Control of taeniasis and cysticercosis in China

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Contents

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Abstract

National surveys suggest that the prevalence of taeniasis has considerably decreased in China, while reported cases indicated *T. solium* cysticercosis was historically highly endemic in northeastern, central and southwestern China. The high prevalence of taeniasis and cysticercosis there was driven by socio-ecological determinants. Cysticercosis may occur in the central nervous system, spinal cord, subcutaneous muscle, eyes, heart and oral cavity. Neurocysticercosis, the clinically most important type, causes epilepsy, increased intracranial pressure and neuropsychiatric symptoms. New molecular diagnostic techniques have been introduced for high sensitivity and discrimination of *Taenia* species. Immunological methods remain useful in the diagnosis of cysticercosis, especially neurocysticercosis. The introduction of imaging techniques including computed tomography and magnetic resonance imaging has significantly improved the diagnosis of neurocysticercosis. Recently, a combination of pumpkin seeds and areca nut has been explored against taeniasis, while praziquantel and albendazole are administrated simultaneously against cysticercosis, with promising efficacy and low side-effects. The widespread adoption of deworming protocols and techniques for inspection, management and treatment of pigs as well as improved sewage management has contributed to the significant decrease of taeniasis and cysticercosis in northern China. The positive results of these techniques should now be extended to highly endemic areas in western China to achieve the national elimination target for taeniasis and cysticercosis. Elimination of taeniasis and cysticercosis in China will not only benefit public health within China but also set an important example for less developed countries.

1. Introduction

Human taeniasis is caused by three *Taenia* spp., namely *T. solium*, *T. saginata* and *T. asiatica* (Ito et al., 2003). The life cycle of all three species involves humans as definitive hosts, who harbour the adult stage of the hermaphrodite worms in their intestines, and either pigs (*T. solium* and *T. asiatica*) or cattle (*T. saginata*) as the intermediate hosts. The intermediate hosts harbour the larval stages of the worm in the form of cysts which establish themselves in several highly oxygenated tissues, such muscles, a condition referred to as cysticercosis. The intermediate hosts become infected by consuming infected human faeces or ingesting food contaminated with infected human faeces. Humans become infected with *Taenia* spp. after consuming undercooked pork meat (*T. solium*), pork viscera (*T. asiatica*) or beef meat (*T. saginata*). Taeniasis caused by these three species has been reported to be generally asymptomatic or associated with very mild symptoms. In the case of *T. solium* infection, humans can serve as accidental intermediate hosts when consuming food contaminated by faeces of humans with taeniasis or through self-infection. Human cysticercosis occurs when

the larvae of *T. solium* migrate to different body tissues. When the larvae migrate to the central nervous system, the cysts establish and cause neurocysticercosis (NCC) (Garcia et al., 2003). NCC is believed to be the most common helminthic infection of the brain and is considered a public health issue in areas endemic for *T. solium* due to its severe sequelae such as epilepsy and severe chronic headaches.

Taeniasis and *T. solium* cysticercosis are believed to be endemic in China and a threat to public health. The goal of this work is to review Chinese data and literature on the epidemiology, risk factors, clinical manifestations, diagnosis and treatment of, and mass control activities for taeniasis and cysticercosis. This review will also serve to identify gaps in knowledge regarding the epidemiology and control of taeniasis and cysticercosis while also identify successes in control which may inspire other developing countries afflicted by taeniasis and cysticercosis.

2. Historical records

Cases of taeniasis have been documented since the early 1900s in China. Dr. C.K. Roys reported that, during 1899–1909, dozens of cases of human *T. solium* and *T. saginata* infections occurred in Qingdao, Shandong province in eastern China, but it is likely that all of these cases were of European origin (Roys, 1910). In 1910, Dr. Henry S. Houghton reported a local *T. saginata* infection from Wuhu General Hospital, Anhui province in central China (Houghton, 1910). During the same period, correspondence issued to members of the China Medical Missionary Association reported several *T. solium* infections in some areas of China according to the Research Committee of China Medical Journal (Research Committee of China Medical Journal, 1910). It is however believed that taeniasis has been present in China for at least 2000 years, as demonstrated by the discovery of *Taenia* spp. eggs in the intestine of an excavated corpse of the Western Han Dynasty in Jiangling county, Hubei province, China in 1975 (Wei et al., 1980). Although differentiation for *Taenia* species was unsuccessful, traces of beef and piglets' skeletons were found buried with the dead.

The first documented case of human cysticercosis occurred in Weihaiwei (now Weihai), Shandong province, China in 1922. Cysts affected various parts of the patient's body (Barnes, 1922). In 1924, Dr. Ralph G. Mills reported cysticercosis of the right side of a patient's chest in Beijing, northern China (Mills, 1924). The case was recorded in 1924 but the symptoms may have appeared up to 12 years before the case was diagnosed.

3. Epidemiological map

3.1 Taeniasis

Three national surveys on parasitic diseases have been conducted in China (Qian et al., 2019). In the first national survey (1988–1992), 2449 out of 1,477,742 sampled individuals in 30 provinces were found to be infected with *Taenia* spp. in 28 provinces (Fig. 1) (Xu et al., 2000). These data led to an estimation of about 1.3 million total *Taenia* spp. infections in the country (Hotez et al., 1997). In the second national survey (2001–2004), 983 from 12 provinces out of 356,629 individuals samples from 31 provinces were found to be infected with *Taenia* spp. (Fig. 2) (Technical Steering Panel for National Survey of Current Status of Major Human Parasitic Diseases, 2008). These data suggested that a total population of 0.55 million was infected (Technical Steering Panel for National Survey of Current Status of Major Human Parasitic Diseases, 2008). In the third national survey between 2014 and 2015, out of 484,210 participants from 31 provinces, 1752 ones were detected with *Taenia* spp. from 12 provinces (Fig. 3). After adjustment by the population structure in total population,

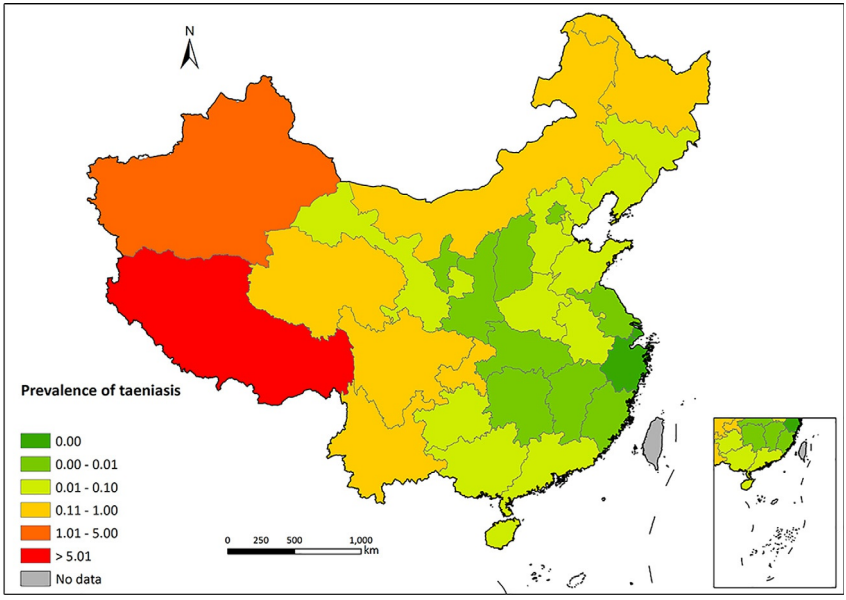

Fig. 1 The prevalence of taeniasis by provinces in China between 1988 and 1992.

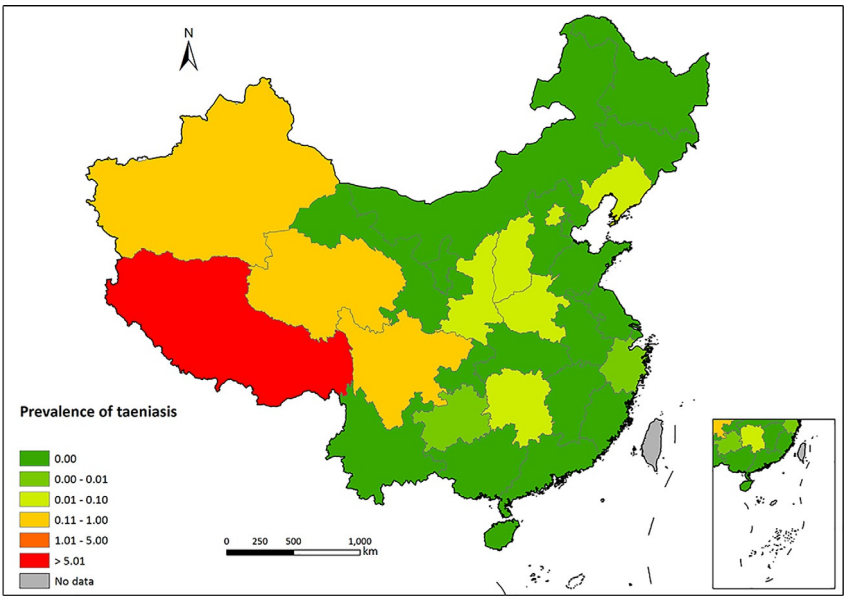

Fig. 2 The prevalence of taeniasis by provinces in China between 2001 and 2004.

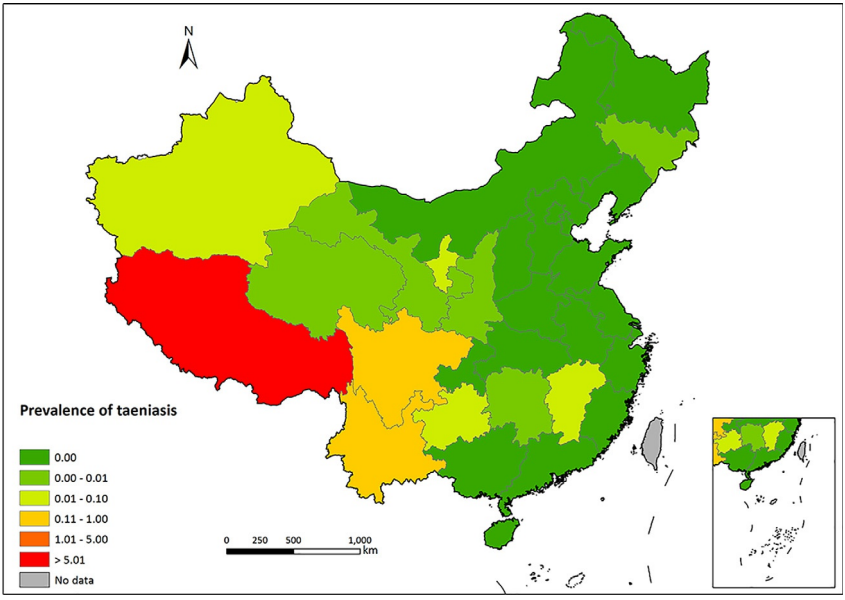

Fig. 3 The prevalence of taeniasis by provinces in China between 2014 and 2015.

a weighted prevalence of 0.06% was estimated, which indicated that 366 thousand persons were infected (Zhou, 2018). In the first survey, species identification techniques were carried out for some patients: 162 cases were identified as *T. solium* distributed across 10 provinces, notably in northeastern China, while 1399 cases were identified as *T. saginata* distributed across four provinces, mostly in western China (Xu et al., 2000). On the basis of the first national survey and the literature reports, *T. solium* and *T. saginata* infections were considered to be endemic in at least 20 and 18 provinces, respectively (Xu et al., 2000). Additionally, *T. asiatica* infection has also been reported in five provinces (Eom et al., 2002; Fan, 1991; Mo et al., 2005; Nkouawa et al., 2012; Zhang et al., 1999).

The three national surveys found no obvious difference in the prevalence of taeniasis among males and females (Technical Steering Panel for National Survey of Current Status of Major Human Parasitic Diseases, 2008; Xu et al., 2000; Zhou, 2018). However, the prevalence usually increased with age and peaked in middle aged people in the two earlier surveys, while it was not significantly different in the third survey (Technical Steering Panel for National Survey of Current Status of Major Human Parasitic Diseases, 2008; Xu et al., 2000; Zhou, 2018).

3.2 Cysticercosis

A retrospective survey in the first national survey of 16,508 cysticercosis cases from 671 counties of 29 provinces demonstrated that most cases occurred in northeastern, central and southwestern regions (Fig. 4) (Xu et al., 1999). The second national survey included a serological study for cysticercosis: of 96,008 individuals sampled in 31 provinces, 553 individuals in 25 provinces tested positive for cysticercosis (prevalence proportion of 0.58%; Fig. 5) (Technical Steering Panel for National Survey of Current Status of Major Human Parasitic Diseases, 2008).

Although the serological survey in the second national survey demonstrated no significant difference in the prevalence of cysticercosis by sex, the proportion of collected cysticercosis cases in the first national survey in males was more than double that in females (Technical Steering Panel for National Survey of Current Status of Major Human Parasitic Diseases, 2008; Xu et al., 1999). However, consistent with the highest serological positivity rate in middle aged people in the serological survey, the highest proportion of collected cases in the retrospective survey was also in middle aged people (Technical Steering Panel for National Survey of Current Status of Major Human Parasitic Diseases, 2008; Xu et al., 1999).

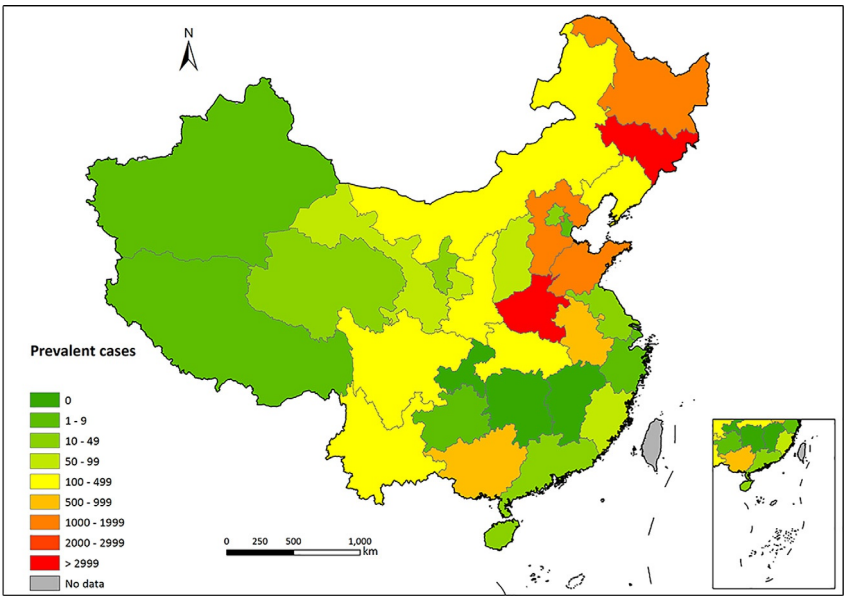

Fig. 4 The distribution of cysticercosis cases by provinces in China in a retrospective survey between 1988 and 1992*.

* The onset or diagnosis time of the cases was not specified.

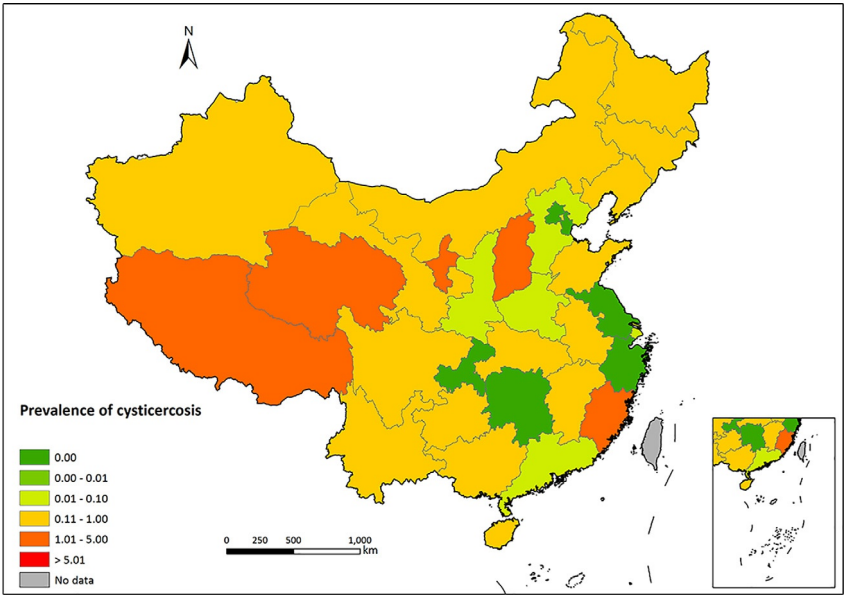

Fig. 5 The positive rate of cysticercosis by provinces in China in the serological survey between 2001 and 2004.

4. Socio-ecological determinants

The endemicity of taeniasis and cysticercosis has complex socio-ecological determinants. It is suspected that the practice of and attitudes towards consuming raw and undercooked meat is an important risk factor for taeniasis. For example, people of the *Bai* ethnicity in Yunnan province often consume completely raw pork, known as *Shengpi* (Yang et al., 2007). While people of the *Han* ethnicity rarely eat completely raw pork, populations in the northern part of China are at risk of consuming undercooked pork meat in the form of dumplings and quick-stick fried pork (Miao et al., 2000; Wang et al., 1999). Dumplings are not boiled for long enough and quick-stick fried pork consists of large pieces of meat not cooked at high enough temperatures to properly cook the meat. Pig cysticercosis remains an issue due to poor human faeces and pig management. In some lower income areas, latrines are poorly constructed or inexistent, and people may defecate openly (Miao et al., 2000; Mo et al., 2005). Further worsening of the situation and cycle of disease is due to the fact that some pigpens are connected with human toilets (Miao et al., 2000). Lastly, the absence of rigorous meat inspection practices in some rural areas leads to contaminated pork meat being sold for human consumption (Liu et al., 1996).

Human cysticercosis is also of concern due to poorly constructed toilets which cause faeces to overflow and contaminate the environment, especially water. Untreated human faeces, called "night soil", are used as fertilizer in local areas, also causing environmental contamination (Pan et al., 1995). The risk of infection is compounded when people consume raw vegetables and drink untreated water, especially in the hot summer (Ji et al., 1997; Miao et al., 2000). Poor personal hygiene can cause subsequent morbidity from cysticercosis in those with taeniasis (Table 1) (Ji et al., 1997; Li et al., 1998; Ma et al., 1988; Miao et al., 2000; Zhang et al., 1990; Zhao et al., 1999). Poor personal hygiene can also lead to a significant high risk of subsequent infection of family members (Li et al., 1998).

It has been argued that the high prevalence of infection with cysticercus in *T. solium* carriers arises from self-infection and auto-infection (Ministry of Health of the People's Republic of China, 2012a). Self-infection occurs when those with taeniasis ingest the eggs from themselves. It has been suggested that the proglottids of *T. solium* may enter the stomach reversely and then eggs from ruptured proglottids cause auto-infection. However, some

Table 1 Co-infection of taeniasis and cysticercosis from field surveys in China.

Location (References)	Time	Number examined	Number with both taeniasis and cysticercosis	Number with taeniasis (percentage with cysticercosis)	Number with cysticercosis (percentage with taeniasis)
Huaiyang county, Henan province (Ma et al., 1988)	1986–87	26,655	33	208 (15.9%)	52 (63.5%)
Kaifeng county, Henan province (Zhang et al., 1990)	1988	2677	11	27 (40.7%)	16 (68.8%)
Haerbin city, Heilongjiang province (Ji et al., 1997)	1993–94	10,525	10	56 (17.9%)	18 (55.6%)
Xiayi county, Henan province (Li et al., 1998)	1994–96	122,310	24	55 (43.6%)	147 (16.3%)
Licheng district, Jinan city, Shandong province (Zhao et al., 1999)	1996–98	238,643	28	75 (37.3%)	73 (38.4%)
Five counties (Yangxin, Qihe, Gaotang, Linqing and Dongying) in Shandong province (Miao et al., 2000)	1999	31,124	1	10 (10.0%)	16 (6.3%)

researchers have cast doubt on the latter assertion, because individuals harbouring a high number of encysted subcutaneous infections had no significantly increased trend of taeniasis (Wei et al., 1986). Additionally, although highly occasional, vertical transmission from mother to foetus has also been documented (Liu, 1987; Zhang, 1998).

5. Clinical manifestations

5.1 Taeniasis

The symptoms of taeniasis arising from all three species are usually not severe. The most typical manifestation is expulsion of proglottids, which is useful in diagnosis (Lang et al., 2004; Ma et al., 1988; Mo et al., 2005). Other nonspecific symptoms include pruritus ani, debilitation, dizziness, headache, drowsiness, anorexia, nausea, abdominal discomfort, diarrhoea and weight loss. *T. solium* occasionally parasitizes the thighs and the thyroid ectopically (Liu, 2013; Zhu and Gao, 1989). An enclosed mass of parasitized tissues is presented and the worms do not usually exceed 20 cm in length.

5.2 Cysticercosis

Cysticercosis is classified on the basis of the tissues affected. It may include but is not limited to NCC, subcutaneous muscle cysticercosis, ocular cysticercosis, heart cysticercosis and oral cavity cysticercosis (Xu et al., 1998). NCC, the most important infection in terms of incidence and morbidity, could account for 65% of total hospital-based cysticercosis cases, and may occur concurrently with other types (Xu et al., 1998). NCC may involve the cerebral parenchyma, cerebral ventricles, meninges or a mixture of these locations (Ma, 2004).

Epilepsy and increased intracranial pressure are the most commonly reported manifestations of NCC (Fang et al., 2009; Ge et al., 1993; Liu et al., 2008). The type of epilepsy is related to the location of cysticercus in the brain, while the frequency of seizure is related to how active the cysticercus is (Xie et al., 1995). In the cerebral cortex, especially precentral gyrus, generalized tonic clonic seizures and simple partial seizures are seen, while complex partial seizures are seen in deep temporal lobe involvement; diverse seizure types may occur when several lesions located in various parts of the brain are present. The frequency of seizure is highest in the degrading stage, reaching as many as one episode per month (Xie et al., 1995). High intracranial pressure is most common when cerebral ventricles are involved (Guo et al., 2001) and is associated positively with the occurrence of seizure (Ma et al., 1998); it also causes severe headache (Guo et al., 2001). Neuropsychiatric symptoms are often reported among people with NCC (Ma et al., 1996; Shen and Li, 2013). Neurasthaenia and anxiety depression are higher in schizophrenia patients with NCC than among those without

NCC (Shen and Li, 2013). Other manifestations (paraesthesia, disturbance of consciousness, dysaudia, aphasia, haemiplegia, hypomnesia and dementia) may also be present in lesser frequencies (Ge et al., 1993; Liu et al., 2008), so do cerebral infarctions (Hu et al., 1994). Spinal cysticercosis is infrequent and usually occurs concurrently with cerebral cysticercosis (Huang et al., 2013). Compression on nerves leads to numbness of the bilateral lower extremities, paraesthesia, changes in muscle strength and dysuria (Huang et al., 2013).

Subcutaneous nodules, the typical sign present in subcutaneous muscle cysticercosis, is most frequently distributed in the trunk, and then the limbs and the neck (Xu et al., 1998). Usually, no obvious symptoms are present when only subcutaneous muscles are involved, but severe infections (multiple nodules) may cause muscular pseudohypertrophy (Guo et al., 1996). Hypermyotrophy is more obvious in the gastrocnemius muscle, and fever and myosalgia are present in the early stage.

Ocular cysticercosis may occur in any part of the eyes, but intravitreal and subretinal cysticercosis are most frequent (Xu et al., 1998). It can lead to the loss of sight and even acroisa from vitreous opacity, detachment of retina, uveitis, endophthalmitis and cataract (Yang et al., 1997). NCC without direct involvement of the eyes may also impact sight (Cui et al., 2000).

Heart cysticercosis is rare (Xu et al., 1998). The order of frequency of cysticercus location in the heart is interventricular septum, left ventricular wall, chordae tendineae and bicuspid valve (Kong et al., 1995). Symptoms are usually mild including cardiopalmus, chest distress, discomfort in praecordium and fear.

Despite being rare, cysticercosis may also occur in the oral and maxillofacial region; the tongue and cheeks are the most frequent locations (Yu, 1988). Clinical presentation is an enclosed mass with a clear boundary, while symptoms may include pain, itching and swelling.

6. Diagnosis

6.1 Taeniasis

The Kato-Katz method and the perianal swab technique were applied in national surveys of parasitic diseases in China (Technical Steering Panel for National Survey of Current Status of Major Human Parasitic Diseases, 2008; Yu, 1991; Zhou, 2018). Although neither techniques specifically targeted *Taenia* spp. (the Kato-Katz method was used to detect many intestinal helminths, especially soil-transmitted helminths, and the perianal swab

technique was used to detect *Enterobius vermicularis*), their application has allowed the mapping of taeniasis epidemiology in China. The direct smear technique is also usually applied because of its simplicity (Han et al., 1981; Yang, 1955). The sensitivity of diagnostic techniques varies with the different *Taenia* species. The perianal swab technique is more sensitive than the direct smear technique for *T. saginata* infection (Yang, 1955), but the reverse is true (the direct smear technique being more sensitive than the perianal swab technique) for *T. solium* infection (Han et al., 1981). However, the major limitation of all these methods is their inability to differentiate *Taenia* species.

When screening for cases in large field surveys, a history of expelling proglottids is the most convenient screening tool, and it can be employed to detect large numbers of cases in a short time (Wang et al., 1987; Wu, 1981). This strategy is usually more sensitive in *T. saginata* infection because the proglottids are expelled automatically without defecation (Yang, 1955). In suspected cases, administration of cesticidal drugs, called "tentative deworming", is also useful because detection of worms after drugs administration could make definite diagnosis (Ito et al., 2013; Ministry of Health of the People's Republic of China, 2012b). This technique can differentiate species, especially when the scolex of intact worm is obtained.

Following the development of molecular methods, many new techniques have been introduced for the diagnosis of taeniasis and species discrimination. When parasite materials become available, multiplex polymerase chain reaction (PCR) techniques based on the cytochrome C oxidase subunit 1 gene (cox1) can be used for the simultaneous detection of any of the three species (Li et al., 2012, 2013). The coproPCR technique, which uses faecal samples for analysis, can also be used for detection of infection and species discrimination (Li et al., 2012, 2013). These PCR tests are expensive and complicated and are thus applied only in the laboratory setting. Recently, the loop-mediated isothermal amplification method (LAMP) was introduced for species discrimination, enabling rapid species identification in field surveys (Nkouawa et al., 2012).

Immunological tests, such as the indirect haemagglutination test (IHA), have also been developed (Qin et al., 1985). Furthermore, enteroscopy is helpful in clinical settings (Meng et al., 2007).

To promote the management of taeniasis in China, the former Ministry of Health issued a diagnostic standard in 2012 (Ministry of Health of the People's Republic of China, 2012b). Three levels of evidence are introduced (epidemiology, clinical manifestations and aetiology) and are employed to draw two categories of diagnostic criteria (suspected cases

and definitive cases). The recommended techniques for etiological diagnosis are faecal examination (for proglottids and eggs), perianal swabs (for eggs) and tentative deworming (for proglottids and adult worms).

6.2 Cysticercosis

Immunodiagnostic techniques have been extensively explored for the diagnosis of cysticercosis in China; these include intradermal test, latex agglutination test, indirect charcoal agglutination test, IHA, enzyme-linked immunosorbent assay (ELISA), dot-immunobinding assay, indirect fluorescent antibody test, enzyme-linked immunoelectro transfer blot and colloid gold immunochromatographic test (Liu, 1988; Liu et al., 2002; Qiu et al., 1998; Shi et al., 1989; Sun et al., 1985; Wu et al., 1994; Yin et al., 1990); IHA and ELISA are mostly applied, especially to support the diagnosis of NCC (Lian et al., 2003; Yang et al., 2008b). In NCC, both sera and cerebrospinal fluid can be applied in IHA and ELISA (Lian et al., 2003; Yang et al., 2008b). The sensitivity of IHA is similar to that of ELISA, and analysis of sera is more sensitive than that of cerebrospinal fluid in both IHA and ELISA tests (Lian et al., 2003; Yang et al., 2008b). The sensitivity of these techniques is positively related to the intensity of infection, namely the number of cysts (Lian et al., 2003). Furthermore, IHA and the classical ELISA detecting total antibody are not suitable to apply in evaluating treatment efficacy due to the persistence of positive results (Yang et al., 2008b). Thus, detection of special IgG4 antibody or cysticercus circulating antigen can be employed (Yang et al., 2008b). The positivity proportion and reaction intensity are higher in those patients in the active stage than those in the inactive stage when circulating antigen is detected (Zhang et al., 1992). Generally, immunological tests are auxiliary because of their insensitivity in some low-intensity infections as well as the false-positive results to other parasitic diseases, especially echinococcosis.

The introduction of imaging techniques including computed tomography (CT) and magnetic resonance imaging (MRI) in the early and late 1980s in China, respectively, has significantly improved the diagnosis of NCC (Ma et al., 1989; Sui et al., 1990). These two techniques are useful not only in definitive diagnosis but also in quantifying, positioning and staging of cysticercosis (Ma et al., 1989; Sui et al., 1990; Wei et al., 1999; Yan et al., 2004; Zhu et al., 1994). Usually, based on CT and/or MRI, four stages are defined (active stage, degeneration stage, inactive (or calcification) stage, and mixed stage which includes two or three stages simultaneously) (Sui et al., 1990; Zhu et al., 1994). Overall, MRI is preferable (to CT)

for diagnosis in active and degeneration stages, while CT is preferable (to MRI) in the calcification stage (Sui et al., 1990). The staging by CT and MRI guides the appropriate choice of treatment (Sui et al., 1990; Zhu et al., 1994).

Electroencephalogram is also helpful in diagnosis of NCC (Wang et al., 2000). Abnormality of electroencephalogram is related to the epilepsy and the characteristics include diffuse or focal irregular slow waves in the frontal, central and anterior temporal lobes (Wang et al., 2004a). The abnormality disappears or improves after treatment (Wang et al., 2004b). Thus, electroencephalogram can be applied with imaging techniques in diagnosis of NCC (Wang et al., 2004a,b).

For suspected NCC cases, "tentative treatment" has been applied (Jia and Ou-yang, 2009; Ministry of Health of the People's Republic of China, 2012a). A high dose of praziquantel is administered and a definite diagnosis is then judged according to efficacy after treatment. Many final ascertained cases with cysticercosis appear with such adverse reactions as headache, dizziness, acroanesthesia, local convulsion, urticaria, pyrexia during the "tentative treatment", which are important indicators for diagnosis. However, ethical questions should be paid attention to.

Additionally, ultrasound can be used in the diagnosis of cysticercosis in the heart, eyes and subcutaneous muscle (Jiang et al., 1999; Li et al., 2011; Shi et al., 2000).

Cysticercosis is complex and involves diverse locations, clinical appearances and types, which could lead to misdiagnosis especially in NCC (Ge et al., 1993; Yang et al., 2008a). Some reports estimate that over 20% of cysticercosis cases have been misdiagnosed before reaching a definitive diagnosis of cysticercosis (Ge et al., 1993). Cysticercosis is usually misdiagnosed as epilepsy unrelated to cysticercosis, viral encephalitis, tuberculous meningitis, perencephaly, cerebrovascular malformation and brain tumour (Ge et al., 1993). Furthermore, many other diseases especially brain tumour can be misdiagnosed as NCC (Yang et al., 2008a).

In 1985 an unofficial diagnostic standard for cysticercosis was first proposed by scholars during the first national seminar on cysticercosis in China (Ma et al., 1989), and then revised several times (Ma, 2004). In 2012 an official diagnostic standard was issued by the former Ministry of Health (Ministry of Health of the People's Republic of China, 2012a). It includes six types of evidence (epidemiology, clinical manifestations, aetiology, immunology, imaging and tentative treatment) to enable classification of cases into three groups (suspected, clinical and definitive).

7. Treatment

7.1 Taeniasis

In the 1970s, Chinese researchers found that extract from the plant *Agrimonia pilosa Ledeb.* was effective against *Taenia* spp. infection. The effective cesticidal component is agrimophol (No authors, 1974). The commercial product (*Shataoling*) has been widely used for treatment of *T. solium* infection in combination with cathartic medicines such as dihydroxyphthalophenone and magnesium sulphate in the field (Wang et al., 1987; Wu, 1981). The cure rate varies from 55% to 95% (No authors, 1974; Wang et al., 1987; Wu, 1981). Another brand (*Qutaojiaonang*) is made also from the plant extract to which cathartic Chinese medicines are added to facilitate administration (Wen et al., 1993). However, it was reported that out of 10,459 cases treated with *Shataoling*, one lethal case occurred due to allergic shock (Wu, 1981). Thus, *Shataoling* should be used with caution.

More than 1000 years ago the Chinese discovered the efficacy of areca nut against taeniasis. In the 1950s, Chinese scientists found that pumpkin seeds acted synergistically with the areca nut extract against taeniasis (Feng, 1956). Recently, it has been demonstrated that a combination of pumpkin seeds and areca nut extract has higher efficacy and lesser time for deworming than any single component (Li et al., 2012). Sequential administration of pumpkin seeds, areca nut extract and cathartic compounds (e.g. magnesium sulphate) usually resulted in a cure rate of 90–100% in those infected with *T. saginata* (Feng, 1956; Gan et al., 1992; Li et al., 1996). However, varying efficacy has been reported with *T. solium* infection, with high efficacy in some cases (Zhang et al., 1985) and in others only 30–40% (Wang and Fang, 2008; Zhang, 2003).

Praziquantel is also administered but mostly in clinical setting (Wang and Fang, 2008; Zhang, 2003). A single dosage (30 mg/kg) followed by a cathartic compound (manicol or natrii sulfas) within 30 min can have a cure rate of over 90%. Furthermore, niclosamide (Zhang et al., 1985), the combination of niclosamide and bitin (Xue and Han, 1981), and paromomycin (Feng et al., 1994) are also effective and are administered. Tribendimidine, a new drug developed in China, has also been documented to be effective against taeniasis in field tests, and may be of great value for use in settings with extensive intestinal polyparasitism, especially soil-transmitted helminthiases (Steinmann et al., 2008).

7.2 Cysticercosis

The high incidence and morbidity of NCC warrant its priority for research on treatment by Chinese scientists. Before the advent of praziquantel, many traditional Chinese medicines were introduced to treat cysticercosis, most of which were either inefficacious or controversial (Liu and Ge, 1978). It has been reported that *Ganwusan* (a combination of lacca sinica exsiccata, pasta ulmi and cinnabar) shows promising efficacy (Ge et al., 1989; Liu and Ge, 1978; Lu et al., 2003). The pharmacodynamic action is mild and side-effects are few. Thus, hospitalization in treatment is not compulsory. However, the major challenge is the need for long term treatment, usually over 1 year.

In the late 1970s, praziquantel was introduced to treat cysticercosis in China (Pan et al., 1981). Initially, efficacy was low because praziquantel was administrated as a single course of treatment and at a low dose (e.g. a total dose of 120–240 mg/kg) (Li et al., 1986; Pan et al., 1981). On the one hand, animal experiment studies showed that the development of the larvae of *T. solium* are not synchronous (Ma et al., 1991). On the other hand, pharmacokinetics studies found that the concentration of praziquantel is lower in cerebrospinal fluid than in blood plasma (Zhu et al., 1993). Thus, a high total dose was gradually applied, of up to 360 mg/kg per course, with administration of two or more courses (Huo et al., 2004; Wu et al., 2013). However, given the intense anthelminthic action of praziquantel, especially in high doses, side-effects are common and severe. These usually appear during the first course of medication (Huo et al., 2004). Major side-effects include the rapid increase of intracranial pressure, and induction or aggravation of seizures (Huo et al., 2004; Meng et al., 1986; Wu et al., 2013). In cases of heavy infection with diffuse location of cysts in the brain, death may result from the severe cysticidal reaction (Wang, 2009). Thus, hospitalization is compulsory when praziquantel is administrated against cysticercosis.

Praziquantel is also administered to treat schistosomiasis and clonorchiasis, both of which are endemic in China (Qian et al., 2016; Zhou et al., 2007). Due to the overlapping distribution with cysticercosis, treatment and mass chemotherapy for schistosomiasis and clonorchiasis in endemic areas could cause serious reactions in those with NCC, and caution must be exercised in these cases (Bi and Wu, 1996; Shu et al., 1992).

In the early 1980s, albendazole was introduced to treat cysticercosis in China (Liu et al., 1987). As with praziquantel, doses have increased from

a low dose (e.g. 10–20 mg/kg per day for 10 days and repetition for three courses) to a high dose (e.g. 60 mg/kg per day for 10 days and repetition for three to five courses) (Liu et al., 1987; Wu et al., 2013). Fewer side-effects occur with albendazole than with praziquantel, but hospitalization is needed with both medicines (Gao et al., 2010). Similarly, side-effects usually occur during the first course of medication (Liu et al., 1987).

In later years, albendazole was combined with praziquantel for treatment of cysticercosis with consideration of the differences in cysticidal mechanisms as well as their sequential side-effects (Li et al., 1995). During the past 20 years, this combination has been increasingly accepted by Chinese scientists (Wu et al., 2013). The following combination strategy is usually applied (Jia et al., 2005; Xu et al., 2002): albendazole and praziquantel are sequentially applied in the first course (albendazole: 20 mg/kg per day for 12 days; praziquantel: 30 mg/kg per day for 12 days); only praziquantel is used in second course (30 or 50 mg/kg per day for 12 days); and only praziquantel is used in the third course (50 mg/kg per day for 12 days). There is an interval of about 2–3 months between the two courses.

Surgery is compulsory in severe cases to decrease intracranial pressure and resolve hydrocephalus (Bu et al., 2009; Yuan et al., 2005). However, antiparasitic therapy cannot be substituted. Given the advances in minimally invasive techniques, minimally invasive neurosurgery can be successfully applied in cases of mild NCC (i.e. only a few cysts), especially in the case of a single cyst (Zhang et al., 2001). Because of the risk of loss of sight from antiparasitic reactions, surgery is the only choice in cysticercosis of the eyes (Cui et al., 2000; Yang et al., 1997).

8. Control

In response to awareness of the harm of pig cysticercosis to the economy and of human cysticercosis to public health, an "Office for Controlling and Eliminating Taeniasis and Cysticercosis" was established in many endemic provinces in northern China during the 1970s–90s involving the departments of commerce, agriculture and health (Liu et al., 1996; Ma et al., 1992). Four major interventions were applied: deworming for taeniasis, inspection of pork, management of human faeces and pigs, and treatment of pigs (Liu et al., 1996; Ma et al., 1992).

Large-scale active screening in villages detected and treated those with taeniasis. The detection method was to request the history of expelling

proglottids, especially during the previous 6 months, while *Shataoling* was widely applied for treatment (Wang et al., 1987; Wu, 1981). For example, during 1979–83 in Hunan province of central China over 140,000 people were found to have a history of expelling proglottids, nearly 100,000 cases of whom accepted treatment (Wang et al., 1987). The expelled worms were collected and managed collectively. It was then found that the incidences of human taeniasis, human cysticercosis and porcine cysticercosis decreased consistently (Wang et al., 1987). Additionally, by tracing the whereabouts of pork infected with larvae of *T. solium*, those eating the pork could be included for treatment (Liu et al., 1996; Ma et al., 1992).

The selling of infected pork is an important component in the transmission of taeniasis. Thus, pork inspection is included among the four arms of the national strategy against taeniasis and cysticercosis. Pork cannot be sold without inspection and those carcasses infected with cysticercosis should be destroyed.

Blocking contact between human faeces and pigs reduces transmission and promotes disease control. To do so, pigs are penned and not allowed to roam freely, and new closed toilets were built. Before applying fertilizer, human faeces are processed through non-hazardous treatment such as thermophilic fermentation.

To avert economic losses, pigs are examined during rearing and treated if infected with larvae of *T. solium*. Many immunological techniques were developed to detect the infection (Gu and Shen, 1998; Liu et al., 1996); albendazole and praziquantel were adopted to treat infected pigs (Han et al., 1983; Liu et al., 1996). Usually, the drugs have no residual effects and the resulting pork is equally nutritious to that without previous infection or treatment (Chen et al., 1991) However, pigs with severe infection are unsuitable for treatment because it may kill the animal and reduce nutritional value (Liu et al., 1996).

Lack of knowledge is an important risk factor of taeniasis and cysticercosis (Cao et al., 1997). Thus, health education is effective in community interventions (Li et al., 1998, 2000). Health education not only promotes knowledge of the disease but also enhances capacity to distinguish infected pork, leading to positive changes in the management of human faeces and rearing of pigs.

In later years the prevalence of taeniasis and cysticercosis decreased significantly and the Office for Controlling and Eliminating Taeniasis and Cysticercosis has been scaled back gradually in many areas. Although no widespread screening and treatment for taeniasis is yet available, proper management of human faeces and pigs and inspection of pigs are occurring

owing to social and economic development. More hygienic toilets are being built and human faeces are no longer an important fertilizer thanks to the production of chemical fertilizers (Department of Comprehensive Statistics of National Bureau of Statistics, 2009). Pigs are usually raised collectively and inspection is more standardized, especially in developed areas.

9. Gap analysis

Despite the achievements in epidemiology, diagnosis and treatment, and control, many gaps still hamper the final elimination of taeniasis and cysticercosis in China. Firstly, the national epidemiological map is inaccurate and the disease burden is unclear. Three national surveys were implemented to include detection of, but not focus on taeniasis (Hotez et al., 1997; Technical Steering Panel for National Survey of Current Status of Major Human Parasitic Diseases, 2008; Xu et al., 2000; Zhou, 2018). On the one hand, national sampling mainly targeted on soil-transmitted helminthiases and thus its representativeness was inadequate for taeniasis. On the other hand, the faecal examinations applied were not very sensitive for *Taenia* spp. However, the decreasing trend of disease incidence provides evidence of social and economic development as well as massive control activities. Although serological investigation was carried out for cysticercosis in the second survey, a national figure for the total infected population was not estimated in the survey report, due to the inaccuracy of serological detection (Technical Steering Panel for National Survey of Current Status of Major Human Parasitic Diseases, 2008). In other literature, a national estimation of 3 million individuals infected was usually mentioned (Lu et al., 2002; Xu, 2002). However, these were only simple estimations and detailed descriptions could not be provided. Another estimation of 7 million infections with cysticercosis was also referred to, based on the rude calculation of national serological data (Yang et al., 2014). According to the Global Burden of Disease Study 2013, the disability-adjusted life years (DALYs) attributed to cysticercosis were 435,100 in 1990 and 341,200 in 2013 worldwide, and the corresponding data in China were 88,900 and 47,000, respectively (GBD DALYs and Hale Collaborators et al., 2015). However, these figures may be severely underestimated, because WHO Foodborne Disease Burden Epidemiology Reference Group estimated that DALYs due to cysticercosis reached 2,780,000 globally in 2010 (Torgerson et al., 2015). Obviously, the unavailability of accurate epidemiological maps in China, especially for cysticercosis, hampers the formulation of further intervention strategies.

Second, research remains inadequate. The cross-reaction of immunological diagnosis with other parasitic diseases especially echinococcosis—another important parasitic disease in China—weakens its large-scale application in fields. No national treatment standard is available for taeniasis and cysticercosis. Although many advances have been made in treatment, gaps still exist. Nowadays, the traditional Chinese medicines *Shataoling* and *Qutaojiaonang* are no longer produced because of the limited demand for treatment of taeniasis in the field. The new method combining pumpkin seeds and areca nut extract should be standardized for the treatment of taeniasis, which is also expected to be commercialized. Although the material is easy to obtain, the quality of effective components should be guaranteed during the process. Although the combination of albendazole and praziquantel is gradually being accepted for the treatment of NCC, large standardized, randomized and controlled clinical studies are still needed, which will promote the wide application of this treatment strategy.

Third, no special intervention programme is being carried out. Following the achievements of control in hyperendemic areas during the 1970s–90s, the Office for Controlling and Eliminating Taeniasis and Cysticercosis was gradually dismantled. Although social and economic development has promoted improvements in environment, hygiene, and pig management and inspection, taeniasis and cysticercosis have not been eliminated and remain endemic in some remote areas, e.g., Yunnan and Sichuan provinces in western China (Li et al., 2019; Zang et al., 2019a, b). Their control has not been included in the updated national control programme for parasitic diseases, although some control pilots are being implemented (Qian et al., 2019). Although active surveillance for human beings has just been established for taeniasis, the coverage is low (Qian et al., 2019). Especially, taeniasis and cysticercosis are excluded from the National Infectious Diseases Reporting System through passive surveillance, which includes many parasitic diseases (amebiasis, schistosomiasis, malaria, visceral leishmaniasis, echinococcosis and filariasis), hampering the acknowledgement of the importance of and subsequent interventions against taeniasis and cysticercosis (Qian et al., 2019).

10. Conclusions and future perspectives

Both in China and globally, cysticercosis has been listed among the eradicable diseases (Ma et al., 1992; Maurice, 2014). However, taeniasis and cysticercosis remain endemic in some poor areas of China. To achieve

the final elimination target, the gaps mentioned above should be filled. Taeniasis and cysticercosis should be included in the National Infectious Diseases Reporting System not only to benefit the establishment of a national epidemiological map but also to promote the clinical management of cases. Similar case management of malaria in China should be used as a reference. For taeniasis, the source of transmission should be traced and those contracting the disease should be examined along with their family members. Cases of cysticercosis should be examined for taeniasis and their family members also included for surveillance. The Office for Controlling and Eliminating Taeniasis and Cysticercosis is expected to be re-established in some hyperendemic areas in order to integrate the efforts of health, agriculture and commerce. New sensitive diagnosis techniques are expected to be developed and national treatment standards should be issued.

WHO has selected China among the first countries in a network to further control and finally eliminate cysticercosis (Maurice, 2014). Thus, under this framework, the National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention is exploring the strategies for the control and elimination of taeniasis and cysticercosis in China. The pilots include one elimination pilot in Henan province, where taeniasis and cysticercosis were highly endemic historically but quite low nowadays, through information, education, and communication and establishment of surveillance system. Another two control pilots are established in Yunnan and Sichuan provinces, respectively, where taeniasis and cysticercosis are still highly endemic. Information, education, and communication, detection and treatment of cases, improvement of sanitation and provision of water are integrated. The control and eventual elimination of taeniasis and cysticercosis in China will promote the health of local people. Successful research and control of taeniasis and cysticercosis in China during the past 40 years have boosted our confidence and provided important experiences. These experiences should be summarized and generalized to benefit those endemic areas in China, as well as other endemic countries.

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