

MOLECULAR AND IMMUNOLOGICAL DIAGNOSIS OF TAENIASIS AND CYSTICERCOSIS IN ASIA AND THE PACIFIC

Akira Ito¹, Yasuhito Sako¹, Minoru Nakao¹, Kazuhiro Nakaya², Munehiro Okamoto³, Toni Wandra^{4,1}, I Nyoman Kandun⁴, Malinee T Anantaphruti^{5,1}, Jitra Waikagul⁵, Tiaoying Li^{6,1} and Dongchuan Qiu⁶

¹Department of Parasitology, ² Animals Laboratory for Medical Research, Asahikawa Medical College;

³Department of Parasitology, School of Veterinary Medicine, Faculty of Agriculture, Tottori University, Japan;

⁴Directorate General Disease Control and Environmental Health, Ministry of Health, Jakarta, Indonesia;

⁵Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;

⁶Institute of Parasitic Diseases, Sichuan Centers for Disease Control and Prevention, China

Abstract. Three human *Taenia* species, *Taenia solium*, *Taenia saginata*, and *Taenia asiatica* have been found and reported from Asia-Pacific region. *T. solium* neurocysticercosis (NCC) is one of the neglected and most lethal parasitic diseases worldwide. Therefore, clinical manifestation, neuroimaging, serology, and molecular identification of resected lesions of NCC are briefly overviewed. The difference between *T. saginata* and *T. asiatica*, as well as the two genotypes of *T. solium* is also overviewed, based on mitochondrial DNA analysis. Epidemiological topics from Indonesia, Thailand, and China through our collaboration projects are also overviewed with religious and socio-cultural background information.

INTRODUCTION

The pork tapeworm, *Taenia solium*, and the beef tapeworm, *Taenia saginata*, are the two major human taeniid cestodes and the major food-borne cestode zoonoses worldwide (Ito *et al*, 2003a, 2006a). The third species, *Taenia asiatica*, has recently been distinguished as an independent species (Eom and Rim, 1993; Hoberg *et al*, 2000; Eom *et al*, 2002; Eom, 2006); although there are some contrary opinions (Bowles and McManus, 1994; McManus and Bowles, 1994; Ito *et al*, 2003a). The number of specimens examined is too small to conclude that there is no hybrid in sympatrically endemic areas (Okamoto *et al*, 2007).

These three species can develop into adult tapeworms in humans exclusively (Hoberg *et al*, 2001). The most interesting species of medical

and public health importance is *T. solium*. It has been speculated that *T. solium* was a human parasite that emerged in Africa several million years ago. Later, the intermediate host shifted from humans to pigs; which means that human cannibalism was essential for completion of the life cycle of this parasite. Molecular analysis of these three species has revealed that *T. solium* is distant from the other two, and *T. saginata* and *T. asiatica* are sister species (Hoberg, 2002; Eom, 2006). The most crucial difference between these two species is not morphological but the intermediate host spectrum. The former develops from an egg into a metacestode, cysticercus, in cattle; whereas, the latter does so in the viscera of pigs (Fan, 1988). As both *T. solium* and *T. asiatica* require swine as the intermediate host, a working hypothesis for cysticercosis of *T. asiatica* was introduced (Ito, 1992). However, it is now established that cysticercosis is exclusively caused by *T. solium*, because both *T. saginata* and *T. asiatica* are sister species, and cysticercosis due to *T. saginata* does not occur (Ito *et al*, 2003a).

In this review article, taeniasis/cysticercosis of *T. solium* is reviewed, initially with molecular and immunological diagnostic tools. Then,

Correspondence: Akira Ito, Department of Parasitology, Asahikawa Medical College, Midorigaoka Higashi 2-1-1-1, Asahikawa 078-8510, Japan.

Tel: +81-166-68-2420; Fax: +81-166-68-2429

E-mail: akiraito@asahikawa-med.ac.jp

taeniasis of *T. saginata* and *T. asiatica*, as well as the two genotypes of *T. solium*, is discussed.

TAENIASIS AND CYSTICERCOSIS OF *T. SOLIUM* IN THE ASIA-PACIFIC REGION

As these all are food-borne zoonotic cestodiasis, it could be expected that these would be eradicable (Schantz *et al*, 1993a, 1998). However, increases in the population of refugees and/or immigrants through economic, political, or religious problems may often cause poverty and social upheaval. The wave of globalization has accelerated this phenomenon worldwide. Such infections are caused by WAFP (contaminated water, air, food, and people) (Ito, 2007). Among the three human *Taenia* species, the most serious species is *T. solium*. *T. solium* neurocysticercosis is one of the most lethal parasitic diseases worldwide and is on the list of neglected tropical diseases (Ito *et al*, 2006a, b; Craig *et al*, 2007). It is found in the majority of developing countries where the people eat pork. However, due to the globalization, outbreaks of *T. solium* cysticercosis have been reported in an orthodox Jewish community in New York (Schantz *et al*, 1993b), and in Muslim communities in Saudi Arabia (Al Shahrani *et al*, 2003) and in Kuwait (Hira *et al*, 2004) through immigrants or visitors from non-Jewish or non-Muslim societies. Recent review articles on the clinical manifestation, neuroimaging, serology, and molecular confirmation of neurocysticercosis have been published (Schantz *et al*, 1998; Ito *et al*, 2006a, b). More information is available from these reviews.

What is *T. solium* neurocysticercosis (NCC) ?

The major clinical manifestations of NCC are epileptic seizures (> 60%) and/or intracranial hypertension (> 30%), and/or meningitis (= 30%). However, these are not specific to NCC. Epilepsy due to NCC is expected, to be the main cause of late-onset

epilepsy in developing countries where NCC of *T. solium* is endemic. Epileptic seizures are the most common symptom (70-90%) of NCC. More important clinical background information is that the majority of NCC cases are asymptomatic until the parasite, cysticercus or cysticerci, will be damaged by the host immune responses or by the treatment with metacestocidal drug such as praziquantel (Sarti *et al*, 1994). Recently, we experienced one asymptomatic NCC patient who harbored *T. saginata* in Bali. This tapeworm carrier was treated with praziquantel, and epileptic seizure attacked within one day (Wandra *et al*, unpublished). Therefore, the basis for suspecting NCC is the following information: 1) neurologic disorders, 2) neuroimaging, and 3) history of traveling to and/or living in *T. solium* endemic areas. Neuroimaging is not always typical, and approximately only 10% of NCC may show typical imaging (Wilson *et al*, 1991; White, 1997). Based on such background information suggesting or suspecting NCC, we have to carry out as an additional test, 4) serology, using highly specific antigens (Ito and Craig, 2003; Ito *et al*, 2006b).

Gold standards for serology to detect NCC

The gold standard for the detection of NCC is immunoblot using purified glycoproteins (GPs) (Tsang *et al*, 1989; Ito *et al*, 1998; Chung *et al*, 1999; Sako *et al*, 2000; Green *et al*, 2000; Hancock *et al*, 2003). Research groups at CDC, Atlanta, USA and Asahikawa Medical College (AMC), Japan have developed immunoblots that use purified GPs, using different tools for purification of GPs. CDC applied lentil-lectin affinity chromatography (Tsang *et al*, 1989); whereas, AMC did isoelectric focusing (Ito *et al*, 1998) to detect specific antibodies. The most interesting and crucial difference in resolution between the two groups was that CDC could recommend immunoblots only; whereas, AMC could recommend both immunoblots and ELISA (antibody-ELISA) with almost same sensitivity and specificity

(Ito *et al.*, 1998; Sako *et al.*, 2000; Sato *et al.*, 2003, 2006). Resolution from recombinant chimeric antigens was similar to or better than that from native GPs, and more than 94% of confirmed NCC cases were easily detected with no cross reactions from highly cross reactive echinococcosis, either cystic or alveolar (Sako *et al.*, 2000).

However, the serology is not always perfect. The sensitivity is 30-60% in solitary NCC cases (Wilson *et al.*, 1991). Therefore, it is not certain that we can detect specific antibodies in NCC cases with a solitary cyst (Ito *et al.*, 1999; Ohsaki *et al.*, 1999; Ishikawa *et al.*, 2007).

We can expect no or poor antibody responses from NCC cases in the following cases: 1) immunodeficiency, 2) single cyst, 3) inactive, calcified lesions only, or 4) other species that may cause zoonotic cysticercosis. In such cases, molecular identification becomes crucial (Ito, 2002; Ito and Craig, 2003; Ito *et al.*, 2006b).

An alternative approach is to detect circulating antigens in patients or domestic animals using monoclonal antibodies by ELISA only. Thus far, we know it is rather complicated to draw the cutoff values using mathematics. Very small differences in OD values have to be evaluated for the differentiation of patients or animals infected with *T. solium* cysticerci. It may often cause false positives from non-infected pigs in developed country in Europe due to how the cutoff values were drawn. There is a crucial difference from antibody-ELISA, where we can differentiate NCC cases from other diseases even by the naked eye (Sato *et al.*, 2003). There is no real blind test to evaluate the specificity or sensitivity of such tools (Dorny *et al.*, 2004). Such tools to detect antigens (antigen-ELISA) are based on the use of monoclonal antibodies, not to the cysticercus of *T. solium* but to that of *T. saginata*, and they are used to detect cross-reactive components of *T. solium* infection. To date, there is no visual immunological, biochemical, or molecular information on the cross-reactive

components. Such tools to detect circulating antigens are therefore expected to be useful for monitoring of progression (Ito and Craig, 2004). If an antigen-ELISA is established based on monoclonal antibodies to species-specific components of *T. solium*, its usefulness is expected to be great, not only for monitoring of progression, but also for diagnosis (Ito and Craig, 2004).

Molecular identification of a cysticercus or cysticerci in histopathological specimens

Surgery is an option recommended in urgent cases of malignant tumors or other diseases in the brain with acute severe symptoms, including neurologic disorders. When NCC cases are admitted without any information from neuroimaging and/or serology supporting NCC, they may have surgical options (Ito *et al.*, 1999; Ohsaki *et al.*, 1999; Ishikawa *et al.*, 2007). Histopathological examination is still the gold standard to confirm rostellar hooks and suckers unique to taeniid species. However, it is not always easy to confirm hooks. In such cases, it is not critical to diagnose them as *T. solium* infections. Such cases were sometimes described as *T. saginata* (Pawlowski and Schultz 1972; Šlais, 1973). There could be rare cysticercosis cases caused by other rare zoonotic species, such as *T. taeniaeformis*, *T. hydatigena*, *T. ovis*, *T. serialis*, *T. multiceps*, *T. crassiceps*, or others. Therefore, molecular approaches using such specimens are now crucial to identify the species (Yamasaki *et al.*, 2004a, b, 2006; Ito *et al.*, 2006b). Development of hooklets is highly variable, including no hook in SCID mice experimentally infected with oncospheres of *T. solium* (Margono *et al.*, 2003; Ito *et al.*, unpublished). As *T. solium* worldwide can be differentiated into two genotypes (Okamoto *et al.*, 2001; Nakao *et al.*, 2002), we can differentiate Asian and African/American genotypes. Furthermore, two polymorphisms in both genotypes have also been found (Campbell *et al.*, 2006; Sudewi *et al.*, 2008).

How to detect carriers of *Taenia* spp

For the prevention of cysticercosis of *T. solium* in human and for production of safe meat or food without the cysticerci of *T. saginata*, *T. asiatica*, or *T. solium*, detection of taeniasis carriers is essential to block the lifecycle of these human *Taenia* spp (Schantz *et al*, 1993b, 1998; Schantz, 2006; Craig and Ito, 2007). There are several tools to detect taeniasis carriers. The most popular tool is copro-ELISA test (Allan *et al*, 1992, 1996; Allan and Craig, 2006). However, it is not a species-specific molecular tool, as the copro-DNA test (Yamasaki *et al*, 2004a) that has been introduced for the confirmative identification of the species. The detection of antibodies specific to adult *Taenia* (Wilkins *et al*, 1999; Nakao *et al*, unpublished) has also been reported, although the species specificity has not always been well evaluated. The most reliable detection of taeniasis carriers is the history of expulsion of gravid proglottids, especially in *T. saginata* and *T. asiatica* (Wandra *et al*, 2006a). It may also be useful for *T. solium* (Flisser *et al*, 2005).

Molecular differentiation of three taeniid species in humans

Based on mitochondrial (mt) DNA analysis, it is relatively easy to differentiate between these three species (Okamoto *et al*, 2001; Nakao *et al*, 2002; Yamasaki *et al*, 2004a). Now, nuclear DNA sequencing data are also available for the differentiation of these three species (Okamoto *et al*, unpublished).

TAENIA SAGINATA AND *T. ASIATICA* IN ASIA-PACIFIC REGIONS

Many researchers working in Asia-Pacific have long recognized a curious phenomenon (Yokogawa, 1935; Huang *et al*, 1966; Kosin *et al*, 1972; Fan, 1988). This puzzle was that adult taeniid tapeworms expelled from people in Asia-Pacific regions seemed to be *T. saginata*, the beef tapeworm, although these people ate pork rather than beef (Simanjuntak *et al*, 1997; Ito *et al*, 2003a). Now it has become clear that it was due to a third species, *T. asiatica* (Eom, 2006). It is rather difficult to differentiate these two species morphologically; although

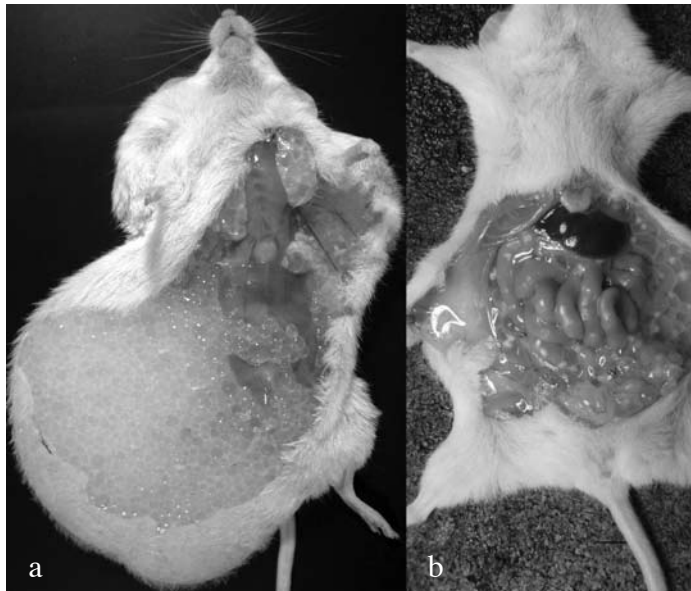


Fig 1- Fully developed cysticerci of *T. asiatica* (a) and *T. saginata* (b) in NOD/Shi-*scid* mice 3 months after subcutaneous and intraperitoneal injections of *in vitro* hatched oncospheres, respectively.

there is a crucial difference in the intermediate host animals as mentioned above. Usually, *T. saginata* cysticercus is much bigger than that of *T. asiatica*. Some different morphological characteristics of the cysticercus of these two species may become clearer when we obtain cysticerci from immunodeficient mice (Fig 1) (Nakaya *et al*, 2006). The cyst wall is much thinner in the cysticerci of *T. asiatica* compared with *T. saginata*. Through our collaboration projects, *T. asiatica* has been confirmed from Taiwan, China, Korea, Indonesia, Philippines, Vietnam, and Thailand (Ito *et al*, unpublished).

TAENIASIS AND CYSTICERCOSIS IN ASIA-PACIFIC REGIONS

In Indonesia

We have been working in three regions in Indonesia: Papua (Irian Jaya), Bali, and Sumatra (Wandra *et al*, 2006a, b). In Papua *T. solium* NCC is a very serious public health problem, because the majority of the people in Papua are Christian. As pigs and dogs have free access to human feces, we checked dog sera and found that more than 10% of dogs showed antibody responses to *T. solium* GPs and recombinant antigens (Sato *et al*, 2003). Approximately 50% of adult population was expected to have been exposed to the eggs of *T. solium* (Wandra *et al*, 2000, 2003; Subahar *et al*, 2001; Ito *et al*, 2002, 2004; Margono *et al*, 2003, 2005, 2006). Dogs as well as humans and swine have been confirmed to be infected with the cysticerci of *T. solium* by molecular and morphological identification of the cysts obtained, based on serological screenings (Subahar *et al*, 2001; Ito *et al*, 2002; Sato *et al*, 2003; Margono *et al*, 2006).

Most recent work on comparison of mtDNA of *T. solium* from Bali and Papua suggests that *T. solium* in Bali and Papua might have different origins (Sudewi *et al*, 2008); although it has been conceived that *T. solium* in Papua was introduced from Bali (Gadjusek, 1978;

Simanjuntak *et al*, 1997). To date, there has been no record of *T. saginata* or *T. asiatica* in Papua.

T. solium has historically been well recognized in Bali; however it is now sporadic (Wandra *et al*, 2006a; Sudewi *et al*, 2008). By contrast, *T. saginata* is rather common in Bali. The majority of Balinese are Hindu but differ from people in India or Nepal because they eat beef. The Balinese like to eat uncooked or undercooked minced beef (beef *lawar*), or minced pork with fresh blood (pork *lawar*), but do not eat uncooked or undercooked viscera. Therefore, there has been no human case of *T. asiatica* (Margono *et al*, 2006; Wandra *et al*, 2006a). Recent fieldwork, in August 2007, in Bali found unique dual infections of *T. saginata* and *T. solium* (asymptomatic NCC) (Wandra *et al*, unpublished).

T. asiatica is well known among the *Batak* people on Samosir Island in North Sumatra. They are Christians and eat uncooked or undercooked pork with viscera, and dog meat with viscera. There was the only record of *T. solium* over 20 years ago (Wandra *et al*, 2006b).

As the majority of Indonesian people are Muslim, *T. saginata* is the only species not expected to be common. Therefore, nowhere in Indonesia do the three human taeniid species occur sympatrically. This is due to the barriers of religion and social culture in each respective area (Wandra *et al*, 2006b, 2007).

In Thailand

To date, there has only been a report demonstrating *T. asiatica* from Thailand (Anantaphruti *et al*, 2007a). *T. saginata* was confirmed from Chiang Mai, Thailand, with molecular tools (Bowles and McManus, 1994; Morakote *et al*, 2000; Anantaphruti *et al*, 2007b). In Kanchanaburi, close to the border to Myanmar, three human taeniid species were found sympatrically. An interesting finding was a dual infection with *T. solium* and *T. asiatica* in one carrier, who harbored two *T. solium* and one *T. asiatica* (Anantaphruti *et al*, 2007a).

In China

Taeniasis and cysticercosis are rather common diseases in China (Chen *et al*, 2005; Ikejima *et al*, 2005). Three human taeniid species have been reported to occur sympatrically in Yunnan (Eom *et al*, 2002; Yamasaki *et al*, 2004a) and in Sichuan Province (Li *et al*, 2006). More information will be available from China as discussed previously (Ito *et al*, 2003b).

PERSPECTIVES

In Asia-Pacific regions, it is now very clear that three human taeniid species are sympatrically occurring in several areas. Therefore, we have to re-examine *T. saginata* in these regions (Ito *et al*, 2003a). To do epidemiological studies in such areas, real-time molecular identification is the best for identification and treatment of worm carriers. Such endemic areas are rather remote, and multiplex PCR is not easily applicable. Therefore, a new molecular tools using LAMP method is expected to be available for such fieldwork in sympatric areas for the three species (Nkauawa and Sako, unpublished).

As Asian people, including immigrants and refugees from Asia-Pacific regions, are moving out of Asia-Pacific and working mainly in Europe, America, and Africa. Simultaneously, people from Africa, Americas, Australia, New Zealand, and Europe are traveling to Asia-Pacific, we have to re-evaluate all specimens of *T. saginata* to determine whether they are real *T. saginata* or *T. asiatica*. There is a similar situation in Japan, because there is no challenge to re-evaluate *T. saginata* cases treated in Japan if they are real *T. saginata* or *T. asiatica*.

CONCLUSION

1) Three human *Taenia* species are occurring in Asia-Pacific regions. Taeniasis may be detected by several tools, including classical morphology, copro-ELISA, and copro-DNA;

2) Molecular identification of these human *Taenia* species is feasible; 3) Serology using purified glycoproteins or recombinant antigens of *T. solium* is highly useful for detection of cysticercosis of *T. solium* in humans, pigs, and dogs. Serology for detection of taeniasis is not yet so sensitive; 4) Confirmation of NCC is based on neuroimaging, serology, histopathology, and molecular identification, although histopathology and molecular identification are options after surgery; 5) *T. saginata* in the world as well as in Asia-Pacific regions should be re-evaluated by molecular tools.

ACKNOWLEDGEMENTS

The projects summarized in this review had financial support from the Japan Society for the Promotion of Science (JSPS) (14256001, 17256002), the Ministry of Education, Japan (Kagaku-Gijutsu Shinko Choseihi 2003-2005), and JSPS-Asia/Africa Science Platform Fund (2006-2008) to A Ito; and from JSPS (16500277, 18406008) to M Okamoto.

REFERENCES

- Al Shahrani D, Frayha HH, Dabbagh O, Al Shail E. First case of neurocysticercosis in Saudi Arabia. *J Trop Pediatr* 2003;49: 58-60.
- Allan JC, Craig PS. Coproantigens in taeniasis and echinococcosis. Proceedings of the 5th International Symposium on Taeniasis/Cysticercosis and Echinococcosis with Focus on Asia and the Pacific, 2005, Asahikawa, Japan. *Parasitol Int* 2006;55 (suppl):75-80.
- Allan JC, Craig PS, Garcia-Noval J, *et al*. Coproantigen detection for the immunodiagnosis of echinococcosis and taeniasis in dogs and humans. *Parasitology* 1992;104:347-55.
- Allan JC, Garcia-Noval R, Torres-Alvarez M, Velasquez-Tohom, Yurrita P. Field

- trial of diagnosis of *Taenia solium* taeniasis by coproantigen enzyme-linked immunosorbent assay. *Am J Trop Med Hyg* 1996;54:352-6.
- Anantaphruti MT, Waikagul J, Yamasaki H, Ito A. Cysticercosis and taeniasis in Thailand. Proceedings of Joint International Tropical Medicine Meeting 2006 and the 5th Seminar on Food- and Water-borne Parasitic Zoonoses, 29 November - 1 December 2006, Bangkok, Thailand. *Southeast Asian J Trop Med Public Health* 2007b;38 (suppl 1):151-8.
- Anantaphruti MT, Yamasaki H, Nakao M, *et al.* Sympatric occurrence of *Taenia solium*, *T. saginata*, and *T. asiatica*, Thailand. *Emerg Infect Dis* 2007a;13:1413-6.
- Bowles J, McManus DP. Genetic characterization of the Asian *Taenia*, a newly described taeniid cestodes of humans. *Am J Trop Med Hyg* 1994;50:33-44.
- Campbell G, Garcia HH, Nakao M, Ito A, Craig PS. Genetic variation in *Taenia solium*. Proceedings of the 5th International Symposium on Taeniasis/Cysticercosis and Echinococcosis with Focus on Asia and the Pacific, Asahikawa, Japan. *Parasitol Int* 2006;55 (suppl):121-6.
- Chen Y, Xu L, Zhou X. Cysticercosis cellulosa in China. *Asian Parasitol* 2005;2:37-83.
- Chung JY, Bahk YY, Huh S, Kang SY, Kong Y, Cho SY. A recombinant 10-kDa protein of *Taenia solium* metacestodes specific to active neurocysticercosis. *J Infect Dis* 1999; 180:1307-15.
- Craig PS, Budke CM, Schantz PM, *et al.* Human echinococcosis: a neglected disease? Proceedings of the Symposium on Cestode Zoonoses in Asia and the Pacific at the 21st Pacific Science Congress, 12-18 June, 2007, Okinawa, Japan. *Trop Med Health* 2007;35:283-92.
- Craig PS, Ito A. Intestinal cestodes. *Curr Opin Infect Dis* 2007;20:524-32.
- Dorny P, Phiri IK, Vercuysse J, *et al.* A Bayesian approach for estimating values for prevalence and diagnostic test characteristics of porcine cysticercosis. *Int J Parasitol* 2004;34:569-76.
- Eom KS. What is Asian *Taenia*? Proceedings of the 5th International Symposium on Taeniasis/Cysticercosis and Echinococcosis with Focus on Asia and the Pacific, 2005, Asahikawa, Japan. *Parasitol Int* 2006;55 (suppl):137-41.
- Eom KS, Jeon HK, Kong Y, *et al.* Identification of *Taenia asiatica* in China: molecular, morphological, and epidemiological analysis of a Luzhai isolate. *J Parasitol* 2002;88:758-64.
- Eom KS, Rim HJ. Morphological descriptions of *Taenia asiatica* sp n. *Korean J Parasitol* 1993;31:1-6.
- Fan PC. Taiwan *Taenia* and taeniasis. *Parasitol Today* 1988;4:86-8.
- Flisser A, Vázquez-Mendoza A, Martínez-Ocaña J, *et al.* Short report: evaluation of a self-detection tool for tapeworm carriers for use in public health. *Am J Trop Med Hyg* 2005;72:510-2.
- Gadjusek DC. Introduction of *Taenia solium* into West New Guinea with a note on an epidemic of burns from cysticercosis epilepsy in the Ekari people of the Wissel Lakes area. *PNG Med J* 1978;21:329-42.
- Green RM, Hancock K, Wilkins PP, *et al.* *Taenia solium*: molecular cloning and serological evaluation of 14- and 18-kDa related, diagnostic antigens. *J Parasitol* 2000;86:1001-7.
- Hancock K, Khan A, Williams FB, *et al.* Characterization of the 8-kilodalton antigens of *Taenia solium* metacestodes and

- evaluation of their use in an enzyme-linked immunosorbent assay for serodiagnosis. *J Clin Microbiol* 2003;41:2577-86.
- Hira PR, Francis I, Abdella NA, *et al.* Cysticercosis: imported and autochthonous infections in Kuwait. *Trans R Soc Trop Med Hyg* 2004;98:233-9.
- Hoberg EP. *Taenia* tapeworms: their biology, evolution and socioeconomic significance. *Microbes Infect* 2002;4:859-66.
- Hoberg EP, Alkire NL, De Queiroz A, Jones A. Out of Africa: origin of the *Taenia* tapeworms in humans. *Proc R Soc Lond B Biol Sci* 2001;268:781-7.
- Hoberg EP, Jones A, Rausch RL, Eom KS, Gardner SL. A phylogenetic hypothesis for species of the genus *Taenia* (Eucestoda: Taeniidae). *J Parasitol* 2000;86:89-98.
- Huang SW, Khaw OK, Liu CY. Studies on *Taenia* species prevalence among the aborigines in Wulai District. *Bull Inst Zool Acad Sinica* 1966;5:87-91.
- Ikejima T, Piao ZX, Sako Y, *et al.* Evaluation of clinical and serological data from *Taenia solium* cysticercosis patients in eastern Inner Mongolia autonomous region, China. *Trans R Soc Trop Med Hyg* 2005;99:625-30.
- Ishikawa E, Komatsu Y, Kikuchi K, *et al.* Neurocysticercosis as solitary parenchymal lesion confirmed by mitochondrial deoxyribonucleic acid sequence analysis. *Neurol Med Chir* 2007;2007;47:40-4.
- Ito A. Cysticercosis in Asia-Pacific regions. *Parasitol Today* 1992;8:181-2.
- Ito A. Serological and molecular diagnosis of zoonotic larval cestode infections. *Parasitol Int* 2002;51:221-35.
- Ito A. Welcome remarks and introduction to symposium on cestodes zoonoses in Asia and the Pacific. Proceedings of Joint International Tropical Medicine Meeting 2006 and the 5th Seminar on Food- and Water-borne Parasitic Zoonoses, 29 November - 1 December 2006, Bangkok, Thailand. *Southeast Asian J Trop Med Public Health* 2007;38 (suppl 1):115-8.
- Ito A, Craig PS. Immunodiagnostic and molecular approaches for the detection of taeniid cestodes infections. *Trends Parasitol* 2003;19:377-81.
- Ito A, Craig PS. Response to Dorny *et al.* Immunodiagnostic approaches for detecting *Taenia solium*. *Trends Parasitol* 2004;20:260-1.
- Ito A, Craig PS, Schantz PM. Taeniasis/cysticercosis and echinococcosis with focus on Asia and the Pacific. Proceedings of the 5th International Symposium on Taeniasis/Cysticercosis and Echinococcosis with Focus on Asia and the Pacific, 2005, Asahikawa, Japan. *Parasitol Int* 2006a;55 (suppl):1.
- Ito A, Nakao M, Ito Y, *et al.* Neurocysticercosis case with a single cyst in the brain showing dramatic drop in specific antibody titers within 1 year after curative surgical resection. *Parasitol Int* 1999;48:95-9.
- Ito A, Nakao M, Wandra T. Human taeniasis and cysticercosis in Asia. *Lancet* 2003a;362:1918-20.
- Ito A, Plancarte A, Ma L, *et al.* Novel antigens for neurocysticercosis: simple method for preparation and evaluation for serodiagnosis. *Am J Trop Med Hyg* 1998; 59:291-4.
- Ito A, Putra MI, Subahar R, *et al.* 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* 2002;76:311-4.
- Ito A, Takayanagui OM, Sako Y, *et al.* Neurocysticercosis: clinical manifestation,

- neuroimaging, serology and molecular confirmation of histopathologic specimens. Proceedings of the Joint International Tropical Medicine Meeting 2005, 30 November – 2 December 2005, Bangkok, Thailand. *Southeast Asian J Trop Med Public Health* 2006b;37 (suppl 3):74-81.
- Ito A, Urbani C, Qiu J, *et al.* Control of echinococcosis and cysticercosis: a public health challenge to international cooperation in China. *Acta Trop* 2003b;86:3-17.
- Ito A, Wandra T, Yamasaki H, *et al.* Cysticercosis/taeniasis in Asia and the Pacific. *Vector-Borne Zoonot Dis* 2004; 4:95-107.
- Kosin E, Depary A, Djohansjah A. [Taeniasis di pulau Samosir]. *Maj Kedok Univ* 1972; 3:5-11.
- Li TY, Craig PS, Ito A, *et al.* Taeniasis/cysticercosis in a Tibetan population in Sichuan province, China. *Acta Trop* 2006; 100:223-31.
- Margono SS, Ito A, Sato MO, *et al.* *Taenia solium* taeniasis/cysticercosis in Papua, Indonesia in 2001: detection of human worm carriers. *J Helminthol* 2003;77:39-42.
- Margono SS, Wandra T, Ito A. Taeniasis and cysticercosis in Indonesia. *Asian Parasitol* 2005;2:115-34.
- Margono SS, Wandra T, Swasono MF, Murni S, Craig PS, Ito A. Taeniasis/cysticercosis in Papua (Irian Jaya), Indonesia. Proceedings of the 5th International Symposium on Taeniasis/Cysticercosis and Echinococcosis with Focus on Asia and the Pacific, 2005, Asahikawa, Japan. *Parasitol Int* 2006;55 (suppl):143-8.
- McManus DP, Bowles J. Asian (Taiwan) *Taenia*: species or strain. *Parasitol Today* 1994;10:273-5.
- Morakote N, Wijit A, Uparanukraw P. Further search for *Taenia saginata asiatica* in Chiang Mai, Thailand. *Ann Trop Med Parasitol* 2000;94:521-4.
- Nakaya K, Mamuti W, Xiao N, *et al.* Usefulness of severe combined immunodeficiency (*scid*) and inbred mice for studies of cysticercosis and echinococcosis. Proceedings of the 5th International Symposium on Taeniasis/Cysticercosis and Echinococcosis with Focus on Asia and the Pacific, 2005, Asahikawa, Japan. *Parasitol Int* 2006;55 (suppl):91-7.
- Nakao M, Okamoto M, Sako Y, Yamasaki H, Ito A. A phylogenetic hypothesis for the distribution of two genotypes of the pig tapeworm *Taenia solium* worldwide. *Parasitology* 2002;124:657-62.
- Ohsaki Y, Matsumoto A, Miyamoto K, *et al.* Neurocysticercosis without detectable specific antibody. *Internal Med* 1999;38:67-70.
- Okamoto M, Nakao M, Sako Y, Ito A. Molecular variation of *Taenia solium* in the world. Proceedings of the 3rd Seminar on Food-Borne Parasitic Zoonoses, 6-8 December 2000, Bangkok, Thailand. *Southeast Asian J Trop Med Public Health* 2001;32 (suppl 2):90-3.
- Okamoto M, Nakao M, Tachi E, *et al.* Asian *Taenia*: species or subspecies? Proceedings of Joint International Tropical Medicine Meeting 2006 and the 5th Seminar on Food- and Water-borne Parasitic Zoonoses, 29 November - 1 December 2006, Bangkok, Thailand. *Southeast Asian J Trop Med Public Health* 2007;38 (suppl 1):125-30.
- Pawlowski Z, Schultz MG. Taeniasis and cysticercosis (*Taenia saginata*). *Adv Parasitol* 1972;10: 69-343.
- Sako Y, Nakao M, Ikejima T, Piao XZ, Nakaya K, Ito A. Molecular characterization and diagnostic value of *Taenia solium* low-

- molecular-weight antigen gene. *J Clin Microbiol* 2000;38:4439-44.
- Sarti E, Schantz PM, Plancarte A, *et al.* Epidemiological investigation of *Taenia solium* taeniasis and cysticercosis in a rural village of Michoacan state, Mexico. *Trans R Soc Trop Med Hyg* 1994;88:49-52.
- Sato MO, Yamasaki Y, Sako Y, *et al.* Evaluation of tongue inspection and serology for diagnosis of *Taenia solium* cysticercosis in swine: usefulness of ELISA using purified glycoproteins and recombinant antigen. *Vet Parasitol* 2003;111:309-22.
- Sato MO, Sako Y, Nakao M, Yamasaki H, Nakaya K, Ito A. Evaluation of purified *Taenia solium* glycoproteins and recombinant antigens in the serologic detection of human and swine cysticercosis. *J Infect Dis* 2006;194:1783-90.
- Schantz PM, Cruz M, Sarti E, Pawlowski Z. Potential eradicability of taeniasis and cystricercosis. *Bull Pan Am Health Organ* 1993a;27:397-403.
- Schantz PM, Moore AC, Munoz JL, *et al.* Neurocysticercosis in an orthodox Jewish community in New York City. *N Engl J Med* 1993b;327:692-5.
- Schantz PM. Progress in diagnosis, treatment and elimination of echinococcosis and cysticercosis. Proceedings of the 5th International Symposium on Taeniasis/Cysticercosis and Echinococcosis with Focus on Asia and the Pacific, Asahikawa, Japan. *Parasitol Int* 2006;55 (suppl 1):7-13.
- Schantz PM, Wilkins PP, Tsang VCW. Immigrants, imaging, and immunoblots: the emergence of neurocysticercosis as a significant public health problem. In: Scheld WM, Craig WA, Hughes JM, eds. *Emerging infections 2*. Washington; AMS, 1998:213-42.
- Simanjuntak GM, Margono SS, Okamoto M, Ito A. Taeniasis/cysticercosis in Indonesia as an emerging disease. *Parasitol Today* 1997;13: 321-3.
- Šlais J. Functional morphology of cestodes larvae. *Adv Parasitol* 1973;11:395-480.
- Subahar R, Hamid A, Purba W, *et al.* *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* 2001;95:388-90.
- Sudewi AAR, Wandra T, Artha A, Nkouawa A, Ito A. *Taenia solium* cysticercosis in Bali, Indonesia: serology and mtDNA analysis. *Trans R Soc Trop Med Hyg* 2008;102:96-8.
- Tsang VC, Brand JA, Boyer AE. An enzyme-linked immunoelectro-transfer blot assay and glycoprotein antigens for diagnosing human cysticercosis. *J Infect Dis* 1989; 159:50-9.
- Wandra T, Depary AA, Sutisna P, *et al.* Taeniasis and cysticercosis in Bali and north Sumatra, Indonesia. Proceedings of the 5th International Symposium on Taeniasis/Cysticercosis and Echinococcosis with Focus on Asia and the Pacific, Asahikawa, Japan. *Parasitol Int* 2006b;55 (suppl):155-60.
- Wandra T, Ito A, Yamasaki H, Margono SS, Suroso T. *Taenia solium* cysticercosis, Irian Jaya, Indonesia. *Emerg Infect Dis* 2003;8 884-5.
- Wandra T, Margono SS, Gafar MS, *et al.* Taeniasis/cysticercosis in Indonesia, 1996-2006. Proceedings of Joint International Tropical Medicine Meeting 2006 and the 5th Seminar on Food- and Waterborne Parasitic Zoonoses, 29 November - 1 December 2006, Bangkok, Thailand. *Southeast Asian J Trop Med Public Health* 2007;38 (suppl 1):140-3.
- Wandra T, Subahar R, Simanjuntak GM,

- et al.* Resurgence of cases epileptic seizures and burns associated with cysticercosis Assologaima, Jayawijaya, Irian Jaya, Indonesia, 1991-95. *Tran R Soc Trop Med Hyg* 2000;94:46-50.
- Wandra T, Sutisna P, Dharmawan NS, *et al.* High prevalence of *Taenia saginata* and status of *Taenia solium* cysticercosis in Bali, Indonesia, 2002-2004. *Trans R Soc Trop Med Hyg* 2006a;100:346-53.
- White AC Jr. Neurocysticercosis: a major cause of neurological disease worldwide. *Clin Infect Dis* 1997;24:101-13.
- Wilkins PP, Allan JC, Verastegui M, *et al.* Development of a serologic assay to detect *Taenia solium* taeniasis. *Am J Trop Med Hyg* 1999;60:199-204.
- Wilson M, Bryan RT, Fried JA, *et al.* Clinical evaluation of the cysticercosis enzyme-linked immunoelectrotransfer blot in patients with neurocysticercosis. *J Infect Dis* 1991;164:1007-9.
- Yamasaki H, Allan JC, Sato MO, *et al.* DNA differential diagnosis of taeniasis and cysticercosis by multiplex PCR. *J Clin Microbiol* 2004a;42:548-53.
- Yamasaki H, Matsunaga S, Yamamura K, *et al.* Solitary neurocysticercosis case caused by Asian genotype of *Taenia solium* confirmed by mitochondrial DNA analysis. *J Clin Microbiol* 2004b;42:3891-3.
- Yamasaki H, Nagase T, Kiyoshige Y, *et al.* A case of intramuscular cysticercosis diagnosed definitively by mitochondrial DNA analysis of extremely calcified cysts. *Parasitol Int* 2006;55:127-30.
- Yokogawa S. On the taeniasis *saginata* among the aborigines in Taiwan. *Nippon Gakujutsu Kyokai Hokoku* 1935;10:497-500.