

The Asian *Taenia* and the possibility of cysticercosis

Maria Teresa GALÁN-PUCHADES* and Màrius V. FUENTES

Department of Parasitology, Faculty of Pharmacy, University of Valencia,
Av. Vicent Andrés Estellés s/n, 46100 Burjassot-Valencia, Spain

Abstract: In certain Asian countries, a third form of human *Taenia*, also known as the Asian *Taenia*, has been discovered. This Asian *Taenia* seems to be an intermediate between *Taenia solium* and *T. saginata* since in morphological terms it is similar to *T. saginata*, yet biologically, as it uses the same intermediate host (pigs), it is more akin to *T. solium*. *Taenia solium* causes human cysticercosis, while *T. saginata* does not. It is not known whether the Asian taeniid is able to develop to the larval stage in humans or not. The arguments proposed by those authors who consider it unlikely that the Asian *Taenia* causes human cysticercosis are: (a) its molecular similarities with *T. saginata*; (b) the absence of cases of human cysticercosis in populations where the Asian adult is highly prevalent; and (c) the unsupporting results derived from an experimental infestation study. These three arguments are debated, although bearing in mind that at present there is still no clear scientific data to support that human cysticercosis can be caused by the Asian *Taenia*.

Key words: Asian *Taenia*, human cysticercosis

Editorial Note: During the past 10 years, medical parasitology field has been excited to identify the third human *Taenia*, which is mainly transmitted via viscera of pigs. It was regarded as *T. saginata* but now it is differentiated as a new species (*T. asiatica*) or a subspecies (*T. saginata asiatica*) according to its morphology, life history, epidemiology, and genetic information. Its nomenclature may be simplified in the near future. The mini-review in this volume was contributed by two Spanish parasitologists, Dr. Maria Teresa Galán-Puchades and Dr. Màrius V. Fuentes. This paper briefly introduces human taeniasis and proposes the possibility of cysticercosis by the third human *Taenia*, which should be confirmed by further studies. We are looking forward to

hearing much progress of studies on human taeniasis and cysticercosis.

INTRODUCTION

In recent years, there have been numerous reports on a new form of human taeniid. Initially designated as Taiwan *Taenia*, it is now known as Asian *Taenia* since it has also been reported in Indonesia, Thailand, Korea, China, Malaysia, and the Philippines (Bowles and McManus, 1994). The salient feature of this third form of tapeworm is that it is an intermediate between the two classically known species, *Taenia solium* and *T. saginata*. Morphologically, the adult Asian *Taenia* is similar to that of the adult *T. saginata*, although the inconsistent presence of both marked and unarmed rostellum on the scolex can differentiate the adult forms (Eom and Rim, 1993; Fan et al., 1995); moreover, the intermediate host involved is not cattle, but

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*Corresponding author (e-mail: Mteresa.Galan@uv.es)

swine (Fan, 1988; Fan et al., 1990). In this context, the larval stage of the Asian taeniid exhibits a liver tropism, though other organs may also be affected (Eom et al., 1992). In the intermediate host, the parasite has a cysticercus more similar to that of *T. solium* because the scolex possesses hooks; however, the cysticerci of the Asian *Taenia* are clearly smaller than those of *T. solium*. Cysticerci that have already lost their hooks may also be detected in swine (Fan, 1988; Eom and Rim, 1993; Fan et al., 1995; Ito et al., 1997).

The main epidemiological feature of this third form of human taeniid is that porcine cysticercosis is linked to the presence of *T. saginata* type adults rather than *T. solium* type adults. This epidemiological characteristic, peculiar to Taiwan (porcine cysticercosis/*T. saginata* type adults in humans), stimulated the research that led to the discovery of this third taeniid time ago (Fan, 1988).

In practical terms, the important point is that humans constitute the definitive host of three taeniids (*T. solium*, *T. saginata* and the Asian *Taenia*) instead of only two, as believed until recently. In addition to serving as the definitive host, humans may also function as the intermediate host for *T. solium* with development of cysticercosis and especially neurocysticercosis, a serious and sometimes fatal disease. This is not the case with *T. saginata*, and it remains to be established whether humans are included in the range of possible intermediate hosts of the Asian taeniid.

This transcendental hypothesis is posed in view of the fact that it is precisely at the intermediate host level where both the Asian *Taenia* and the *T. solium* behave similarly and distinct to *T. saginata*. In this context, pigs serve as the intermediate host for both *T. solium* and Asian *Taenia*. Thus, if these parasites effectively share one intermediate host, the question may be posed of whether they are also able to share another, in this case, humans.

Another consideration to investigate is whether the case of *T. saginata* is exceptional or not, since in many cestodes (mostly taeniids) with life cycles that develop in mammals close to humankind, humans are

introduced in the cycle as intermediate host. This is the case for the cycles of *T. solium*, *T. crassiceps*, *Echinococcus granulosus*, *E. multilocularis*, *Multiceps multiceps*, *M. serialis* or *Spirometra* spp.

TAXONOMIC STATUS OF THE ASIAN TAENIA

At present there are two opinions regarding the taxonomic status of the Asian *Taenia*. [Eom and Rim \(1993\)](#) described the cestode under the new specific designation of *Taenia asiatica*, as a function of its geographical distribution. Prior to this description, however, [Zarlenga et al. \(1991\)](#), based on genetic studies and supplementing the observed larval biological and morphological differences, suggested that despite the clear relations to *T. saginata*, the parasite should not be regarded simply as a variant of this species. On the other hand, a number of specialists who have examined the morphological and molecular characteristics of the tapeworm opine that the Asian taeniid should not be recognized at a species level but rather as a strain or subspecies of *Taenia saginata* ([Bowles and McManus, 1994](#); Fan et al., 1995). Consequently in 1995, Fan et al. redescribed the taeniid as a subspecies of *T. saginata* specifically, the name *T. saginata asiatica* was given to the taeniid.

Subsequently, however, [Zarlenga and George \(1995\)](#), on the basis of their mitochondrial DNA findings, considered the parasite at a species level. Soon after, epidemiological and sanitary aspects were addressed by [Galán-Puchades and Mas-Coma \(1996\)](#), with the argument that this form would be more usefully considered as a separate species. More recently, [Queiroz and Alkire \(1998\)](#), in phylogenetic studies of species pertaining to the genus *Taenia*, also considered the parasite at the species level.

The interest in this labelling debate would be restricted to those in systematic or taxonomic academia were it not for its repercussions upon public health. To regard the parasite as a subspecies of *T. saginata* and taking into consideration its inability to cause human cysticercosis suggests that the Asian taeniid is unable to produce human

infestation.

THE ASIAN *TAENIA* AND CYSTICERCOSIS

To date, no clear evidence exists to substantiate the fact that the Asian *Taenia* causes human cysticercosis. This is the main remaining point to be clarified, in view of its importance to human health.

Two opinions have been presented in recent literature. On the one hand, some authors consider on the basis of the importance of human cysticercosis presence in those Asian countries that taeniasis and porcine and human cysticercosis is caused by the Asian *Taenia* (Ito, 1992; Simanjuntak et al., 1997). On the other hand, other investigators are of the opinion that this parasite is not a causal factor in the development of human cysticercosis (Bowles and McManus, 1994; McManus and Bowles, 1994; Fall et al., 1995).

The three main criteria of those authors who consider it unlikely that the Asian *Taenia* causes human cysticercosis are: (a) the molecular similarities between the Asian taeniid and *T. saginata* (which does not cause human cysticercosis); (b) the lack of case evidence of human cysticercosis or neurocysticercosis in populations where the Asian adult is highly prevalent (Taiwan and Samosir Island in Indonesia), which is in opposition to the criteria of the above mentioned authors (Ito, 1992; Simanjuntak et al., 1997); and (c) the unsupportive results derived from an experimental infection study.

A point by point analysis following these three arguments are given to establish whether they do or do not suffice the assumption of the Asian taeniid as a possible cause of human cysticercosis.

Molecular similarities between *T. saginata* and the Asian *Taenia*

In regards to molecular affinities, McManus and Bowles (1994) summarized the molecular genetic study conducted by Zarlenga et al. (1991) and Bowles and McManus (1994) and concluded that the Asian *Taenia* is a genetically distinct entity nevertheless, closely related to *T. saginata*. They developed PCR-RFLP (polymerase chain reaction-restriction

fragment length polymorphism) methods that allowed rapid discrimination of Asian *Taenia* from other human taeniids. Likewise, these authors carried out a comparative study of mitochondrial COI (cytochrome c oxidase I) and nuclear rDNA 28S sequences. These DNA analyses indicated that the Asian *Taenia* is much more closely related to *T. saginata* than other recognized taeniid species are to each other. Thus, and based upon these genetic affinities observed between *T. saginata* and the Asian form, McManus and Bowles (1994) concluded that the latter seems unlikely to cause human cysticercosis.

Following the above studies, new molecular findings have widened the gap between the Asian taeniid and *T. saginata*. In effect, Zarlenga and George (1995) observed a 4.6% divergence in nucleotide sequencing between the Asian taeniid and *T. saginata*, calculated from mitochondrial banding patterns; this figure being higher than the 2.6% estimated from the COI mitochondrial gene fragment sequence data obtained by Bowles and McManus (1994). Zarlenga and George (1995) added that this level of mitochondrial DNA nucleotide substitution is often associated with species level differences in mammalian systems, as previously commented by George (1982).

Eom et al. (1996) also detected genetic differences among the different isolates of the Asian taeniid, particularly between the Korean and Taiwanese specimens. These authors related the possible existence of biological and morphological differences between the two isolates to the observed genetic differences. In addition, Eom and Rim (1998) detected new morphological and genetic differences between *T. asiatica* and *T. saginata* at metacestode level.

The possible non-implication of the Asian *Taenia* in the production of human cysticercosis, as concluded from the initial molecular biology findings is substantiated by the fact that *T. saginata* is unable to produce human cysticercosis. In this case then, the Asian taeniid would also be an unlikely cause of porcine cysticercosis since *T. saginata* is not a causal factor for the disease. Nevertheless, swine represents the best natural intermediate

host known for the Asian taeniid (Fan, 1988; Fan et al., 1990; Eom and Rim, 1993). Therefore, the natural infective activities of the Asian *Taenia* and *T. solium* eggs (the latter being responsible for human cysticercosis) are very similar, and yet different from that of *T. saginata* eggs.

Lack of cases of human cysticercosis in Taiwan and Samosir Island (Indonesia)

The second criterion of those authors who consider it unlikely that the Asian taeniid causes human cysticercosis is the absence of evidence of human cysticercosis or neurocysticercosis in human populations where the intestinal Asian taeniasis is highly prevalent (Taiwan and Samosir Island in Indonesia).

Firstly, it should be taken into account that autopsies of warfare and traffic accident victims have revealed a large proportion of cysticercosis and, more accurately, of asymptomatic neurocysticercosis accidentally discovered at necropsy (Evans, 1996). Frequently, multiple parenchymal calcifications have been incidentally detected in asymptomatic individuals during imaging studies. The individuals harboring these parasites presumably have a “silent immune response” and a remarkable tolerance to the parasite (Carpio et al., 1998).

Secondly, this absence of evidence of human cysticercosis or neurocysticercosis is only indicative of a low prevalence of *T. solium*; thus, it should not be used as an indication that the Asian taeniid is unable to produce human cysticercosis.

Taenia solium and the Asian *Taenia* - considering the latter at either a specific or subspecific level - are different species in which both the tropism and size of the larval forms differ. In the pig, the larva of *T. solium* exhibits no defined tropism (Fan et al., 1994), and its size ranges from 0.5-1.5 cm (Rabiela et al., 1989). In contrast, the larva of the Asian *Taenia* exhibits marked liver tropism in the pig, and reaches a size of only about 2 mm (Fan, 1988; Eom and Rim, 1993).

In humans, the cysticercus of *T. solium* has a behavior similar to that observed in the pig (its usual intermediate host). In humans, however, and in many cases depending on

geographical factors, the preferred organs for parasitisation are the brain and eye, as well as muscles and viscera. It is precisely in humans where *T. solium* can give rise to aberrant larval forms in the brain (i.e., the racemose cysticercus and the intermediate form between the latter and cellulose cysticercus). These aberrant forms are related to the more severe presentations of neurocysticercosis (Rabiela et al., 1989).

In regards to the Asian *Taenia*, Fan et al. (1988) were able to experimentally infect monkeys, calves and goats, yielding (as in the case of the pig) hepatic metacestodes. If, as would be expected, the cysticercus of the Asian *Taenia* follows the same developmental course in humans, the preferred parasitisation organ would be the liver thus giving rise to hepatic cysticercosis with the presence of considerably smaller larvae than in the case of *T. solium*. Therefore, such cases of cysticercosis could be either symptomatic or asymptomatic, depending on the number of larvae and their location within the liver. A few hepatic cysticerci, if any, may be asymptomatic and practically unnoticed.

The liver tropism of the larva of the Asian *Taenia* in the pig is also a frequent phenomenon in the larval stages of other taeniids. Thus, *E. granulosus*, *E. multilocularis*, *Taenia taeniaeformis* or *T. hydatigena* are all examples of parasites that, in their habitual intermediate hosts, exhibit liver tropism though in the case of *E. granulosus* or *T. hydatigena* they are also able to reach other locations. As pointed out above, humans also act as intermediate hosts for species of the genus *Echinococcus*, where the developed larva maintains liver tropism; this phenomenon being more accentuated in the case of *E. multilocularis*. Therefore, in the situation where the eggs of the Asian taeniid are infective in humans, the larva might be expected to preferentially develop in the liver. Thus, the symptoms of possible Asian taeniid cysticercosis would be different to those known for “classical” cysticercosis or neurocysticercosis caused by *T. solium*.

The clinical risk of this possible larval parasitisation on the part of the Asian taeniid could be similar to that of classical cysti-

cercosis, provided the larvae also reach other, different locations in humans (as in the case of both *T. solium* and *E. granulosus*) or develop aberrant forms. In this context, at the experimental level, larvae of the Asian taeniid have been successfully developed in non-hepatic regions (Eom et al., 1992) and moreover, can reach larger body sizes in hosts other than pigs (Ito et al., 1997).

To summarize, firstly, the absence of evidence of cysticercosis as classically defined in human populations where the Asian taeniid is prevalent should not serve to exclude the possible presence of human cysticercosis caused by this parasite. Secondly, and/or until demonstrated otherwise, the Asian taeniid - possibly depending on different strains (it should be remembered that Eom and Rim (1996) detected genetic variations among *T. asiatica* isolates from Taiwan and Korea) - could also give rise to clinical manifestations compatible with the attributes of *T. solium* cysticercosis in the event that other human organs are affected in which larger or anomalous larval forms develop.

Experimental infections

In regards to the experimental study carried out by Fall et al. (1995), in order to evaluate the infectivity of the eggs of Asian *Taenia* for humans, these authors administered eggs from a Korean isolate of the Asian taeniid to three baboons (*Papio hamadryas*). The absence of successful parasitisation observations suggested that the eggs of the Asian taeniid may not be infective in humans. Regardless, the authors recognized that is difficult to suggest whether a baboon is a suitable model or not to test the infectivity of Asian *Taenia* eggs for man.

Lastly, as has been mentioned above, Fan et al. (1988) were previously able to infect four monkeys with eggs of the Asian taeniid. Thus, to date, the results of experimentally induced infections neither confirm nor discard the possibility that such eggs may also infect humans.

DISCUSSION

The question of whether humans may or

may not serve as an intermediate host for the Asian taeniid is important, for it is not simply a sporadic parasite. Indeed, Fan et al. (1997) recently showed that the adult of the Asian form is markedly prevalent. According to this author, in endemic areas of Taiwan, Korea and Indonesia, up to 21% of the human population has been found to be affected, with annual losses of over 18 million U.S. dollars. In northern Sumatra, 10% of the population is affected, and 23% of all examined pigs were found to harbour larvae (Murrell et al., 1996).

Moreover, its true geographical distribution remains uncertain, and need not be limited to the Asian region as previously thought. Many other controversial epidemiological situations resembling that recorded in Taiwan have occurred in different parts of the world, including Mexico, the former-USSR, Spain and certain African countries (Galán-Puchades and Mas-Coma, 1995), where humans are much more commonly affected by *T. saginata* than *T. solium* and while bovine cysticercosis is only rarely observed. In Mexico, for example, for each human case of *T. solium* there are 14 human cases of *T. saginata*, though nevertheless both human and porcine cysticercosis pose a major health and economical problem.

In Brazil, due to the health care problem posed by human cysticercosis, and in view of the high prevalence of *T. saginata* taeniasis among the population, the larva of this species have been accused as the possible cause of such human cysticercosis (Santos, 1996). In our opinion, the situation observed in Brazil is perhaps attributable to two causes. Firstly, *T. saginata* might effectively produce human cysticercosis. Immunological methods could contribute to resolve this question by applying EITB 100% specific for *T. solium* in affected patients. Secondly, the Asian taeniid might also be implicated the adult worm of which is the same as that of *T. saginata*, contributing with *T. solium* to the mentioned human cysticercosis.

It should be taken into consideration that for many years this Asian *Taenia* was systematically confused with *T. saginata*. This same misdiagnosis may be happening in other non-Asian countries, since at the human host level these parasites are commonly diagnosed

by observing the gravid proglottids, which are not clearly differentiated by taxonomic criteria. In the same way, and in the absence of morphological studies reporting the measurements of the scolex hooks, the porcine cysticerci attributed to *T. solium* could include the Asian form.

In order to clarify both issues, i.e., humans acting as an intermediate host for the Asian taeniid, and the true geographical distribution of the parasite, it will be necessary to find the larval forms at the intermediate host level since the gravid proglottids of the adult stage in humans are indistinguishable from those of *T. saginata* when using only routine diagnostic techniques. This search should thus focus on two levels: humans and pigs. If the Asian *Taenia* larvae were detected in pigs from another continent, it might prove possible to explain the controversial epidemiological situations found in certain countries, as outlined above.

The question would be resolved if the cysticercus were to be found in humans, or if human volunteers were to ingest viable eggs of the cestode. There have indeed been cases of humans who voluntarily ingested viable metacestodes of the Asian *Taenia* (Eom and Rim, 1993; Fall et al., 1995). However, the authors of this study are convinced that even those researchers who support the hypothesis that humans are unlikely to become infested by the eggs of the Asian taeniid would prefer to not conduct such studies on humans.

The task is therefore not easy, for it implies a thorough and worldwide morphological study of cysticerci in both pigs (especially at liver level) and humans, in order to establish a differential diagnosis with *T. solium*. Although the size is smaller in the larva of the Asian *Taenia* this datum may not be sufficient, for in other hosts the larva of the Asian form grows to larger sizes than reported in the pig (Ito et al., 1997). A definitive conclusion could be reached by studying the scolex hooks which in the cysticercus of *T. solium* possess dimensions similar to those found in the adult stage, while the cysticercus of the Asian form exhibits small vestigial hooks or even none at all (Fan et al., 1995; Ito et al., 1997).

A morphological and/or molecular study is

the only solution, since the problem posed by cross reactions presently limits the application of specific immunological diagnostic techniques in humans with cysticercosis. It has been demonstrated that the serum of pigs infested with the larva of the Asian taeniid cross-reacts with the EITB assay that is 100% specific for *T. solium* (Pilcher et al., 1991).

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