CHAPTER 8

Cestodes

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8.1 PREFACE

Cestodes, or tapeworms, belong to the class Cestoidea of the phylum Platyhelminthes. Members of this family vary greatly in size and behavior; however, they share the same basic body plan. They attach to the intestinal wall of definitive hosts by the scolex, or head. The scolex is followed by the neck, behind which grow the body segments, or proglottids. The proglottids together form the strobila, or body, of the worm; the number of proglottids in the adult worm depends on the species. Proglottids have both longitudinal and transverse muscles and are motile. Each proglottid also has both male and female reproductive organs, but mating usually occurs with adjacent segments rather than by self-fertilization. The oldest proglottids are farthest from the scolex and contain the tapeworm's eggs. Cestodes have no digestive or circulatory system and must absorb nutrients from the lumen of the host's small intestine through microvilli. These cover the surface of each proglottid and excrete waste through a pair of excretory tubules. Tapeworms do have a rudimentary nervous system consisting of ganglia in the scolex and nerves in the proglottids.

8.2 TAENIA

Three *Taenia* species, members of the Cyclophyllidea order, claim human beings as their definitive hosts: *T. saginata*, *T. solium*, and *T. asiatica*. Humans acquire intestinal infection with the worms by ingestion of undercooked meat—pork in the cases of *T. solium* and *T. asiatica*, and beef in the case of *T. saginata*—that contains encysted larvae. *T. solium* is presumably the only parasite of the three to cause significant human pathology in the form of human cysticercosis, although the pathogenicity of *T. asiatica* in humans has not been fully characterized. *T. saginata* and *T. asiatica* are morphologically very similar and closely related genetically. They cause limited pathology in humans, but their economic impact on the livestock market is significant.

Cestodes of the order Cyclophyllidea typically require two hosts in order to complete their life cycles (Fig. 8.1). The life cycles of *Taenia* species are similar, and differences will be highlighted in the "Biology" section in the discussions of the individual species. In general, Taenia eggs are ingested by an intermediate host, allowing larva to mature to the metacestaode stage of development. The metacestode stage is the encysted, infective larva that is referred to as a cysticercus. Maturation to the adult tapeworm continues once the cyticercus is ingested by a definitive host, at which point egg production and release into the environment permits the life cycle to continue.

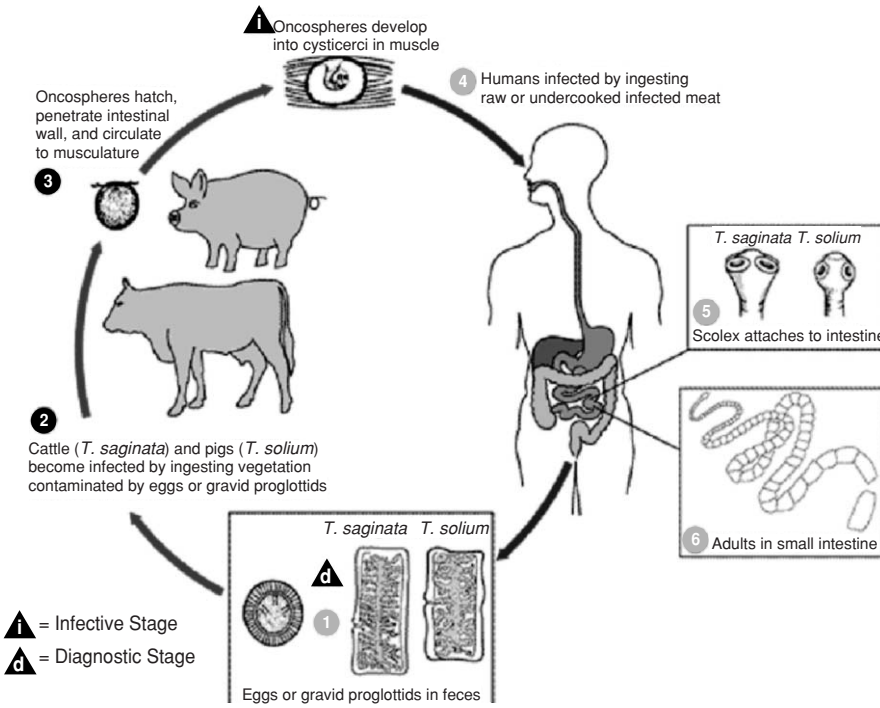

Figure 8.1. Life cycle of *Taenia* species. http://www.dpd.cdc.gov/dpdx

The adult tapeworms of all three *Taenia* species consist of a scolex characterized by four suckers, a short neck, and a strobila of varying length. Morphologic differences detectable by microscopy are the most reliable method of distinguishing between the three species. Injection of India ink into the uterus of the gravid proglottid allows for visualization of uterine branches and provides a means of species identification. *T. saginata* has 15–20 uterine branches per side, *T. asiatica* has 12–30, and *T. solium* has 7–13. Other notable morphologic species differences detectable by microscopy include the presence (*T. saginata*, *T. asiatica*) or absence (*T. solium*) of the vaginal sphincter muscle and the unilobed (*T. solium*) or bilobed (*T. saginata*, *T. asiatica*) ovary (Table 8.1). Polymerase chain reaction with restriction enzyme analysis (PCR-REA) can be used to distinguish the species (Mayta *et al.*, 2000). Eggs of all three species are identical and therefore do not permit species identification by microscopy. They are spherical, typically 31–43 μm in diameter, with a thick brown shell easily recognized by its radially striated appearance (Fig. 8.2). Within each egg is an embryonated larva, or oncosphere, with six hooks.

8.2.1 *Taenia solium*

8.2.1.1 Biology

The adult *T. solium* tapeworm lives in the human small intestine, attaching to the gut wall by its scolex; causing mild inflammation at the attachment site. The *T. solium* adult has a scolex with four suckers and a rostellum armed with a double row of hooklets followed by a narrow neck. A mature tapeworm can reach a length of

Table 8.1. Morphological differences between *Taenia solium*, *Taenia saginata*, and *Taenia asiatica.*

	1 T. solium	*2 T. saginata*	*3 T. asiatica*
Intermediate host	Pig	Cattle	Pig
Human pathology	Taeniasis; cysticercosis	Taeniasis	Taeniasis; unknown capacity for cysticercosis
Rostrellum	Double row of hooklets	unarmed	Rudimentary, wart-like formation
Strobila	≤1000 proglottids	>1000 proglottids	<1000 proglottids
Uterine branches	7–13 per side	15–20 per side	12–30 per side
Vaginal sphincter muscle	Absent	Present	Present
Ovary	Unilobed	Bilobed	Bilobed
Metacestode cysts	0.5–1.5 cm	7–10 mm	2 mm

2–4 m, containing up to 1000 hermaphroditic proglottids, and can live for several years in the upper jejunum, absorbing food through its tegument. Maturation to the reproductive adult stage occurs in the upper jejunum and requires 10–12 weeks. Egg release begins approximately 2 months postinfection and occurs via the passage of 3–5 whole proglottids at a time in the human feces. Each proglottid can contain 50,000 eggs, which can survive for months in the external environment. Once an

Figure 8.2. Taeniid egg with embryonated oncosphere with six hooklets within a characteristic radially striated brown shell. http://www.dpd.cdc.gov/dpdx

intermediate host ingests the eggs, they hatch in the host's gastrointestinal tract, releasing oncospheres that penetrate the intestinal wall and migrate to other tissues through the bloodstream. The larvae encyst in various tissues, particularly striated muscle in the neck, tongue, and trunk of pigs, and the central nervous system and skeletal muscle of humans. The encysted metacestode (cysticercus) matures over 60–90 days reaching a size of approximately 1 cm (Fig. 8.1). Normally, the encysted organism consists of only a scolex and can exist for many years in the host tissue. The cysticercus suppresses the host's immune response; thus, there is little or no inflammation while the cyst remains alive. Once the cyst begins to degenerate, however, there is a localized cellular immune response that may result in edema and scarring.

8.2.1.2 Epidemiology

Taenia solium has a worldwide distribution, but is most common in South America, Africa, India, and Southeast Asia. Prevalence is highest in rural areas where humans and pigs live in close proximity and good hygiene and sanitation are lacking. In many non-Muslim developing nations, where pork is a common food source, *T. solium* is the most common helminthic infection (Carangelo *et al.*, 2001; Garcia-Noval *et al.*, 2001). *T. solium* is no longer endemic in industrialized nations, but the prevalence there has been increasing in recent years due to immigration; identification increased due to improved diagnostic techniques. Although neurocysticercosis is much more common in developing nations, there are more than one thousand cases in the United States each year, mainly in immigrants from endemic areas (García *et al.*, 1999). In a recent study of emergency room patients with seizures, neurocysticercosis was diagnosed in 10% of the patients in Los Angeles, California and in 6% of those in New Mexico (Craig 2002). Outbreaks have even occurred in highly unlikely populations such as in a community of orthodox Jews in New York City who contracted *T. solium* cysticercosis from infected employees who had recently immigrated to the United States from tapeworm-endemic areas in Latin America. The infected employees were shedding eggs, which were then ingested in contaminated food (Schantz *et al.*, 1992).

In endemic regions, large portions of the population may be infected. In these areas up to 6% of people can have intestinal worms at a given time and serve as a source of infectious eggs that cause cysticercosis (Allan 1996a; Cruz *et al.*, 1989). Between 10 and 25% of people may be seropositive, and of these, 10–18% have abnormal CT findings suggestive of cysticercosis (Cruz *et al.*, 1999; Garcia-Noval *et al.*, 2001; Sánchez *et al.*, 1999; Schantz *et al.*, 1994). In general, prevalence is higher among females. There is an association between socioeconomic status and seroprevalence, but because of the transmission of *T. solium* eggs, the disease is certainly not limited to poor populations. Other risk factors for infection include age, open sewers and improper disposal of human feces, poor education, inability to recognize infected pigs, and inadequate inspection of pork. Local techniques for food preparation can also influence the spread of the disease.

T. solium is a major societal problem in many areas because of the morbidity associated with neurocysticercosis, which is of public health and economic concern. A large proportion of the patients admitted to neurology wards in developing

countries suffer from neurocysticercosis (Garcia, 2003). In areas where *T. solium* infection is endemic, neurocysticercosis is a major cause of epilepsy, and in many areas, is the leading cause of epilepsy. The prevalence of epilepsy in these countries is 3–6 times higher than in industrialized nations: 1.7% in Ecuador, 2.1% in Colombia, and 3.7% in Nigeria (Commission on Tropical Diseases, 1994; Jimenez, 1991; Nicoletti *et al.*, 2002; Osuntokun and Schoenberg, 1982; Placenceia, 1992). Seropositive people have a two- to threefold greater risk of developing epilepsy compared to seronegative people (Sánchez *et al.*, 1999; Schantz *et al.*, 1994). In Peru, 5% of seropositive people have a seizure disorder, 19,000–31,000 in total, and 23,500–39,000 Peruvians have some form of symptomatic neurocysticercosis. When similar analysis is applied to all of Latin America, it is estimated that 400,000 people have symptomatic neurocysticercosis. One-quarter to one-half of adult seizure disorders in tapeworm-endemic areas can be attributed to *T. solium* neurocysticercosis (Bern, 1999). Because neurocysticercosis tends to affect older children and young adults, it has a disproportionate economic effect due to lost wages. Hospitalization costs are also very high, estimated at $15 million per year in Mexico alone (Flisser *et al.*, 1998). Loss of livestock also has a large economic impact on the pork industry in endemic nations, where 30–60% of pigs may be infected.

8.2.1.3 Transmission

The human is the only definitive host for *T. solium.* The intermediate host is usually the pig, but humans can also act as intermediate hosts. Other species such as dogs, cats, and sheep can occasionally be infected, but rarely develop significant disease. Infection in the intermediate host, known as cysticercosis, is manifested by encysted metacestode larvae in skeletal muscle or other tissue. Humans may develop numerous cysts in muscle or in the central nervous system, a disease known as neurocysticercosis. Infection by the oncosphere does not always result in cysticercosis because the host immune system is often capable of resolving light infections in the early stages. People do not need to have an intestinal worm to acquire cysticercosis since cysticercosis is caused by ingestion of eggs, but about 15% of patients with neurocysticercosis do harbor a tapeworm at the time of diagnosis (García *et al.*, 1999; Gilman *et al.*, 2000) and 25% report having had one at some point (Dixon and Lipscomb, 1961).

The cestode life cycle is propagated via foodborne and fecal-oral transmission. Taeniasis, human gastrointestinal infection by the adult worm, occurs when people eat undercooked pork that contains live cysticerci (Fig. 8.3). Cysticercosis in the intermediate host is a result of the ingestion of the cestode's eggs, usually in contaminated food. Pigs can acquire cysticercosis through exposure to raw sewage containing infected human waste. Autoinfection can occur in people when gravid proglottids of an intestinal worm rupture and hatching oncospheres are activated in the small intestine, rendering them capable of causing cysticercosis. The prevalence of antibodies to oncospheres suggests that this occurs more frequently than previously thought. Human-to-human spread can occur by fecal-oral transmission if poor hygiene is practiced when preparing food. Infections are often clustered in households, a phenomenon likely related to food preparation practices. *T. solium*, therefore, can become a problem anywhere that pigs are raised and fed in places

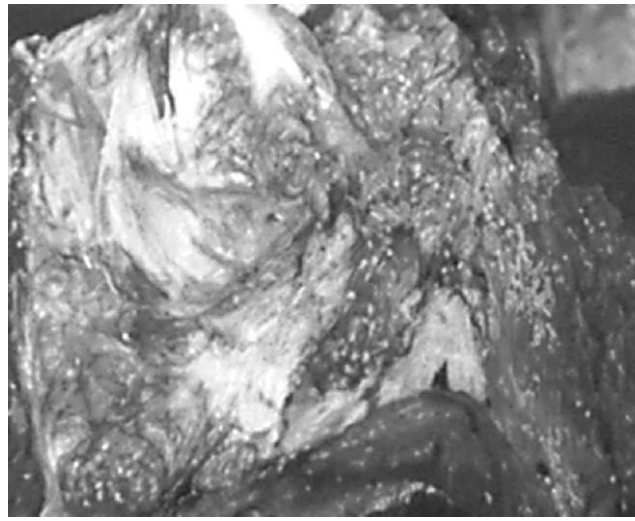

Figure 8.3. Pork flesh containing *T. solium* cysticerci.

contaminated with human feces, and where pork is not cooked thoroughly before eating. *T. solium* infection almost never occurs in industrialized countries, where nearly all pigs are raised commercially under heavy regulation, ensuring that there is no possibility of contact with human feces.

8.2.1.4 Clinical Aspects

Taeniasis, the infection of the human gut with the adult *T. solium*, is usually asymptomatic, but may occasionally cause epigastric pain, nausea, diarrhea, sensation of hunger, or weight loss. In contrast to the mobile proglottids of *T. saginata*, immobile *T. solium* proglottids can be visible in the person's stool, but usually pass unnoticed. *T. solium* cysticercosis can occur in almost any part of the body. In humans, cysticerci are most commonly found in skeletal muscles and in the brain. They are also found in the skin, subcutaneous tissue, eye, and heart. Cysticerci in the tissues are rarely symptomatic unless they encyst in the eye or in neural tissue, a condition known as neurocysticercosis. Cysticercosis can also cause subcutaneous nodules in the skin and muscular pseudohypertrophy when there is very high worm burden in skeletal muscles.

In the brain or other neural tissues, the cysticercus resembles a tumor and can cause many problems, including hydrocephaly, meningitis, and seizures. Cysts can be located in the brain parenchyma, especially at the grey-white junction, in the subarachnoid space, in the ventricles, and in the spinal cord. Cysts in the central nervous system are usually larger than cysts in other tissues. When cysticerci are found in the ventricular systems, they most commonly reside in the fourth ventricle, followed by the third ventricle. The racemose form of the disease consists of a large, frequently lobulated, translucent cyst without a scolex that is usually found in the ventricles or at the base of the brain (Fig. 8.4). This form of disease carries a high mortality rate due to hydrocephalus. Typical presentation of neurocysticercosis

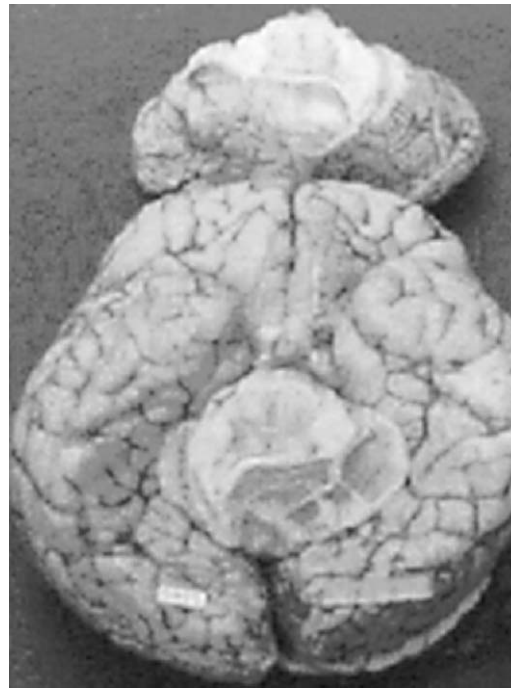

Figure 8.4. *Taenia solium* racemose cyst in the brain of a neurocysticercosis patient.

varies by geographical location: single brain lesions are most common in Asia while the presence of several viable cysts is more common in Latin America. Symptoms depend on the location of the cysticerci, the amount of inflammation or scarring, and the parasite load. The signs and symptoms of neurocysticercosis are usually due to inflammation, but the cyst can have a mass effect when located in the cerebrospinal fluid system or in the parenchyma when they are exceptionally large.

Parenchymal cysts are rarely fatal, but they can cause significant morbidity. Epilepsy is the most common symptom of neurocysticercosis. In fact, cysticercosis is the most common cause of epilepsy in the developing world. In endemic areas, new onset of seizures in adolescence or young or middle adulthood is suggestive of neurocysticercosis. Between 50 and 80% of people with parenchymal brain cysts have at least one seizure (Commission on Tropical Diseases, 1994; Chopra *et al.*, 1981; Del Brutto *et al.*, 1992). The resulting seizures can be partial or general, and EEG will often reveal focal slowing in the region of the lesion. Cysticerci have been reported to cause psychiatric symptoms as well, including one case report of binge-eating disorder (Fernandez-Aranda *et al.*, 2001). In contrast to parenchymal cysts, intraventricular cysts can frequently be fatal if they cause hydrocephalus. Twenty to thirty percent of patients develop increased intracranial pressure or hydrocephalus when CSF outflow is impeded (García *et al.*, 2003), causing headache, nausea or vomiting, dizziness, visual problems, ataxia, confusion, or papilloedema. Cysticerci in the subarachnoid space can cause stroke. Neurocysticercosis can also

cause encephalitis (especially in younger adults or children and in females), meningitis, or arachnoiditis. About 1% of patients with spinal cord neurocysticercosis develop spinal cord compression (García *et al.*, 2003).

In the eye, the cysticercus may invade the anterior chamber, the vitreous humor, or the retina, giving rise to visual problems. Only 1–3% of infected patients have ocular cysts, but, nevertheless, *T. solium* is the most common intraocular parasite. Subretinal cysticerci can cause retinal detachment and vision loss. Intraocular cysts can often be seen on fundoscopic examination. Rarely, cysts form in the optic nerve or extraocular muscles.

8.2.1.5 Diagnosis

Diagnosis of intestinal infection can be difficult because stool microscopy is not very sensitive and the eggs of *T. solium* are identical to those of other *Taenia* and *Echinococcus* species. Eggs from different species can, however, be distinguished with PCR, enzyme electrophoresis, or immunological tests. Diagnosis becomes easier if proglottids or the scolex are recovered. Use of a purgative before and after administration of treatment improves the chances of recovering the worm's scolex and strobila. The proglottids of *T. solium* and *T. saginata* can be differentiated by the anatomy of the female reproductive organs: *T. solium* has 5–10 uterine branches on each side, no vaginal sphincter muscle, and only one ovarian lobe while *T. saginata* has at least 15 uterine branches, a vaginal sphincter muscle, and two ovarian lobes. Sensitivity for the detection of eggs in stool may be improved by using concentration techniques. Sedimentation, as opposed to flotation, techniques for the isolation of eggs are required due to the density of *Taenia* eggs. Of note, it is important to fix eggs or proglottids before examination to prevent infection of laboratory personnel. There is also a coproantigen ELISA that is about 95% sensitive and 99% specific (Allan, 1990; Allan AJTMH, 1996).

Species differentiation is a difficult but important part of the diagnosis of taeniasis. Overlapping geographic distributions and the morphologic similarities make speciation a challenging endeavor. Nonetheless, it is important for clinical as well as investigational purposes. Clinically, *T. solium* infection must be ruled out in order to identify potential cases of human cysticercosis, which can be worsened by inappropriate antiparasitic therapy.

Diagnosis of *T. solium* cysticercosis is not straightforward and must take into account history, examination, epidemiology, radiological studies, and serology. Del Brutto, *et al.* established a detailed set of criteria to diagnose definite or probable neurocysticercosis. Their system includes a weighted list of absolute, major, minor, and epidemiological diagnostic criteria (Table 8.2). A definitive diagnosis of neurocysticercosis is established by the presence of one absolute criterion or the presence of two major, one minor, and one epidemiologic criterion. A probable diagnosis is established by one of three combinations of criteria: (1) one major plus two minor criteria; (2) one major plus one minor and one epidemiologic criterion; or (3) three minor plus one epidemiologic criterion (Del Brutto *et al.*, 2001).

Examination of cerebrospinal fluid may show pleocystosis with a predominance of lymphocytes, neutrophils or eosinophils, increased protein, and normal or low

Table 8.2. Criteria for diagnosis of neurocysticercosis (Del Brutto, 2001).

Absolute Criteria	1. Histological demonstration of the parasite from biopsy of a brain or spinal cord lesion 2. Cystic lesions showing the scolex on CT or MRI 3. Direct visualization of subretinal parasites by fundoscopic examination
Major Criteria	1. Lesions highly suggestive of neurocysticercosis on neuroimaging studies 2. Positive serum EITB for the detection of anticysticercal antibodies 3. Resolution of intracranial cystic lesions after therapy with albendazole or praziquantel 4. Spontaneous resolution of small single enhancing lesions
Minor Criteria	1. Lesions compatible with neurocysticercosis on neuroimaging studies 2. Clinical manifestations suggestive of neurocysticercosis 3. Positive CSF ELISA for detection of anticysticercal antibodies of cysticercal antigens 4. Cysticercosis outside the CNS
Epidemiological Criteria	1. Evidence of a household contact with *Taenia solium* infection 2. Individuals coming from or living in an area where cysticercosis is endemic 3. History of frequent travel to disease-endemic areas

glucose. In particular, eosinophils in the CSF are suggestive of neurocysticercosis, but they are found in only about 40% of cases.

Neuroimaging is one of the most important elements of diagnosis and is important for discovering the number, size, and location of cysts. CT is about 95% sensitive and specific for neurocysticercosis. Cysticerci typically appear as hypodense lesions with well-defined edges and with a hyperdense lesion inside. As the cyst degenerates and causes inflammation, the lesion enhances with contrast. Dead, calcified cysts usually do not enhance, but the presence of inflammation is predictive of relapse of symptoms. Because cyst fluid is isodense with CSF and cysts have thin walls, it is difficult to see cysticerci in the CSF. CT is better at identifying calcified lesions, but MRI is better to visualize cystic lesions, intraventricular cysts, or enhancing lesions. MRI is also more useful to stage lesions; although it cannot detect calcifications. Gradient refocused echo MRI is the best modality to visualize the scolex in a calcified lesion. Periventricular enhancement on MRI can distinguish neurocysticercosis from lymphoma or other infections. MRI and B-scan ultrasonography are superior to CT for diagnosis of ocular cysticercosis.

Immunological testing is also extremely useful for diagnosis of neurocysticercosis, though antibodies can disappear over time. Cysticercosis causes an increase in the serum levels of specific IgA, IgE, IgG, and IgM antibodies. ELISA for IgG is sensitive (88.5%) and specific (93.2%) (Odashima *et al.*, 2002), especially IgG4 (Huang *et al.*, 2002). Antigen detection by enzyme-linked immunoelectrotransfer blot assay (EITB) is even better, with 98 to 99.4% sensitivity and 100% specificity (García *et al.*, 2003; Gekeler *et al.*, 2002). This test is less sensitive if the patient has only one cyst. Because ELISA frequently cross-reacts with antibodies to *Hymenolepis nana* and *Echinococcus granulosus*, it is best used for screening only, and

positive results should be confirmed by EITB. EITB is useful for screening and in clinical settings and is the current test of choice. Antibodies may persist for weeks after the cyst degenerates even with treatment.

8.2.1.6 Treatment

Niclosamide and praziquantel are the drugs used to treat intestinal *T. solium* infection. Both are effective in a single dose—2 g for niclosamide or 5–10 mg/kg for praziquantel. Praziquantel is cysticidal and can cause inflammation around dying cysts in patients with cysticercosis; this may trigger seizures or other symptoms. Praziquantel-induced seizures can be problematic when the drug is used in mass-treatment campaigns. Because niclosamide is not absorbed from the gastrointestinal tract, it does not cause an inflammatory response and is considered the drug of choice for intestinal taeniasis.

Treatment of cysticercosis, especially neurocysticercosis, can be difficult and must be individualized. Cysticercosis outside of the central nervous system is usually asymptomatic and does not require therapy. Symptomatic treatment of seizures and increased intracranial pressure in neurocysticercosis is crucial. Anticonvulsants usually control seizures. They can be discontinued after 2 years if the patient remains seizure-free and intracranial paranchymal lesions resolve without calcifications. In patients with hydrocephalus, antiparasitic treatment should be avoided until the increased intracranial pressure has resolved, to avoid worsening of the patient's condition due to drug-induced inflammation. Hydrocephalus due to neurocysticercosis should be treated as with other diseases, using techniques such as ventriculoperitoneal shunt or removal of the cysticercus by craniotomy or ventriculoscopy if necessary. Arachnoiditis and associated vasculitis usually respond to steroids. Ocular cysticerci or spinal medullary lesions usually require surgery because inflammation in these areas can cause irreversible damage.

There is controversy about treatment of parenchymal brain cysticerci because as the cysts die in response to medication, surrounding inflammation can cause transient worsening of symptoms. Certain groups of patients have definite benefit from antiparasitic therapy, like those with giant cysts, subarachnoid cysts, or growing cysts. One argument against the use of antiparasitic therapy for other types of neurocysticercosis is that most cysts will resolve on their own; however, there is some evidence that treatment results in less scarring as lesions heal (García *et al.*, 2004; Padma *et al.*, 1995). García *et al.*, performed a placebo-controlled trial that showed treatment with 800 mg of albendazole daily, with adjuvant steroid therapy, reduced the frequency of generalized seizures. In the first month after treatment, the albendazole group had more seizures than the placebo group, but this relationship reversed at 2 months and at 30 months, when treated patients had significantly fewer generalized seizures. Intracranial lesions also resolved more quickly in the albendazole group (García *et al.*, 2004). Both albendazole (15 mg/kg/day for 8 days) and praziquantel (50–60 mg/kg/day for 15 days) kill encysted worms, though albendazole appears to penetrate the brain more effectively. Concurrent administration of glucocorticoids and, if needed, anticonvulsants, can control the increased inflammation. Steroids, however, increase first-pass hepatic metabolism of praziquantel, so cimetidine should also be coadministered to inhibit hepatic enzymes and maintain

therapeutic concentrations of praziquantel. All patients with seizures should receive antiepileptic drugs.

8.2.1.7 Control

As with other food-borne diseases, good hygiene and sanitation are crucial measures to control the spread of *T. solium*. Only humans with intestinal infections and pigs with cysticercosis transmit the parasite, so control measures should be targeted at these stages. Proper management of human waste disposal, such as the construction of latrines, decreases human-pig and human-human transmission. Improved sanitation in pig husbandry and the pork industry is also important. Regulation and effective screening in slaughterhouses, proper housing and care of pigs on farms or in peridomestic areas, and preparation of pork by salt pickling, freezing at -10°C for at least 9 days or cooking above 65°C, decreases transmission from pigs to humans. Implementation of these measures can be difficult in developing countries, where the pork industry is often not well-regulated and many pigs are raised and slaughtered in private settings outside slaughterhouses. Because pigs are cheaper than cows, easy to feed with garbage, and easy to sell or eat, people in developing countries often raise them in their homes and sell them, without having them inspected for cysticercosis. In Peru, for example, more than half of pigs entering the pork market do so illegally, and many are infected with *T. solium.* Diseased pork is much cheaper, so pork sellers may disguise infected pork or mix it with uninfected meat (Cysticercosis Working Group in Peru, 1993). Public education on the need to isolate pigs from human feces is necessary to change habits in these areas. Because of economic pressures on poor rural populations, however, economic incentives like compensation or introduction of other agricultural products must complement education (Gonzales *et al.*, 2003).

Medical interventions also play an important role in prevention of transmission. Treatment of human intestinal infections with niclosamide or praziquantel reduces cysticercosis. In some areas, mass treatment of the population with praziquantel reduced the prevalence of intestinal infection by 53%, seizures by 70%, and the prevalence of antibodies in both pigs and humans (Sarti *et al.*, 2000). Pigs can be treated as well with a single dose of oxfendazole 30 mg /kg (Gonzales *et al.*, 1997).

Difficulty with large-scale propagation of cestodes *in vivo* or *in vitro* thwarted vaccine development efforts prior to the introduction of recombinant DNA technology. However, advances in molecular science have led to the successful development of recombinant vaccines for *Taenia* cestodes in their intermediate hosts. A vaccine has been developed for use in pigs; it remains to be seen if it will be economically feasible for widespread use in endemic areas.

8.2.2 *Taenia saginata*

8.2.2.1 Biology

Taenia saginata has a scolex characterized by four suckers and a unique, retracted, unarmed rostellum. The size of the mature proglottids ranges from 2.1–4.5 mm and gravid proglottids range from 0.3–2.2 cm. Proglottids are longer than they are wide and have a large central genital pore, and each hermaphroditic proglottid is capable of producing thousands of eggs per day. On average *T. saginata* grows to a length of

5–10 m and can have more than 1000 proglottids. The intact proglottids are mobile and can occasionally be seen moving in the stool.

The life cycle of *T. saginata* occurs in cattle and human beings, although llamas, buffalo, and giraffes occasionally can act as intermediate hosts (Fig. 8.1). Cattle are infected when they ingest eggs on local vegetation that has been contaminated by human feces. Cattle develop cysticerci in skeletal muscles, which are then ingested by humans in undercooked beef. The life cycle of *T. saginata* is essentially identical to that of *T. solium*, with two notable exceptions: the cow, not the pig, is the intermediate host of *T. saginata*, and the human, the definitive host, never acts as an intermediate host of *T. saginata.*

8.2.2.2 Epidemiology

Taenia saginata is a ubiquitous parasite, and human taeniasis occurs in all countries where raw or undercooked beef is consumed. The World Health Organization estimates that over 60 million people are infected with taeniasis worldwide (WHO report, 1992). The *T. saginata* tapeworm is most prevalent in Sub-Saharan Africa and the Middle East; other regions with high prevalence of *T. saginata* (defined as greater than 10% of the population) include Central Asia, the Near East, and Central and Eastern Africa. Areas of low prevalence (defined as less than 1% of the population) include Europe, the United States, Southeast Asia, and Central and South America.

Bovine cysticercosis resulting from *T. saginata* infection is a global problem occurring in cattle rearing regions of the world and resulting in significant financial loss. Bovine cysticercosis renders beef unmarketable, and is globally responsible for over 2 billion dollars in yearly economic losses (Hoberg, 2002).

8.2.2.3 Transmission

Taenia saginata transmission and propagation is closely tied to both food consumption and sanitary habits. Human taeniasis results from the consumption of contaminated beef that has not been frozen or thoroughly cooked. Cows subsequently become infected by ingesting eggs excreted by humans. Once eggs are released into the environment, they can remain viable for months to years until an appropriate intermediate host ingests them and the life cycle resumes. Perpetuation of bovine and human disease in an agricultural setting can occur in several ways (Hoberg, 2002), including direct transmission to cattle through fecal contamination of pastureland by agricultural workers, application of untreated human sewage onto pastureland, and indirect contamination of the cattle food or water supply.

8.2.2.4 Clinical Aspects and Diagnosis

Human taeniasis caused by *T. saginata* is typically asymptomatic. Patients may become aware of infection upon the passage of proglottids, or even several feet of strobila, in the stool. Proglottids are often motile, thus causing discomfort with discharge. A small percentage of patients complain of colicky abdominal pain, nausea, changes in appetite, weakness, weight loss, constipation or diarrhea, pruritis ani, and general malaise. Abdominal discomfort and nausea are the most common complaints and are often relieved with the ingestion of food. In infants, increased irritability may be the only sign of infection. Complications from *T. saginata* infection

are rare and are a result of the motile nature of the proglottids. Migrating proglottids rarely cause biliary duct, pancreatic duct, or appendiceal obstruction.

Clinically, taeniasis may be associated with an elevated serum IgE and a mild eosinophilia of 5–15% in a minority of patients. Definitive diagnosis of taeniasis, however, is made by direct visualization of eggs or proglottids in the stool or by cellophane tape swab of the perianal region. *T. solium* releases eggs or proglottids into the stool erratically, in contrast to *T. saginata*, which releases eggs or proglottids on a daily basis. Large sections of *T. saginata* strobila can break off in a day, without subsequent release of eggs or gravid proglottids for several days thereafter; therefore, collection of multiple stool samples is recommended.

8.2.2.5 Treatment

A single 5–10 mg/kg dose of praziquantel is highly effective for cestode infections. Alternatively, a single dose of niclosamide is also effective. Dosing of niclosamide is 2 g for adults, 1.5 g for children greater than 34 kg, and 1 g for children 11–34 kg. Both praziquantel and niclosamide are class B drugs, although treatment can and should be delayed until after pregnancy unless clinically indicated. Since praziquantel is released in breast milk and safety in children under 4 years of age has not been investigated, it is recommended that nursing mothers should not breastfeed for 72 h after treatment.

8.2.2.6 Control

There is a *T. saginata* recombinant vaccine developed based upon the identification of homologues to host protective antigens of *T. ovis*. The vaccination of cattle using a combination of the *T. saginata* proteins tsa9 and tsa18 has resulted in 94–99% protection against parasite infection (Lightowlers *et al.*, 2003). Research to develop a more practical and affordable vaccine is ongoing.

In the meantime, disease prevention depends upon interrupting the parasite life cycle through public health efforts directed at raising awareness of disease transmission mechanisms and at improving sanitary practices. Cysticerci in beef can be inactivated by cooking meat at least 56°C or freezing meat at −10°C for at least 9 days. Reliable meat inspection to remove infected meat from the market and proper disposal of human feces to interrupt transmission to cattle are also important preventive measures.

8.2.3 *Taenia asiatica*

Taenia asiatica is a relatively recently described species of *Taenia* that closely resembles *T. saginata* both morphologically and genetically. Debate is ongoing as to whether or not the "Asian *Taenia*" should be considered a subspecies of *T. saginata*, and it is still referred to as *T. saginata-asiatica* in some current literature. Genetic studies of ribosomal genes and the mitochondrial cytochrome C oxidase I (COI) gene identified a close relationship between *T. saginata* and *T. asiatica*, supporting the subspecies theory (Flisser *et al.*, 2004). However, comparative morphologic studies and life cycle differences lend support to the idea that the "Asian *Taenia*" may be closely related to *T. saginata*, but is an individual species nonetheless (Galan-Puchades and Fuentes, 2000).

8.2.3.1 Biology

The life cycle of *T. asiatica* is almost identical to that of *T. solium* (Fig. 8.1) with the exception that humans probably cannot act as intermediate hosts for *T. asiatica*. The pig is the primary intermediate host, but other intermediate hosts include cattle, goat, monkey, and wild boar. While *T. asiatica* cysticercosis can occur in many organs, the larva seems to have a special tropism for the liver. When the definitive human host ingests the cysticercus in undercooked pork, maturation to adulthood occurs in the small intestine.

The scolex of *T. asiatica* has four suckers and a rostellum armed with rudimentary hooklets referred to as wart-like formations (Flisser *et al.*, 2004). The strobila typically is composed of fewer than 1000 hermaphroditic proglottid segments. Like *T. saginata*, a vaginal sphincter muscle is present in mature proglottids, and gravid proglottids have a central uterus with 12–30 uterine branches per side. However, *T. asiatica* has more than 57 uterine twigs per side, with a larger ratio of uterine twig: Uterine branches than other *Taenia* species. The prominent protuberance on posterior aspect of *T. asiatica* gravid proglottids is also unique. The metacestode cysts contain rudimentary hooklets and typically measure 2 mm, compared with the 7–10 mm cysts of *T. saginata*, and 0.5–1.5 cm cysts of *T. solium*.

8.2.3.2 Epidemiology

Thus far, *T. asiatica* has been identified in Taiwan, Indonesia, Thailand, Korea, China, Malaysia, Vietnam, and the Philippines. Prevalence of the tapeworm can be as high as 21% (Galan-Puchades and Fuentes, 2000) in some endemic regions, particularly where people eat undercooked pork with viscera. The distribution of *T. asiatica* may not be limited to Asia, as the same epidemiological conditions that led to its discovery in Taiwan have been noted in other parts of the non-Asian world as well.

8.2.3.3 Transmission

Taenia asiatica was identified using basic epidemiology combined with knowledge of the food consumption habits in the effected population. Investigators in Taiwan noted that the prevalence of *T. saginata* did not correlate well with the food consumption habits of the local people. Pork is a staple part of the diet in Southeast Asia. In fact, it is a common practice in many rural parts to house pigs and other animals under the floor of the house, creating an ideal environment for *Taenia* spp. transmission. Consumption of pig meat and viscera was far more common than that of beef, yet *T. solium* had a surprising low prevalence compared to *T. saginata*. This observation led investigators to hypothesize that perhaps there was another *Taenia* parasite present that closely resembled *T. saginata*, and *T. asiatica* was subsequently classified.

8.2.3.4 Clinical Aspects and Diagnosis

The debate over whether or not *T. asiatica* is its own species or a subspecies of *T. saginata* has importance beyond the merely academic. It has yet to be definitively determined whether or not *T. asiatica* is capable of causing human cysticercosis. Evidence suggesting that it does not cause human cysticercosis includes its genetic and morphologic similarities with *T. saginata*. In addition, in regions of the world

where the prevalence of *T. asiatica* is highest, namely regions of Taiwan and Samosir Island (Indonesia), there are very few cases of human cysticercosis. Evidence suggesting that it could cause human cysticercosis includes the fact that, similar to *T. solium*, pigs are the primary intermediate hosts of *T. asiatica*. Additionally, *T. asiatica* cysticerci demonstrate liver tropism in porcine models, suggesting cases of human *T. asiatica* cysticercosis may not present like the traditional neurocysticercosis cases of *T. solium*. The potential for *T. asiatica* to cause human cysticercosis needs further investigation (Galan-Puchades and Fuentes, 2000).

Definitive diagnosis of *T. asiatica* taeniasis is by microscopic examination of stool. Since the eggs of all *Taenia* species are identical, only by noting morphologic differences in proglottids or scolex, if expelled, is speciation possible. If resources permit, observations can be confirmed by PCR analysis of DNA. Coproantigen testing can also be performed on stool samples, but this methodology is only specific to the level of genus.

8.2.3.5 Treatment

Effective treatment for *T. asiatica* taeniasis includes single doses of praziquantel or niclosamide, using the same dosage for taeniasis as for other *Taenia* species (see *T. solium*, 1.2.1.6 Treatment).

8.2.3.6 Control

Preventive measures involve improving hygiene and education regarding the tapeworm lifecycle. Meat inspection for cysticerci, keeping pigs indoors and without contact with human feces, and avoiding the consumption of undercooked pork or pig viscera are other important measures of prevention. Although yet to be demonstrated, it is hoped that the recombinant vaccine for *T. saginata* will be equally successful for *T. asiatica*, given their genetic and morphologic similarities.

8.3 DIPHYLLOBOTHRIUM

8.3.1 *Diphyllobothrium Latum*

8.3.1.1 Biology

Diphyllobothrium latum, also known as the fish tapeworm or broad tapeworm, is the longest of the human tapeworms, reaching lengths of 10–20 mm/cm, with 3000–4000 proglottids. Pseudophyllidea typically have a scolex with two sucking grooves, as opposed to the four true suckers of cestodes of the Cyclophilidea order. The sucking grooves, or bothria, are located along opposite sides of the scolex. Proglottids are wider than they are long, typically measuring 2 to 4 mm by 10 to 12 mm. The gravid proglottid has a central, coiled uterus with a distinctive rosette-like appearance. The central ventral genital pore is the site of egg expulsion. Eggs are yellow, oval, and distinctly operculated at one end. On the end opposite the operculum is a small knob like feature. Eggs measure 58 to 76 μm by 40 to 51 μm, and are passed in the stool unembryonated (Fig. 8.5).

Diphyllobothrium latum belongs to the order Pseudophyllidea, and its life cycle requires three hosts. The life cycle of *D. latum* (Fig. 8.6) requires two intermediate

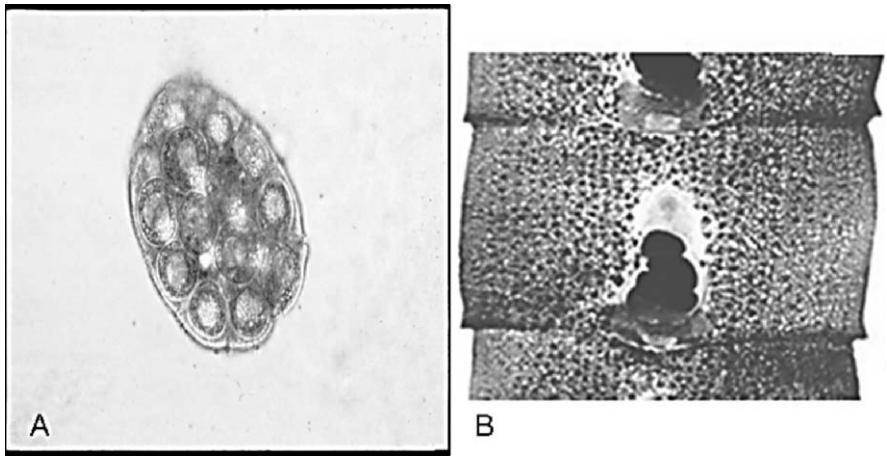

Figure 8.5. (a) *Diphyllobothrium* egg packet. (b) Proglottid with central coiled uterus. http://www.dpd.cdc.gov/dpdx

marine hosts before adulthood is reached in the definitive mammalian host. Immature eggs released with the feces must promptly be deposited into fresh water, where they mature and eventually release a freely swimming, ciliated, six hooked embryo, called a coracidium, from the opened operculum. The coracidia are ingested by crustaceans such as copepods or water fleas, where the first larval, or procercoid, stage of development occurs. The procercoid larva develops in the crustacean tissue and maturation is arrested until it is ingested once again by a larger fish. In the muscle tissue of the larger fish, the procercoid larva matures into a plerocercoid cyst, or sparganum. The sparganum grows to 6 mm and can be transmitted up the food chain to progressively larger fish, until finally it is ingested by a definitive mammalian host and can mature to adulthood. Interestingly, as progressively larger fish consume the sparganum it does not mature; but rather re-encysts in the fish muscle tissue. Once consumed by the definitive host, the sparganum matures to adulthood in the small intestine. The tapeworm attaches to the gut mucosa utilizing its bothria, and attains adulthood in 3–6 weeks. Definitive hosts can include, but are not limited to, humans, dogs, cats, foxes, bears, and pigs.

8.3.1.2 Epidemiology

Diphyllobothrium latum has a worldwide distribution and is most common in regions where undercooked or raw fish are consumed. Areas of high endemnicity (>2%) include lake and delta areas of Siberia, parts of Europe, particularly Scandinavian countries, North America, Japan, Peru, and Chile. *D. latum* primarily infects older children and adults, and those who eat or prepare raw fish for home or for commercial distribution are at greatest risk. The prevalence in the United States is estimated to be less than 0.5% (Masci, 2004), though outbreaks have been associated with increased availability of fresh salmon and sushi.

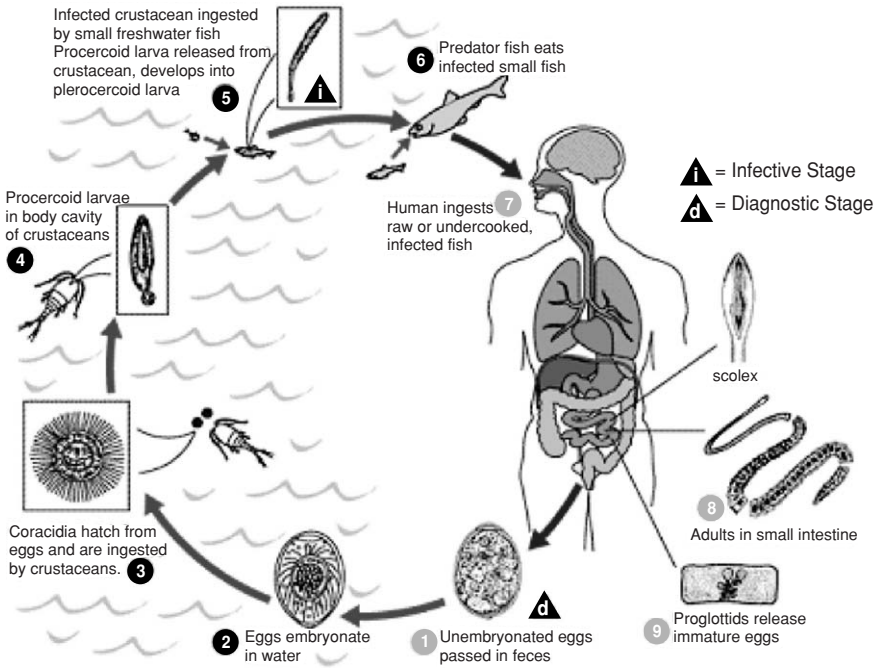

Figure 8.6. *Diphyllobothrium latum* life cycle. http://www.dpd.cdc.gov/dpdx

8.3.1.3 Transmission

Human infection is most commonly associated with the consumption of salmon, whitefish, rainbow trout, pike, walleye, perch, turbot, and ruff, particularly in areas where raw, marinated, or undercooked fish are eaten.

8.3.1.4 Clinical Aspects and Diagnosis

The majority of *D. latum* infections are asymptomatic, although infection can be associated with diarrhea, abdominal distension, flatulence, abdominal cramping, and general malaise in a minority of patients. Rare complications include intestinal obstruction due to high worm burden and megaloblastic anemia due to impaired vitamin B_{12} absorption in up to 2% of those infected (King, 2000). The adult tapeworm affects vitamin B_{12} absorption through two mechanisms. First, the tapeworm is a scavenger of vitamin B_{12}, which is important for worm growth and development. Second, *D. latum* can uncouple the vitamin B_{12}-intrinsic factor complex, thus preventing ileal B_{12} absorption. Historically, anemia had been described with heavy worm burden (the presence of multiple worms) and prolonged infection in the Scandinavian population. It is currently very rare to find and may only result in genetically predisposed individuals.

Diagnosis is made by visualizing eggs in the stool. They are usually so numerous that concentration techniques are unnecessary. Their characteristic operculum is evident on microscopy. Egg discharge can be intermittent, and diagnosis may be

missed with only one stool sample. Scolex and proglottids are unlikely to be passed in with the feces, although case reports have described parts of the strobila emitted in vomitus (Richards, 2003).

8.3.1.5 Treatment

Single doses of 5–10 mg/kg of praziquantel or 2 g (adult)/50 mg/kg (children) of niclosamide are highly effective. Stool should be reexamined in 6 weeks to determine disease persistence. Cobalamin injections are recommended for severe anemia resulting from B_{12} deficiency.

8.3.1.6 Control

Altering human eating habits is the only effective means of interrupting the *D. latum* life cycle. Regulating proper disposal of human sewage is not sufficient because egg deposition into fresh water occurs from many of the animal sources that act as definitive hosts. Brief cooking of fish at 56°C for 5 minutes or freezing at –18°C for 24 h will effectively kill the sparganum. Importantly, sparganum remain viable in dried or smoked fish.

8.3.2 *Diphyllobothrium pacificum*

8.3.2.1 Life Cycle

Causal agents of human diphyllobothriasis include *D. latum* and *D. pacificum*. The life cycle of *D. pacificum* is similar to that described for *D. latum*, with the exception that the second intermediate, or paratenic, hosts are salt water species rather than fresh water species of fish. The typical definitive hosts for *D. pacificum* are sea lions, with humans infrequently becoming accidental definitive hosts upon ingestion of raw or under-prepared marine fish infected with *D. pacificum* plerocercoid larvae.

8.3.2.2 Epidemiology

Diphyllobothrium pacificum was first identified in South America. It is considered endemic to Peru, with the prevalence reaching 2% on the southern coast, particularly in underdeveloped urban areas. To date, it is the only known cause of human diphyllobothriasis in Peru (Medina Flores *et al.*, 2002). Sixteen commercially important species of fish have been identified as paratenic hosts (Cabrera, 2001) including Jurel (*Trachurus symmetricus murphyi*), Bonito (*Sarda chiliensis*), Coco (*Paralonchurus peruanus*), Perico (*Coryphaena hippurus*), and Lisa (*Mugil cephalus*).

Cases of *D. pacificum* diphyllobothriasis in Chile have been associated with the El Niño phenomenon, presumably due to changes in water temperatures resulting in the southern displacement of fish native to Peruvian waters and the creation of conditions favorable for the overgrowth of copepods, the first intermediate host of *D. pacificum* (Sagua *et al.*, 2001).

8.3.2.3 Transmission

Human infection is related to the consumption of raw or undercooked fish, common practice in Peruvian coastal regions. *D. pacificum* infection has been associated with dishes such as cebiche (raw fish prepared with lemon juice and ají), tiradito (raw fish prepared with a lemon, garlic, and ají sauce), and chinguirito (raw fish prepared with lemons and red peppers).

8.3.2.4 Clinical Presentation and Diagnosis

Diphyllobothrium pacificum diphyllobothriasis can be asymptomatic or can present with abdominal pain, vomiting, or diarrhea. There is no association between *D. pacificum* infection and pernicious anemia (Medina Flores *et al.*, 2002). Diagnosis is made upon visualization of the expulsed proglottids or eggs in the feces. Eggs typically measure 48 to 60μm long by 35 to 40μm wide. Infection can be successfully treated with niclosamide.

8.3.2.5 Control

Human *D. pacificum* diphyllobothriasis results from the consumption of raw or improperly prepared marine fish. Prevention measures include thoroughly cooking fish in endemic regions or adequately freezing fish prior to food preparation.

8.4 SPIROMETRA

8.4.1 *Spirometra mansoides*

8.4.1.1 Biology and Transmission

Spirometra mansoides is a common tapeworm of dogs, cats, and other carnivores. It is a member of the Pseudophyllidea order, and thus requires two intermediate hosts in order to complete its life cycle. Eggs are discharged into freshwater, and, similar to *D. latum*, hatch to release a free-swimming, ciliated coracidium. The first intermediate host, a copepod, ingests the coracidium where it develops into a procercoid larva. At this point, the life cycle of *S. mansoides* diverges from that of *D. latum*, because the former cannot have a fish as the second intermediate host. Rather, the second intermediate, or paratenic, host of *S. mansoides* may be a reptile, amphibian, bird, or other mammal. Within the paratenic host, the procercoid larva migrates through the intestinal mucosa and eventually into muscle or connective tissue where it encysts and develops into the plerocercoid larva. This process will continue until the paratenic host is consumed by a definitive host, usually a dog, cat, or raccoon. In the small intestine of the definitive host, the tapeworm develops to adulthood, reaching maturity in 10–30 days. Eggs are discharged from gravid proglottids and passed with the feces. Eggs are brown and approximately 57 μm by 39 μm. The proglottids have a pinkish hue and a coiled uterus when gravid.

8.4.1.2 Epidemiology

Spirometra mansoides is an uncommon parasite, but widespread in warm climates. Human cases of sparganosis are most common in Asia, though cases have been reported in North and South America, Europe, and Africa.

8.4.1.3 Transmission

Humans are an accidental paratenic host, and infection can occur in several ways. If infected copepods, such as cyclops (water fleas), are ingested through contaminated water, the procercoid will continue to mature to the plerocercoid stage in human tissue. Similarly, ingestion of undercooked, infected paratenic hosts will likewise result in human infection with the plerocercoid larvae. Transfer of plerocercoids can also occur through direct contact with the skin or organs of infected paratenic

hosts. Skin or eye poultices sometimes used in ritualistic healing practices provide an unusual conduit for the migrating plerocercoid cyst to infect humans.

8.4.1.4 Clinical Aspects and Diagnosis

Plerocercoid encystment or reencystment in human tissue results in sparganosis. Larva may grow up to 30 cm and slowly migrate, resulting in cutaneous or visceral migrans, depending on the site of infection. Skin and intestinal mucosa are the two most common sites of plerocercoid encystment. Sparganosis may present as an erythematous, pruritic, subcutaneous swelling that slowly migrates through the skin. Migration into the eye can occur through direct contact with a poultice and leads to significant inflammatory pathology with pain, periorbital swelling, and conjuntivitis. Invasion of the CNS and bowel perforation have been reported.

8.4.1.5 Treatment

Treatment of sparganosis with antihelminthic agents has not proven to be beneficial. Surgical excision for localized sparganosis is the only effective therapy.

8.4.1.6 Control

Most cases of human sparganosis result from the consumption of water contaminated with infected copepods and the consumption of a paretenic host. Control can be achieved through proper water purification and food preparation techniques in endemic regions. Education regarding the dangers posed by application of poultices in healing practices should also be addressed.

8.5 ECHINOCOCCUS

The Echinococcus species are small tapeworms that usually reside in canine or feline definitive hosts and herbivore intermediate hosts. Humans are accidental intermediate hosts. There are several species of Echinococcus that can cause disease in humans, but by far the most important are *Echinococcus granulosus*, which causes cystic echinococcosis, and *Echinococcus multilocularis*, which causes alveolar echinococcosis. Although *Echinococcus* is not a truly food-borne human parasite, it is included here because of its importance as a human pathogen.

8.5.1 *Echinococcus granulosus*

8.5.1.1 Biology

Echinococcus granulosus is a small tapeworm in the Taenidiae family that infects humans in its larval form. The adult worm inhabits a variety of canine definitive hosts, with the domestic dog being the most important from the standpoint of human health. The intermediate hosts include sheep and other ungulates, camels, goats, and cattle. Infrequently, humans are intermediate hosts for the tapeworm.

A mature *E. granulosus* worm is 3–6 mm long and contains only three proglottids, one immature, one mature, and one gravid. Dogs are infected by consuming infected tissue, most commonly raw sheep viscera (Fig. 8.7). The tapeworm matures over 4–5 weeks in the dog's intestine and survives for 5 to 20 months. The gravid proglottid ruptures to release fertilized eggs. Upon ingestion by the intermediate

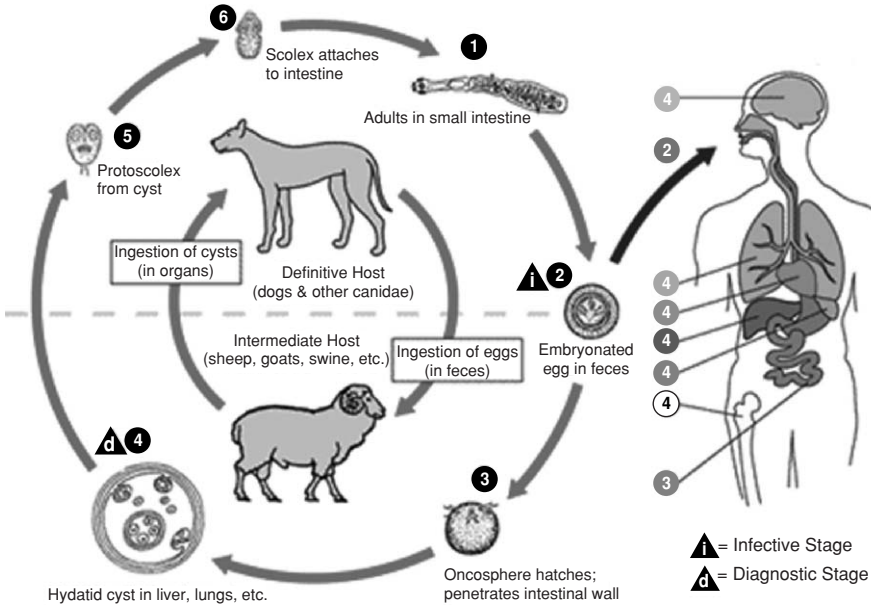

Figure 8.7. *Echinococcus granulosus* life cycle. http://www.dpd.cdc.gov/dpdx

host, the egg hatches and the released larva migrates through the intestinal wall and travels through the bloodstream to other sites, most notably the liver and the lung in humans, where the larva encysts.

8.5.1.2 Epidemiology

Echinococcus granulosus has a worldwide distribution and is the most common *Echinococcus* infection in humans. There are two forms of the disease, "European" and "Northern." The European form is globally distributed in domestic animals while the Northern form is restricted to the tundra and taiga of North America and Eurasia. There are several sylvatic cycles that may bring the parasite in contact with humans, including a cycle involving dingoes and marsupials in Australia (Thompson and McManus, 2001) and a cycle involving wolves or sled dogs and cervids in North America and Eurasia (Castrodale *et al.*, 1999). Sylvatic strains appear to have less severe clinical manifestations in humans than the more widespread domestic forms. There is considerable genetic variability between strains in different geographical regions, and often demonstrate host specificity. Regions with the highest prevalence are Eurasia, especially Russia, China, and various Mediterranean nations, northern and eastern Africa, Australia, and South America. Prevalence is highest where people raise sheep, especially when dogs are involved in the care of sheep.

Prevalence in humans varies widely. In some endemic areas such as rural Greece, prevalence can be as high as 29% in the general population (Sotiraki *et al.*, 2003). Hydatid disease appears to be more common in women than in men in many endemic areas. Risk factors for infection include occupation as a hunter and ownership of many sheep, and in children, infected family members, a father who slaughters

sheep, and heavy exposure to dogs in the first year of life (Bai *et al.*, 2002; Larrieu, 2002). Drinking tap water (rather than from another source) appears protective, probably because tap water is unlikely to be contaminated with dog feces (Larrieu 2002).

8.5.1.3 Transmission

Dogs become infected with *E. granulosus* when they eat raw sheep viscera containing protoscolices, the larval worms. Worm burden can be very high; therefore, a single dog can disseminate a large quantity of eggs. The eggs may be carried by the wind and can survive for years in the environment. Transmission of *E. granulosus* to humans is by the fecal-oral route, predominantly through contact with surfaces, food, or water contaminated with dog feces. Humans do not develop intestinal infections from consuming contaminated sheep flesh, so transmission is predominantly associated with contact with infected dogs.

8.5.1.4 Clinical Aspects

Echinococcus granulosus infection usually occurs during childhood, and because the cyst grows slowly, is often asymptomatic for many years before it causes symptoms or is discovered incidentally on an imaging study. Up to 60% of infected persons may remain asymptomatic throughout life, but when symptomatic disease does occur, it is usually diagnosed during childhood or young adulthood. *E. granulosus* cysts are usually unilocular and filled with fluid, and they may have internal membranes. The outer acellular membrane protects the parasite from the host's immune response. The inner layer consists of a germinal membrane that produces new larvae, called protoscolices, daughter cysts, and brood capsules. Protoscolices and parasite hooklets accumulate in the cystic fluid to form a substance called hydatid sand. There may also be a layer of host granulomatous tissue surrounding the cyst. Symptoms are usually the result of the space-occupying effect and depend on the location of the cyst. More emergent symptoms may result with cyst rupture, when the release of cyst contents can cause fever, urticaria, pruritis, eosinophilia, and anaphylaxis. The cysts rarely metastasize or seed other body parts unless they rupture. Cystic echinococcosis appears to provoke a protective immune response that prevents reinfection.

Echinococcus granulosus can encyst in nearly any part of the body, but the liver is the site in more than half of patients. The average size of hepatic cysts is 12 cm. People usually present with abdominal pain or mass. Hepatic cysts can cause hepatobiliary problems by mass effect, cyst rupture, or communication with the biliary tree, causing jaundice, cholestasis, cholecystitis, cholangitis, or fistula formation. Hepatic cyst rupture can occur with blunt trauma, frequently in a motor vehicle accident, and may cause hepatobiliary symptoms, pain, or anaphylaxis. The lung is the second most common site of hydatid cyst formation, occurring in approximately 25% of patients and typically unilaterally. Pulmonary cysts may cause pain, fever, dyspnea, cough, and hemoptysis, and sputum may contain protoscolices or hooklets. Complications of pulmonary cysts include pleural or pericardial disease, pneumothorax, empyema, and fistula formation. Patients also may have cysts in both the liver and the lungs, a syndrome called hepatopulmonary hydatidosis. Bone cysts, most commonly in the spine or pelvic bones, are not common but can cause

Table 8.3. Classification of hepatic cystic echinococcosis lesions based on ultrasound examination (Pawlowski, I., Eckert, J., Vuitton, D., *et al.*, 2001).

Type	*Active*	*Fertile*	*Cyst Wall*	*Remarks*
CL*	Yes	No	Not visible	If cysts are due to cystic Echinococcus—early stage of development.
CE1	Yes	Yes	Visible	Unilocular, anechoic, or "snowflake sign."
CE2	Yes	Yes	Visible	Multiseptate and multivesicular, daughter cysts present.
CE3	Transitional	Yes	Visible	Anechoic content with detached laminated membrane ("waterlilly sign"). Decreased intracystic pressure. Cyst starting to degenerate.
CE4*	Inactive	No	Not visible	Heterogeneous hyperechoic or hypoechoic contents. No visible daughter cysts. "Ball of wool" sign due to degenerate membranes. Usually no viable protoscolices.
CE5*	Inactive	No	Calcified	Thick, variably calcified wall producing a cone-shaped shadow. Usually no viable protoscolices.

Cysts subclassified according to size: small <5 cm; medium 5–10 cm; large >10 cm.
*Further tests required to ascertain a diagnosis of cystic echinococcosis.

significant morbidity. Hydatid disease occurs rarely in other organs. Twenty to forty percent of patients have multiple cysts.

8.5.1.5 Diagnosis

Radiological imaging is the cornerstone of diagnosis of cystic echinococcosis in humans. Ultrasonography is excellent for screening and diagnosis because it is safe and noninvasive, provides immediate results, and can often be performed in the community. CT and MRI are also quite sensitive, but are only available in hospitals. CT may be better than ultrasonography for the diagnosis of extrahepatic hydatid disease (Gottstein and Reichen, 1996). The visualization of daughter cysts on ultrasound, CT, or MRI is pathognomonic for cystic echinococcosis; another characteristic finding is wall calcification. The World Health Organization has developed a classification system for the staging of hepatic cystic echinococcosis based on ultrasound findings (Table 8.3). Plain film chest X-ray is also useful for the diagnosis of pulmonary cysts or calcified hepatic cysts. On X-ray, pulmonary cysts appear as irregular rounded masses of uniform density. Endoscopic retrograde cholangiography can be used preoperatively to distinguish simple from complicated cysts, and endoscopic retrograde cholangiopancreatography can be used after surgery to look for biliary tree damage.

Serologic testing is also useful for diagnosis of cystic echinococcosis. Antigen and antibody tests exist, but both have problems with specificity. Serologic testing by enzyme-linked immunotransfer blot (EITB) is positive in 80% of patients with hepatic cysts, but in only 56% of patients with pulmonary cysts or cysts in multiple

organs. Specificity approaches 100%, yet there are reports of cross-reactivity in patients with *T. solium* cysticercosis. An ELISA based on swine hydatid fluid had similar sensitivity, but was less specific, while a double diffusion test (DD5) based on sheep hydatid fluid was only 47% sensitive, although very specific (Verastegui *et al.*, 1992). Serology can also be used to assess the effectiveness of surgery or chemotherapy.

The diagnosis of echinococcosis can also be made by identification of hydatid sand in aspirates of cystic fluid, but because of the high risk of seeding new cysts or provoking anaphylaxis, aspiration is discouraged, except in PAIR procedures described below. In histological specimens, hooklets are acid-fast and the cyst capsule is periodic acid-Schiff positive.

8.5.1.6 Treatment

Treatment is generally deferred unless the patient is symptomatic or the cyst is a threat to an anatomical structure. Surgical removal of the cyst is considered the gold standard. Relative contraindications for surgery are the presence of multiple cysts or anatomical location. Radical surgery carries a higher risk of complications, but a lower rate of relapse. Use of protoscolicidal agents intraoperatively is controversial. Commonly used agents include 70–90% ethanol, 15–20% saline solution, and 0.5% cetrimide, and these should be left in the cystic cavity for at least 15 minutes. Patients should also receive preoperative and postoperative chemotherapy for several weeks with albendazole.

PAIR (Puncture, Aspiration, Injection, Reaspiration) is a less invasive treatment performed under ultrasound guidance. The physician inserts the needle into the cyst and aspirates the contents. A protoscolicidal agent, which kills the protoscolex larval form of the tapeworm, is then injected into the cavity, dwells for several minutes, and is reaspirated. All daughter cysts within the main cysts must be punctured as well. PAIR should only be performed with intensive care support because of the risk of anaphylaxis. Patients should receive chemotherapy before and after the procedure. PAIR reduces complication rates from 28 to 5–10% compared to surgery (Aygun *et al.*, 2001, Men *et al.*, 1999, Pelaez *et al.*, 2000). PAIR is contraindicated if the cyst is superficial, contains thick internal septae, or communicates with the biliary tree.

Medical treatment alone is rarely curative, but is an option for patients who are not surgical candidates. Albendazole 10mg/kg divided into two daily doses is the best, and when used alone for 12 weeks to 6 months cures 30% of patients and improves in 50% of the remaining patients. Some physicians recommend two-week rest periods off the drug to decrease toxicity, but recent data does not suggest that this decreases side effects (McManus, 2003). Praziquantel 25 mg/kg daily may also provide some improvement. Studies in sheep suggest that weekly use of praziquantel is also effective and may cause fewer side effects (Dueger *et al.*, 1999).

8.5.1.7 Control

Good animal husbandry practices and good hygiene and sanitation are currently the most practical and effective methods to control *E. granulosus* infection. Dogs should not be allowed to eat raw flesh from domestic animals, particularly sheep, and humans should use good hygiene to avoid contamination of food and water by dog feces. It is very important that dogs be kept away from places where sheep are

slaughtered. Limiting the number of stray dogs living in the community may also decrease prevalence in humans. Infected dogs have been successfully treated with praziquantel. Programs based on periodic treatment of dogs and restriction of dogs from slaughterhouses have successfully eradicated *E. granulosus* in Iceland and have greatly decreased the prevalence of the disease in New Zealand, Tasmania, Cyprus, Chile, and Argentina. Vaccine development holds great promise for future control of the disease. In particular, the recombinant vaccine EG95 has been effective in trials in sheep in Australia, New Zealand, and Argentina and it seems to provide some protection in goats and cattle as well (Lightowers, 1999, 2001, 2003). Studies on dog vaccines are in their infancy, but show promise for decreasing egg excretion. Dog vaccination with an effective vaccine, in combination with periodic pharmacological treatment, would be the most efficacious method to control hydatid disease.

8.5.2 *Echinococcus multilocularis*

8.5.2.1 Biology

The definitive hosts are foxes, especially red and arctic foxes, wild dogs, and domestic dogs. Rodents are the main intermediate hosts, although the cestode can also infect pigs, monkeys, horses, and European beavers. Canines become infected with *E. multilocularis* when they eat the larval form of the worm in an infected rodent. The larva attaches to the small intestine and matures over about 4 weeks. Adult tapeworms are 1.2–4.5 mm long and have 2–6 proglottids, with an average of 5 proglottids. The round or oval eggs, measuring 30–36 μm in diameter, are released from the gravid proglottid and expelled in feces. Eggs can survive for extended periods of time in the environment. The life cycle is very similar to that of *E. granulosus* (Fig. 8.7).

However, the cysts of *E. multilocularis* are different from the cysts of *E. granulosus*. *E. multilocularis* larvae remain in a proliferative state, forming multilocular cysts with vesicles that grow out from the germinal layer to invade adjacent tissues. The cysts vary in size between 1 and 20 mm. Protoscolices and hydatid sand are rarely seen in humans. Cysts are very aggressive, destroying the liver and even metastasizing hematogenously to other organs. The cyst of *E. multilocularis* contains a laminated and a germinal layer, but the laminated layer does not provide an effective host-parasite barrier. Cellular immunity appears to be more important than humoral immunity, and the parasite may be capable of modifying the host's immune response to enhance its own odds of survival (Vuitton, 2003).

8.5.2.2 Epidemiology

Echinococcus multilocularis is found only in the northern hemisphere, in arctic, subarctic, or mountainous areas of Canada, the United States, central and northern Europe, and Asia. It predominantly participates in a sylvatic cycle in foxes and wild rodents, though domestic dogs and cats can also harbor the parasite. In recent years, there is evidence that the infection has the potential to emerge in urban populations; as foxes move into more urban habitats and come into greater contact with domestic animals. Alveolar echinococcosis is a rare disease, but is medically important because it is frequently fatal when untreated. Prevalence in humans varies with location and is not always correlated with the presence of foxes or other hosts. Men

and women have similar prevalence rates. Fur trappers and their families have the highest risk of infection due to contact with contaminated fur.

8.5.2.3 Transmission

Humans are accidental intermediate hosts of *E. multilocularis*, and they acquire the infection by ingesting eggs from contaminated food or by contact with contaminated furs.

8.5.2.4 Clinical Relevance and Diagnosis

Alveolar echinococcosis has a long asymptomatic period lasting 5–15 years. The cysts grow at an average of 15 ml per year and can ultimately involve areas 15–20 cm in diameter. About 10% of cysts metastasize hematogenously. Liver cysts, usually in the right lobe, are found in 99% of patients, and 13% of patients have multiorgan disease. Patients usually become symptomatic between 50 and 70 years of age and can present with a variety of symptoms. One third present with right upper quadrant or epigastric pain and one third with cholestatic jaundice. Other signs and symptoms include hepatomegaly, weight loss, and fatigue. Patients can form amyloids in the liver and develop biliary cirrhosis. Complications include abscess formation, cholangitis, sepsis, portal hypertension, and Budd-Chiari syndrome. Metastatic disease can cause a myriad of other organ-specific signs, symptoms, and complications. The cysts provoke an inflammatory reaction, but liver enzymes are rarely significantly elevated. The levels of all types of immunoglobins, particularly IgE, increase, but they are usually not marked eosinophilia.

Imaging studies, especially ultrasonography, are the most useful diagnostic tools. Ultrasonography is 88–98% sensitive and more than 95% specific for alveolar echinococcosis (Raether and Hänel, 2003). On plain film chest X-rays, lung metastases appear as multiple small solid masses at the peripheries of the lobes. On CT, liver masses are irregular, heterogeneous, and hypodense with central necrosis and calcifications, and they do not enhance with contrast. MRI is less sensitive because it does not detect calcifications, but it is useful to distinguish cystic and alveolar lesions in the brain. Serological testing is also useful for diagnosis. Specific IgE levels are 73.6% sensitive for diagnosis and can be used to follow treatment success as well (Wellinghausen and Kern, 2001). Em2 is a species-specific native antigen ELISA that is useful for screening, diagnosis, and monitoring treatment. This test is even better when used with II/3–10, a recombinant antigen; demonstrating 97% sensitivity and 99% specificity (Gottstein *et al.*, 1993).

8.5.2.5 Treatment

Surgery is the cornerstone of treatment for alveolar echinococcosis. When possible, the lesion is usually treated like hepatic cancer with radical resection of tissue containing the cysts. Early diagnosis is essential because early treatment carries a better prognosis, though even after surgery, 10–20% of patients have a recurrence. If the cyst cannot be removed in entirety, improving biliary drainage may increase quality of life. Patients should receive preoperative and postoperative chemotherapy, usually with albendazole. Because albendazole is only parasitostatic, patients need up to 2 years of therapy after surgery. Use of up to 20 mg/kg per day postoperatively has been associated with 80% survival at 10 years. Liver transplant has also been used

to treat alveolar echinococcosis. While it has been successful in many cases, there is considerable risk of proliferation of undiagnosed metastatic lesions or remaining cystic material due to post-transplant immunosuppressive therapy.

Albendazole, mebendazole, and praziquantel have all been used as chemotherapeutic agents against *E. multilocularis* infection. Albendazole is superior to mebendazole. Praziquantel is the most scolicidal, but does not prevent cyst expansion; albendazole is best to control cyst growth. Although cure is difficult with medical therapy alone, medication may be able to convert patients who are not suitable for surgery into operative candidates.

8.5.2.6 Control

Echinococcus multilocularis is very difficult to control because it is predominantly sylvatic. Limiting the number of stray dogs in the community and treating infected dogs with praziquantel can reduce human incidence, and placing praziquantel baits for foxes can decrease infection in this population. Elimination of *E. multilocularis* has only been successful on the Japanese island of Rebun, but this was only accomplished by elimination of all dogs and foxes from the island.

8.6 HYMENOLEPIS

8.6.1 *Hymenolepis nana*

8.6.1.1 Biology

Hymenolepis nana, known as the dwarf tapeworm, is a member of the order Cyclophyllidea and is the only cestode that does not require two distinct hosts, as the life cycle can occur entirely in humans. With a length of only 2–5 cm, it is the smallest cestode that infects humans. Its scolex has four suckers and one row of hooks. When mature, the strobila consists of 150–200 proglottids that are wider than they are long. The round or oval eggs, 40–50 μm in diameter, are transparent and white with a double membrane. The life span of the tapeworm is 4–10 weeks, but because of autoinfection, infected persons may harbor worms for much longer periods of time.

Hymenolepis nana has a direct life cycle (Fig 8.8), meaning that humans can serve as the only hosts for the parasite—it does not require a separate intermediate host although rats and insects often participate in transmission. *H. nana* is acquired by ingestion of eggs or metacestodes in food or on fomites; autoinfection can also occur when gravid proglottids release eggs that hatch inside the gut. Eggs hatch in the small intestine, liberating the oncosphere embryo, which then penetrates the lamina propria of the intestinal villi. The oncosphere encysts inside the villi for 4–5 days and then reenters the lumen of the small intestine. The worm then attaches to the small intestine wall with its scolex and matures over 3–4 weeks. If the metacestode (cysticercoid) form is eaten, it will attach directly to the small intestine wall without penetrating the lamina propria and will mature into an adult tapeworm in about 2 weeks. Gravid proglottids are released from the distal end of the worm and disintegrate in the small intestine so that only fertilized eggs are

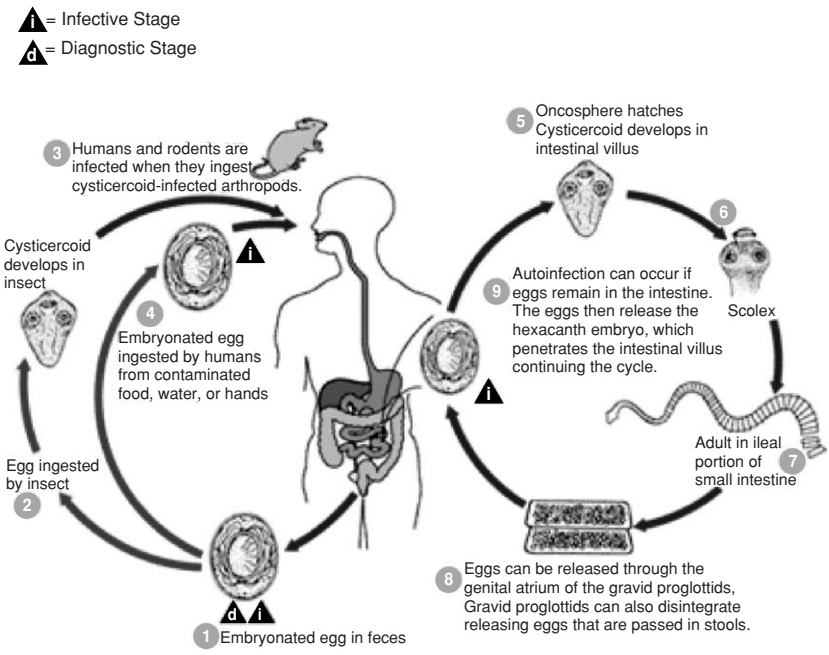

Figure 8.8. *Hymenolepis nana* life cycle. http://www.dpd.cdc.gov/dpdx

released in feces. They are infectious from the moment they are expelled in human feces.

8.6.1.2 Epidemiology

Hymenolepis nana is a ubiquitous human parasite, found worldwide, but it is especially common in Asia, Africa, Central and South America, and southern and eastern Europe. Children are the most commonly infected, possibly due to the immaturity of their immune systems. It is especially common in institutionalized children, where up to 8% may be infected (Yoeli *et al.*, 1972), and in immunocompromised or malnourished people. In tropical nations, where infection is most common, prevalence is about 1% (Botero *et al.*, 1998), but in certain endemic areas it can exceed 25% (King, 2000).

8.6.1.3 Transmission

Transmission occurs mainly through a fecal-oral route or by accidental ingestion of infected insects. Both eggs and metacestode larvae are infective for humans. The eggs may be eaten by rodents or beetle larvae, or may contaminate food when people do not follow good hygienic practices in the kitchen. Food, especially cereals and grains, becomes contaminated with human or rat feces containing eggs, or with mealworm larvae containing metacestodes, which is then eaten by humans.

8.6.1.4 Clinical Aspects and Diagnosis

Infection with *H. nana* is usually asymptomatic. Both cellular and humoral immunity appear important for clearance of the infection. In adults, the infection is cleared quickly because most adults rapidly mount a protective immune response, but children can have more prolonged infections. Very heavily infected people may have symptoms such as loss of appetite and abdominal pain. Diarrhea can result from damage to the intestinal mucosa.

Definitive diagnosis of *H. nana* infection is by identification of the eggs in stool microscopy. If the entire worm is recovered, diagnosis can be made by inspection of the scolex or by expressing eggs from gravid proglottids and identifying them as *H. nana*. There is an enzyme-linked immunosorbent (ELISA) assay that is approximately 80% sensitive, but it is not specific and frequently cross-reacts with other parasites (Castillo *et al.*, 1991).

8.6.1.5 Treatment

The infection is treated with either niclosamide or praziquantel. The cysticercoid form in the lamina propria is somewhat resistant to medical therapy, so patients may require higher doses or longer courses of the medications than are used for other helminthic infections. Praziquantal is advantageous because it kills both adult and larval forms and can be administered in a single dose of 25 mg/kg. The recommended dose of niclosamide is 2 g for adults or 1.5 g for children for the first dose, followed by 1g for adults or 0.5 g for children daily for 1 week in order to insure that any emerging cysts are killed. Because of the tapeworm's relative resistance to chemotherapy and the potential for autoinfection, the patient's stool should be checked for eggs 1 and 3 months after completion of treatment. If the stool contains eggs, the patient should receive another course of treatment.

8.6.1.6 Control

Good personal hygiene and sanitation to prevent contamination of food with human feces are the most effective ways to control *H. nana* infection. Controlling rodent populations may also decrease transmission by eliminating reservoir hosts. In epidemics, mass chemotherapy has been effective to prevent spread of the infection.

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