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Human Taeniasis and cysticercosis in Asia

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Akira Ito, Minoru Nakao, Toni Wandra

Context Human taeniasis caused by the pork tapeworm, *Taenia solium* and by the beef tapeworm, *Taenia saginata* are meat-borne parasitic diseases, and require pork and beef contaminated with metacestodes, the larval stage of these parasites, respectively. Taeniasis of *T. solium* has serious medical or public health problems, since it simultaneously causes cysticercosis, especially neurocysticercosis (NCC), threatening human life through accidental ingestion of eggs released from taeniasis patients. Approximately 70% of human population who has the custom to eat pork is risky for taeniasis/cysticercosis of *T. solium*. In contrast, taeniasis of *T. saginata* appears to be more widely distributed and common than *T. solium*. Over several decades it has been generally noticed that adult taeniid tapeworms expelled from local people in Asia appeared to be *T. saginata* (so called Asian *Taenia*), although they ate pork. It is now named *Taenia asiatica* and has been found from Taiwan, Korea, China, Vietnam and Indonesia, at least. (152 words)

Starting point Recent work on taeniasis in Asia indicates a third taeniid species, *Taenia asiatica* (AL Willingham and others. SE Asian J Trop Med Pub Health 2003; **34** (Suppl 1): 35-50) which is still unfamiliar even for the majority of parasitologists. Phylogenetic analysis of *Taenia* spp. and historical, ecological and biogeographic analyses by EP Hoberg and others (Proc Roy Soc London (B) 2001; **268**: 781-787) has indicated that *T. asiatica* is an independent species and the sister species of *T. saginata* and strongly suggested that (i) a molecular clock (conservative) estimate indicates divergence of these sister species, *T. asiatica* and *T. saginata*, at a minimum > 160,000 years ago, and (ii) *T. solium* is only distantly related and emerged in Africa several million years ago as a parasite unique to *Homo erectus*. M Nakao and others (Parasitology 2002; **124**: 657-662) provided the first "clock" evidence for the timing of the speciation event of two (Asian and American/African) genotypes of *T. solium* worldwide. Molecular techniques available for phylogeny, evolution, diagnosis by several groups including the authors' group and vaccination by MW Lightowlers and other (Int J Parasitol 2003; **33**: 1207-17) against taeniasis and cysticercosis of human taeniid infections have greatly advanced over the past decade. It, therefore, is timely to review these all. (210 words)

Where next Molecular and immunological techniques including vaccine and development of experimental animal models for differentiation of taeniid species in humans have greatly advanced over the past decade. What is clinical importance of infections by these taeniids in humans including *T. asiatica*? Where are they distributed in Asia? What is the potential for cysticercosis attributable to *T. asiatica* in humans? And what is the present situation for cysticercosis linked to *T. solium* in Asia? (72 words)

(Total words for peg: 434 words)

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The life history of Asian *Taenia* was experimentally demonstrated by Fan and his colleagues in Taiwan.¹ In contrast to *T. saginata*, pigs are required intermediate hosts, and infective metacestodes, or cysticerci of small dimensions (e.g., 2 mm in diameter) develop in the liver and survive for a relatively short period of 2-3 months. The metacestodes in pigs have only rudimentary or vestigial hooks, but strobilate adults lack rostellar armature and in this regard are similar to *T. saginata*. It is clear that Asian *Taenia* is biologically unique. However, if it was found to be related to *T. solium* rather than *T. saginata*, it might have indicated the potential for human cysticercosis.²

Eom and Rim³ described and differentiated Asian *Taenia* based on comparative morphology and designated a new species, *Taenia asiatica*. The most recent phylogenetic studies based on mitochondrial DNA (mtDNA) or comparative morphology have shown the validity and independence of *T. asiatica* as the sister species of *T. saginata*, both are distantly related to *T. solium*.⁴⁻⁷ Major characteristics of three species of *Taenia* that develop as adults in human definitive hosts are summarized in Table 1.⁸

Asian *Taenia* is *Taenia asiatica*, the sister species of *Taenia saginata*

Additional evidence supporting this concept is no hybrid of *T. asiatica* and *T. saginata* found in sympatric zones in China.^{9,10} Thus, if these two sister species are discrete biological entities, with separate histories, as indicated by phylogeny and an array of diagnostic criteria,³⁻⁸ and they are now sympatric,^{9,10} then *T. asiatica* can not justifiably be reduced as a subspecies of *T. saginata*. There is just one minor comment on the lack of definitive cross breeding experiments.^{11,12} Species definition aside, the multiple lines of evidence for *T. asiatica* support it an independent, sister species of *T. saginata*.

Where is *T. asiatica* distributed in Asia?

This parasite has been known to be present in Taiwan, Korea, China (several provinces), Indonesia (North Sumatra) and Vietnam at least where local people have the custom to eat uncooked pork with viscera after killing pigs at home.^{1, 13}

It has been reported that *T. saginata*, *T. asiatica* and *T. solium* coexist in Guangxi Autonomous Region and in Yunnan Province, China and in Vietnam.^{9,10,14}

Is the pig suitable intermediate host of *T. asiatica*?

Based on the stunted cysticerci of *T. asiatica* in pigs, there is some doubt if pigs are the really suitable intermediate hosts

or if this parasite has well adapted to use pigs as its intermediate hosts.

When non-obese diabetic severe combined immunodeficient (NOD/Shi-*scid*) mice were used for preparation of cysticerci of these three taeniid species, oncosphere embryos of *T. asiatica* and *T. saginata* developed into cysticerci of approximately 10 mm in diameter with similar morphology and differed from those of *T. solium*.¹⁵

Does cysticercosis of *T. asiatica* exist in humans?

Based solely on this association demonstrated in both molecular and morphological studies, it is predicted that cysticercosis in humans attributable to *T. asiatica* does not occur, because it is a phenomenon unknown in its sister-species, *T. saginata*.^{2,5-7}

***Taenia solium* worldwide**

Recent topics on Evolution and two genotypes of *T. solium*

The most serious taeniid species for humans is *T. solium*, since it induces neurocysticercosis in humans. Hoberg and others⁶ launched a hypothesis that (i) *T. solium* emerged in Africa several million years ago (MYA) as a parasite of *Homo erectus* and came out from Africa, (ii) *T. solium* is only distantly related with *T. saginata*, and has its own independent

evolutionary trajectory and historical ecology. Recently, Nakao and others¹⁶⁻¹⁸ indicated that (i) *T. solium* in the world can be divided into Asian and African/American genotypes which diverged approximately 1 MYA in western Palearctic (Europe) and Asia, (ii) the tapeworm was maintained and diverged in early human colonies through a 'human-human' cycle (cannibalism) and a 'human-wild suids' cycle (hunting), and (iii) European (western Palearctic) genotype was introduced into Africa, southern part of the Sahara desert, and America through European exploration and colonization since 1500s. These two research groups stress that *T. solium* is originally human parasite through cannibalism. Although there is no critical evidence of pathological differences between Asian and African/American genotypes, it is crucial to identify two genotypes of *T. solium*, since it travels with human carriers.^{11,18,19}

***T. solium* taeniasis/cysticercosis in Asia**

The highly endemic areas in Asia locate everywhere the local people consume pork: China, India, Vietnam, Lao PD, Cambodia, Nepal, Myanmar, Philippines, Indonesia where local pigs roam around with free access to human feces. From Japan and South Korea, it has been eradicated.^{20,21} Situations in India and Indonesia are of particular interest. The majority of people in India are vegetarians but NCC with solitary cyst is very

common.^{20,22} By contrast, the majority of people in Indonesia are Muslim but NCC is spreading in several islands where the majority is Hindu or Christian.^{20,23,24}

***T. solium* taeniasis/cysticercosis in Papua, Indonesia**

The present situation in Papua (= former Irian Jaya), Indonesia appears to be the worst in the world. There are several brief reviews on the history of introduction of NCC into Papua.^{22,24} It has been revealed that approximately 46% of local people \geq 18 years old examined in Jayawijaya District in 1996-1997 were expected to be cysticercosis of *T. solium*, either symptomatic or asymptomatic.^{24,26} Approximately > 8% and 32% of local people living in the local capital city, Wamena, Jayawijaya examined in 2001 harbored adult tapeworms of *T. solium* and expected to be suffering from cysticercosis, respectively.²⁷ The genotype of *T. solium* in Papua has been confirmed to be the Asian type using expelled proglottids, eggs and subcutaneous cysts resected.^{24,26,27} Local people live with pigs and dogs together and these pigs and dogs function as scavengers and therefore highly infected with cysticerci of *T. solium*.^{28,29} As eating dog meat is still not rare in Asia, especially in Korea, China, Vietnam and some parts of Indonesia including North Sumatra. Some ethnics living in Java, Sulawesi, Papua have custom to eat dog meat. Therefore, there might be some contribution for

maintenance of the life history of *T. solium* through the dog-human cycle as well as the well-known the pig-human cycle.²⁹

It is urgent for us to check the situation of *T. solium* taeniasis/cysticercosis in other islands in Indonesia and the neighboring countries including East Timor and Papua New Guinea.²⁴

Present situation of taeniasis in Sumatra and taeniasis/cysticercosis in Bali

In North Sumatra, the ethnic groups living in Samosir Island in the Lake Toba are Christians and used to eat uncooked minced pork with viscera and blood¹³ similar in Bali where local Hindi people still eat uncooked minced pork with fresh blood and recently have started eating of uncooked minced beef too (Wandra et al. unpublished).²³ There is no crucial evidence of taeniasis/cysticercosis of *T. solium* in Samosir Island and taeniasis of *T. asiatica*, which has well been recognized as endemic disease there¹³, is now not so common in 2003 (Wandra et al. unpublished). Similarly, taeniasis/cysticercosis of *T. solium* which was common in Bali one decade ago³⁰ is becoming rare. In contrast, a rapid increase in the number of taeniasis of *T. saginata* with prevalence rate of more than 20% of local people in several villages has most recently become evident (Wandra et al, unpublished). There is no critical evidence of

T. asiatica in humans in Bali so far. It is interesting to understand the situation in these two areas in Indonesia. It is strongly suggested that taeniasis/cysticercosis of *T. solium* in Bali and taeniasis of *T. asiatica* in North Sumatra have become not common through changes in pig husbandry to keep pigs indoor without direct contact with human feces, improvement of sanitation, and sustainable education to boil pork before eat (Wandra et al. unpublished).

Importance of identification of human *Taenia*

It is actually most important to know who is infected with *T. solium* due to the issue of neurocysticercosis (NCC) in humans. This drives the necessity to accurately and rapidly identify any species of *Taenia* in a human definitive host; and to accurately identify any cysticerci resulting from recovery of metacestodes from infected humans.

It is crucial to identify and differentiate *T. asiatica* from *T. saginata* for epidemiological or public health concerns. The life cycle of *T. asiatica* appears to be completed in rather remote areas where pigs can roam around with free access to human feces in many Southeast Asian countries as similar as that of *T. solium* in Asia, Latin America and Africa.³¹

The most accurate approaches for identification of species are based on total evidence whether molecular and immunological

diagnostics are combined with comparative morphology.^{7,33} Multiplex PCR to identify *T. asiatica*, *T. saginata*, and Asian and Africa/America genotypes of *T. solium* is now available.^{10,32} Serology for cysticercosis in humans, pigs and dogs are available and serology for taeniasis in humans as well as copro-antigen test and copro-DNA test for taeniasis are available.³³ The human cases of taeniasis of *T. saginata* in the world, especially at least in Asia should be re-evaluated based on mtDNA and epidemiological study for differentiation of *T. asiatica*. Much of this material may not be accessible by current molecular techniques due to methods of preservation, or the possibility that specimens no longer exist. Thus, it would be necessary to engage in new and broad-based surveys across this region.

Prevention and control of human *Taeniasis*

Clinical manifestation of taeniasis of *T. asiatica* appears to be similar to that of *T. saginata* but differs from that of *T. solium*. Almost every day, singled proglottids of either *T. asiatica* or *T. saginata* actively and spontaneously come out from our anus. It is the most common symptom that tapeworm carriers themselves easily recognize by themselves. Therefore for diagnosing of outpatients and for epidemiological survey, it is important to show expelled proglottids for demonstration.

Treatment with a single dose of praziquantel or nicrosamide is sufficient to expel adult worms of *T. saginata* or *T. asiatica* or even *T. solium*.²¹

There are two strategies for control of taeniasis other than improvement of meat inspection. *The first* is for foreign visitors and local people in endemic areas not to eat such local food with uncooked or undercooked meat with viscera. *The second* is to keep pigs indoor with no contact with human feces which has greatly been proven for prevention of cysticercosis of *T. solium* in developed countries³¹ and in Bali. Cut-off the life cycle of *T. solium* may depend on sustainable public health education (i) not to eat uncooked or undercooked but well cooked meat or viscera with improvement of meat inspections, and (ii) to block the direct contact of domestic animals with human feces through improvement of sanitation and the style of husbandry of animals.

Alternative strategy for control of cysticercosis is through vaccination and chemotherapy of domestic animals.^{33,34} Recent work on vaccination of pigs and cattle against *T. solium* and *T. saginata*, respectively, is highly promising.³⁴ It is expected to be informative if the gene homology of vaccine candidate proteins between *T. saginata* and *T. asiatica* is very high, it may work against *T. asiatica* too. Another strategy for control of *T. solium* is chemotherapy of pigs by single dose

of oxfendazole.^{33,35} These techniques for domestic animals and treatment of humans infected with *Taenia* should be carried out simultaneously and under sustainable financial support with sustainable education of the local people living with these parasites.³³

Conclusion Current evidence would support recognition of *T. asiatica* as a valid species that is distinct from *T. saginata*. It has been found from Taiwan, Korea, Indonesia, Vietnam and China so far where local people or the ethnic groups eat uncooked home-made pork with viscera. A sister-species relationship for *T. asiatica* and *T. saginata* and the predictive nature of phylogenetic information suggest that cysticercosis in humans attributable to the former species is unlikely.

(1940 words)

Addendum

For such international collaborations through technical transfer, the Ministry of Education, Japan (MEXT) has decided for the senior author to establish the network for control of taeniasis/cysticercosis and echinococcosis in Asia from 2003 for three years.

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Table 1. Several major characteristics of three species of human *Taenia* (modified from ^{8,15})

Characteristics	<i>T. solium</i>	<i>T. asiatica</i>	<i>T. saginata</i>
Cysticercus			
Intermediate hosts (IH)	pigs, humans ^a , dogs, wild boar	pigs, cattle, goat, monkey, wild boar	cattle, reindeer ^c
Localization in IH	muscle, brain, skin, eye, tongue	viscera mainly liver	muscle, viscera, brain ^c
Size of cysticercus (mm)	5-8 x 3-6	2 x 2 ^b	7-10 x 4-6
Scolex	rostellum with hooklets	rostellum with rudimentary hooks	no rostellum, no hook
Adult tapeworm			
Scolex	rostellum with hooklets	rostellum with no hooks	no rostellum, no hook
Number of uterine branches in a gravid proglottids	7-12	16-21	18-32
Expulsion from human	mainly in groups, passively	single, actively	single, actively

^a: neurocysticercosis is the most serious.

^b: the size and morphology of cysticercus of *T. asiatica* becomes to be similar to that of *T. saginata* in NOD/Shi-*scid* mice.¹⁵

^c: cysticerci are found from the brain of the reindeer.