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Advances in research on echinococcoses epidemiology in China

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ABSTRACT

Echinococcoses are serious zoonotic diseases in China's vast, western and north-western pastoral areas that has one of the highest prevalence in the world. The two most common forms, cystic echinococcosis (CE) and alveolar echinococcosis (AE), are co-epidemic in some areas causing a grave threat to people's health and economic development. *Echinococcus* spp. are transmitted through domestic, sylvatic and mixed cycles involving many kinds of host. Successful transmission requires a favourable environment for the growth of the parasites and survival of their eggs, while the unique customs and religious beliefs in the endemic areas pose a challenge to the prevention and control of these parasites. Based on previous epidemiological studies, this paper reviews the particular factors affecting the transmission of *Echinococcus* parasites in China, with a focus on biological (parasite genotype and the species, age, sex and density of hosts), environmental (landscape and climate) and social (age, gender, ethnicity, education, occupation, life style, cultural customs, living conditions and hygiene practices of humans in the endemic areas). These three factors interact with each other and jointly determine the parasites' transmission intensity, the study of which supports the formulation of the strategies and measures that are significant for control of these infections.

Introduction

Echinococcoses are zoonotic parasitic infections caused by the larval stages of taeniid cestodes belonging to the genus *Echinococcus* (Otero-Abad and Torgerson, 2013; Qian et al., 2017), and considered as neglected parasitic diseases (NTDs) by the World Health Organization (WHO) (WHO, 2015). The classification of this genus has long been controversial due to the lack of evidence of geographical and/or ecological segregation and common sympatric occurrence as well as inadequate descriptions and lack of phenotypic characterization (McManus, 2013; Xiao et al., 2005). Before molecular genetics were widely used, a total of 16 species and 13 subspecies of the genus had been reported based on morphology and host-parasite specificity, but most of them were finally considered to be *Echinococcus granulosus sensu lato* (*E. granulosus s.l.*) (Lymbery, 2017; McManus, 2013; Xiao et al., 2005). At present, according to the latest taxonomic revision, 9 species are recognized (Cadavid Restrepo et al., 2016; Lymbery, 2017; Vuitton et al., 2020). Four of them, *E. granulosus s.l., E. multilocularis, E. oligarthra* and *E. vogeli* are pathogenic to humans (Han et al., 2015b; Rausch and Bernstein, 1972; Thompson and McManus, 2001), with the former two particularly harmful as they cause cystic echinococcosis (CE) and alveolar echinococcosis (AE), respectively. Both are widely distributed and thus represent diseases of important public health significance (McManus et al., 2003; Moro and Schantz, 2009; Tappe et al., 2010). *E. vogeli* and *E. oligarthra* cause neotropical echinococcosis in South, Central, and North America but have so far not been found elsewhere (Lymbery, 2017; Vuitton et al., 2020).

Echinococcus spp. basically need two mammalian hosts to complete their life cycle, with ungulate herbivores and rodents acting as intermediate hosts and carnivore as the definitive ones (canids, felids, etc.)

Abbreviations: Xinjiang PCC, Xinjiang Production and Construction Corps.

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(Jenkins, 2001), while humans are accidental hosts who play no part in the parasite life cycle (Colombe et al., 2017). CE and AE are both serious, life-threatening diseases with the former commonly chronic with absence of initial symptoms that first emerge when the growing cysts become large and/or complex (Islami Parkoohi et al., 2018). The clinical presentation depends on the organ(s) affected, the size of the cyst(s) and where they are localized (McManus et al., 2003). The cyst(s) can rapture then cause systemic or local allergic reactions (Liu et al., 2018b), even death (Khachatryan, 2017). Treatment is complicated and the prognosis poor, with a post-operative mortality of 2.2% and post-treatment relapses of 6.5% (WHO, 2020). AE, on the other hand, is a highly fatal disease that generally causes widespread, serious damage to the body reminiscent of malignant tumours. The vast majority of primary lesions in AE are in the liver, but the metacestodes can spread to lung, brain and other organs by infiltration, hematogenous and lymphatic metastasis (Jenkins et al., 2001, 2005). It has a 10-year fatality rate of 94% for untreated or inadequately managed patients (Jura et al., 1996), which has led to the name "worm cancer" for this form of the disease (Qucuo et al., 2020).

Echinococcoses not only endanger human health but also have effect on the economy in the area and country affected. Each year about 200,000 human cases of echinococcoses are diagnosed globally, and a total of 2-3 million people are currently infected producing an estimated burden of diseases amounting to 871,000 disability-adjusted life years (DALYs) (Cadavid Restrepo et al., 2016; Schurer et al., 2015; WHO, 2020). Among those infected, approximately 1 million suffer from CE (Torgerson and Macpherson, 2011) and 0.3-0.5 million from AE, with an addition of more than 18,000 new cases of AE annually (Torgerson et al., 2010). Furthermore, more than 1 million people globally are at risk of developing AE and CE, and the economic cost incurred is approximately USD 3 billion per year (Yu et al., 2018a). CE results in an economic loss of USD 1.92 billion, and the associated livestock production is estimated at USD 2.19 billion (Budke et al., 2006). The burden of CE is at least 1 million DALYs, and that of AE is estimated at 670,000 DALYs (Chen et al., 2017; Torgerson et al., 2010).

Echinococcoses are highly prevalent diseases in China. The annual economic loss caused by CE in China is 4.61 billion Chinese Yuan (RMB) corresponding to USD 0.66 billion, and the loss of animal husbandry related to CE is almost 1 billion RMB (USD 0.14 billion) (Yang et al., 2015c). The disease burden of CE patients in China amounts to nearly 400,000 DALYs, accounting for 40% of the global CE disease burden (Budke et al., 2006). Of all new AE cases worldwide, 91% occur in China and this corresponds to 95% of the world's total DALYs (Torgerson et al., 2010). There is thus no doubt that echinococcoses are major public health and socio-economic problems in China.

The complicated life cycle of *Echinococcus* spp., involving multiple host species, diverse and widely distributed of intermediate and definitive hosts coupled with the unique natural environment, customs and religious beliefs in China's endemic areas have led to a high prevalence there. This has created a serious local situation, with many particular challenges with respect to prevention and control. This review analyzes the epidemic situation of echinococcoses in China based on previously published data, summarizing factors related to the epidemic as well as determining the key factors affecting the transmission of *Echinococcus* parasites in order to provide a reference for modelling approaches. The overall aim is to predict the prevalence of echinococcoses and contribute to the formulation of targeted control measures that can effectively reduce the prevalence.

1. Epidemiology of echinococcoses in China

Both forms of echinococcoses - CE and AE – are highly prevalent in the agricultural and pastoral areas in the West and North of China (Liu et al., 2018b). Since 1949, the Ministry of Health of China has organized three population-based, large-scale, national epidemiological surveys, the most recent in 2012-2016, which found these diseases in 368 endemic counties distributed in 9 provinces and autonomous regions, including Inner Mongolia, Sichuan, Tibet Autonomous Region (TAR), Gansu, Qinghai, Ningxia Hui Autonomous Region (NHAR), Yunnan, Shaanxi and Xinjiang Uygur Autonomous Region (XUAR) (Wu et al., 2018a). A total of 5,133 cases of echinococcoses were detected, including 3,992 cases of CE and 1,074 of AE. The ultrasound detection rate of the infection was 0.51% and the overall prevalence was estimated at 0.28% (Wu et al., 2018a). Compared to the 2001-2004 survey (Ministry of Health, 2007), the population detection rate had decreased from 1.08%, probably attributed to the comprehensive control strategy under the adopted slogan "focus on the source of infection in combination with controlling intermediate hosts plus patient investigation and treatment". In addition, Xiao et al. (2005) isolated a new species in Shiqu County of Sichuan Province, i.e. *E. shiquicus* in the Tibetan fox *Vulpes ferrilata* and in the plateau pika *Ochotona curzoniae,* a small, mountain-dwelling mammal. This *Echinococcus* species has subsequently been reported in Tibetan voles, pikas and Tibetan foxes in other areas of the Qinghai-Tibet Plateau (Han et al., 2009; Wu et al., 2007; Zhang and Wang, 2007). In the eastern Tibetan plateau, Boufana et al. (2013) first reported dog faeces positive for *E. shiquicus* by genetic techniques. However, so far no human infection with *E. shiquicus* has been described.

1.1. Cystic echinococcosis (CE)

In China, the first case of human CE was found in Qingdao, Shandong Province in 1905 (Chi et al., 1990), while *E. granulosus s.l.* was first found in dogs in Beijing in 1911 (Craig et al., 1991). Today, human CE cases have been reported in almost all provinces, mainly in western and north-western China (Wang et al., 2010a), such as Xinjiang, Qinghai, Tibet, Sichuan, Yunnan, Gansu, Ningxia, Shaanxi and Inner Mongolia that are all highly endemic.

The prevalence of CE in all endemic provinces and autonomous regions in the past 10 years is shown in Table 1. It is noted that the Tibetan areas in Sichuan Province and on the Qinghai-Tibet Plateau remain one of the most serious areas for echinococcoses in the world. The latest survey found that the prevalence of human echinococcoses in 35 endemic counties in Sichuan was 1.08% in 2012, with levels in Shiqu and Seda counties of 12.09% and 6.30%, respectively (Sichuan Center for Disease Control and Prevention, 2014), while the corresponding human CE cases amounted to 229 (7.16%) and 150 (4.69%) (Sichuan Center for Disease Control and Prevention, 2014). The epidemiological investigation in Tibet recorded the greatest prevalence of human CE (6.22%) in Naqu County (Shu et al., 2015). In addition, the CE prevalence in Yushu and Guoluo counties in Qinghai Province between 2013 and 2014 was 4.03% (Han et al., 2019b), while that in Xinjiang in 2016 was 1.03% (Qi, 2014).

The results of the national retrospective survey of echinococcoses in China carried out in 1992 showed that 25,696 cases of CE diagnosed in 1949-1996 were reported in 344 counties of 23 provinces (autonomous regions, municipalities) (Xu et al., 1999). So far, 31 provinces (autonomous regions, municipalities) have reported the primary CE cases (Wang et al., 2010a) and already the number of provinces (autonomous regions, municipalities) reporting primary cases has increased to 27 in 2008 (Zhang et al., 2015). This indicates that more and more regions are endemic, and that CE tends to spread from the endemic areas in the West to the non-endemic areas in the East. Wu et al. (2018a) haven shown that CE can be imported from endemic areas to non-endemic areas in various ways, e.g., the occurrence of cases in Liyang City of Jiangsu Province was related to the export of infected livestock, while others in Jiyuan City of Henan Province were related to the fur processing industry. In addition, the positive rate of faecal antigens of pet dogs in Horchin District, Tongliao City, Inner Mongolia was 16.49% (Hu et al., 2011). These examples underline the role in transmission by exchange of people, livestock trades, livestock products as well as the increasing number of imported dogs between the western and eastern regions of China. This important finding suggests that quarantine practises of

Table 1
Prevalence of human AE and CE in China in the period 2010 to 2020 confirmed by mass ultrasound screening

Administrative region	Period	Scope of investigation	People examined (no.)	CE cases (no.)	Estimated CE prevalence % (95% *CI*)	AE cases (no.)	Estimated AE prevalence % (95% *CI*)	Mixed infection no. (% prevalence)	References
Inner Mongolia	Jan.-Dec. 2012	Whole autonomous region (16 counties of 5 leagues/cities)	53,313	56	0.11 (0.08-0.13)	0	0	-	Song et al., 2017b
	2012-2015	Whole autonomous region (8 areas)	7,373	5	0.07 (0.01-0.13)	0	0	-	Zhang et al., 2018
	2012-2016	Whole autonomous region	70,161	64	0.09 (0.07-0.12)	0	0	0	Wu et al., 2018a
	2018	Whole autonomous region	58,814	30	0.05 (0.03-0.07)	0	0	0	Unpublished*
Sichuan	2012	35 counties in 4 cities (prefectures) of Ganze, Aba, Liangshan and Yaan	112,605	1,012	0.90 (0.84-0.95)	317	0.28 (0.25-0.31)	18 (0.02)	Sichuan Center for Disease Control and Prevention, 2014
		Ganze (Shiqu County)	3,198	229	7.16 (6.27-8.06)	143	4.47 (3.76-5.19)	-	
		Ganze (Seda County)	3,199	150	4.69 (3.96-5.42)	70	2.19 (1.68-2.70)	-	
	2013-2014	Ganze (303 townships in 17 counties)	280,851	278	0.10 (0.09-0.11)	134	0.05 (0.04-0.06)	-	Zhao, 2015
		Dege County	13,910	48	0.35 (0.25-0.44)	18	0.13 (0.07-0.19)	-	
		Shiqu County	32,567	112	0.34 (0.28-0.41)	75	0.23 (0.18-0.28)	-	
		Ganzi County	16,306	20	0.12 (0.07-0.18)	29	0.18 (0.11-0.24)	-	
	May-Nov. 2016	Whole province [a]	1,258	21	1.67 (0.96-2.38)	-	-	-	Yuan et al., 2017
	Dec.2015-May 2017	Ganze (Shiqu County)	84,526	1,949	2.31 (2.21-2.41)	3,028	3.58 (3.46-3.71)	59 (0.07)	Yu et al., 2018b
	Oct. 2018	Ganze (Ganzi County)	17,650	174	1.00 (0.84-1.13)	637	3.61 (3.33-3.88)	-	Xie et al., 2020
	2018	Whole province	809,376	215	0.03 (0.023-0.030)	90	0.01 (0.009-0.0130)	8 (<0.01)	Unpublished*
Yunnan	2012-2016	Whole province	56,163	28	0.05 (0.03-0.07)	0	0	0	Wu et al., 2018a
	2012-2017	Whole province (24 counties (cities, districts))	105,555	67	0.06 (0.05-0.08)	0	0	0	Li et al., 2019b
	2018	Whole province	42,421	9	0.02 (0.01-0.04)	0	0	0	Unpublished*
Tibet Autonomous Region	2012-2016	Whole province	80,834	1,202	1.49 (1.40-1.57)	153	0.19 (0.16-0.22)	0	Li et al., 2019a; Gongsang et al., 2017; Wu et al., 2018a
	Mar.-Jun. 2014	Nagqu	933	58	6.22 (4.66-7.77)	6	0.64 (0.13-1.16)	-	Shu et al., 2015
	May-Nov. 2016	Whole province [a]	996	25	2.51 (1.54-3.48)	-	-	-	Yuan et al., 2017
	Aug.-Oct. 2016	Ali	4,740	94	1.98 (1.59-2.38)	13	0.27 (0.13-0.42)	-	Xiao et al., 2018
	Aug.-Oct. 2016	Nagqu	11,897	339	2.85 (2.55-3.15)	33	0.28 (0.18-0.37)	-	Danzhen et al., 2018
	Aug.-Oct. 2016	Nyingchi	5,016	42	0.84 (0.56-1.09)	5	0.10 (0.01-0.19)	-	Wang et al., 2018a
	Aug.-Oct. 2016	Whole province (70 counties) [b]	13,651	49	0.36 (0.26-0.46)	6	0.04 (0.01-0.08)	-	Xue et al., 2018a
	Aug.-Oct. 2016	Shannan	10,287	100	0.97 (0.78-1.16)	3	0.03 (0.00-0.06)	-	Baiba et al., 2018b
	Aug.-Oct. 2016	Changdu	14,289	167	1.17 (0.10-1.35)	39	0.27 (0.19-0.36)	-	Gongsang et al., 2018
	Aug.-Oct. 2016	Shigatse	21,497	261	1.21 (1.07-1.36)	26	0.12 (0.07-0.17)	-	Bianba et al., 2018
	Aug.-Dec. 2016	364 villages from 70 counties of 7 prefectures (cities) –Lhasa, Nyingchi, Shannan,	77,049	1,078	1.40 (1.32-1.48)	136	0.18 (0.15-0.21)	-	Chen et al., 2018

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Table 1 (*continued*)

Administrative region	Period	Scope of investigation	People examined (no.)	CE cases (no.)	Estimated CE prevalence % (95% *CI*)	AE cases (no.)	Estimated AE prevalence % (95% *CI*)	Mixed infection no. (% prevalence)	References
		Changdu, Shigatse, Naqu, Ali							
	Aug.-Dec. 2016	Lhasa	10,917	124	1.14 (0.94-1.34)	27	0.25 (0.15-0.34)	-	Ciren et al., 2018
	2018	Whole province	630,476	966	0.15 (0.14-0.16)	48	<0.01 (0.006-0.010)	22 (<0.01)	Unpublished*
Shaanxi	2012-2016	Whole province	10,138	8	0.08 (0.02-0.13)	0	0	0	Wu et al., 2018a
	2018	Whole province	14,199	2	0.01 (0.00-0.03)	0	0	0	Unpublished*
Gansu	2010	Zhangye (Huangcheng town of Sunan County)	3,989	38	0.95 (0.65-1.25)	0	0	0	Niu and An, 2012
	-	Zhangye (Minle County) [c]	362	1	0.28 (-0.30-0.8)	1	0.28 (-0.30-0.80)	-	Han et al., 2015b
	Jun.-Dec. 2011	Baiyin City	17,699	52	0.29 (0.21-0.37)	0	0	0	He and Qiang, 2014
	Sep. 2011-Jun. 2012	10 Tibetan autonomous prefectures (counties) of Gannan, Wuwei and Zhangye	37,815	223	0.59 (0.51-0.67)	1	<0.01 (0.00-0.01)	0	Wang et al., 2017a
	2010-2013	Gannan	220,501	374	0.17 (0.15-0.19)	1	<0.01 (0.000-0.001)	-	Ma and Shang, 2015
	2009-2015	Dingxi (Zhang County)	118,476	75	0.06 (0.05-0.08)	40	0.03 (0.02-0.04)	-	Ma et al., 2016
	2012-2016	Whole province	198,131	483	0.24 (0.22-0.27)	10	<0.01 (0.00-0.01)	0	Wu et al., 2018a
	May-Nov. 2016	Whole province [a]	1,123	11	0.98 (0.40-1.56)	-	-	-	Yuan et al., 2017
	Sep.-Nov. 2017	Gannan (Hezuo city)	4,000	7	0.18 (0.05-0.31)	-	-	-	Yang and Zhang, 2018
	2018	Gannan	59,127	51	0.09 (0.06-0.11)	0	0	0	Shang, 2020
	2018	Whole province	384,216	319	0.08 (0.07-0.09)	1	<0.01 (0.000-0.001)	0	Unpublished*
Ningxia Hui Autonomous Region	2012-2016	Whole province	62,348	112	0.18 (0.15-0.21)	13	0.02 (0.01-0.03)	0	Wu et al., 2018a
	2018	Whole province	112,957	113	0.10 (0.08-0.12)	7	0.01 (0.002-0.011)	1 (<0.01)	Unpublished*
Qinghai	2011	Guoluo (Maqin, Gander, Dari, Jiuzhi, and Banma) [b]	11,260	89	0.79 (0.63-0.95)	146	1.30 (1.09-1.51)	1 (<0.01)	Cai et al., 2017
	2011-2012	Yushu [b]	7,454	27	0.36 (0.23-0.50)	31	0.42 (0.27-0.56)	-	Han et al., 2018
		Guoluo [b]	12,175	92	0.76 (0.60-0.91)	191	1.57 (1.35-1.79)	-	
	2012	Hainan Tibetan Autonomous Prefecture	15,788	35	0.22 (0.15-0.30)	1	0.01 (0.00-0.02)	-	Cai et al., 2016
	Apr.-Oct. 2012	Haibei Tibetan Autonomous Prefecture	13,241	33	0.25 (0.16-0.33)	0	0	0	Wang et al., 2017c
	2011-2013	Guoluo (Dari)	7,354	198	2.69 (2.32-3.06)	662	9.00 (8.35-9.66)	13 (0.18)	Ma, 2014a
	Jul. 2013-Aug. 2014	Yushu (Chengduo and Yushu Counties), Guoluo (Dari and Banma Counties)	2,856	115	4.03 (3.31-4.75)	20	0.70 (0.39-1.01)	1 (0.04)	Han et al., 2019b
	Jul.-Aug. 2014	Guoluo (Banma County)	1,801	47	2.61 (1.87-3.35)	170	9.44 (8.09-10.79)	-	Ren et al., 2016
	2012-2016	Whole province	109,122	746	0.68 (0.64-0.73)	573	0.53 (0.48-0.57)	14 (0.01)	Wu et al., 2018a
	May-Nov. 2016	Whole province [a]	1,072	19	1.77 (0.98-2.56)	-	-	-	Yuan et al., 2017
	Jul.-Dec. 2018	Guoluo (Jiuzhi County)	23,505	126	0.54 (0.44-0.63)	219	0.93 (0.81-1.06)	-	Gao et al., 2019
	2018	Whole province	666,211	346	0.05 (0.046-0.057)	124	0.02 (0.015-0.022)	5 (<0.01)	Unpublished*
	2011-2012	Kizilsu Kirgiz Autonomous Prefecture	12,000	60	0.50 (0.37-0.63)	0	0	0	Chen et al., 2016b

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Table 1 (*continued*)

Administrative region	Period	Scope of investigation	People examined (no.)	CE cases (no.)	Estimated CE prevalence % (95% *CI*)	AE cases (no.)	Estimated AE prevalence % (95% *CI*)	Mixed infection no. (% prevalence)	References
Xinjiang Uygur Autonomous Region									
	2012	Xinjiang Production and Construction Corps	44,617	31	0.07 (0.05-0.09)	0	0	1 (<0.01)	Wang, 2016
	2010-2014	Bortala prefecture (Wenquan County)	43,708	120	0.27 (0.23-0.32)	0	0	0	Polat et al., 2016
	2012-2016	Whole autonomous region	302,121	356	0.12 (0.11-0.13)	24	0.01 (0.005-0.011)	20 (<0.01)	Wu et al., 2018a
	May-Nov. 2016	Whole autonomous region [a]	1,365	14	1.03 (0.49-1.56)	-	-	-	Yuan et al., 2017
	2015-2017	Tacheng	277,615	683	0.25 (0.23-0.26)	0	0	0	Adalaiti et al., 2018
	2018	Whole autonomous region	708,026	1,147	0.16 (0.15-0.17)	15	<0.01 (0.001-0.003)	4 (<0.01)	Unpublished*
	2018	Xinjiang Production and Construction Corps	41,150	101	0.25 (0.20-0.29)	5	0.01 (0.002-0.023)	0	Unpublished*

[a] Herding families
[b] Students participants ≤18 years old
[c] Additional previously confirmed cases of AE (not new cases in this study)
[*] National annual report on echinococcoses control in 2018
[−] No data given.

livestock in the endemic areas needs to be strengthened and the circulation of infected animals restricted to prevent the spread of echinococcosis.

1.2. Alveolar echinococcosis (AE)

Human AE cases are known in China since the 1950s (Wang, 1978), but the first patient was not described until 1965 when Yao (1965) formally reported a patient admitted to the First Teaching Hospital at Xinjiang Medical College in Urumqi City with hepatic AE localized to the liver. Zhu et al. (1983) first detected *E. multilocularis* in a stray dog during an epidemiological investigation in Datangba Village, Ganzi County, Sichuan Province. Initially, AE was considered to be rare and sporadic in China, however by the 1970s, convincing reports of human AE cases in Gansu, Xinjiang, Qinghai, Ningxia and Sichuan had appeared (Chen et al., 1979; Jiang, 1981), and a large number of AE cases were found in Zhang County, Gansu Province, Shiqu County, Sichuan Province from the early 1980s (Craig et al., 1992; Qiu et al., 1988). Not much later, this form of echinococcosis was reported in Xiji County, Ningxia, and also in other places (Craig et al., 1992; Wang et al., 1991) indicating that AE in fact has been, and still is, highly prevalent in China.

As can be seen from Table 1, human AE cases are mainly distributed in Sichuan, Tibet, Gansu, Ningxia, Qinghai and Xinjiang. In addition, the first national survey on the distribution of human parasites, carried out from 1988 to 1992, found four human AE cases in three counties of Heilongjiang Province (Yu 1994) and Fu (2005) reported the first case of human AE in Qinling District, Shaanxi Province in 2002. While *E. multilocularis* was detected in small rodents and the Corsac fox (*Vulpes corsac*) in Inner Mongolia, no human AE cases have been reported there so far. Currently, Yili Kazakh Autonomous Prefecture of Xinjiang; the counties Xiji, Haiyuan and Guyuan in Ningxia; Zhang and Min Counties in Gansu; Ganze and Aba in the Tibetan Autonomous Prefectures of Sichuan; and Yushu, Guoluo and Huangnan in the Tibetan Autonomous Prefectures of Qinghai, all include highly endemic areas for human AE (Han et al., 2015b). In 2012, the prevalence of AE in Shiqu and Seda counties in Sichuan were 4.47% and 2.19%, respectively, as reported by the Sichuan Center for Disease Control and Prevention (2014) (Table 1). In an ultrasound screening study conducted in Dari County, Qinghai Province, 662 of 7,354 individuals examined were found to have been infected, which corresponds to an overall prevalence of 9.00% in 2011-2013 (Ma, 2014a) (Table 1). Furthermore, another survey detected as many as 170 AE cases among 1,801 participants (corresponding to 9.44% prevalence) in Banma County, Qinghai Province in July-August 2014 (Ren et al., 2016) (Table 1). Besides, a relatively recent ultrasound investigation carried out by Craig et al. (2000) indicated a 4.05% mean prevalence of AE in Zhang and Min counties, which reached as high as 15.80% in some villages. These data underline how severe the disease in China is.

Generally, human CE and AE are co-endemic in a few areas in the world, e.g., eastern Asia minor, Siberia apart from central and eastern Asia (Craig, 2003). In China, the two types of echinococcoses coexist in Sichuan, Qinghai, Gansu, Ningxia, Tibet and Xinjiang, where a few rare cases of mixed CE and AE infection have been found (Table 1). Eleven pastoral counties in the two neighbouring provinces Sichuan and Qinghai on the eastern edge of the Tibetan Plateau stand out with respect to high levels of co-endemicity, in fact they show the highest prevalence in the world reported so far (Li et al., 2010). Furthermore, some studies have proved triple coexistence by *E. granulosus, E. multilocularis*, and *E. shiquicus* in Shiqu County, Sichuan Province, a fact that emphasizes the gravity of the problem in this area (Li et al., 2010; Xiao et al., 2005). Given the common problem of CE and AE in western China, prevention and control activities need to be significantly strengthened in these areas.

2. Factors affecting the transmission of *Echinococcus* parasites

2.1. Biological factors

2.1.1. *E. granulosus s.l.* and animal hosts

Over the past 60 years, studies have revealed significant phenotypic variability between *Echinococcus* spp. isolates; *E. granulosus s.l.* showed especially extensive genetic diversity. The different *E. granulosus s.l.* genotypes found in different geographical and ecological environments and hosts (McManus, 2006; Thompson and McManus, 2002) exhibited differences in antigenicity, infectivity, pathogenicity, host specificity, transmission dynamic, epidemiology and drug sensitivity (Romig et al., 2015; Thompson, 2008; Thompson and McManus, 2001, 2002). Analysis of mitochondrial DNA has shown that *E. granulosus s.l.* include 5 species (Kinkar et al., 2017; Maksimov et al., 2020; Ohiolei et al., 2019; Wassermann et al., 2016), i.e. *E. granulosus sensu stricto (s.s.)* consists of

G1 and G3 genotypes, with G2 considered a microvariant of G3, with sheep usually acting as intermediate host. *E. equinus*, formerly known as G4 genotype, is associated with horse; *E. ortleppi*, formerly known as G5 genotype, is associated with cattle; *E. canadensis* is composed of G6, G7, G8 and G10, with G9 probably being a variant of the G7, with camels and goats as intermediate hosts for the G6 genotype, pigs for the G7 genotype and cervids for the G8 and G10 genotypes. *E. felidis* was formerly known as the "lion strain", because it was initially identified from a lion in the sub-Saharan part of Africa. In addition, the genotype of the isolate found by Wassermann et al. (2016) in a patient in south-western Ethiopia is a new genotype, named Gomo, provisionally retained under *E. granulosus s.s.* for the time being. To date human CE cases reported in China have been associated with the G1, G3, G5, G6, G7, G10, G1-G3 and G6-G10 genotypes, and studies on domestic animals have shown the G1, G6 and G1-G3 genotypes in sheep, yaks and dogs, while the G6-G10 genotypes have been detected in sheep and goats (Table 2). CE in both humans and domestic animals, such as sheep, goats, cattle, yaks and camels, are mainly caused by the G1 genotype (Table 2). Moreover, through sequence analysis of the CO1 gene of 17 *E. granulosus s.l.* isolates in Xinjiang, Zhang et al. (2005) found mixed infections with the G1 and G6 genotypes in one dog, while Yang et al. (2009a) were the first to report that the ground squirrel is naturally infected with *E. granulosus s.l.* of the G1 genotype.

Importantly, while the prevalence of *E. granulosus s.l.* varies between the many different hosts mentioned above, sheep (the principal intermediate host in China and elsewhere) has the highest prevalence and the number of slaughtered sheep is higher than that of any other livestock (Yang et al., 2015c). In the Chinese regions with high CE prevalence, the *E. granulosus s.l.* prevalence was reported to be between 0.00% and 36.93% for sheep, while that of yaks and goats varied between 20.83% and 23.68%, respectively; *E. granulosus s.l.* was detected in horses and camels in Xinjiang, with a prevalence of 4.26% and 6.77%, respectively (Table 3). Besides, dogs play a crucial role in the transmission of *E. granulosus s.l.* in China, with prevalence varying between 0.45% and 52.78% (Table 4).

In addition to the genotype and host species, age and sex of the intermediate host also affect the transmission cycle of *E. granulosus s.l.*. Based on conditional logistic regression Li et al. (2017) found age influencing the prevalence of *E. granulosus s.l.* in yaks, with animals aged 2-4 years running a five times higher risk than that of yaks aged 0-1 years. From 2012 to 2016, Wu et al. (2018a) investigated the infection in sheep in 342 endemic counties in 9 provinces and autonomous regions of China showing that the CE prevalence increased significantly with the age of the sheep. Chang et al. (2011) and Li et al. (2019) found that increased age of cattle and sheep was associated with an increased risk of *E. granulosus s.l.* infection. At present, there are different reports about the influence of the sex of the intermediate host on the prevalence of *E. granulosus s.l.* (Erbeto et al., 2010; Ibrahim, 2010; Ming et al., 1992). A survey conducted in Xinjiang showed that female sheep had a higher CE prevalence than male ones, and that the difference was significant, with the prevalence increasing with age for both female and male sheep (Ming et al., 1992).

CE has also been detected in wild species in China, involving blue sheep (*Pseudois nayaur*), Tibetan gazelles (*Procapra picticaudata*) as well as the Tibetan wild ass (*Equus kiang*) and the black-lipped pika (*O. curzoniae*) (Jiang, 1996; Wang et al., 2014b; Zhang and Wang, 2007). A survey showed that the *E. granulosus s.l.* prevalence of blue sheep and Tibetan gazelles on the Qingnan Plateau of Qinghai were 6.42% and 6.57%, respectively (Zhang and Wang, 2007). Interestingly, foxes and wolves, infected with *E. granulosus s.l.* have also been reported as definitive hosts for these parasites (Wang et al., 2014b). However, because of the tough conditions in the field and the practical difficulty with this approach, very few studies on CE in wildlife have been carried out in China.

2.1.2. *E. multilocularis* in wild hosts

Compared to the obvious genetic variation of *E. granulosus s.l.*, the genes of *E. multilocularis* are more conserved and the genetic variation therefore limited. Asian, European, North American and Mongolian genotypes have been described based on the analysis of genetic diversity of *E. multilocularis* by using nuclear and mitochondrial genes (Nakao et al., 2009). There have been studies using the highly polymorphic EmsB microsatellite marker to assess the genetic diversity of *E. multilocularis* isolates from different origins. The genetic diversity analyzed this marker is greater than that done by traditional mitochondrial gene analysis (Knapp et al., 2020). However, *E. multilocularis* typing based on the marker is still rare in China. At present, Asian, European, North American and Mongolian genotypes all exist in China, with the Asian genotype being predominant (Table 5). It is worth mentioning that Tang et al. (2001a, b), when investigating the pathgen of *E. multilocularis* in the Hulunbeir Pasture, Inner Mongolia during 1985-1999, found two independent species of *E. multilocularis* in *Lasiopodomys brandtii* and *V. corsac*, i.e. *E. multilocularis* (Leuckart, 1863) and *E. sibiricesis* (later considered to be the Mongolian genotype and found to be conspecific with the former). At the same time, *E. multilocularis, Alveolaris hulunbeierensis*, a newly discovered species that subsequently was confirmed to be *E. multilocularis*, was also found in this area. On the other hand, no human AE case caused by these Mongolian genotypes has been found in Inner Mongolia so far. However, when Nakao et al. (2009) re-analyzed two isolates of *E. multilocularis* obtained by Tang's team from *V. corsac* in Inner Mongolia, they classified these isolates as mitochondrial haplotype O1. As the sample retained most of the variant mtDNA the variation of the haplotype O1 was deemed intraspecific, which is of great significance for the study of the evolutionary history of *E. multilocularis*.

From a global perspective, the intermediate hosts of *E. multilocularis* include 9 families, 26 genera and 46 species of small mammals. In China, 14 species of rodents and lagomorphs belonging to 6 families and 10 genera have been reported as natural hosts (Lin et al., 2012). Dogs and foxes are the main definitive hosts in China but also wolves can play this role. The Tibetan fox (*V. ferrilata*), the red fox (*V. Vulpes*) and the corsac fox are important in this group. A recent study has shown that the prevalence in red foxes was as high as 50.00% in Zhaosu Basin, Xinjiang (Ma, 2014b). The prevalence in dogs in the endemic areas varies between 1.29% and 14.13% (Table 6). *E. multilocularis* infection in wild animals and the intermediate hosts of this parasite found in China are shown in Table 6 and Table 7.

From Table 6 and Table 7, we find that there are a large number of small mammal species on the Qinghai-Tibet plateau, which is a highly-endemic area in China, and almost all species can be infected with *E. multilocularis*. Further analysis reveals that studies have mainly focused on *O. curzoniae* and *L. fuscus*, while information on *E. multilocularis* infection status in other small mammals is limited. *E. multilocularis* prevalence in these intermediate hosts vary from high to low, so it is difficult to determine which hosts are important for parasite transmission just by comparing the prevalence of these small mammals. Thus, the dynamics of small mammal populations and their importance for transmission needs to be further investigated. Giraudoux et al. (2003) have pointed out that the transmission intensity of *E. multilocularis* depends on the age structure and the density of the host populations after having compared the epidemiology and ecology of AE in southern Gansu, China with Doubs, a department, in eastern France. Applying regression analysis, Wang et al. (2018b) found that individuals with a lager relative head to body length, i.e. older individuals of the small mammals, were more likely to be infected, which is consistent with the results reported by Giraudoux et al. (2003). Moreover, the model established by Wang et al. (2006b) for infection of *E. multilocularis* in dogs and the density of small mammals also supports the likelihood that a higher density of small mammals is linked to a higher prevalence of *E. multilocularis* in dogs. This indicates that the larger number of small mammals, the greater the chance that dogs will prey on them. In

Table 2
Distribution of *Echinococcus granulosus sensu lato* genotypes in humans and animals in China

Administrative region	Period	Gene(s) analyzed or methodology	Genotype	No. of samples	Human genotype (samples no.)	Host genotype (no. of samples)							References
						sheep	yak	goat	cattle	camel	squirrel	dog	
Sichuan	2000-2005	*atp6*	G1	13	4	4	5						Yang et al., 2009b
	Jun. 2010-Nov.2011	*nad1, atp6*	G1, G3	84	G1(20), G3 (2)		G1 (8)						Yan et al., 2013
	2011-2013	*cox2*	G1	72	23		1						Hu et al., 2015
	2014-2016	*cox1, ND2*	G1-G3, G6/7	191	G1-G3 (115), G6/7(1)		G1-G3 (2)						Shang et al., 2019*; Wang et al., 2014a*
Tibet	Jun. 2010-Nov.2011	*nad1, atp6*	G1	84		11	1						Yan et al., 2013
	2011-2013	*cox2*	G1, G6	72		G1 (10), G6(2)	G1 (1)						Hu et al., 2015
	Dec. 2015-Nov. 2016	*cox1, nad1*	G1, G3, G6/7	23	G1(12), G3 (1), G6/7 (1)								Cao et al., 2018
	Oct.-Dec. 2017	*nad2, nad5*	G1, G3, G6	85		G1-sheep and yak: (77) G3-sheep and yak: (6) G6-sheep & yak: (1) [a]							Ohiolei et al., 2019
Gansu	Oct. 2016	*cox1, nad1*	G1-G3, G10	33		G1-G3 (32), G10 (1)							Wu et al., 2018c
	2005 [b]	*atp6*	G1	70	1								Yang et al., 2005
	2004 [b]	CO1, ND1, ITS2	G1	24		12							Yang et al., 2004
Ningxia	Apr. 2001	*atp6*	G1-G3	1	1								Yang et al., 2006
	2005 [b]	*atp6*	G1	70	12	14		1					Yang et al., 2005
	2009 [b]	*cox1*	G1	1							1		Yang et al., 2009a
Qinghai	Aug.-Sep. 2007	PCR-RFLP	G1	24		5	14					1	Han et al., 2009
	Jun. 2010-Nov. 2011	*nad1, atp6*	G1	84		38	4						Yan et al., 2013
	2011-2013	*cox2*	G1	72		35							Hu et al., 2015
	Dec. 2015-Nov. 2016	*cox1, nad1*	G1	23	1								Cao et al., 2018
	2010-2017	*cox1*	G1	244	93	38	91						Han et al., 2019a
	2004 [b], 2005 [b]	*atp6,* CO1, ND1, ITS2	G1	94	1	19	3		12				Yang et al., 2004*;Yang et al., 2005*
	2013 [b], 2015 [b]	*cox1, nad1, 16S rRNA*	G1-G3, G6-G10	617	G6-G10(1)	G1-G3 (35) G6-G10 (5)	G1-G3 (22)	G1-G3 (2) G6-G10 (2)				G1-G3(4)	Boufana et al., 2015 *; Liu et al., 2013*; Ma et al., 2015*; Wang et al., 2015*

(*continued on next page*)

Table 2 (*continued*)

Administrative region	Period	Gene(s) analyzed or methodology	Genotype	No. of samples	Human genotype (samples no.)	Host genotype (no. of samples)							References
						sheep	yak	goat	cattle	camel	squirrel	dog	
Xinjiang	Feb.-Jul. 2005, Oct. 2004-May 2005	*cox1*	G1, G6	92	G1(45), G6 (2)							G1 (42), G6(3)	Bart et al., 2006
	Oct. 2004-Apr. 2005	CO1	G1, G6	17								G1 (17), G1 and G6(1) [c]	YL et al., 2005
	Jun. 2016	*cox1*	G1	1	1								Xue et al., 2018b
	2016-2017	12S rRNA, CO1	G1	55		45			10				Yan et al., 2018
	2016, 2018	*cox1*, NADH1	G1	18		10			8				Mayila et al., 2019
	1998 [b], 1999 [b]	*cox1, nad1*	G1, G6	68	G1(3)	G1 (16), G6(2)			G1(5)	G1(1), G6(9)			Zhang et al., 1998*; Zhang et al., 1999*
Heilongjiang	May-Dec. 2013	*cox1, cytb, nad1*	G1, G7	10	G1(6), G7 (4)								Zhang et al., 2014
	Feb. 2014	*cox1, cytb, nad1*	G10	1	1								Yang et al., 2015a
Liaoning	Jun. 2015	*cox1*	G1	1	1								Wang et al., 2017b; Xue et al., 2018b
Inner Mongolia	Dec. 2015-Nov. 2016	*cox1, nad1*	G1	23	7								Cao et al., 2018
Guangxi	2017	*cox1, nad1*	G5	1	1								Shi et al., 2019

[a] 83 hydatid cysts in sheep and yak identified as *E. granulosus s.s.* comprising genotype G1 (n =77), genotype G3 (n=6) and 2 identified as *E.canadensis* (genotype G6)
[b] Date of the publication
[c] Mixed infection of G6 and G1 were found in one dog
[*] integration of relevant data in the listed references.

addition, as infected small mammals are more likely to be caught by the dogs, an increased risk of *E. multilocularis* infection in dogs should be expected. Continuing their line of study, Giraudoux et al. (2013a) identified and mapped four spatially distinct types of transmission ecosystems in China by combining climate, land cover and intermediate host species distribution data, each characterized by a different flagship species, i.e., *Ellobius tancrei* (in northern Xinjiang), *O. curzoniae* (on the eastern Tibetan plateau), *L. brandtii* (in Inner Mongolia) and *Eospalax fontanierii* (in southern Gansu and southern Ningxia), respectively. However, although these small mammal species are common in the endemic ecosystems, it does not mean that they play the main role for transmission. Therefore, rather than exclusively look at the intermediate host richness, both landscape characteristics and climate conditions need to be considered when attempting to predict the AE infection risk for humans (Craig et al., 2019).

Studies on the genetic variability of *E. granulosus s.l.* is of great significance for the development of a more practical CE control programme, as well as efficient vaccines and diagnostic reagents. However, classification of genotypes G1-G3 and G6-G10 is still under dispute (Kinkar et al., 2017; Laurimäe et al., 2018). Due to lack of comprehensive genotype investigations and an analysis of the pathogens in different foci in China, it is still not clear how many, and which of the *E. granulosus s.l.* genotypes, are infectious to humans. On the other hand, since the G5 genotype is the dominant strain in Nepal (Ito et al., 2010), it is likely that this genotype also exists in China. The first report of a case of human infection with *E. ortleppi* by Shi et al. (2019) in the Guangxi Zhuang Autonomous Region, a non-endemic region in China, is a strong indication that the G5 genotype exists in China. However, neither is the source of the *E. ortleppi* known, nor is the epidemiological situation of G5 in other parts of China fully evaluated. Moreover, the prevalence of *E. multilocularis* in intermediate and definitive hosts in Inner Mongolia is equal to, or even higher, than that in other regions epidemic for AE (Table 6). There are human AE cases in other endemic areas and such patients have been reported in Mongolia and Heilongjiang, which both border Inner Mongolia (Ito et al., 2010; Yu et al., 1994; Zhang et al., 2018). On the other hand, no one in Inner Mongolia has so far been reported to be infected with *E. multilocularis*. Therefore, this phenomenon deserves consideration. For example, with respect to Heilongjiang, where human AE and CE cases coexist, only a few studies on livestock have been published and no studies at all on wild animals.

2.2. *Environmental factors*

In China, *E. granulosus s.l.* is mainly transmitted through domestic cycles and *E. multilocularis* through sylvatic ones. Both species involve multi-host systems affected by environmental factors, which influence host species abundance, habitats, density as well as predator-prey relationships and egg survival (Cadavid Restrepo et al., 2018a; Giraudoux

Table 3
Echinococcus granulosus sensu lato infections in livestock in China

Administrative region	Period	Prevalence (%)							References
		Sheep	Goat	Cattle	Yak	Pig	Horse	Camel	
Inner Mongolia	2012-2016	0.70 (146/20745)		0.00 (0/314)					Wu et al., 2018a
Sichuan	2012-2016	0.09 (1/1074)		4.70 (774/16476)					Wu et al., 2018a
	2014	5.34 (351/6573)							Yang et al., 2016
	2014-2016				3.43 (11/321)				Li et al., 2017
Yunnan	2012-2016	0.00 (0/957)		0.00 (0/730)		0.03 (1/3151)			Wu et al., 2018a
Tibet									
	2012-2016	18.24 (191/1047)		9.15 (91/995)		0.99 (1/101)			Wu et al., 2018a
Nyingchi prefecture	2014-2015					7.27 (33/454)			Li et al., 2017
	2014-2016				8.63 (22/255)				Li et al., 2017
Shannan City	Aug.-Oct. 2016	18.23 (35/192)		0.00 (0/115)					Baima et al., 2018b
Nagqu Prefecture	Aug.-Oct. 2016	13.33 (16/120)		2.03 (5/246)					Danzhen et al., 2018
Shigatse City	Aug.-Oct. 2016	12.01 (58/483)		9.57 (9/94)					Bianba et al., 2018
Shaanxi	2012-2016	1.82 (36/1973)							Wu et al., 2018a
Gansu									
Sunan County	2010		23.68 (9/38)		20.83 (20/96)				Niu and An, 2012
Gannan Prefecture	2010-2013	1.84 (324/17562)		2.49 (172/6910)					Ma and Shang, 2015
Tianzhu, Maqu and Huan counties	2011-2013	6.09 (206/3384)		5.91 (108/1828)					Zhan et al., 2015
	2012-2016	1.94 (787/40639)		0.96 (105/10986)					Wu et al., 2018a
	2014-2016				5.50 (33/600)				Li et al., 2017
Qinghai	2012-2016	8.36 (1371/16394)		12.65 (635/5019)					Wu et al., 2018a
	2014-2016				11.79 (23/195)				Li et al., 2017
Ningxia	2012-2016	1.34 (138/10317)		0.3 (9/3046)					Wu et al., 2018a
	2017	1.40 (87/6226)							Duan et al., 2019
Xinjiang									
Kizilsu Kirgiz Prefecture	2011-2012	8.62 (283/3283)	0.00 (0/4)	1.04 (3/288)	1.92 (3/156)		3.08 (2/65)		Chen et al., 2016b
Urumqi, Yining, Tacheng, and Altay areas	2011-2012	9.75 (1223/12539) [a]		8.39 (118/1407)			4.26 (15/352)	6.77 (13/192)	Meng et al., 2014
Xinjiang PCC [b]	2012	4.02 (429/10672)		0.44 (2/450)					Han et al., 2014
Northern Xinjiang	2012-2013	6.47 (1550/23943)	3.18 (30/943)	2.89 (36/1247)	0.00 (0/36)		0.00 (0/1)		Maimai et al., 2017
Emin County	2010-2013	1.82 (236/12936)							Yang et al., 2015c
Quaker Wusu area of Bayinbuluke	Jul. 2014	36.93 (137/371)							Dong et al., 2015
	2012-2016	0.50 (429/85800)		4.14 (122/2944)					Wu et al., 2018a
Yili	2018	17.03 (689/4046)		13.03 (291/2234)					Mayila et al., 2019

[a] Prevalence of *E. granulosus s.l.* in sheep and goats
[b] PCC: Production and construction Corps.

Table 4
Echinococcus granulosus sensu lato dog infections in China

Administrative region	Period	Prevalence (%)	References
Sichuan			
Maerkang and Songpan Counties	Mar. 2010	4.79 (8/167)	Yu et al., 2012
Ganze and Aba prefecture	2014	22.46 (2065/9194)	Yang et al., 2016
Inner Mongolia			
Inner Mongolia Border Area	2008-2010	13.16 (278/2112)	Chang et al., 2011
Horchin district	2010	16.49 (16/97)	Hu et al., 2011*
Gansu			
Sunan County	Mar.-Oct. 2011	9.04 (167/1848)	Li and Niu, 2012
Tianzhu, Maqu and Huan Counties	2011-2013	4.38 (55/1255)	Zhan et al., 2015
Tianzhu County	2011-2016	4.70 (706/15020)	Zhang and Cai, 2018
Qinghai			
Guoluo Prefecture	2010-2011	18.89 (29/180)	Li et al., 2014
Gonghe County	Dec.2015	52.78 (19/36)	Tao, 2016
Menyuan County	Jan.-Dec. 2016	42.86 (3/7)	Zhang, 2017
Ningxia			
Xiji County	2012	16.53 (124/750)	Liu et al., 2018a
	Jun.-Dec. 2015	4.05 (187/4620)	Zhou et al., 2016
Xinjiang			
Kizilsu Kirgiz Autonomous Prefecture	2012	3.33 (74/2219)	Chen et al., 2016a
Xinjiang Production and Construction Corps	2011-2013	3.15 (991/31493)	Han et al., 2015a
Wensu County	2011-2013	9.73 (71/730)	Yang et al., 2015b
Hobukesar County	Apr. 2013	42.11 (16/38)	Van Kesteren et al., 2015
14 different areas of Xinjiang	2014	9.84 (378/3842)	Nusilaiti et al., 2016
Urumqi	2016	0.45 (18/3970)	Song et al., 2017a
Yili	2018	17.18 (101/588)	Mayila et al., 2019

* Study in pet dogs.

et al., 2013b; Ma, 2014b; Xu et al., 2011).

Few studies have focused on the influence of environmental factors on the prevalence of *E. granulosus s.l.*. However, Chinese studies have shown forest, shrub-lands and water coverage to be positively correlated with CE infection risk (Cadavid Restrepo et al., 2018a), with altitude, winter mean temperature (10-year lag), early winter and early summer also positively correlated (Cadavid Restrepo et al., 2018b; Hu et al., 2014; Yu et al., 2012), while precipitation during summer and winter and land surface temperature are negatively associated (Cadavid Restrepo et al., 2018a; Hu et al., 2014).

With respect to AE, on the other hand, many relevant studies have pointed out the various environmental factors playing a critical role for its prevalence as shown in Table 8. Landscape factors (vegetation type, vegetation coverage, grassland ratio and elevation) as well as climatic factors (temperature and humidity) are the main environmental factors affecting the prevalence of AE. In 1994 - 1997, the survey results of Zhang and Min counties in Gansu Province indicated that the positive correlation between AE and proximity of villages to forested areas as well as to grassland and scrublands, and this survey also noted that AE prevalence was negatively associated with cultivated land areas, although without correlation to the ratio of grassland to scrublands around the villages (Danson et al., 2004). Craig et al. (2000) carried out an additional investigation in Zhang County and found that the transmission of *E. multilocularis* mainly occurred in mixed landscapes of sub-alpine scrublands, grassland and farmland. The village AE prevalence was high especially in a high ratio of scrublands to grasslands, while AE prevalence was found to increase exponentially with the ratio of alpine meadows and decrease with the ratio of forest in the eastern Tibetan Plateau (Giraudoux et al., 2013b). Unlike the findings in Zhang County, the abundance of reforested lowland herbage was associated with higher prevalence of human AE risk (Cadavid Restrepo et al., 2018a, b; Pleydell et al., 2008). In 2008, a survey conducted by Wang (2009) in Chengduo County, Qinghai Province, indicated that the density of *O. curzoniae* was negatively correlated with grass height, while the soil type affected the distribution of intermediate hosts: the density of *O. curzoniae* and *L. fuscus* on alpine meadow soil was 1.94 times higher than that on the alpine grasslands soil. In China, Giraudoux et al. (2003) were first to reveal that the landscape can affect the transmission of *E. multilocularis* through interaction with small mammal communities and population dynamics. Based on the ratio of optimal to marginal path areas (ROMPA) hypothesis, they speculated that the deforestation in Zhang and Puma counties of Gansu in the 1970s led to a significant increase of scrublands and grassland, resulting in an increase of suitable habitats for *M. limnophilus* and *C. longicaudatus*. Therefore, it was expected that these two rodents populations would surge when the ROMPA reached a certain critical value. This hypothesis was supported by reports of these two rodents infestations in southern Gansu in the early 1980s, while human AE prevalence increased in the following 5-15 years. Subsequently, Giraudoux et al. (2019) conducted follow-up eco-epidemiological surveys in the same area in 2005/2006 and 2014 and described the evolution of local AE under landscape and social ecological changes in a retrospective study of Gansu covering 25 years. This work proved that landscape, climate and hosts jointly affect the

Table 5
Distribution of the *Echinococcus multilocularis* genotypes in humans and animals in China

Administrative Region	Gene analyzed	Genotype	Sample (no.)	Human sample (no.)	Host (no. identified)	References
Sichuan	*cob, nad2, cox1*	Asian	76	5	Dog (10), Voles (7)	Nakao et al., 2009
Gansu	*atp6*	Eurasian	70	0	Mouse (1)	Yang et al., 2005
Ningxia	*atp6*	Eurasian	70	1	-*	Yang et al., 2005
Qinghai	*cox1*	Asian	17	0	Qinghai voles (11)	Cai et al., 2018
Xinjiang	*nad2*	Asian	5	5	-*	Zheng et al., 2017
Inner Mongolia	-*	Mongolian haplotype	-*	0	*Microtus brandti, Vulpes corsac*	Tang et al., 2001a**, b**
Western China (Ningxia, Xinjiang, Qinghai, Sichuan and Gansu)	*cob* and *nad2*	Asian, Europe, North America	62	Asian (56)	Wild small mammals: *Microtus spp.*, Mongolian jirds, voles	Wu et al., 2017***

* Relevant information not available
** Number of samples not stated in the listed papers
*** *E. multilocularis* isolates collected from wild small mammals (n=6) and AE patients (n=56) from western China. (small mammal genotypes not clearly indicated in the paper).

Table 6
Echinococcus multilocularis infections in wild hosts in China

Intermediate host					Definitive host				
Host	Period	Prevalence (%)	Province/region	References	Host	Period	Prevalence (%)	Province/region	References
Lasiopodomys brandtii	1985	2.43 (64/2635)	Inner Mongolia (Hulunbeier)	Tang et al., 1988	Tibetan fox (*Vulpes ferrilata*)	1991	59.09 (13/22)	Sichuan (Shiqu County)	Qiu et al., 1995
	1988-1999	9.94 (67/679)	Inner Mongolia (Xinbaerhu West County)	Tang et al., 2004		1992-1999	19.04 (4/21)	Qinghai	Wang et al., 2000b
	1988-1999	5.28 (131/2483)	Inner Mongoia (Ewenke County)	Tang et al., 2004		1997-1998	44.44 (76/171)	Sichuan (Shiqu and Ganzi Counties)	He et al., 2000
Meriones unguiculatus	1985	16.67 (1/6)	Inner Mongolia (Hulunbeier)	Tang et al., 1988		Aug.-Sep. 2004	4.35 (1/23)	Qinghai (Banma County)	Han et al. 2006
Microtus ilaeus	1999	0.76 (7/916)	Xinjiang (Nileke County)	Xu et al., 2002		2006, 2007	15.40 (-/-)	Sichuan (Shiqu County)	Vaniscotte et al., 2011
	2000	5.88 (2/34)	Xinjiang (Yining County)	Xu et al., 2002		2012*	35.00 (42/120)	Sichuan (Shiqu County)	Jiang et al., 2012
Ochotona curzoniae	1991	9.36 (24/256)	Sichuan (Shiqu County)	Qiu et al., 1995	Red fox (*Vulpes Vulpes*)	1982-1983	27.27 (3/11)	Ningxia (Guyuan district)	Li et al., 1985
	1991	8.70 (4/46)	Tibet (Naqu County)	Qiu et al., 1995		1987-1988	30.56 (11/36)	Xinjiang (Tacheng area)	Wang et al., 1989
	1991	3.54 (4/113)	Tibet (Chengduo County)	Qiu et al., 1995		1991	57.14(12/21)	Sichuan (Shiqu County)	Qiu et al., 1995
	1992-1999	3.45 (11/319)	Qinghai	Wang et al., 2000b		1998-2001	40.00 (2/5)	Inner Mongolia (Hulunbeier)	Wang et al., 2002
	1995-2005	4.24 (34/801)	Qinghai (South Qinghai Plateau)	Wang et al., 2006a		2012*	33.33 (2/6)	Sichuan (Shiqu County)	Jiang et al., 2012
	1997-1998	5.58 (13/233)	Sichuan (Shiqu and Ganzi Counties)	He et al., 2000		Feb.2014	50.00 (3/6)	Xinjiang (Zhaosu Basin)	Ma, 2014b
	1997-1998	15.18 (34/224)	Qinghai (South Qinghai Plateau)	Zhao, 2002	Corsac fox (*Vulpes corsac*)	1985	33.33 (2/6)	Inner Mongolia (Hulunbeier)	Tang et al., 1988
	2014	1.48 (2/135)	Sichuan (Shiqu County)	Wang et al., 2018b		2001	12.58 (19/151)	Inner Mongolia (Hulunbeier)	Tang et al., 2006
	2018*	4.08 (2/29)	Qinghai (Jiuzhi County)	Li et al., 2018	Dog (*Canis familiaris*)	2003	3.33 (1/30)	Xinjiang (Hejing County)	Wen et al., 2006
Lepus Oiostolus	1991	6.67 (5/75)	Sichuan (Shiqu County)	Qiu et al., 1995		2005	8.33 (1/12)	Qinghai (Jiuzhi County)	Yu et al., 2008
	1959-1998	12.50 (1/8)	Qinghai (South Qinghai Plateau)	Wang et al., 2000a		2006	5.96 (35/587)	Sichuan (Ganze Prefecture)	Moss et al., 2013
	1997-1998	20.00 (1/5)	Qinghai (South Qinghai Plateau)	Zhao, 2002		2006	11.23 (31/276)	Sichuan (Shiqu county)	Moss et al., 2013
	1997-1998	7.14 (1/14)	Sichuan (Ganze Prefecture)	He et al., 2000		2006	1.29 (4/311)	Sichuan (Honglong)	Moss et al., 2013
Spermophilus dauricus	1985	1.37 (9/656)	Ningxia (Guyuan district)	Hong and Lin, 1987		1990-2010	10.86 (98/902)	Qinghai	Cai et al., 2012
	1982-1983	0.20 (3/1500)	Ningxia (Guyuan district)	Li et al., 1985		2012	14.13 (106/750)	Ningxia (Xiji County)	Liu et al., 2018a
	2004	1.15 (1/87)	Gansu (Gannan Prefecture)	Zhao et al., 2009	Wolf (*Canis lupus*)	1987-1988	50.00 (1/2)	Xinjiang (Tacheng area)	Wang et al., 1989
Eospalax fontanierii	1985	0.31 (1/320)	Ningxia (Guyuan district)	Hong and Lin, 1987					
	2004	2.27 (3/132)	Gansu (Gannan Prefecture)	Zhao et al., 2009					
Mus musculus	1997-1998	11.11 (1/9)	Qinghai (South Qinghai Plateau)	Zhao, 2002					
	2012-2013	0.77 (25/3234)	Northern Xinjiang	Maimaitijiang et al., 2017					
Microtus (Stenocranius) gregalis	2013	8.37 (21/251)	Xinjiang (Zhaosu Basin)	Ma, 2014b					
Rhombomys opimus	2013-2014	3.48 (8/230)	Xinjiang (Ala-shankou Port)	Xiao et al., 2015					
Meriones (Pallasiomys) libycus	2013-2014	2.22 (1/45)	Xinjiang (Ala-shankou Port)	Xiao et al., 2015					
Rattus norvegicus	2013-2014	1.85 (1/54)	Xinjiang (Ala-shankou Port)	Xiao et al., 2015					
Microtus limnophilus	2014	11.36 (5/44)	Sichuan (Shiqu County)	Wang et al., 2018b					

(*continued on next page*)

Table 6 (*continued*)

Intermediate host					Definitive host				
Host	Period	Prevalence (%)	Province/region	References	Host	Period	Prevalence (%)	Province/region	References
	Not given	14.71 (5/34)	Sichuan	Giraudoux et al., 2006					
Lasiopodomys fuscus	1995-2005	0.45 (1/224)	Qinghai (South Qinghai Plateau)	Wang et al., 2006a					
	1997-1998	20.00 (1/5)	Qinghai (South Qinghai Plateau)	Zhao, 2002					
	2014	11.11 (16/144)	Sichuan (Shiqu County)	Wang et al., 2018b					
	2015	22.00 (11/50)	Qinghai (Guoluo Prefecture)	Cai et al., 2018					
	2018*	29.41 (30/102)	Qinghai (Jiuzhi County)	Li et al., 2018					
Neodon irene	1997-1998	25.00 (3/12)	Sichuan (Shiqu and Ganzi Counties)	He et al., 2000					
Cricetulus migratorius	1992-1999	2.86 (1/35)	Qinghai (Caidamu Basin)	Wang et al., 2000b					
	1995-2005	1.80 (3/167)	Qinghai (South Qinghai Plateau)	Wang et al., 2006a					
Arvicola amphibius	May 2001	1.64 (1/61)	Xinjiang (Emin County)	Fu et al., 2001					
Cricetulus kamensis	Not given	5.26 (1/19)	Sichuan	Giraudoux et al., 2006					

* Exact period not given.

transmission intensity of *E. multilocularis*.

Climate and season change mainly affect the geographical distribution of intermediate and definitive hosts by influencing the survival of parasite eggs and the reproduction of the intermediate hosts. AE prevalence is said to be correlated to rainfall and temperature, information that has been confirmed by studies conducted in China's AE-endemic regions (Cadavid Restrepo et al., 2018a, b; Giraudoux et al., 2013b). A study carried out in eastern part of the Tibetan Plateau showed that the risk of human AE increased with rainfall and temperature up to a maximum of 564 mm and -5.62 °C, respectively (Giraudoux et al., 2013b). Based on Bayesian geostatistical models with environmental and demographic covariates, Cadavid Restrepo et al. (2018a, b) found that the odds of *E. multilocularis* seropositivity per 1mm increase of summer mean precipitation increased by 0.60%, while it decreased by 10.60% per 1 mm increase in winter mean precipitation. They also noted that there was an increase of 82.60% in the odds of seropositivity for *E. multilocularis* per 1.00% increase in water coverage (five-year lag), and the risk of human AE infection decreased by 65.70% and 97.40% per 1 °C increase in average winter temperature and annual mean temperature, respectively (Cadavid Restrepo et al., 2018a, b). Furthermore, Ma (2014b) reported that the *E. multilocularis* prevalence in *M. gregalis* in April 2013 (20.93%) was significantly higher than that in September 2013 (5.71%) in Zhaosu Basin, Xinjiang. Some studies have also reported that early spring and early winter are the main infectious seasons for dogs (Huang et al., 2018; Wang et al., 2016). This may be explained by the temperature in early spring and winter being suitable for the survival of the parasite eggs, while some intermediate hosts species would die due to extreme cold and food shortages. This increases the potential for predation by dogs and foxes, leading to a high infection in these definitive hosts.

The situation is further complicated by anthropogenic impact and factors such as livestock density, levels of overgrazing, expansion of townships and increased use of pasture fencing leading to change of the natural landscape. Studies carried out by Wang et al. (2004, 2007) in Shiqu County, Sichuan Province, revealed that the burrow density of small mammals in open pastures is higher than that in adjacent privately fenced pastures. Counter-intuitively, this is linked with a significantly higher risk of AE infection for people living in villages with fenced pastures due to the following explanation: in the 1980s, rearrangements of land rights led to increased fencing of privately owned property (Wang et al., 2004), which is mainly used to secure forage for weak, young or pregnant livestock during winter and early spring when forage is extremely limited. This has led to increased grazing pressure in the open pastures, which provide suitable habitats for small mammals and thus result in an overall higher transmission of *E. multilocularis* in the villages. Besides, extensive deforestation and modified agricultural practices, e.g., as a result of the great increase of population in Ningxia, exists in many other areas of China (Yang et al., 2012) and this has led to widespread biodiversity changes affecting the prevalence of AE in the endemic areas.

The current development of spatial analysis techniques, such as remote sensing (RS) and geographical information systems (GIS), has made it easier to study the correlation between echinococcoses and environmental factors. Since RS supplies continuously updated spatial landscape information and GIS provides the means to manage and analyse the data collected, supporting the determination of AE risk zones and prediction of transmission trends, this approach has been widely used (Danson et al., 2003, 2004; Giraudoux et al., 2013b; Graham et al., 2004; Pleydell et al., 2008). Moreover, studies in Switzerland, Chile and the United Kingdom have investigated the association between the *Echinococcus* spp. infection status and type of urbanization, showing that although the prevalence in foxes and dogs in rural areas is higher than that in urban areas, there is still a high infection pressure by foxes and dogs in the periphery of the cities (Acosta-Jamett et al., 2010; Harris and Rayner, 1986; Otero-Abad et al., 2017). At present, the investigations on *Echinococcus* spp. infection status in rural host animals are exhaustive, especially in the Tibetan Plateau (Craig et al., 2019); Regrettably, there is no research on the association between the *Echinococcus* spp. infection status and urbanization. This phenomenon should be brought to attention even if it is rare in China for wild animals that live in the suburbs to enter the cities.

2.3. Social factors

An analysis of research related to echinococcoses in China carried out over the past 10 years shows socioeconomic variables, such as demographics, occupation, life style and education can all influence the transmission of parasites of the genus *Echinococcus* (Table 9). These

Table 7
The intermediate host animals of *Echinococcus multilocularis* found in China

Host species	Administrative region	References
Lasiopodomys fuscus	Sichuan	Wang et al., 2018b;
	Qinghai	Cai et al., 2018; Li et al., 2018; Wang et al., 2006a; Zhao, 2002
Lasiopodomys brandtii	Inner Mongolia	Tang et al., 1988; Tang et al., 2004
Microtus ilaeus	Xinjiang	Xu et al., 2002
Microtus (Stenocranius) gregalis	Xinjiang	Ma, 2014b
Microtus limnophilus	Sichuan	Giraudoux et al., 2006; Wang et al., 2018b
Neodon irene	Sichuan	He et al. 2000
Micotus agreastis	Xinjiang	Maimaitijiang et al., 2017
Meriones unguiculatus	Inner Mongolia	Tang et al., 1988
Rhombomys opimus	Xinjiang	Xiao et al., 2015
Meriones (Pallasiomys) libycus	Xinjiang	Xiao et al., 2015
Meriones meridianus	Ningxia, Xinjiang	Israin et al., 1998
Eospalax fontanierii	Gansu	Zhao et al., 2009
	Ningxia	Hong and Lin, 1987
Mus musculus	Qinghai	Zhao, 2002
Rattus norvegicus	Xinjiang	Xiao et al., 2015
Arvicola amphibius	Xinjiang	Fu et al., 2001
Dipodidae	Xinjiang	Maimaitijiang et al., 2017
Ellobius (Ellobius) talpinus	Xinjiang	Maimaitijiang et al., 2017
Apodemus sylvaticcus	Xinjiang	Maimaitijiang et al., 2017
Lagurus lagurus	Xinjiang	Israin et al., 2000; Maimaitijiang et al., 2017
Eolagurus luteus	Xinjiang	Maimaitijiang et al., 2017
Cricetulus migratorius	Qinghai	Wang et al., 2000b; Wang et al., 2006a
	Xinjiang	Maimaitijiang et al., 2017
Cricetulus kamensis	Sichuan	Giraudoux et al., 2006
Cricetulus longicaudatus	Gansu	Giraudoux et al., 2003
Citellus dauricus	Ningxiia	Li et al., 2011
Citellus erythrogenys	Xinjiang	Jiang et al., 2000; Lin et al., 1993; Maimaitijiang et al., 2017
Spermophilus undulatus	Xinjiang	Maimaitijiang et al., 2017
Ochotona curzoniae	Sichuan	He et al., 2000; Qiu et al., 1995; Wang et al., 2018b
	Qinghai	Li et al., 2018; Wang et al., 2000b; Wang et al., 2006a; Zhao, 2002
	Tibet	Danzhen et al., 2018; Qiu et al., 1995
Spermophilus dauricus	Gansu	Zhao et al., 2009
	Ningxia	Hong and Lin, 1987; Li et al., 1985
Lepus oiostolus	Qinghai	Wang et al., 2000a; Zhao, 2002
	Sichuan	He et al., 2000; Qiu et al., 1995
Marmota (Marmota) bobak	Xinjiang	Maimaitijiang et al., 2017

studies show that age, gender, ethnicity and occupation can affect the epidemic of echinococcoses (including CE and AE). Although there are variations between the results of the studies due to different demographic and social structures in different endemic regions, the majority of them hold that people aged ≥60 and of female gender are more likely to be infected than others, something that applies also for herdsmen and lama (religious teachers in Tibetan Buddhism) as well as all those of Tibetan and Mongolian ethnicity (Baima et al., 2018a; Chen et al., 2018; Li et al., 2019a; Luo et al., 2014; Ma et al., 2020; Zhang et al., 2017). Regarding age, prevalence obviously increases with the time spent in an endemic environment as the disease is chronic with temporal accumulation of cysts as well as recurrent of infections (Zhang et al., 2017). For women this may be due to the fact that they in daily life not only participate in production activities, but also undertake a large number of domestic activities, such as feeding dogs and livestock,

Table 8
Environmental factors related to the transmission of *Echinococcus multilocularis* in China

Environmental factors	Study information	Statistical method	References
Landscapes			
Variation of scrub/ grassland ratios	Ultrasound examination of 2,482 people in Min and Zhang counties, Gansu Province.	Univariate analysis	Craig et al., 2000
Forest, grassland, shrub-lands vegetation and areas of cultivated land	Analysis of the relationship between AE prevalence in 31 villages and surrounding landscape in Gansu Province.	Stepwise linear regression	Danson et al., 2004
Alpine, subalpine meadow and forest	17,589 people screened by abdominal ultrasound in Sichuan and Qinghai provinces.	Generalized additive mixed models	Giraudoux et al., 2013b
Bare-land, areas half-bare and grassland	Correlation analysis between the density of rodents/ lagomorph burrows and different landscape types in Shiqu County, Sichuan Province.	Regression analysis	Xu et al., 2011
Mountain and lowland pastures	Screening 3,205 individuals by abdominal ultrasound in Xiji County, Ningxia Hui Autonomous Region.	Generalized additive mixed models	Pleydell et al., 2008
Bare-land/artificial surface coverage	Analysis of the relationship between environmental variables and 4,472 cases of AE and CE diagnosed in hospital in Ningxia Hui Autonomous Region.	Bayesian spatio-temporal conditional autoregressive model	Cadavid Restrepo et al., 2018b
Extent of shrub-lands and water bodies	Detection of 5,110 children aged 6-18 by ELISA in Xiji County, Ningxia Hui Autonomous Region.	Bayesian geostatistical models	Cadavid Restrepo et al., 2018a
Vegetation types	Spatial analysis of *Ochotona curzoniae* and *Lasiopodomys fuscus* in Chenduo County, Qinghai Province.	Negative binomial distribution regression model	Wang, 2009
Vegetation coverage	Spatial analysis of *Ochotona curzoniae* and *Lasiopodomys fuscus* in Chenduo County, Qinghai Province.	Negative binomial distribution regression model	Wang, 2009
Grass height	Spatial analysis of *Ochotona curzoniae* and *Lasiopodomys fuscus* in Chenduo County, Qinghai Province.	Negative binomial distribution regression model	Wang, 2009
	Arecoline purgation of 228 domestic dogs	Generalized linear models	Wang et al., 2010b

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Table 8 (*continued*)

Environmental factors	Study information	Statistical method	References
	in Shiqu, Sichuan Province.		
Pasture type (open/ fenced, winter/ summer)	Spatial analysis of *Ochotona curzoniae* and *Lasiopodomys fuscus* in Chenduo County, Qinghai Province.	Negative binomial distribution regression model	Wang, 2009
Pasture type (open/ fenced)	Ultrasound examination was carried out in 4,036 people and copro-PCR test of 252 dogs sampled for faeces in Shiqu County, Sichuan Province.	Multiple logistic regression	Wang et al., 2004, 2007
Pasture type (open/ fenced)	Coproantigen examination of 334 faecal samples from dogs in Shiqu County, Sichuan Province.	Multiple logistic regression	Wang et al., 2006b
Pasture type (winter/summer)	Correlation analysis between the density of rodents/ lagomorph burrows and different landscape types in Shiqu County, Sichuan Province.	Regression analysis	Xu et al., 2011
Type of soil	Spatial analysis of *Ochotona curzoniae* and *Lasiopodomys fuscus* in Chenduo County, Qinghai Province.	Negative binomial distribution regression model	Wang, 2009
Altitude	Screening of 17,589 people by abdominal ultrasound in Sichuan and Qinghai provinces.	Generalized additive mixed models	Giraudoux et al., 2013b
Rainfall	Screening of 17,589 people by abdominal ultrasound in Sichuan and Qinghai provinces.	Generalized additive mixed models	Giraudoux et al., 2013b
Rainfall (summer/ winter precipitation)	Investigation of 5,110 children aged 6-18 by ELISA in Xiji County, Ningxia Hui Autonomous Region.	Bayesian geostatistical models	Cadavid Restrepo et al., 2018a
Temperature	Screening of 17,589 people by abdominal ultrasound in Sichuan and Qinghai provinces.	Generalized additive mixed models	Giraudoux et al., 2013b
Temperature (winter/annual mean temperature)	Analysis of the relationship between environmental variables and 4,472 cases of AE and CE diagnosed in hospital, Ningxia Hui Autonomous Region.	Bayesian spatio-temporal conditional autoregressive model	Cadavid Restrepo et al., 2018b
Season	Post mortem examination and biopsy of 251 captured rats in Zhaosu Basin in Xinjiang.	Univariate analysis	Ma, 2014b

Table 9

References dealing with social risk factors identified for human echinococcoses in China (2010-2020)

Significant social risk factor	Echinococcoses in general	CE	AE
Age≥60 (a particularly strong risk factor for echinococcoses)	Baima et al., 2018a, b; Chen et al., 2018; Luo et al., 2014; Xiao et al., 2018	Chen et al., 2018; He et al., 2019b; Ren et al., 2016	Gongsang et al., 2017; Ren et al., 2016
Female gender	Baima et al., 2018a; Cai et al., 2017[a]; Gesang et al., 2020; Li et al., 2019a; Luo et al., 2014; Ma et al., 2020[b]; Ren et al., 2016; Zhang et al., 2017	Cai et al., 2017[a]; Ren et al., 2016; Song et al., 2017b	Cai et al., 2017[a]; Gongsang et al., 2017; Ren et al., 2016
Tibetan and Mongolian ethnicity	Luo et al., 2014; Zhang et al., 2017	Song et al., 2017b	
Herder or lama	Gesang et al., 2020; Li et al., 2019a; Luo et al., 2014; Ma et al., 2020[b]; Ren et al., 2016; Song et al., 2017b; Zhang et al., 2017	Chen et al., 2018; Ren et al., 2016; Song et al., 2017b	Gongsang et al., 2017; Ren et al., 2016
Poor education and knowledge	Li et al., 2019a; Ma et al., 2020[b]; Baima et al., 2018a; Gesang et al., 2020; He et al., 2019a		Gongsang et al., 2017
Production types (pastoral area)	Li et al., 2019a; Baima et al., 2018a; Gesang et al., 2020; Zhang et al., 2017; Zhao, 2015	Chen et al., 2018; Song et al., 2017b; Zhao, 2015	Gongsang et al., 2017; Zhao, 2015
Semi-nomadic lifestyle	Baima et al., 2018a; Gesang et al., 2020	He et al., 2019b	
High number of domestic dogs	He et al., 2019a	He et al., 2019b; Zeng et al., 2020[c]	
High number of sheep owned		He et al., 2019b; Zeng et al., 2020[c]	
High number of cattle owned		He et al., 2019b	
Home slaughter		Chu et al., 2010; Wang et al., 2001; Yuan et al., 2017[d]	
Dogs fed offal		Li et al., 2015; Wu et al., 2018b; Yuan et al., 2017[d]	
Dogs able to roam freely		Yuan et al., 2017[d]	
People feed the dogs themselves		Li et al., 2015	
Without access to piped water	Ma et al., 2020[b]	Wu et al., 2018b; Yuan et al., 2017[d]; Zeng et al., 2020[c]	
Drinking non-boiled water		Yuan et al., 2017[d]	
Eating raw vegetables		Yuan et al., 2017[d]	
No hand washing before meals	Ma et al., 2020[b]	Yuan et al., 2017[d] He et al., 2019b	

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Table 9 (*continued*)

Significant social risk factor	Echinococcoses in general	CE	AE
High density of dog faeces in the courtyard			
Presence of stray dogs or wild animals	Ma et al., 2020[b]	Wu et al., 2018b; Yuan et al., 2017[d]	

[a] Participants were schoolchildren 6-16 years old
[b] Participants were all Tibetans
[c] Survey conducted in non-Qinghai Tibetan Plateau Regions of China
[d] Herding families.

milking, etc. On the Tibetan Plateau they also often responsible for collecting, drying and burning yak dung that is used as fuel on the Tibetan rangelands, which increases close contact with dogs, livestock and in particular faeces (Craig et al., 2019; Li et al., 2019a). In October 2005, Yu et al. (2008) conducted an epidemiological survey of echinococcoses in Jiuzhi County, Guoluo Tibetan Autonomous Prefecture, Qinghai Province. The investigation showed that herdsmen (16.6%) and lama (15%) are occupations with high prevalence, which is consistent with the results of other studies (Li et al., 2019a; Ren et al., 2016; Wu et al., 2018a; Zhang et al., 2017). In addition, 9 of 12 stray dogs captured were found to be infected with *Echinococcus* spp.in their study, with the prevalence as high as 75% (Yu et al., 2008). This is clearly a high level of prevalence even if it may be biased to some degree because of the limited number of stray dogs examined. The lama constitute a particularly high-risk occupation because Tibetan Buddhist teaching does not accept killing of animals, which leads to the large number of infected stray dogs around the temples in Tibetan areas. The lama are at enhanced risk of infection because of their protection and feeding of the stray dogs. Herdsmen run the same risk due to their frequent contacts with both livestock and dogs (Wu et al., 2018a). Furthermore, Gesang et al. (2020) and Baima et al. (2018a) both reported a higher echinococcoses prevalence among nomadic and semi-nomadic people (settled in winter and nomadic in summer) compared with those with a fully settled lifestyle. The same difference was also found in Inner Mongolia (Zhang et al., 2018) and Sichuan (He et al., 2019b), a result that may be related to poor living conditions of nomads and semi-nomads, a higher contact with livestock and dogs, less dog deworming and heavier environmental contamination.

The economic backwardness, poor infrastructure, low education levels and poor hygiene habits make people particularly vulnerable to echinococcoses in the underdeveloped rural areas of western China (Gesang et al., 2020; Gongsang et al., 2017; He et al., 2019a). Most surveys find that the education level is closely associated with echinococcoses, which is not surprising given that illiteracy (Baima et al., 2018a; Gongsang et al., 2017; Ren et al., 2016) and lack of biological knowledge make it impossible for these people to understand these diseases. Naturally, this situation has a negative impact on prevention and control (Li et al., 2019a). Studies carried out by Yuan et al. (2017) and Ma et al. (2020) show that residents in endemic areas habitually drink water without boiling it first, eat raw vegetables and do not wash their hands before meals. Because of the lack of piped water, people rely mainly on natural sources (river, spring water, rain collection, etc.), which also increases the risk of transmission of these parasites. A case-control study carried out by He et al. (2019b) in Shiqu County, Sichuan Province between 2015 and 2017 revealed that the number of cattle, the number of sheep and the number of dogs in a family were all strongly associated with human CE, where the mean number of dogs per family had the greatest impact. Indeed, the prevalence of CE increased by 5.28 for every 1 dog kept (He et al., 2019a). Similar to these results, Zeng et al., 2020 showed that each dog or sheep added to the household in the non-Qinghai Tibetan Plateau increased the human CE prevalence by 2.06% and 4.31%, respectively. These results highlight the critical role of dogs and livestock in the transmission of *Echinococcus* parasites. The backward production and life style in western or north-western China, where residents mainly engaged in animal husbandry and keep various livestock for a long time together with many domestic dogs, the risk of echinococcoses in intermediate as well as definitive hosts is high (Li et al., 2019a). Home slaughter of livestock, where dogs are habitually fed the offal (Li et al., 2015; Wu et al., 2018b; Yuan et al., 2017), adds to the problem and has been shown to be associated with the transmission of *E. granulosus s.l.*in five provinces in China (Xinjiang, Tibet, Gansu, Sichuan and Qinghai) (Chu et al., 2010; Wang et al., 2001; Yuan et al., 2017). Additional note that the presence of stray dogs and wild animals near habitations is a significant additional risk factor (Ma et al., 2020; Wu et al., 2018b; Yuan et al., 2017).

A good first approach to improve the situation described above, would be to strengthen health education of key people, improve infrastructures and provision of sanitation facilities in regions endemic for echinococcoses. In addition, deworming domestic and stray dogs should be promoted, as well as assist harmless disposal of infected animals and viscera, so as to reduce the exposure risk and effectively prevent and control these diseases.

Conclusions

Human CE and AE are particularly pathogenic helminthic zoonoses and the prevalence of both are high in China, where the transmission of *Echinococcus* parasites involves wild animals and domestic animals, which participate and interact with each other. The vast north-western pastoral areas present a favourable environment for the growth of the parasite and the survival of its eggs, a situation that is further exacerbated by the local way of life, unique customs and religious beliefs, which are hard to change.

Transmission of parasites of the genus *Echinococcus* depend on three main factors:

- Biological factors: parasite genotypes, intermediate and definitive host species and characteristics, such as age, sex and host densities;
- Environmental factors: landscape type and climate in the endemic areas;
- Social factors: age, gender, occupation, ethnicity, education level, lifestyle, cultural customs, living condition and hygiene.

These three factors modulate the parasite-host-human interplay at different spatial and temporal scales by interacting and influencing each other to jointly determine the overall transmission intensity. Due to the current limitations of research and methodology, all influencing factors have not all been measured and investigated accurately. However, available biological, environmental and social factors have a high impact and are useful for prediction of the epidemic trends as well as identification of high-risk populations and endemic areas. Research based on data provided by these three attributes is essential for the formulation and implementation of effective prevention and control strategies.

Remaining problems and challenges in the research of epidemical factors of echinococcoses in China include:

- Research on the molecular epidemiology is needed to confirm genotypes and the genetic variation characteristic of *Echinococcus* spp. in China. *E. granulosus s.l.* genotypes G1, G3, G5, G6, G7, G10, G1-G3 and G6-G10 together with Asian, European, North American and Mongolian genotypes of *E. multilocularis* have all been reported in the country. It would also be useful to explore the epidemic status of G5 in regions outside the Guangxi Zhuang Autonomous Region, including the original source of *E. ortleppi*, as this would provide reference for the design and development of diagnostic reagents, vaccines and drugs;

- Preliminary investigation should be conducted in Inner Mongolia and Heilongjiang Province to learn more about the epidemic range and degree of AE there and to explore the reasons for the increase of CE sporadic cases in recent years in Heilongjiang Province. Research also needs to focus on the infection status for livestock echinococcosis and host species of AE in Heilongjiang Province and surrounding areas;
- In China, the diversity of small mammal shown to be capable as intermediate hosts is a remarkable feature of the transmission ecology of *E. multilocularis*. However, it is difficult to quantify their relative contribution to the overall transmission of *E. multilocularis* due to the extremely complex multi-population dynamics. So far, most studies are limited to a minor number of host species, e.g., *O. curzoniae, L. fuscus*, etc., so the best course would be to treat transmission as an ecosystem grouping together all known transmission factors, including biotic and abiotic characteristics. This approach can at least provide information on transmission patterns that would help decision-makers to implement effective surveillance and prevention for AE;
- Dogs, especially stray dogs, play an important role in sustaining transmission in the regions endemic for *Echinococcus* spp. in China. The implementation of the slogan "deworming month by month and administering drugs dog by dog" has achieved remarkable control effects. However, it is difficult to consolidate and maintain the effect of this approach due to various other field infection sources that need consideration as we move forward;
- Geospatial techniques, such as RS and GIS, prove a unique advantage in

  exploring environmental factors affecting the transmission of *Echinococcus* parasites. We should strengthen the application of RS/GIS and implement spatiotemporal epidemic surveillance in humans and animals, so as to establish the mechanisms for early-warning and risk-assessment;

- The interaction between biological factors, environmental factors and social factors should be explored with the aim of attempting to understand the role and mechanisms at play for each link of *Echinococcus* parasites transmission comprehensively and systematically.

The prevalence of echinococcoses in China remains a serious problem, and the number of threatened populations and patients across the country still ranks the highest in the world. The prevalence varies greatly among different regions, especially in the Tibetan areas where the Qinghai-Tibet plateau is highly endemic. Therefore, targeted prevention and control measures should be carried out according to the degree of endemicity in different regions, especially in heavily prevalent areas, we should strengthen training as well as technical guidance adhering to the comprehensive control strategy of "focusing on the control of the source of infection, combination of controlling intermediate hosts and patient investigation and treatment"; Second, the epidemic of CE tends to be exported or spread in various ways, such as the exchange of people, the livestock trades and livestock products, as well as the increasing number of imported dogs, so it is necessary to strengthen the quarantine of host animals in the endemic areas, restrict the circulation of infected animals and prevent the spread of the disease. Moreover, targeted health education should be conducted in combination with key groups (such as females, aged ≥60 years, herders, lama, etc.) to improve prevention and control awareness of the population and effectively prevent these diseases. Finally, policy decision-makers should consider changing land-use policy and strengthen control of domestic dogs and small mammal populations to aid diseases prevention.

Author contributions

Mei-Hua Fu: Conceptualization, Data Curation, Writing- Original draft, Visualization. **Xu Wang:** Formal analysis. **Shuai Han:** Resources. **Ya-Yi Guan:** Writing-Review & Editing, Supervision. **Robert Bergquist:** Writing-Review & Editing. **Wei-Ping Wu:** Conceptualization, Writing-Review & Editing, Supervision.

Declarations

All authors consent to the publication.

Ethics approval and consent to participate

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Availability of data and materials

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Declaration of Competing Interest

None.

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