Cystic echinococcoses in Mongolia: molecular identification, serology and risk factors.

CHAPTER 51

Cysticercosis and taeniosis: 
*Taenia solium*, *Taenia saginata* and *Taenia asiatica*

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Summary

The pork and beef tapeworms, *Taenia solium* and *Taenia saginata* respectively, are taeniid cestodes and major food-borne or meat-borne zoonoses. Human tapeworms and swine cysticerci have been known since Egyptian and Greek cultures. Nevertheless their association as part of the life cycle of the same parasite was only demonstrated during the nineteenth century. Kuchenmeister fed convicts with cysticerci excised from pork meat and found adult tapeworms in the intestine after autopsy, while van Beneden fed *T. solium* eggs to pigs and found numerous cysticerci in muscles after slaughter (Grove 1990).

*T. solium* is the only causative agent of neurocysticercosis in humans and is, therefore, the more important of these species in public health. This chapter describes classical aspects of the morphology of the parasites as well as clinical aspects of the diseases they cause. Most importantly, detailed explanations of taxonomic aspects, specially related to the newly recognized *Taenia asiatica* are given. Furthermore, the epidemiology and transmission dynamics of the parasites, as well as intervention measures such as health education, mass drug treatment and vaccination, are described in detail. The chapter concludes with considerations on the surveillance and a discussion on prospects for the control of these cestode zoonoses.

Taxonomy

The classification of human *Taenia* is as follows:

- Kingdom: Animalia
- Phylum: Platyhelminthes
- Class: Cestoidea
- Subclass: Eucestoda
- Order: Cyclophyllidea
- Family: Taeniidae
- Genus: Taenia
- Species: *Taenia solium* Linnaeus (1758),
- Species: *Taenia saginata* Goeze (1782),

*Taeniidae* are mammalian parasites with adults found in carnivores and larvae in herbivores. In the adult parasite, the scolex, which is the anchorage organ aided by suckers, usually bears 2 rows of hooks that rarely are absent. The genital pore is irregularly alternated along the strobila with a single set of reproductive organs in each proglottid. Eggs have a radial striated appearance because of the embryophore formed by embryophoric organs in each proglottid. Adult *Taenia solium* and *Taenia saginata* are found in the human intestine. The larval stage or metacestode (cysticercus) is found in pigs (*T. solium*) and bovines (*T. saginata*).

*Taenia asiatica* has been recognized in Asia and the Pacific. Adult tapeworms appear to be *T. saginata* but infected people eat pork rather than beef (Huang et al. 1966; Kosin et al. 1972; Fan 1988). It has been called the Asian *Taenia* and expected to be a new species (Fan 1988; reviewed by Simanjuntak et al. 1997). Subsequent molecular studies revealed very small differences from *T. saginata* and it was classified as a subspecies of *T. saginata* (*T. saginata asiatica*, Fan et al. 1993), which used different intermediate hosts distributed in Asia and the Pacific (Fan 1988, 1995; McManus and Bowles 1994). Later, it was described as *Taenia asiatica*, an independent but sister species of *T. saginata* (reviewed by Ito et al. 2003; Eom 2006; Hoberg 2006). Separate species are believed to be valid as *T. saginata* and *T. asiatica* are distribute sympatrically but to data no hybrids between the two have been identified which would be expected if they were subspecies or strains of the same species. However, the numbers of specimens to date examined is small. (Hoberg 2006). Fig. 51.1 illustrates a summary of the molecular phylogeny of taeniid cestodes (modified from Okamoto et al. 2007).

Molecular phylogeny

Molecular tools have been used to further characterize the 3 human *Taenia* species (McManus and Ito 2005) and their epidemiology and possible origin. Mitochondrial DNA data strongly suggest that *T. saginata* and *T. asiatica* are very closely related to each other and
that *T. solium* is divided into two genotypes, the Asian and the American/African genotypes (Fig. 51.2). Minor diversity within the genotypes has been demonstrated in samples from Peru and Mexico (Nakao et al. 2002; Campbell et al. 2006; Maravilla et al. 2003, 2008; Sudewi et al. 2008). Molecular phylogenic studies (Sudewi et al. 2008) suggest that *T. solium* in Papua originated elsewhere in Asia rather than from nearby Bali as suggested by Gajdusek (1978).

*T. saginata* mitochondrial DNA analysis shows large variations (Rodriguez-Hidalgo et al. 2002; Myadagsuren et al. 2007) pointing to a higher complexity of this parasite than that of *T. solium*.

*T. solium* emerged in Africa several millions years ago as a parasite of early hominids that probably evolved from parasites of hyaenids (Hoberg 2001, 2006).

Detection of parasite DNA using faecal samples and multiplex PCR for identification of human *Taenia* should be used in endemic areas for *T. solium*, *T. saginata* and *T. asiatica*, because their sympatric distribution may complicate surveillance of cysticercosis control (Ananthaphruti et al. 2007).

**Morphology**

**Tapeworm**

Tapeworms are flat long helminths: adults measuring 1.5 to 10 m. The head or scolex, has four suckers and a rostellum, which may be armed with hooks (*T. solium*), unarmed (*T. saginata*) or have a sunken or unarmed rostellum (*T. asiatica*, Fig. 51.3). Hooks are organized as a two row crown of 22 to 32 hooks that ranges in size from 159 to 173 μm. The most conspicuous part of the tapeworm is the chain of segments that forms the strobila. It has the appearance of a ribbon and is constituted by more than a thousand proglottids (proper name for segments). Tapeworms do not have digestive organs, thus feed passively through their tegument. In contrast they have a well formed excretory system that contains numerous collecting ducts and flame cells. Proglottids develop from the neck region behind the scolex. Proximal proglottids are immature, they are followed by mature ones that contain several

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**Fig. 51.1** Molecular phylogeny of genus *Taenia*. Modified from Okamoto et al. (2007).

**Fig. 51.2** Two genotypes of *T. solium* in the world. The neighbour-joining phylogenetic tree of taeniid tapeworms inferred from the complete nucleotide sequences of mitochondrial *cox1* gene. The scale bar represents the estimated number of nucleotide substitutions per nucleotide site. The isolates of *T. solium* were obtained from Bolivia (BOL), Ecuador (ECU), Brazil (BRA), Cameroon (CAM), Peru (PER), Mexico (MEX), Mozambique (MOZ), Tanzania (TAN), Iran Jaya (IRI), China (CH1 and CH2), India (IND) and Thailand (THA). Modified from Nakao et al. (2002).
Each egg contains an embryo, which is a multi-cellular structure that has six hooks, therefore it is also named hexacanth embryo or oncosphere. When eggs are released from the definitive host, many are fully embryonated and infective whilst others are at different stages of maturation and not infective. The embryophore appears as a rigid structure that protects the oncosphere while the egg is in the environment, making eggs extremely resistant. When eggs are ingested by the intermediate host, the cementing substance that joins embryophoric blocks is susceptible to enzymatic digestion which allows the oncosphere to be released (Laclette et al. 1982; Fan et al. 1995). Aided by their hooks and by enzymes released in vesicles, the oncospheres invade the intestinal mucosa and, after circulating, develop in the intermediate host.

Cysticercus

*T. solium* cysticerci have been identified in liver, brain and skeletal muscles of pigs six days after infection measuring around 0.3 mm. By 60 to 70 days after infection cysticerci have a fully developed scolex and measured between 6 to 9 mm (Yoshino 1933a, b, c). The mature cysticercus is usually spherical or oval, white or yellow, measures 0.5 and 1.5 cm and has a translucent bladder wall, through which the scolex can be seen. Young cysticerci have minimal inflammatory reaction surrounding them, while older parasites or those that are in pigs that were treated with a cestocidal drug, have an intense reaction that includes eosinophils, lymphocytes and macrophages (Flisser et al. 1990a; Aluja and Vargas 1989; Aluja et al. 1998). Cysticerci have two chambers: an inner one contains the scolex and the spiral canal and is surrounded by an outer compartment that contains the vesicular fluid, usually less than 0.5 ml. When a cysticercus is ingested by the definitive host, the first event that takes place is the widening of the pore of the bladder wall for the scolex and neck to emerge, leaving the bladder wall and vesicular fluid to disintegrate in the digestive tract of the definitive host (Rabiela et al. 2000).

*T. solium* cysticerci may also establish in humans causing cysticercosis in the central nervous system, eye, striated and heart muscle and subcutaneous tissue. Two morphological types of metacestodes develop in humans: cellulose and racemose. The cellulose cysticercus is as previously described and is present in swine and in humans. This type of cysticercus is generally separated from the host tissue by a thin collagenous capsule, within which it remains alive (Escobar 1983; Aluja and Vargas 1988; Aluja et al. 1998). The racemose cysticercus appears either as a large, round or lobulated bladder circumscribed by a delicate wall, or resembles a cluster of grapes, it measures up to 10 or even 20 cm and may contain 60 ml fluid. Cellulose cysticerci grow and transform into racemose in spacious areas such as basal cisterns, especially optic, carotid, Sylvian and peduncular cisterns. The most important characteristic of this type of cysticercus is that usually the scolex cannot be seen, in some cases only detailed histological studies reveal its remains (Berman et al. 1981; Jung et al. 1981; Rabiela et al. 1989).

*Taenia saginata* cysticerci, (*cysticercus bovis*), is an oval bladder less than 1cm long, fluid filled and containing the invaginated scolex but does not have hooks. Cysticerci lodge in the skeletal muscle of cattle and sporadic reports of unarmored cysticerci in llamas, pronghorn, oryx, topi and other antelopes, bushbucks, gazelles, wildebeest, oryx and giraffes, have appeared in the literature (Nelson et al. 1965; Pawlowski and Schultz 1972; Gemmell et al. 1983). Intermediate host acquire the infection when grazing on contaminated pasture.

**Eggs**

Eggs are spherical, range in size from 20 to 50 μm and are morphologically indistinguishable from eggs of other taeniid species.

*Fig. 51.3* Three Taenia worms of two species were expelled from one woman in Kanchanaburi, Thailand in 2004 (2 *T. solium* and 1 Asian *Taenia*) and from one Tibetan girl in 2007 (2 *T. saginata* and 1 *T. solium*). Fig (a) and (b) show the scolex of one of the 2 *T. solium* and one Asian *Taenia* from Kanchanaburi which were confirmed by DNA analysis. Fig (a) was morphologically identified to be *T. saginata*, since there was no evidence on the distribution of Asian *Taenia* in Thailand before this study. Fig (c) shows two *T. saginata* and one *T. solium* from a Tibetan girl (Dr LI TY unpublished data). In these areas, three species have been confirmed to be occurring sympatrically. (Ananthaphruti et al. 2007; Li et al. 2006).

hundred testes and two to three ovary lobes per segment. Tapeworms are hermaphrodites; self-fertilization occurs and eggs develop in the multi-branched sac-like uterus of gravid proglottids, at the end of the strobila, which contain between 50,000 and 80,000 eggs per gravid segment. Distal proglottids become bigger, measuring from a couple of mm to up to 2 cm long. *T. solium* has 7–14 lateral uterine branches in the proglottid whilst *T. saginata* has 14–32. This feature is very important for species identification when the scolex cannot be found (Eom and Rim 1993; Fan et al. 1995; Flisser et al. 2004a; Andreassen 2005).

The adult tapeworm dwells in the human small intestine. An autoradiographic analysis of the germinative tissue in evaginated cysticerci identified stem cells that proliferate continuously, differentiate and migrate to the tegument, constituting the main process by which these worms grow (Merchant et al. 1998). Adult *T. solium* has been established experimentally in one gibbon, one chacma baboon, many golden hamsters and, recently, in gerbils and chinchillas (Verster 1965; 1974; Cadigan et al. 1967; Maravilla et al. 1998). Experimentally infected hamsters develop mature segments and, when rodents are immunosuppressed with steroids, long lasting gut infections (1–3 months) are attained, pre-gravid proglottids develop in hamsters and in gerbils, while gravid proglottids and mature eggs may develop in chinchillas (Maravilla et al. 1998). The inflammatory, humoral and cellular immune responses have been characterized in non immunosuppressed hamsters (Avila et al. 2006). Experimental infections with adult *T. saginata* have been established in immunosuppressed golden hamsters without obtaining mature or gravid proglottids (Verster 1974) but their study has not been followed.

**Eggs**

Eggs are spherical, range in size from 20 to 50 μm and are morphologically indistinguishable from eggs of other taeniid species.
**T. asiatica** cysticerci are smaller than those of *T. saginata* measuring approximately 2–3 mm in diameter. Both metacestodes have a scolex with a round rostellum surrounded by four symmetrically placed conspicuous suckers, while *T. asiatica* has two rows of rudimentary hooklets, considered as a wart-like formation that usually do not develop into morphologically identifiable hooks. *T. asiatica* cysticerci are found in domestic pigs and wild boar (Fan et al. 1995) and develop in liver but not in muscle. Most importantly, *T. asiatica* does not appear to cause cysticercosis in humans. This supports the hypothesis that it is a sister species of *T. saginata*. Both *T. saginata* and *T. asiatica* may be found sympatrically in Asia and the Pacific (Flisser et al. 2004; Ito et al. 2008). The main features of tapeworms, cysticerci and eggs are shown in Table 51.1.

### Table 51.1 Morphological characteristics of human tapeworms

<table>
<thead>
<tr>
<th></th>
<th><em>Taenia solium</em></th>
<th><em>Taenia saginata</em></th>
<th><em>Taenia asiatica</em></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Entire body</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length (m)</td>
<td>1–5</td>
<td>4–12</td>
<td>1–8</td>
</tr>
<tr>
<td>Width (mm)</td>
<td>7–10</td>
<td>12–14</td>
<td>9–12</td>
</tr>
<tr>
<td>Proglottids (number)</td>
<td>700–1,000</td>
<td>1,000–1,500</td>
<td>200–1,200</td>
</tr>
<tr>
<td><strong>Scolex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diameter (mm)</td>
<td>0.6–1.0</td>
<td>1.5–2.0</td>
<td>0.2–2.0</td>
</tr>
<tr>
<td>Suckers (number)</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Rostellum</td>
<td>Present</td>
<td>Absent</td>
<td>Present, small</td>
</tr>
<tr>
<td>Hooks (number)</td>
<td>22–32</td>
<td>Absent</td>
<td>Vestigial***</td>
</tr>
<tr>
<td><strong>Mature proglottid</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tectes (number)</td>
<td>350–600</td>
<td>800–1,200</td>
<td>300–1,200</td>
</tr>
<tr>
<td>Ovary (number of lobes)</td>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Vaginal sphincter</td>
<td>Absent</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Length (mm)</td>
<td>2.1–2.5</td>
<td>2.1–4.5</td>
<td>2.8–3.5</td>
</tr>
<tr>
<td>Width (mm)</td>
<td>2.8–3.5</td>
<td>3.1–6.7</td>
<td></td>
</tr>
<tr>
<td><strong>Gravid proglottid</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uterus (number of branches)</td>
<td>7–11</td>
<td>14–32</td>
<td>12–26</td>
</tr>
<tr>
<td>Posterior protuberance</td>
<td>Absent</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Length (mm)</td>
<td>3.1–10</td>
<td>10–20</td>
<td>4–22</td>
</tr>
<tr>
<td>Width (mm)</td>
<td>3.8–8.7</td>
<td>6.5–9.5</td>
<td>3–12</td>
</tr>
<tr>
<td><strong>Cysticercus</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Size (mm)</td>
<td>8–15**</td>
<td>6–10</td>
<td>0.4–35</td>
</tr>
<tr>
<td>Fluid contents (ml)</td>
<td>&lt;0.5**</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Hooks in scolex</td>
<td>Present</td>
<td>Absent</td>
<td>Rudimentary</td>
</tr>
<tr>
<td><strong>Egg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Size (μm)</td>
<td>26–34</td>
<td>26–34</td>
<td>16–45</td>
</tr>
<tr>
<td>Hooks (number)</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
</tbody>
</table>

* In humans racemose type cysticerci measure up to 20 cm.
** In humans racemose type cysticerci contain up to 60 ml.
*** Hooks are sunken and rudimentary NR – not reported.

### Life cycle

Life cycles of the human *Taenia* are shown in Fig. 51.4. When a person ingests raw or semi-cooked pork or beef with viable cysticerci, the scolex evaginates and attaches to the intestinal mucosa in the upper third section of the small intestine (duodenum–jejunum). Gravid proglottids are released with faeces and/or spontaneously, starting at 8–12 weeks after infection. Although some sources state that tapeworms can survive for about 25 years, published original articles indicate that *T. saginata* can be found in the intestine of the host for approximately two years. Recent experience indicates that *T. solium* remains for shorter periods. Tapeworms release a few gravid proglottids, full of eggs, daily or 2–3 times per week (Andreassen 2005; Flisser et al. 2005a, 2006).

When swine or cattle ingest eggs, bile and enzymes disaggregate the embryophoric blocks and digest the oncospheral membrane. Cysticerci establish primarily in skeletal and cardiac muscle, as well as in the brain of pigs, a process that takes approximately 12 weeks. They remain viable for at least one year, when pigs are usually sent to slaughter. In cattle, cysticerci are usually calcified in adult animals, indicating that for *T. saginata* cysticercus life span is short. The main distinguishing feature of the life cycle of *T. asiatica* compared to *T. saginata* is the viscerotropic nature of cysticerci in pigs (especially to the liver), in contrast to the musculotropic cysticerci of *T. saginata* in cattle. Metacestodes from beef and swine become infective to humans about 8 to 10 weeks post-infection. Humans only acquire cysticercosis when they consume eggs in food handled by people infected by adult *T. solium* or through the faecal oral route (Eom and Rim 1993; Fan et al. 1995, Eom 2006).

### Clinical aspects

#### Intestinal taeniosis

Intestinal taeniosis, caused by *T. solium* or *T. saginata*, is normally non-pathogenic. It is identified because proglottids are frequently released (Craig and Ito 2007). Observations on a total of 3,100 affected people, show that by far the most frequent symptom is the discharge of proglottids (93%) (Pawlowski and Schultz 1972). This is a distinctive sign because of a sensation in the rectum followed by a crawling sensation in the perianal region and the thighs due to the discharge and movement of the proglottids. Up to 35% of tapeworm carriers felt abdominal pain and/or nausea. Weight loss only occurred in 21%, change in appetite in 17% and 15% reported headaches. In Ethiopia, 18 of 26 *T. saginata* carriers reported independent migration of segments from the anus (Tesfa-Yohannes 1990). Voluntary self-infections of humans with cysticerci of *T. saginata* reported release of 5–15 segments per day starting 10–12 weeks post infection (Craig and Ito 2007). As a result of worm migration to unusual sites or due to mechanical effects, various rare acute conditions or complications may occur, including appendicitis, invasion of the pancreatic and bile ducts, intestinal obstruction and perforation, vomiting of proglottids, or even vaginal bleeding due to a tapeworm in the uterus (reviewed in Flisser 1995, Jongwutiwes et al. 2004, Ahsan et al. 2005, Liu et al. 2005, Karanikas et al. 2007). Of greater importance in avoiding *T. solium* adult infections is that the tapeworm carrier is the main risk factor for acquiring cysticercosis (Flisser and Gyorkos 2007).
Taeniosis has been diagnosed for over a half a century by detecting eggs in stools under microscopy or proglottids with the naked eye (Hall et al. 1981). These approaches are not very sensitive because they depend on the natural release of segments and on technical expertise. Coproantigens are parasite-specific products present in host faeces that can be detected by immunologic techniques. These products are associated with adult parasite metabolism and are present independently of eggs or proglottids. In addition, they are undetectable in the faeces shortly after removal of the adult worms and therefore can indicate treatment success. Detecting human taeniosis by an enzyme-linked immunosorbent assay (ELISA), without necessarily observing eggs in the stool, represents a significant advance in diagnosis. The assay can detect as little as 35 ng protein/ml of adult parasite antigen products. The sensitivity depends on the assay format employed and the quality of the immunized rabbit serum used. A high titre rabbit serum offers a higher sensitivity. Rabbit anti-*Taenia* antiserum is not commercially available at this time so that antibody titres and avidity may vary. Coproantigen detection by ELISA have already been applied for screening of taeniosis (including *T. asiatica*) in several field studies (Flisser 2002a; Allan and Craig 2006; Wandra et al. 2006b; Flisser and Gyorkos 2007).
**Neurocysticercosis**

Neurocysticercosis (NCC) is due to the development of *T. solium* cysticerci in the human central nervous system, where parasites can be found in the parenchyma, the subarachnoid tissue, and the ventricles. Clinical manifestations are polymorphic and depend on the location, number and development or involution stages of the parasites as well as characteristics of the immune response of the host. The most important sign is epilepsy that occurs mainly when cysticerci are lodged in the brain parenchyma. Extraparenchymal cysticerci can cause hydrocephalus due to mechanical obstruction of ventricular circulation of cerebrospinal fluid or to inflammatory reaction in basal cisterns. Symptoms usually occur after the cyst has initiated its degenerative process and are due mainly to the inflammatory response they induce or to residual scarring. In contrast, living cysticerci induce minimal inflammation, and can stay in this condition for several years because parasites evade the immune response. When the immune response becomes exacerbated it produces a cascade of immunological mechanisms that cause parasite death, but also severe damage to the neighbouring structures in the host, especially to basal blood vessels. These include dense collagen walls around cysticerci, astroglitic gliosis, microglia and capillary vessel proliferation. When cysticerci start to degenerate they have an appearance of colloidal, whitish vesicles, this stage is followed by a granulomatous one and finally parasites become calcified due to mineralization of the nodule, with surrounding intense gliosis and multinucleated giant cells, typical of a chronic inflammatory reaction to a foreign body. Parasites in different stages of involution are frequently found in the same brain, which suggests either recurrent infections, parasites with different survival abilities or different immune response in different parasites or sites in the host. 

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Diagnosis of NCC is based on two types of techniques. Imaging techniques (computed tomography, CT, and magnetic resonance, MR) allow the definition of the number, stage, location and extent of the lesions. Immunologic assays identify anticysticercus antibodies and parasite antigens. Based on these techniques and epidemiologic data, several criteria have been established for diagnosis. 

1. **Absolute**, when there is a histological demonstration of the parasite from biopsy of a brain or spinal cord lesion, cystic lesions showing the scolex on CT or MR, and direct visualization of subretinal parasites by fundoscopic examination.

2. **Major**, when there are lesions highly suggestive of NCC on imaging studies, positive western blot in serum for the detection of cysticercus antibodies and parasite antigens. Based on these techniques and epidemiologic data, several criteria have been established for diagnosis.

3. **Minor**, when there are lesions compatible with neurocysticercosis on imaging studies, clinical manifestations suggestive of NCC, positive ELISA for detection of anticysticercus antibodies or cysticercus antigens, and cysticercosis outside the central nervous system.

4. **Epidemiologic**, when there is evidence of a household contact with *T. solium*, individuals coming from or living in an area where cysticercosis is endemic, history of frequent travel to disease-endemic areas. Interpretation of these criteria allows two degrees of diagnostic certainty. Definitive diagnosis is in patients who have one absolute criterion or in those who have two major plus one minor and one epidemiologic criterion. Probable diagnosis, in patients who have one major plus two minor criteria, or one major plus one minor and one epidemiologic criterion, and in those who have three minor plus one epidemiologic criterion (Del Brutto et al. 2001). 

In imaging studies, a parenchymal living cysticercus generally is small, round and hypodense (CT) or hypointense (MR). When the parasite is colloidal, an external ring of inflammation appears with contrast fluid. A hyperdense (CT) or hyperintense (MR) invaginated scolex can be seen in both cases. Big living or colloidal cysticerci, up to 5 cm diameter, can be found in the subarachnoidal space or in the ventricles. Calcified parasites are round (hyperdense) and are better detected by CT (Sotelo and Del Brutto 2002, Amara et al. 2003; Arriada et al. 2003; Ito et al. 2006). For immunodiagnostic purposes currently the best technique is immunoblot using a semi-purified fraction obtained from a crude extract of cysticerci with a lentil-lectin column. Seven glycoprotein (GP) bands (with molecular masses of 50, 39–42, 24, 21, 18, 14 and 13 kDa) show 100% specificity for the detection of human cysticercosis. Sensitivity is related to the number of cysticerci in the brain and their viability: 98% sensitivity was found with three or more cysticerci, while only 65% sensitivity was obtained with one or two parasites (Tsang et al. 1989; Wilson et al. 1991). Also immunoblot has been standardized using GP purified by preparative isoelectric-focusing, which allow successfully using them also in ELISA with almost complete sensitivity and specificity (Ito et al. 1998, 2002a, 2006; Sako et al. 2000; Sato et al. 2003, 2006).

Treatment of NCC includes cestocidal drugs (praziquantel and albendazole) to kill living parasites and surgical procedures to remove intraventricular or subarachnoidal cysticerci or to place a ventricular shunt. Drugs to control symptoms are frequently used in order to reduce inflammation (corticoids), to control convulsive crisis (antiepileptics) or to reduce pain (analgesics). Pharmacokinetic and toxicological studies performed in humans with either cestocidal drug have shown that these agents have a fast absorption and, in general, lack toxic effects. Efficacy of cestocidal treatment is measured by the reduction in the number and size of cysticerci seen in CT or MR, by clinical improvement, elimination of corticoids or anticonvulsants and by the correction of ventricular dilatation. The most frequent surgical intervention is placement of ventricular shunts to deviate the cerebrospinal fluid to the peritoneal cavity in order to control hydrocephalus. Solitary intraventricular cysticerci can be surgically removed, nowadays even by endoscopy, in order to rapidly improve the patient’s health (Bergsneider et al. 2000; Del Brutto et al. 2001; Colli et al. 2002; Sotelo and Del Brutto 2002; Psarros et al. 2003; Jung et al. 2008; Suri et al. 2008).

As with *T. saginata*, no proven cases have been reported of human cysticercosis caused by *T. asiatica*, and although the possibility remains it is probably unlikely. At least one study failed to experimentally infect non-human primates (baboons) dosed orally with eggs of *T. asiatica* (Fall et al. 1995).

**Epidemiology**

The family Taeniidae comprises around 33 species of tapeworms including the 3 human species. For *Taenia* of non-human hosts,
studies of host ecology and transmission biology are most important, while for the human Taenia species human behaviour, husbandry practices and socio-economic risk factors contribute to transmission, therefore epidemiological studies are essential.

**Taenia solium**

*T. solium* and human cysticercosis are widely distributed, with highest transmission in Latin America, India and Southeast (SE) Asia (WHO 1983). Studies indicate under-recognized but significant transmission of the parasite in several countries of sub-Saharan Africa (Geerts et al. 2002), Papua, Indonesia (Gajdusek 1978; Simanjuntak et al. 1997; Margono et al. 2006; Wandra et al. 2007) and of China and SE Asia (Simanjuntak et al. 1997; Roman et al. 2000; Singh et al. 2002; Craig and Ito 2007; Li et al. 2007). Nevertheless no global burden for human cysticercosis has yet been calculated (Carabin et al. 2005). Epidemiologic studies estimate 5–6 million cases worldwide (Craig et al. 1996), including at least 400,000 symptomatic cases in Latin America (Bern et al. 1999), 1.5–3 million cases in sub-Saharan Africa (A. L. Willing personal communication), and 3 million cysticercosis cases estimated for China (Li et al. 2007). Furthermore, due to migration there are many neurological cases in developed countries, such as USA, and also recently, tapeworm carriers in the USA and Muslim countries have expanded interest in cysticercosis proposing it as an emerging infectious disease (Schantz et al. 1998, Flisser et al. 2004a). The economic impact of human and porcine cysticercosis, both in monetary burden and societal losses, is significant (Carabin et al. 2005, Rajkotia et al. 2007). There has been a formal proposal to declare NCC an international reportable disease (Roman et al. 2000), and *T. solium* has been included in a priority list of six human diseases (polio, mumps, rubella, dracunculiasis, lymphatic filariasis and cysticercosis) targeted for global eradication (ITFDE 1993; WHO/DFID-AHP 2006).

The epidemiology of *T. solium* taeniosis/cysticercosis is primarily linked to three main transmission features that must occur in an endemic community:

1. Keeping/raising pigs that have access to human faeces,
2. Lack of latrines or latrines accessible by pigs,
3. Eating undercooked or raw pork as part of local cuisine and/or because of poor cooking.

Human cysticercosis (including neurocysticercosis) is caused only by ingestion of the microscopic eggs or gravid proglottids. Main transmission pathways for human cysticercosis occur when eggs contaminate the hands a tapeworm carrier which increases the chance of self-infection as up to 30% of neurocysticercosis patients report a history of taeniosis (Gilman et al. 2000). Eggs may contaminate persons that have contact with a tapeworm carrier, or contaminate food prepared by a carrier, or contaminate vegetables close to indiscriminate sites of human defecation, or vegetables may be contaminated by eggs via human faeces as fertilizer (the latter practice remains common in parts of China and south east Asia). Other possible routes for egg contamination in humans may occur, such as deliberate use of proglottids as traditional medications (for example in South Africa) (Heinz and Macnab 1965). Note therefore that absence of pork eating may not prevent occurrence of human cysticercosis in a *T. solium* endemic area or even infection in low-risk groups, as long as at least one tapeworm carrier occurs in a household or local community (Schantz et al. 1992, WHO/FAO/OIE 2005).

In endemic communities in Latin America prevalence of human taeniosis based on microscopy/coproantigen ELISA is usually below 3%, porcine cysticercosis seropositivity or tongue palpation prevalence range from 1–50%, and human cysticercosis seropositivity from 3–25% (Allan et al. 1996; Garcia-Noval et al. 1996; Rodriguez-Canul et al. 1999; Flisser et al. 2003; Garcia et al. 2003a, b; Flisser and Gyorkos 2007). The incidence of epilepsy/seizures/convulsions (the main symptom of neurocysticercosis) was 18–29 per 1,000 in Central American communities, of which 40% of cases may have detectable lesions compatible with NCC. However, there is not always a clear association between seropositivity and seizure history and/or a CT scan positive image (Garcia-Noval et al. 2001, 2002). Official abattoir slaughter rates for porcine cysticercosis, while useful in identification of potential hotspots, are usually of little practical value because most pigs from poor rural endemic communities are slaughtered at home or within a village setting. For example, in one highly endemic *T. solium* area of SW China, only 1.3% of pigs slaughtered at abattoirs were positive by meat inspection (Li et al. 2007). Epidemiological studies in Latin America, especially in Mexico, Guatemala, Honduras, Ecuador, Bolivia and Peru, have helped to identify major risk factors for taeniosis and human and porcine cysticercosis in rural endemic communities in that region. These are summarized below.

### Risk of human taeniosis

These include eating undercooked pork, living in a household with infected pigs, female, age 10–39 years, Taenia carriers in the household and seropositivity for anti-cysticercus antibodies (Sarti et al. 1988, 1992, 1997, 2000; Allan et al. 1996a; Rodriguez-Canul et al. 1999; Garcia et al. 2003b).

### Risk of human cysticercosis

A history of taeniosis (Gilman et al. 2000); person older than 10 years (Garcia et al. 1995, 946 patients); presence of a tapeworm carrier (person who is taenid egg positive, coproantigen positive, and/or passed proglottids) in a household/family or in a neighbouring house or housing cluster (Sarti et al. 1988, 1994, 2000; Diaz-Camacho et al. 1990; Sanchez et al. 1998; Garcia-Noval et al. 1999; Garcia et al. 2003b); raising pigs; presence of cysticercosis positive pigs (tongue palpation, immunoblot seropositive, or necropsy positive) in a household (Garcia et al. 2003b); presence in family/household of a person with a history of late-onset (>18 years of age) seizures/epilepsy; immunoblot seropositive for antibodies against low molecular weight (<50KDa) *T. solium* metacestode glycoproteins (Garcia-Noval et al. 1996; Garcia et al. 2003b).

### Risk of porcine cysticercosis

Presence of a human tapeworm carrier in a household (Sarti et al. 1988; Lescano et al. 2007); lack of latrine (Sarti et al. 1994; Allan et al. 1996b; Vazquez et al. 2001); presence of free-range backyard or wandering pigs in communities that practice home-slaughter (Rodriguez-Canul et al. 1998, 1999); a seropositive pig within 50–500 metres of a house with a *Taenia* carrier (Lescano et al. 2007).

Whilst transmission of *T. solium* occurs mainly in rural areas of under-developed regions where pig ownership is high (Flisser et al. 2004), transmission or outbreaks of human cysticercosis have also been described in urban foci in endemic countries such as...
Ecuador and Peru (Goodman et al. 1999; Huisa et al. 2005). Furthermore, serological surveys revealed 12–15% cysticercosis seropositivity in soldiers living in Tegucigalpa (capital city of Honduras) and in Mexico City (Sanchez et al. 1998; Garcia-Garcia et al. 1999). Also, NCC cases have occurred in extremely low risk individuals in affluent households in New York City as a result of transmission of *T. solium* eggs from tapeworm positive housemaids (Schantz et al. 1992).

As previously discussed, recent molecular genotypic analysis of mitochondrial DNA extracted from *T. solium* isolates from different world regions, indicated two main genotypes, clades or strains, i.e., an Asian type and an African/Latin American type (Nakao et al. 2002). These have since been confirmed in several studies. However, it is not yet clear if the two genotypes exhibit differing epidemiology, transmission patterns or pathology (Craig and Ito 2007).

**Taenia saginata**

The human beef tapeworm, *T. saginata*, is the commonest taeniid of humans with an estimated 60,000–70,000 carriers worldwide (Flisser and Craig 2005; Craig and Ito 2007). In highly endemic regions, for example Ethiopia, Bali and Tibet, 22–27% prevalences of human *T. saginata* taeniosis have been recorded (Li et al. 2006; Wandra et al. 2006a, b; Craig and Ito 2007). In Europe and Australia beef tapeworm infection remains endemic, albeit at low prevalence (usually <0.05%), probably maintained in part due to the practice of application of sewage sludge on to pastures (Rickard et al. 1977; Cabaret et al. 2002; Boone et al. 2007). Human cysticercosis cannot be caused by ingestion of *T. saginata* eggs and therefore the public health impact for this parasite is limited to gut infection of humans (taeniosis). Consequently the epidemiology of this tapeworm species chiefly concerns transmission from human carriers to cattle, yak or other bovines. Bovine cysticercosis is however of economic importance because it may be responsible for condemnation of carcass or downgrading of meat, and even prevent development of potential beef export markets in resource-poor economies (Kebede 2008).

The risk factor for human *T. saginata* taeniosis is eating raw or under-cooked beef. Therefore *T. saginata* is more prevalent in communities or populations where dietary practices or cuisines include under-cooked and/or raw beef. For example in Sichuan and Yunnan provinces of SW China, and in Bali, Indonesia, raw beef is a delicacy. Consequently in their rural populations *T. saginata* taeniosis prevalence may be >20% (Li et al. 2006; Wandra et al. 2006b). In Bali, Indonesia 56/60 cases of suspected *T. saginata* were detected by questionnaire in a community study (n = 398) and confirmed as *T. saginata* by PCR. Males had a significantly higher prevalence and the risk age group was 30–44 years (Wandra et al. 2006). A similar cross-sectional epidemiological study (n = 661) in a Tibetan area of western Sichuan Province (China) found that 31% of persons reported a history of proglottid expulsion, and 18 of 21 proglottids positives tested by PCR were confirmed as *T. saginata* and three as *T. asiatica*. Of the 21 faecal samples from *Taenia* carriers 18 were also coproantigen ELISA positive (Li et al. 2007). In these 2 studies risk factors for taeniosis were consumption of raw beef, a history of passing proglottids in the previous 1–2 years, owning cattle/yak, poor hygiene/hand-washing and low level of education. Mean age of first infection (anamnesis) in 26 *T. saginata* cases treated in Addis Ababa was 12.2 years (Tesfa-Yohannes 1990).

**Taenia asiatica**

*Taenia asiatica* has been found in Taiwan, Korea, China, Vietnam, Philippines, Indonesia and Thailand. It is expected to also occur in Lao PD, Cambodia and Myanmar (Ito et al. 2007, 2008). *T. asiatica* was only described formally as a new tapeworm of humans in 1993 (Eom and Rim 1993). Prior to that in rural communities of south east Asia it was attributed to *T. saginata*, to which it closely resembles morphologically, but was often described in patients that consumed raw pig liver but not beef (Isobe 1922; Huang et al. 1966; Chao et al. 1979; Fan 1988; Fan et al. 1990; Eom and Rim 1993; Ito et al. 2003). It appears that spontaneous release of motile segments occurs in *T. asiatica* infections in the same way as for *T. saginata* and similarly therefore *T. asiatica* carriers are usually aware of their infection (Craig and Ito 2007; Wandra et al. 2007).

There have been relatively few epidemiological studies in known *T. asiatica* endemic communities, because previous studies were unable to differentiate *T. asiatica* and *T. saginata*, and so the majority of infections were classed as *T. saginata* (Eom and Rim 2001; Ito et al. 2003). One recent specific epidemiologic study on *T. asiatica* was undertaken in a rural Batak ethnic community in Ambarita village on Samosir Island, Lake Toba, Sumatra (Wandra et al. 2006). A total of 240 persons were voluntarily registered and answered a questionnaire, which indicated eight persons with a history of passing proglottids, and six (2.5% total prevalence) of these passed *T. asiatica* tapeworms (confirmed by PCR). Interestingly all six cases were coproparasitologically negative for *Taenia* eggs, but four that were tested by coproantigen ELISA were positive. Risk factors for *T. asiatica* taeniosis in the Lake Toba community were: consumption of pork (only 2.5% of population ate beef), home slaughter of pigs, predilection for raw pig liver and lack of sanitary facilities (Wandra et al. 2006, 2007). Since experimental infections in pigs performed with eggs from *T. asiatica* (Lake Toba isolate) developed cysticerci in the liver and not in the muscles or other locations (Fan et al. 1990, 2006), it is likely that in parts of Southeast Asia the distribution of *T. asiatica* and *T. solium* will be sympatric. This appears to be the case, at least, in Tibetan and Bai ethnic groups in SW China (Li et al. 2006) and in Karen ethnic communities on the Thai-Myanmar border (Anantaphruti et al. 2007). In the latter study in Kanchanaburi Province Thailand, all three human *Taenia* species occurred in those communities where under-cooked pork and beef were consumed, and at least one dual infection with *T. solium* and *T. asiatica* adult tapeworms was confirmed after DNA analysis (Fig. 51.3).

**Transmission dynamics**

There have been relatively few quantitative studies in relation to the transmission dynamics of the human *Taenia* spp. In contrast, a significant number of experimental and field studies were used to construct transmission models for the common taeniid species of livestock. Animal studies with *Taenia* species can be used to understand transmission dynamics of *T. solium* (Lawson and Gemmell 1989).

At any one time a *Taenia* parasite population will be in one of three states: the egg, the metacestode (cysticercus), or the adult; all three states can happen simultaneously in one community and even in the same human host in the case of *T. solium*. The effects of environmental factors such as temperature, humidity, dispersal (rain, arthropods) on eggs in the environment were important in
consideration of transmission of dog-sheep taeniid species (Lawson and Gemmell, 1983). For T. solium however the rapid direct ingestion of human faeces by pigs is common so that eggs may not be exposed for long periods in an endemic environment (Martinez-Mayo et al. 2000). A recent study based on experimental pig infections further indicates that pig-pig transmission may occur through coprophagy i.e. pig-human coprophagy followed by pig-pig coprophagy (Gonzalez et al. 2006). The distribution of cestode larvae in the pig intermediate host is usually over-dispersed, with acquired immunity stimulated by egg/oncosphere challenge and age-specific resistance also occurring probably within 15 days (Gemmell et al. 1987) the duration of immunity is not clear but probably lasts three months in the absence of egg challenge (Kvysgaard et al. 2007). Pigs may be protected against T. solium egg infection from probably as little as 10 eggs, and immunity can be passively transferred from pregnant sow to new born piglets to provide up to 2–4 months protection (Gemmell et al. 1987; Gonzalez et al. 2002). In humans the biotic potential of a gravid adult T. solium tapeworm is relatively high with possibly 200,000 eggs passed per day, though the size (approximately 2–3 m) and life-span (probably months to a few years) of this species appears to be significantly below that for T. saginata (Allan et al. 1996a; Flisser 2006; Craig and Ito 2007). The basic reproductive number (Ro) for T. solium has been assumed to be close to one (Gonzalez et al. 2002), nevertheless a relatively low prevalence (~1%) of human taeniosis can still sustain transmission of T. solium (WHO/FAO/OIE, 2005). In addition to these parasite factors, transmission dynamics of T. solium will be affected by human/pig interrelations, pig behaviour, human sanitary habits and local socio-economic factors (Lawson and Gemmell 1989; Sarti et al. 1997; Gonzalez et al. 2002; Kvysgaard et al. 2007). Knowledge of the transmission dynamics will assist in development of rational intervention simulations and control programs.

**Prevention and control**

In theory it should be relatively easy to prevent the occurrence of human taeniosis/cysticercosis and to break the parasitic life-cycle of the three human Taenia species. This is because humans are the only natural definitive host, and domestic pigs and cattle, the only important intermediate hosts. Consequently T. solium was added to the list of eradicable diseases (ITFDE 1993; Schantz et al. 1993). However, in practice it will be very difficult to implement control measures in poor rural areas of developing countries in which T. solium is highly endemic and where sanitation is poor or absent, where there exists cultural preference for under-cooked pork, where home-slaughter is the norm, and where pigs are bred un-penned and allowed to roam free. Furthermore, pork is the most popular meat consumed worldwide with at least 300 million pigs in endemic regions (Flisser et al. 2003, 2006). The demand for household pig rearing and pork protein is growing rapidly in resource-poor regions which will increase the transmission potential of T. solium and the probability of exposure to human taeniosis/cysticercosis (Lekule and Kvysgaard 2003; WHO/DFID-AHP, 2006).

Prevention and control of cysticercosis/taeniosis can be considered as a long-term horizontal approach eg, improved sanitation, husbandry, slaughter regulations, meat inspection, and general education. Education is making a difference in Mexico. But control measures can be more focused or vertically directed interventions that aim to break the transmission cycle over shorter periods. There are 4 main options for such directed shorter-term intervention approaches:

1. Directed health/husbandry education,
2. Mass treatment against human taeniosis,
3. Mass chemotherapy against porcine cysticercosis,
4. Anti-cysticercosis livestock vaccines.

Of course combinations of some of the above interventions are likely to further improve control efficacy, especially against T. solium. In addition appropriate surveillance methods and systems, including modern computer simulations to model cost-effective intervention approaches, are required at local and regional scales to measure control effect and monitor progress.

**Animal husbandry, meat inspection, sanitation and socio-economic development**

Pork ‘measles’ was known in ancient Greece and described by Aristotle. Furthermore pork vendors in ancient Rome had to guarantee that pig meat was free of measles. In the Middle Ages the Ausburg Charter of 1276 stated, ‘If a butcher kills a measly hog, he shall sell it to no one without a statement of this fact’ (Discussed in Viljoen 1937). An understanding of the life-cycle of T. solium after its elucidation and publication by Kuchenmeister in Germany in 1855, quickly resulted in formal recommendations about the dangers of eating under-cooked pork, and also clarified why the infection was rare in Jewish and Muslim communities (Grove 1990). Over the next 100 years the prevalence of human and porcine cysticercosis slowly declined across Western Europe, primarily through gradual improvements in sanitation, the adoption of formal meat inspection measures, less consumption of raw pork (in part because of historic out-breaks of trichinellosis in continental Europe), and the move to more intensive rearing of pigs (Grove 1990; WHO/FAO/OIE 2005). Endemic foci of T. solium however remain today in parts of rural Portugal and Spain where free-range pig husbandry is still not uncommon (Overbosch 2002; WHO/FAO/OIE 2005).

The connection between bovine cysticercosis (‘beef measles’) and an outbreak of human taeniosis in soldiers in South Africa was noted by Knox in 1819 and, following these observations, the role of cattle in the life-cycle of T. saginata was elucidated in 1861 by Leuckart (Viljoen 1937). Several authors by the late nineteenth and early twentieth centuries already advocated the inspection of slaughtered cattle, treatment of measly beef by freezing (-10°C for 2–6 days), and cooking or heating infected beef (Grove 1990). For T. solium, cysticerci are killed at -20°C for 1–3 days (Sotelo et al. 1986; Garcia et al. 2007) and proper salting of pork (12–24 hours) is also effective (Rodriguez-Canal et al. 2002). In most of Europe the prevalence of T. saginata taeniosis has declined to levels below 0.1% (range 0.01–2%), while prevalence of bovine cysticercosis at meat inspection ranges between 0.02 and 7% (Cabaret et al., 2002). Improved sanitation in Europe has no doubt reduced the likelihood of direct contamination of grazing pastures. However indiscriminate defecation by campers, walkers, travellers etc, and the use of treated urban sewage sludge to irrigate pastures, has probably maintained transmission of T. saginata in several parts of the developed world (Rickard et al. 1977; Cabaret et al. 2002). In Switzerland during 2005 and 2006, 119 farms with infected cattle were identified at slaughter as compared to 66 randomly selected...
farms with cattle slaughtered in the same period but with no evidence or history of infection. The presence of a railway line or a car park close to areas grazed by cattle, leisure activities around these areas, use of purchased roughage and organized public activities on farms attracting visitors, were the risk factors, pointing to outdoor defecation by tapeworm carriers (Flutsch et al. 2008).

Routine meat inspection usually involves up to five knife cuts in specific sites on the carcass (e.g. masseters, upper foreleg, hind-leg, heart, tongue). However >30% of infected cattle or pig carcasses (especially with light infections) may not be detected by these methods (WHO/FAO/OIE 2005; Phiri et al. 2006; Geysen et al. 2007). Restraint or corolling of pigs in resource-poor settings is effective in preventing ingestion of human faeces (Vazquez et al. 2001). In practice this is not easy to implement because of economic constraints. Furthermore in parts on India, Indonesia and China pigs are restrained or penned deliberately under or close to latrines so that they are able to remove human faecal waste from the household environment (PS Craig, unpublished observation). Backyard-free-roaming pigs or semi-confined household pigs in southern Mexico had significantly higher T. solium seropositive rates compared to more intensively farmed animals (Sarti et al. 1994, 1997, 2000; Rodriguez-Canal et al. 1998). Reports of restraint of pigs that were normally free-roaming have indicated decrease in swine cysticercosis rates in Peru and China (Bern et al. 1999; Vazquez et al. 2001; Pawlowski et al. 2005).

Health education

Humans can acquire cysticercosis after accidentally ingesting T. solium eggs. Furthermore, the prevalence of taeniosis among patients with neurocysticercosis is higher than previously reported. In addition, a clear association between the presence of taeniosis and the severity of neurocysticercosis was seen, since most massive cerebral infections (with more than 100 cysticerci) were present in patients who harboured the adult tapeworm in the intestine. Therefore, the perception that tapeworms are silent guests, causing no harm to humans, is erroneous and tapeworm carriers should be regarded as potential risks to themselves and to those living in their close environment (Gilman et al. 2000). Consequently, an important risk factor is the presence of a tapeworm carrier in the household or neighbourhood (Sarti et al. 1988; Flisser 2002b, Flisser and Gyorkos 2007). A study performed in a Mexican municipality with around 750,000 inhabitants showed that self-identification of tapeworm carriers is a feasible tool for control of T. solium (Flisser et al. 2005b). Also, identified tapeworm carriers can be treated with a high degree of efficacy (Jeri et al. 2004).

Health education in relation to taeniosis/cysticercosis could, in theory, lead to the acquisition of appropriate knowledge required to understand the life-cycle of the parasite. That knowledge could result in a change in risk-behaviours and/or husbandry practices that help propagate transmission, with a resultant reduction in human and livestock infection/exposure indices. There are only a few modern examples of specific education programmes in relation to T. solium, and very few, if any, reported for T. saginata or T. asiatica. In the late 1980s and early 1990s community based epidemiologic studies on T. solium in Mexico began to identify some of the sociological/behavioural risk factors for human and porcine infection (Sarti et al. 1988, 1992; Schantz et al. 1994). As a consequence, two educational intervention programs were developed and applied to rural communities in Mexico. In Guerrero State, 131 families were given health education about the parasite and associated risk factors, and after two years 76% of children but only 2% of adults acquired specific knowledge. Disappointingly the pre-intervention prevalence of tongue palpable cysticerci in one year old pigs increased from 6% to 11% (Keilbach et al. 1989). In Morelos State, a rural population (n = 1,931) was subjected to intense health education which used knowledge acquisition questionnaires, tongue palpation with immunoblot serology in pigs, and microscopy and coproantigen tests in humans, as pre-intervention and post-intervention indicators of transmission. Although there was no significant difference in human taeniosis rates before and after the educational programme, health education increased villagers’ knowledge about the parasite and transmission, despite an apparent lack of observed major behavioural changes. Nevertheless in this case there was significantly reduced porcine infection and exposure rates after six months (Sarti et al. 1997), which remained up to 42 months (A Flisser, unpublished observations).

A health education intervention trial was also recently applied in north eastern Tanzania—but differed from the Mexican one in that the study was a randomized control programme (n = 827 households, including 418 as household controls), targeted towards pig husbandry including building proper pig pens, as well as pit latrines, and safe disposal of human faeces; sentinel pigs were employed as transmission indicators over a one year period. Similar to the Morelos study, despite significant gain in knowledge acquisition, there was no improvement in observed risk practices amongst targeted or control households. However the porcine incidence rate based on tongue palpation and circulating antigen testing in sentinel pigs (given to each family) was significantly lower in the health education intervention household group, as was reported pork consumption (Ngowi et al. 2008). Long-term follow-up was not reported and it remains to be seen whether public health education alone could provide sustained decrease in transmission of T. solium in resource-poor communities in Latin America, Sub-Saharan Africa or elsewhere. Interestingly rigorous health education programmes for cystic echinococcosis in resource-rich countries/regions were not always effective for long-term sustained reduction of transmission of Echinococcus granulosus (Craig and Larrieu 2006).

Taeniosis mass drug treatment

The life-cycles of T. solium, T. saginata and Taenia asiatica involve humans as the only obligatory definitive host. Therefore, effective anthelmintic mass treatment of human populations in endemic areas could result in control of transmission or even elimination of the parasite (Pawlowski 1990). Furthermore, the provision of annual or sub-annual mass treatment for school age children using albendazole for gastrointestinal nematode and other infections has been very successful in reducing the burden of chronic helminth infections in under-developed regions (Molyneux et al. 2005; Flisser et al. 2008). Consequently, the approach of mass treatment against human taeniosis has gained support. Furthermore, effective tapeworm treatment could remove any (or more than one) of the three Taenia species (as well as Hymenolepis nana) where they are sympatric (Allan et al. 2002; WHO/FAO/OIE 2005; Ananthapruthi et al. 2007; Craig and Ito 2007).

There are several factors to consider in relation to mass treatment for human taeniosis however, that are different from directly transmitted gastrointestinal nematodes.
1) The age-specific prevalence of *T. solium* taeniosis is distributed mainly above the school-age group (ie. >15 years old) (Allan et al. 1996b; Sarti et al. 1997, 2000, Garcia et al. 2003b), and thus targeted treatment to schools would not be so effective.

2) The prevalence of human *T. solium* taeniosis is usually below 3.5% in endemic communities and therefore very high population coverage is required.

3) Pigs if untreated, act as a reservoir of infection back to the human population.

4) The most effective anthelmintic drug against human taeniosis is praziquantel (not albendazole the preferred drug in mass-treatment of gastrointestinal nematodes), but this drug is also used to treat neurocysticercosis and therefore has the potential to cause cerebral inflammation in asymptomatic neurocysticercosis cases. Despite that risk for mass administration of praziquantel such clinical effects have to date only rarely been reported (Cruz et al. 1989; Flisser et al. 1993). In relation to praziquantel safety, that drug has been extensively used in China and Africa at higher dosage for mass treatment campaigns against schistosomosis without apparent adverse effects on asymptomatic neurocysticercosis (Pawlowski 2006).

At the present time (2008) only six studies have been reported internationally since 1989 in which mass drug administration was used to control *T. solium* transmission, and all of these were carried out in Latin America (summarized in Table 51.2). Five of these studies used praziquantel and one niclosamide as the taenicide agent. Niclosamide is slightly less efficacious (85–90%) than praziquantel (>95%) and is five times more expensive and has a more limited shelf-life (Pawlowski et al. 2005). Niclosamide however has the advantage that the drug is poorly absorbed from the gut and therefore would not cause potential inadvertent effects on asymptomatic neurocysticercosis. Also *Taenia* tapeworms are usually passed intact after niclosamide treatment which facilitates identification (Allan et al. 1996b, 2002).

The endemic *T. solium* rural populations targeted ranged in size from <400 in Sinaloa Mexico to 10,000 in the Loja/El Oro region of south Ecuador. Follow-up occurred at various periods from four to 40 months but the average was one year. Pre and post intervention surveillance was mainly based on human taeniosis prevalence (stool examination and/or coproantigen test), and porcine cysticercosis prevalence/incidence in pig cohorts born after the intervention (necropsy, tongue palpation and/or serology). In one study in Peru the pig population was also subjected to mass treatment with the drug oxendazole (Garcia et al. 2006). Other factors, such as health education and changes in behaviour as well as improved sanitation and pig husbandry may have occurred in parallel as a result of the programme design, or indirectly occurred in the community, and thus could have influenced the effect of taeniosis mass-treatment (Allan et al. 2002). Five of the six mass treatment programmes (see Table 51.2), where human taeniosis was monitored, showed a statistically significant decrease in the prevalence of taeniosis within one year of mass treatment, with no taeniosis cases being detected post-intervention in three of those studies (Cruz et al. 1989; Keilbach et al. 1989; Diaz-Camacho et al. 1991). In all but one intervention study, porcine cysticercosis rates were also significantly reduced after 1–3.5 years follow-up, but pig infection was not eliminated (Sarti et al. 2000). Even when two rounds of oxendazole dosing of pigs was included with a taeniosis mass treatment program for the human population, the parasite persisted in the pig population despite significant decrease in porcine seroprevalence and seroconversion rates (Garcia et al. 2006).

Taenicial drug coverage of the human population was never above 70–90% in these six mass treatment programmes and therefore persistence of a handful of tapeworm carriers in a treated community could still maintain transmission because of the high biotic potential of the parasite. Nevertheless these studies demonstrate that at least short-term reduction (within one year) in transmission of *T. solium* may occur after taeniosis mass-treatment. Long term assessments have not been carried out except in Morelos (Mexico) where 42 months after mass administration with a single dose of praziquantel, human taeniosis prevalence remained 56% below the pre-intervention rate, pig tongue palpation rates were 52% lower and the seroprevalence of human cysticercus antibodies was 75% reduced (Sarti et al. 2000). In this study 5mg/kg instead of 10 mg/pg praziquantel were used (as recommended by WHO, Pawlowski 1990), and therefore drug efficacy was 50% instead of 95%. Mass treatment alone will therefore probably not be enough to interrupt transmission of *T. solium*, which appears to return to pre-intervention levels within 2–3 years (Garcia et al. 2007). Therefore options should consider more frequent drug administration and ensure that >95% of the population is treated (Gonzalez et al. 2002). Alternatively specific identification and treatment of tapeworm carriers should be also considered (Flisser et al. 2005b).

Mass treatment for *T. saginata* taeniosis is unlikely to be cost-effective because this parasite does not cause sufficient economic or public health impacts. However in some regions where *T. saginata* is common, self-medication on a large scale may occur; for example in Addis Ababa (Ethiopia) where >80% of the adult population regularly take taenidical drugs (Tefsia-Yohannes 1990; Pawlowski 2006). Prophylactic use of taenidical drugs by workers in cattle feed-lots may also reduce the risk of local outbreaks of bovine cysticercosis in both developed and resource-poor settings (Dorny et al. 2002).

**Anthelmintic mass drug treatment of livestock**

The possibility to use anti-metacestode drugs to control the transmission of *T. solium* from pigs to humans has also been investigated. Both praziquantel and albendazole can affect the viability of *T. solium* cysticerci in pigs, and the latter was 100% effective in killing muscle cysticerci (non viable cysts were present) though viable cysts remained in the brain (Flisser et al. 1989; Peniche-Cardenas et al. 2002). Praziquantel was highly effective even at one day treatment (Torres et al. 1992). The overall efficacy of both drugs, however, was not as great as oxendazole for treatment of porcine cysticercosis (Gonzalez et al. 1996), although this latter drug was used at a higher dose than the one commercially available. A single dose (30mg/kg) of oxendazole caused cyst death and disappearance within 3 months of treating infected pigs, and pigs also appeared refractory to further infection for another 3 months (Gonzalez et al. 1996; 2001). In rural Latin America and in other resource-poor regions, pigs are usually about 9 months old at slaughter, so a single dose of oxendazole or praziquantel (or better two doses at 3 months and 6 months) could in theory keep pigs free of cysticerci for that period with the added advantage of full economic return on the carcass (Torres et al. 1992; Gonzalez et al. 2003).
Despite these results, an intervention trial that used mass administration of oxfendazole to pigs in parallel with mass praziquantel administration to the human population in Peru, reduced transmission but did not eliminate human taeniosis or porcine cysticercosis after 18 months (Garcia et al. 2006).

**Cysticercosis vaccines for livestock**

The marked protective immune response of sheep and cattle to experimental egg challenge or vaccination with oncosphere antigen extracts of various *Taenia* species, lead the development of protective sub-unit vaccines against cysticercosis and echinococcosis (Lightowlers and Gauci 2001; Lightowlers 2003; reviewed by Flisser and Lightowlers 2008). In 1989 the first recombinant sub-unit anti-parasite vaccine (To45W) was developed, and this was for *Taenia ovis*, the cause of ovine cysticercosis, a non-zoonotic metacestode disease of economic importance (Johnson et al. 1989). Following that success, which was based on the use of a recombinant oncosphere peptide antigen, the homologous genes were identified in *T. saginata* and the expressed peptides (TSA-9/TSA-18) given intramuscularly with adjuvant to cattle resulted in 99.5–100% protection against porcine cysticercosis vaccines are available for practical use (Lightowlers 2006).

**Table 51.2** Summary of 6 control programmes for *T. solium* in rural communities in Latin America where mass treatment of human taeniosis was applied

<table>
<thead>
<tr>
<th>Country (site/start year of programme)</th>
<th>Human Pop.</th>
<th>Drug mg/kg, no. doses (% cover)</th>
<th>Follow-up period</th>
<th>Taen-iais pre-(%)</th>
<th>Taen-iais post-(%)</th>
<th>Pig Cystic pre-(%)</th>
<th>Pig Cystic post-(%)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ecuador (Loja/1986)</td>
<td>10,000</td>
<td>PZQ 5mg/kg, x1 (76%)</td>
<td>1 year</td>
<td>1.6 +</td>
<td>0 (n = 539)</td>
<td>11.4+</td>
<td>2.6 (n = 113)</td>
<td>Cruz et al. (1989)</td>
</tr>
<tr>
<td>Mexico (Guerrero/1986)</td>
<td>530</td>
<td>PZQ 5mg/kg, x1 (60%)</td>
<td>4mths-1year</td>
<td>3.2 +</td>
<td>0 (n = 440)</td>
<td>6**</td>
<td>11</td>
<td>Keilbach et al. (1989)</td>
</tr>
<tr>
<td>Mexico (Sinaloa/1989)</td>
<td>339</td>
<td>PZQ 5mg/kg, x1 (71%)</td>
<td>1 year</td>
<td>1.3 +</td>
<td>0 (n = 238)</td>
<td>ND</td>
<td>ND</td>
<td>Camacho et al. (1991)</td>
</tr>
<tr>
<td>Mexico (Morelos/1991)</td>
<td>1865</td>
<td>PZQ 10mg/kg, x1 (87%)</td>
<td>3.5 yrs</td>
<td>1.1+++</td>
<td>0.5 (n = 605)</td>
<td>1.2**</td>
<td>4.8+</td>
<td>Sarti et al. (2000)</td>
</tr>
<tr>
<td>Guatemala (Santa Gertrudis/1994)</td>
<td>1582</td>
<td>Niclosamide 1gm, x1 (75%)</td>
<td>10 months</td>
<td>3.5+++</td>
<td>1.0</td>
<td>55+</td>
<td>7 (n = 330)</td>
<td>Allan et al. (1997)</td>
</tr>
<tr>
<td>Peru (Quilcas/1996)</td>
<td>2100</td>
<td>PZQ 5mg/kg, x1 (75%)</td>
<td>18 months</td>
<td>ND</td>
<td>ND</td>
<td>0.57+* plus OXF</td>
<td>0.40</td>
<td>Garcia et al. (2006)</td>
</tr>
</tbody>
</table>

* Stool exam/worm recovery; +: coproantigen/worm recovery; * pig necropsy 
** pig tongue palpation; + pig serology; ^ total mean sero-incidence; plus OXF additional treatment of two rounds oxfendazole in pigs (n = 3177) at 30mg/kg; PZQ praziquantel.

**Surveillance methods**

Prevention and control of any infectious/parasitic disease cannot be reliably undertaken without appropriate surveillance tools. Several approaches and tools have been developed for taeniosis/cysticercosis, especially in relation to epidemiological and intervention studies for *T. solium*. Surveillance is important in the human population for taeniosis and cysticercosis, and in the pig population for cysticercosis. In addition, health education acquisition by the target population can be measured by questionnaires and observational studies. A number of diagnostic or detection methods have been developed for *T. solium* (Schantz and Sarti 1989; Garcia et al. 2003a).

**Taeniosis**

Clinical out-patient records are not very useful for human taeniosis because many people self-treat within the community. Self-identification by tapeworm carriers is also of variable value, but most reliable for *T. saginata* or *T. asiatica* because of the frequency of anamnesis in carriers (i.e. spontaneous escape of motile segments), but contradictory data have been published for *T. solium* (Hall et al. 1981; Flisser et al. 2005b; Wandra et al. 2006b). Use of questionnaire and demonstration of proglottid recognition has been reported to be useful in identification of human *T. saginata* and *T. asiatica*, but also for *T. solium* taeniosis carriers (Fan et al. 1992; Wandra et al. 2006a; Flisser et al. 2005b). Stool microscopy for detection of *Taenia* spp eggs and coproantigen ELISA for *Taenia* spp faecal antigen detection, have overall been most effective methods for surveillance of human taeniosis, the latter test being up to

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**Note:**

The table and text content is extracted from the book "Parasitic Zoonoses" by Palmer et al. (2011). The data and information provided are intended for educational purposes and should not be used for clinical or research purposes without further verification.
Surveys for cysticercosis (Aranda-Alvarez 2000) and also lower prevalence rates than for taeniosis likewise has proved useful in some epidemiological studies (1996; Dorny 1998; Flisser and Gyorkos 2007; Lescano 1998; Flisser 2002a; Garcia-Noval et al. 1997, 2000; Rodriguez-Canul et al. 2003b, c, 2006; Sato et al. 2008). Serodiagnostic tests for porcine and bovine cysticercosis have been developed based on specific serum antibody or circulating antigen detection (Craig and Rickard 1980; Gonzalez et al. 1990; Dorny et al. 2002; WHO/FAO/OIE 2005; Abuseir et al. 2004). Antibody tests based on recognition of low molecular weight T. solium metacestode glycoproteins show high specificity in immunoblots for both human and porcine cysticercosis, and even for dog cysticercosis, and have also been purified or cloned for high through-put screening ELISAs (Ito et al. 2002; Hancock et al. 2006; Sato et al. 2006; Flisser and Gyorkos 2007). The surveillance value of porcine serology in several epidemiological studies has in general been shown to be very useful and an important indicator of transmission before and after application of control intervention (Allan et al. 1996b, 1998; Sarti et al. 1997, 2000; Rodriguez-Canul et al. 1998; Flisser 2002a; Garcia et al. 2003b, c, 2006; Sato et al. 2003; Flisser and Gyorkos 2007; Lescano et al. 2007). The advantage of circulating antigen detection rather than serum antibodies is its association with current viable cyst infection, and these assays have been particularly useful in seroepidemiological studies of bovine cysticercosis where both infection prevalence and intensity are usually lower than in porcine cysticercosis (Onyango-Abuge et al. 1996; Dorny et al. 2000). Serum antigen ELISA for porcine cysticercosis likewise has proved useful in some epidemiological studies on T. solium (Sikasunge et al. 2008) as well as for human cysticercosis (Aranda-Alvarez et al. 1995; Correa et al. 1999). Surveys for T. asiatica cysticercosis in pigs are more difficult at routine meat inspection because of the small cyst size (2–3mm) in the liver and also lower prevalence rates than for T. solium cysticercosis, for example 0.01% viable cysts of T. asiatica were found in >25,000 pigs inspected in Chongju, Korea (Eom and Rim 2001). Currently there is no serological test available for T. asiatica porcine cysticercosis.

### Human cysticercosis

Hospital records for neurocysticercosis have proved useful in establishing public health impact, the burden of disease, and in advocating surveillance and control both historically and currently (Roman et al. 2000; Flisser 2002a, Garcia et al. 2007; Li et al. 2007). In highly endemic communities prevalence of epilepsy, with serological and/or CT image confirmation is also an important indicator of disease burden due to neurocysticercosis (Schantz et al. 1994; Garcia-Noval et al. 1999; Carabin et al. 2005). Active mass screening is probably the most effective way to establish true prevalence of human cysticercosis and should comprise the following: questionnaire (including history of convulsions, taeniosis), brief clinical examination (presence skin nodules, headache, epilepsy, other symptoms of neurocysticercosis) and blood sample for serology using a species-specific test. Ideally individuals with clinical data related to cysticercosis and/or seropositive persons should also be followed up by an imaging technique of the brain to confirm presence of neurocysticercosis. In one study a proportion of healthy persons (ie. clinically normal, circulating antibody/antigen seronegative, taeniosis negative, no reports of history of convulsions, etc) were also shown to have CT images of brain lesions (usually calcified) indicative of neurocysticercosis (Garcia-Noval et al. 2001). Furthermore, some seropositive persons may sero-revert over a period of months/years and thus specific anti-T. solium cysticercosis antibodies may also be transient (Garcia et al. 2001; Meza et al. 2003). Interpretation of the results of such comprehensive mass screenings can be difficult, so long-term follow-up studies are recommended.

### Prospects/options for control

Of the three human Taenia species, T. solium is by far the most important from a public health perspective and it has recently been considered priority for control by several international agencies (ITFDE 1993; Roman et al. 2000; WHO/FAO/OIE 2005; WHO/DFID-AHP 2006). Because T. solium is both a food-borne zoonoses and a sanitary-associated transmitted parasite, active control measures need to target both humans and pigs, and therefore requires intersectoral cooperation between medical and veterinary services (Pawlowski et al. 2005; Willingham and Engels 2006). A combination of several measures, including mass treatment of humans, mass treatment of pigs, porcine vaccination, economic incentives and health education, with application of appropriate surveillance tools, carried out under the direction of an integrated control authority, is likely to be most effective approach for control of T. solium over short time periods (<10 years). In the coming decades rural developments in sanitation, poverty reduction and improvements in pig husbandry and local economies will probably increase chances for the control of T. solium.

Application of quantitative models using parasite transmission parameters and cost-benefit analysis has only recently been developed for computer-assisted simulations of intervention measures against T. solium. Such models are still relatively crude because of the lack of accurate hard data for several transmission parameters including the biotic potential of the parasite, its basic reproductive number, role of immunity in pigs and humans, longevity of adult tapeworms, human taeniosis reinfection rates, survival of eggs in the environment, etc. (Sciutto et al. 2008). Despite the need for further data, informed prior assumptions can be made especially...
using Bayesian/stochastic statistical approaches (Basanez et al. 2004), so that groups/packages of interventions for T. solium control have been modelled to identify optimal cost-effective options (Gonzalez et al. 2002; Kyvsgaard et al. 2007).

Two simplified transmission intervention simulation models assessed the following 4 main interventions against T. solium:

1) Horizontal-type measures (latrines, meat inspection, proper cooking),
2) Mass treatment of humans for taeniosis,
3) Mass treatment of humans and pigs,
4) Identification and targeted treatment of taeniosis carriers and pig vaccination (TSOL18).

The simulations used hypothetical communities of 1,000 or 2,000 individuals with interventions over a period of 5 years or 10 years. Assumptions were that the Ro for the parasite was between 1–1.75, the vaccine was 100% protective against porcine cysticercosis (with 90% coverage) and mass drug treatment had 100% coverage in humans and 90% in pigs. In summary, the most important findings of the simulations were:

1) Human mass treatment can result in short-term significant reduction in transmission (within 48 months) but was insufficient alone to eliminate transmission which returned to pre-control levels unless more than 11 interventions occurred at 90 day intervals with 100% cover (probably unachievable).
2) If mass treatment (or targeted treatment) of humans was followed by at least 2 treatments of pigs, or followed by porcine vaccination, then significant reduction in transmission was possible within 5 years.
3) Horizontal measures required 5–10 years to result in significant reductions in human and porcine rates but infection still remained at low prevalence (~0.5% human taeniosis; ~10% porcine cysticercosis (Gonzalez et al. 2002; Kyvsgaard et al. 2007).

A multiple intervention approach against T. solium appears to have the biggest chance of reducing transmission as judged by the few real intervention programmes and these were supported by the simulation models. Cost-benefit analysis showed that economic considerations are likely to be very important in whether a Ministry of Agriculture and/or Health decides to support a long-term costly intervention (Lawson and Gemmell 1989; Gonzalez et al. 2002; Flisser et al. 2003, 2006). The health and economic benefits, logistics of scale and out-reach achieved by combining interventions for several zoonotic diseases (especially the group of so called neglected zoonotic diseases i.e. cysticercosis, brucellosis, anthrax, rabies, echinococcosis, zoonotic trypanosomiasis, zoonotic mycobacterium infections) as well as possibly other infectious diseases (Zinstaag et al. 2005) has gained support for the route to more effective disease control and poverty-reduction in resource-poor regions of the world (WHO/DFID-AHP 2006).

Acknowledgements

The authors dedicate this chapter to the memory of Dr P. C. Fan, who worked at the Department of Parasitology, Institute of Tropical Medicine, National Yang-Ming University School of Medicine, Taipei, Taiwan, and passed away on September 2nd, 2008.

References

Anantaphruti, M.T. et al. (2007). Study of stage-specific immunity against porcine cysticercosis (with 90% cover) and mass drug treatment had 100% coverage in humans and 90% in pigs. In summary, the most important findings of the simulations were:

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CHAPTER 51 CYSTICERCOSIS AND TAENIOSIS: TAENIA SOLIUM, TAenia SAGINATA AND TAenia ASIatica


