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Cestodes

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INTRODUCTION

The true tapeworms, Class Cestoda, belong to the Phylum Platyhelminthes and those of medical importance are placed in two orders: the Pseudophyllidea and the Cyclophyllidea. Platyhelminthes are among the oldest invertebrates in the animal kingdom, with bilateral symmetry and specialized tissues that support complex male and female reproductive organs that generate millions of infective embryos, called oncospheres, capable of developing into new tapeworms. Tapeworms are hemaphrodites, with one of the highest reproductive capabilities in biology (Bruce-Conn, 1993): a single tapeworm in the human intestine can grow several meters long and produce 20–30 million eggs a year. With the exception of *Hymenolepis nana*, cestode oncospheres are enclosed in a keratin shell (embryophore) that protects them from environmental variations. The persistence of these tapeworms in endemic areas is supported by their enormous reproductive capacity and the built-in protection from environmental factors.

The cestodes are segmented, ribbon-like flatworms that normally reside in the intestines of their definitive mammalian hosts. Their life-cycle includes at least one intermediary host, in which the tapeworm develops from the embryo to the larval stage. In this chapter, only tapeworms that cause significant disease in humans are discussed: *Taenia solium*, *Taenia saginata*, Asian *Taenia* and *Hymenolepis nana* belonging to the Order Cyclophyllidea and *Diphyllobothrium latum*, belonging to the Order Pseudophyllidea. *Echinococcus granulosus*, which is also a cyclophyllidean cestode, will be described in a separate chapter. *T. solium*, *T. saginata*, Asian *Taenia* and *H. nana* still cause widespread disease in developing countries of Asia, Africa and Latin-America (Bao, *et al*., 1995; Dada *et al*., 1993; Díaz *et al*., 1992; Díaz-Camacho *et al*., 1991; Sarti *et al*., 1994; Sánchez *et al*., 1997). The taeniid tapeworms are responsible for zoonoses almost always associated with ignorance and poverty.

TAENIA

DESCRIPTION OF THE ORGANISM

Adult Tapeworm Morphology

Adult tapeworms are attached to the upper third of the duodenum of the human intestine. Humans are the only known natural definitive hosts for taeniids. The adult tapeworm has a **scolex** at the anterior end bearing **bothria** (in pseudophyllideans, such as *Diphyllobothrium latum*) or **suckers** (in cyclophyllideans, such as Taenidae and Hymenolepidae), followed by a

neck region of undifferentiated tissue, which gives rise to a chain of **proglottids** (segments). Each proglottid can be considered an independent reproductive unit, as it contains both male and female organs (Schmidt, 1986).

As proglottids progress distally along the chain (also known as the **strobila**), they mature and produce a large number of eggs in the uterus, which are fertilized by sperm released from the testes. The resulting embryos, known as **oncospheres**, are then encapsulated in a protective keratin shell and eventually released with the gravid proglottid, each of which contains thousands of infective oncospheres (encapsulated embryos).

Tapeworms can be identified by differences in the morphology of the scolex, proglottids, length of the strobila and number of worms per infection: *T. solium*, *T. saginata* (1.5–12 m) and *D. latum* (up to 10 m, or 30 feet) being very long and usually found as single worms, with *H. nana* measuring 2–3 cm and generally found as a multiple infection.

The external surface of adult tapeworms consists of a tegument, a continuous protoplasmic band joined to cell bodies (tegumentary cytons) by cytoplasmic processes and separated from the rest of the parasite wall by a basement membrane. All cestode tegumentary surfaces have a brush border covered by microvilli or microtriches, structures that are in contact with the host tissue. Beneath the basement membrane are found various cell types: flame cells, myocytes, calcareous corpuscle cells and glycogen storage cells within a loose matrix of connective tissue fibers. The parenchyma of proglottids is divided into cortical and medullary tissues by a system of longitudinal and transverse muscle fibers. Reproductive structures are located within the medullary portion. Interspersed throughout the cortical area are calcareous corpuscles, structures unique to cestodes, oval-shaped with a whorled appearance and a complex chemical composition that includes calcium carbonate.

Larval (Metacestode) Morphology

Since *T. solium* metacestodes (larval stage) are the best studied larvae, both by light and electron microscopy, we will use them to illustrate the main structures (Lumsden *et al.*, 1982).

The larvae are extracellular parasites, visible to the naked eye, seen as bladders 0.5–1.5 cm in diameter, with an invaginated scolex, observed as a white opaque sphere suspended within the vesicle. In pig muscle infections they are readily apparent (Figure 23.1A, B). Under the light microscope, the external surface is a tegumentary tissue, similar to that found in the adult worm, with microvilli or microtriches projecting from it and in direct contact with the host tissue (Figure 23.2). The bladder wall contains various cell types surrounded by loose connective tissue and calcareous corpuscles that blend into the vesicular fluid, which makes up about 90% of the larval contents. In human infections, these larvae can survive for a number of years. An immune response eventually elicits an inflammatory reaction of the granulomatous type, with a large number of eosinophils degranulating on the surface of the parasite. Dead parasite tissue is reabsorbed slowly, leaving a calcified concretion in both muscle and brain tissue.

Oncosphere, Egg Morphology

Mature eggs from *T. solium* and *T. saginata* are indistinguishable. As shown in Figure 23.3, they can be seen under the light microscope as 50 μm diameter spheres, with a striated border corresponding to the keratin envelope and frequently a triple set of hooks within. Their presence in stool is diagnostic of *Taenia* sp. Electron micrographs of sections through these eggs illustrate the oncospheres with a number of cells; the hooks and several cell types have been identified (Figure 23.4). In addition, the embryo is surrounded by several membranes. The protective envelope (embryophore) is made up of keratin blocks, which are cemented together and become unglued when the egg comes into contact with hydrochloric acid, digestive enzymes and bile in the small intestine, thus liberating the oncosphere, which can penetrate the intestinal wall and reach the blood or lymphatic vessels of the mesentery, from where it is passively transported to the host tissues.

Once the oncosphere has reached an extracellular site (the mechanisms by which the

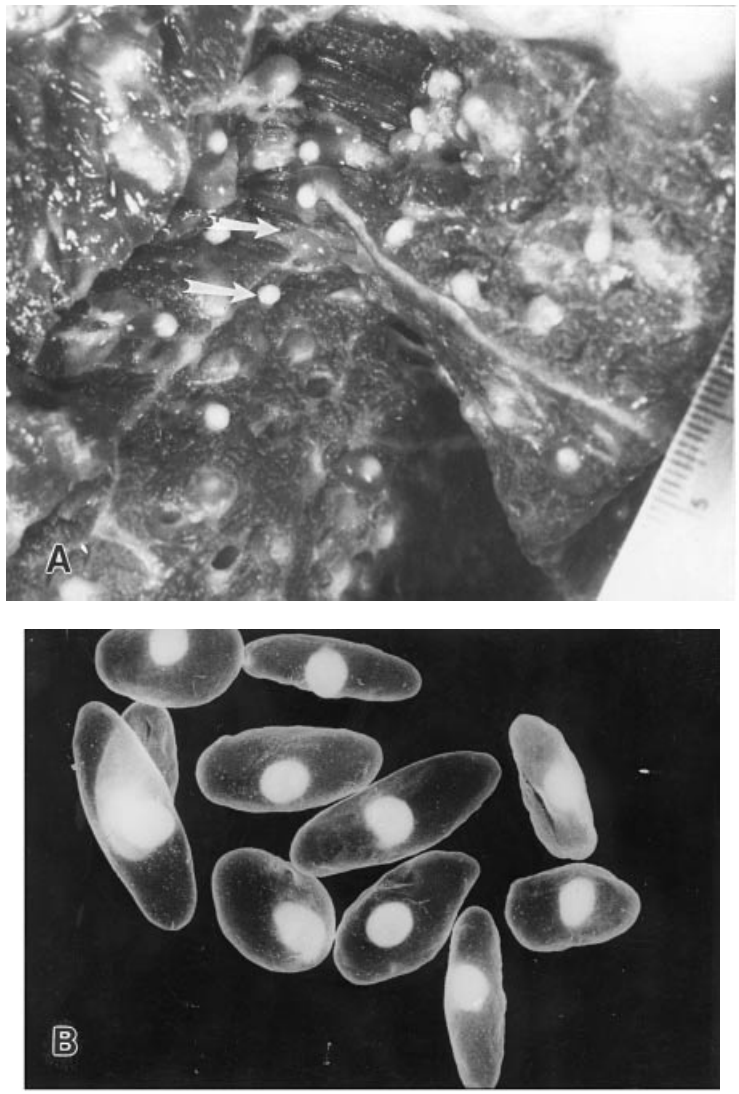

Fig. 23.1 (A) Light micrograph of infected pork meat, showing a large number of cysticerci (arrows). Bar=1 cm. (B) *Taenia solium* larval metacestodes dissected from infected pork

oncosphere traverses the intestinal and vessel walls are not understood), it develops to the larval stage, a process that takes about 8 weeks.

LIFE-CYCLE

Taenia saginata (*Taeniarhynchus saginatus*) (Beef Tapeworm) (Figure 23.5)

The adult tapeworm lives only in the small intestine of humans and so far has never been found naturally in any other definitive host. Experimental infections have been established in immunosuppressed golden hamsters, but without obtaining gravid proglottids (Verster, 1971). The tapeworm is acquired by ingesting raw or undercooked beef infected with larvae. The larvae evaginate in the small intestine of the host. After digestive juices and bile promote the evagination of the scolex through the bladder wall, this structure attaches to the intestinal wall, probably by burrowing through the intestinal villi with the unarmed rostellum, penetrating a crypt of Lieberkühn while simultaneously anchoring to

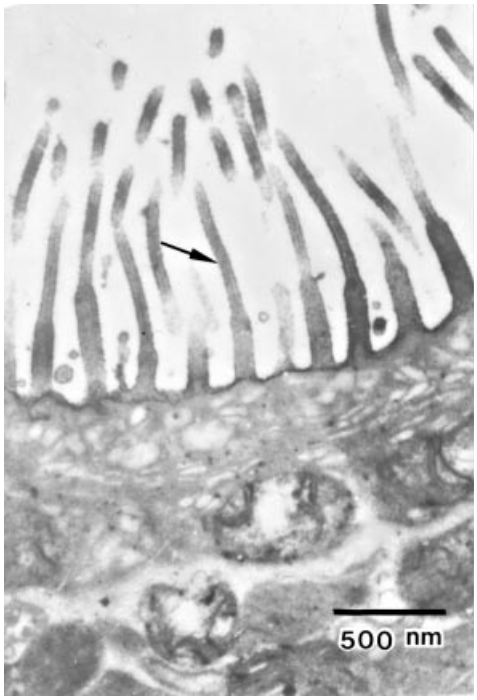

Fig. 23.2 Electron micrograph of *Taenia solium* metacestode surface, illustrating microvilli (arrow)

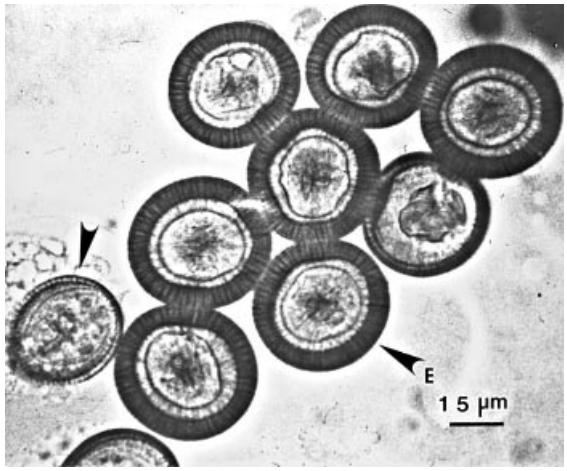

Fig. 23.3 *Taenia* sp. eggs. Light micrograph showing typical embryophore outer shell (arrow, E). Reproduced by permission from Flisser *et al.* (1982)

neighboring villi by all four suckers, similar to the mechanism that has been identified for *Echinococcus granulosus* in experimental dogs and in experimental *T. solium* infections in hamsters.

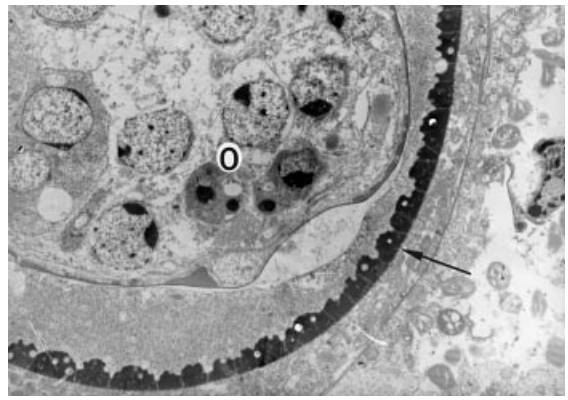

Fig. 23.4 Transmission electron micrograph through *Taenia solium* egg. Arrow, embryophore. O, oncosphere

Growth of the adult tapeworm then proceeds continuously from the neck region by an ever-lengthening chain of proglottids; 4–6 months after infection, the tapeworm begins to eliminate gravid proglottids containing 50 000–80 000 infective eggs, which are shed in the stool.

When infective eggs are ingested by cattle in contaminated fodder or water, the oncospheres penetrate the intestinal wall and are carried to various tissues, mostly the heart and masseter muscles but also throughout the musculature, where they develop into larvae or cysticerci. Ingestion of viable larvae in raw or undercooked beef by humans can then produce a new adult tapeworm.

Taenia solium (Pork Tapeworm) (Figure 23.6)

Taenia solium is the most important human tapeworm, because it is the only intestinal parasite responsible for human cysticercosis as well as pig cysticercosis. *T. solium* continues to be an endemic parasitic disease in many countries of Central and South America, South Africa and Asia. Humans are the only natural definitive host. Tapeworms attach to the epithelial wall of the small bowel and grow in segments (proglottids) which contain male and female sex organs. Its importance resides in the capacity of the embryos to traverse the intestinal wall and lodge in muscle masses or in the brain, where they develop into the larval (metacestode) stage of the

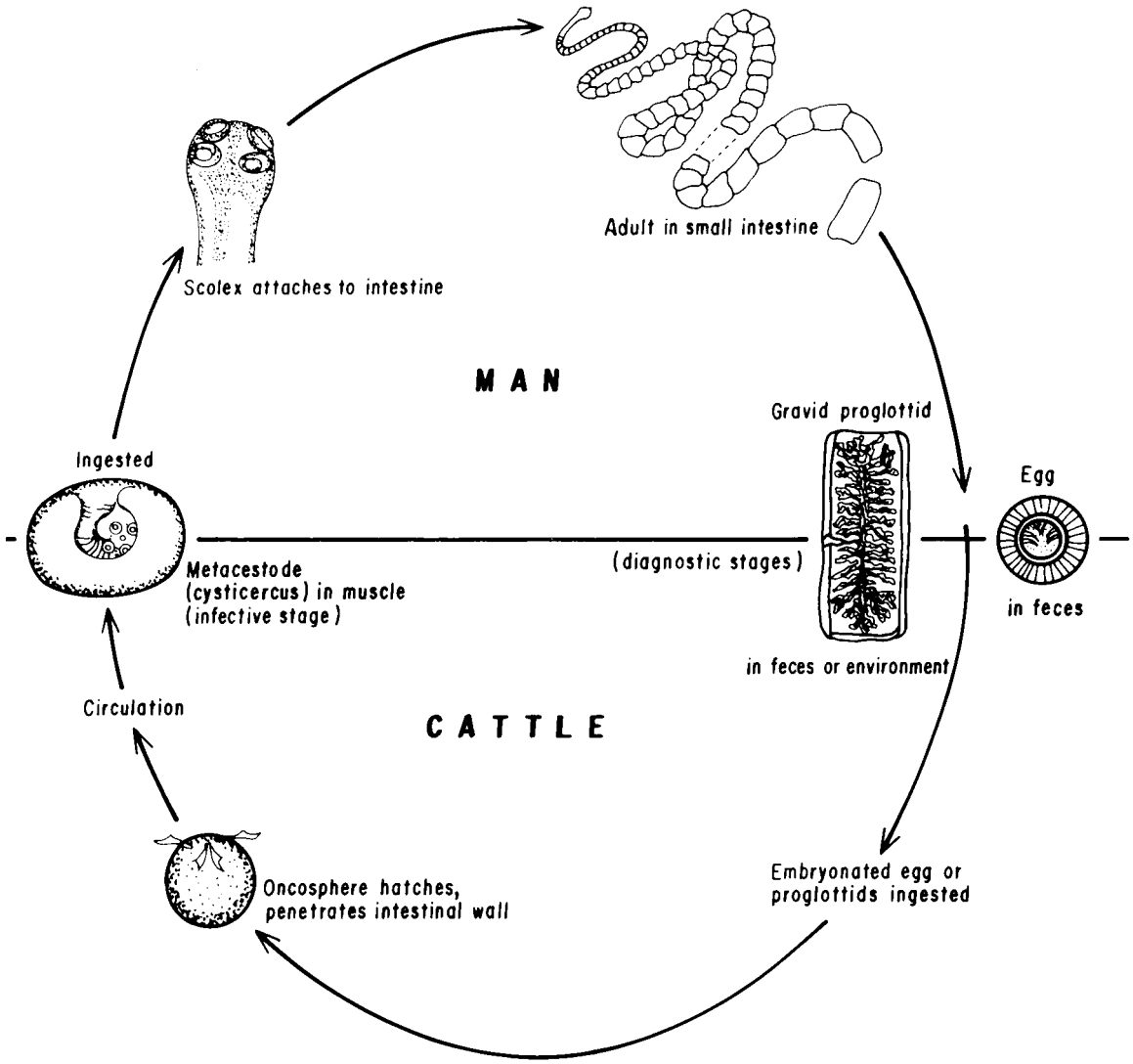

Fig. 23.5 Life-cycle of *Taenia saginata*

parasite. In humans, neurocysticercosis (NC) is by far the most important disease caused by this parasite. Pigs are the intermediate host for the larval stage, which they acquire by ingesting feces containing adult tapeworm proglottids. The life-cycle thrives in rural areas with poor sanitation, without water or drainage and where pigs are left to roam and scavenge on human excrement and garbage. It has been recognized for many years that the larval stage can survive for long periods in the host before being destroyed or attacked by the immune response. The classic work of Dixon and Lipscomb (1961), showed that British soldiers returning in 1948 from India, a country with a high prevalence of *Taenia solium*, took an average of 2–5 years to develop symptoms of NC, suggesting that the parasite, lodged in the nervous tissue, either does not release antigens or has evasion mechanisms that allow survival for long periods.

The adult worm has an armed scolex (Figure 23.7) which consists of a rostellum bearing two rows of hooks (22–32). Recent experimental evidence, obtained by infection of golden

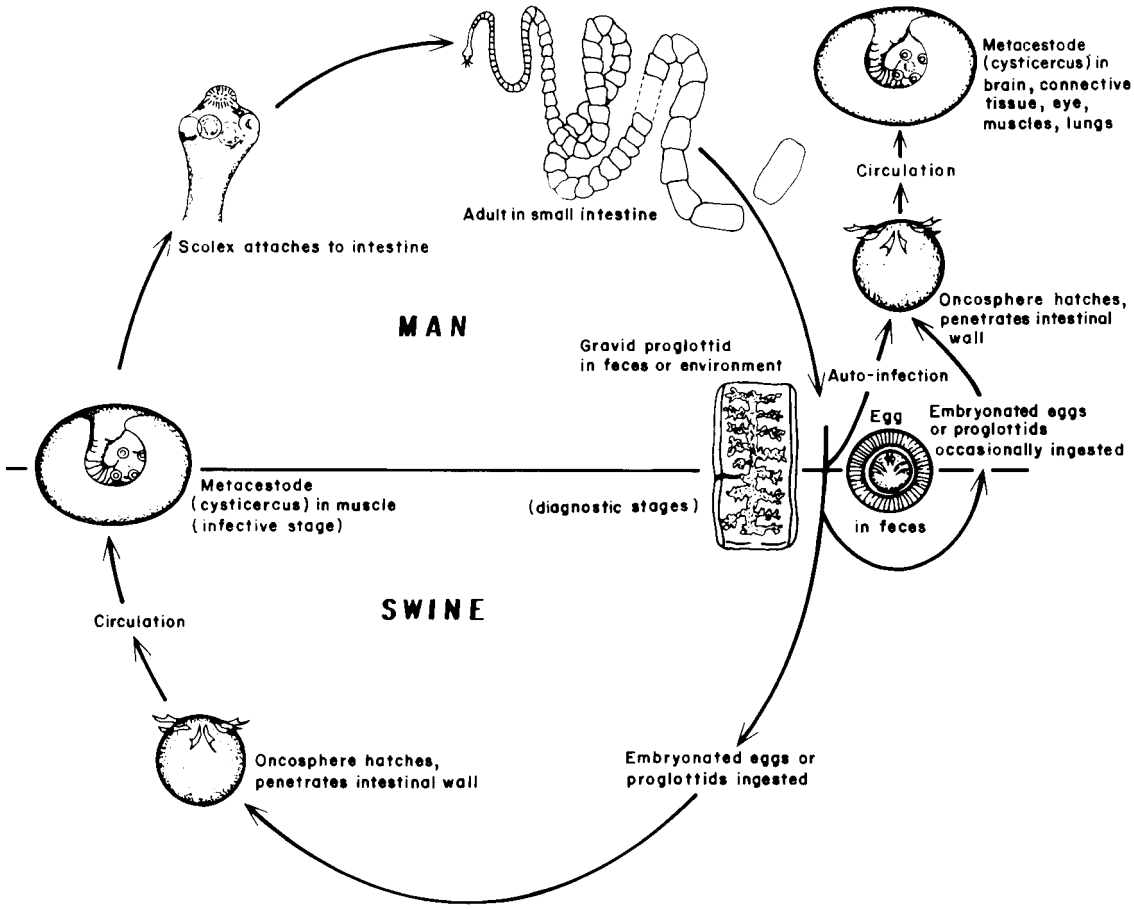

Fig. 23.6 Life-cycle of *Taenia solium*

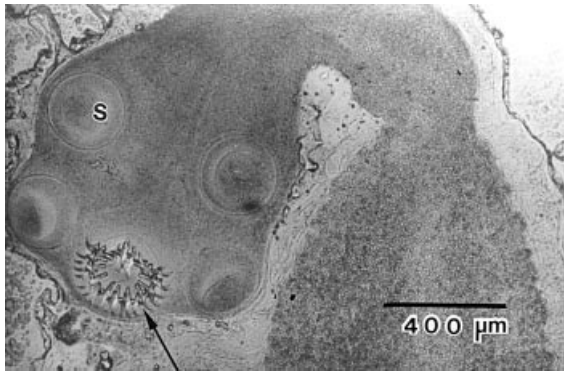

Fig. 23.7 Light micrograph of *Taenia solium* whole worm preparation, to show scolex with four suckers (s) and rostellum with double row of hooks (arrow)

hamsters, has shown that the scolex implants in the upper third of the duodenum (Merchant *et al*., 1998), by engulfing intestinal villi in the four suckers (Figure 23.8) and burrowing the rostellar pad into the crypts of Lieberkuhn of the submucosa, similar to what has been described for the dog tapeworm, *Echinococcus granulosus* (Figure 23.9).

EPIDEMIOLOGY

Taenia saginata

Taenia saginata continues to be a frequent helminthic disease in developing countries

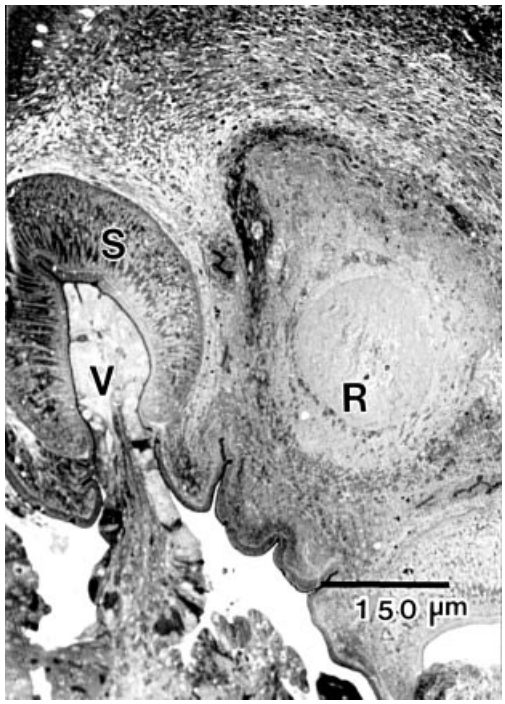

Fig. 23.8 Light micrograph of section through hamster duodenum, showing implanted *Taenia solium* and sucker engulfing intestinal villus. S, sucker; V, villus; R, worm rostellum

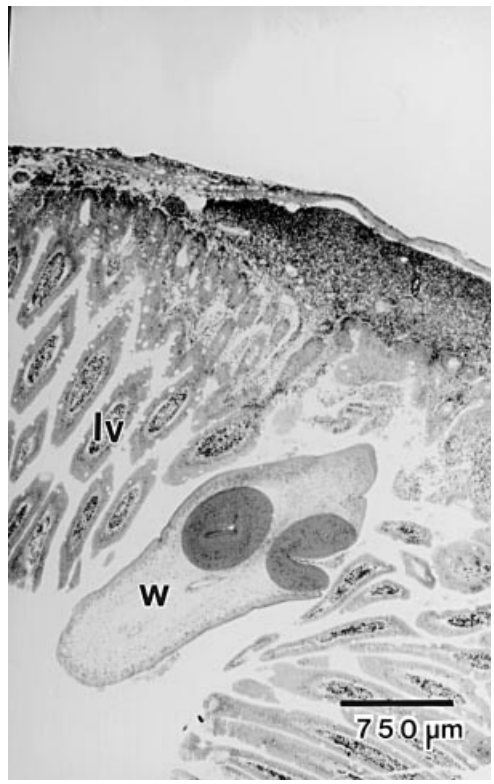

Fig. 23.9 Light micrograph of section through hamster intestine, showing implantation site of *Taenia solium*. Iv, intestinal villi; W, worm

(Pawlowski, 1982). This is due to several difficulties in diagnosing tapeworm infections, particularly in isolated rural areas (where human excrement is disposed of on open ground), the absence of symptoms in otherwise healthy carriers, poor personal hygiene and lack of adequate meat inspection in many countries (Mobius, 1993).

Taeniasis/Cysticercosis

The life-cycle of *T. solium* has been understood since Küchenmeister (1855) proved that the ingestion of cysts obtained from infected pork and mixed with food gave rise to adult tapeworms in the intestine in prisoners (Figure 23.7). Two years earlier, in 1853, Van Beneden had shown that the ingestion of *T. solium* proglottids caused cysticercosis in pigs. Rigorous meat inspection practices, the development of an increasing number of farms in which pigs are reared under highly controlled conditions, and significant improvement in hygiene standards and sanitary installations in Europe and North America have contributed to the eradication of taeniasis and human cysticercosis in the majority of developed countries (Gemmel *et al*., 1983). Population mobility has, however, contributed to the appearance of an increasing number of cases of NC in the USA among Latin-American immigrants. In 1992, cases of autoctonous NC were reported in the Bronx, NY, which were probably transmitted by a Mexican domestic worker who was diagnosed with intestinal *T. solium* (Schantz *et al*., 1992). During the past 15 years a number of epidemiological studies have been carried out in Mexico, Guatemala, Honduras and Peru (Díaz-Camacho *et al*., 1991; Sarti *et al*., 1992; Allan *et al*., 1996; Sánchez *et al* 1997; García *et al*., 1995) in order to obtain more precise information on the frequency and geographic distribution of *Taenia* NC parasitosis.

Seroepidemiological surveys carried out in Mexico have indicated a high percentage of individuals with antibodies against *T. solium* antigens in areas of porciculture, an observation which has been interpreted as frequent contact with cestode antigens (Larralde *et al.*, 1992). Detailed studies in small rural communities have found up to 10% of individuals infected with adult tapeworms, high seropositivity rates, the presence of infected pigs reared domestically, as well as the practice of human defecation on open ground. Studies of small rural communities in Mexico indicate a significant association between the number of *T. solium* carriers and the practice of defecating on open ground (Sarti *et al.*, 1992). The studies of Diaz-Camacho *et al.* (1991) in small rural communities revealed that sharing living quarters with a tapeworm carrier increased the number of individuals with antibodies to cestode antigens five-fold over inhabitants who had no contact with such carriers. Daily domestic contact with a tapeworm carrier also increases the risk of acquiring NC, as has been shown by the studies of Sarti *et al.* (1992). These results emphasize the importance of treating tapeworm carriers opportunely with anthelminthics. The elimination of *T. solium* tapeworms in endemic areas should become a public health priority, since it has been shown that persons living with a tapeworm carrier have a significantly higher risk of acquiring NC.

Asian *Taenia*

This cestode was originally described in Taiwanese aborigines (Eom and Rim, 1993) and has since been found in Korea, Indonesia, Thailand and The Philippines. Genetic characterization of this cestode, as well as the macroscopic morphology of an unarmed scolex, a large number of uterine branches and a posterior protuberance, has pointed to a close genetic relationship with *T. saginata* (Bowles and McManus, 1994). The larval stages are viscerotropic and infect the liver of pigs and cattle. Humans acquire the adult tapeworm after ingesting raw viscera (Fan *et al.*, 1992). The prevalence of this taeniasis appears to be high in Asia and the South Pacific basin and is therefore an important public health problem. However, due to its close relationship with *T. saginata*, it is unlikely to be a causal agent of human cysticercosis.

CLINICAL FEATURES AND PATHOLOGY

Taenia saginata

Symptomatology in *Taenia* carriers is vague and may include abdominal pain, nausea, dizziness, headache, weight loss, increased appetite, pruritus ani and excitation. Presence of the tapeworm can often be detected by the carrier after observing proglottids in the stool or active migration of segments through the anus. It should be stressed that many infections may go undetected. *T. saginata* should be suspected in a patient who ingests raw beef and who describes elimination of tapeworm segments in the stool and/or has recovered segments migrating through the anus.

Taenia solium

The intestinal symptoms of *T. solium* infection are similar to infection with *T. saginata*. The most important complication of clinical syndrome is cysticercosis. It is the larval stage (metacestode) of *Taenia solium* that produces cysticercosis. Three sites are preferred targets for cysticerci: the nervous system, the muscle and the eye (Willms, 1998). Exceptionally, cysticercosis has been described in other organs, such as the placenta, liver, heart, peritoneum, etc. By far the most frequent and most important form of human cysticercosis is neurocysticercosis (NC). Cysticercosis is endemic in most countries of Latin America, Asia, Africa and some European countries. With the exception of populations in which the life-cycle of *T. solium* cannot prosper because pork meat is not consumed, the disease is endemic in the developing world. In recent years, the disease has spread as a consequence of immigration from endemic areas to developed countries, where the disease had previously been controlled by strict meat inspection practices, as well as sanitary and hygiene measures. Thus, cysticercosis is increasingly seen in countries of

North America and Europe where, despite sanitary measures that impede the perpetuation of the parasite life-cycle, immigrants infected in an endemic country transport the disease that may manifest clinically months or years after the infection was acquired.

The feces of human carriers with the intestinal cestode *T. solium* contain mature proglottids, each with several thousand viable eggs that contaminate the environment of places without sanitation and vegetables irrigated with sewage contaminated with human feces. Both humans and pigs can become infected by ingesting water and raw fruit or vegetables contaminated with *Taenia* eggs. The eggs lose their keratin coat when they come in contact with the digestive enzymes, and free oncospheres traverse the intestinal wall and enter the blood stream, which will carry them to the nervous system. In most endemic areas the popular belief is that cysticercosis is acquired after eating infected pork, and the link between human carriers of the adult intestinal worm and pig cysticercosis is not understood (Nieto, 1982). Ignorance of basic facts of the life-cycle of taeniasis/cysticercosis prevents the instrumentation of simple hygiene measures, such as washing vegetables and drinking boiled water to prevent the ingestion of taeniid eggs.

Pathology

The complex host–parasite relationship in cysticercosis is still poorly understood. Some patients present a remarkable tolerance to the parasite, which can live in the brain for long periods without inducing a noticeable immune reaction (Pitella, 1997); in others, the immune response is unable to destroy the parasite, but is an important cause of damage to the surrounding tissue; in still other patients, the immune response is intense, leading to rapid destruction of the larva. The reasons for this variable response between individuals are not yet understood. Some HLA antigens have been weakly associated either to increased resistance (HLA DQw2) or susceptibility (HLA A28) to infection. It has also been shown that the parenchymal inflammatory response is more intense in females than in males; however, the reasons for these differences have not been explained (Monteiro *et al*., 1993; Rangel *et al*., 1987; Del Brutto *et al*., 1988).

The sequence of events corresponding to the stage of the parasite in the brain begins when the hexacanth embryo (oncosphere) is passively carried by the systemic circulation to the brain parenchyma, where it differentiates into a larva 1–1.5 cm in diameter within 2 months. Different events will follow, depending on the immune response of the host to the newly established parasite (Figure 23.10) (Pitella, 1997):

1. If immune tolerance develops, the cyst can remain in the tissue for several years (up to 12 years have been documented by neuroimaging studies). In most of these cases, the cysts will continue to grow undisturbed; some may develop into cysts 10–15 cm in diameter years after infection (Figure 23.11). In many other cases, although the cysts grew undisturbed for long periods, the sudden appearance of a host immune reaction will induce an intense inflammation around the cyst, an event which seems to trigger death of the cysticercus. When the size of the cyst exceeds 2 cm in diameter, most of them lose the scolex due to a degenerative process that nevertheless allows the tegumentary membranes of the cysticercus to continue proliferating. The membranes can produce a giant cyst containing up to 50 ml fluid without an identifiable scolex in its interior.
2. Within 2 months of implantation, the cysticercus will acquire its typical morphological features of a 1 cm diameter cyst filled with a clear fluid and containing the scolex and neck, with the characteristic features of the cestode, a worm-like body with a head composed by four suckers and a double crown of hooks. If the immune response is strong enough to induce death of the parasite, it will undergo hyaline degeneration of the cystic fluid, followed, a few weeks later, by macrophage infiltration and the formation of a granulomatous lesion, which in turn will either disappear without evident damage to the surrounding tissue or remain as a permanent granuloma, composed mostly of fibrotic scar tissue. Over 2–7 years this granuloma will

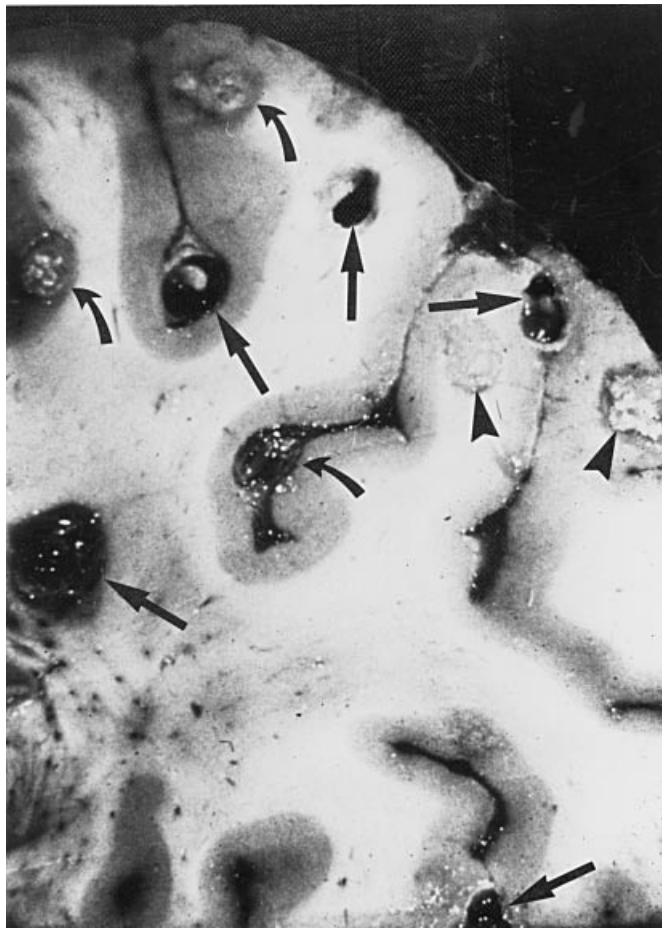

Fig. 23.10 Brain slice from a patient with neurocysticercosis, showing multiple lesions in different stages; live cysts with the characteristic metacestode inside (straight arrows), granulomas (curved arrows) and calcifications (arrowheads)

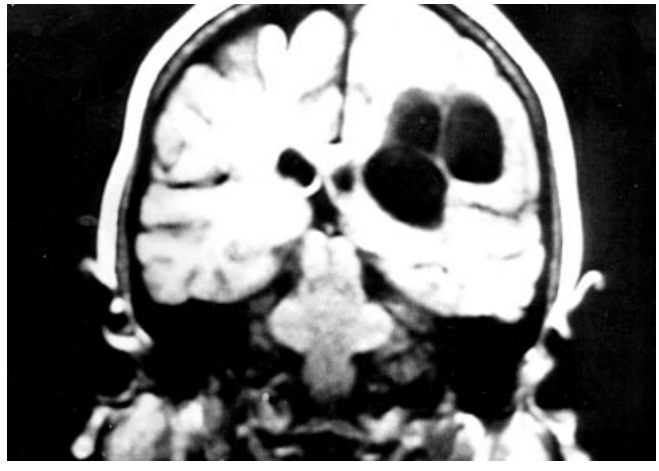

Fig. 23.11 Magnetic resonance imaging, showing a clump of three large cysts producing a space-occupying lesion

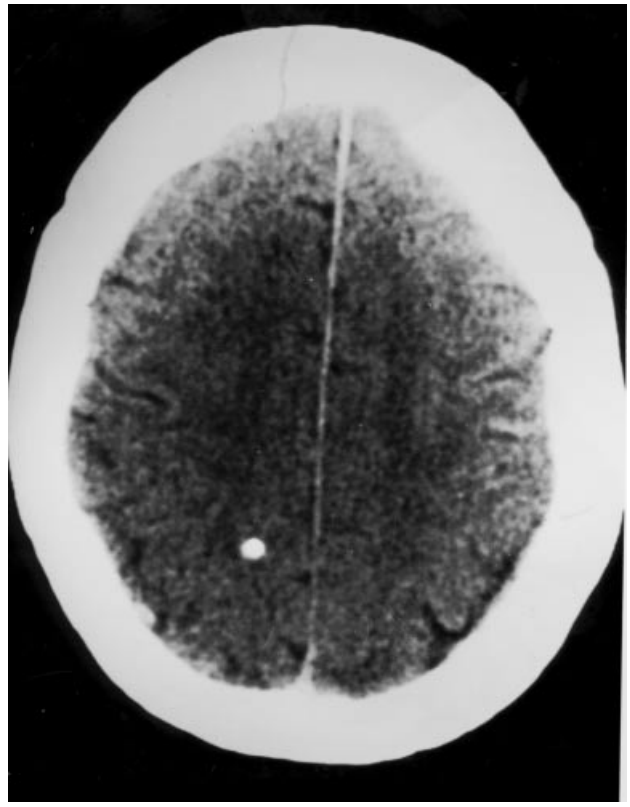

Fig. 23.12 Computed tomography, showing a parenchymal brain calcification, the most conspicuous sequel of neurocysticercosis and a frequent cause of epilepsy in endemic areas

gradually calcify, becoming a permanent calcification which is easily observed in a simple X-ray study of the skull (Figure 23.12).

3. The two patterns described above in the natural history of brain parenchyma cysticercosis represent opposite pictures that depend on either immune tolerance or a hyperimmune response of the host (Estañol *et al.*, 1986). However, in many patients the immune response is mild and chronic, not enough to destroy the parasite but sufficient to induce damage in neighboring tissues, such as vasculitis, fibrosis and astrogliosis. The parasites may remain for long periods in this stage. Thus, by imaging studies, many patients are found to have degenerating cysts that remain unchanged and surrounded by a thick capsule of fibrous tissue secondary to chronic perilesional inflammation. An intriguing feature of NC is the frequent finding of various parenchymal lesions in different stages, i.e. live cysticerci without signs of surrounding inflammation, hyaline cysts, granulomas and calcifications. This combination of lesions indicates either that the intensity of the local immune response varies from one site to another in the same host or that the cysticerci were the result of different infections (see Figure 23.10). Both possibilities appear feasible.

When cysticerci are lodged in cavities, such as the ventricular system or the vitreous cavity of the eye, the cysticercus may remain viable, floating within the fluid for long periods. In the case of ventricular cysticercosis, the parasite may lodge in the third or fourth ventricle and occlude

the cerebrospinal fluid (CSF) circulation causing subacute hydrocephalus. Meningeal cysticercosis is the most severe form of the disease (Lobato *et al*., 1981; Estañol *et al*., 1983). When cysticerci infect the arachnoid membrane, the inflammatory response is intense, and may last for several years and be a persistent source of tissue damage, which, in contrast with parenchymal cysticercosis, is not restricted to the infection site. The CSF circulation disseminates the inflammatory cells and cytokines throughout the central nervous system, causing cerebritis, vasculitis (Del Brutto, 1992), fibrous entrapment of cranial nerves and fibrotic obstruction of CSF absorption at the arachnoid villi, which in turn will induce chronic hydrocephalus in most patients (Sotelo and Marín, 1987). The intense inflammation of the meninges and its dissemination by the CSF circulation are the source of severe neurological damage, evidenced as brain infarctions, amaurosis, diplopia, other cranial nerve dysfunctions, intracraneal hypertension and dementia. In meningeal cysticercosis, the inflammatory response of the host is the source of most of the pathological features.

Clinical Manifestations

The clinical manifestations of cysticercosis depend to a great extent on the location of the parasites (Earnest *et al*., 1987; Salgado *et al*., 1997). Parenchymal cysticercosis induces epilepsy in most cases (López-Hernández and Garaizar, 1982; Grisolia and Wiederholt, 1982; Chandy *et al*., 1989; Monteiro *et al*., 1991). When the number of parasites is large, mental disturbances or focal neurological symptoms may be present. Giant cysticerci may induce a tumor-like picture. The severity of neurological disturbances depends on the intensity of perilesional inflammation, where cerebritis and vasculitis magnify the parenchymal lesions.

In endemic areas, the diagnosis of NC (either active or inactive) in the form of residual granulomas accounts for more than 50% of late-onset epilepsy (Figure 23.12) (Rajshekhar, 1991; Del Brutto *et al*., 1992a). Therefore, in patients or immigrants from endemic areas who present a first seizure after the age of 20, a neuroimaging study is mandatory to investigate a possible case of cysticercosis (Monteiro *et al*., 1995; Medina *et al*., 1990).

Ventricular cysticercosis in most cases induces a subacute picture of hydrocephalus, due to the valvular occlusion of the CSF fluid circulation; usually a single cyst is visually located in the fourth ventricle, in some cases ependymitis is associated with signs of brainstem dysfunction.

Meningeal cysticercosis is the most severe form of the disease. When cysticerci are located at the base of the brain, widespread vasculitis ensues, with vascular headache and, in severe cases, small and large brain infarctions may appear in distant sites. Clinical manifestations are either mental deterioration or acute motor abnormalities. Chronic inflammation of the arachnoid membranes, disseminated by the CSF circulation, leads to fibrosis and dysfunction of the mechanisms of CSF absorption, with the progressive development of hydrocephalus and intracraneal hypertension, gait disturbances and mental deterioration (Sotelo and Marín, 1987). The same mechanisms induce fibrotic entrapment of the cranial nerves, the most frequent clinical manifestation being diplopia, due to dysfunction of the oculomotor nerves.

Muscle cysticercosis is usually asymptomatic, with the finding on clinical examination of subcutaneous nodules. In severe cases muscle pseudohypertrophy develops, due to massive infection of the muscle by countless cysticerci (Wadia *et al*., 1988). In contrast to the other host for cysticercosis, pigs, which usually present muscle cysticercosis, in humans this is a rare location.

Ocular cysticercosis is also rare. The parasite lodges in either the vitreous cavity or the subretinal space. In both cases, visual abnormalities develop. The diagnosis is made by fundoscope examination (Keane, 1982; Kruger-Leite *et al*., 1985; Corona *et al*., 1986). Cysticerci located in other organs are rare; in most cases they are an autopsy finding associated with severe cases of disseminated cysticercosis.

DIAGNOSIS

Intestinal Taeniasis

Taeniasis can be diagnosed on the basis of the following findings: (a) a history of ingesting raw

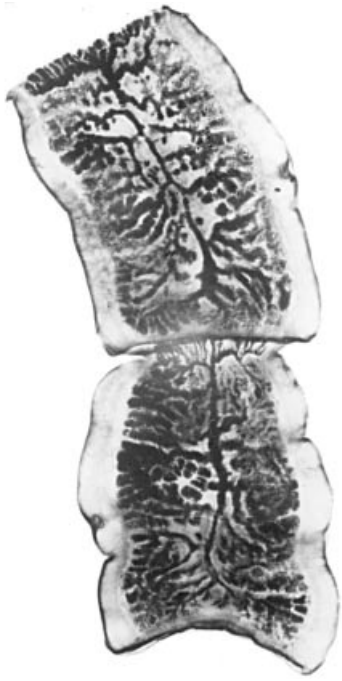

Fig. 23.13 Proglottids of *Taenia solium*. Reproduced from Willms (1998) by permission of WB Saunders Company

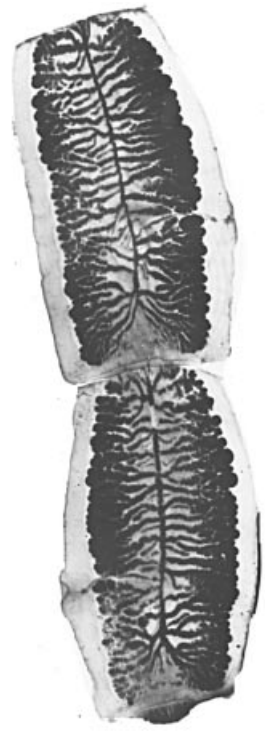

Fig. 23.14 Proglottids of *Taenia saginata*. Reproduced from Willms (1998) by permission of WB Saunders Company

or undercooked pork (homemade sausages) or beef; (b) discharging of proglottids or worm segments in the stool or the presence of loose proglottids in underclothing or bedding, which has been reported in *T. saginata* infections; (c) coprological analysis—three consecutive stool examinations using the methods of Faust *et al.* (1938), Ritchie (1948) or Kato are recommended. The perianal swab method of Graham (1941) may also be used. If proglottids are available, an effort should be made to identify the number of uterine branches under a microscope, by fixing the segments in formalin and dehydrating in glycerol. Less than 12 uterine branches is indicative of *T. solium* and the patient should be given anthelminthic treatment as soon as possible, as he/she is a potential risk to other humans (Figures 23.13 and 23.14). The patient should be asked to recover the tapeworm and bring it to the laboratory for definitive diagnosis. Care should be taken to identify the scolex to ascertain whether it has an armed or unarmed rostellum (Figure 23.15). If the scolex is not present, the

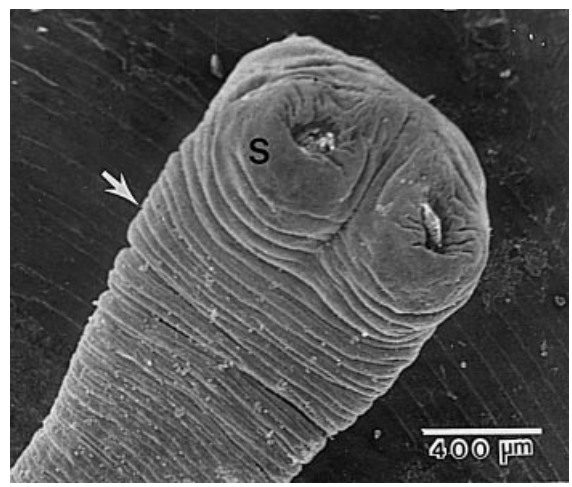

Fig. 23.15 Scanning electron micrograph of *Taenia saginata* scolex. S, sucker. Arrow, neck

proglottids should be prepared for microscopic observation. Patients should be re-examined 4–6 months after treatment, particularly if the scolex was not found or the proglottids were too

macerated to be identified. It should be emphasized that the eggs of *T. solium* and *T. saginata* are identical under the light microscope. The morphological identification of proglottids and scolices requires laboratory facilities and trained personnel, which are frequently not available in rural areas of developing countries. Recently, several groups have worked out an antigen capture method based on an ELISA technique (Allan *et al.*, 1993) as well as the preparation of specific DNA probes for the detection of *Taenia* eggs in stool samples, methods which promise rapid and efficacious results and that should be helpful in epidemiological surveys (Chapman *et al.*, 1995).

Cysticercosis

Neuroimaging studies, magnetic resonance imaging (MRI) and computed tomography (CT), are irreplaceable studies for proper diagnosis and characterization of active and inactive neurocysticercosis (NC) (Martínez *et al.*, 1989). Cysts, granulomas, infarctions and hydrocephalus are clearly identified by these studies. Also, the degree of inflammation can be determined; a conspicuous lesion of cysticercosis can be determined in brain parenchyma through the aid of neuroimaging studies. Immuno-diagnostic tests in serum are useful as a screening procedure for epidemiological studies (Simac *et al.*, 1995; Ramos-Kuri *et al.*, 1992) but not as a diagnostic tool for individual cases, as patients with single lesions or with sequelae such as granulomas and calcifications are frequently seronegative (Chang *et al.*, 1988). Analyses of CSF, including immunodiagnostic tests, are very useful for NC cases as they give reliable information on the degree of inflammation in the subarachnoid space (Ramos-Kuri *et al.*, 1992; Miller *et al.*, 1985), which are of paramount importance for anti-inflammatory steroid therapy.

TREATMENT

Intestinal Taeniasis

Two anthelminthics have been used successfully for the treatment of intestinal taeniasis: praziquantel and albendazole. Both have shown a high cure ratio and have also been used for the treatment of human NC (see below) (Pawlowski, 1989; Groll, 1980). The recommended dose of praziquantel in adults is 2.5–10 mg/kg, given in a single dose. For albendazole, the recommended dose in adults is 6.6 mg/kg or two doses, each of 200 mg/day on 3 consecutive days. This drug should not be used in children under 2 years old or during pregnancy, owing to embryotoxic and teratogenic effects observed in experimental animals.

Several publications have emphasized the positive results of population or individual case treatment for the elimination of tapeworms in endemic areas (Anderson and May, 1982). Treatment is innocuous and inexpensive. A note of caution should be introduced: although large-scale anthelminthic treatment has been effective in temporarily reducing the number of tapeworm carriers in a community, the increasing number of reports on drug resistance to praziquantel and other antiparasitic drugs in wide use support the policy that anthelminthics should be administered only in individually diagnosed cases.

Cysticercosis

After more than a decade since the first descriptions of cysticidal drugs, great advances have been made on the optimal schedules for the treatment against both the parasites and inflammation (Robles, 1982; Colli *et al.*, 1986; Sotelo *et al.*, 1990; Corral *et al.*, 1996; Sotelo and Flisser, 1997). Two drugs, albendazole (Takayanagui and Jardim, 1992; Botero *et al.*, 1993; Rajshekhar, 1993) and praziquantel (Wadia *et al.*, 1988; Robles *et al.*, 1987; Bittencourt *et al.*, 1990) are very effective cysticidal drugs. They are indicated in all cases of parenchymal or arachnoid cysticercosis (Martínez *et al.*, 1995; Vázquez and Sotelo, 1992), so that nowadays surgical extirpation of cysts is reserved only for cases of therapeutic failure with cysticidal drugs (Del Brutto, 1993; Del Brutto and Sotelo, 1990).

A novel schedule for praziquantel therapy has reduced the treatment to a single day, with results similar to those obtained with the 2 week treatment schedule (Corona *et al.*, 1996; Sotelo, 1997). In the 'single-day' schedule, praziquantel therapy is administered in a total dose of 75 mg/kg, divided into three administrations of 25 mg/kg

each at 2 hour intervals (e.g. at 7, 9 and 11 a.m.). Five hours later (e.g. at 4 p.m.) 20 mg of dexamethasone i.m. are administered; the same dose of dexamethasone is repeated the next 2 days in the morning. With this schedule, a plateau of about 6 hours of high plasma concentrations of praziquantel is obtained, exposing the parasites to a longer and continuous period of cysticidal concentration of the drug (Jung *et al*., 1997; Sotelo and Jung, 1998). In contrast with earlier schedules, in which the drug is administered every 8 hours, achieving very brief periods of high praziquantel concentrations, whose half-life in plasma is less than 3 hours, the 'single-day' schedule of praziquantel produces the same cysticidal effects (destruction of about 70% of parenchymal cysticerci) with the advantage of administering less than 10% the total dose, significantly diminishing the time of treatment and the cost of the drug. Dexamethasone is administered 5 hours later, at the time when most of the praziquantel has been cleared from the blood and its cysticidal action has already taken place. In this way, the treatment against the parasite and the inflammation that follows its destruction are given sequentially, without pharmacological interference between the two drugs.

Albendazole is also given in a brief course, in this case during 8 days, in doses of 15 mg/kg/day divided into two doses, every 12 hours (Sotelo and Jung, 1998; Cruz *et al*., 1995). With this schedule, around 80% of parenchymal and subarachnoid cysts are destroyed. Albendazole is also effective in ocular and ventricular cysticercosis (Santos *et al*., 1984; Lozano-Elizondo and Barbosa-Horta, 1990; Del Brutto *et al*., 1992b). As no pharmacological interference between albendazole and dexamethasone exists (Takayanagui *et al*., 1997), during the first 4 days of therapy 10–20 mg of i.m. dexamethasone are given to prevent reactions secondary to acute inflammation triggered by the sudden destruction of parasites (Sotelo and Jung, 1998).

In cases of meningeal cysticercosis with intense inflammation, diagnosed by CSF analysis, chronic administration of steroids must be contemplated. A useful schedule is 50 mg prednisone in the morning, three times a week (e.g. Monday, Wednesday and Friday) for long periods (up to years). The continuation of therapy must be decided on the basis of sequential analysis of CSF (Suastegui-Roman *et al*., 1996).

PREVENTION

Several measures can be taken to interfere with the life-cycle of taeniasis/cysticercosis. The most important and affordable is public education on the life-cycle of the parasite to implement simple measures aimed at preventing infection, such as proper disposal of human feces whenever feasible, the routine freezing of pork, proper cooking of pork at $> 70^{\circ}C$, identification and treatment of taenia carriers, confinement of pigs, and preventing irrigation of vegetables with water contaminated with human feces. Porcine vaccination with recombinant *Taenia* antigens seems a technological possibility in the near future (Sciutto *et al*., 1990), a measure designed to reduce cysticercosis in pigs in endemic areas and interruption of the life-cycle.

Tapeworm infections can be prevented by eating only well-cooked pork or beef, and avoiding the ingestion of uncooked sausages. Education of residents in small communities in which domestic animals are slaughtered by the owners without the benefit of meat inspection should be attempted, by explaining the necessity of cooking meat properly in order to kill viable larvae, which are the source of tapeworms. Domestic animals, in this case pigs and cows, should be kept away from human excrement, particularly pigs. Systematic treatment of tapeworm carriers should be encouraged, especially since treatment is inexpensive and innocuous.

HYMENOLEPIS NANA

LIFE-CYCLE (FIGURE 23.16)

H. nana belongs to the Family Hymenolepididae, originally described in rodents and discovered in humans by Theodor Bilharz in 1851, in an autopsy carried out on a child in Egypt. It is the only human tapeworm capable of completing the parasite cycle in one host. The scolex has four

suckers and an armed rostellum with 8–30 hooks. The adult worm is 2–3 cm, its length being proportional to the number of individual worms present in the small intestine. The scolices attach to the upper third of the duodenum and the gravid proglottids rupture into the lumen, releasing the embryonated eggs (40–50 µm in diameter), which hatch in the intestinal lumen and lodge between the intestinal villi, where they develop into cysticercoids. The cysticercoids mature to adult worms in 15–20 days, when they began to release infective eggs.

EPIDEMIOLOGY

Hymenolepiosis is also a disease of populations living under conditions of poor hygiene and poverty. It is prevalent in school children in tropical and subtropical climates. The disease is acquired by ingestion of water and food contaminated with mouse feces, and can also be transmitted from one child to another by passing infective eggs on dirty hands.

H. nana infections induce humoral and cellular immunity, which probably accounts for the

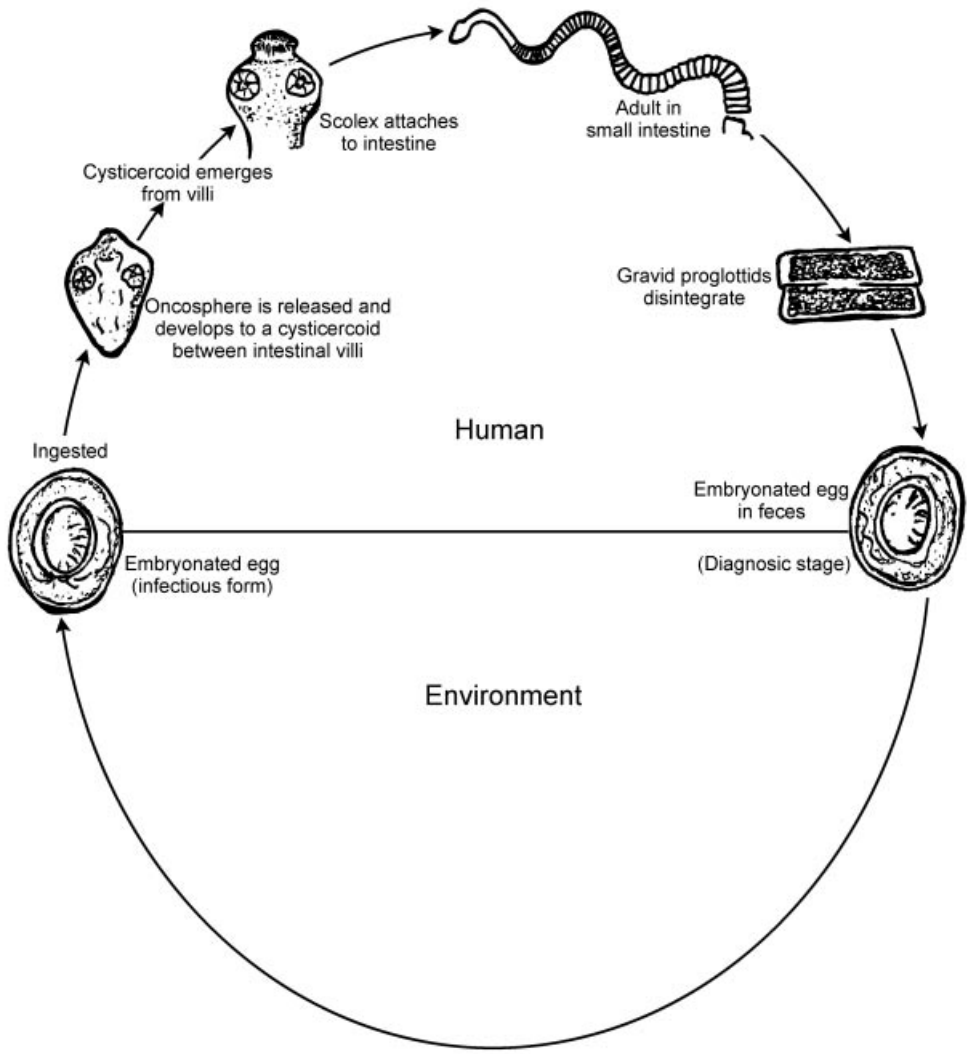

Fig. 23.16 Life-cycle of *Hymenolepis nana*

lower prevalence of this parasitosis observed in adults living in endemic communities. Experimental evidence has demonstrated that IgE and mast cells are involved in the expulsion of adult worms from the intestine (Watanabe *et al.*, 1994).

CLINICAL MANIFESTATIONS

Hymenolepis infections are found mainly in children under 8 years of age (Mason and Patterson, 1994). It is estimated that the majority of infections are asymptomatic and are probably associated with a low number of parasites. Symptoms are vague abdominal distress in light infections, but this can be accompanied by abdominal pain, nausea, vomiting, weight loss, diarrhea and irritability in multiple infections.

DIAGNOSIS

The diagnosis can be made on coprologic analysis of serial stool samples, by identification of the eggs, which are ovoid and do not have a striated outer embryophore, as they are not covered by a protective keratin shell. The adult worms may also be found in multiple infections, and can be identified by their length and armed rostellum.

TREATMENT

Praziquantel at a dose of 25 mg/kg has been reported to cure 95% of infections. In countries where niclosamide is available, a dose of 2 g daily for 5 consecutive days is recommended.

DIPHYLLOBOTHRIUM LATUM (BROAD FISH TAPEWORM)

LIFE-CYCLE (FIGURE 23.17)

In contrast to the taeniid tapeworms, Diphyllobothridae require two intermediate hosts to complete their life-cycle and have a free-living stage in freshwater. The scolex of *D. latum* is conformed by bothria and the worms can be very long (6–9 m), with 3000–4000 proglottids, which tend to be wider than long. A single worm can shed 1 million eggs per day. The eggs are not completely mature when released from the proglottids and, when deposited in freshwater bodies, take up to 12 days to mature. The egg hatches the embryo, which is released into the water as the coracidium, a free-swimming form which can be ingested by a small crustacean (copepod), where it develops into a procercoid larva measuring up to 600 µm long. When the copepod is ingested by a fish, the larvae dislodge and penetrate the intestinal wall of the fish, from whence they eventually lodge in muscle masses or viscera to become plerocercoid larvae. Plerocercoids measure 1–5 cm and may remain viable for the lifetime of the fish. The life-cycle is completed when a human ingests raw or undercooked infected freshwater fish. Other definitive hosts are dogs, cats, pigs, wolves, foxes and bears. The worms attach to the small intestine and may survive for many years (Von Bonsdorff and Bylund, 1982).

CLINICAL MANIFESTATIONS

Symptoms include abdominal pain, weight loss and a unique form of pernicious anemia, a consequence of the worms' capacity for taking up vitamin B_{12} in the small intestine.

EPIDEMIOLOGY

D. latum is found in various terrestrial and marine fish-eating carnivores. The adult worm also parasitizes humans. It has been reported in geographic areas with fresh-water lakes in the subarctic and Eurasia, in the Siberian rivers Ob and Yenisei and in the Baltic Sea. A high prevalence has been observed in the Volga basin and Finland, the lake district of Italy and

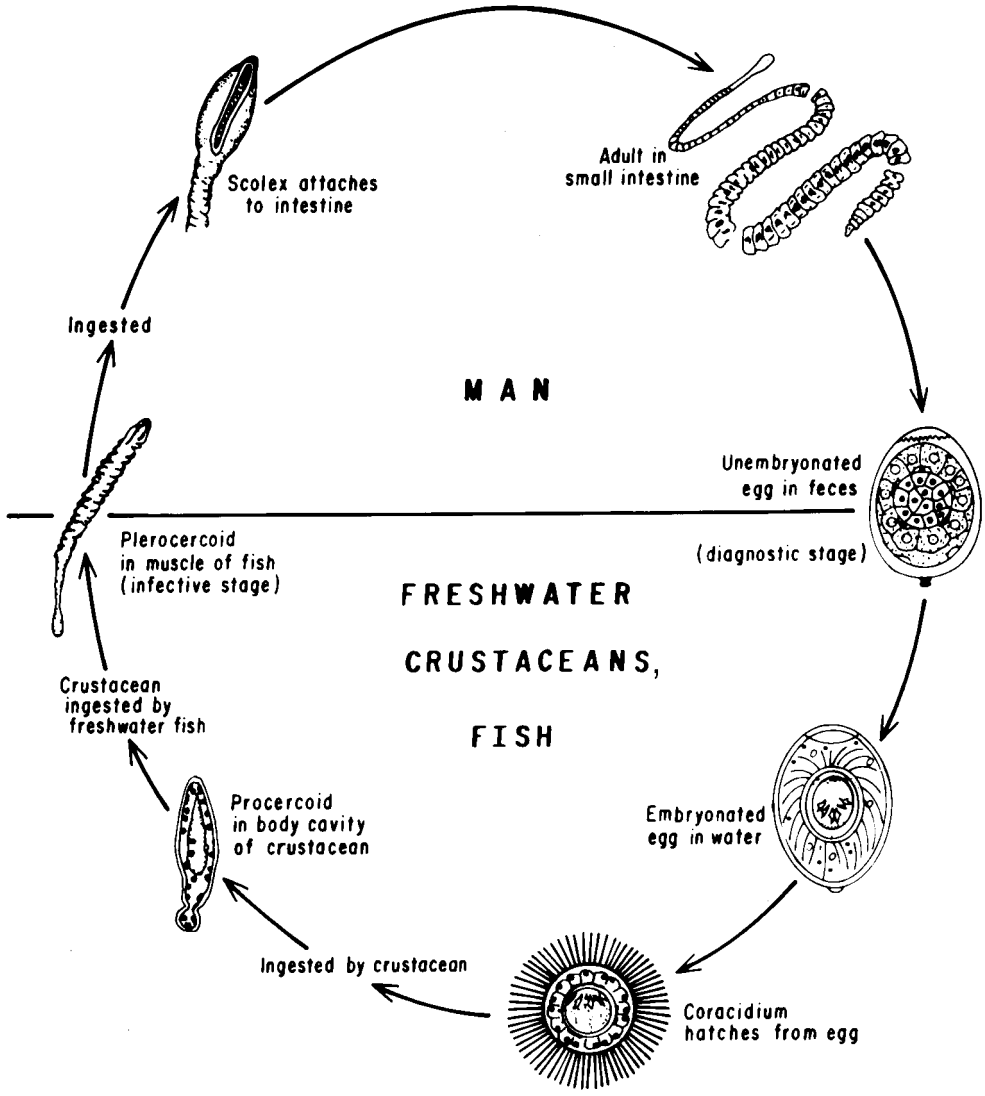

Fig. 23.17 Life-cycle of *Diphyllobothrium latum*

Switzerland. Immigration has transported the disease to North and South America. It has been reported in a number of fish species: pike, perch, ruff, rainbow trout and turbot in Chile, and whitefish and salmon in the USA.

DIAGNOSIS

The parasitosis should be suspected in persons with a history of eating raw or undercooked fish, by identification of proglottids and oval-shaped eggs with a characteristic operculum.

TREATMENT

The administration of 5–10 mg/kg praziquantel in a single dose has been shown to be effective.

PREVENTION

This tapeworm infection can be avoided by not ingesting raw or undercooked fish in known endemic areas. Direct drainage of sewage into freshwater lakes should be avoided.

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REFERENCES

Allan JC, Mencos F, Garcia Noval J *et al*. (1993). Dipstick dot ELISA for the detection of *Taenia* coproantigens in humans. *Parasitology* **107**: 79–85.

Allan JC, Velazquez M, Garcia Noval J *et al*. (1996). Epidemiology of intestinal taeniasis in four rural Guatemalan communities. *Am Trop Med Parasitol* **90** (2): 157–65.

Anderson RM, May RM (1982). Population dynamics of human helminth infections: control by chemotheraphy. *Nature* **297**: 557–63.

Bao ME, Bogh HO, Kassuku AA *et al*. (1995). The prevalence of *Taenia solium* metacestodes in pigs in northern Tanzania. *J Helminthol* **69** (2): 113–17.

Bittencourt PRM, Gracia CM, Gorz AM *et al*. (1990). High-dose praziquantel for neurocysticercosis: serum and CSF concentrations. *Acta Neurol Scand* **82**: 28–33.

Botero D, Uribe CS, Sanchez JL *et al*. (1993). Short course albendazole treatment for neurocysticercosis in Columbia. *Trans R Soc Trop Med Hyg* **87**: 576–7.

Bowles J, McManus DP (1994). Genetic characterization of the Asian *Taenia* a newly described taeniid cestode of humans. *Am J Trop Med Hyg* **50**: 33.

Bruce-Conn D (1993). Ultrastructure of the gravid uterus of *Hymenolepis diminuta* (Platyhelminthes: Cestoda). *J Parasitol* **79** (4): 583–90.

Chandy MJ, Rajshekhar V, Prakash S *et al*. (1989). Cysticercosis causing single, small CT lesions in Indian patients with seizures. *Lancet* **8634**: 390–1.

Chang KH, Kim WS, Cho SY *et al*. (1988). Comparative evaluation of brain CT and ELISA in the diagnosis of neurocysticercosis. *Am J Neurol Res* **8**: 125–30.

Chapman A, Vallejo V, Mossie KG *et al*. (1995). Isolation and characterization of species-specific DNA probes from *Taenia solium* and *Taenia saginata* and their use in an egg detection assay. *Clin Microbiol* **33**: 1283.

Colli BO, Martelli N, Assirati JA *et al*. (1986). Results of surgical treatment of neurocysticercosis in 69 cases. *J Neurosurg* **65**: 309–15.

Corona T, Lugo R, Medina R *et al*. (1996). Single-day praziquantel therapy for neurocysticercosis. *N Engl J Med* **334**: 125.

Corona T, Pascoe D, González-Barranco D *et al*. (1986). Anticysticercus antibodies in serum and cerebrospinal fluid in patients with cerebral cysticercosis. *J Neurol Neurosurg Psychiat* **49**: 1044–9.

Corral I, Quereda C, Moreno A *et al*. (1996). Intramedullary cysticercosis cured with drug treatment. *Spine* **21**: 2284–7.

Cruz I, Cruz ME, Carrasco F, Horton J (1995). Neurocysticercosis: optimal dose treatment with albendazole. *J Neurol Sci* **133**: 152–4.

Dada EO, Adeiyongo CM (1993). Observations on the epidemiology of human taeniasis amongst the Goemi tribe of northern Nigeria. *Appl Parasitol* **34** (4): 251–7.

Del Brutto OH, Santibañez R, Noboa CA *et al*. (1992). Epilepsy due to neurocysticercosis: analysis of 203 patients. *Neurology* **42**: 389–92.

Del Brutto OH (1992). Cysticercosis and cerebrovascular disease: a review. *J Neurol Neurosurg Psychiat* **55**: 252–4.

Del Brutto OH (1993). The use of albendazole in patients with single lesions enhanced on contrast CT. *N Engl J Med* **328**: 356–7.

Del Brutto OH, García E, Talamás O *et al*. (1988). Sex-related severity of inflammation in parenchymal brain cysticercosis. *Arch Intern Med* **148**: 544–6.

Del Brutto OH, Sotelo J (1990). Albendazole therapy for subarachnoid and ventricular cysticercosis. Case report. *J Neurosurg* **72**: 816–17.

Del Brutto OH, Sotelo J, Aguirre R *et al*. (1992b). Albendazole therapy for giant subarachnoid cysticerci. *Arch Neurol* **49**: 535–8.

Díaz-Camacho S, Candil Ruiz A, Uribe-Beltrán M *et al*. (1991). Epidemiological study and control of *Taenia solium*: infections with praziquantel in a rural village of Mexico. *Am J Trop Med Hyg* **45** (4): 522–31.

Díaz F, García HH, Gilman RH *et al*. (1992). Epidemiology of taeniasis and cysticercosis in a Peruvian village. The Cysticercosis Working Group in Peru. *Am J Epidemiol* **135** (8): 875–82.

Dixon H, Lipscomb F (1961). *Cysticercosis: An Analysis and Follow-up of 450 Cases*. Medical Resource Council Special Report No. 299. London: HMSO.

Earnest MP, Reller LB, Filley CM *et al*. (1987). Neurocysticercosis in the United States: 35 cases and a review. *Rev Infect Dis* **9**: 961–79.

Eom KS, Rim HJ (1993) Morphologic descriptions of *Taenia asiatica* sp. *Korean J Parasitol* **31**: 1.

Estañol B, Corona T, Abad P (1986). A prognostic classification of cerebral cysticercosis: therapeutic implications. *J Neurol Neurosurg Psychiatr* **49**: 1131–4.

Estañol B, Kleriga E, Loyo M *et al*. (1983). Mechanisms of hydrocephalus in cerebral cysticercosis: implications for therapy. *Neurosurgery* **13**: 119–23.

Fan PC, Chung WC, Lin CY *et al*. (1992). Clinical manifestations of taeniasis in Taiwan aborigenes. *J Helminthol* **66**: 118.

Faust EC, Antoni JS, Odom V *et al*. (1938). A critical study of clinical laboratory techniques for the diagnosis of protozoan, cyst and helminth eggs in faeces. *Am J Trop Med Hyg* **18**: 169.

Garcia HH, Gilman RH, Tovar MA *et al*. (1995). Factors associated with *Taenia solium*: cysticercosis: analysis of 946 Peruvian neurologic patients. Cysticercosis Working Group in Peru (CWG). *Am J Trop Med Hyg* **52** (2): 145–8.

Gemmel MM, Matyas Z, Pawlowski Z *et al*. (eds) (1983). *Guidelines for the Surveillance, Prevention, and Control of Taeniasis/Cysticercosis*. World Health Organization: Geneva.

Graham CF (1941). A device for the diagnosis of *Enterobius* infection. *Am J Trop Med Hyg* **21**: 159.

Grisolia JS, Wiederholt WC (1982). CNS cysticercosis. *Arch Neurol* **39**: 540–4.

Groll E (1980). Praziquantel for cestode infections in man. *Acta Trop* **37**: 293.

Jung H, Medina R, Castro N *et al*. (1997). Pharmacokinetic study of praziquantel administered alone and in combination with cimetidine in a single-day therapeutic regimen. *Antimicrob Agents Chemother* **41**: 1256–9.

Keane JR (1982). Neuro-ophthalmologic signs and symptoms of cysticercosis. *Arch Ophthalmol* **100**: 1445–8.

Kruger-Leite E, Jalkh AE, Quiroz H *et al*. (1985). Intraocular cysticercosis. *Am J Ophthalmol* **99**: 252–7.

Küchenmeister F (1855). Offenes Sendschreiben an die k.k. Gesellschaft der Aerzte zu Wien. Experimentelles Nachweisen dass *Cysticercus cellulosae* inerhalb des menschlichen Darmkanales in *Taenia solium* umwandelt. *Wien Med Wochenschr* **5**: 1–4.

Larralde C, Padilla A, Hernandez M *et al*. (1992). Seroepidemiology of cysticercosis in Mexico. *Salud Pub Mexico* **34**: 197–210.

Lobato RD, Lamas E, Portillo JM (1981). Hydrocephalus in cerebral cysticercosis. Pathogenic and therapeutic considerations. *J Neurosurg* **55**: 786–93.

López-Hernández A, Garaizar C (1982). Childhood cerebral cysticercosis: clinical features and computed tomographic findings in 89 Mexican children. *Can J Neurol Sci* **9**: 401–7.

Lozano-Elizondo D, Barbosa-Horta, S. (1990). Tratamiento con albendazol de la cisticercosis intraocular. *Rev Mex Oftalmolol* **64**: 15–28.

Lumsden R, Voge M, Sogandares-Bernal F (1982). The metacestode tegument: fine structure, development, topochemistry and interactions with the host. In Flisser A, Beltran F, Larralde C *et al*. (eds), *Cysticercosis: Present State of Knowledge and Perspectives*. Academic Press: New York; 307–61.

Martinez HR, Rangel-Guerra R, Arredondo-Estrada JH *et al*. (1995). Medical and surgical treatment in neurocysticercosis a magnetic resonance study of 161 cases. *J Neurol Sci* **130**: 25–34.

Martinez HR, Rangel-Guerra R, Elizondo G *et al*. (1989). MR imaging of neurocysticercosis: a study of 56 cases. *Am J Neurol Res* **10**: 1011–19.

Mason PR, Patterson BA (1994). Epidemiology of *Hymenolepis nana* infections in primary school children in urban and rural communities in Zimbawe. *J of Parasitol* **80** (2): 245–50.

Medina MT, Rosas E, Rubio F *et al*. (1990). Neurocysticercosis as the main cause of late-onset epilepsy in Mexico. *Arch Intern Med* **150**: 325–7.

Merchant MT, Aguilar L, Avila G *et al*. (1998). *Taenia solium*: description of the intestinal implantation sites in experimental hamster infections. *J Parasitol* **84** (4): 681–5.

Miller BL, Staugaitis SM, Tourtellotte WW *et al*. (1985). Intra-blood–brain barrier IgG synthesis in cerebral cysticercosis. *Arch Neurol* **42**: 782–4.

Mobius G (1993). Epidemiologic studies of *C. bovis* and *T. saginata* infections in eastern and western Germany. *Deutsche Tierärztl Wochenschr* **100** (3): 110–14.

Monteiro L, Almeida-Pinto J, Stocker A *et al*. (1993). Active neurocysticercosis, parenchymal and extraparenchymal: a study of 38 patients. *J Neurol* **241**: 15–21.

Monteiro L, Martins da Silva A, Nunes B *et al*. (1991). Epilepsy in neurocysticercosis: electroclinical aspects in 138 patients. *Epilepsia* **32**: 104.

Monteiro L, Nunes B, Mendoca D *et al*. (1995). Spectrum of epilepsy in neurocysticercosis: a long-term follow-up of 143 patients. *Acta Neurol Scand* **92**: 33–40.

Nieto D (1982). Historical notes on cysticercosis. In Flisser A, Beltran F, Larralde C *et al*. (eds), *Cysticercosis, Present State of Knowledge and Perspectives*. Academic Press: New York; 1–7.

Pawlowski ZS (1989). Efficiency of low doses of praziquantel in taeniasis. *Acta Trop* **48**: 83.

Pawlowski ZS (1982). Epidemiology of *Taenia saginata* infection. In Flisser A, Beltran F, Larralde C *et al*. (eds), *Cysticercosis: Present State of Knowledge and Perspectives*. Academic Press: New York; 69–85

Pitella JEH (1997). Neurocysticercosis. *Brain Pathol* **7**: 681–93.

Rajshekhar V (1991). Etiology and management of single small CT lesions in patients with seizures: Understanding a controversy. *Acta Neurol Scand* **84**: 465–70.

Rajshekhar V (1993). Albendazole therapy for persistent, solitary cysticercus granulomas in patients with seizures. *Neurology* **43**: 1238–40.

Ramos-Kuri M, Montoya RM, Padilla A *et al*. (1992). Immunodiagnosis of neurocysticercosis: disappointing performance of serology (enzyme-linked immunosorbent assay) in an unbiased sample of neurological patients. *Arch Neurol* **49**: 633–6.

Rangel R, Torres B, Del Brutto OH *et al*. (1987). Cysticercotic encephalitis: a severe form in young females. *Am J Trop Med Hyg* **36**: 387–92.

Ritchie LS (1948). An ether sedimentation technique for routine stool examinations. *Bull US Army Dept* **8**: 326.

Robles C, Sedano AN, Vargas-Tentori N *et al*. (1987). Long-term results of praziquantel therapy in neurocysticercosis. *J Neurosurg* **66**: 359–63.

Robles C (1982). Resultados tardíos en el tratamiento de la cisticercosis cerebral por praziquantel. *Salud Públ Méx* **24**: 625–7.

Salgado P, Rojas R, Sotelo J (1997). Cysticercosis: clinical classification based on imaging studies. *Arch Intern Med* **157**: 1991–7.

Sanchez AL, Gomez O, Allebecj P *et al*. (1997). Epidemiologic study of *Taenia solium* infection in a Rural Village in Honduras. *Ann Trop Med Parasitol* **91** (2): 163–171.

Santos R, Chavarría M, Aguirre AE (1984). Failure of medical treatment in two cases of intraocular cysticercosis. *Am J Ophthalmol* **97**: 249–50.

Sarti E, Schantz PM, Plancarte A *et al*. (1994). Epidemiological investigation of *Taenia solium* taeniasis and cysticercosis in a rural village of Michoacan state, Mexico. *Trans R Soc Trop Med Hyg* **88** (1): 49–52.

Sarti E, Schantz PM, Plancarte A *et al*. (1992). Prevalence and risk factors of *Taenia solium* taeniasis and cysticercosis in humans and pigs in a village in Morelos, Mexico. *Am J Trop Med Hyg* **46**: 677–85.

Schantz PM, Moore AC, Muñoz JL *et al*. (1992). Neurocysticercosis in an Orthodox Jewish community in New York City. *N Engl J Med* **327**: 692–5.

Schmidt GD (1986). *Handbook of Tapeworm Identification. Key to the General Taeniidae*. CRC Press: Boca Raton, FL; 221–7.

Sciutto E, Fragoso G, Trueba L *et al*. (1990). Cysticercosis vaccine: cross protecting immunity with *T. solium* antigens against experimental murine *T. crassiceps* cysticercosis. *Parasite Immunol* **12**: 687–96.

Simac C, Michel P, Andriantsimahavandy A *et al*. (1995). Use of enzyme-linked immunosorbent assay and enzyme-linked immunoelectrotransfer blot for the diagnosis and monitoring of neurocysticercosis. *Parasitol Res* **81**: 132–6.

Sotelo J, Jung H (1998). Pharmacokinetic optimization of the treatment of neurocysticercosis. *Clin Pharmacokinet* **34** (6): 503–15.

Sotelo J, Flisser A (1997). Neurocysticercosis: practical treatment guidelines. *CNS Drugs* **7**: 17–25.

Sotelo J, Del Brutto OH, Penagos P *et al*. (1990). Comparison of therapeutic regimen of anticysticercal drugs for parenchymal brain cysticercosis. *J Neurol* **237**: 69–72.

Sotelo J, Marín C (1987). Hydrocephalus secondary to cysticercotic arachnoiditis. A long-term follow-up review of 92 cases. *J Neurosurg* **66**: 686–9.

Sotelo J (1997). Treatment of brain cysticercosis. *Surg Neurol* **48**: 110–12.

Suastegui-Roman RA, Soto-Hernández JL, Sotelo J (1996). Effects of prednisone on ventriculoperitoneal shunt function in hydrocephalus secondary to cysticercosis: a preliminary study. *J Neurosurg* **84**: 629–33.

Takayanagui OM, Lanchote VL, Marques MPC (1997). Therapy for neurocysticercosis: pharmacokinetic interaction of albendazole sulfoxide with dexamethasone. *Therapeut Drug Monitor* **19**: 51–5.

Takayanagui OM, Jardim E (1992). Therapy for neurocysticercosis. Comparison between albendazole and praziquantel. *Arch Neurol* **49**: 290–4.

Vázquez V, Sotelo J (1992). The course of seizures after treatment for cerebral cysticercosis. *N Engl J Med* **327**: 696–701.

Verster A (1971). Preliminary report on the golden hamster as a definitive host of *Taenia solium* Linnaeus 1758 and *Taenia saginata* Goeze 1792. *Onderstepoort J Vet Res* **38** (1): 63–4.

Von Bonsdorff B, Bylund G (1992). The ecology of *Diphyllobothrium latum*. *Ecology Dis* **1**: 21.

Wadia N, Desai S, Bhatt M (1988). Disseminated cysticercosis. New observations, including CT scan findings and experience with treatment by praziquantel. *Brain* **111**: 597–614.

Watanabe N, Nawa Y, Okamoto K *et al*. (1994). Expulsion of *Hymenolepis nana* from mice with congenital deficiencies of IgE production or of mast cell development. *Parasite Immunol* **16**: 137.

Willms K (1998). Cestodes (tapeworms). In Gorbach SL, Bartlett JG, Blacklow NR (eds), *Infectious Diseases*, 2nd edn. WB Saunders: Philadelphia; 2481–99.