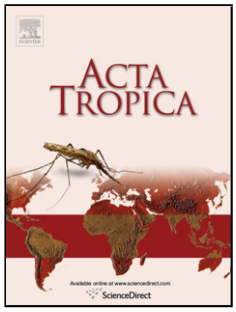

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Cysticercosis/Taeniasis Endemicity in Southeast Asia: Current Status and Control Measures

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Highlights:

Cysticercosis/taeniasis remains a neglected zoonosis in most Southeast Asia countries due to the lack of information about its presence and societal impact.

We provided an overview of the disease endemicity mainly based on literatures published after 2009.

It is imperative to evaluate current serological tools under multi-central evaluation systems with double-blinded testing.

Taeniasis and cysticercosis control programs should be adopted with consideration toward differences in culture, religion, socio-economic status and level of education.

Introduction

Cysticercosis is caused by the larval stage (cysticercus, cysticerci) infection of *Taenia solium* (*T. solium*) in both humans and pigs. In humans, the commonly infested body organs are skeletal muscles, subcutaneous tissues, eyes and brain with the most pathogenic infection, neurocysticercosis (NCC), occurring due to the invasion into the central nervous system (CNS). In pigs, cysticercosis makes pork unsafe to eat and causes economic losses due to the loss of market value.

The life cycle of *T. solium* involves humans and pigs. Humans are the only carriers of eggs that can spread cysticercosis. Humans acquire adult tapeworm infection (taeniasis) when eating raw or undercooked pork containing cysticerci. Following ingestion, the larval tapeworm grows into an adult worm within approximately two months in the human small intestine. Eggs or the most distal worm segments (proglottids) containing mature eggs are released/detach from the worm intermittently and then are passed out into the environment with human faeces. These eggs can infect the same (auto-infection) or other humans through faecal-oral transmission from direct contact with tapeworm carriers or consumption of water or food contaminated with human faeces. Pigs become infected through consumption of human feces where open human defecation occurs as well as through contaminated food, water and soil.

Cysticercosis is one of the 17 major Neglected Tropical Diseases (NTDs) identified by the WHO as a focus for research and control (WHO, 2011b). It is a severe helminth infection responsible for neurological damage, occurring in many resource-poor countries, especially those with warm and mild climates in the regions of Latin America (LA), Asia and Sub-Saharan Africa (SSA). In areas where *T. solium* is endemic, cysticercosis is known to be a leading cause of seizure/epilepsy (Del Brutto, 2012; Del Brutto and Garcia, 2012; Moyano et al., 2014). Systematic reviews indicate that seizure/epilepsy was the most common manifestation among diagnosed NCC patients (Carabin et al., 2011) and the proportion of NCC cases among people with epilepsy in endemic countries was estimated to be 29.0% (Ndimubanzi et al., 2010). The prevalence of human cysticercosis is marked in those areas where sanitation is poor and people are traditionally keen to consume raw or insufficiently cooked pork and/or where the husbandry of pigs is improper. The global burden of NCC has been estimated to be over 2 million DALYs per annum (Torgerson and Macpherson, 2011). The number of human cysticercosis cases has recently been estimated at 3-6 million in China and 11-29 million in the Latin America region (WHO, 2013). Notably, large-scale control initiatives are lacking in all regions (Lustigman et al., 2012).

This review focuses on the current endemic status of cysticercosis/taeniasis caused by *T. solium* in both humans and pigs living in Southeast Asian countries including China. We also emphasize epidemiological data as well as prevention and control measures for human NCC.

Current status

Cases of taeniasis caused by *Taenia solium, Taenia saginata and Taenia asiatica* have been reported from Southeast Asian countries of Cambodia, Indonesia, Japan, Lao PDR, Malaysia, Nepal, Thailand, The Philippines, PR China and Vietnam (Ash et al., 2015; Conlan et al., 2008; Deckers and Dorny, 2010; Ito et al., 2003a; 2011; 2014; 2015; Van De et al., 2014; Verle et al., 2003; Wandra et al., 2015; Willingham et al., 2010; Wu et al., 2012; Xiao et al., 2013; Yanagida et al., 2012). While adult tapeworms of other taeniid species, such as, *T. saginata* and *T. asiatica*, also infect humans, only *T. solium*

can cause human cysticercosis. There have been no reports of metacestodes (cysticerci) of these other species infecting human organs (Ale et al., 2014; Ito et al., 2003a; Yamane et al., 2012).

Approximately 50 million people are suffering from NCC due to *T. solium* globally with more than 50,000 deaths per year attributable to this disease (Wandra et al., 2015). Although accurate estimates of the extent of the infection and disease are not available for most endemic regions, many studies suggest a higher prevalence of cysticercosis disease burden than has been appreciated by the public health service systems (Hotez et al., 2008; Montano et al., 2005).

Cambodia:

No nationwide survey data about either *T. solium* or cysticercosis prevalence in Cambodia are currently available. However, human cysticercosis does occur in Cambodia according to case reports in the local literature (Dorny et al., 2004b). However, there are very few literature looks into situation of taeniasis/cysticercosis in Cambodia besides reports by the Korea Association of Health Promotion (KAHP) and the Cambodian National Center for Parasitology, Entomology, and Malaria Control (CNM) since 2006(Cho et al., 2014; Jeon et al., 2011; Yong et al., 2012). It is estimated that the overall prevalence of *Taenia* spp. ranged from 0.3% to 1.5% between 2006 and 2009 with mainly *T. saginata* infection. In 2007, KAHP and CNM surveyed inhabitants and primary school children in Koh Kong, Kam Pot and Kampong Som Provinces and performed single stool examination using the Kato-Katz thick smear technique. Out of the 2,824 fecal specimens collected, 42 taeniid positive samples were found in Koh Kong province (4.6%, 42/904), which is the single province among the three known for eating raw beef and pork (Jeon et al., 2011). *Taenia* spp. eggs were isolated from the stools of 21 patients in Koh Kong and subjected to DNA sequencing and multiplex PCR to identify species. Among those, 2 patients were identified as infested by *T. solium* and the remaining 19 as *T. saginata*. In 2012, a study focused on *Opisthorchis viverrini* carried out by KAHP revealed a 0.06% of *Taenia* spp. egg positive rate using the single stool Kato-Katz thick smear technique with a total of 1,341 stool samples collected. This stool

survey was conducted in the riverside villages of Ang Svay Chek area approximately 45 km south of Phnom Pen (Yong et al., 2012).

There is no recent report on porcine cysticercosis in Cambodia besides data cited in a 2010 review which stated that positive pigs were detected from eight of the nine provinces supplying pigs to the central slaughterhouse in Phnom Penh, with prevalence ranging from 5.3% to 36.4% (Willingham et al., 2010).

Indonesia:

There are three human *Taenia* spp. species reported in Indonesia: *T solium* mainly from Papua and Bali, *T. saginata* from Bali, and *T. asiatica* from Samosir island, North Sumatra. Cysticercosis has been confirmed in Indonesia in humans, pigs and even dogs (Ito et al., 2002; Margono et al., 2006; Simanjuntak et al., 1997; Wandra et al., 2007; 2015) From year 2000 and on, the prevalence of cysticercosis decreased dramatically in Bali. Wandra et al. reported 2 sero-positive NCC cases were detected among the 660 people from the 9 districts in Bali where epidemiological surveys for taeniasis/cysticercosis were conducted from 2002 -2009 (Wandra et al., 2011). Most recently, an ocular cysticercosis (OCC) case of a 9-year-old girl who lived in the northeastern part of Bali was reported as the first case report of OCC from Indonesia (Swastika et al., 2012). Notably, a paper discussing the transmission hypothesis of solitary ocular cysticercosis is in publication (Sahu and Ito, 2015). Even though serologic tests by either ELISA or immunoblot showed negative results, mitochondrial DNA examination of the cysticercus indicated that the cox1 gene sequence of the cysticercus from the left eye of the patient was 99.9% identical to that of *T. solium* collected in Papua, Indonesia. Throughout a 10-year field survey directed in Bali, no *T. solium* adult worms were detected by community-based surveys until 2011. All tapeworms discharged by 110 people were identified as *T. saginata*. However, in 2011 and 2012, three *T. solium* carriers were identified among the 227 people surveyed from two neighboring villages in Karangasem, Bali including a 4 years old girl and a 35 year old man from Datah village, and a 35 year old woman from Dukuh village (Swastika et al., unpublished).

Cysticercosis is believed to be decreasing in Bali due to improvements in household sanitation and pig husbandry as a result of sustainable public health education campaigns and economic advancement (Wandra et al., 2011). In 2009, a slaughterhouse survey of 108 pigs slaughtered in East Flores district did not find any cysticercosis infections in areas where sporadic human taeniasis cases have been reported (Willingham et al., 2010). Nevertheless, taeniid species for those human taeniasis cases needs to be determined.

In contrast, it has been very difficult to control cysticercosis in Papua (Ito et al., 1999; 2004; Salim et al., 2009; Wandra et al., 2013). In 2011, sero-prevalence surveys of human cysticercosis were conducted by a Japan and Indonesia joint field team in Papua and Bali in villages with confirmed *T. solium* carriers. Cysticercosis sero-positive rates are 21% (60/286) and 6% (11/176) in adults reside in Wamena, Papua and northeast Bali, respectively using recombinant antigen-specific ELISA and confirmed by immunoblot (Sako et al., 2000; Sato et al., 2003; 2006). More than 50% of the cases in Papua were strong positives, whereas all positives in Bali were weak in ELISA. Cysticercosis sero-prevalence appears to have decreased slightly in 2011 comparing with the data collected in 1996 from Wamena, Papua, but is still in the considerably high range (Swastika et al., unpublished). Similar serological data in Papua were reported by other groups as well (Salim et al., 2009).

In Papua, porcine cysticercosis prevalence appears to be higher than that of Bali (Subahar et al., 2001). A slaughterhouse survey was conducted in the traditional market of Wamena, Jayawijaya district, in which 27 of 35 (77%) pigs slaughtered were found infected with porcine cysticercosis (Willingham et al., 2010). It is worth noting that not only pigs but also dogs in Papua have been found infected with *T. solium* cysticerci (Ito et al., 2002). Dog meat is consumed in several Southeast Asian countries, including Indonesia, Korea, China, Vietnam, and Thailand, however, it is usually well-cooked. Therefore, the risk of taeniasis from eating *T. solium* cysticerci contaminated dog meat is likely to be low, but should be investigated (Ito and Budke, 2014; Ito et al., 2013a; Wandra et al., 2015).

Japan:

T. solium infection is not considered endemic in Japan where there are only sporadically reported imported cases of cysticercosis (Kobayashi et al., 2013). Yanagida et al. (2012) recently published a review about the status of *T. solium* infection in Japan as an attempt to prevent further outbreaks of this fecal-oral transmitted parasitic disease. Due to globalization, Japan is no longer absolutely free of taeniasis and cysticercosis. Business personnel and tourists visiting endemic countries may return with infections of any species of *Taenia* spp. There are reports of imported cysticercosis and taeniasis cases from East Asian countries including China and North and South Korea (Yanagida et al., 2012). A single taeniasis patient or *T. solium* carrier may cause cysticercosis in numerous others through *T. solium* eggs discharged. Thus, family members and colleagues of the identified *T. solium* infected are recommended to take serological test for cysticercosis in Japan. The research lab at the Asahikawa Medical University in Japan has functioned as a national reference lab using both serological and molecular diagnostic tools since 1998. The serological and mitochondrial DNA (MtDNA) and nuclear DNA analyses performed have also been introduced to other cysticercosis endemic areas in Asia and Africa with the financial support from the Ministry of Education, Japan from 2003 onward (Ito et al., 2007). Thus, those tests have been highly useful to assess the infection not only in Japan but also worldwide (Ito, 1998; 2006; 2007; Nkouawa, 2009; Yamasaki, 2006). More recently, a rapid immunochromatographic kit for detection of cysticercosis or NCC has become commercially available in Japan, which uses fresh blood samples and provides the results within 20 minutes (ICST Co. Ltd. Saitama, Japan) (Ito and Budke, 2014).

South Korea:

Historically, cysticercosis due to *T. solium* was rather common in South Korea and probably the same in DPR Korea (North Korea) (Chai, 2013; Cho et al., 2014; Rajshekhar et al., 2003; Singh et al., 2002). A drastic drop in the number of human and swine cysticercosis cases in South Korea is considered to be due to improved sanitation and economic situation. A nationwide human serological study on a total of 74,448 serum samples from 121 hospitals collected during 1993 to 2006 revealed that the IgG positive rate for *T. solium* cysticerci antigens in 1993 was 8.3%, but reduced to 2.2% in 2006 (Lee et al., 2010).

However, antigens used for this IgG ELISA were collected from the cyst fluid of *T. solium* metacestodes recovered from pigs (Cho et al., 1986). As there are some recent advances in preparation of diagnostic antigens with higher specificity (Chung et al., 2002; Ito et al., 1998; Lee et al., 2005a; 2005b; Sako et al., 2000; Sato et al., 2006), seroepidemiological surveys using better antigens are necessary to evaluate the current situation of cysticercosis in South Korea and to distinguish it from other potentially cross-reactive helminthiases such as clonorchiasis, paragonimiasis and sparganosis that have also been endemic in South Korea.

Cysticercosis is currently not considered actively endemic in South Korea with only a few case reports from elderly people and immigrants (Choi et al., 2014; Kim et al., 2014; Shin et al., 2012).

Lao PDR:

The parasitic zoonoses of human cysticercosis (*T. solium*) and taeniasis (other *Taenia* spp. species) are endemic in the Lao People's Democratic Republic (Lao PDR) with an estimated taeniasis prevalence throughout the country ranging from 0-14% although documented data regarding human cysticercosis and taeniasis, as well as porcine cysticercosis are quite limited (Ash et al., 2015; Choudhury et al., 2013; Jeon et al., 2013; Okello et al., 2014).

In 2009, a serological survey for cysticercosis was conducted in 24 randomly selected villages from the 4 northern provinces of Laos PDR consisting of Oudomxay, Luangprabang, Huaphan, and Xiengkhuang. Based on 1,306 serum samples tested, cysticercosis antigen ELISA positive rate was 2.2%, ranging at the village level from 0 to 11.3% (Conlan et al., 2012) using the ELISA for *Taenia* spp. metacestodes circulating antigens (Dorny et al., 2004a). In the same study population cited, Conlan et al. reported that prevalence of taeniid egg positive rate by single stool Kato-Katz method to be 2.9%, while estimated taeniasis prevalence (egg positive plus self-reported) was 8.4%. MtDNA tests on the tapeworms expelled from 35 persons showed that 33 tapeworms were *T. saginata* and 2 were *T. solium*. These data likely underestimate the endemicity of taeniasis in northern Lao PDR due to the limited sensitivity of the microscopic technique used (Conlan et al., 2008). During 2005 - 2006, a hospital-based

human intestinal helminthiasis survey was carried out in southern Laos. Pooled results from 3 stools from each person tested by the Kato-Katz thick smear method and quantitative formalin ethyl-acetate concentration technique (FETC) showed that out of 232 participants (age ≥15 yr), 53 were taeniid egg positive, indicating an infection rate of at least 22.8% among residents from the southern region of Laos (Sayasone et al., 2009). Recently, a community survey of taeniasis in the village of Om Phalong in Phongsaly province of northern Lao PDR reported 26.1% taeniasis prevalence by a combination of microscopy and copro-antigen ELISA analysis (Okello et al., 2014). Ninety-two participants representing 27.9% of the total village population provided single stool samples and among them 13 submitted blood samples during the 2013 dry season. Generic taeniid PCR and sequencing determined that 5 of the successfully sequenced samples 100% identified with *T. solium*. Results of circulating cysticerci antigen test (4/13 positive) and the fact that neither *T. saginata* nor *T. asiatica* were detected in any of the genotyped samples led the authors to suggest that *T. solium* exists within the human population of Om Phalong at significantly higher levels than indicated in previously published studies from Lao PDR (Conlan et al., 2012; Okello et al., 2014). However, recent field studies on soil transmitted helminthes in Sepon province of Lao PDR close to Vietnam have revealed that the three human *Taenia* spp. species are sympatrically distributed (Sato et al., unpublished).

So far, there are no means to estimate the true prevalence of swine cysticercosis from the very limited slaughterhouse data available in Lao PDR. A significant proportion of pigs are slaughtered and sold outside official channels without carcass inspection. Routine inspection data is unreliable and the maximum likely prevalence estimates of swine cysticercosis range from 2.8 to 4.2% in northern Lao PDR (Choudhury et al., 2013).

Cross-sectional human and animal surveys of *Taenia* spp. showed that *T. solium* was one of the four species endemic in Lao PDR, where three species cause taeniasis in humans (*T. solium, T. saginata,* and *T. asiatica*) and three species cause cysticercosis in pigs (*T. solium, T. asiatica,* and *T. hydatigena*) (Conlan et al., 2012).

Malaysia:

Cysticercosis does not traditionally occur in Malaysia where Islam is the major religion. There are only sporadic case-reports, most of the cases had a history of travelling to endemic countries like China (Arasu et al., 2005; Ito et al., 2013a; 2014; Nor Zainura et al., 2005). However, there are several ethnic minorities in Malaysia who are known to consume pork and are in close contact with domesticated wild boars or pigs in Sabah, Sarawak and Peninsular Malaysia. In 2006, a sero-prevalence survey of humans living in a rural district of Sabah showed 2.2% cysticercosis antibody sero-positive rate in a community where people customarily keep domesticated wild boars under their houses (Noor Azian et al., 2006). This study used a commercial ELISA kit to analyze 135 human blood samples collected and stored for approximately ten years. These conditions may have underestimated the true prevalence suggesting that the potential of cysticercosis in rural communities in Malaysia should not be ignored.

Myanmar:

So far, there are no nationwide studies regarding cysticercosis endemic status in Myanmar (formerly Burma) except a report by Coker-Vann et al (1981). This report demonstrated 6% anti-*T. solium* cysticerci antibody positive rate by ELISA. However, the appearing case reports on NCC among refugees from Myanmar indicate cysticercosis endemicity in this region. A recent serological survey using enzyme-linked immunoelectrotransfer blot (EITB LLGP, CDC, US) (O'Neal et al., 2012) detected 24.9% positive rate of antibodies against *T. solium* cysts in 499 anonymous samples of refugees from Myanmar collected during 2004 to 2007. Even though seroprevalence is not generalizable to the broader population in Myanmar, one should not underestimate the epidemiology of cysticercosis in this country apart from the known fact that the EITB LLGP has low sensitivity for detecting single parenchymal cysts and calcified cysts alone (Prabhakaran et al., 2004; Singh et al., 1999). Recent studies involving refugees from Myanmar to Thailand also showed that taeniasis and cysticercosis due to *T. solium* is not rare in Myanmar (2010; Anantaphruti et al., 2007).

Nepal:

Nepal was previously considered to be highly endemic for taeniasis and cysticercosis, especially based on the study by Amatya and Kimula in 1999 (Amatya and Kimula, 1999), even though there are very limited data and no systematic evaluations on epidemiology of cysticercosis in Nepal (Agarwal, 2011; Azzopardi and Quirk, 2012; Pant et al., 2011; Yanagida et al., 2010). In a recent editorial of Kathmandu University Medical Journal, Agrawal JP (2011) stated that the available data suggest cysticercosis prevalence ranges from 0.002 – 0.1% in the general population of Nepal noting that many clinical studies reported from Nepal had variable presentations, and outcome in terms of diagnosis and treatment responses. In 2013, a retrospective study about the etiological diagnosis of children with seizure revealed that 12% of seizure disorder is diagnosed as NCC among children aged 1-15yrs. The data is retrieved from the records maintained in the Department of Pediatrics, Manipal Teaching Hospital in Western Nepal from 2007 to July31, 2011 (Adhikari et al., 2013).

Interestingly, a recent community based survey (Devleesschauwer et al., 2012) in the eastern Terai of Nepal revealed an unexpected result in the region with a high density of pigs and pork consuming individuals. In the community of Dum, a remarkably high prevalence of 13.5% (71/524) was determined among tapeworm carriers, but molecular diagnosis disclosed that of the 16 tapeworms collected from these carriers all were identified to be *T. asiatica*, not *T. solium.* Further research is warranted to assess the actual health impact of *Taenia* spp. and cysticercosis in Nepal (Devleesschauwer et al., 2013a; 2013b).

Sri Lanka:

Information on cestode zoonoses in Sri Lanka is extremely limited. Residents in Sri Lanka traditionally eat raw or uncooked meat rarely if at all, thus, NCC is not considered occurring in this country (Juyal et al., 2008). However, in a brief update about parasitic zoonoses in Sri Lanka, Dissanaike (2002) claimed that there are cases of *T. solium* treated by clinicians and parasitologists, but not reported. Clinical case reports on taeniasis and cysticercosis are needed to help estimating the situation of cysticercosis in Sri Lanka.

Thailand:

Cysticercosis cases have often been reported in hospitals in Thailand (Waikagul et al., 2006; Wiwanitkit and Wiwanitkit, 2015). In 1992, Jongsuksuntigul et al (1992 as quoted by Waikagul, et al., 2006) reported a nationwide stool survey in Thailand and revealed 1-2% of taeniasis infection in the north and northeast of the country, with <1% in the central region, and almost none in the south. A community–based coprological and serological survey was conducted in 2 villages in central Thailand with 667 participants aged 5 years and older during 2007 and 2008 (Anantaphruti et al., 2010). This study revealed that 9 out of the 159 (5.7%) villagers who provided serum samples were highly suspected of having cysticercosis due to sero-positivity against GPsAg (glycoproteins antigen) while 4 out of 159 (2.5%) were immunoblot positive using RecAg (recombinant antigen) (Sato et al., 2006). Interestingly, none of the cysticercosis participants were detected to be *T. solium* carriers by either Kato-Katz fecal egg examination or molecular approach of multiplex PCR using expelled worms. Although two of the cysticercosis participants (including one confirmed NCC case) had a history of expelling proglottids in feces one year before the investigation, suggesting that even though carriers of *T. solium* tapeworms are at great risk of contracting cysticercosis, we should also pay attention to person to person transmission especially among family members and neighbours (Gonzalez et al., 2006).

So far, there is no prevalence data on pigs with cysticercosis in Thailand. A study conducted in Karen refugees' villages on the Thai-Myanmar border in Tak province (2010-2012) indicated at least 10 pigs owned by the *T. solium* carriers or their neighbors are infected with cysticerci of *T. solium* and/or *T. hydatigena*, but no human cysticercosis case has been identified thus far (Kusolsuk et al., unpublished).

The Philippines:

T. saginata and *T. solium* adult worms found in human stools was first reported in the Philippines in 1901 (Garrison, 1907). Although previous studies disclosed taeniasis prevalence ranging between 10-15% (Arambulo et al., 1976; Cruz, 1991), to date, no systematic nationwide survey on taeniasis or cysticercosis have been documented in the Philippines. The overall NCC case numbers reported in the

literature are quite low (Arambulo et al., 1976; Atilano and Pena, 2000; de Leon, 2005; Nakajima et al., 2002). Recently, through the IDRC's EcoHealth program (ECO-EID in SE Asia: Helminthes), a study surveying taeniasis/cysticercosis prevalence using the Kato-Katz technique and a commercial anti-cyst IgG-ELISA kit in a newly defined schistosomiasis endemic area in Cagayan valley, northern Philippines was reported (personnel communication). Residents in the area are known to eat uncooked pork of a local dish "kinilaw". Out of the 1212 stool samples collected from residents aged ≥ 18 years, taeniid eggs were detected in 28 (4%) individuals, but the *s* spp. species was not identified. A subset of 627 participants submitted blood samples. An ELISA kit using cyst fluid as detection antigens defined 218 (35%) of these as antibody positive for cysticercosis. Another community-based study conducted in Leyte, central Philippines using the same ELISA kit revealed a 24.6% of seropositive rate among 497 participants aged 7-30 years old (Xu et al., 2010). These sero-prevalence data warrant the need for a thorough investigation on cysticercosis in the Philippines, even though antibody detection assays might overestimate cysticercosis prevalence due to the cross-reactivity with other *Taenia* spp. infection, and/or other parasitic infections such as *Schistosoma japonicum*, which are highly endemic in the above mentioned two areas (Anantaphruti et al., 2010; Carod et al., 2012; Flisser and Gyorkos, 2007). There is also a need to clarify which tapeworms (*T. solium*, *T. saginata*, *T. asiatica*) are infecting people (Ale et al., 2014; Eom et al., 2009; Ito, 2015; Ito and Budke, 2014; Ito et al., 2014; Jeon et al., 2009).

Vietnam:

A recent review compiling data from the local literature and case reports indicated that human taeniasis was occurring in more than 50 provinces in Vietnam. The prevalence of taeniasis was 0.5-12% in the north of the country, 0.2-2.8% in the middle, 0.3-1.5% in the south, and 3.8-10.1% in the highlands (Van De et al., 2014). Although information on cysticercosis is available at some hospitals across the country in Vietnam, there are limited studies on clear estimation of the burden of the disease in Vietnam. In 2006, Somers et al (2006) reported community-based studies in the northern mountainous province of Bac Kan and the coastal province of Ha Tinh. Among the 303 and 175 participants from the

mountainous and coastal regions, circulating cysticerci antigen positive rate were 5.3% and 0.6%, respectively, by a monoclonal antibody-based sandwich ELISA, indicating active cysticercosis infection prevalence in those rural areas. Kato-Katz stool examination detected 1 and 3 taeniid egg positive participants in the 2 chosen research areas respectively. Among those individuals screened positive for taeniasis/cysticercosis, 14 were further examined with CT and biopsy, which confirmed 1 case of NCC and 5 subcutaneous cysticercosis cases in Bac Kan. A recent study estimated the seroprevalence (Praet et al., 2010b) of cysticercosis in selected epileptic, headache and subcutaneous cyst patient populations living in rural areas of Northern Vietnam is less than 10% (Trung et al., 2013).

Slaughterhouse-based surveys in either Hanoi or the surrounding provinces showed that cysticercosis prevalence in pigs is low between 0.018% and 0.9% (Dorny et al., 2004b). Unfortunately, large-scale, up-to-date prevalence data is still limited despite the fact that human cysticercosis and taeniasis have been found in most of the provinces in Vietnam and hundreds of cases of NCC and subcutaneous cysticercosis have been diagnosed and treated at the referral hospitals (Dorny et al., 2004b; Willingham et al., 2010). Based on local reports (Van De et al., 2014), the infection rate of cysticercosis in pigs was 0.04% at Hanoi slaughterhouses, 0.03-0.31% at provincial slaughterhouses in the north, and 0.9% in provincial slaughterhouses in the southern region of Vietnam.

People's Republic of China:

Cysticercosis/taeniasis is considered as one of the major foodborne parasitic diseases in China and was reported in all provinces, autonomous regions and municipalities (P/A/M) of P. R. China (Ikejima et al., 2005; Ito et al., 2003b; 2013b; Li et al., 2006; Ministry of Health and Diseases, 2005; Xu and Gu, 2010; Yu et al., 1994). There have been surveillance and intervention measures for cysticercosis/taeniasis in endemic areas across the country since the 1970s through government programs of health education and promotion. Comprehensive control consists of chemotherapy for taeniid tapeworm carriers, cysticercosis patients and pigs in the communities and government initiatives for food safety laws, and meat inspections and regulations (Wu et al., 2012). A cysticercosis survey was

also included in the "First Nationwide Investigation of Human Parasites in China" during 1989 to 1992. This national parasitic diseases survey finished in 2004 and disclosed that the prevalence of cysticercosis/taeniasis decreased dramatically compared to the prevalence in 1960 (Xu and Gu, 2010). Government and international funds have continuously supported the community-based surveys of cysticercosis and taeniasis to advance the efforts of disease control since 2004. Sporadically high distribution of taeniasis/cysticercosis foci appear mainly in the southwest of China, such as Yunnan, Guizhou, Guangxi and Sichuan provinces where a fair portion of the residents have the habit of consuming raw or undercooked pork. In 2010, a survey on taeniasis/cysticercosis was conducted in 3 counties of Pu-Er city, Yunnan province where relatively high prevalences were reported before and 50.35% of residents self-reported eating raw pork (Xu et al., 2012). Cyst-fluid crude antigen-specific antibody ELISA (Xu et al., 2010) showed an overall sero-positive rate of 38.61% among the 2,870 participants. Li X (2009) reported a survey on food-borne parasitic diseases and dietary habits in Guangxi during 2002 to 2005. Within 10 of the 109 counties that commonly reported raw meat consumption, 22,772 residents were surveyed with questionnaires regarding raw meat eating habits and history of proglottid discharge. Among them, taeniid egg positive rate was evaluated by Kato-Katz while cysticercosis seroprevalence was determined using cyst-fluid antigen-specific antibody ELISA (Xu et al., 2010). The highest taeniid egg positive rate is 43.3% (151/349) in Rongshui County, while the overall prevalence of taeniasis by detected eggs in stool is 24.8% (range 0 to 43.3%) within the 10 counties investigated. Of note, cysticercosis seropositive rate is relatively low at 2.1% in Rongshui County (12/565) with an average 0.7% seropositive rate for the 10 counties surveyed. In 2007, Li T suggested that human cysticercosis was highly endemic in some regions of Guizhou Province based on a porcine cysticercosis prevalence of 3.7-12.1% in 4,292 pigs owned by the minority ethnic residents in Guizhou by postmortem inspection in 1998 (Li et al., 2007). In Sichuan, a cross-sectional study of human taeniasis/cysticercosis was carried out in 2005 among Tibetan populations in Yajiang County (Li et al., 2006). History of expulsion of *Taenia* spp. proglottids within the previous year was reported by 30.6%

(202/661) of the subjects. Among those participants, 20 (4%) were antibody positive to *T. solium* cyst glycoproteins from a pH 8.1 fraction purified by preparative isoelectric focusing (Ito et al., 1998). A significant higher sero-positive rate of 16.4% (9/55) was observed among people experienced epilepsy than that of 2.5% (11/445) in those without epilepsy episodes. *Taenia* spp. proglottids from 21 individuals were tested by multiplex PCR, and 18 were identified as *T. saginata*, 3 were confirmed as *T. asiatica*, while no *T. solium* tapeworms were detected.

The estimated number of individuals with epilepsy due to NCC in China is 300,000 – 700,000 based on the assumption that 10% of seropositive *T. solium* infection is attributable to NCC in the Chinese population (Coyle et al., 2012; Wu et al., 2013). In a retrospective study detecting specific antibodies for cysticercosis in 2,736 patients suffering CNS diseases who visited the clinic of the Center for Disease Control in Guangxi during the years 2000-2008, an 18.7% cysticercosis seropositive rate was observed among 812 of the patients with a history of seizures compared to the overall seropositive rate of 14.7% in all patients seeking medical care for CNS symptoms of unknown cause (Li et al., 2010).

Taiwan:

Tapeworm infection is very rare in Taiwan except in mountainous areas inhabited by aborigines. Although aborigines traditionally consume uncooked pork and viscera, most documented *Taenia* spp. worms collected from them were reported to be *T. saginata* (Fan, 1988). This issue was clarified later when those worms were identified as actually being the *T. saginata*-like species of *T. asiatica* (Eom and Rim, 1993; Fan et al., 2001; Ito et al., 2003a; 2014; 2015; Simanjuntak et al., 1997). The few cysticercosis cases reported in Taiwan were foreigners (Shih et al., 2010; Yeh and Wu, 2008). However, in recent years, immigration from other Asian countries has increased rapidly, and the number of reports of *T. solium* cases among foreigners living in Taiwan is increasing by literature. There is a risk of an unexpected outbreak of cysticercosis if the *T. solium* life cycle is established by tapeworm carriers from foreign countries among the aborigines who like to eat raw pork and keep the pigs around the household (Yanagida et al., 2012).

Control measures

The spread of human taeniasis/cysticercosis is facilitated by poor hygiene, inadequate sanitation, the use of untreated or partially treated human waste in agriculture, improper food-handling, lack of knowledge concerning the risk of infection while visiting endemic countries, and the consumption of raw or undercooked pork, particularly in/from regions where pigs are raised under poor conditions (Li et al., 2006; Swastika et al., 2012). Importantly, cysticercosis can occur in individuals who do not raise pigs or consume pork (Hira et al., 2004; Schantz et al., 1992). In addition, person-to-person transmission should not be ignored (Gonzalez et al., 2006; Rajshekhar et al., 2003). Control and prevention of *Taenia* spp. infections and cysticercosis should include enhancing sanitation and health education to improve sanitary and food hygiene practices, interventions consisting of human chemotherapy with better diagnostic tools for taeniasis, and porcine chemotherapy and immunization (Gauci et al., 2012). Available information suggests that implementing a single approach to *T. solium* control is insufficient, thus a combination of approaches is needed to ensure sustainable prevention and control (WHO, 2011a).

Diagnosis

Human tapeworm carriers and infected pigs are the only sources of transmission. Rapid diagnosis together with timely treatment in the field is specifically valuable in the endemic areas. Human tapeworm carriers can routinely be diagnosed by detection of proglottids or eggs in feces, or by using more sensitive methods such as the detection of *Taenia* spp. antigens in stools or specific antibodies in serum (Bustos et al., 2012). Unfortunately, these methods come with the caveats of low sensitivity (detection of proglottids) or non-specific indicators of teaniid infection and not specifically *T. solium* infection (detection of eggs), or non-active *T. solium* infection (immunological assays). Nkouawa A reported the field application of a loop-mediated isothermal amplification method (LAMP) for rapid identification of human *Taenia* spp. species, which suggested that this LAMP method (Nkouawa et al, 2009; 2010; 2011;

2012) would be very useful in the field to detect *T. solium* carriers for early and effective treatment. Immunodiagnosis, especially circulating antigen detection (Ag-ELISA) assays are currently preferred for taeniasis/cysticercosis surveillance and monitoring of control programs (Gabriel et al., 2012; WHO, 2011a). However, there is no clear evaluation of the immunodiagnosis without knowing its mechanisms plus its effectiveness for conducting pig surveys (Ito, 2015).

Confirmation of human cysticercosis cases, in particular NCC cases, relies mostly on biopsy (e.g. subcutaneous nodules) and neuroimaging techniques, even though specific immunoblot assays for the diagnosis of human cysticercosis has drastically improved over the past two decades and enzyme-linked immunoelectrophoresis blot (EITB) has provided a reliable immunodiagnostic tool and improved the accuracy of seroprevalence studies (Ito et al., 1998; Rodriguez et al., 2009; Tsang et al., 1989). Recently, Sako Y established a very simple method for purification of diagnostic antigens of *T. solium* from cyst fluid (Sako et al., 2013). The quality of the antigens purified by a cation exchange chromatography appears to be very similar or higher than those prepared using lentil lectin affinity chromatography (Tsang et al., 1989) or preparative isoelectric focusing (Ito, 2015; Ito et al., 1998; 1999; 2002). From a clinical disease management point of view, in the absence of neuroimaging, serological tests, such as EITB or Ag-ELISA, cannot be a standalone diagnostic technique for NCC (Ito, 2013, 2015). Although Ag-ELISA testing has recently been proposed as one of the criteria for NCC diagnosis (Gabriel et al., 2012), it still needs to be evaluated as discussed above.

However, immuno-diagnosis methods are preferred for defining baseline prevalence in the suspected endemic areas (Garcia et al., 2012). When using serology for community-based surveys in Southeast Asia, the use of EITB deserves further consideration due to the findings that EITB may not be sensitive enough in areas where a majority of NCC cases have only a single parenchymal cyst (Prabhakaran et al., 2004). More investigations about serological diagnostic methods are needed. A specific antigen detection method that works well in detecting asymptomatic NCC cases would be highly appreciated, especially in resource-poor Southeast Asian countries.

Immunodiagnosis for detection of human cysticercosis or NCC cases is rather easy by antibody or antigen detection, since *T. solium* is the only species that infects humans by eggs. In contrast, it is difficult for detection of pigs especially in endemic areas in developing countries (Ito, 2015; Ito et al., 2015). Thus far, there is no discussion about the cross-reactive components of *T. solium* in pigs infected with other taeniid species, such as *T. asiatica and T. hydatigena*. Almost all components highly useful for detection of human cysticercosis cases are shared by other taeniid species in pigs. Therefore, further researches on detection markers for the infection of *T. solium* in pigs are needed to develop more reliable and practical screening tests (Swastika et al. in prep).

An alternative but perhaps better idea for detection of humans and pigs infected with cysticerci of *T. solium* is the introduction of a simple tool for detection of species specific DNA, RNA or any other biomarkers such as metabolites using blood, saliva or urine samples. Thus far, there is only a preliminary report on this issue (Almeida et al., 2006).

Treatment and prevention in swine

Interventions focused on pigs will not only control the source of taeniasis transmission but also potentially increase the economic value of the pigs. Preventing pigs from becoming infected with *T. solium* and treating pigs with cysticercosis will offer a financial benefit to the farmers and will potentially lead to increased compliance with other control activities including community-based screening, therapy, and health education (O'Neal et al., 2011). Oxfendazole has proven to be an effective drug for curing pigs by eliminating the cysts and providing resistance to further infection. Educating farmers about the importance of a source management strategy for this infection will help to promote their willingness to spend more on the pigs.

In pig keeping practices, even in rural areas, it is recognized that vaccinations of farm animals can prevent pathogenic infections and therefore improve the commercial value of the pork. Recently, a vaccine for preventing porcine cysticercosis (TSOL18) has been proven to be highly effective against naturally acquired infection with *T. solium* in pigs in several field trials (Assana et al., 2010; Garcia et al.,

2007; Gauci et al., 2012; 2012; Gonzalez et al., 2011; 2012a; Jayashi et al., 2012b; Martinez-Ocana et al., 2011; Pina et al., 2011; Rueda et al., 2011; Verle et al., 2003; Zimic et al., 2011). It will be a great tool for combating cysticercosis (Lightowlers, 2013; WHO, 2011a). Proof of concept for actively eliminating *T. solium* transmission using pig vaccinations has been provided in recent years in endemic areas of Peru and in Cameroon (Assana et al., 2010; Bethony et al., 2011). Application of the porcine cysticercosis vaccine TSOL18 (developed at the University of Melbourne, Australia) together with a single treatment of pigs with oxfendazole has also been shown to completely eliminate transmission of *T. solium* among pigs involved in a field trial in Cameroon (Assana et al., 2010).

In addition, meat inspection of pigs at slaughter is an important public health measure to prevent *T. solium* transmission to humans. Unfortunately, in many of the Southeast Asian countries, national pork inspection guidelines are insufficient in regard to detection of cysticercosis, especially, illegal slaughter occurs often when pigs were suspected of being infected with cysticercosis to avoid economic loss due to confiscation (Praet et al., 2010a). Another risk factor is that meat inspection is usually only effective in detecting heavily infected carcasses and is not quite reliable for detecting lightly infected carcasses being dependent on the expertise of the meat inspector (Geysen et al., 2007). Cysticerci can be confused with sarcocystis, milk spots, hydatid cysts and even unstructured pieces of fat and left over muscle fasciae (Chiesa et al., 2010; Geysen et al., 2007). Recently, PCR has been used for detecting *T. solium* cysticercosis in pigs using the suspected lesion samples (Sreedevi et al., 2012), this may provide a better solution for meat inspection.

Treatment and prevention in humans

Mass treatment of taeniasis is a cost-effective control strategy in taeniasis/cysticercosis endemic areas (Alexander et al., 2011). Praziquantel (PZQ) and niclosamide are considered to be effective anthelminthics to treat human tapeworm carriers (Allan et al., 1997; Pawlowski, 1990, 2006). Additionally, persons with asymptomatic NCC being treated with PZQ for taeniasis or other parasites (e.g. schistosomiasis, fish-borne trematodes) may be at risk for developing symptomatic NCC such as serious

headache or epileptic seizure (Ito et al., 2003a; Pawlowski, 2006; Wandra et al., 2011). The effectiveness of other drugs for treating taeniasis such as the traditional Chinese remedy of pumpkin seeds combined with areca nut extract (Li et al., 2012), and nitazoxanide are being tested in field settings (Lateef et al., 2008).

Treatment of NCC must be individualized at a minimum dosing, based on the location of the lesions, level of disease progress, and the host's immune response. The first line of management usually includes a combination of symptomatic and cysticidal drugs including PZQ and albendazole (Del Brutto, 2012; Takayanagui et al., 2011; Wiwanitkit, 2012), though NCC treatment failure using PZQ has been noted (Koul et al., 1999; Vermund et al., 1986). Recently, attention has been given to the intraventricular form of NCC (IVNCC), which has a rapidly progressive course and is seen in 15-54% of NCC cases (Sinha and Sharma, 2012). The treatment for IVNCC depends on clinical presentation, location within the ventricular system and development stage of the parasite. Albendazole is preferred over PZQ in IVNCC because of its efficacy and absence of drug interactions with corticosteroids and anti-epileptic drugs (del Brutto and Sotelo, 1990; Sotelo et al., 1988). The efficacy of antihelminthic treatment in IVNCC may require further collaborative clinical trials. Endoscopic approaches have recently become a favored treatment option for IVNCC with hydrocephalus (Kelesidis and Thian, 2011; Ramos-Zuniga et al., 2011). The indication for surgical removal should only be considered when serious increased intracranial pressure has occurred due to obstructive hydrocephalus (Wiwanitkit, 2012). Recently, microsurgery has been reported as an option for the management of parenchymal cysticercosis in selected patients (Ou et al., 2012).

Co-infection of multiple helminthes and other parasites is very common in the regions and countries where cysticercosis is endemic. Health systems and services should take into consideration the presence of the different parasites in order to develop effective integrated parasite control programs.

Conclusion and future direction

Cysticercosis/taeniasis remains a neglected zoonosis in most Southeast Asia countries due to the lack of information about its presence and societal impact. Here we provided an overview of the disease endemicity mainly based on literatures published after 2009 (Table 1). Large-scale, community-based surveys on cysticercosis and accurate hospital data collection, as well as distribution maps for countries are urgently needed to better understand the epidemiology of cysticercosis/taeniasis in areas considered at risk in the region (Xiao et al., 2013).

We would like to put forward the following issues into account when considering current cysticercosis/taeniasis status and control measures in Southeast Asia. First, the prevalence of human taeniasis should not be translated into cysticercosis since other teaniid species (e.g. *T. saginata, T. asiatica*) that infect humans may be present in cysticercosis-affected regions. As a matter of fact, so far, *T. asiatica* has been identified in remote areas in most of the Southeast Asian countries including Taiwan, South-central China, Indonesia, Japan (imported), Nepal, South Korea, the Philippines, Thailand and Vietnam(Ale et al., 2014). To our knowledge, only *T. solium* causes human cysticercosis, while the potential of *T. asiatica* to cause human cysticercosis still needs to be clarified(Ito et al., 2015). Second, person-to-person transmission of cysticercosis among family members, neighbors and co-workers accounts for a substantial number of cases and should not be overlooked. Third, while reports using serological data from each country are a great source of information on the present situation of cysticercosis and taeniasis, additional direct evidence by MRI or CT should be obtained on serologically suspected NCC cases. Fourth, serology survey data in pigs should be interpreted with caution given that it often does not distinguish between *T. solium* and *T. hydatigena* and only the former causes porcine cysticercosis. Fifth, control efforts for *T. solium* infections should be integrated with that of schistosomiasis and fish-borne trematode infections (e.g. opisthorchiasis, clonorchiasis) where their endemicity overlaps in Southeast Asia. However, cautions have to be taken when using Praziquantel for treatment, since the drug may elicit seizures within one day among those with asymptomatic cysticercosis (Ito et al., 2013a). Finally, to obtain a clear picture of cysticercosis endemicity in Southeast

Asia, it is imperative to evaluate current serological tools under multi-central evaluation systems with double-blinded testing. Serological work without blind testing should be questioned on its scientific soundness for interpreting the epidemic status of cysticercosis.

In Southeast Asian countries, few countries like China has a government control program in place, or as in Japan, setup a robust disease monitoring system. Continuous efforts are critical to evaluate the disease situation in the region and to continue building the necessary infrastructure for disease control. Taeniasis and cysticercosis control programs should be adopted with consideration toward differences in culture, religion, socio-economic status and level of education.

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Reference:

Adhikari, S., Sathian, B., Koirala, D.P., Rao, K.S., 2013. Profile of children admitted with seizures in a tertiary care hospital of Western Nepal. BMC Pediatr 13, 43.

Agarwal, J.P., 2011. Neurocysticercosis in Nepal and it's global perspective. Kathmandu Univ Med J (KUMJ) 9, 1-2.

Ale, A., Victor, B., Praet, N., Gabriel, S., Speybroeck, N., Dorny, P., Devleesschauwer, B., 2014. Epidemiology and genetic diversity of Taenia asiatica: a systematic review. Parasit Vectors 7, 45.

Alexander, A., John, K.R., Jayaraman, T., Oommen, A., Venkata Raghava, M., Dorny, P., Rajshekhar, V., 2011. Economic implications of three strategies for the control of taeniasis. Trop Med Int Health 16, 1410-1416.

Allan, J.C., Velasquez-Tohom, M., Fletes, C., Torres-Alvarez, R., Lopez-Virula, G., Yurrita, P., Soto de Alfaro, H., Rivera, A., Garcia-Noval, J., 1997. Mass chemotherapy for intestinal Taenia solium infection: effect on prevalence in humans and pigs. Trans R Soc Trop Med Hyg 91, 595-598.

Almeida, C.R., Ojopi, E.P., Nunes, C.M., Machado, L.R., Takayanagui, O.M., Livramento, J.A., Abraham, R., Gattaz, W.F., Vaz, A.J., Dias-Neto, E., 2006. Taenia solium DNA is present in the cerebrospinal fluid of neurocysticercosis patients and can be used for diagnosis. Eur Arch Psychiatry Clin Neurosci 256, 307-310.

Amatya, B.M., Kimula, Y., 1999. Cysticercosis in Nepal: a histopathologic study of sixty-two cases. Am J Surg Pathol 23, 1276-1279.

Anantaphruti, M.T., Okamoto, M., Yoonuan, T., Saguankiat, S., Kusolsuk, T., Sato, M., Sato, M.O., Sako, Y., Waikagul, J., Ito, A., 2010. Molecular and serological survey on taeniasis and cysticercosis in Kanchanaburi Province, Thailand. Parasitol Int 59, 326-330.

Anantaphruti, M.T., Yamasaki, H., Nakao, M., Waikagul, J., Watthanakulpanich, D., Nuamtanong, S., Maipanich, W., Pubampen, S., Sanguankiat, S., Muennoo, C., Nakaya, K., Sato, M.O., Sako, Y., Okamoto, M., Ito, A., 2007. Sympatric occurrence of Taenia solium, T. saginata, and T. asiatica, Thailand. Emerg Infect Dis 13, 1413-1416.

Arambulo, P.V., 3rd, Cabrera, B.D., Tongson, M.S., 1976. Studies on the zoonotic cycle of Taenia saginata taeniasis and cysticercosis in the Philippines. Int J Zoonoses 3, 77-104.

Arasu, K., Khairul, A., Waran, V., 2005. Neurocysticercosis an uncommon intra-cerebral infection in Malaysia. Med J Malaysia 60, 514-516.

Ash, A., Okello, A., Khamlome, B., Inthavong, P., Allen, J., Thompson, R.C., 2015. Controlling Taenia solium and soil transmitted helminths in a northern Lao PDR village: Impact of a triple dose albendazole regime. Acta Trop.

Assana, E., Kyngdon, C.T., Gauci, C.G., Geerts, S., Dorny, P., De Deken, R., Anderson, G.A., Zoli, A.P., Lightowlers, M.W., 2010. Elimination of Taenia solium transmission to pigs in a field trial of the TSOL18 vaccine in Cameroon. Int J Parasitol 40, 515-519.

Atilano, M.A.G., Pena, A.C., 2000. Neurocysticercosis. Phil J Microbiol Infect Dis 29, 41-47.

Azzopardi, L., Quirk, J., 2012. An acquired source of seizures. BMJ 344, e2991.

Bethony, J.M., Cole, R.N., Guo, X., Kamhawi, S., Lightowlers, M.W., Loukas, A., Petri, W., Reed, S., Valenzuela, J.G., Hotez, P.J., 2011. Vaccines to combat the neglected tropical diseases. Immunol Rev 239, 237-270.

Bustos, J.A., Rodriguez, S., Jimenez, J.A., Moyano, L.M., Castillo, Y., Ayvar, V., Allan, J.C., Craig, P.S., Gonzalez, A.E., Gilman, R.H., Tsang, V.C., Garcia, H.H., 2012. Detection of Taenia solium taeniasis coproantigen is an early indicator of treatment failure for taeniasis. Clin Vaccine Immunol 19, 570-573.

Carabin, H., Ndimubanzi, P.C., Budke, C.M., Nguyen, H., Qian, Y., Cowan, L.D., Stoner, J.A., Rainwater, E., Dickey, M., 2011. Clinical manifestations associated with neurocysticercosis: a systematic review. PLoS Negl Trop Dis 5, e1152.

Carod, J.F., Randrianarison, M., Razafimahefa, J., Ramahefarisoa, R.M., Rakotondrazaka, M., Debruyne, M., Dautigny, M., Cazal, P., Andriantseheno, M.L., Charles, E.R., 2012. Evaluation of the performance of 5 commercialized enzyme immunoassays for the detection of Taenia solium antibodies and for the diagnosis of neurocysticercosis. Diagn Microbiol Infect Dis 72, 85-89.

Chai, J.Y., 2013. Human taeniasis in the Republic of Korea: hidden or gone? Korean J Parasitol 51, 9-17.

Chiesa, F., Dalmasso, A., Bellio, A., Martinetti, M., Gili, S., Civera, T., 2010. Development of a biomolecular assay for postmortem diagnosis of Taenia saginata Cysticercosis. Foodborne Pathog Dis 7, 1171-1175.

Cho, J., Jung, B.K., Lim, H., Kim, M.J., Yooyen, T., Lee, D., Eom, K.S., Shin, E.H., Chai, J.Y., 2014. Four cases of Taenia saginata infection with an analysis of COX1 gene. Korean J Parasitol 52, 79-83.

Cho, S.Y., Kim, S.I., Kang, S.Y., Choi, D.Y., Suk, J.S., Choi, K.S., Ha, Y.S., Chung, C.S., Myung, H.J., 1986. Evaluation of enzyme-linked immunosorbent assay in serological diagnosis of human neurocysticercosis using paired samples of serum and cerebrospinal fluid. Kisaengchunghak Chapchi 24, 25-41.

Choi, S.C., Lee, S.Y., Song, H.O., Ryu, J.S., Ahn, M.H., 2014. Parasitic infections based on 320 clinical samples submitted to Hanyang University, Korea (2004-2011). Korean J Parasitol 52, 215-220.

Choudhury, A.A., Conlan, J.V., Racloz, V.N., Reid, S.A., Blacksell, S.D., Fenwick, S.G., Thompson, A.R., Khamlome, B., Vongxay, K., Whittaker, M., 2013. The economic impact of pig-associated parasitic zoonosis in Northern Lao PDR. Ecohealth 10, 54-62.

Chung, J.Y., Yun, D.H., Eom, K.S., Kang, S.Y., Kong, Y., Cho, S.Y., 2002. Taenia solium: identification of specific antibody binding regions of metacestode 10-kDa protein. Exp Parasitol 100, 87-94.

Coker-Vann, M.R., Subianto, D.B., Brown, P., Diwan, A.R., Desowitz, R., Garruto, R.M., Gibbs, C.J., Jr., Gajdusek, D.C., 1981. ELISA antibodies to cysticerci of Taenia solium in human populations in New Guinea, Oceania, and Southeast Asia. Southeast Asian J Trop Med Public Health 12, 499-505.

Conlan, J., Khounsy, S., Inthavong, P., Fenwick, S., Blacksell, S., Thompson, R.C., 2008. A review of taeniasis and cysticercosis in the Lao People's Democratic Republic. Parasitol Int 57, 252-255.

Conlan, J.V., Vongxay, K., Khamlome, B., Dorny, P., Sripa, B., Elliot, A., Blacksell, S.D., Fenwick, S., Thompson, R.C., 2012. A cross-sectional study of Taenia solium in a multiple taeniid-endemic region reveals competition may be protective. Am J Trop Med Hyg 87, 281-291.

Coyle, C.M., Mahanty, S., Zunt, J.R., Wallin, M.T., Cantey, P.T., White, A.C., Jr., O'Neal, S.E., Serpa, J.A., Southern, P.M., Wilkins, P., McCarthy, A.E., Higgs, E.S., Nash, T.E., 2012. Neurocysticercosis: neglected but not forgotten. PLoS Negl Trop Dis 6, e1500.

Cruz, A.C., 1991. Treatment of human taeniasis in the Philippines: a review. Southeast Asian J Trop Med Public Health 22 Suppl, 271-274.

de Leon, W.U., 2005. Taeniasis and Cysticercosis in the Philippines. Federation of Asian Parasitologists, Asian Parasitology Series Monograph. Volume 2. Taeniasis/Cysticercosis and Echinococcosis in Asia. Chiba, Japan.

Deckers, N., Dorny, P., 2010. Immunodiagnosis of Taenia solium taeniosis/cysticercosis. Trends Parasitol 26, 137-144.

Del Brutto, O.H., 2012. Neurocysticercosis: a review. The Sci World J 2012, ID159821.

Del Brutto, O.H., Garcia, H.H., 2012. Neurocysticercosis in nonendemic countries: time for a reappraisal. Neuroepidemiology 39, 145-146.

del Brutto, O.H., Sotelo, J., 1990. Albendazole therapy for subarachnoid and ventricular cysticercosis. Case report. J Neurosurg 72, 816-817.

Devleesschauwer, B., Aryal, A., Joshi, D.D., Rijal, S., Sherchand, J.B., Praet, N., Speybroeck, N., Duchateau, L., Vercruysse, J., Dorny, P., 2012. Epidemiology of Taenia solium in Nepal: is it influenced by the social characteristics of the population and the presence of Taenia asiatica? Trop Med Int Health 17, 1019-1022.

Devleesschauwer, B., Aryal, A., Tharmalingam, J., Joshi, D.D., Rijal, S., Speybroeck, N., Gabriel, S., Victor, B., Dorny, P., 2013a. Complexities in using sentinel pigs to study Taenia solium transmission dynamics under field conditions. Vet Parasitol 193, 172-178.

Devleesschauwer, B., Pruvot, M., Joshi, D.D., De Craeye, S., Jennes, M., Ale, A., Welinski, A., Lama, S., Aryal, A., Victor, B., Duchateau, L., Speybroeck, N., Vercruysse, J., Dorny, P., 2013b. Seroprevalence of zoonotic parasites in pigs slaughtered in the Kathmandu Valley of Nepal. Vector Borne Zoonotic Dis 13, 872-876.

Dissanaike, A.S., 2002. Parasitic zoonoses in Sri Lanka: an update. Ceylon Med J 47, 46-47.

Dorny, P., Phiri, I.K., Vercruysse, J., Gabriel, S., Willingham, A.L., 3rd, Brandt, J., Victor, B., Speybroeck, N., Berkvens, D., 2004a. A Bayesian approach for estimating values for prevalence and diagnostic test characteristics of porcine cysticercosis. Int J Parasitol 34, 569-576.

Dorny, P., Somers, R., Dang, T.C.T., Nguyen, V.K., Vercruysse, J., 2004b. Cysticercosis in Camboida, Lao PDR and Vietnam. Southeast Asian J Trop Med Public Health 35 Suppl 1, 223-226.

Eom, K.S., Jeon, H.K., Rim, H.J., 2009. Geographical distribution of Taenia asiatica and related species. Korean J Parasitol 47 Suppl, S115-124.

Eom, K.S., Rim, H.J., 1993. Morphologic descriptions of Taenia asiatica sp. n. Korean J Parasitol 31, 1-6.

Fan, P.C., 1988. Taiwan taenia and taeniasis. Parasitol Today 4, 86-88.

Fan, P.C., Chung, W.C., Chen, E.R., 2001. [Parasitic infections among the aborigines in Taiwan with special emphasis on Taeniasis asiatica]. Kaohsiung J Med Sci 17, 1-15.

Flisser, A., Gyorkos, T.W., 2007. Contribution of immunodiagnostic tests to epidemiological/intervention studies of cysticercosis/taeniosis in Mexico. Parasite Immunol 29, 637-649.

Gabriel, S., Blocher, J., Dorny, P., Abatih, E.N., Schmutzhard, E., Ombay, M., Mathias, B., Winkler, A.S., 2012. Added value of antigen ELISA in the diagnosis of neurocysticercosis in resource poor settings. PLoS Negl Trop Dis 6, e1851.

Garcia, H.H., Gonzalez, A.E., Del Brutto, O.H., Tsang, V.C., Llanos-Zavalaga, F., Gonzalvez, G., Romero, J., Gilman, R.H., 2007. Strategies for the elimination of taeniasis/cysticercosis. J Neurol Sci 262, 153-157.

Garcia, H.H., Rodriguez, S., Gilman, R.H., Gonzalez, A.E., Tsang, V.C., 2012. Neurocysticercosis: is serology useful in the absence of brain imaging? Trop Med Int Health 17, 1014-1018.

Garrison, P.E., 1907. A preliminary report upon the scientific identity of cestode parasites of man in the Philippines Islands, with a description of a new species of Taenia. Philippine J Sci, B2, 537-550.

Gauci, C.G., Jayashi, C.M., Gonzalez, A.E., Lackenby, J., Lightowlers, M.W., 2012. Protection of pigs against Taenia solium cysticercosis by immunization with novel recombinant antigens. Vaccine 30, 3824-3828.

Geysen, D., Kanobana, K., Victor, B., Rodriguez-Hidalgo, R., De Borchgrave, J., Brandt, J., Dorny, P., 2007. Validation of meat inspection results for Taenia saginata cysticercosis by PCR-restriction fragment length polymorphism. J Food Prot 70, 236-240.

Gonzalez, A.E., Bustos, J.A., Jimenez, J.A., Rodriguez, M.L., Ramirez, M.G., Gilman, R.H., Garcia, H.H., 2012. Efficacy of diverse antiparasitic treatments for cysticercosis in the pig model. Am J Trop Med Hyg 87, 292-296.

Gonzalez, A.E., Lopez-Urbina, T., Tsang, B., Gavidia, C., Garcia, H.H., Silva, M.E., Ramos, D.D., Manzanedo, R., Sanchez-Hidalgo, L., Gilman, R.H., Tsang, V.C., cysticercosis working group in, P., 2006. Transmission dynamics of Taenia solium and potential for pig-to-pig transmission. Parasitol Int 55 Suppl, S131-135.

Gonzalez, L.M., Ramiro, R., Garcia, L., Parkhouse, R.M., McManus, D.P., Garate, T., 2011. Genetic variability of the 18 kDa/HP6 protective antigen in Taenia saginata and Taenia asiatica: implications for vaccine development. Mol Biochem Parasitol 176, 131-134.

Hira, P.R., Francis, I., Abdella, N.A., Gupta, R., Ai-Ali, F.M., Grover, S., Khalid, N., Abdeen, S., Iqbal, J., Wilson, M., Tsang, V.C., 2004. Cysticercosis: imported and autochthonous infections in Kuwait. Trans R Soc Trop Med Hyg 98, 233-239.

Hotez, P.J., Bottazzi, M.E., Franco-Paredes, C., Ault, S.K., Periago, M.R., 2008. The neglected tropical diseases of Latin America and the Caribbean: a review of disease burden and distribution and a roadmap for control and elimination. PLoS Negl Trop Dis 2, e300.

Ikejima, T., Piao, Z.X., Sako, Y., Sato, M.O., Bao, S., Si, R., Yu, F., Zhang, C.L., Nakao, M., Yamasaki, H., Nakaya, K., Kanazawa, T., Ito, A., 2005. Evaluation of clinical and serological data from Taenia solium cysticercosis patients in eastern Inner Mongolia Autonomous Region, China. Trans R Soc Trop Med Hyg 99, 625-630.

Ito, A., 2013. Nothing is perfect! Trouble-shooting in immunological and molecular studies of cestode infections. Parasitology 140, 1551-1565.

Ito, A., 2015. Basic and applied problems in developmental biology and immunobiology of cestode infections: Hymenolepis, Taenia and Echinococcus. Parasite Immunol 37, 53-69.

Ito, A., Budke, C.M., 2014. Culinary delights and travel? A review of zoonotic cestodiases and metacestodiases. Travel Med Infect Dis 12, 582-591.

Ito, A., Li, T., Chen, X., Long, C., Yanagida, T., Nakao, M., Sako, Y., Okamoto, M., Wu, Y., Raoul, F., Giraudoux, P., Craig, P.S., 2013a. Mini review on chemotherapy of taeniasis and cysticercosis due to Taenia solium in Asia, and a case report with 20 tapeworms in China. Trop Biomed 30, 164-173.

Ito, A., Nakao, M., Wandra, T., 2003a. Human Taeniasis and cysticercosis in Asia. Lancet 362, 1918-1920.

Ito, A., Okamoto, M., Li, T., Wandra, T., Dharmawan, N.S., Swastika, K.I., Dekumyoy, P., Kusolsuk, T., Davvajav, A., Davaasuren, A., Dorjsuren, T., Mekonnen, S.M., Negasi, Z.H., Yanagida, T., Sako, Y., Nakao, M.,

Nakaya, K., Lavikainen, A.J., Nkouawa, A., Mohammadzadeh, T., 2011. The first workshop towards the control of cestode zoonoses in Asia and Africa. Parasit Vectors 4, 114.

Ito, A., Okamoto, M., Wandra, T., Wibisono, H., Anantaphruti, M.T., Waikagul, J., Li, T., Qiu, L., 2007. The present situation of taeniasis and cysticercosis in Asia and the Pacific. Southeast Asian J Trop Med Public Health 38 Suppl 1, 115-118.

Ito, A., Plancarte, A., Ma, L., Kong, Y., Flisser, A., Cho, S.Y., Liu, Y.H., Kamhawi, S., Lightowlers, M.W., Schantz, P.M., 1998. Novel antigens for neurocysticercosis: simple method for preparation and evaluation for serodiagnosis. Am J Trop Med Hyg 59, 291-294.

Ito, A., Plancarte, A., Nakao, M., Nakaya, K., Ikejima, T., Piao, Z.X., Kanazawa, T., Margono, S.S., 1999. ELISA and immunoblot using purified glycoproteins for serodiagnosis of cysticercosis in pigs naturally infected with Taenia solium. J Helminthol 73, 363-365.

Ito, A., Putra, M.I., Subahar, R., Sato, M.O., Okamoto, M., Sako, Y., Nakao, M., Yamasaki, H., Nakaya, K., Craig, P.S., Margono, S.S., 2002. Dogs as alternative intermediate hosts of Taenia solium in Papua (Irian Jaya), Indonesia confirmed by highly specific ELISA and immunoblot using native and recombinant antigens and mitochondrial DNA analysis. J Helminthol 76, 311-314.

Ito, A., Urbani, C., Jiamin, Q., Vuitton, D.A., Dongchuan, Q., Heath, D.D., Craig, P.S., Zheng, F., Schantz, P.M., 2003b. Control of echinococcosis and cysticercosis: a public health challenge to international cooperation in China. Acta Trop 86, 3-17.

Ito, A., Wandra, T., Li, T., Dekumyoy, P., Nkouawa, A., Okamoto, M., Budke, C.M., 2014. The present situation of human taeniases and cysticercosis in Asia. Recent Pat Antiinfect Drug Discov 9, 173-185.

Ito, A., Wandra, T., Yamasaki, H., Nakao, M., Sako, Y., Nakaya, K., Margono, S.S., Suroso, T., Gauci, C., Lightowlers, M.W., 2004. Cysticercosis/taeniasis in Asia and the Pacific. Vector Borne Zoonotic Dis 4, 95-107.

Ito, A., Yanagida, T., Nakao, M., 2015. Recent advances and perspectives in molecular epidemiology of Taenia solium cysticercosis. Infect Genet Evol doi: 10.1016/j.meegid.2015.06.022. [Epub ahead of print].

Ito, A., Zhou, X.N., Craig, P.S., Giraudoux, P., 2013b. Control of cestode zoonoses in Asia: role of basic and applied science. Preface. Parasitology 140, 1547-1550.

Jayashi, C.M., Gonzalez, A.E., Castillo Neyra, R., Kyngdon, C.T., Gauci, C.G., Lightowlers, M.W., 2012a. Characterisation of antibody responses in pigs induced by recombinant oncosphere antigens from Taenia solium. Vaccine.

Jayashi, C.M., Kyngdon, C.T., Gauci, C.G., Gonzalez, A.E., Lightowlers, M.W., 2012b. Successful immunization of naturally reared pigs against porcine cysticercosis with a recombinant oncosphere antigen vaccine. Vet Parasitol 188, 261-267.

Jeon, H.K., Chai, J.Y., Kong, Y., Waikagul, J., Insisiengmay, B., Rim, H.J., Eom, K.S., 2009. Differential diagnosis of Taenia asiatica using multiplex PCR. Exp Parasitol 121, 151-156.

Jeon, H.K., Yong, T.S., Sohn, W.M., Chai, J.Y., Hong, S.J., Han, E.T., Jeong, H.G., Chhakda, T., Sinuon, M., Socheat, D., Eom, K.S., 2011. Molecular identification of Taenia tapeworms by Cox1 gene in Koh Kong, Cambodia. Korean J Parasitol 49, 195-197.

Jeon, H.K., Yong, T.S., Sohn, W.M., Chai, J.Y., Min, D.Y., Rim, H.J., Insisiengmay, B., Eom, K.S., 2013. Human neurocysticercosis case and an endemic focus of Taenia solium in Lao PDR. Korean J Parasitol 51, 599-602.

Juyal, P.D., Sharma, R., Singh, N.K., Singh, G., 2008. Epidemiology and Control Strategies Against Cysticercosis (due to Taenia solium) with Special Reference to Swine and Human in Asia. J Vet Anim Sci 1, 1-10.

Kelesidis, T., Thian, N., 2011. Multiple intraventricular neurocysticercal cysts treated with endoscopy without antiparasitic therapy. Am J Trop Med Hyg 85, 1-2.

Kim, S.W., Wang, H.S., Ju, C.I., Kim, D.M., 2014. Acute hydrocephalus caused by intraspinal neurocysticercosis: case report. BMC Res Notes 7, 2.

Kobayashi, K., Nakamura-Uchiyama, F., Nishiguchi, T., Isoda, K., Kokubo, Y., Ando, K., Katurahara, M., Sako, Y., Yanagida, T., Ito, A., Iwabuchi, S., Ohnishi, K., 2013. Rare case of disseminated cysticercosis and taeniasis in a Japanese traveler after returning from India. Am J Trop Med Hyg 89, 58-62.

Koul, P.A., Waheed, A., Hayat, M., Sofi, B.A., 1999. Praziquantel in niclosamide-resistant Taenia saginata infection. Scand J Infect Dis 31, 603-604.

Lateef, M., Zargar, S.A., Khan, A.R., Nazir, M., Shoukat, A., 2008. Successful treatment of niclosamide- and praziquantel-resistant beef tapeworm infection with nitazoxanide. Int J Infect Dis 12, 80-82.

Lee, E.G., Bae, Y.A., Jeong, Y.T., Chung, J.Y., Je, E.Y., Kim, S.H., Na, B.K., Ju, J.W., Kim, T.S., Ma, L., Cho, S.Y., Kong, Y., 2005a. Proteomic analysis of a 120 kDa protein complex in cyst fluid of Taenia solium metacestode and preliminary evaluation of its value for the serodiagnosis of neurocysticercosis. Parasitology 131, 867-879.

Lee, E.G., Lee, M.Y., Chung, J.Y., Je, E.Y., Bae, Y.A., Na, B.K., Kim, T.S., Eom, K.S., Cho, S.Y., Kong, Y., 2005b. Feasibility of baculovirus-expressed recombinant 10-kDa antigen in the serodiagnosis of Taenia solium neurocysticercosis. Trans R Soc Trop Med Hyg 99, 919-926.

Lee, M.K., Hong, S.J., Kim, H.R., 2010. Seroprevalence of tissue invading parasitic infections diagnosed by ELISA in Korea. J Korean Med Sci 25, 1272-1276.

Li, S.L., Xu, H.B., Yang, Y.C., Su, A.R., Zhang, W.W., Wan, X.L., Zhang, H.M., 2010. [Survey on Cysticercosis cellulosase in fection in patients with center nerve system disease and epidemiological analysis of Cysticercosis in Guangxi]. Journal of Tropical Diseases and Parasitology 8, 135-136.

Li, T., Craig, P.S., Ito, A., Chen, X., Qiu, D., Qiu, J., Sato, M.O., Wandra, T., Bradshaw, H., Li, L., Yang, Y., Wang, Q., 2006. Taeniasis/cysticercosis in a Tibetan population in Sichuan Province, China. Acta Trop 100, 223-231.

Li, T., Ito, A., Chen, X., Long, C., Okamoto, M., Raoul, F., Giraudoux, P., Yanagida, T., Nakao, M., Sako, Y., Xiao, N., Craig, P.S., 2012. Usefulness of pumpkin seeds combined with areca nut extract in community-based treatment of human taeniasis in northwest Sichuan Province, China. Acta Trop 124, 152-157.

Li, T., Ito, A., Craig, P.S., Chen, X., Qiu, D., Zhou, X., Xiao, N., Qiu, J., 2007. Taeniasis/cysticercosis in China. Southeast Asian J Trop Med Public Health 38 Suppl 1, 131-139.

Li, X.M., Ouyang, Y., Yang, Y.C., Lin, R., Xu, H.B., Xie, Z.Y., Li, S.L., Shang, S.M., 2009. [Distribution of food-borne parasitic diseases and dietary habits in human population in Guangxi]. Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi 27, 151-155.

Lightowlers, M.W., 2013. Control of Taenia solium taeniasis/cysticercosis: past practices and new possibilities. Parasitology 140, 1566-1577.

Lustigman, S., Prichard, R.K., Gazzinelli, A., Grant, W.N., Boatin, B.A., McCarthy, J.S., Basanez, M.G., 2012. A research agenda for helminth diseases of humans: the problem of helminthiases. PLoS Negl Trop Dis 6, e1582.

Margono, S.S., Wandra, T., Swasono, M.F., Murni, S., Craig, P.S., Ito, A., 2006. Taeniasis/cysticercosis in Papua (Irian Jaya), Indonesia. Parasitol Int 55 Suppl, S143-148.

Martinez-Ocana, J., Romero-Valdovinos, M., de Kaminsky, R.G., Maravilla, P., Flisser, A., 2011. Immunolocalization of TSOL18 and TSOL45-1A, the successful protective peptides against porcine cysticercosis, in Taenia solium oncospheres. Parasit Vectors 4, 3.

Ministry of Health, C., Diseases, C.O.o.t.N.S.o.t.I.H.P., 2005. [A national survey on current status of the important parasitic diseases in human population]. Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi 23, 332-340.

Montano, S.M., Villaran, M.V., Ylquimiche, L., Figueroa, J.J., Rodriguez, S., Bautista, C.T., Gonzalez, A.E., Tsang, V.C., Gilman, R.H., Garcia, H.H., 2005. Neurocysticercosis: association between seizures, serology, and brain CT in rural Peru. Neurology 65, 229-233.

Moyano, L.M., Saito, M., Montano, S.M., Gonzalvez, G., Olaya, S., Ayvar, V., Gonzalez, I., Larrauri, L., Tsang, V.C., Llanos, F., Rodriguez, S., Gonzalez, A.E., Gilman, R.H., Garcia, H.H., Cysticercosis Working Group in, P., 2014. Neurocysticercosis as a cause of epilepsy and seizures in two community-based studies in a cysticercosis-endemic region in Peru. PLoS Negl Trop Dis 8, e2692.

Nakajima, M., Tashima, K., Hirano, T., Nakamura-Uchiyama, F., Nawa, Y., Uchino, M., 2002. [A case of neurocysticercosis suggestive of a reinfection, 20 years after the initial onset]. Rinsho Shinkeigaku 42, 18-23.

Ndimubanzi, P.C., Carabin, H., Budke, C.M., Nguyen, H., Qian, Y.J., Rainwater, E., Dickey, M., Reynolds, S., Stoner, J.A., 2010. A systematic review of the frequency of neurocyticercosis with a focus on people with epilepsy. PLoS Negl Trop Dis 4, e870.

Noor Azian, M.Y., Hakim, S.L., Sumiati, A., Norhafizah, M., 2006. Seroprevalence of cysticercosis in a rural village of Ranau, Sabah, Malaysia. Southeast Asian J Trop Med Public Health 37, 58-61.

Nor Zainura, Z., Barkeh, H.J., Wong, J.S., Muhaya, M., 2005. A rare case of subretinal cysticercosis. Med J Malaysia 60, 650-652.

O'Neal, S., Winthrop, K., Gonzalez, A., 2011. Cysticercosis control: bringing advances to the field. J Glob Infect Dis 3, 156-160.

O'Neal, S.E., Townes, J.M., Wilkins, P.P., Noh, J.C., Lee, D., Rodriguez, S., Garcia, H.H., Stauffer, W.M., 2012. Seroprevalence of antibodies against Taenia solium cysticerci among refugees resettled in United States. Emerg Infect Dis 18, 431-438.

Okello, A., Ash, A., Keokhamphet, C., Hobbs, E., Khamlome, B., Dorny, P., Thomas, L., Allen, J., 2014. Investigating a hyper-endemic focus of Taenia solium in northern Lao PDR. Parasit Vectors 7, 134.

Ou, S.W., Wang, J., Wang, Y.J., Tao, J., Li, X.G., 2012. Microsurgical management of cerebral parenchymal cysticercosis. Clin Neurol Neurosurg 114, 385-388.

Pant, B., Devleesschauwer, B., Shrestha, P., Shrestha, I., Praet, N., Dorny, P., 2011. Intraventricular Taenia solium neurocysticercosis: a report of three cases. J Nepal Med Assoc 51, 192-195.

Pawlowski, Z.S., 1990. Efficacy of low doses of praziquantel in taeniasis. Acta Trop 48, 83-88.

Pawlowski, Z.S., 2006. Role of chemotherapy of taeniasis in prevention of neurocysticercosis. Parasitol Int 55 Suppl, S105-109.

Pina, R., Gutierrez, A.H., Gilman, R.H., Rueda, D., Sifuentes, C., Flores, M., Sheen, P., Rodriguez, S., Garcia, H.H., Zimic, M., 2011. A dot-ELISA using a partially purified cathepsin-L-like protein fraction from Taenia solium cysticerci, for the diagnosis of human neurocysticercosis. Ann Trop Med Parasitol 105, 311-318.

Prabhakaran, V., Rajshekhar, V., Murrell, K.D., Oommen, A., 2004. Taenia solium metacestode glycoproteins as diagnostic antigens for solitary cysticercus granuloma in Indian patients. Trans R Soc Trop Med Hyg 98, 478-484.

Praet, N., Kanobana, K., Kabwe, C., Maketa, V., Lukanu, P., Lutumba, P., Polman, K., Matondo, P., Speybroeck, N., Dorny, P., Sumbu, J., 2010a. Taenia solium cysticercosis in the Democratic Republic of Congo: how does pork trade affect the transmission of the parasite? PLoS Negl Trop Dis 4, e817.

Praet, N., Speybroeck, N., Rodriguez-Hidalgo, R., Benitez-Ortiz, W., Berkvens, D., Brandt, J., Saegerman, C., Dorny, P., 2010b. Age-related infection and transmission patterns of human cysticercosis. Int J Parasitol 40, 85-90.

Rajshekhar, V., Joshi, D.D., Doanh, N.Q., van De, N., Xiaonong, Z., 2003. Taenia solium taeniosis/cysticercosis in Asia: epidemiology, impact and issues. Acta Trop 87, 53-60.

Ramos-Zuniga, R., de La Cruz-Ramirez, J., Casillas-Espinosa, P.M., Sanchez-Prieto, J.A., Lopez-Hernandez, M.D., 2011. "Full moon" endoscopic sign in intraventricular neurocysticercosis. Minim Invasive Neurosurg 54, 90-94.

Rodriguez, S., Dorny, P., Tsang, V.C., Pretell, E.J., Brandt, J., Lescano, A.G., Gonzalez, A.E., Gilman, R.H., Garcia, H.H., 2009. Detection of Taenia solium antigens and anti-T. solium antibodies in paired serum and cerebrospinal fluid samples from patients with intraparenchymal or extraparenchymal neurocysticercosis. J Infect Dis 199, 1345-1352.

Rueda, A., Sifuentes, C., Gilman, R.H., Gutierrez, A.H., Pina, R., Chile, N., Carrasco, S., Larson, S., Mayta, H., Verastegui, M., Rodriguez, S., Gutierrez-Correa, M., Garcia, H.H., Sheen, P., Zimic, M., 2011. TsAg5, a Taenia solium cysticercus protein with a marginal trypsin-like activity in the diagnosis of human neurocysticercosis. Mol Biochem Parasitol 180, 115-119.

Sahu, P.S., Ito, A., 2015. Solitary cysticercosis in eye: Literature review and a hypothesis on transmission of infection. J Ocular Dis Therapeutics 3. In press.

Sako, Y., Itoh, S., Okamoto, M., Nakaya, K., Ito, A., 2013. Simple and reliable preparation of immunodiagnostic antigens for Taenia solium cysticercosis. Parasitology 140, 1589-1594.

Sako, Y., Nakao, M., Ikejima, T., Piao, X.Z., Nakaya, K., Ito, A., 2000. Molecular characterization and diagnostic value of Taenia solium low-molecular-weight antigen genes. J Clin Microbiol 38, 4439-4444.

Salim, L., Ang, A., Handali, S., Tsang, V.C., 2009. Seroepidemiologic survey of cysticercosis-taeniasis in four central highland districts of Papua, Indonesia. Am J Trop Med Hyg 80, 384-388.

Sato, M.O., Sako, Y., Nakao, M., Yamasaki, H., Nakaya, K., Ito, A., 2006. Evaluation of purified Taenia solium glycoproteins and recombinant antigens in the serologic detection of human and swine cysticercosis. J Infect Dis 194, 1783-1790.

Sayasone, S., Vonghajack, Y., Vanmany, M., Rasphone, O., Tesana, S., Utzinger, J., Akkhavong, K., Odermatt, P., 2009. Diversity of human intestinal helminthiasis in Lao PDR. Trans R Soc Trop Med Hyg 103, 247-254.

Schantz, P.M., Moore, A.C., Munoz, J.L., Hartman, B.J., Schaefer, J.A., Aron, A.M., Persaud, D., Sarti, E., Wilson, M., Flisser, A., 1992. Neurocysticercosis in an Orthodox Jewish community in New York City. N Engl J Med 327, 692-695.

Shih, Y.C., Chen, C.M., Huang, Y.H., Liao, C.W., Fan, C.K., Yang, C.H., 2010. Subcutaneous cysticercosis diagnosed by mitochondrial DNA analysis. Int J Dermatol 49, 672-675.

Shin, S.H., Hwang, B.W., Lee, S.J., Lee, S.H., 2012. Primary extensive spinal subarachnoid cysticercosis. Spine (Phila Pa 1976) 37, E1221-1224.

Simanjuntak, G.M., Margono, S.S., Okamoto, M., Ito, A., 1997. Taeniasis/cysticercosis in Indonesia as an emerging disease. Parasitology Today 13, 321-323.

Singh, G., Kaushal, V., Ram, S., Kaushal, R.K., Dhanuka, A.K., Khurana, S., 1999. Cysticercus immunoblot assay in patients with single, small enhancing lesions and multilesional neurocysticercosis. J Assoc Physicians India 47, 476-479.

Singh, G., Prabhakar, S., Ito, A., Cho, S.Y., Qiu, D.C., 2002. Taenia solium taeniasis and cysticercosis in Asia, Taenia solium Cysticercosis: from basic to clinical science. CABI Publishing, Oxon, UK, pp. 111-127.

Sinha, S., Sharma, B.S., 2012. Intraventricular neurocysticercosis: a review of current status and management issues. Br J Neurosurg 26, 305-309.

Somers, R., Dorny, P., Nguyen, V.K., Dang, T.C., Goddeeris, B., Craig, P.S., Vercruysse, J., 2006. Taenia solium taeniasis and cysticercosis in three communities in north Vietnam. Trop Med Int Health 11, 65-72.

Sotelo, J., Escobedo, F., Penagos, P., 1988. Albendazole vs praziquantel for therapy for neurocysticercosis. A controlled trial. Arch Neurol 45, 532-534.

Sreedevi, C., Hafeez, M., Kumar, P.A., Rayulu, V.C., Subramanyam, K.V., Sudhakar, K., 2012. PCR test for detecting Taenia solium cysticercosis in pig carcasses. Trop Anim Health Prod 44, 95-99.

Subahar, R., Hamid, A., Purba, W., Wandra, T., Karma, C., Sako, Y., Margono, S.S., Craig, P.S., Ito, A., 2001. Taenia solium infection in Irian Jaya (west Papua), Indonesia: a pilot serological survey of human and porcine cysticercosis in Jayawijaya district. Trans R Soc Trop Med Hyg 95, 388-390.

Swastika, K., Dewiyani, C.I., Yanagida, T., Sako, Y., Sudarmaja, M., Sutisna, P., Wandra, T., Dharmawan, N.S., Nakaya, K., Okamoto, M., Ito, A., 2012. An ocular cysticercosis in Bali, Indonesia caused by Taenia solium Asian genotype. Parasitol Int 61, 378-380.

Takayanagui, O.M., Odashima, N.S., Bonato, P.S., Lima, J.E., Lanchote, V.L., 2011. Medical management of neurocysticercosis. Expert Opin Pharmacother 12, 2845-2856.

Torgerson, P.R., Macpherson, C.N., 2011. The socioeconomic burden of parasitic zoonoses: global trends. Vet Parasitol 182, 79-95.

Trung, D.D., Praet, N., Cam, T.D., Lam, B.V., Manh, H.N., Gabriel, S., Dorny, P., 2013. Assessing the burden of human cysticercosis in Vietnam. Trop Med Int Health 18, 352-356.

Tsang, V.C., Brand, J.A., Boyer, A.E., 1989. An enzyme-linked immunoelectrotransfer blot assay and glycoprotein antigens for diagnosing human cysticercosis (Taenia solium). J Infect Dis 159, 50-59.

Van De, N., Le, T.H., Lien, P.T., Eom, K.S., 2014. Current status of taeniasis and cysticercosis in Vietnam. Korean J Parasitol 52, 125-129.

Verle, P., Kongs, A., De, N.V., Thieu, N.Q., Depraetere, K., Kim, H.T., Dorny, P., 2003. Prevalence of intestinal parasitic infections in northern Vietnam. Trop Med Int Health 8, 961-964.

Vermund, S.H., MacLeod, S., Goldstein, R.G., 1986. Taeniasis unresponsive to a single dose of niclosamide: case report of persistent infection with Taenia saginata and a review of therapy. Rev Infect Dis 8, 423-426.

Waikagul, J., Dekumyoy, P., Anantaphruti, M.T., 2006. Taeniasis, cysticercosis and echinococcosis in Thailand. Parasitol Int 55 Suppl, S175-180.

Wandra, T., Ito, A., Swastika, K., Dharmawan, N.S., Sako, Y., Okamoto, M., 2013. Taeniases and cysticercosis in Indonesia: past and present situations. Parasitology 140, 1608-1616.

Wandra, T., Margono, S.S., Gafar, M.S., Saragih, J.M., Sutisna, P., Sudewi, A.A.R., Depary, A.A., Yulfi, H., Darla, D.M., Okamoto, M., Sato, M.O., Sako, Y., Nakao, M., Nakaya, K., Craig, P.S., Ito, A., 2007. Current Situation of Taeniasis and Cysticercosis in Indonesia Trop Med Health 35, 323-328.

Wandra, T., Sudewi, A.A., Swastika, I.K., Sutisna, P., Dharmawan, N.S., Yulfi, H., Darlan, D.M., Kapti, I.N., Samaan, G., Sato, M.O., Okamoto, M., Sako, Y., Ito, A., 2011. Taeniasis/cysticercosis in Bali, Indonesia. Southeast Asian J Trop Med Public Health 42, 793-802.

Wandra, T., Swastika, K., Dharmawan, N.S., Purba, I.E., Sudarmaja, I.M., Yoshida, T., Sako, Y., Okamoto, M., Eka Diarthini, N.L., Sri Laksemi, D.A., Yanagida, T., Nakao, M., Ito, A., 2015. The present situation and towards the prevention and control of neurocysticercosis on the tropical island, Bali, Indonesia. Parasit Vectors 8, 148.

WHO, 2011a. Report of the WHO Expert Consultation on Food-Borne Trematode Infections and

Taeniasis/Cysticercosis., Vientiane, Lao People's Democratic Republic, 12–16 October 2009. Geneva, World Health Organization.

WHO, 2011b. Working to overcome the global impact of neglected tropical diseases - Summary. Wkly Epidemiol Rec 86, 113-120.

WHO, 2013. Sustaining the drive to overcome the global impact of neglected tropical diseases: second WHO report on neglected diseases. Geneva, World Health Organization., in: Crompton, D.W. (Ed.). World Health Organization, p. 153.

Willingham, A.L., 3rd, Wu, H.W., Conlan, J., Satrija, F., 2010. Combating Taenia solium cysticercosis in Southeast Asia an opportunity for improving human health and livestock production. Adv Parasitol 72, 235-266.

Wiwanitkit, S., Wiwanitkit, V., 2015. Racemose cysticercosis: A summary of 5 reported Thai cases. J Neurosci Rural Pract 6, 451.

Wiwanitkit, V., 2012. Microsurgery for cerebral cysticercosis. Clin Neurol Neurosurg 114, 1117.

Wu, W., Jia, F., Wang, W., Huang, Y., Huang, Y., 2013. Antiparasitic treatment of cerebral cysticercosis: lessons and experiences from China. Parasitol Res 112, 2879-2890.

Wu, W., Qian, X., Huang, Y., Hong, Q., 2012. A review of the control of clonorchiasis sinensis and Taenia solium taeniasis/cysticercosis in China. Parasitol Res 111, 1879-1884.

Xiao, N., Yao, J.W., Ding, W., Giraudoux, P., Craig, P.S., Ito, A., 2013. Priorities for research and control of cestode zoonoses in Asia. Infect Dis Poverty 2, 16.

Xu, A., Gu, J., 2010. [The current situation and the prevalenct trend of cysticercosis in China]. China Tropical Medicine 10, 239-240.

Xu, A., Wang, L., Zhao, G., Wu, S., Jin, Q., Gu, J., 2012. [Epidemiological survey of taeniasis/cysticercosis in Puer area of Yuannan Province]. China Tropical Medicine 12, 1031-1032.

Xu, J.M., Acosta, L.P., Hou, M., Manalo, D.L., Jiz, M., Jarilla, B., Pablo, A.O., Ovleda, R.M., Langdon, G., McGarvey, S.T., Kurtis, J.D., Friedman, J.F., Wu, H.W., 2010. Seroprevalence of cysticercosis in children and young adults living in a helminth endemic community in leyte, the Philippines. J Trop Med 2010, 603174.

Yamane, K., Suzuki, Y., Tachi, E., Li, T., Chen, X., Nakao, M., Nkouawa, A., Yanagida, T., Sako, Y., Ito, A., Sato, H., Okamoto, M., 2012. Recent hybridization between Taenia asiatica and Taenia saginata. Parasitol Int 61, 351-355.

Yanagida, T., Sako, Y., Nakao, M., Nakaya, K., Ito, A., 2012. Taeniasis and cysticercosis due to Taenia solium in Japan. Parasit Vectors 5, 18.

Yanagida, T., Yuzawa, I., Joshi, D.D., Sako, Y., Nakao, M., Nakaya, K., Kawano, N., Oka, H., Fujii, K., Ito, A., 2010. Neurocysticercosis: assessing where the infection was acquired from. J Travel Med 17, 206-208.

Yeh, S.J., Wu, R.M., 2008. Neurocysticercosis presenting with epilepsia partialis continua: a clinicopathologic report and literature review. J Formos Med Assoc 107, 576-581.

Yong, T.S., Shin, E.H., Chai, J.Y., Sohn, W.M., Eom, K.S., Lee, D.M., Park, K., Jeoung, H.G., Hoang, E.H., Lee, Y.H., Woo, H.J., Lee, J.H., Kang, S.I., Cha, J.K., Lee, K.H., Yoon, C.H., Sinuon, M., Socheat, D., 2012. High prevalence of Opisthorchis viverrini infection in a riparian population in Takeo Province, Cambodia. Korean J Parasitol 50, 173-176.

Yu, S., Xu, L., Jiang, Z., Xu, S., Han, J.J., Zhu, Y., Chang, J., Lin, J.X., Xu, F., 1994. [Report on the first nationwide survey of the distribution of human parasites in China. I. Regional distribution of parasite species]. Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi 12, 241-247.

Zimic, M., Gutierrez, A.H., Gilman, R.H., Lopez, C., Quiliano, M., Evangelista, W., Gonzales, A., Garcia, H.H., Sheen, P., 2011. Immunoinformatics prediction of linear epitopes from Taenia solium TSOL18. Bioinformation 6, 271-274.

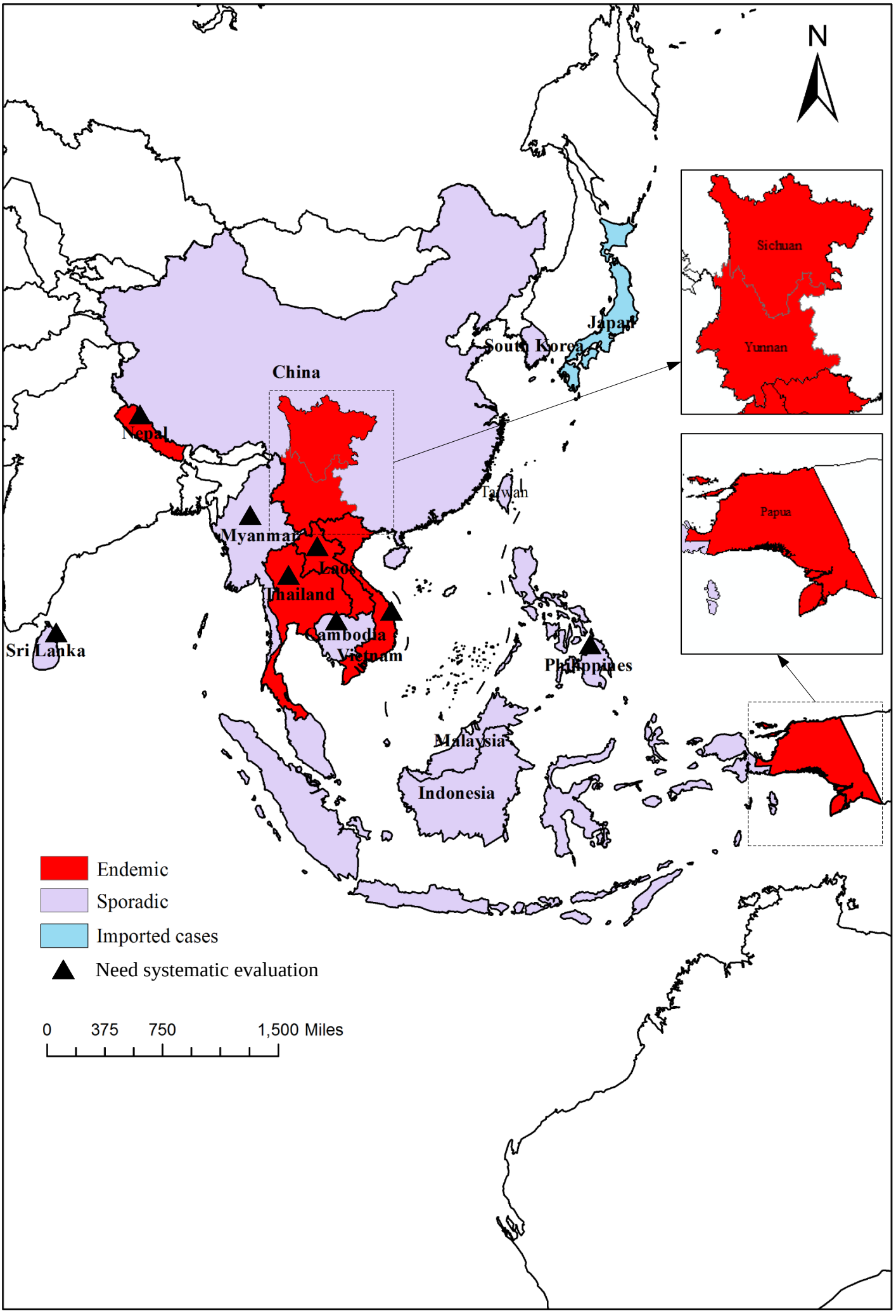
N
Sichuan
Yunnan
Papua
China
Japan
South Korea
Nepal
Taiwan
Myanmar
Laos
Thailand
Cambodia
Vietnam
Sri Lanka
Philippines
Malaysia
Indonesia
Endemic
Sporadic
Imported cases
Need systematic evaluation
0
375
750
1,500 Miles

Table1. Summary of the human cysticercosis and taeniasis infection rate in Southeast Asia by countries

Country	Area (total number of participants)	Taeniasis		Cysticercosis		Citations
		Detection Method	Positivity	Detection Method	Positivity	
Cambodia	Koh Kong (904)	Kato-Katz	4.60%	N/A	N/A	Jeon et al., 2011
	Kam Pot (1,002)	Kato-Katz	0	N/A	N/A	Jeon et al., 2011
	Kampong Som (918)	Kato-Katz	0.10%	N/A	N/A	Jeon et al., 2011
	Ang Svay Chek (1,341)	Kato-Katz	0.06%	N/A	N/A	Yong et al., 2012
Indonesia	Papua (286)	N/A	N/A	ELISA & EITB	21%	Swastika et al., 2011
	Bali	N/A	N/A	ELISA & EITB	6%	unpublished
Japan	Imported cases	N/A	N/A	PCR	N/A	Yanagida et al., 2012
South Korea	nationwide（74,448）	N/A	N/A	ELISA (IgG antibody)	8.30% in 1993; 2.20% in 2006	Lee et al., 2010
Lao PDR	Northern Region (1,306)	Kato-Katz	2.90%	ELISA (Antibody)	2.20%	Conlan et al., 2012
	Southern Region (232)	Kato-Katz; FECT	22.8%	N/A	N/A	Sayasone et al., 2009
	Om Phalong (92)	Kato-Katz; corpo-ELISA	26.1%	ELISA (Antigen)	30.7%(4/13)	Okello et al., 2014
Malaysia	Pinawantai (135)	N/A	N/A	ELISA (Antibody)	2.20%	Noor Azian et al., 2006
Myanmar	Refugees in the US (499)	N/A	N/A	EITB LLGP	24.9%	O'Neal et al., 2012
Nepal	Dum (524)	Kato-Katz	13.5%	N/A	N/A	Devleesschauwer et al., 2012
	Serizure patients aged 1-15yr in a hospital	N/A	N/A	imaging	12%	Adhikari et al., 2013
Sri Lanka	N/A	N/A	N/A	N/A	N/A	N/A
Thailand	Kanchanaburi (159)	N/A	N/A	ELISA (GpsAg)	5.70%	Anantaphruti et al., 2010
				ELISA (RecAg)	2.50%	
Philippines	Cagayan village (1,212)	Kato-Katz	4.00%	ELISA (Antibody)	35.0%	Acosta et al., unpublished
		N/A	N/A	ELISA (Antibody)	24.6%	Xu et al., 2010
Vietnam	Bac Kan (303)	Kato-Katz	0.33%	ELISA (Antigen)	5.30%	Somers et al., 2006
	Ha Tinh (175)	Kato-Katz	1.71%	ELISA (Antigen)	0.60%	Somers et al., 2006
	Northern Vietnam	N/A	N/A	ELISA (Antigen)	<10%	Trung et al., 2013
China	National parasitic diseases survey (96,008)	N/A	N/A	ELISA (Antibody)	0.58%	Xu et al. 2010

Taiwan	N/A	N/A	N/A	PCR	N/A	Shih et al., 2010

NOTE: N/A: not applicable/available