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CLINICAL REVIEW

Diagnosis, treatment, and management of echinococcosis

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Echinococcosis (hydatid disease) is caused by the larvae of dog and fox tapeworms (cestodes) of the genus *Echinococcus* (family Taeniidae).[1-3] This zoonosis is characterised by long term growth of metacestode (hydatid) cysts in humans and mammalian intermediate hosts. The two major species that infect humans are *E granulosus* and *E multilocularis*, which cause cystic echinococcosis (CE) and alveolar echinococcosis (AE). A few reported cases of polycystic echinococcosis in Central and South America are caused by *E vogeli* and *E oligarthrus*.[2 w1 w2] The clinical potential of two other *Echinococcus* species (*E shiquicus* and *E felidis*) is unknown.[1 2]

Cystic echinococcosis (CE) and alveolar echinococcosis (AE) are serious chronic diseases with poor prognosis and high mortality if managed inadequately.[1-3] Of the estimated two to three million cases of echinococcosis globally, most are cystic.[2 4] Published reports and the Office International des Epizooties databases suggest that the global burden for human CE exceeds one million disability adjusted life years (DALYs), resulting in a loss of $760m (£490m; €612m) a year,[4] although these figures are probably underestimates.[2] Case series and small clinical trials show a mortality rate of 2-4% for CE, but this increases markedly with poor treatment and care.[5 6] There are 0.4 million cases of human AE, and survival analysis has shown that, if untreated or if treatment is limited, mortality exceeds 90% 10-15 years after diagnosis.[5 7] About 18 000 new cases of AE occur annually, with a total annual burden of 666 434 DALYs.[8]

Here, we introduce the *Echinococcus* parasites and the diseases they cause, and we discuss current methods for the diagnosis, treatment, and management of both types of echinococcosis. The life cycle characteristics of *Echinococcus* spp and the causes and immunology of echinococcosis have been described extensively.[1-3 9-14 w3-w16]

Where and how is echinococcosis acquired?

Figure 1⇓ shows the distribution of echinococcosis, according to statistics from the World Health Organization. *E granulosus* occurs worldwide, with high endemic areas concentrated in north east Africa, South America, and Eurasia.[10 12] *E multilocularis* is restricted to the northern hemisphere.[10 12] Figure 2⇓ illustrates the *E granulosus* and *E multilocularis* life cycles and shows how humans become infected. Human co-infection with *E granulosus* and *E multilocularis* is not common, although these two species are co-endemic in some specific foci, notably the northwest of the People's Republic of China.[10] Figure 3⇓ is an ultrasound image of a patient with both types of echinococcosis.

What are the clinical features of echinococcosis?

Most (>90%) CE cysts occur in liver, lung, or both organs.[12 w17] In general, the initial stages of CE do not cause symptoms—small cysts can remain asymptomatic for many years.[1] Because of the parasite's slow growth most cases are diagnosed in adults.[3] The onset of symptoms depends on the infected organ, the size and position of the cyst(s), their effect on the organ and adjacent tissues, and complications arising from the rupture of a cyst or a secondary infection.[1 12] Recurrent (secondary) CE can arise after primary cyst surgery, owing to spillage of the cyst contents, or if there is spontaneous or trauma induced cyst rupture and release of larvae, which can grow into secondary cysts.[10] Leakage or rupture of CE cysts can induce systemic immunological reactions and other complications, including cholangitis.[1 12]

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Summary points

- Echinococcosis is a parasitic zoonosis caused by *Echinococcus* cestode worms
- The two major species of medical importance are *Echinococcus granulosus* and *E multilocularis*, which cause cystic echinococcosis (CE) and alveolar echinococcosis (AE), respectively
- CE and especially AE are life threatening chronic diseases with a high fatality rate and poor prognosis if careful clinical management is not carried out
- Human CE is cosmopolitan and the more common presentation, accounting for most of the estimated two to three million global echinococcosis cases. AE has an extensive geographical range in the northern hemisphere
- Diagnosis is based on clinical findings, imaging (radiology, ultrasonography, computed axial tomography, magnetic resonance imaging), and serology
- Treatment options for CE are: surgery, percutaneous sterilisation, drugs, and observation (watch and wait). Surgery is the basis of treatment for early AE, but patients not suitable for surgery and those who have had surgical resection of parasite lesions must be treated with benzimidazoles (albendazole, mebendazole) for several years

Sources and selection criteria

We obtained information from personal reference archives, personal experience, and extensive literature searches of the PubMed and Cochrane databases. We sourced English language papers that were fully published mainly between 2000 and March 2012 using appropriate index terms. Keywords included: "*Echinococcus*", "*Echinococcus granulosus*", "*Echinococcus multilocularis*", "echinococcal cysts", "hydatid cysts", "hydatid disease", "cystic echinococcosis", "alveolar echinococcosis", "hydatidosis", "hydatid", "surgery", "liver transplant", "mebendazole", "albendazole", "benzimidazole", "chemotherapy", "PAIR", "percutaneous treatment", "percutaneous drainage", "ultrasound"; and "*Echinococcus*" with "diagnosis", "serology", "treatment", "clinical", "review", "meta analysis"; and "echinococcosis" with diagnosis", "serology", "treatment", "clinical", "review", and "meta analysis".

AE generally has a longer latent phase (up to 15 years) before the onset of chronic disease.[1 12 w18] *E multilocularis* usually develops in the right liver lobe and AE lesions range from a few millimetres to 15-20 cm in diameter in areas of infiltration.[1 12] Extrahepatic primary disease is uncommon.[1 12 w18 w19] Metastasis formation leads to secondary AE with infiltration of the lung, spleen, or brain. Symptoms of AE usually include epigastric pain or cholestatic jaundice.[12]

How is echinococcosis diagnosed?

The box shows the best indicators of disease. The diagnosis of CE is based on clinical findings, imaging results, and serology.[1-3 6 7 11 12 15-17] Clinical manifestations may indicate cyst rupture, secondary bacterial infection, allergic reactions, or anaphylaxis.[1 17] Patients with symptoms should immediately be advised to undergo imaging and serology.

Ultrasound is a crucially important tool for the diagnosis, staging, and follow-up of abdominal CE cysts, although it has low sensitivity for detecting small cysts. The first generally accepted ultrasound classification for CE was developed in 1981.[w21] A series of meetings by a WHO informal working group on echinococcosis (WHO-IWGE) resulted in an international standardised ultrasound classification of CE cysts into three groups (fig 4⇓).[6 12 16] Microscopy of cystic fluid for brood capsules or protoscoleces provides proof of infection and cyst viability.[6] Polymerase chain reaction (PCR) analysis of biopsy material can also provide a definitive diagnosis.[6] High field magnetic resonance spectroscopy is also useful for determining cyst viability and for staging.[1 w22]

CE serology is a helpful diagnostic adjunct and can be used to monitor patients after surgery or drug treatment. However, although used widely, particularly in developing countries where imaging techniques may not be readily available, questions remain with regard to its effectiveness for clinical detection and screening.[17 w23 w24] Serum antibody measurement is more sensitive than detection of circulating *E granulosus* antigens,[1 11 w8] but available tests lack standardisation.[11 17] Current serology for human CE mainly tests for IgG antibodies against native or recombinant antigen B by enzyme linked immunosorbent assay or western blotting.[2 11 w25] Test specificity is affected by immunological crossreactivity with antigens found in other helminth infections, cancers, and liver cirrhosis and by the presence of anti-P1 antibodies.[2 11] Although not thoroughly tested,[17] serodiagnostic performance seems to depend also on cyst location, cyst size, and stage.

The seriousness of human AE means early detection is crucial so that treatment can start.[1 5 12] Diagnosis is analogous to that for CE including clinical findings and use of imaging techniques and serology.[1 5 12] Ultrasound is the main diagnostic test for AE in the abdomen,[5] and the imaging based WHO-IWGE PNM classification system (table 1⇓; fig 5⇓) is the recognised benchmark for standardised evaluation of diagnosis and treatment.[5 12 18]

As with CE, serodiagnosis of AE is used as an adjunct to other detection procedures.[11 w8 w26 w27] Conventional PCR can detect *E multilocularis* specific nucleic acids in tissue biopsies and real time PCR can be used to assess viability.[5 w28 w29] Notably, however, for both diseases a negative real time PCR result does not reflect complete parasite inactivity and a negative PCR cannot rule out disease.[5 w29]

How is CE treated and managed?

The WHO-IWGE classification provides the basis for choosing basically four treatment and management options for CE: surgery, percutaneous sterilisation, drug treatment, and observation (watch and wait).[5 6 17] However, there is no optimum treatment for CE and no clinical trials have compared the different modalities.[5] Table 2⇓ shows the current expert consensus on the management of liver CE.[5]

Surgery

Surgery is the classic treatment but, despite being curative, it does not totally prevent recurrence.[5] Furthermore, in the absence of specific clinical trials, the evidence for the surgical treatment of complicated liver and disseminated CE is limited.[5 w30] Surgery is, however, the choice for large or infected cysts, cysts likely to rupture, and cysts in important organ locations.[1 5] Surgery may not be practical for patients with multiple cysts in several organs.[1 5] Open cystectomy, pericystectomy, partial hepatectomy or lobectomy, cyst extrusion (Barrett's technique), and drainage of infected cysts are some of the surgical options available.[1] In cases where cyst resection is incomplete, or if small lesions

Key indicators for a positive diagnosis of echinococcosis

Medical history

- Have you travelled to or emigrated from an endemic country (about five to 10 years ago)? If so, from where? (fig 1)
- Have you had contact with dogs, foxes, or livestock during the past five to 10 years?
- Have you worked in a pastoral area where you may have had contact with wildlife during the past five to 10 years?
- Have you worked in an abattoir during the past five to 10 years?

Cystic echinococcosis

- Upper abdominal discomfort
- Poor appetite

Alveolar echinococcosis

- Vague abdominal pain (right upper quadrant; 30% cases) (most cases originate in the liver)
- Jaundice (25% cases)
- Fatigue, weight loss, fever, chills

Physical examination

Cystic echinococcosis

- On palpation of the abdomen a mass may be found on the surface of organs (the liver is affected in two thirds of patients); hepatomegaly or abdominal distension may also be seen
- Chest pain, cough, and haemoptysis can be indicative of cysts in the lung; cyst rupture into the bronchi may result in the expulsion of hydatid material and cystic membranes
- Cyst rupture can induce fever, urticaria, eosinophilia, and anaphylactic shock

Alveolar echinococcosis

- On palpation of the abdomen, hepatomegaly may be detected
- Splenomegaly may be present in cases complicated by portal hypertension
- Collateral circulation between the inferior and superior vena cava may be present on the skin in the thoracic and abdominal regions in advanced cases
- Other physical symptoms are dictated by the location of metastatic legions (see lung involvement for cystic echinococcosis)

Laboratory investigations

- General laboratory investigations show non-specific results
- Serology can help form a definitive diagnosis
- Ultrasound guided fine needle biopsy can also be used to examine hydatid cyst fluid for the presence of protoscoleces or DNA using molecular techniques (polymerase chain reaction)

Radiology

- Ultrasound (figs 4 and 5), computed tomography, and magnetic resonance imaging are the procedures of choice for the definitive diagnosis of echinococcosis
- Imaging should be used to examine not only the liver but also the entire abdomen and thorax, and they are able to determine metastatic locations in alveolar echinococcosis

remain undetected, disease can recur.[1] Postoperative fatality is about 2% but can be higher if additional surgery is needed or if medical facilities are inadequate.[12 15]

Percutaneous sterilisation techniques

These include PAIR (puncture, aspiration, injection, reaspiration), which destroys the cyst's germinal layer,[w31-w33] and modified catheterisation approaches, which evacuate the complete cyst.[1 5 12] PAIR, developed in the 1980s, involves ultrasound assisted percutaneous needle puncture aspiration of the cyst, followed by injection of a suitable protoscolicide (such as 20% sodium chloride or 95% ethanol) and cyst reaspiration after 15-20 minutes.[1] Anaphylaxis is a risk. Assess cyst fluid for protoscoleces and bilirubin, and, to minimise the risk of secondary CE, co-administer benzimidazole. CE2 and CE3b stages (fig 4) are problematic because they have many compartments that require individual puncture, and these commonly relapse after PAIR.[17] Large bore catheters, combined with suitable aspiration equipment, may in future replace PAIR for these stages,[17] but their true effectiveness needs to be established.[5] The choice of between surgery or percutaneous sterilisation can be difficult. Comparison of the two procedures requires large carefully designed clinical studies, which have yet to be done.[17]

Antiparasite drug treatment

The benzimidazoles—albendazole and mebendazole—are generally regarded as the most effective drugs for treating uncomplicated CE cysts and as an alternative to invasive surgery. Mebendazole was used in the 1970 and 1980s, but albendazole is now the drug of choice. It is administered in 10 mg/kg doses (usually 400 mg) twice daily; mebendazole (40-50 mg/kg a day in three doses) is less effective than albendazole.[19] However, studies carried out with both drugs have been small, and heterogeneity in methodology has prevented meta-analysis.[17] Furthermore, a recent pooled study of individual data from patients with CE (six treatment centres; five countries) suggested that the overall efficacy of these drugs may have been overstated.[20] Systematic randomised controlled trials that compare standardised treatment with benzimidazoles at different cyst stages with other options are needed,[20] especially as these drugs seem to work better against some cyst stages (such as small CE1 cysts). Indeed, benzimidazoles are not effective against large cysts (>10 cm), being diluted by the volume of fluid present.[5] The degree and type of side effects of sustained use of benzimidazoles also warrant rigorous study.[5] Benzimidazoles should not be used in early pregnancy or against cysts at risk of rupture.[1 5] Thorough assessment of other anthelmintics (such as praziquantel and nitazoxanide) and

combinations of anthelmintics (such as albendazole plus praziquantel) that have been used to treat CE is also needed.[w34-w37]

Watch and wait

Leaving uncomplicated cyst types (CE4 and CE5) untreated and just monitoring them by imaging (particularly ultrasound) is a logical management option given that a proportion of cysts calcify over time and become completely inactive; such cysts do not compromise organ function or cause discomfort.[15 w38] Such an approach is attractive but requires systematic study to define fully its indications and limitations.

How is AE treated and managed?

Table 3⇓ details a stage specific approach to treating AE. Historically, surgery has been the recommended treatment for early disease.[1 5] Early diagnosis reduces the need for radical surgery and results in fewer unresectable lesions.[1 5] Long term treatment with benzimidazoles is essential for patients with inoperable AE or after resection of *E multilocularis* lesions.[1 5 12] Benzimidazoles are parasitostatic—they inhibit larval proliferation but do not kill metacestodes.[w39] They should be given for a minimum of two years and patients monitored for at least 10 years for relapse.[w40] Benzimidazoles are not recommended before surgery.[5] As for CE, the drugs are given orally with fat-rich meals (10-l5 mg/kg/day, in two doses), although they have been given at a higher dose of 20 mg per kg per day for 4.5 years.[5] Continuous treatment with albendazole is tolerated well, having been used for more than 20 years in some patients; intermittent use is not recommended.[5] Mebendazole, given at a dose of 40-50 mg per kg per day over three days with a fatty meal, is an alternative to albendazole.[5] Figure 6⇓ shows the effect of albendazole treatment on a P4 AE lesion. Neither praziquantel nor nitazoxanide is clinically effective against AE.[5 w41-w43]

Allotransplantation of the liver has been carried out in patients with end stage AE.[w44-w46] However, the essential use of immunosuppressive treatment can stimulate the proliferation of parasitic remnants in the lung or brain.[w45] A long term prospective follow-up of patients with AE treated by palliative liver transplantation in the 1980s found that some patients survived for 20 years.[21] Ex vivo liver resection, followed by autotransplantation of AE-free lateral segments,[22] may offer a radical approach to improving prognosis, but this procedure needs to be fully evaluated.

What are the future challenges?

Considerable recent progress has been made in the diagnosis, treatment, and management of echinococcosis, but challenges remain. Clinical trial data systematically evaluating existing treatments are not available and ideal treatment options are lacking. Treatment indicators are often complicated, being based on cyst characteristics, availability of medical and surgical expertise and equipment, and patient compliance in long term monitoring programmes.[5]

Comparable and standardised procedures and terminology need to be established by the medical fraternity.[5] PAIR should be undertaken only by experienced doctors and trained teams capable of managing anaphylactic shock.[1] PAIR needs to be studied systematically, via randomised controlled trials, to assess its efficacy compared with surgery and other available options for treatment of uncomplicated hepatic cysts.[23]

Given recent concerns about the cost and treatment efficacy of the benzimidazoles,[17] new drugs are needed to combat both AE and CE. Strategies aimed at defining new compounds need to be pursued.[24]

The WHO-IWGE consensus recommendations for the ultrasound imaging based classification of CE cysts need to be more wider disseminated to clinicians because they are useful when choosing treatment options.[5] Similarly, the WHO-IWGE classification for AE should be advocated as the international classification because it can help determine whether an *E multilocularis* lesion should be excised or otherwise treated, give some indications for improved prognosis, and help determine the best treatment option for the individual patient.[5]

The current clinical diagnosis of AE and CE relies mainly on the detection of parasite lesions by imaging methods, but the procedures are expensive and are generally not available in resource poor settings. Furthermore, they are not useful for detecting the early stages of infection, which is a major disadvantage because earlier diagnosis results in more effective and successful treatment. Serodiagnosis can play a role in early detection because specific anti-*Echinococcus* antibodies appear in the blood system four to eight weeks after infection. Most available immunodiagnostic techniques have been used in the diagnosis of echinococcosis.[11] However, most of these tests have not been systematically compared by independent laboratories, they are mainly used for research purposes, and few have found general acceptance by clinicians.

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A patient's perspective

I am a 31 year old farmer of the Hui minority from Ningxia, China. I was first admitted to hospital in May 2003 with extreme fatigue, cough, and difficulty breathing. A chest radiograph showed that my lungs were scattered with dark shadows and the doctors diagnosed me with a form of cancer and sent me home. In September 2003 a specialist doctor reviewed my case and asked me to come back to the hospital for further tests. The specialist doctor asked me many questions, performed a physical examination, and ran some tests including an ultrasound. The ultrasound and blood test showed that I did not have cancer but had alveolar echinococcosis. The parasite started in my liver and had spread to my lungs. I was given daily treatment with a drug called albendazole and after six months another chest radiograph showed that my lungs were clear and I felt much better. I was told to continue taking the drug to stop the parasite spreading from my liver to other organs. Today I am still taking albendazole and am feeling well.

Zhang Yin Gui, *Xiji County, Ningxia Hui Autonomous Region, Peoples' Republic of China*

Tips for non-specialists

- Refer symptomatic patients who travelled to, or emigrated from, an echinococcosis endemic area about five to 10 years ago, and had contact with dogs or wildlife, to an infectious disease physician
- Serology provides supportive information for diagnosis but imaging studies provide the definitive diagnosis
- Differential diagnosis is important because alveolar echinococcosis often presents with cancer-like symptoms
- Imaging studies should examine the entire thorax and abdomen, not just the liver
- Treatment may involve the use of drugs (albendazole, mebendazole) or surgery (or both)

Additional educational resources

- Wikipedia (http://en.wikipedia.org/wiki/Echinococcosis)—Information on the *Echinococcus* parasites and echinococcosis for patients and the public
- Wikipedia (http://en.wikipedia.org/wiki/Alveolar_hydatid_disease)—Brief fact sheet on alveolar echinococcosis for patients and the public
- US Centers for Disease Control and Prevention (http://www.cdc.gov/parasites/echinococcosis/)—Fact sheet on the *Echinococcus* parasites and echinococcosis for professionals, patients, and the public
- US Centers for Disease Control and Prevention (www.dpd.cdc.gov/dpdx/HTML/Echinococcosis.htm)—Description of the *Echinococcus* parasites and echinococcosis for professionals, patients, and the public
- Patient.co.uk (www.patient.co.uk/doctor/Hydatid-Disease.htm)—Fact sheet of the *Echinococcus* parasites and echinococcosis for professionals, patients and the public
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Tables

Table 1| WHO informal working group on echinococcosis PNM classification of alveolar echinococcosis

PMN	Characteristics
P	Hepatic localisation of the parasite
PX	Primary tumour cannot be assessed
P0	No detectable tumour in the liver
P1	Peripheral lesions without proximal vascular or biliary involvement
P2	Central lesions with proximal vascular or biliary involvement of one lobe*
P3	Central lesions with hilar vascular or biliary involvement of both lobes or with involvement of two hepatic veins
P4	Any liver lesion with extension along the vessels† and the biliary tree
N	Extrahepatic involvement of neighbouring organs (diaphragm, lung, pleura, pericardium, heart, gastric and duodenal wall, adrenal glands, peritoneum, retroperitoneum, parietal wall (muscles, skin, bone), pancreas, regional lymph nodes, liver ligaments, kidney)
NX	Not evaluable
N0	No regional involvement
N1	Regional involvement of contiguous organs or tissues
M	The absence or presence of distant metastases (lung, distant lymph nodes, spleen, central nervous system, orbit of the eye, bone, skin, muscle, kidney, distant peritoneum, retroperitoneum)
MX	Not completely evaluated
M0	No metastasis‡
M1	Metastasis

*For classification, the plane projecting between the bed of the gall bladder and the inferior vena cava divides the liver into two lobes.

†Inferior vena cava, portal vein, and arteries.

‡Negative on chest radiography and cerebral computed tomography.

Table 2| Suggested stage specific approach to treatment of uncomplicated cystic echinococcosis of the liver. Adapted from Brunetti and colleagues,5 with permission from Elsevier

WHO classification	Surgery	Percutaneous treatment	Drug treatment	Suggested treatment	Resource setting
CE1	No	Yes	Yes	<5 cm: albendazole	Optimal
				<5 cm: PAIR	Minimal
				>5 cm: PAIR + albendazole	Optimal
				>5 cm: PAIR	Minimal
CE2	Yes	Yes	Yes	Other PT + albendazole	Optimal
				Other PT	Minimal
CE3a	No	Yes	Yes	<5 cm: albendazole	Optimal
				<5 cm: PAIR	Minimal
				>5cm: PAIR + albendazole	Optimal
				>5cm: PAIR	Minimal
CE3b	Yes	Yes	Yes	Non-PAIR PT + albendazole	Optimal
				Non-PAIR PT	Minimal
CE4				Watch and wait	Optimal*
CE5				Watch and wait	Optimal*

*Minimal may not be applicable here because in low resourced remote endemic areas it may be impossible or too expensive to travel to the nearest hospital just to obtain a diagnosis.

PAIR= puncture, aspiration, injection, reaspiration; PT=percutaneous treatment.

Table 3| **Suggested stage specific approach to treatment of alveolar echinococcosis. Adapted from Brunetti and colleagues,5 with permission from Elsevier**

WHO classification	Surgery	Interventional treatment	Drug treatment	Suggested treatment	Resource setting
P1N0M0	Yes	No	Yes	Radical resection (RO); benzimidazoles for 2 years; PET/CT controls	Optimal
				Radical resection (RO); benzimidazoles for 3 months	Minimal
P2N0M0	Yes	No	Yes	Radical resection (RO); benzimidazoles for 2 years	Optimal
				Radical resection (RO); benzimidazoles for 3 months	Minimal
P3N0M0	No	No	Yes	Benzimidazoles continuously; PET/CT /MRI scan initially and at 2 year intervals	Optimal
				Benzimidazoles continuously	Minimal
P3N1M0	No	Yes	Yes	Benzimidazoles continuously; PET/CT/MRI scan initially and at 2 year intervals	Optimal
				Surgery if indicated	Minimal
P4N0M0	No	Yes	Yes	Benzimidazoles continuously; PET/CT/MRI scan initially and at 2 year intervals	Optimal
				Surgery, if indicated	Minimal
P4N1M1	No	Yes	Yes	Benzimidazoles continuously; PET/CT/MRI scan initially and at 2 year intervals	Optimal
				Surgery if indicated	Minimal

CT=computed tomography; MRI=magnetic resonance imaging; PET=positron emission tomography; RO=complete removal of alveolar echinococcosis lesion.

Figures

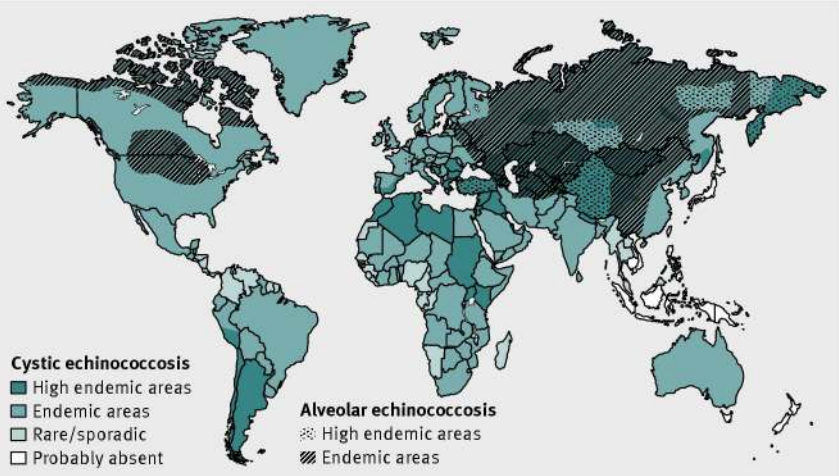

Fig 1 Global distribution of echinococcosis

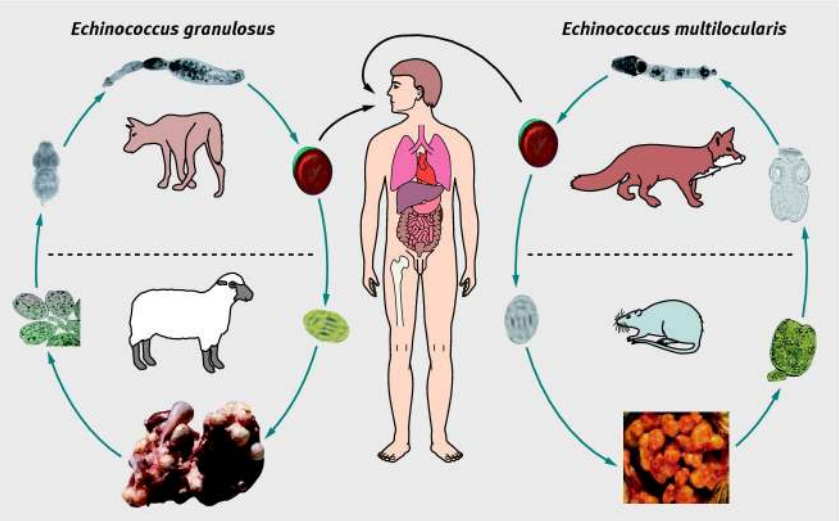

Fig 2 Life cycles of *E granulosus* and *E multilocularis*. Swallowed *Echinococcus* eggs hatch in the intestine to release oncospheres which pass through the gut wall and are carried in the blood system to various internal organs where they develop into hydatid cysts. *E granulosus* cysts are found mainly in the liver or lungs of humans and intermediate hosts. Dogs and other canines, which act as definitive hosts for *E granulosus*, become infected by eating offal with fertile hydatid cysts containing larval protoscoleces. These larvae evaginate, attach to the canine gut, and develop into sexually mature adult parasites. Eggs and gravid proglottids are released in faeces. Humans are typically "dead end" hosts, but not always.[w20] *E multilocularis* develops mainly in the liver of humans. Wild carnivores, such as the red fox (*Vulpes vulpes*) and the arctic fox (*Alopex lagopis*) are the major definitive hosts for *E multilocularis,* with small mammals acting as intermediate hosts. As with *E granulosus*, humans are exposed to *E multilocularis* eggs by handling infected definitive hosts or by eating contaminated food

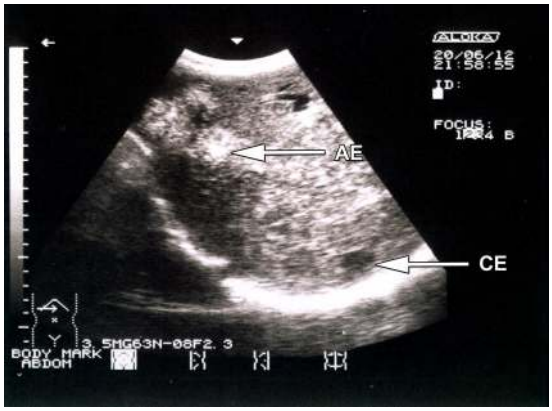

Fig 3 Ultrasound image of simultaneous alveolar (AE) (stage P3) and cystic (CE) (stage CE4) echinococcosis in the right liver of a patient from the People's Republic of China

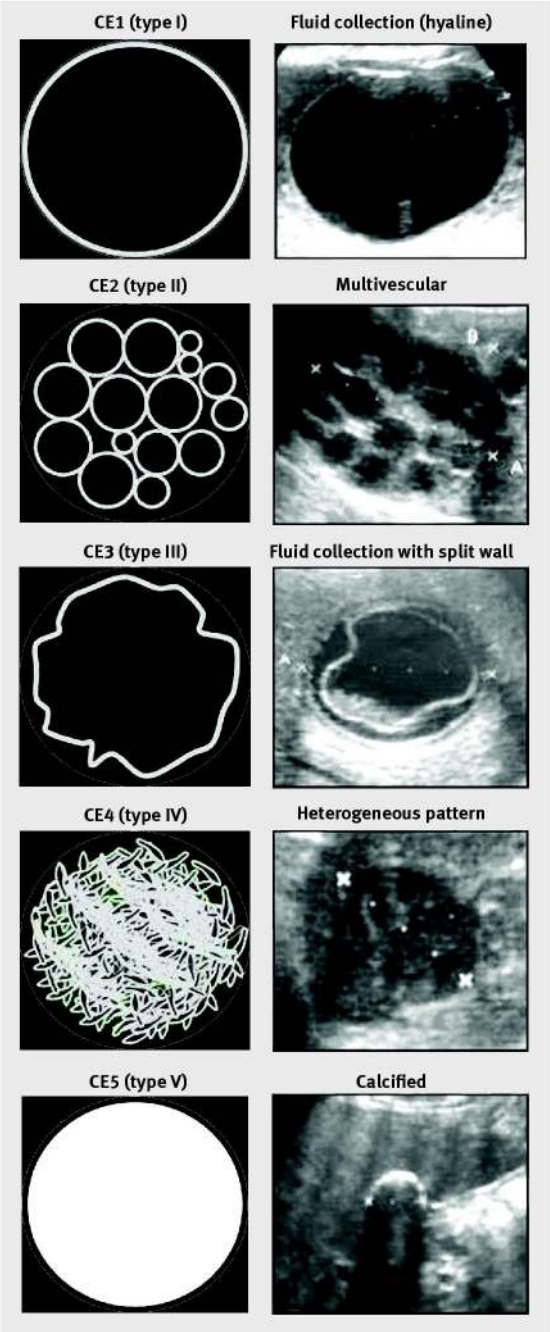

Fig 4 Ultrasound classification of CE cysts. The WHO informal working group on echinococcosis classification differs from that of Gharbi and colleagues[w21] by the addition of a "cystic lesion" (CL) stage (undifferentiated) (not shown), and by reversing the order of CE types 2 and 3. CE3 transitional cysts may be differentiated into CE3a (with detached endocyst) and CE3b (predominantly solid with daughter vesicles).[15] CE1 and CE3a are early stage cysts and CE4 and CE5 late stage cysts

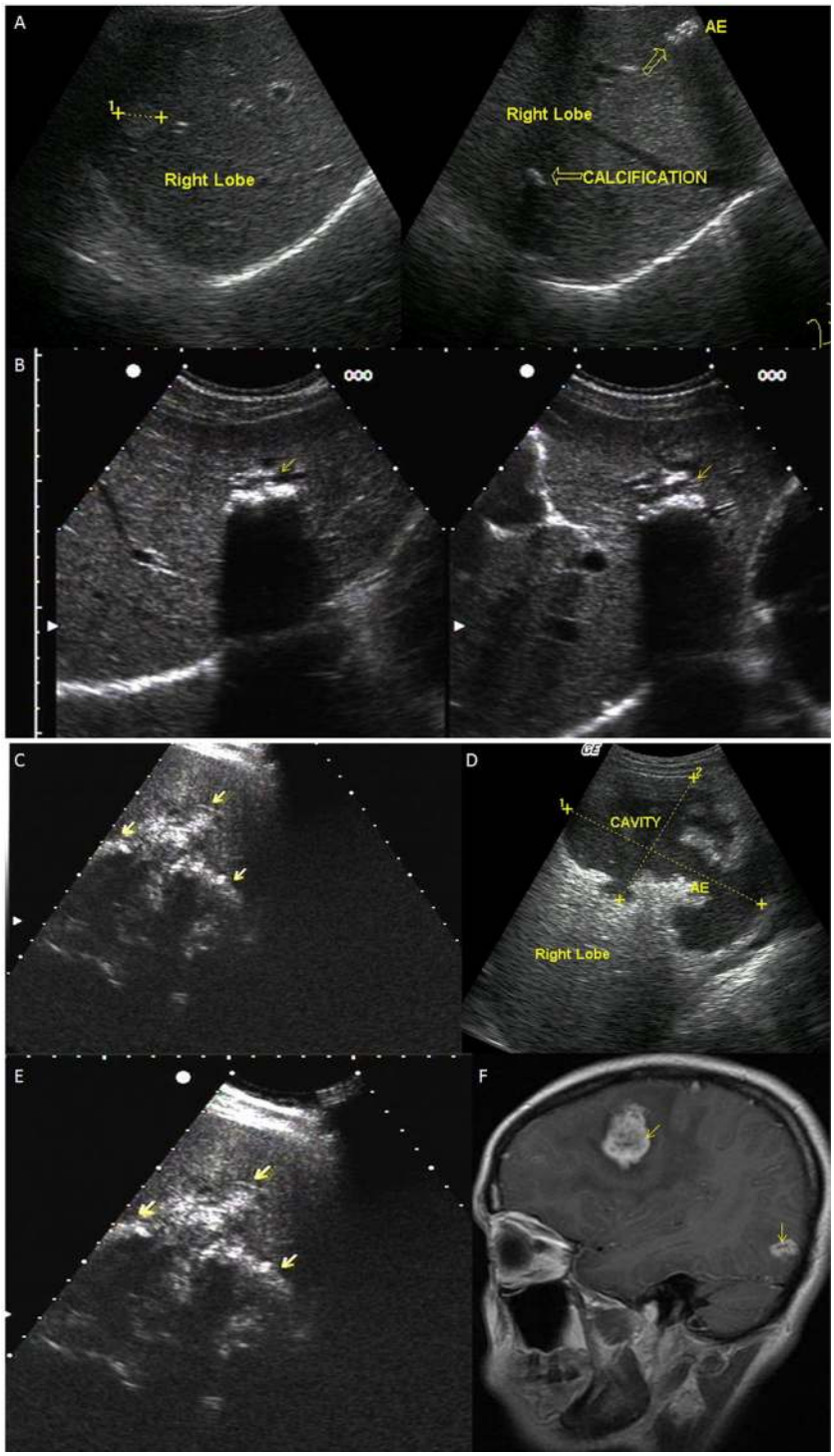

Fig 5 Staging of AE lesions according to the WHO informal working group on echinococcosis PNM classification system, based on ultrasound observations. (A) P1; (B) P2; (C) P3; (D) P4; (E) and (F) P4 NO M1—panel E shows primary lesion in the right liver lobe; panel F shows secondary metastatic lesions in the brain

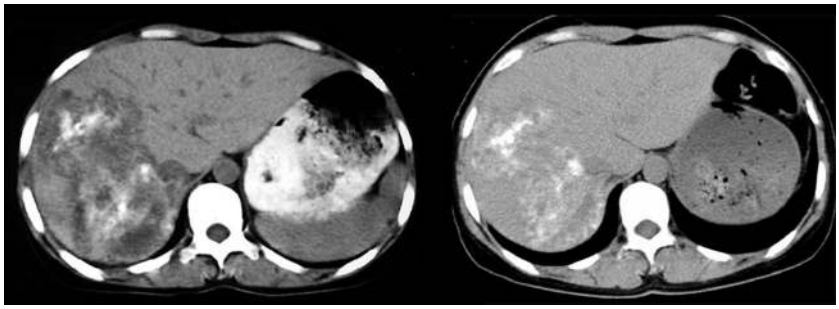

Fig 6 Computed tomography scan of the liver showing a large irregular AE lesion in the right lobe containing scattered calcifications and liquefactions (left panel). After five years of treatment with albendazole, the lesion had not changed in size but the areas of calcification had increased and those of liquefaction had decreased (right panel)