Echinococcosis on the Tibetan Plateau: prevalence and risk factors for cystic and alveolar echinococcosis in Tibetan populations in Qinghai Province, China

P. M. SCHANTZ[1]*, H. WANG[2], J. QIU[3], F. J. LIU[4], E. SAITO[1], A. EMSHOFF[1], A. ITO[5], J. M. ROBERTS[1] *and* C. DELKER[6]

[1] *Division of Parasitic Diseases, National Center For Infectious Diseases, Centers For Disease Control and Prevention, Atlanta, GA 30341, USA*
[2] *Qinghai University Medical School, Xining, Qinghai Province, China*
[3] *Sichuan Center For Disease Control, Chengdu, China*
[4] *National Hydatid Disease Control Center, Urumqi, Xinjiang Province, China*
[5] *Department of Parasitology, Asahikawa Medical College, Asahikawa, Japan*
[6] *Boulder-Lhasa Sister City Project, Boulder, CO, USA*

SUMMARY

Infections by larval stages of tapeworms of the genus *Echinococcus* (echinococcosis or hydatid disease) are zoonotic infections of major public health importance throughout much of the world. Humans become infected through accidental ingestion of eggs passed in faeces of canid definitive hosts. Tibetan populations of China have some of the highest documented levels of infections by both *Echinococcus granulosus* and *E. multilocularis*, the causes of cystic and alveolar echinococcosis, respectively. In this study we measured the prevalence of cystic (CE) and alveolar (AE) echinococcosis disease in Tibetan communities in Qinghai, Province, China, and identified putative risk factors for both infections in these communities. 3703 volunteers in three predominately Tibetan counties of Qinghai were surveyed between June 1997 and June 1998. Parasitic lesions were diagnosed by imaging of characteristic space-occupying lesions in abdominal organs (ultrasound) or the lungs (radiographs). Specific serodiagnostic assays (Dot-ELISA and Em2-ELISA) were performed on sera of positively imaged subjects to further distinguish the disease agent. All participants completed a questionnaire documenting age, sex, education level, occupation, lifestyle (nomadic or settled), slaughter practices, drinking water source, hygienic practice and association with dogs. Data were analyzed using SAS version 8. 6·6% of the volunteers had image-confirmed infection with *E. granulosus* (CE) and 0·8% had *E. multilocularis* (AE) infection. The significant univariate factors for echinococcal infection (both CE and AE) included livestock ownership, Tibetan ethnicity, female gender, low income, herding occupation, limited education, water source, age greater than 25 years old, poor hygienic practices, offal disposal practices and dog care. Multivariate analysis revealed that livestock ownership was a significant risk factor for both forms of the disease, as well as age greater than 25 years, female gender, herding occupation, and being nomadic (*vs* semi-nomadic or settled). No additional significant risk factors were identified among the 344 nomadic participants. Being female and being older than 25 years of age were significant factors among the 1906 semi-nomadic participants. Among the 1445 settled participants, allowing dogs to sleep indoors was statistically significant. Issues such as inadequate assessment of animal ownership, selection bias, disease misclassification, and loss of information may have led to reduction in strength of some risk factor associations and need to be addressed in future epidemiologic analysis of echinococcosis in this population.

Key words: Alveolar echinococcosis, cystic echinococcosis, hydatid disease, China, epidemiology, risk factors.

INTRODUCTION

The echinococcoses are important human and livestock animal health problems in many parts of the world (Schantz *et al.* 1995; Eckert *et al.* 2001). Cystic echinococcosis (CE), infection by *Echinococcus granulosus*, affects human, canine and livestock animal populations on all major continents and is highly prevalent in sheep-raising regions throughout the world. Alveolar echinococcosis (AE), caused by *E. multilocularis*, is a relatively less widespread and prevalent, but often fatal, zoonotic disease. *E. multilocularis* occurs in life cycles involving small mammals and wild and domestic canids and is found primarily in northern latitudes of Central Europe, Eurasia and North America. Qinghai Province, China, has the unusual distinction of being endemic for both AE and CE.

This investigation measured the prevalence of CE and AE in rural populations of Qinghai Province and evaluated demographic and behavioural factors suspected to influence exposure to infections by larval *Echinococcus* spp. Previous research in China reported that the primary risk factors for echinococcosis were living in close proximity to domestic

* Corresponding author: Division of Parasitic Diseases, NCID, Centers For Disease Control and Prevention, Mailstop F22, 4770 Buford Highway, Atlanta, GA 30341, USA. Tel: 770 488-7792. Fax: 770 488-7761. E-mail: PSchantz@cdc.gov

Parasitology (2003), **127**, S109–S120.
DOI: 10.1017/S0031182003004165 Printed in the United Kingdom

animals, a low level of personal sanitation, and ignorance of the disease (Chi *et al*. 1990). The variables surveyed in this study include age, sex, occupation, cultural and lifestyle factors, socioeconomic status, general educational level, dog ownership, drinking water source, presence and use of medical facilities, personal hygiene, and animal slaughter practices. Few previous studies have examined all of these potential risks using such a large population.

MATERIALS AND METHODS

Investigator field teams examined 3703 volunteers residing in three counties (Chindu, Zeko and Gade) of Qinghai Province, China, between June 1997 and June 1998. All subjects (or their guardians) were recruited by local village leaders or monks and volunteers were assured free diagnosis and treatment (if indicated) for larval echinococcosis (hydatid disease). Participants were made aware of the risks and benefits of the study and provided a written consent form that required an individual signature or mark (thumbprint) prior to participation. There were no restrictions to participation. Study participants ranged in age from 1 to 86 years with a median of 26 years. Fifty-three percent (1972) were male and 47% (1731) were female. Persons of Zang (Tibetan) nationality comprised 94·8% of the sampled population. The other participants listed their nationality as Han (4·1%), Hui (1%) or other (0·1%). Nearly half of the participants (49·2%) raised livestock as the primary source of their income. Other listed occupations included government worker (10·4%), student (25·7%), housewife (2·7%), farmer (6·7%), lama (monk) (2·0%), labourer (1·6%), or other (1·6%).

Questionnaire

Participants completed a questionnaire designed to obtain information on demographics, animal ownership and lifestyle practices. Risk factors evaluated in this study focused on occupation, family income, education level, lifestyle, ethnic group, at-home slaughter practice, animal ownership, dog care, presence of stray dogs in the community, primary water source, hygienic practices and offal disposal practices.

Screening and diagnosis of infection in humans

Investigators diagnosed alveolar or cystic echinococcosis in study participants by abdominal ultrasonogram, chest radiograph and serodiagnostic tests. All participants were imaged using abdominal ultrasound (US) and thoracic X-ray and blood was obtained by finger-prick for antibody testing using Dot-ELISA. Persons with space-occupying lesions detected by imaging examinations had venous blood drawn for detection of specific *E. multilocularis* antibody (Em18 immunoblot, Ito *et al*. 2000). Cases were defined as follows: (1) CE: a. those who had characteristic cyst-like images detected on abdominal ultrasound or chest radiographs and were positive in the dot-ELISA; or b. those with distinct cyst-like images detected on chest radiographs, but negative on both the dot-ELISA and EM-18; (2) AE: those with distinctive tumour-like lesions detected on abdominal ultrasound who were positive on the dot-ELISA and on the EM-18. Persons without visualized lesions were considered non-cases, regardless of serologic results. For evaluation of risk factors, AE or CE cases were compared with disease-free non-cases.

Statistical analysis

Multivariate logistic regression was used to calculate adjusted odds ratios to assess the relationship of animal ownership to *Echinococcus* spp. infection while controlling for such factors as hygiene, at-home slaughter, offal disposal practices, age, gender, allowing dogs to sleep indoors, playing with dogs, occupation, cultural and lifestyle differences and socioeconomic status. Univariate odds ratios were used to determine independent associations of risks, the study population was stratified by lifestyle (nomadic, semi-nomadic, settled) to detect possible differing trends in risks associated with these different lifestyles. Chi-square test for linear trend was used to detect the increase in prevalence associated with age. All analyses were performed using SAS version 8.0 and Epi Info version 6.0. Statistical significance was set at alpha = 0·05.

Diagnosis of infection in lower animal hosts

The lungs and livers of yaks and sheep slaughtered in the surveyed communities were obtained for examination. Ascertainment of larval stage infections (CE and AE) was carried out by careful visual examination and palpation of lungs and livers. Potential intermediate hosts for *E. multilocularis* were obtained by trapping and shooting small mammals in the vicinity surrounding the human settlements. Tissue lesions of questionable identity were sectioned and stained prior to examination.

RESULTS

Of the 3703 participants evaluated in this study, one or the other form of echinococcosis was diagnosed in 274 or 7·4% – 243 (6·6%) with CE and 31 (0·8%) with AE. No persons were diagnosed with both AE and CE. Prevalence of both CE and AE increased significantly with age for both sexes reaching 10·2% for CE and 1·5% for AE in persons 31 years of age or older (Tables 1 and 2; Figs 1 and 2).

The populations sampled varied according to several demographic, environmental and lifestyle

Table 1. Prevalence of cystic echinococcosis by age

Age in years	Cases*	Prevalence	Odds ratio
0 to 15	17/1054	1·61%	1·00
16 to 30	79/1178	6·71%	4·38
31 and over	147/1440	10·21%	6·33

Chi square test for linear trend = 71·946, *P* value < 0·001.

Table 2. Prevalence of alveolar echinococcosis by age

Age in years	Cases*	Prevalence	Odds ratio
0 to 15	3/1040	0·29%	1·00
16 to 30	9/1108	0·81%	2·83
31 and over	19/1312	1·45%	5·08

Chi square test for linear trend = 8·887, *P* value = 0·003.
* Note for Tables 1 and 2: Denominators are different for alveolar echinococcosis and cystic echinococcosis because non-cases are defined as those free from either infection (i.e. cystic echinococcosis cases are compared only with disease-free individuals and not alveolar echinococcosis cases; and alveolar echinococcosis cases, as well, are only compared with disease-free individuals). This was done because it was suspected that the two diseases may share some of the same risk factors.

practices presumed to be associated with risk of infection by *E. granulosus* and/or *E. multilocularis*. In addition to age, sex, ethnicity and county of residence these risk factor variables included occupation, lifestyle (nomadic, semi-nomadic or exclusively settled), ownership of dogs and livestock, and livestock slaughter practices. Because of the relatively low prevalence of AE in this population and because preliminary analysis revealed similar risk factors for both forms of echinococcosis, cases of CE and AE were combined and analyzed as a single group. Estimated prevalence odds ratios of each potential risk factor for cases of echinococcosis obtained by univariate analyses are presented in Table 3. Significant independent risk factors for infection included: being older than 25 years of age, herding livestock as primary occupation, being female, being of Tibetan ethnicity, earning less than 2000 Yuan (~112.3 EURO) a year, having no education, living in Chenduo County, practising a semi-nomadic lifestyle, owning both livestock and dogs, using stream or river water as the primary source of drinking water, never washing hands before eating, never boiling water before consumption, never playing with dogs and feeding offal to the dogs. Those who did not own livestock animals, drank water from non-stream/non-river water sources, discarded offal beyond reach of dogs (i.e. burning or burying offal) or were Han Chinese were less likely to have CE or AE.

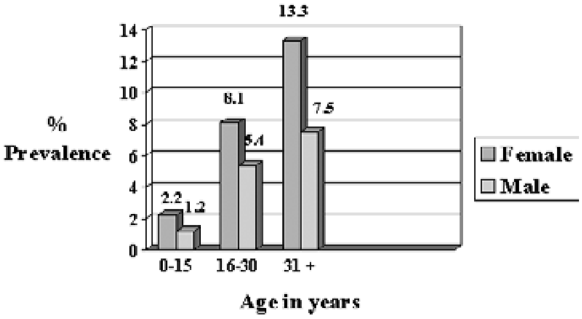

Fig. 1. Prevalence of CE by age and sex.

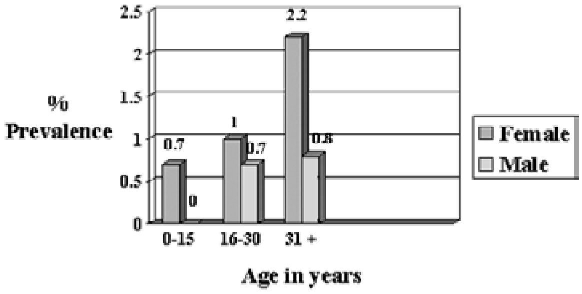

Fig. 2. Prevalence of AE by age and sex.

The study population was stratified by major lifestyle (nomadic, semi-nomadic and settled) and risk factors for each subpopulations were determined separately (below).

Nomadic subpopulation

Among the 344 nomadic participants, 18 (5·2%) were diagnosed with echinococcosis – 17 (4·9%) with CE and 1 (0·3%) with AE. The age of individuals in this group ranged from 1 to 71 years, with a median of 31 years; 228 (66·3%) were at least 26 years old and 181 (52·6%) were male. Living in Chenduo County and using stream water were the only significant independent risk factors for infection (Table 4). Those living in Zeku County and using piped water were significantly less likely to be diagnosed with echinococcosis. Ownership of dogs, livestock or both were not significantly associated with infection in this sub-population. Offal disposal, boiling water and county of residence were significantly correlated with slaughter practice. Presence of stray dogs was correlated with animal ownership. In multivariate analysis none of the predictors, including ownership of dogs and livestock, were significant (Table 7).

Semi-nomadic subpopulation

Among the 1906 semi-nomadic participants, 179 (9·4%) were diagnosed with echinococcosis – 160 (8·4%) with CE and 19 (1·0%) with AE. These rates were the highest among the sub-populations evaluated (Table 3).

Multiple significant risk factors were found among this group (Table 5). The odds of echinococcosis

https://doi.org/10.1017/S0031182003004165 Published online by Cambridge University Press

Table 3. Frequency of cases of echinococcosis (CE and AE) and measures of association of potential risk factors in 3703 people in three regions of Qinghai Province, China (274 cases)

Cases of echinococcosis

Risk factor	Risk factor present? Yes *n*, freq (%)	No *n*, freq (%)	OR*	95% C.I.**
Demographics				
Age >25 years	201/1935 (10·4)	73/1768 (4·1)	2·69	2·04–3·55
Herder	218/1910 (11·4)	56/1790 (3·1)	3·99	2·95–5·39
Male	107/1972 (5·4)	167/1731 (9·7)	0·54	0·42–0·69
Family income ⩾2000 Yuan	65/1331 (4·9)	78/2038 (8·7)	0·54	0·40–0·72
Education	54/1681 (3·2)	220/2016 (10·9)	0·27	0·20–0·37
Ethnicity				
Tibetan	269/3509 (7·7)	5/194 (2·6)	3·14	1·28–7·69
Hui	1/38 (2·6)	273/3665 (7·5)	0·34	0·05–2·46
Han	3/151 (2·0)	271/3552 (7·6)	0·25	0·08–0·77
Other	1/5 (20·0)	273/3698 (7·4)	3·14	0·35–28·16
County/region				
Zeku	73/1048 (7·0)	201/2655 (7·6)	0·91	0·69–1·21
Gande	81/1403 (5·9)	193/2300 (8·4)	0·67	0·51–0·87
Chenduo	120/1252 (9·6)	154/2451 (6·3)	1·58	1·23–2·03
Lifestyle				
Nomadic	18/344 (6·2)	256/3351 (7·6)	0·67	0·41–1·09
Semi-nomadic	179/1906 (9·4)	95/1789 (5·3)	1·85	1·43–2·39
Settled	77/1445 (5·3)	197/2250 (8·9)	0·59	0·45–0·77
Slaughter practices				
In winter only	11/133 (8·3)	236/3200 (7·4)	1·13	0·60–2·13
Scattered throughout the year	90/1328 (6·8)	157/2005 (7·8)	0·86	0·65–1·12
Both	146/1872 (7·8)	101/1461 (6·9)	1·14	0·88–1·48
Animal ownership				
Livestock only	17/247 (6·9)	253/3360 (7·5)	0·91	0·55–1·51
Dogs only	10/269 (3·7)	260/3338 (7·8)	0·46	0·24–0·87
Both	229/2655 (8·6)	41/952 (4·3)	2·10	1·49–2·95
None	14/436 (3·2)	256/3171 (8·1)	0·38	0·22–0·65
Others dogs in area				
Neighbours have dogs	252/3426 (7·4)	13/240 (5·4)	1·39	0·78–2·46
Stray dogs present	205/2735 (7·5)	44/785 (5·6)	1·36	0·98–1·91
Water source				
Stream	5/43 (11·6)	264/3636 (7·3)	1·68	0·66–4·31
River	151/1583 (9·5)	118/2096 (5·6)	1·77	1·38–2·27
Piped Water	74/1163 (6·4)	195/2516 (7·8)	0·81	0·61–1·07
Other	39/890 (4·4)	230/2789 (8·3)	0·51	0·36–0·72
Water storage/hygienic practices				
Kept covered	26/426 (6·1)	241/3204 (7·5)	0·80	0·53–1·21
Boil before drinking	192/2818 (6·8)	61/577 (10·6)	0·62	0·46–0·84
Washes hands	55/986 (5·6)	214/2691 (8·0)	0·68	0·50–0·93
What is done with offal				
Discarded	42/966 (4·4)	227/2705 (8·4)	0·50	0·35–0·70
Eaten by people	133/1830 (7·3)	136/1841 (7·4)	0·98	0·77–1·26
Fed to dogs	94/875 (10·7)	175/2796 (6·3)	1·80	1·39–2·35
Dog care				
Dog sleeps indoors	69/789 (8·8)	199/2841 (7·0)	1·27	0·96–1·69
Play with dogs	104/1810 (5·8)	163/1863 (8·8)	0·63	0·49–0·82
Purpose of dog				
Shepherding	9/108 (8·3)	93/1217 (7·6)	1·10	0·54–2·24
Guarding	90/1165 (7·7)	12/160 (7·5)	1·03	0·55–1·93
Pet	3/52 (5·8)	99/1273 (7·8)	0·73	0·22–2·37

* Mantel–Haenszel estimate of the Prevalence Odds Ratio.
** Test-based Confidence Interval, $\alpha = 0{\cdot}05$.

Table 4. Frequency of cases of echinococcosis and measures of association of potential risk factors among 344 nomadic persons in three regions of Qinghai Province, China (18 cases)

Cases of echinococcosis

Risk factor	Risk factor present? Yes *n*, freq (%)	No *n*, freq (%)	OR*	95% C.I.**
Demographics				
Age > 25 years	14/228 (6·1)	4/116 (3·5)	1·83	0·59–5·70
Herder	17/288 (5·9)	1/56 (1·8)	3·45	0·45–24·47
Male	10/181 (5·5)	8/163 (4·9)	1·13	0·44–2·94
Family income ⩾2000 Yuan	4/68 (5·9)	13/269 (4·8)	1·23	0·39–3·90
Education	0/60 (0·0)	18/284 (6·3)	0·12	0·01–2·00
Ethnicity				
Tibetan	18/342 (5·3)	0/2 (0·0)	0·29	0·01–6·15
Hui	0/0	18/344 (5·2)	N/A	N/A
Han	0/2 (0·0)	18/342 (5·3)	3·51	0·16–75·74
Other	0/0	18/344 (5·3)	N/A	N/A
County/region				
Zeku	3/140 (2·1)	15/204 (7·4)	0·28	0·08–0·97
Gande	7/123 (5·7)	11/221 (5·0)	1·15	0·43–3·05
Chenduo	8/81 (9·9)	10/263 (3·8)	2·77	1·06–7·28
Slaughter practices				
In winter only	1/8 (12·5)	16/323 (5·0)	2·74	0·32–23·64
Scattered throughout the year	4/134 (3·0)	13/197 (6·6)	0·44	0·14–1·37
Both	12/189 (6·4)	5/142 (3·5)	1·86	0·64–5·40
Animal ownership				
Livestock only	1/15 (6·7)	17/326 (5·2)	1·30	0·16–10·46
Dogs only	0/3 (0·0)	18/338 (5·3)	2·47	0·12–49·71
Both	17/320 (5·3)	1/21 (4·8)	1·12	0·14–8·87
None	0/3 (0·0)	18/338 (5·3)	2·47	0·12–49·71
Other dogs in area				
Neighbours have dogs	15/315 (4·8)	1/25 (4·0)	1·20	0·15–9·48
Stray dogs present	6/188 (3·2)	7/124 (5·7)	0·55	0·18–1·68
Water source				
Stream	2/5 (40·0)	14/337 (4·2)	15·38	2·38–99·55
River	14/173 (6·9)	12/169 (2·4)	3·88	0·97–9·73
Piped Water	1/151 (0·7)	15/191 (7·9)	0·08	0·01–0·60
Other	1/13 (7·7)	15/329 (4·6)	1·74	0·21–14·31
Water storage/hygienic practices				
Kept covered	1/24 (4·2)	15/312 (4·8)	0·86	0·11–6·81
Boil before drinking	13/274 (4·7)	1/7 (14·3)	0·30	0·04–2·67
Washes hands	1/43 (2·3)	2/298 (5·0)	0·45	0·06–3·49
What is done with offal				
Discarded	0/8 (0·0)	16/334 (4·8)	1·14	0·06–20·53
Eaten by people	9/223 (4·0)	7/119 (5·9)	0·67	0·24–1·85
Fed to dogs	7/111 (6·3)	9/231 (3·9)	1·66	0·60–4·58
Dog care				
Dog sleeps indoor	3/89 (3·4)	13/249 (5·2)	0·63	0·18–2·28
Play with dogs	6/192 (3·1)	10/149 (6·7)	0·45	0·16–1·26

* Mantel–Haenszel estimate of the Prevalence Odds Ratio.
** Test-based Confidence Interval, $\alpha = 0{\cdot}05$.
N/A = calculation not applicable/unable to be calculated.

significantly increased among those being older than 25 years, being female, being livestock herders, earning less than 2000 Yuan a year, limited education, living in Chenduo County, never boiling water before consumption, playing with dogs and slaughtering animals throughout the year. Persons who practised slaughtering throughout the year and did not allow dogs to eat offal by discarding or eating

https://doi.org/10.1017/S0031182003004165 Published online by Cambridge University Press

Table 5. Frequency of cases of echinococcosis and measures of association of potential risk factors among 1906 semi-nomadic persons in three regions of Qinghai Province, China (179 cases)

Cases of echinococcosis				
	Risk factor present?			
Risk factor	Yes *n*, freq (%)	No *n*, freq (%)	OR*	95% C.I.**
Demographics				
Age >25 years	137/986 (13·9)	42/920 (4·6)	3·37	2·36–4·83
Herder	165/1326 (8·7)	14/580 (2·4)	5·75	3·30–10·01
Male	61/990 (6·2)	118/916 (12·9)	0·44	0·32–0·61
Family Income ⩾2000 Yuan	32/478 (6·7)	132/1313 (10·1)	0·64	0·43–0·96
Education	20/580 (3·5)	159/1325 (12·0)	0·26	0·16–0·42
Ethnicity				
Tibetan	179/1900 (0·1)	0/6 (0·0)	1·36	0·08–24·16
Hui	0/4 (0·0)	179/1902 (9·4)	1·07	0·06–19·90
Han	0/1 (0·0)	179/1905 (9·4)	3·21	0·13–78·99
Other	0/1 (0·0)	179/1905 (9·4)	3·21	0·13–78·99
County/region				
Zeku	66/775 (8·5)	113/1131 (10·0)	0·84	0·61–1·15
Gande	50/661 (7·6)	129/1245 (10·4)	0·71	0·50–1·00
Chenduo	63/470 (13·4)	116/1436 (8·1)	1·76	1·27–2·44
Slaughter practices				
In winter only	0/19 (0·0)	175/1826 (9·6)	0·24	0·01–4·01
Scattered throughout the year	79/1047 (7·6)	96/798 (12·0)	0·60	0·44–0·82
Both	96/779 (12·3)	79/1066 (7·4)	1·76	1·28–2·40
Animal ownership				
Livestock only	14/104 (13·5)	163/1782 (9·2)	1·55	0·86–2·78
Dogs only	0/12 (0·0)	177/1874 (9·5)	0·38	0·02–6·49
Both	163/1761 (9·3)	14/125 (11·2)	0·81	0·45–1·44
None	0/9 (0·0)	177/1877 (9·4)	0·50	0·03–8·70
Other dogs in area				
Neighbours have dogs	173/1866 (9·3)	5/34 (14·7)	0·59	0·23–1·55
Stray dogs present	145/1532 (9·5)	22/289 (7·6)	1·27	0·80–2·02
Water source				
Stream	3/21 (14·3)	176/1882 (9·4)	1·62	0·47–5·54
River	107/1018 (10·5)	72/885 (8·1)	1·33	0·97–1·81
Piped Water	65/809 (8·0)	114/1094 (10·4)	0·75	0·55–1·03
Other	4/55 (7·3)	175/1848 (9·5)	0·75	0·27–2·10
Water storage/hygienic practices				
Kept covered	4/88 (4·6)	172/1781 (9·7)	0·45	0·16–1·23
Boil before drinking	135/1569 (8·6)	31/180 (17·2)	0·45	0·30–0·69
Washes hands	18/157 (11·5)	160/1744 (9·2)	1·28	0·76–2·15
What is done with offal				
Discarded	17/284 (6·0)	162/1615 (10·0)	0·57	0·34–0·96
Eaten by people	99/1185 (8·4)	80/714 (11·2)	0·72	0·53–0·99
Fed to dogs	63/430 (14·6)	116/1469 (7·9)	2·02	0·44–2·78
Dog care				
Dog sleeps indoor	48/532 (9·0)	129/1346 (9·6)	0·94	0·66–1·32
Play with dogs	76/1137 (6·8)	102/757 (13·5)	0·46	0·34–0·63

* Mantal–Haenszel estimate of the Prevalence Odds Ratio.

** Test-based Confidence Interval, $\alpha = 0{\cdot}05$.

the offal themselves were less likely to have disease. In multivariate analysis, ownership of dogs or livestock, or both were not statistically significant, but being older than 25 years and being female were significant factors for echinococcosis (Table 7).

Settled subpopulation

Of 1445 permanently settled participants, 77 (5·3%) were diagnosed with echinococcosis – 66 (4·6%) with CE and 11 (0·8%) with AE. Significant independent

Table 6. Frequency of cases of echinococcosis and measures of association of potential risk factors among 1445 settled persons in three regions of Qinghai Province, China (77 cases)

Risk factor	Cases of echinococcosis: Yes *n*, freq (%)	Cases of echinococcosis: No *n*, freq (%)	OR*	95% C.I.**
Demographics				
Age >25 years	50/717 (7·0)	27/728 (3·7)	1·95	1·20–3·14
Herder	36/292 (12·3)	41/1151 (3·6)	3·81	2·38–6·09
Male	36/797 (4·5)	41/648 (6·3)	0·70	0·44–1·11
Family income ⩾2000 Yuan	29/785 (3·7)	33/451 (7·3)	0·49	0·29–0·82
Education	34/1040 (3·3)	43/401 (10·7)	0·28	0·18–0·45
Ethnicity				
Tibetan	72/1260 (5·7)	5/185 (2·7)	2·18	0·87–5·47
Hui	1/33 (3·0)	76/1412 (5·4)	0·55	0·07–4·07
Han	3/148 (2·0)	74/1297 (5·7)	0·34	0·11–1·10
Other	1/4 (25·0)	76/1441 (5·3)	5·99	0·62–58·24
County/region				
Zeku	4/127 (3·2)	73/1318 (5·5)	0·55	0·20–1·54
Gande	24/617 (3·9)	53/828 (6·4)	0·59	0·36–0·97
Chenduo	49/701 (9·0)	28/744 (3·8)	1·92	1·19–3·09
Slaughter practices				
In winter only	10/106 (9·4)	45/1046 (4·3)	2·32	1·13–4·74
Scattered throughout the year	7/142 (4·9)	48/1010 (4·9)	1·04	0·46–2·34
Both	38/904 (4·2)	17/248 (6·9)	0·60	0·33–1·08
Animal ownership				
Livestock only	2/128 (1·6)	73/1247 (5·9)	0·26	0·06–1·05
Dogs only	10/254 (3·9)	65/1121 (5·8)	0·67	0·34–1·31
Both	49/569 (8·6)	26/806 (3·2)	2·83	1·73–4·61
None	14/424 (3·3)	61/951 (6·4)	0·50	0·28–0·90
Other dogs in area				
Neighbours have dogs	64/1238 (5·2)	7/181 (3·9)	1·36	0·61–3·00
Stray dogs present	54/1008 (5·4)	15/372 (4·0)	1·35	0·75–2·42
Water source				
Stream	0/17 (0·0)	74/1410 (5·3)	0·51	0·03–8·60
River	32/392 (8·2)	42/1035 (4·1)	2·10	1·31–3·38
Piped Water	8/197 (4·1)	66/1230 (5·4)	0·75	0·35–1·58
Other	34/821 (4·1)	40/606 (6·6)	0·61	0·38–0·98
Water storage/hygienic practices				
Kept covered	21/313 (6·7)	54/1104 (4·9)	1·40	0·83–2·35
Boil before drinking	44/970 (4·5)	29/390 (7·4)	0·59	0·36–0·96
Washes hands	36/785 (4·6)	39/642 (6·1)	0·74	0·47–1·18
What is done with offal				
Discarded	25/672 (3·7)	49/750 (6·5)	0·55	0·34–0·91
Eaten by people	25/416 (6·0)	49/1006 (4·9)	1·25	0·76–2·05
Fed to dogs	24/334 (7·2)	50/1088 (4·6)	1·61	0·97–2·66
Dog care				
Dog sleeps indoor	18/163 (11·0)	57/1243 (4·6)	2·58	1·48–4·51
Play with dogs	22/475 (4·6)	51/945 (5·4)	0·85	0·51–1·42

* Mantel–Haenszel estimate of the Prevalence Odds Ratio.

** Test-based Confidence Interval, $\alpha = 0{\cdot}05$.

risk factors for echinococcosis in this group included: being older than 25 years of age, earning less than 2000 Yuan a year, being a herder, having no education, living in Chenduo County, slaughtering animals in the winter only, owning both livestock and dogs, consuming river water, never boiling the water and allowing dogs to sleep indoors at night (Table 6). In multivariate analysis, only the practice of allowing dogs to sleep indoors was a statistically significant risk factor for CE/AE (Table 7).

https://doi.org/10.1017/S0031182003004165 Published online by Cambridge University Press

Table 7. Multivariate logistic regression model of the relationship of animal ownership and echinococcosis, controlling for potential confounding factors, among participants from Qinghai Province, China – by lifestyle

Risk factor	Nomadic OR* (95% C.I.**)	Semi-Nomadic OR* (95% C.I.**)	Settled OR* (95% C.I.**)
Exposure Variables			
Own dogs only	not in model	not in model	0·40 (0·05, 3·53)
Own livestock only	not in model	not in model	0·32 (0·04, 2·87)
Own both	1·10 (0·13, 9·35)	0·61 (0·33, 1·14)	2·71 (0·94, 7·87)
Other Risk Factors			
Dog sleeps indoors	0·88 (0·19, 3·97)	1·02 (0·71, 1·47)	2·81 (1·28, 6·15)
Plays with dogs	0·68 (0·17, 2·72)	0·69 (0·47, 1·01)	0·68 (0·30, 1·51)
Older than 25 years	1·69 (0·45, 6·39)	2·91 (1·99, 4·25)	1·60 (0·83, 3·12)
Male	0·93 (0·33, 2·61)	0·43 (0·30, 0·60)	1·07 (0·58, 1·96)
Herder	2·96 (0·34, 26·05)	not in model	1·78 (0·88, 3·56)
Slaughter scattered throughout year	0·49 (0·09, 2·70)	0·80 (0·55, 1·17)	1·06 (0·37, 3·07)
Slaughter in winter only	4·34 (0·32, 58·96)	not in model	1·61 (0·58, 4·47)
Stray dogs present	not in model	not in model	1·69 (0·73, 3·88)
Feeding offal to dogs	not in model	not in model	1·50 (0·64, 3·50)
Eating offal	not in model	not in model	1·38 (0·60, 3·18)
Goodness-of-Fit***			
χ^2	5·4871	3·5895	5·5168
Degrees of freedom	7	7	8
P-value	0·6007	0·8257	0·7012

* Adjusted Prevalence Odds Ratio, controlling for other factors in model.

** Test-based Confidence Interval, $\alpha = 0{\cdot}05$.

*** Hosmer–Lemeshow Goodness-of-Fit Test, $\alpha = 0{\cdot}05$.

Table 8. Prevalence of *Echinococcus granulosus* in livestock intermediate hosts in Qinghai Province, China, 1998–99

Species	No. examined	No. infected %
Sheep	1002	666 (66·5)
Yak	728	521 (71·6)
Pig	426	0

Table 9. Prevalence of *Echinococcus* spp. in definitive hosts examined in Qinghai Province, China, 1998–99

Host species	No. examined	No. infected % *E. granulosus*	No. infected % *E. multilocularis*
Dog	59	27 (45·8)	3 (5·1)
Fox	12	—	4 (33·3)
Wolf	1	1	—

Echinococcosis in animal hosts

During the course of the diagnostic surveys in human populations, *Echinococcus* larval-stage infection data were collected by examination of potential intermediate (Table 8) and definitive (Table 9) host animals. Two-thirds (66·5%) of sheep and 71·6% of yaks examined at slaughter were infected with larval *E. granulosus*. Rates of infection in sheep and yak intermediate hosts were similarly high in all three counties (Chindu, Zeko and Gade). *Echinococcus* spp. infection was not detected in pigs ($n = 426$) examined at slaughter. *E. multilocularis* infections were detected in 11 (3·5%) of 319 conies (*Ochotona curzoniae*), a small lagomorph, examined at autopsy.

Adult-stage infections with *E. granulosus* were detected at necropsy of intestines in 45·8% of stray dogs and in none of 12 foxes examined at autopsy (Table 9). By contrast *E. multilocularis* infection was identified in 5·1 % of the same sample of dogs and in 4 (33·3%) of the foxes.

DISCUSSION

Although echinococcosis has been recognized in humans and animals since antiquity, it was only reported in China during the last century. The first case of CE (*E. granulosus*) in humans was reported in 1905 (Chi *et al*. 1990), and AE (*E. multilocularis*) in 1965 (Yao *et al*. 1965). Since then, 22 of 31 of China's provinces and autonomous regions, approximately 87% of China's territory, have reported cases (Schantz *et al*. 1995; Wen & Yang, 1997; Craig *et al*. 2000; Eckert *et al*. 2001) and the population at risk for one or both forms of infection is estimated at 60 million (Ito *et al*. 2003). Although both forms of echinococcosis are associated with morbidity and mortality, infection with *E. multilocularis* causes alveolar-like metacestode growth (AE) that resembles and behaves like malignant tumours in affected human hosts. Case-fatality of alveolar echinococcosis

https://doi.org/10.1017/S0031182003004165 Published online by Cambridge University Press

Fig. 3. Map of China showing geographic position of Qinghai Province.

may be as high as 75% in progressive cases; however, early diagnosis and treatment reduces mortality (Schantz, 1994).

Most earlier reports of series of cases of CE/AE depended on case identification by surgical/clinical presentation and patients' ages were highly skewed toward adults (Pawlowski *et al*. 2001). Abdominal ultrasound imaging of the Qinghai Tibetan population indicates incident infection in the first decade of life with increasing prevalence with age suggesting susceptibility and risk for infection throughout the lifespan (Tables 1 and 2; Figs 1 and 2). Recent advances in diagnostic imaging technology and specific serodiagnosis have allowed the identification of earlier stages of disease, before onset of clinical symptoms, thus reducing the time between infection and diagnosis (Macpherson & Milner, 2003). This shorter period may allow better assessment of risk factors for echinococcosis. This study has utilized such techniques to help identify the importance of animal ownership, as well as other lifestyle covariates, in echinococcosis in the overall study group, as well as among the nomadic, the semi-nomadic and the settled participants.

Qinghai Province located on the Tibetan Plateau of western China is especially burdened as both cystic and alveolar echinococcosis occur in this frontier province (Fig. 3). An extensive medical record review of Qinghai hospitals reported a high incidence of surgical cases of both *E. granulosus* and *E. multilocularis* infections in the local population (Wang *et al*. 1999). The record review of 40 years' experience found 3679 cases of CE and 107 cases of AE in the region. Persons of Tibetan nationality were 'over-represented' among the patients in comparison with their representation in the overall provincial population. The province is approximately 721 100 square kilometers with an ethnically diverse population of 4·5 million persons (1990 census data). Han (Chinese), Zang (Tibetan), Mongol and Hui (Chinese Muslims) reside within the province; 2·4% of China's Tibetan population, approximately 119 000 persons, reside in this province and were the primary focus of this study.

In our population survey the prevalence of AE was low in comparison with prevalence of CE (0·8% *vs* 6·6%) and, since preliminary analysis of risk factors for infection identified contact with dogs rather than foxes as the primary source of both infections, cases of CE and AE were combined for further analysis. The univariate analysis for echinococcosis identified independent risk factors similar to that found in previous studies – poor hygienic practices, female gender, herding occupation, limited education, lower income, age greater than 25 years, presence of stray dogs, inadequate offal disposal practices, and ownership of both livestock and dogs were found to be significant risk factors for both CE and AE (Table 5). Socioeconomic indicators that were significant included low income and limited education. These indicators support previous observations that, in an environment in which cyclic transmission is occurring, lower SES status, and the associated hygienic practices, are associated with higher risk of acquiring echinococcosis. The multivariate analysis showed that those owning livestock, with or without dogs, have tripled the risk of being diagnosed with echinococcosis in comparison with those without livestock. Other significant covariates included being older than 25 years, female gender, herding occupation, and living a nomadic (*vs* permanently settled) lifestyle. The increased odds of diagnosing infection in those older than 25 years indicates chronic exposure and the lack of acquired immunity. Analysis of potential risk factors in all populations indicated that girls and women were at increased risk of infection in comparison with males. This may be associated with the observation that women and girls are primarily responsible for dog care and collection of yak faeces for fuel (the latter may be mixed with canine faeces). Herders tend to own both livestock and dogs and consequently these factors are confounded. The nomadic participants may be at comparatively decreased risk of infection due to their periodic movement from region to region, decreasing their actual exposure to the parasite and infection pressure.

Among the nomadic population, univariate analysis identified only living in Chenduo County and use of streams and rivers as regular water source as significant risk factors for echinococcosis. The practical significance of this latter association is uncertain – the water sources of the nomads would be dependent on their location at the time of the survey. It did not necessarily reflect where they were residing or where they were obtaining their water prior to interview at the time of infection/exposure. It is possible that these responses would have been different in another season or another year. The number of nomads was relatively small (less than 10% of the study group were nomadic and less than 7% of the cases were among the nomadic) and the precision of many estimates of the prevalence odds ratios was poor, as indicated by large confidence intervals. The method of recruiting participants (moving village to village over the course of 1 year) likely affected the ability to reach the nomads, thus the relatively low number of nomadic participants.

Persons classified in our study as 'semi-nomadic' practised a nomadic lifestyle for most months of the year, however, they resided in permanent dwellings usually within or close to large settlements during all or part of the winter. Their relatively large numbers gave strength to the analysis and permitted identification of practices associated with the 'nomadic herding' lifestyle that were associated with infection. Among the semi-nomadic participants, age, herding occupation, female gender, income, education, slaughter practices, offal disposal practices, and playing with dogs were significant risk factors, similar to findings in the overall group. Multivariate analysis indicated that being older than 25 years and being female conferred higher risk of infection, as was found in the overall assessment.

Among the settled participants, age, herding occupation, income, education, county, slaughtering in winter only, ownership of both dogs and livestock, water source, boiling water, offal disposal and allowing dogs to sleep indoors (the family dwelling) were significant univariate risk factors. The multivariate analyses did not find livestock ownership and dog ownership to be significantly associated with echinococcosis; however, allowing dogs to sleep inside the family dwelling was a significant risk factor for infection. More than 85% of participants reported neighbors owning dogs and over 70% reported the presence of stray dogs in the area. Consequently, because of the common presence of dogs in these villages, personal ownership of dogs may not significantly increase exposure – *Echinococcus* eggs may occur relatively commonly in soil, water and vegetation as a result of widespread defecation by infected dogs. Allowing dogs to sleep indoors, however, may reflect a more intense exposure to eggs in this sub-population, and thus, explain why this factor significantly increased risk for echinococcosis.

The presence in the environment of *E. granulosus* and *E. multilocularis* and certain lifestyle practices place the Tibetan population of this region at high risk for cystic and alveolar echinococcosis. These two cestodes have different life cycles but in the Tibetan environment in Qinghai both appear to be primarily acquired from domestic dogs. Livestock husbandry with sheep, yak and pigs, all intermediate hosts for *E. granulosus*, is practised in 90% of the area. People in this region live in close proximity to dogs that may be fed offal from livestock slaughter and butchered game animals. Unrestrained dogs commonly prey upon conies, believed to be the most important local intermediate host for *E. multilocularis*.

E. granulosus, the cause of CE in humans, is maintained throughout most of its worldwide distribution in dogs and domestic ungulates and exposure and risk of infection in humans is strongly influenced by human behaviour in relation to husbandry practices and contact with these hosts (Eckert *et al.* 2001). In contrast, *E. multilocularis* is mainly limited to sylvatic hosts and its survival and transmission is determined by the predator–prey relationships between foxes and local species of small mammals. Prevalences of AE in humans are comparatively low in comparison with those of CE and risk factors for infection are usually poorly defined (Schantz *et al.* 1995). Consequently, the geographic distribution and public health impact of *E. granulosus* (CE) is usually greater than that of *E. multilocularis* (AE). Recent investigations in China reveal that these generalizations may not apply and that dogs are the primary definitive host of *E. multilocularis* responsible for zoonotic transmission of infection to humans (Craig *et al.* 1992; Qiu, Liu & Schantz, 1998; Liu, Qiu & Schantz, 1999; Ito *et al.* 2003; see also Vuitton *et al.* this supplement). Among the Tibetan populations on the Qinghai Tibetan Plateau where both species of *Echinococcus* occur, the rates of AE in humans exceed those documented in most other other areas where investigations have been performed and the prevalence of AE is comparable and sometimes exceeds that of CE. The enzootic foci of AE among Tibetan populations in Qinghai and Sichuan Provinces (Qiu *et al.* 1998; Wang *et al.* 2001) are representative of this special situation. Parasitological surveys of wildlife in the Tibetan plateau document high prevalences ($>50\%$) of *E. multilocularis* in several species of fox and stray dogs. Intermediate hosts involved in the maintenance of *E. multilocularis* include rodents (*Microtus irene*) and conies. The latter appears to be a major prey species for foraging dogs in the vicinity of the human communities (see Vuitton *et al.* in this supplement). Although maintenance of *E. multilocularis* in nature in this region involves the sylvatic cycle in foxes and their rodent and lagomorph prey (Table 8), more intense zoonotic exposures of humans are related to synanthropic cycles involving dogs.

Overgrazing may be a key factor causing grassland degradation and increases in small mammal populations, including *Ochotona*. It has been observed that the construction of 'fenced enclosures' for grazing livestock in the vicinity of the Tibetan villages leads to overgrazing, thus creating a habitat more favourable to increase of conie populations, the primary local intermediate hosts for transhumant cycles of *E. multilocularis*. Conies are a popular prey species for local dogs, thus leading to intense transmission of *E. multilocularis* near human settlements and, consequently, increasing risk for zoonotic transmission (Wang Q. *et al.* unpublished data). This may be a partial explanation for the high prevalence of *E. multilocularis* in *O. curzoniae* that has been documented in Qinghai and Sichuan Provinces (Table 9; Qiu *et al.* 1998).

Tibetan populations on the Qinghai Tibetan plateau of China are exposed to and suffer some of the highest prevalences of cystic and alveolar echinococcosis in the world. The close association of the people with livestock and dogs, combined with low levels of hygiene and lack of knowledge of the disease, contribute to the maintenance of the transmission cycles of these zoonotic tapeworms. Dogs are routinely fed offal of butchered livestock leading to canine infections with *E. granulosus* and contamination of the environment with tapeworm eggs. Commensal lagomorph and rodent populations exist close to the villages and provide a food source for stray and free-roaming owned dogs resulting in peridomestic *E. multilocularis* infection. Ownership of dogs is associated with increased prevalence of both diseases in humans, implying that treatment and control of domestic dogs could play a major role in decreasing infection risk in this population.

Most of the factors associated with the diseases result from human behaviours that can be addressed to prevent continued transmission. Treating and controlling dogs should be the focus of control programmes in Qinghai, especially as dogs appear to be a major risk factor for both cystic and alveolar echinococcosis.

ACKNOWLEDGEMENTS

This work was supported in part by a grant from the Thrasher Research Fund, Salt Lake City, Utah, USA.

REFERENCES

CHI, P., ZHANG, W., ZHANG, Z., HASYET, M., LIU, F., DING, Z., ANDERSON, F. L., TOLLEY, H. D. & SCHANTZ, P. M. (1990). Cystic echinococcosis in the Xinjiang Uyger Autonomous Region, People's Republic of China. I. Demographic and epidemiologic data. *Tropical Medicine and Parasitolgy* **41**, 157–162.

CRAIG, P. S., DESHAN, L., MACPHERSON, C. N., DAZHONG, S., REYNOLDS, D., BARNISH, G., GOTTSTEIN, B. & ZHIRONG, W. (1992). A large focus of alveolar echinococcosis in central China. *Lancet* **340** (8823), 826–831.

CRAIG, P. S., GIRAUDOUX, P., SHI, D., BARTHOLOMOT, B., BARNISH, G., DELATTRE, P., QUERE, J. P., HARRAGA, S., BAO, G., WANG, Y., LU, F., ITO, A. & VUITTON, D. A. (2000). An epidemiological and ecological study of human alveolar echinococcosis transmission in south Gansu, China. *Acta Tropica* **77**, 167–177.

ECKERT, J., SCHANTZ, P. M., GASSER, R. B., TORGERSON, P. R., BESSONOV, A. S., MOVSESSIAN, S. O., THAKUR, A., GRIMM, F. & NIKOGOSSIAN, M. A. (2001). Geographic distribution and prevalence. In *WHO/OIE Manual on Echinococcosis* *in Humans and Animals: A Public Health Problem of Global Concern* (ed. Eckert, J., Gemmel, M. A., Meslin, F.-X. & Pawlowski, Z. S.), pp. 100–141. World Organisation for Animal Health, Paris, France.

ITO, A., MA, L., SCHANTZ, P. M., GOTTSTEIN, B., LIU, Y.-H., CHAI, J.-J., ABDEL HAFEZ, S., ALTINTAS, N., JOSHI, D. D., LIGHTOWLERS, M. W. & PAWLOWSKI, Z. S. (2000). Differential serodiagnosis for cystic and alveolar echinococcosis and *E. multilocularis* protoscolex (EM18). *American Journal of Tropical Medicine and Hygiene* **60**, 188–192.

ITO, A., URBANI, C., QIU, J., VUITTON, D. A., QIU, D., HEATH, D. D., CRAIG, P. S., ZHENG, F. & SCHANTZ, P. M. (2003). Control of echinococcosis and cysticercosis: a public health challenge to international cooperation in China. *Acta Tropica* **86**, 3–17.

LIU, F. J., QIU, J. M. & SCHANTZ, P. M. (1999). Epidemiology of echinococcosis in a Tibetan community in Western Sichuan. In *Proceedings, Workshop on Echinococcosis Control Strategy in China*. Urumqi, Institute for Endemic Disease Research and Control. (In Chinese.)

MACPHERSON, C. N. L. & MILNER, R. (2003). Performance characteristics and quality control of community based ultrasound surveys for cystic and alveolar echinococcosis. *Acta Tropica* **85**, 203–209.

PAWLOWSKI, Z. S., ECKERT, J., VUITTON, D. A., AMMANN, R. W., KERN, P., CRAIG, P. S., DAR, K. F., DE ROSA, F., FILICE, C., GOTTSTEIN, B., GRIMM, F., MACPHERSON, C. N. L., SATO, N., TODOROV, T., UCHINO, J., VON SINNER, W. & WEN, H. (2001). Echinococcosis in humans: clinical aspects, diagnosis and treatment. In *WHO/OIE Manual on Echinococcosis in Humans and Animals: A Public Health Problem of Global Concern* (ed. Eckert, J., Gemmel, M. A., Meslin, F.-X. & Pawlowski, Z. S.), pp. 20–71. Wld. Org. Anim. Hlth., Paris, France.

QIU, J. M., LIU, F. J. & SCHANTZ, P. M. (1998). Epidemiology and transmisssion of alveolar echinococcosis in East Tibetan Plateau. In *Proceedings First National Hydatidology Conference of Imaging and Therapeutics and International Symposium on Transmission and Control of* Echinococcus *Infection*, pp. 104–108. Urumqi, Xinjiang Medical University. (In Chinese.)

SCHANTZ, P. M. (1994). Larval cestodiases. In *Infectious Diseases*. Fifth Edn. (ed. Hoeprich, P., Jordan, C. & Wilson, R.), pp. 850–860. Philadelphia: J.B. Lippincott.

SCHANTZ, P. M., CHAI, J., CRAIG, P. S., ECKERT, J., JENKINS, D. J., MACPHERSON, C. N. L. & THAKUR, A. (1995). Epidemiology and control of hydatid disease. In *Echinococcus and Hydatid Disease* (ed. Thompson, R. C. A. & Lymbery, A. J.), pp. 233–331. CAB International, UK.

WANG, H., LIU, F., SCHANTZ, P. M., ITO, A., DELKER, C., CAO, D., MA, S. & ZHAO, H. (1999). A survey of hydatid disease in Tibetan populations in Qinghai Province: prevalence, distribution and risk factors for cystic and alveolar echinocococcosis. *Archivos Internacionales Hidatidosis* **XXXIII**, 316.

WANG, Q., QIU, J. M., SCHANTZ, P. M., HE, J. G., ITO, A. & LIU, F. (2001). Investigation of risk factors for development of human hydatidiosis among households raising livestock in Tibetan areas of Western Sichuan Province. *Chinese Journal of Parasitology and Parasitic Diseases* **19**, 289–293.

WEN, H. & YANG, W.-G. (1997). Public health importance of cystic echinococcosis in China. *Acta Tropica* **67**, 133–145.

YAO, P. L., HUANG, N. Q., FU, L. M. & FANG, H. (1965). Hepatic alveolar hydatid disease. *China Surgery Journal* **13** (5), 400–401.