

CLINICAL DIAGNOSIS AND TREATMENT FOR HUMAN ECHINOCOCCOSIS IN CHINA

Wen Hao, Luan Meixiang, Xu Mingqian, Peng Xinyu, Shao Yingmei, Gao Yongshen, Feng Xiaohui, Cheng Xinhua, and Li Haitao

Clinical Division, Xinjiang Hydatid Clinical Research Institute, Urumqi, PR China

INTRODUCTION

Human echinococcosis is still a major public health problem, especially in northwestern, northern, and central parts of China, such as Xinjiang, Gansu, Tibet, Inner Mongolia, Qinghai, Ningxia and Sichuan. Based on the China CDC meeting in Urumqi and Dunhuang, approximately 1,000,000 hydatid patients have been recorded in hospital data involving a 20,000,000 population and 80,000,000 RMB loss by this endemic disease in China. In general, the incidence of human cystic echinococcosis (CE) was 95~97%, and alveolar echinococcosis (AE) was 3~5%. Some local regions only showed a high incidence of human AE, like Zhang County and Ming County in Gansu, and also Guyuan Prefecture in Ningxia, while the majority of the provinces and Autonomous Regions had mixed distributions of human AE and CE. Only in the clinical division of the First Teaching Hospital, Xinjiang Hydatid Clinical Research Institute (XHCRI), 4,728 patients have been recorded as 3,154 (65.3%) cases in the liver, 1,119 (23.2%) in the lungs, 150 (3.1%) in the abdominal/pelvic cavity, 100 (2.1%) in the brain, and 304 (6.3%) in other organs, including the kidney, bone, spleen, pancreas, and heart. Human CE was 97% and AE 3% in this center.

CLINICAL DIAGNOSIS

Technologically, the two key procedures for diagnosis of human echinococcosis are imaging techniques and serology. US and CT have now been firmly established in the diagnosis of echinococcosis and are becoming more and more useful for clinical diagnosis and epidemiological survey. Under CT or US scanning, a typical CE cyst appears as a round or ovoid space-occupying lesion or a hypoechogenic area,

and 'double layers and arc calcification' can be considered specific for hydatid cyst caused by *E. granulosus* infection rather than other cyst diseases, ie congenital cyst in the liver or kidney. US and CT imaging can recognize rupture of the endocyst by showing a folded detached endocyst. An AE lesion is transonically characterized by an irregular parenchyma focus or hyperechogenic area with calcification either in nodular spots and/or ring forms. US may show a characteristic association with echogenic areas due to fibrosis, and transonic zones due to necrosis inside the parasitic lesion. US may also show hilar involvement and biliary dilatation with the classical 'shotgun' sign, or stenosis of the portal vein and/or the inferior vena cava with parasitic lesions. A correlative study on CT scan for diagnosis of AE patients shows a typical geographical map pattern with irregular contours. Inside the lesion, hypodense areas due to necrosis are associated with hyperdensity due to calcification. A retrospective comparison between imaging and histopathological findings in 67 AE patients with 100 separate lesions indicated that the radiological features were correlated directly with the pathological specimens from each patient, and moreover, the CT appearance was more specific for clinical diagnosis, while the US had an advantage in screening as well as for intraoperative use. Magnetic resonance imaging (MRI) has also been used to examine the relationship among AE lesions to large vessels and the heart, as well as directly for cardiac hydatid cysts.

An international imaging classification for human AE has been made by WHO/IWGE through 3 Hydatidology Congresses (XVII, XVIII, and XIX). Based on the high foci of human AE experience in the world, human AE is classified as Parasite, Nodes, and Metastasis (PNM). Meanwhile, the ultrasonographic classification for human cystic echinococcosis has been officially agreed as five patterns: CE I (simple cyst), CE II (multiple daughter cyst), CE III (ruptured cyst), CE IV (solid cyst), and CE V (calcified cyst), based on Garbi's classification in 1981. From the clinical point of view, more information needs to be demonstrated through the classification, for physicians and surgeons; thus, a new recommended classification is shown in Table 1.

Correspondence: Dr Wen Hao, Clinical Division, Xinjiang Hydatid Research Institute, First Xinjiang Medical University, No 1 Liyushan Road, Urumqi, PR China.

Tel: 008-6991-4363776

E-mail: haowen2000@yahoo.com

Table 1
Comparison of different classifications for cystic echinococcosis.

Chabi * T _{I-VI} (1981)	WHO/ IWGE CE ₁₋₅ (1995~2001)	XHCRI T ₀₋₅ D _{n1,n2} ...C _{o-f-r-i-b} (2001~2002)
Type I	CE ₀ Cyst lesion	T ₀ \bar{D}_n C ₀
Type II	CE ₁ Simple cyst	T ₁ \bar{D}_n C ₀
Type III	CE ₂ Multiple daughter cyst	T ₂ \bar{D}_n C ₀
Type IV	CE ₃ Ruptured cyst	T ₃ \bar{D}_n C ₀
Type V	CE ₄ Solid cyst	T ₄ \bar{D}_n C ₀
Type VI	CE ₅ Calcified cyst	T ₅ \bar{D}_n C ₀

D: average diameter for cyst, \bar{D} : $(\phi_{max}+\phi_{min})/2$, C_o: non-complication C_f: fever, C_r: recurrence, C_i: icterus, C_b: biliary fistula.

Table 2
Blinded test for DIGFA in sera.

Countries	Testing sera	Negatives	Positives		Positive rate (%)	Final clinical confirmation rate ^a (%)
			CE	AE		
China	461	183	216	62	60.3	92.8%
Britain	112	53	29	30	52.7	84.3%
France	128	66	23	39	48.4	77.9%

^aThe rate means positive rate combined with clinical confirmation (DIGFA positives/clinical confirmation cases ×100%).

Generally, IgG antibodies are produced more than other classes, though IgM, IgA, and IgE may be detectable. ELISA tests using the *E. multilocularis* Em2 fraction appear to be the most sensitive and specific serological tests, with up to 90% sensitivity in both diseases, especially for human AE. The above serological methods serve to confirm the diagnosis and provide a ‘bench mark’ for post-therapy surveillance of the patient. Em2-ELISA has been routinely used for epidemiological surveys and laboratory diagnosis for AE patients. A mixture of the native antigen Em2 and the recombinant antigen II/3-10 has been reported to further increase sensitivity and specificity, up to 95%. An immunoblot test, using Em18 from a crude *E. multilocularis* protoscolex extraction, showed reasonably high sensitivity and specificity in Japanese and Chinese AE patients. Detection of the specific IgG subclass antibodies of IgG1 and IgG4 isotypes in human CE and AE is also of potential significance, and may provide the possibility of differentiation of early and chronic infections, as well as better correlation with hydatid patient prognosis following medical treatment.

‘A fast immunodiagnostic kit’ for clinical confirmation and differentiation of human cystic and alveolar echinococcosis with over 90% sensitivity and specificity, which can be conveniently and economically used in both clinic and mass screening.

SURGICAL TREATMENT

Surgery has been and is still considered the principal form of treatment for both cystic and alveolar echinococcosis in China. Major intervention with indication protocol and key points has been introduced, as follows:

Surgery for CE cases

1. **Intact pericystectomy for hepatic CE.** Based on surgical experience with over 200 CE cases, great improvements in technique have been developed in three hydatid centers, in Xinjiang (Shihezi, Urumqi, and Yining), called radical pericystectomy, which could remove the whole cyst without any remaining cavity. The indication being considered is for a CE cyst located

Table 3
Comparison of DIGFA test with imaging and surgery confirmation.

Samples		DIGFA		Imaging (Ultrasound)	Surgery/Pathology
		Positives	Negatives		
CE cases	EgCF	321	29	350	350
	EgP	319	31		
	EgB	316	34		
	Em2	14	336		
AE cases	EgCF	92	68	160	102
	EgP	80	80		
	EgB	72	88		
	Em2	140	20		
Normal control	EgCF	22	227	249	-
	EgP	22	227		
	EgB	13	236		
	Em2	7	242		
Combined sensitivity ^a	CE			91.7%(321/350)	
	AE			87.5%(140/160)	
Combined specificity ^b	CE			91.2%(227/249)	
	AE			97.2%(242/249)	

^a Sensitivity: CE sensitivity means antigen EgCF/EgP/EgB combined maximum true positive rate and AE sensitivity means antigen Em2 true positive rate.

^b Specificity: CE specificity means antigen EgCF/EgP/EgB combined minimum true negative rate and AE specificity means antigen Em2 true negative rate.

on the surface of the liver or not too close to a large vessel. The technique can, ideally, eliminate major complications, such as recurrence and biliary fistula, completely.

Well exposure and protection of CE cyst from neighbor tissues and organs. Open liver theca around the CE cysts, and try to find potential space between CE out layer membrane and hepatic parenchyme. During stripping process, by electrotome combined with dull separation, the vessels, especially intrahepatic duct through into the cyst, must be carefully recognized, ligated and cut off, which can be considered as key point for perfect stripping and voiding postoperative bleeding and biliary leakage.

The qualified stripping should be just left a thin membrane onto the vessels and liver without rupture of the cyst. Well control of electrome combined with dull separation just along into the potential space can be considered as key technique point, since it can only keep real subadventitial strip without unexpected injury both of the cyst and vessels.

Remove the whole cyst completely without puncture it. Stop bleeding on the traumatic surface should be coagulated with electrotome and surgical

tube placed. The vessels or ducts can be easily seen through very thin membrane.

2. Punctured endocystectomy for CE. The common indications should be considered as: 1) majority of cystic echinococcosis in liver; 2) postoperative recurrence of cystic echinococcosis in liver; 3) ruptured or infected cystic echinococcosis.

Surgical protocol: epidural or general anesthesia has been commonly employed. Median, right rectus abdominis, or right subcostal incisions can be taken according to location of cystic echinococcosis in liver. The cyst location and number should be clarified after while opened the abdominal cavity, operation should be taken under direct complete exposure of the cysts, and liver can be liberated when necessary. In case of the probability of the spillage of cystic fluid and protoscolices, the cysts must be isolated from abdominal cavity by large carbasus with 20% hypertonic saline, surrounding liver tissues of the puncture point be also protected with carbasus strips with 20% hypertonic saline.

Management of the cysts: puncture at the point of the cyst protruding the liver surface combined vacuum aspiration should be taken; then fluid with clear or

yellow color can be seen during aspiration. While operating the external cystic wall with scalpels, collapsed internal cyst or daughter cysts can be seen after aspiration of the cystic fluid, intracystic injection of hypertonic saline (15-20%) or alcohol (75-95%) should be taken until the cyst fulfilled and remained for 10 minutes, meanwhile, the external cystic wall should be wiped repeatedly and carefully in order to kill all the protoscolices in the residual cavity, clip out the internal cyst or daughter cysts, then wipe the cyst wall with alcohol (70%) carbasus.

Residual cavity management: external capsule can be resected properly for reducing the residual cavity, and closed by suturing, or left it for open. Drainage of the residual cavity: drainage with tubes can be done if seen any biliary fistula signals, like yellow color cystic fluid or severe infection.

Attention points: 1. hydrocortisone (100~200mg) should be used as anti-anaphylactic drug in the beginning of the operation; well-preparation should be taken in case anaphylactic shock with sudden cessation of the heart beating and breathing. 2. Prevention of the cystic fluid and protoscolices spillage. 3. Protection of the operating field carefully by enclosing the cysts with carbasus soaked hypertonic saline; puncture the cysts must be under vacuum aspiration in case of the cystic fluid leakage. 4. Anti-hydatid drugs: protoscolicidal solution should be remained in residual cavity for 10 minutes at least in order to kill all the protoscolices. Albendazole or mebendazole chemotherapy is recommended for 3 days pre-operation and 1 month post-operation so as to prevent the recurrence.

Retrospective analysis was made on 552 child patients with cystic echinococcosis in the liver and abdomen admitted between 1957~1997 undergoing surgical treatment. Infection was common in childhood and the morbidity increased with the patient age. The cyst usually grows fast, the calcification was much less common and the postoperative residual cavity rapidly shrank or disappeared because child's liver enjoys bumper blood supply. In 66% of the cases, the lesion was multiple cysts or multiple organ cysts, and the multiple daughter cysts were encountered in only 7.6% of all cases. The postoperative complications mainly developed in over 6-year age group. For serodiagnosis of echinococcosis, in general, the positive reaction in children was weaker than that in adult. Endocystectomy with suture of exocystic wall was major surgical management for the child cystic echinococcosis (82%). An early diagnosis can be obtained by analysing the clinical feature, ultrasonic examination and sero-

diagnosis. Endocystectomy was relatively less traumatic, simple procedure with quick recovery.

3. **PAIR.** Since 1980s, over two thousands CE patients with inoperable or recurrent lesions of the liver, peritoneum, spleen, kidneys have been treated by procedures following the method of puncture, aspiration, injection and reaspiration (PAIR), and under ultrasonographic guidance in northwestern China (Qinghai, Xinjiang, Ningxia). Satisfactory results were obtained in 70% of these patients with diminishment of the cyst size. Approximately 5% patients had minor allergic response such as tickle, skin eruption, and palpitation, etc, but 2% cases suffered from anaphylactic shock, which needed urgent management.

Surgery for AE cases

Hepatectomy is an effective way of the treatment of surgery AE cases. The resection area can be determined by the parasitic lesion and the focal character, the surgical intervention can be divided as following procedures.

Radical hepatectomy: in order to eliminate the active proliferating part of AE, 1~2cm from edge of the normal liver tissue to the lesion is required to be resected with the parasite lesion. In about 30% of cases, the parasitic mass can infiltrate the hepatic hilum, and extended hemihepatectomy with resection of the extrahepatic bile duct had to be performed. In such cases, involvement of retrohepatic vena cava or portal vein are common and may used a specific reconstruction. For example, extended right hepatectomy should include resection of the right liver, segment IV and entire caudate lobe. The biliary tract may need reconstruct with intrahepatic biliary enterostomy using a Roux-en-Y loop with segments 2 and 3 bile ducts. As the complications of liver failure, retroactive involvement of the right liver was rather low due to the remaining liver became hypertrophy, thus, there was major risk of post-operative failure. If biliary leakage, a small tube on a stent may be inserted in each of biliary ducts for prevention of biliary leakage. The tube should be taken off 3-6 months later, if no major complications.

Attentive procedures: (1) Palliative hepatectomy: resected area requires to minimize the remaining liver lesion, incisal edge of the resected lesion commonly without bleeding, resect to see leaking yellow viscous fluid from necrotic space. (2) Simple external drainage: for the patients in whom the location of the lesion and general condition is not suitable to palliative hepatectomy. **Indications:** Radical hepatectomy is the most acceptable method for patients in whom lesions

limited in single lobe or several segments, and without significant invasion to the diaphragm and other adjacent organs. Palliative hepatectomy is for those patients who could not tolerate the radical hepatectomy or when radical hepatectomy is impossible. Simple external drainage is for the patients with severe biliary tract infection and jaundice, the lesion can hardly be resected. Liver transplantation can be considered for the latest stage of the hepatic alveolar echinococcosis combined with jaundice and radical hepatectomy could not be taken. Long-term administration of the anti-hydatid drugs (albendazole, mebendazole) is necessary after any kind of surgical treatments, according to the WHO/IWGE guideline, and the period should be more than one year at least.

The surgical treatment of AE cases is usually more difficult and a different approach is used. (1) When the lesions are sufficiently localized within half of the liver, then regular hepatectomy or hepatolobectomy is the method of choice. (2) When the lesions occupy more than half the liver, then tentative irregular hepatectomy or hepatolobectomy can be effective, but this requires excision of large, necrotic, purulent cavities. (3) When the lesions are unresectable, then surgical drainage procedures are performed, which include drainage of liver abscesses or biliary ducts. Since Yao and colleagues reported in 1965 the first five AE cases in China, over 500 AE patients has been diagnosed and treated in Xinjiang, Qinghai, Gansu and Sichuan, in which approximately 28% were treated by radical hepatectomy, 50% by partial hepatectomy, or clearance of necrotic cavities and surgical drainage, and 22% were too advanced to be treated by surgery. The mortality at five years follow-up was 10 - 15% and the longest survivor in the series was over 30 years after operation.

At Besançon Central Hospital (France), twenty-one patients with incurable AE were treated by liver transplant between 1986-1995. Survival rate at 72 months was 66% and the longest survival 106 months. Orthotopic liver transplantation is feasible, particularly for AE patients who combined with severe complications (Budd-Chiari syndrome or secondary biliary cirrhosis). Liver transplantation for AE patients should be considered as final choice of surgical approach due to its high cost, relatively more serious complications and also recurrence or metastasis. Based on our surgical experience from Besançon Central Hospital by Prof Gillet and Prof Manton, the first AE patient in China was successfully transplanted by side-to-side piggyback procedures on 27th December 2000 in XHCRI and the following was done, in Sichuan and Chongqing centers.

Recurrence

One of the major surgical complications for echinococcosis is recurring secondary CE after primary intervention. CE recurrence rates of between 2-11% were reported by Schantz (USA). A 10-2% recurrence rate was recorded in Xinjiang. Obviously, use of an effective protoscolicidal adjunct to proper hydatid (CE) surgery may play an important role for the reduction of the recurrent rate. The following procedure was recommended: puncture of hydatid cyst, aspiration of cystic fluid, injection of 70-95% alcohol or 15-20% sodium chloride solution into each cyst for 10 minutes and reaspiration, removal of endocyst, washing with physiological saline solution, scrubbing of the exocystic wall with a small gauze soaked 70% ethanol 3 times and finally, suturing of the wall be carried out. Oral administration of albendazole or other anti-hydatid drugs should also be considered in the pre- and post-surgery periods for the prevention of hydatid recurrence after surgical intervention.

CHEMOTHERAPY

Since the early 1980s, studies with chemotherapy for human echinococcosis have been carried out in north-western China. Thirteen inoperable AE patients were treated with mebendazole, the dosage was 1.2-1.5 g daily for a course of 30 days with an interval of 2 weeks between courses. After 6-16 courses of therapy, most patients remained stable. A total of 20 AE cases were treated by Liu with continuous albendazole at an oral dose of 10 mg/kg every 12 hours without inter 35 months (range 13-60 months). In 7 cases judged as cured, the hepatic lesions were almost completely calcified, while in 3 improved cases incomplete calcification around the hepatic lesions was observed. The remaining AE cases still showed active lesions with heterogeneous hypodense areas in the liver. They found that long-term continuous albendazole therapy could result in a parasiticidal effect for human AE in their clinical experience.

More than 500 human AE have been treated by albendazole with 10-20 mg/kg/day either continuous or interval administration orally from endemic regions in western and central China. Approximately one fourth of hydatid cases were cured or showed clinical improvements, half showed clinical improvements or stabilization, and the remaining one quarter had no effects clinically or morphologically. One hundred and one CE patients were also treated by praziquantel at a dosage of 25 mg/kg/d for 10 days and found to be effective based on histopathology and clinical follow-up. Twenty-five CE patients (12 cysts in liver, 13 in lungs) were treated by

oral praziquantel every 8 hrs at dosage of 40 mg/kg/day for 7 days, then by surgery. The eosin uptake rates of protoscolexes were higher in hepatic hydatid group (62.7%) than that in the pulmonary hydatid group (36.6%). The mean concentrations of praziquantel in the hepatic group were 0.533 ng/ml in blood, 0.087 ng/ml in cystic fluid and 0.149 ng/ml in the cystic wall which was higher than the 0.494 ng/ml in blood, 0.026 ng/ml in cystic fluid and 0.067 ng/ml in the cystic wall in pulmonary group at 4 hours after taking the morning dose. The clinical results in both groups, compared with 60 CE cases in the surgery-only control group, indicated that praziquantel was an effective anti-hydatid drug. Chinese herbs (*ie* hamalar seeds) alone and mixed with albendazole have been encouragingly reported for initial clinical trial in a few hundred patients with better tolerance and unexpecting responses, especially for the patients who already underwent albendazole or mebendazole chemotherapy alone with no effect. Recent years, over 500 hydatid patients (major CE) have been orally treated by emulsion albendazole, based on positive animal trial data. Approximately 85% cases were effective and improvement when given the drug between 3-12 months.

In a combination chemotherapy trial, concentrations of albendazole (ABZ) were measured, by high-pressure liquid chromatography. Nineteen CE patients were treated by ABZ plus cimetidine or ABZ alone with 4-week courses of albendazole (20 mg/kg/day), separated by 10-day-long drug-free intervals. Seven patients also received three courses of cimetidine (10 mg/kg/day). Concentrations of albendazole sulphoxide (ABZSX) were significantly higher in samples of bile and hydatid cyst fluid from the patients receiving albendazole and cimetidine than in those from patients receiving albendazole alone ($p < 0.05$). The therapeutic benefit of the combined drug treatment was more than that with albendazole alone. An initial clinical trial using praziquantel combined with albendazole in treatment of 5 AE patients showed that one case improved with evidence of diminishing lesion size, and four patients were in a stable condition after 3-6 years follow-up. These AE patients were treated with praziquantel at an oral dose of 20-25 mg/kg for 20 days with 20-day intervals, and in combination with albendazole 15 mg/kg/day for 30 days with 10-day intervals for 6-10 cycles of combination therapy.

Although the doses of mebendazole and albendazole given were well tolerated by most patients, the following clinical symptoms and signs were interpreted as possible or probable adverse drug reactions: abdominal pain, nausea and/or vomiting, dizziness, vertigo and/or headache, fever, skin eruptions and/or pruritus, hair loss, clinical jaundice, serum transaminase level

above 100U/l, leukocyte counts down to 4,000/mm³, and hemoglobin level below 9 g/l. Such side effects were recorded 29 of the 253 (11.5%) CE and AE patients, and 13 out of 79 (10.3%) patients. In 3-5% of hydatid patients, medical treatment was stopped temporarily or permanently because of suspected adverse effects. In the albendazole toxicity study, no evidence of teratogenic or embryotoxic reaction occurred in C57BL/6J and NIH mice with *E. granulosus* after given 200 mg/kg/day for 8 weeks by gavage. Nevertheless, all females of reproductive age should be warned about albendazole, particular for long-term chemotherapy.

NEW TOOLS FOR CONTROL OF HUMAN ECHINOCOCCOSIS

1. Liposomal albendazole (L-ABZ) has been considered as an effective formulation with higher bioavailability and targeting function, which can make aggregation against *Echinococcus* infections. Liposomal formulation strongly changed free albendazole in tissue distribution in rodents (mice, gerbils, and cotton rats). Targeting function was experimentally confirmed in liver, lungs, spleen etc, which showed L-ABZ has significantly organ selection and high bioavailability. Initial clinical trial with a total of 71 hydatid patients (12 cases for AE and 59 for CE), had a positive effect with minor side effects. In addition, L-ABZ efficacy against *E. multilocularis* in rodents (mice and gerbils) by abdominal cavity injection had better effect than that by administered orally. Emulsion albendazole formulation has also been used to treat over a hundred hydatid patients, which showed encouraging results in liver, lung cases, especially some recurrent cases.

2. Multiple Antigen Enzyme Linked Immunosorbent Assay Kits (MA-ELISA) can be effectively applied to improve sensitivity and accuracy in clinical immunodiagnosis.

3. Dot Immunogold Filtration Assay (MADIGFA) was an effective, fast, and economical tool for immunodiagnosis of human echinococcosis. Blind tests have been carried out in China, the UK, and France, which showed 91% sensitivity and 89% specificity. Great advantages are initial differentiation of cystic and alveolar echinococcosis, and convenience and practicability for screening in the field. Over 1,000 patients have been tested in our hospital, with 92% coincidence of imaging and surgery.

4. The application of the coproantigen ELISA test for echinococcus infection in dogs for diagnosis and

Table 4
Clinical observation on L-ABZ effect against human echinococcosis.

Classification	Effect				Total
	Cured	Effective	Partial effective	Ineffective	
CE ₁	13	3	3	2	21
CE ₂	8	20	5	5	38
AE	0	8	4	0	12
Total	21	31	12	7	71

survey of dog infections indicated many advantages, compared to the old arecoline testing method. Relatively high sensitivity and specificity made it suitable for application either in screening communities (Habahe and Herbokesar County) or in veterinary clinics.

5. Human phage display technique has been initiated for production of human Echinococcus-specific antibodies, which can be employed in patho-biochemistry and immunodiagnosis. Furthermore, it may play a role in making 'bio-missiles' for both diagnosis and treatment in future.

REFERENCES

- Ding ZX, Wen H. Atlas of *Echinococcosis*. Xinjiang: Xinjiang People's Publisher, 2000.
- Jiang C. Today's regional distribution of echinococcosis in China. *Chin Med J* 2002;115:1244-7 (In English).
- Gharbi HA, Hanipe W, Brauner MW, *et al.* Ultrasound examination of the hydatid liver. *Radiology* 1981; 139:459-63.
- Craig PS, Deshan L, Macpherson CNL, *et al.* A large focus of alveolar echinococcosis in Central China. *Lancet* 1992;340:826-31.
- Ito A, Wen H, Craig PS, *et al.* Antibody responses against Em18 and Em16 serodiagnostic markers in alveolar and cystic echinococcosis patients from northwest China. *Jpn J Med Sci Biol* 1997;50:19-26.
- Schantz PM, Gottotien B, Ammann A, Lanier A. Hydatid and the Artic. *Parasitol Today* 1991;7:35-6.
- Wen H, New RR, Craig PS. Diagnosis and treatment of human hydatidosis. *Br J Clin Pharmacol* 1993; 35:565-74.
- Wen H, Zhang HW, Muhmut M, Zou PF, New RR, Craig PS. Initial observation on albendazole in combination with cimetidine for the treatment of human cystic echinococcosis. *Ann Trop Med Parasitol* 1994;88:49-52.
- Wen H, Zou PF, Yang WG, *et al.* Albendazole chemotherapy for human cystic and alveolar echinococcosis in north-western China. *Trans R Soc Trop Med Hyg* 1994;88:340-3.
- Wen H, Craig PS. Immunoglobulin G subclass responses in human cystic and alveolar echinococcosis. *Am J Trop Med Hyg* 1994;51:741-8.
- Wen H, New RR, Muhmut M, *et al.* Pharmacology and efficacy of liposome-entrapped albendazole in experimental secondary alveolar echinococcosis and effect of co-administration with cimetidine. *Parasitology* 1996;113 (Pt 2):111-21.
- Wen H, Yang WG. Public health importance of cystic echinococcosis in China. *Acta Trop* 1997;67:133-45.
- Zheng H, Wen H, Xu ZX, Zhang ZX, Yin JF. Experimental observation on anaphylaxis induced by Echinococcus infection in *Meriones unguiculatus*. *Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi* 2000;18:109-12 (In Chinese).
- Zhou HX, Chai SX, Craig PS, *et al.* Epidemiology of alveolar echinococcosis in Xinjiang Uygur autonomous region, China: a Preliminary analysis. *Ann Trop Med Parasitol* 2000;94:715-29.
- Eckert J, Schantz PM, Gasser RB, *et al.* Geographic distribution and prevalence, In: Eckert J, Gemmell MA, Meslin FX, Palowski ZS, eds. WHO/OIE Manual on echinococcosis in humans and animals: a public health problem of global concern. Office International des Epizooties, 2001:30-50.
- Shambesh MK, Craig PS, Wen H, Rogan MT, Paolillo E. IgG1 and IgG4 serum antibody responses in asymptomatic and clinically expressed cystic echinococcosis patients. *Acta Trop* 1997;64:53-63.

TAENIA SOLIUM CYSTICERCOSIS: THE ASIAN AND AFRICAN PERSPECTIVE

KD Murrell and AL Willingham

WHO/FAO Collaborating Center for Emerging Parasitic Zoonoses, Danish Center for Experimental Parasitology, Royal Veterinary and Agricultural University, Fredericksberg, Denmark

Cysticercosis, caused by the pork tapeworm *Taenia solium*, long a relatively neglected foodborne parasitic zoonosis, is receiving increasing attention as its global impact on health and agriculture becomes better understood. It has been estimated that over 50 million people are affected worldwide. However, this estimate is probably most accurate for Latin America, where for several decades concerted research and control efforts have been conducted. More attention is now being given to the cysticercosis situation in Sub-Saharan Africa, spurred, perhaps by the recognition in campaigns against epilepsy that neurocysticercosis is an important factor in that affliction. Concern is also being raised in that region in connection with the recent rapid increase in smallholder pig rearing, under conditions that may favor the transmission of *T. solium*. The demand for increased production of animal protein as well as household income makes intervention and control urgent.

In Asia, cysticercosis has been recognized for several hundred years, but for reasons not clear, it has been a truly neglected zoonosis. This may be in large part due to poor information on the scope and severity of the zoonosis, and to the general inaccessibility of data that have been gathered. The genesis of this symposium was to present information on the status of cysticercosis in India, where the prevalence of the parasite has recently been revealed to be unexpectedly

high, and where the clinical manifestation of neurological involvement appears to be unique in comparison with that reported in Latin America. A project funded by the Danish International Development Agency (Danida) in India has produced new information and progress in the immunodiagnosis of single cyst granulomas due to *T. solium*. It was decided to organize a larger symposium to both present these data, and to increase the awareness of the zoonosis throughout the Asia region. Because of the many similarities between the two regions, investigators working in Africa have been invited to present overviews of the situation in Africa and to discuss the approaches being developed there for surveillance, prevention, and control of *T. solium* infections. An important action taken in the Eastern and Southern Africa region is the formation of a multinational, multisectoral working group to coordinate research and control activities. The potential value of this for Asian researchers will be discussed. Also included in this symposium will be a presentation on the vital need to gather socioeconomic impact data necessary for national and international assistance priority setting. The outcome of the symposium is expected to be, in addition to increased awareness, recommendations for further actions in Asia to assess the burden of cysticercosis and establish mechanisms for collective decision making with regard to research and control needs and strategies.

Correspondence: KD Murrell, WHO/FAO Collaborating Center for Emerging Parasitic Zoonoses, Danish Center for Experimental Parasitology, Royal Veterinary and Agricultural University, 185 Fredericksberg, Denmark.

E-mail: kdmurrell@comcast.net