Hydatid Disease in China

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Hydatid disease is one of the world's most geographically widespread zoonoses. It is present on all inhabited continents and occurs in tropical, subtropical, temperate, sub-arctic and arctic regions. The two countries with the greatest areas over which transmission occurs are almost certainly the Soviet Union and China. Until recently, however, very little information about hydatidosis in China was available outside the country. Since the ‘open-door’ policy over the past few years the great importance of hydatid disease in north and western China is gradually being realized.

Hydatid disease is caused by infection with the larval (metacestode) stage of taenid tapeworms belonging to the genus Echinococcus. Transmission occurs in predator-prey mammalian cycles between carnivore definitive hosts and herbivorous intermediate hosts. Although there are four recognized species, i.e. E. granulosus, E. multilocularis, E. vogeli and E. oligarthrus, only E. granulosus and E. multilocularis are of significant public health importance. They also have the broadest geographical distribution. E. vogeli and E. oligarthrus are confined to sylvatic transmission cycles in Central and South America. The minute adult tapeworms of each species are always found in the small intestine of the definitive host. All except E. oligarthrus have been identified as zoonoses in which the larval stage causes a chronic debilitating and sometimes fatal disease known as hydatidosis. Hydatidosis is primarily characterized by slow-growing fluid-filled cystic or vesiculated lesions in the liver, although the nature and form of the metacestode varies between the species. Human infection with the fluid-filled cysts of E. granulosus, the most widespread of the four species, has been described from almost all parts of the body in addition to the primary liver location. Surgery is still the main treatment for cystic and alveolar hydatid disease.

E. granulosus, the cause of cystic hydatid disease (CHD), is very well adapted to synanthropic cycles involving domesticated animals and is most often typified by transmission between the domestic dog and sheep. In consequence, E. granulosus is geographically widespread and its distribution closely parallels the areas of the world where pastoralism is the main occupation. Therefore, it is not surprising that CHD is an important endemic disease over large parts of South America, East Africa, Australasia, Central Europe, Central Asia and the Mediterranean littoral including North Africa. Local control programmes have been implemented with some success in a few countries, notably New Zealand and Chile.

General situation in China

E. granulosus has been recorded in 21 of China’s 31 provinces, municipalities and autonomous regions (approximately 87% of China’s territories) and is probably one of the most important infectious diseases in the vast pastoral areas of northwest China. Under the World Health Organization’s classification of hyperendemicity for E. granulosus, i.e. annual surgical incidence of >10 per 100,000 population, and >50% prevalence rates in sheep, virtually the whole of west and northwest China can be included (Figs 1 and 2). This covers an area of approximately 4.2 million km² (about 44% of the total area of China) containing an estimated population of 50 million people, 100 million livestock (including >50% of all China’s sheep) and 5–6 million dogs.

In this highly endemic region of China, as in most other endemic areas of the world, the domestic dog is the main definitive host of E. granulosus, with sheep acting as the main intermediate host. This parasite is also frequently found in other domestic livestock (Fig. 3). In some livestock species, economic loss through offal condemnation may be significant. No wildlife cycles of E. granulosus have as yet been described in China, but they could possibly occur.

Fig. 1. Map of China showing provincial borders and main distribution of E. granulosus (lines) and E. multilocularis (stippled, overlaps with E. granulosus). Key provinces and autonomous regions (AR) are numbered: (1) Xinjiang (AR), (2) Gansu, (3) Qinghai, (4) Sichuan, (5) Ningxia (AR), (6) Tibet (AR), (7) Shaanxi, (8) Inner Mongolia (AR), (9) Shanxi.
Unfortunately, accurate data on national or even local annual incidence rates for CHD are unknown. In addition to the large city hospitals, for which incidence rates could be obtained, small rural hospitals of less than 100 beds may treat as many as 50 hydatid patients per year and collation of surgical rates for all hospitals would be difficult. Nevertheless, one calculation puts the number of surgical interventions for hydatidosis between 1949 and 1984 at 15,888 (Ref. 6). The importance of CHD in China has recently been recognized at the national level and in 1984, hydatidosis was added to the Ministry of Public Health’s list of diseases designated for special attention. In 1989, a purpose-built institute in Urumqi (Xinjiang) was designated as the National Hydatid Disease Centre for China.

Alveolar hydatid disease (AHD) is often considered as one of the most lethal helminth infections of humans and is characterized by multivesiculated tumour-like lesions in the liver. Up to 30% of AHD cases in China are misdiagnosed as hepatic carcinoma. In China’s northern latitudes, AHD, caused by *E. multilocularis*, is primarily transmitted in sylvatic cycles between foxes and rodents (Figs 1 and 2). However, the small adult tapeworms of *E. multilocularis* have also been found in the domestic dog in some areas and semi-domestic transmission may therefore be possible for this species. Numbers of reported AHD cases are significantly lower than those for CHD but the greater severity of the parasitic lesions and the infiltrative nature of AHD makes it more difficult to treat by either surgery or chemotherapy and the prognosis is poorer. Jiang Cipeng reported on 90 cases of AHD originating from Gansu, Xinjiang and Qinghai provinces, of which 64% were able only to have exploratory laparotomy due to the advanced nature of the lesions.

Owing to the lack of accurate data at the national level for human and animal echinococcosis, we have focused on Xinjiang Uyghur Autonomous Region and Gansu province in the northwest of China where the disease is highly endemic.

**Hydatidosis in Xinjiang**

At 1.65 million km², Xinjiang is China’s largest administrative region (capital city, Urumqi). It has extensive international borders with the Soviet Union and Mongolia. The human population of the region is approximately 13 million, consisting of more than ten nationalities, including Uygur, Kazakh and Hui moslem groups as well as Han (who make up >95% of China’s population). There are an estimated 23 million sheep and two million dogs in Xinjiang. Xinjiang probably has the highest prevalence rates of CHD in China, with the disease occurring over most of the region but especially along the Tianshan and Altai mountain areas (Fig. 2). Relatively little transmission occurs in the Tarim and Junggar desert basins where the density of people and livestock is low.
mountains, 16–40% of dogs have been found infected (Ding Zhaoxun, unpublished) and also in that region, Hutubi County abattoir recorded that 88% of sheep and 56% of goats were infected. Two morphologically distinct adult forms of *E. granulosus* have been reported from dogs in north Xinjiang and may represent variant strains, although this needs further investigation. Application of DNA probes will help and preliminary DNA hybridization using protoscolex DNA extracted from both sheep and human hydatid cysts indicate identity with the domestic sheep strain of *E. granulosus* (D. McManus and Ding Zhaoxun, unpublished).

The prevalence of human cystic hydatidosis for the whole of Xinjiang is not clear and provincial incidence data are not available. The First Teaching Hospital of Xinjiang Medical College recorded 966 surgical CHD cases between 1978 and 1988, more than 80% of which were for hepatic hydatidosis, but this is only one of five large hospitals in Urumqi that treat hydatid patients. Currently, up to 1000 CHD cases may be expected to be treated annually in Xinjiang. Over the same ten year period, surgeons at Xinjiang Medical College were also treating approximately ten AHD cases per year, with 14 AHD patients receiving surgical treatment in 1988. The extremely rare presentation of both cystic and alveolar hydatid lesions in the liver of the same patient has also been confirmed surgically in the same hospital.

Medical and veterinary research groups from Xinjiang have begun to assess local disease rates for some rural communities in the high prevalence areas near the Tianshan and Altai mountains. Chi et al. obtained an annual surgical case incidence rate of 43.8 per 100 000 from a baseline survey of two communities including 85 permanent villages in Hutubi County, where 70% of the population was Han and 78% of households kept sheep. In 1986, a community survey was carried out on 1400 people in the Fuhai area near Altai. Portable ultrasound was used primarily for the detection of liver cysts, X rays for lung cysts, and an enzyme immunoassay (ELISA) for serum antibody detection. This survey identified 41 (ie. an infection rate of 2.9%) CHD cases (31 cases of cysts in the liver, three in the kidneys, five in the lungs and two of mixed location). In the same Fuhai community an ELISA seropositivity rate of 21.3% was obtained, with most seroreactors being in the 15–24 age group. This represented an overall sensitivity of 64% when measured against ultrasound and X ray. The cyst imaging rate and seropositivity rates were similar for the over-45s, at about 15%. In another survey, 10% of Kazakh and Uygurs were seropositive compared with 4.2% for Han. Also in this area, in a more recent survey, 79% of ‘ultrasound-negative’ Kazakhs were found to be seropositive for antibodies against the invasive oncosphere stage (IgG-immunofluorescence test), which also suggests a high level of exposure (P.S. Craig and H. Wen, unpublished).

**Fig. 3.** Large hydatid cyst of *E. granulosus* removed from a naturally infected yak in South Gansu.
Hydatidosis in Gansu

North Gansu forms a desert border with southeast Xinjiang and has traditionally been the main route for travellers through northwest China, forming part of the Great Silk Road. Although smaller than Xinjiang, Gansu Province covers an area of 450,000 km² with a human population of 19 million (capital city, Lanzhou). With an average per capita income of £50, it is also one of the six poorest provinces in China. Although hydatidosis occurs virtually over the whole province (Fig. 2) and all nationalities are exposed, the greatest prevalence is in the south on the edge of the Tibetan plateau where the majority of the region’s 5–6 million sheep are concentrated. Data from the Animal Husbandry Bureau (1986) show a 7.78% hydatid prevalence in sheep for Gansu but, in parts of Gannan Prefecture, up to 88% of sheep and 80% of yaks are infected (Liu Deshan, unpublished).

Most Tibetans keep livestock, especially yaks and sheep, and many still practice traditional seminomadic pastoralism, a lifestyle where dogs are important for protecting livestock. In Gannan, Liu Deshan (unpublished) has recorded 26% of dogs infected with adult *E. granulosus* tapeworms but wild canids have so far been found to be free of infection. The dog–sheep cycle for *E. granulosus* is predominant in Gansu, although a dog–yak transmission cycle cannot be excluded in the autonomous Tibetan areas, as home slaughter is commonplace and the older beasts that do not survive winter are scavenged by dogs.

As in Xinjiang, no figures for CHD incidence rates are available for Gansu, although some local figures have been collated. In Xia He Town hospital (54 beds) in the west of Gannan Prefecture, 3–4% of all surgical cases in 1987 were for CHD. Furthermore, the hospital records 60 surgical cases of CHD (mostly Tibetans) over a three-year period, which represents an annual incidence of 43 per 100,000 for the Xia He region. In Hezou hospital (Gannan), 76% of all CHD cases are also Tibetans and the rest are mostly Han. A recent human serological survey in the Tienzhu region found a 4.8% overall seropositivity rate which comprised a 11.1% seropositivity rate for Tibetan nationals and a 2% rate for Han (Liu Deshan, pers. commun.).

Part of the main focus of AHD in central China occurs in south Gansu (Figs 1 and 2). *E. multilocularis* has a high endemicity in the south of Zhang County although very few studies have been carried out in the isolated communities that live in this mountainous region. Between 1986 and 1989, records from three of the county’s hospitals, combined with liver palpation examination and positive serology, indicated that there were 54 cases of AHD with a median age at diagnosis of 42 years. Interestingly, a 2:1 ratio of female to male AHD cases was also apparent.

No detailed surveys of fox or wild rodent populations in this region have been carried out yet. However, a recent survey in the Cao Tan area found that six out of 58 (10.3%) necropsied dogs were infected with *E. multilocularis* (P.S. Craig and Liu Deshan, unpublished). This indicates that *E. multilocularis* could also be transmitted in a semi-domestic cycle, and could help to explain the higher prevalence in women, who probably spend a greater time in the home area with dogs than do men. The most important rodent prey species for dogs in the Cao Tan valley appears to be the mole-rat, *Myospalax fontanieri*, which is also heavily predated by foxes, *Vulpes* spp. As yet, no confirmed reports of infected mole-rats have been made in the Cao Tan region of Zhang County, although *Myospalax, Microtus* and *Cetellus* have been reported infected in other parts of China (Tang Changti, pers. commun.)

**Treatment**

In China, surgery remains the main form of treatment for both diseases, although a significant proportion of cases are complicated or inoperable, especially in cases of AHD. Radical liver resection has resulted in a 10% cure rate for AHD patients treated in Xinjiang Medical College. The use of anthelmintic drugs such as benzimidazoles, especially albendazole, for CHD and AHD has proved useful in other areas of the world. Albendazole is also manufactured in China, and some centres like Xinjiang Medical College are using the drug to treat large numbers of hydatid patients. In a recent study at Xinjiang Medical College using albendazole (20 mg per kg per day for one month, total of three courses with ten-day rest intervals) for the treatment of 38 inoperable CHD cases, eight were considered successful, 21 showed clinical improvement and in nine, the drug had no observed effect on the cysts. Benzimidazole treatment for AHD is usually less effective but has resulted in cure for a small number of patients, and diminished alveolar liver masses in about 25% of cases.

In Xinjiang Medical College, a combination of albendazole chemotherapy and surgery (where appropriate) is currently viewed as the best approach for the treatment of human hydatidosis.

**Control**

No provincial control programmes for cystic echinococcosis have been implemented, although co-ordinated local control efforts have begun in some provinces and in some cases have been preceded by the collection of baseline data. In parts of Xinjiang, large numbers of stray dogs have been destroyed; remaining animals must be registered, and families can own no more than two dogs. Also, regular six-weekly dosing of dogs with a biscuit formulation of praziquantel, developed by Chi Puseng and colleagues at the Veterinary Research Institute, Urumqi, at a cost of 0.25 Yuan (0.03p) per dog has been implemented in some communities in combination with a health education programme particularly directed at school children (developed by Ding Zhaoxun, Xinjiang Medical College).
Control programmes will be logistically difficult to implement in many of the remote areas of northwest China. However, once organized, the mobilization of staff can be impressive. For example, between 1986–1989, in a local control programme in the Altai region of Xinjiang, 672 ‘bare-foot’ vets and 144 qualified veterinary officers treated 7000 dogs from 14 000 pastoral families (72 villages) with praziquantel an average of eight times per year.

Control of the transmission of *E. multilocularis* in its sylvatic cycles will be extremely difficult, if not impossible. However, in communities where significant infection pressure on humans may be provided by domestic dogs rather than any other source, anthelmintic treatment of dogs will be important. For instance, an organized dog-management and dosing programme may help to reduce the incidence of AHD in the Cao Tan focus in Gansu. However, unlike many control programmes for *E. granulosus*, dosing of dogs against *E. multilocularis* will need to be continued for as long as sylvatic transmission occurs within the same locality.

The inclusion of hydatidosis onto the Chinese government’s priority disease listing and the creation of the National Hydatid Disease Centre in Xinjiang have helped to focus attention on quantifying the problem of hydatidosis and will undoubtedly lead to the establishment of control programmes in many endemic areas of China.

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