

# Chapter 7

## Taeniasis and Neurocysticercosis: Emerging Public Health Problems



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**Abstract** *Taenia*, one of the earliest recognized helminths, is a comparatively large genus with 42 known valid species. Three most commonly recognized species of human importance are *T. solium* and *T. asiatica* (pork tapeworms) and *T. saginata* (beef tapeworm). Adult tapeworms reside in human intestine, and the disease is called taeniasis. The larva (cysticercus) of only *T. solium* can infect internal organs of human, known as cysticercosis; when the larva infects the central nervous system (CNS) of the host, it is known as neurocysticercosis (NCC). NCC is the most severe form of the disease with considerable morbidity and mortality. It is considered as the most common cause of community-acquired epileptic seizure disorders. The life cycle of *T. solium* involves two hosts: humans are the only definitive host and accidental intermediate host, while pig is the natural intermediate host. The eggs passed through faeces by *T. solium* carriers contaminate the environment. Both human and pig can get infection (cysticercosis/NCC) through ingestion of eggs, while human acquires taeniasis through consumption of cysticercotic pork. *T. solium* infection is highly endemic in Africa, Asia and Latin America. Now developed world is also facing this problem due to human migration from *Taenia* endemic areas. Therapeutic measures for NCC-related active epilepsy include anti-epileptic drug(s) with or without steroids: surgery/placement of shunt is indicated for patients with raised intracranial pressure. Antiparasitic drug to kill the brain cysticerci remains controversial. Treatment of choice for taeniasis is niclosamide; alternatives are praziquantel and albendazole. The following measures such as antiparasitic therapy to eliminate *Taenia* carriers in endemic populations, health education, toilet facilities and handwash with soap, control on sale of measly pork, restriction on pig roaming and pig vaccination, etc. may help to control the disease.

**Keywords** Albendazole · Cysticercosis · Neurocysticercosis · Praziquantel · Taeniasis · Vaccination

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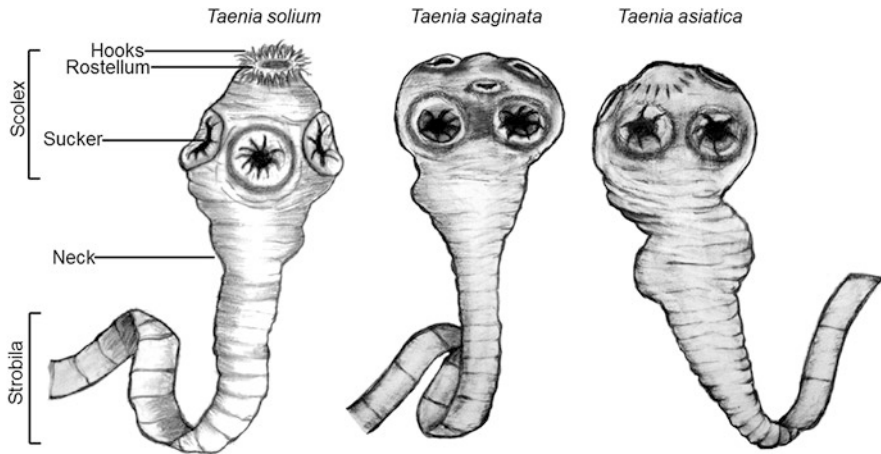
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## 7.1 Introduction

*Taenia* species are among the earliest recognized helminths. Life history and ecology of *Taenia* species are well studied and drawn considerable attention among the eucestodes. *Taenia* is a comparatively large genus with 42 known valid species and 3 subspecies (Hoberg 2006). Morphologically, they are ribbon-like structure with series of well-defined segments known as proglottids and therefore the name *Taenia* (Greek ταινία meaning ribbon/strip). The most common species infecting humans are the pork tapeworm *T. solium* and *T. asiatica* and the beef tapeworm *T. saginata*. Infection with adult tapeworms of *T. solium*, *T. asiatica* or *T. saginata* leads to taeniasis in humans. Among all the species of *Taenia*, the larval form (cysticercus) of only *T. solium* can infect internal organs of human, and the disease is called cysticercosis. When the larva of *T. solium* is lodged in the brain, it is known as neurocysticercosis (NCC). NCC is considered as the severe form of the disease with considerable morbidity and mortality. The life cycle of *T. solium* involves two hosts; viz. human (definitive host) and pig (intermediate host). Human harbours the adult tapeworm, which produces thousands of eggs for years. These eggs are excreted through faeces and disseminated in the environment. When free-roaming pigs ingest egg-loaded human faeces, the hexacanth embryos are liberated from the eggs, which penetrate the mucosal layer of the intestinal wall and enter into the blood circulation and subsequently develop into cysticerci (larval forms) in different internal organs, especially in the muscles of pigs. Human can also develop cysticercosis/NCC through consumption of food (raw vegetables and salads, etc.) and water contaminated by *T. solium* eggs. When human eats undercooked cysticercotic pork, the larva (cysticercus) develops into an adult worm in human intestine, and the disease is called taeniasis. In brief, both human and swine can get cysticercosis/NCC by ingestion of *T. solium* eggs excreted by the adult worm carriers. Clinical features of NCC may vary from mild form with little or no symptoms to life-threatening medical emergency. *T. solium* infection is cosmopolitan but highly endemic in African, Asian and Latin American countries where open-field defaecation practice is common and pigs roam freely with easy access to human faeces, and humans consume undercooked pig meat and hygienic standards are poor.

## 7.2 Morphology/Structure

The body of a classical adult eucestode is divided into three distinct parts, namely, scolex, neck and strobila. The scolex, responsible for attachment to the host tissue, is present at the anterior end. The size and morphological features of scolex are used to identify the worms. The neck is present immediately posterior to the scolex. It is the narrowest unsegmented and poorly differentiated region. New segments or proglottids differentiate from the neck region, and they push the older segments gradually posterior forming a chain of proglottids called strobila, which is the last part of



**Fig. 7.1** Diagrammatic representation of the comparative morphological features of adult tapeworms, *Taenia solium*, *T. saginata* and *T. asiatica*

the adult parasite. As each proglottid moves posteriorly, its reproductive system starts maturing progressively. Therefore, the posterior most proglottids have the fully developed reproductive systems. The progressive maturity of the reproductive systems divides strobila into immature, mature and gravid proglottids (filled with egg) with often atrophied reproductive organs.

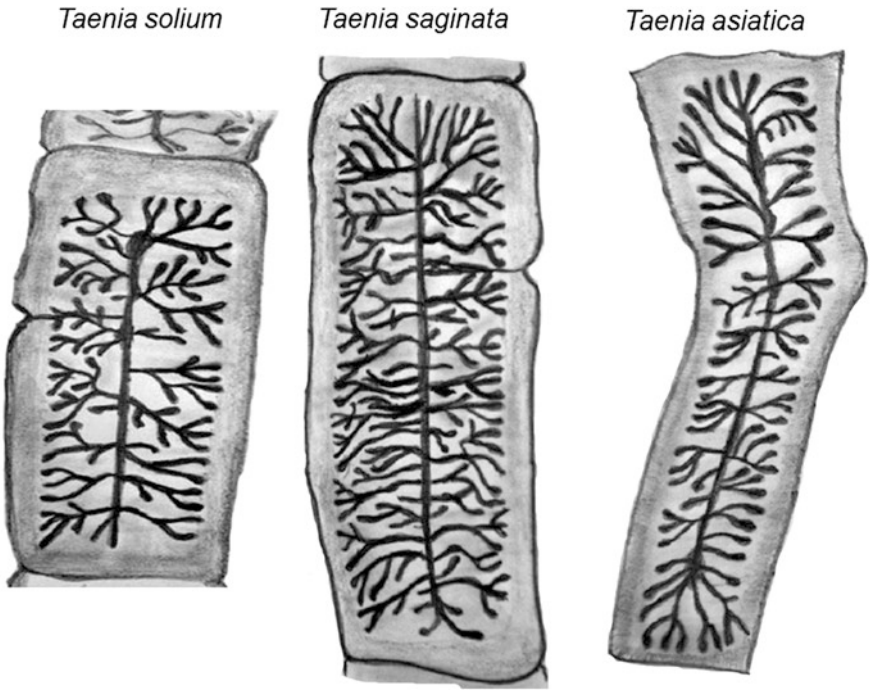
Three species of the *Taenia* genus, *T. solium*, *T. saginata* and *T. asiatica*, can cause taeniasis (intestinal infection) in humans. However, only the first two species have been considered for centuries except *T. asiatica* that remained undiscovered till recently. These tapeworms are flat and opaque white or yellowish with long segments measuring 1–12 m in the adult stage. An adult tapeworm has three segments: scolex, narrow neck and large strobila with hundreds of proglottids. The scolex is the organ for attachment with four suckers and a rostellum. Rostellum may be armed with hooks as in *T. solium*, or unarmed and sunken (*T. saginata*), or with rudimentary hooklets (*T. asiatica*) (Fig. 7.1) (Eom and Rim 1993; Flisser 1994). The scolex is a muscular structure with mesenchymal tissues that lodges the main part of the nervous system of the parasite and nephridial canals. Proximal segments are immature, followed by mature and gravid proglottids filled with eggs. Mature proglottids are hermaphrodites and contain thousands of testes. The female sexual organs have one lobulated ovary, connected to an oviduct. Gravid proglottids are full of  $50\text{--}60 \times 10^3$  fertile eggs. The egg-containing uterus develops 7–32 lateral branches; this feature allows identification of species. *T. solium* has 7–16 and *T. saginata* has 14–32 branches. The eggs are spherical and their size varies from 31 to 43  $\mu\text{m}$  in diameter. When eggs are excreted, most of them are fully embryonated and infective, while others may be at different stages of maturation. The main features of tapeworms and eggs are shown in Table 7.1 and Fig. 7.2 (Eom and Rim 1993; Flisser 2013; Galan-Puchades and Fuentes 2013).

**Table 7.1** Morphological differences among *Taenia solium*, *T. saginata* and *T. asiatica*

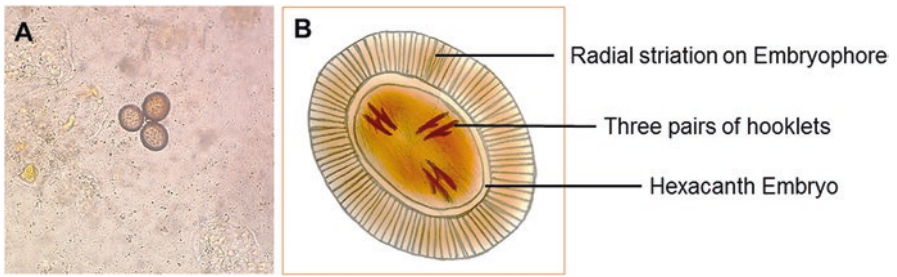
Morphological features	<i>T. solium</i>	<i>T. saginata</i>	<i>T. asiatica</i>
<b>Scolex</b>			
Shape	Globular	Quadrilateral	Quadrilateral
Rostellum	+	–	+
Number of hooks	22–32	–	–
Diameter (mm)	0.6–1.0	1.5–2.0	0.8
<b>Mature proglottid</b>			
Testis (number)	375–575	800–1200	324–1216
Ovary (number of lobes)	3	2	2
Vaginal sphincter	–	+	+
<b>Gravid proglottid</b>			
Uterine branches (each side number)	7–16	14–32	11–31
Pattern of uterine branching	Dendritic	Dichotomous	Dichotomous
Posterior protuberance	–	+	+
Size (length × width; mm)	3.1–10 × 3.8–8.7	10–20 × 6.5–9.5, longer than wide	4–22 × 3–12
<b>Adult tapeworm</b>			
Length (m)	1–5	4–12	1–8
Number of proglottids	700–1000	1000–1500	200–1200
<b>Cysticercus</b>			
Size (mm)	5–8 × 3–6	6–10 × 4–6	2 × 2
Hooks in scolex	+	–	Rudimentary

+ Present; – absent

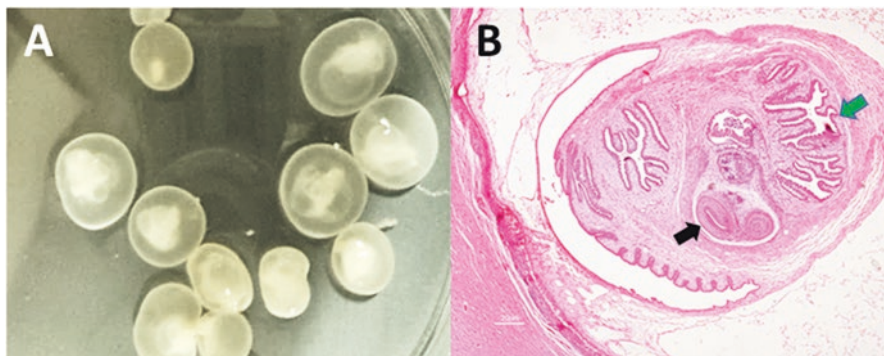
After 15–48 h of ingestion of eggs, hexacanth embryos (oncospheres) are liberated in the intestine of the host that pierce the intestine and enter into the blood circulation. When the embryos are lodged in the internal organs, they develop into the larval forms called cysticercus, which is a fluid-filled bladder-like structure with invaginated whitish scolex (de Aluja et al. 1998). When definitive host (human) consumes the viable cysticercus present in the muscles of intermediate host (pork/beef), bladder wall pore widens that allows the scolex and neck to evaginate, and the adult tapeworm develops (de Queiroz and Alkire 1998). The adult tapeworm resides in the small intestine of humans, the only definitive hosts. Stages of taeniid development are as follows: embryo inside the egg, circulating oncosphere or larva, post-oncosphere that is transformed into the cysticercus or metacystode in tissues (the post-larval or pre-adult stage) and the adult worm. Eggs and embryos are microscopic (Fig. 7.3), while cysticerci (Fig. 7.4) and adult worms are macroscopic (Fig. 7.1).



**Fig. 7.2** Differences in uterine branching pattern of *Taenia solium*, *T. saginata* and *T. asiatica* proglottids



**Fig. 7.3** Egg of *Taenia*: (a) as seen under microscope, (b) schematic diagram



**Fig. 7.4** (a) Cysticerci of *Taenia solium* obtained from pig muscles, (b) histologic section of *T. solium* cysticercus showing canalicular system (green arrow) and suckers (black arrows)

## 7.3 Biology/Life Cycle

### 7.3.1 *T. solium*

It is commonly known as pork tapeworm. Humans are the only definite host and harbour the adult tapeworm in their intestine. Both swine and human act as the intermediate hosts harbouring larvae in different internal organs (Fig. 7.5). The adult tapeworm residing in the small intestine of human produces thousands of eggs daily which are disseminated into the environment through faeces. The intermediate host (pig) ingests these eggs, which develop into cysticerci in different internal organs like muscles and brain. When human consumes cysticercotic pork, these cysts develop into adult worms residing the human intestine. The gravid proglottids start to separate from the distal end and are excreted in the faeces after 2 months of intestinal infection. Every day around four to five proglottids break off from the adult worm, and each segment has  $50\text{--}60 \times 10^3$  fertile eggs. The eggs are spherical ( $31\text{--}43 \mu\text{m}$  in diameter) with thick striated cover containing oncosphere. Both swine and man can ingest the eggs, and these eggs reach digestive tract and lose their coat due to action of the gastric acid and pancreatic enzymes resulting in release of hexacanth embryos or oncospheres. Oncospheres pierce the intestinal wall using their hooklets to reach the blood circulation and further reach the different organs such as subcutaneous tissue, skeletal muscles, central nervous system (CNS) and eyes. Now, the oncospheres drop their hooklets, take a vesicular shape and develop into cysticerci by gradual invagination of scolex, and it takes approximately 2 months to develop (Escobar and Nieto 1972). Its life cycle is completed when human consumes the undercooked measily pork. After reaching the small intestine, the scolex evaginates from the cysticerci and attaches itself to the mucosal wall and gradually evolves into the adult tapeworm. However, humans may also be infected with eggs



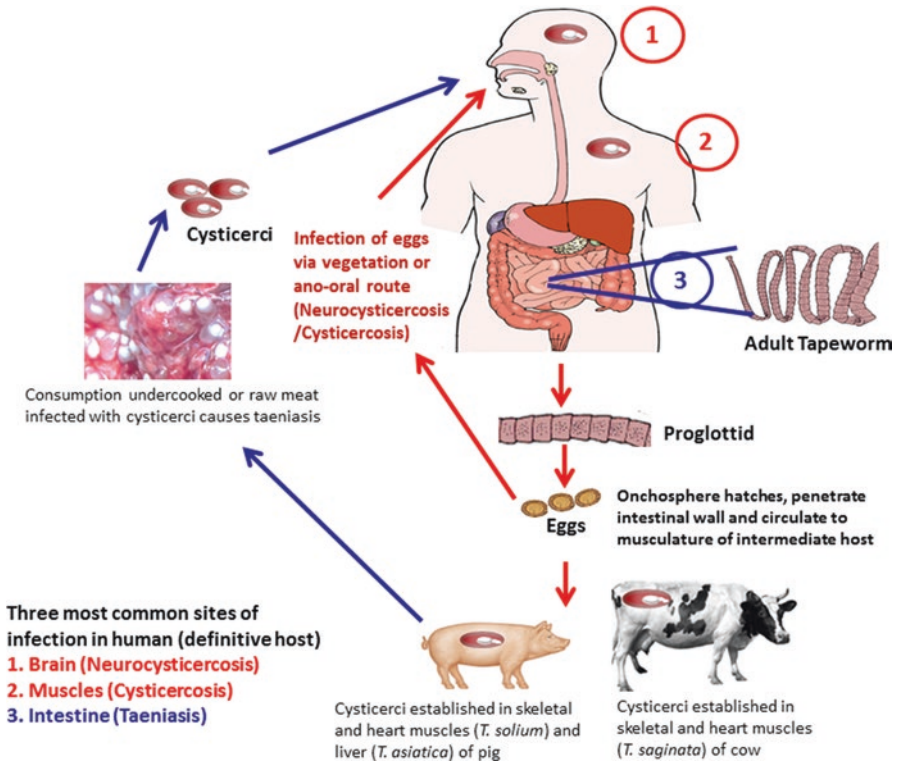


Fig. 7.5 Life cycles of three human *Taenia* tapeworms

in one of the following ways: (1) by hetero-infection through consumption of food/water contaminated with eggs of *Taenia*, (2) by exogenous autoinfection caused by ano-oral ingestion in *Taenia* carriers and (3) by endogenous autoinfection, in which the eggs present in the small intestine reach to the stomach due to reverse peristalsis. Hetero-infection is the most common route, while the last two modes of infection are very uncommon. The eggs of *Taenia* are sticky, and they may remain stuck to nail and nail beds of *Taenia* carriers if the hands are not properly washed with soap after defaecation. While handling such carriers can contaminate the food and disseminate the disease (cysticercosis/NCC).

In human, the parasite has a predilection to the brain and spinal cord, and when it gets lodged in these organs, it results in NCC. The larval stage also infects other tissues, especially those with pulsatile or contractile property and enriched in cholinergic innervations like skeletal muscle, diaphragm, heart, tissue and cavities subjected to contractile, rhythmic pulsatile movement by the internal organs like peritoneum, pleura and subcutaneous tissue (Del Brutto and Sotelo 1988).

Other animals have also been reported to harbour cysticerci of *T. solium*. An Indonesian study revealed that sera from 7 of 64 dogs were highly positive for

*T. solium* infection by ELISA and immunoblot. Subsequent examination of two such dogs showed *T. solium* cysticerci in their brain and heart muscle. Mitochondrial DNA analyses revealed that cysticerci from these dogs were similar with cysticerci obtained previously from swine and biopsies of local people (Ito et al. 2002). *T. solium* cysticercus had also been reported from the brain of a cat (Schwan et al. 2002).

### 7.3.2 *T. saginata*

Humans get infection through consumption of raw/undercooked beef infected with larvae of *T. saginata* (Fig. 7.5). The developmental stages of both *T. saginata* and *T. solium* are similar. After 3 months, *T. saginata* becomes sexually mature and produce gravid proglottids, which are expelled in faeces. Gravid proglottids may contain  $50\text{--}80 \times 10^3$  eggs, with different maturation stages. Eggs are only infective to cattle, the intermediate host; hence *T. saginata* does not cause cysticercosis in human. When ingested eggs by the intermediate host (cattle) come in contact with gastric and intestinal juices, the active embryos are liberated, which penetrate the intestinal wall and reach the blood circulatory system. Generally, oncospheres develop in to cysticercus in cardiac and skeletal muscles and seldom in fat and visceral organs, and become infective to human by 10 week time. Cysticerci may start degenerating within a few months after infection, and a substantial numbers of cysticerci are usually dead and calcified by about 9 months (Pawlowski and Murell 2000).

### 7.3.3 *T. asiatica*

*T. asiatica* was first reported in Taiwan and later on in many other Asian countries such as Indonesia, Korea, the Philippines, and Thailand (Eom et al. 1992). It has recently been reported from India (Singh et al. 2016). Morphologically, *T. asiatica* is related to *T. saginata*; it has scolex without hooklets, a large number of dichotomous pattern of uterine branches in gravid proglottids and a posterior protuberance (Table 7.1). *T. asiatica* cysticerci develop in visceral organs of pigs such as the liver, omentum, lungs and serosa; however, *T. saginata* cysticerci infect only muscles of cattle. In general, *T. asiatica* life cycle is similar to *T. solium*; specifically the adult stage develops in humans (Fig. 7.5; Eom et al. 1992). Taeniasis due to *T. asiatica* occurs in human after consumption of raw/undercooked meat or viscera of pigs infected with cysticerci. Cysticercosis in human due to *T. asiatica* has not been reported till date.



## 7.4 Epidemiology

The incidence of *T. solium* infection significantly varies according to sanitation, eating habits and pig husbandry practices in a region. However, it is hard to estimate the exact prevalence of *T. solium*-associated taeniasis, because eggs of different *Taenia* species are indistinguishable by microscopic method.

Cysticercosis is an under-reported disease because of involvement of different internal organs. However, NCC is considered the severe form of the disease, and epilepsy is the common clinical manifestation of parenchymal NCC. Extra-parenchymal location of the cysticerci in the brain leads to raised intracranial pressure and hydrocephalus. The World Health Organization estimates approximately 50,000 deaths every year due to NCC. Overall, NCC is identified as a cause of active epilepsy in 26.3–53.8% of seizure disorders in the developing world (Del Brutto et al. 2005; Montano et al. 2005; Prasad et al. 2009a, b). It is prevalent in Asian countries such as China, Cambodia, India, Indonesia, Mongolia, Myanmar, Nepal, Thailand and Vietnam. *T. solium* infection has been eradicated from Japan and South Korea. Seroprevalence studies in Asian countries (Vietnam, China, Korea and Indonesia) indicate high rates of exposure to the parasite ranging from 0.02% to 12.6% (Kong et al. 1993; Margono et al. 2001; Rajshekhar et al. 2003).

Reports have demonstrated a potentially high risk of *T. solium* infection for inhabitants of many Latin American countries with variable incidence rates suggesting an active transmission involving pig and human cycle in the region (Fleury et al. 2006; Garcia-Noval et al. 1996). Studies from Guatemala, Honduras, Peru and Mexico demonstrated NCC infection in rural populations between 9% and 18% (Flisser et al. 2003). A study from Mexico had shown that up to 50% of patients with evidence of NCC were neurologically and systematically asymptomatic (Chavarria et al. 2003). Swine cysticercosis is also often reported at meat inspection in the slaughterhouses of Latin America.

*T. solium* is an emerging and expanding zoonosis in African countries like Cameroon, Mozambique, Nigeria, South Africa, Tanzania, Zimbabwe, etc. Data from African countries show low incidence of human infection and a high prevalence in pig populations. This discrepancy may be due to lack of suitable surveillance, monitoring and reporting systems. Moreover, a high prevalence of pig cysticercosis (20–40%) is reported from East and Southern Africa (Phiri et al. 2002).

NCC is now becoming prevalent in developed countries because of increased human travel from endemic areas and migration of tapeworm carriers (Burneo et al. 2009; Schantz et al. 1992). Individuals who have never gone outside the USA as well as those who travel to disease-endemic regions are at risk acquiring infection. Hospital-based data analysis showed that up to 2% of admissions in neurosciences in southern California were due to NCC (McCormick 1985). The USA reports more than 1000 cases of NCC per year (Shandera et al. 1994).

Only few population-based data are available that provide evidence about the community burden, risk factors, and geographical distribution of cysticercosis in India. Studies from India reported that 28.4–48.3% cases of active epilepsy are due

to NCC by neuroimaging techniques such as CT and MRI (Prasad et al. 2009a, b; Rajshekhar et al. 2006). In Indian subcontinent, single cyst infection is more frequently reported, and its prevalence ranges from 47.7% to 53.4% of NCC cases (Prabhakaran et al. 2007).

## 7.5 Clinical Features

### 7.5.1 *Clinical Manifestations of Taeniasis*

Most people having taeniasis are either asymptomatic or have low to moderate symptoms. The most frequent complaint is passage of proglottids with slight discomfort. Other common symptoms are abdominal pain often colicky in nature (frequent in children), loss of appetite, nausea, constipation/diarrhoea, dizziness, headache, weakness, hyper-excitability, etc. These clinical symptoms may appear when the tapeworms become fully mature in human intestine, usually 6–8 weeks after ingestion of measly meat of swine (Ooi et al. 2013). Stomach pain and nausea are more frequent in the morning which is reduced after having small amounts of food. These symptoms are most common in children than adults and often lead to increased or decreased appetite. Infants may have diarrhoea, fever, irritability, vomiting and weight loss. The most severe complication of taeniasis is appendicitis.

### 7.5.2 *Clinical Manifestations of NCC*

The clinical manifestations of NCC vary with location, stage and number of *T. solium* cysticerci in the brain and immune response of the host to the parasite. It can affect the parenchyma, subarachnoid space or intraventricular systems within the CNS and rarely ocular and spinal region.

### 7.5.3 *Parenchymal NCC*

In parenchymal NCC, the most common clinical manifestation is seizure. It accounts up to 80% of patients (Ndimubanzi et al. 2010). Generalized tonic-clonic or simple partial seizure with motor symptomatology is mostly associated with NCC. However, some patients may have myoclonic, truncal or complex partial seizures (Sotelo et al. 1985). Presence of multiple degenerating parenchymal cysts with massive pericystic oedema may lead to cysticercotic encephalitis. The other most common clinical feature is headache (37% of NCC cases) followed by altered mental state (28% cases), neuro-focal deficits (16% cases), signs of increased intracranial pressure (12% cases) and cognitive decline (5% cases) (Carabin et al. 2011).

### **7.5.4 Subarachnoid NCC**

Hydrocephalus is the most common clinical presentation of subarachnoid NCC due to increased intracranial pressure followed by stroke in about 12% of cases (Marquez and Arauz 2012). A variety of stroke syndromes have been described in patients with NCC such as cerebral infarctions, intracranial haemorrhages and transient ischemic attacks. Other manifestations are acute meningitis and cranial nerve involvement.

### **7.5.5 Ventricular NCC**

The main clinical manifestation of intraventricular NCC is obstruction of cerebrospinal fluid (CSF) flow that leads to increased intracranial pressure leading to acute hydrocephalus. It usually happens when freely moving cysticerci reach the third ventricle from lateral ventricles or move up to cerebral aqueduct from fourth ventricle leading to blockage of CSF flow. It is an acute emergency and may need urgent shunt placement. Cysticerci present in the lateral ventricles may compress nearby tissues and are generally associated with focal neurological symptoms. Cysticerci present in the fourth ventricle may cause brainstem dysfunction because of compression of fourth ventricle floor (Madrazo et al. 1983; Sinha and Sharma 2012).

### **7.5.6 Spinal Cord NCC**

In NCC, spinal cord involvement is very rare (1–5%); however, introduction of MRI has significantly improved the diagnosis. Generally, cysts are single or clusters of multiple cysts and present in the spinal cord parenchyma or spinal cord subarachnoid space, and the clinical symptoms are radicular pain and motor deficits of sub-acute onset with progressive course (Bandres et al. 1992; Park et al. 2011).

### **7.5.7 Ophthalmic Cysticercosis**

Intraocular cysticerci (ophthalmic cysticercosis) may be found in the anterior chamber, the lens, the vitreous and the sub-retinal space. Although it is often asymptomatic, inflamed degenerating cysticerci cause progressive decrease in vision with symptoms like proptosis, diplopia, chorioretinitis, retinal detachment or vasculitis (Kruger-Leite et al. 1985; Madigubba et al. 2007).

### 7.5.8 Systemic Cysticercosis

Cysticerci can develop in almost any body site but tend to have a predilection for muscle or subcutaneous tissues. Cysticerci at these sites are usually asymptomatic, but the patient may notice subcutaneous, pealike or walnut-sized nodules. Subcutaneous nodules are more common in patients from Asia and Africa than from Latin America. In cases of major muscle involvement, acute myopathy can develop (Sawhney et al. 1976).

## 7.6 Pathogenesis of NCC

*T. solium* cysticercus is a structurally complex helminthic larva, which expresses diverse sets of antigens mounting variable immune response that leads to various clinical manifestations of the disease. Histological investigations on human and pig brain tissues have shown a very low or no inflammatory response around viable cysticerci. Viable cysticerci escape the host's immune response by blocking/inhibiting the complement system. The viable cysticerci produce excretory/secretory molecules such as paramyosin which inhibits Clq (Laclette et al. 1987); taeniaestatin identified in *T. taeniaeformis* inhibits both classical and alternate pathways of complement system. Taeniaestatin also decreases IL-1 and IL-2 production and lymphocyte proliferation (White et al. 1992). Cysticerci cell wall is rich in sulphated polysaccharides, which are to a large extent immunologically inert. Moreover, sulphated polysaccharides activate and consume complement and evade its response. Cysticercal cysteine proteinase degrades the host immunoglobulins, and its prostaglandin E2 (PGE2) induces Th2 response and suppresses the inflammation (Garcia et al. 2014; Terrazas 2008). However, when the cysticerci start to die/degenerate, granuloma is formed with inflammation around the dying cysts in both human and pig (Singh et al. 2013, 2015a, b). Immune cells such as eosinophils, lymphocytes, macrophages, and plasma cells infiltrate around the dying cysticerci to form granuloma. These cells secrete cytokines, chemokines and other inflammatory mediators that cause the various symptoms in patients. The infiltrating cells produce high level of Th1 (IFN- $\gamma$ , TGF- $\beta$  and IL-18) and lower level of Th2 cytokines (IL-4, IL-13 and IL-10) in the brain tissue surrounding dying cyst (Restrepo et al. 2001). Anti-helminthic treatment also induces Th1 (IFN- $\gamma$ ) and pleiotropic (IL-6) cytokine response with leukocyte infiltration around dead cysticerci in swine (Singh et al. 2015a, b).

The host immune response against cysticerci can be of two types, i.e. humoral and cellular. In humoral immune response, a number of immunoglobulin classes as specific antibodies against the parasite are produced. The most common immunoglobulin is IgG detected in patient's CSF, serum and saliva which is suggestive of long duration of infection (Grogl et al. 1985; Zini et al. 1990). The immune response against *T. solium* cysticerci display both Th1 and Th2 type; however, the basic mechanisms are not clear. Probably, the parasite is destroyed by eosinophils, which is supposed to be

mediated by Th2 cytokines (Ostrosky-Zeichner and Estanol 1999). The inflammatory response that kills the parasite and leads to resolution of fibrosis is mediated by Th1 cytokines. Peripheral immune response is associated with reduced lymphocytic proliferation, inhibition of granulocyte aggregation and induction of Th2 response (IL-4, IL-5 and IL-13) (White et al. 1997). In chronic NCC, pro-inflammatory cytokines, up-regulated cellular adhesion molecules such as ICAM-1 and activation of MMP-9 and MMP-2 contribute to blood-brain barrier disruption resulting in seizure disorder (Alvarez et al. 2002; Prasad et al. 2009a, b; Verma et al. 2011). It has been reported that individuals with glutathione S-transferase (GST)-M1 and (GST)-T1 deletions (null genotypes) are low producers of GST enzymes and such individuals are at higher risk to develop seizures in NCC. GST enzymes are essential for the protection of cells from damage caused by reactive oxygen species (ROS) generated during inflammation. Hence, higher GST activity may maintain asymptomatic condition, possibly by neutralizing the ROS and free radicals (Singh et al. 2017).

## 7.7 Diagnosis

### 7.7.1 *Diagnosis of Taeniasis*

Intestinal *Taenia* infections in humans are diagnosed by the detection of gravid segments or eggs in faecal samples. However, there are various tools for diagnosis of taeniasis with variable sensitivity and specificity.

### 7.7.2 *Microscopy*

Traditional microscopy to detect *Taenia* eggs in the stool has poor sensitivity but a very high specificity. However, concentration methods, preferably using sedimentation, increase the sensitivity. *Taenia* egg appears as a thick radiate cover and hooks under the microscope. However, eggs of different *Taenia* species (*T. solium*, *T. asiatica* and *T. saginata*) cannot be differentiated by microscopic examination (Garcia and Del Brutto 2003). Detection of gravid segment with its uterine branching is a reliable test to differentiate different *Taenia* species.

### 7.7.3 *Antigen Detection in Stool*

Copro-antigen detection in stool by capture ELISA has enhanced the sensitivity two to three times for diagnosis of taeniasis. To detect tapeworm antigen in stool, generally polyclonal antibody is used against the adult tapeworm in copro-antigen ELISA (Bustos et al. 2012).

### **7.7.4 Molecular Method**

The differentiation of the different species of *Taenia* is possible by mitochondrial DNA (*cox1*, *cob* and NADH dehydrogenase 1 gene)-based PCR, and the results are consistent if tapeworm material is available (Gonzalez et al. 2000, 2002; Yamasaki et al. 2004). However, the sensitivity of direct PCR assays in stool samples is yet to be defined.

### **7.7.5 Diagnosis of NCC**

The clinical diagnosis of NCC is hard due to its polymorphic/nonspecific disease symptoms. However, a precise diagnosis can be done if clinical and epidemiologic data is interpreted together with the neuroimaging findings and the results of specific immunological tests.

### **7.7.6 Immunodiagnostic Techniques**

In immunodiagnosis, specific antibodies and circulating cysts antigens are detected in serum or CSF. Various techniques such as complement fixation test, ELISA, indirect haemagglutination test, latex agglutination, radioimmunoassay and enzyme-linked immune-electrotransfer blot (EITB) have been used to detect antibodies. The serum-based ELISA to detect antibody is not reliable to diagnose NCC; however, it is very much in use due to simplicity of the technique. EITB is the most specific test so far. This immune-blot uses fractions of glycoproteins (50, 39–42, 24, 21, 18, 14 and 13 kDa) from crude extracts purified using a lentil-lectin column (Tsang et al. 1989).

### **7.7.7 Neuroimaging Techniques**

Neuroimaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) have significantly enhanced the diagnostic precision of NCC. CT is found to be more sensitive for the detection of calcified cysts; however, MRI is the most accurate as it gives information on the number and topography of lesions, stage of the cysts and the intensity of inflammatory response.

MRI has particular advantages such as it is non-invasive, it does not use any ionizing radiation and it has a high soft-tissue resolution. It may also provide both morphological and functional information. MRI is found to be accurate neuroimag-



ing tool for the detection of dying and viable cysts, whereas CT is good for calcified lesions, but it cannot differentiate the stage of the parasite (Garcia and Del Brutto 2003). Moreover, a study has shown that MRI with gradient echo sequence phase imaging is equally good as CT for the detection of the scolex in lesions and also the calcified stage (Gupta et al. 2001).

## 7.8 Treatment

### 7.8.1 *Anti-helminthic Therapy*

Although treatment for NCC with anticysticercal drugs such as albendazole, mebendazole, praziquantel, metrifphonate and flubendazole has been used, there has been a debate over safety and usefulness of such drugs due to lack of clinical trials to define doses and duration of therapy. Cysts location in the brain is a major factor that decides the success of anti-helminthic treatment. When the parasite infects the brain parenchyma, treatment with these drugs show radiological and clinical improvement in majority of patients with only a low adverse effect in some cases (Carpio et al. 2008; Del Brutto et al. 2006). However, when the parasite infects the subarachnoid basal cisterns, the prognosis is uncertain, and in such cases, either albendazole or praziquantel is preferred (Sotelo et al. 1988). However, controversies still persist about the use antiparasitic drugs in treatment of NCC, especially on seizure occurrence and other neurological disorders that result from inflammatory response triggered by antiparasitic treatment. Albendazole has been found to be more effective than praziquantel in clinical trials (Takayanagui and Jardim 1992). Another benefit of using albendazole is that it can also kill subarachnoid and ventricular cysts and has relatively less interaction with steroids and anti-epileptic drugs. However, increased dose of praziquantel (up to 30 mg/kg/day) or more prolonged or even repeated use has been recommended for treatment of patients with large subarachnoid cyst (Fleury et al. 2011). Further, surgery is also recommended by some clinicians as the best option for this form of infection. Albendazole is effective on 75–90% of cysts in the parenchyma when 15 mg/kg/day of albendazole is administered; however, the duration of treatment in such patients varies from 8 to 30 days (Castro et al. 2009). Further, antiparasitic therapy is recommended only in patients with low number of parenchymal cyst since the dying parasites release antigens to the surrounding tissues that initiate a strong inflammatory immune response, thus aggravating the symptoms. In order to reduce the risk, concomitant corticosteroids should be given, especially if there are large numbers of cysts. However, antiparasitic therapy is not recommended in patients with cysticercotic encephalitis. Recommendations for the treatment of NCC are given in Table 7.2 (Garcia et al. 2002).

**Table 7.2** Guidelines for the use of antiparasitic treatment of neurocysticercosis (NCC)

<i>Parenchymal NCC</i>		
Viable cysts	1–5 cysts	Antiparasitic + steroid treatment
	More than 5 cysts	Antiparasitic + steroid treatment
	More than 100 cysts	Antiparasitic treatment + high-dose steroid Alternatively, chronic steroid management; no antiparasitic treatment
Enhancing lesion (dying cysts)	Mild or moderate	No antiparasitic treatment; neuroimaging follow-up. Alternatively, antiparasitic + steroids treatment
	Heavy (cysticercotic encephalitis)	No antiparasitic treatment + high-dose steroids and osmotic diuretics
Calcified cysticerci	Any number	No antiparasitic treatment
<i>Extra-parenchymal NCC</i>		
Ventricular cysticercosis		Neuroendoscopic removal, if not available: CSF diversion followed by antiparasitic + steroids treatment or open surgery
Subarachnoid cysts (racemose cysticercosis and chronic meningitis)		Antiparasitic + steroids treatment, ventricular shunt if there is hydrocephalus
Hydrocephalus with no visible cysts on neuroimaging		Ventricular shunt; no antiparasitic treatment
<i>Other locations</i>		
Spinal cysticercosis		Primarily surgical; anecdotal reports of successful use of albendazole with steroids
Ophthalmic cysticercosis		Surgery

### 7.8.2 Anti-inflammatory Therapy

Corticosteroids are commonly used to reduce the inflammatory response that leads to various neurological symptoms due to degenerating cysticerci. Drug of choice for this therapy is dexamethasone; dose varies between 4.5 and 12 mg/day. It is also used in chronic cysticercosis arachnoiditis or encephalitis, where up to 32 mg/day of dexamethasone may be given to decrease the brain oedema (Del Brutto et al. 1993). Another drug, prednisone at 1 mg/kg/day, may replace dexamethasone when long-term corticosteroid is given (Suastegui et al. 1996). To reduce the raised acute intracranial pressure secondary to NCC, mannitol (2 g/kg/day) is also recommended as an osmotic agent.

### 7.9 Anti-epileptic Drug Therapy

Other drugs generally used to treat symptomatic NCC patients are anti-epileptic drugs (AEDs). Carbamazepine, phenytoin and phenobarbitone are the first-line AEDs more often used for the control of seizures due to NCC. In recurrent severe

headache associated with seizures, valproic acid/topiramate is preferred. Addition of praziquantel and albendazole with AED may improve seizure control. One study showed that 83% patients were seizure-free when treated with combination of anti-epileptic and anticysticercal drugs, whereas only 26% patients were seizure-free when treated with AEDs alone over a period of 28 months. However, despite better seizure control, albendazole and praziquantel may not be a definitive therapy for NCC-related active epilepsy, and AEDs need to be continued (Del Brutto et al. 1992). There is no definite time frame how long the anti-epileptic treatment should be given. Generally, AED is prescribed until a 2-year seizure-free period followed by gradual withdrawal.

## 7.10 Prevention

Cysticercosis/NCC is recognized as an eradicable disease. Eradication of swine cysticercosis through better animal husbandry and pig meat inspection are the important parameters adopted by the developed countries. These measures helped in breaking the transmission cycle of *T. solium* infection in the USA and Western Europe (Ferreira et al. 1997). Tapeworm carriers are the main target for anti-helminthic therapy for effective control of *T. solium* infection, since a small number of such carriers are likely to infect large numbers of healthy individuals. In developing countries the control measures should focus on mass administration of anti-helminthic drugs in endemic regions to cure tapeworm carriers and public awareness programme through health education. Other measures include toilet facilities to discourage open-field defaecation, handwash with soap after defaecation, restriction on sale of measily pork, restriction on pig roaming and pig vaccination, etc. Mass treatment of pigs in highly endemic regions with albendazole for 1 week followed by at least 2 weeks window period before slaughter for human consumption can reduce the incidence of *T. solium* carriers.

## 7.11 Treatment of Taeniasis

The only source of NCC/cysticercosis both for humans and pigs is the adult *T. solium* carrier individuals; a single tapeworm carrier can infect large number of hosts. Therefore, tapeworm carriers are the appealing target for control of the disease. Tapeworm carriers can be cured either by individualized or mass treatment of the population in the endemic area with a single oral dose of either niclosamide (2 g in adults) or praziquantel (5–10 mg/kg; Garcia et al. 2007). Albendazole 15 mg/kg is a good alternative to praziquantel especially in the developing countries.

## 7.12 Vaccination of Swine

Vaccination/immunization of porcine population in endemic region may be good approach to interrupt the *T. solium* life cycle thus preventing taeniasis and NCC. Many research groups had evaluated several parasite antigens derived from different developmental stages of the related cestodes (*T. crassiceps*, *T. solium*, *T. saginata* and *T. ovis*) or of synthetic origin with variable results. Three different protective antigens (TSOL18, TSOL45-1A and TSOL16) were identified from *T. solium* oncospheres and evaluated as vaccines (Lightowlers 2004). These antigens were found to induce almost complete protection in vaccinated pigs challenged with *T. solium* in experiments. Studies showed that the two doses of TSOL18 vaccine had given almost complete protection from infection in swine population (Flisser et al. 2004; Gonzalez et al. 2005).

## 7.13 Treatment of Infected Swine

Treatment of cysticercotic swine can reduce the taeniasis burden and help in *T. solium* elimination. Praziquantel and albendazole are proven to be highly effective in treatment of swine cysticercosis. However, oxfendazole at a single oral dose of 30 mg/kg demonstrated 100% effective to kill muscle cysts with no major side effects (Pondja et al. 2012). In naturally infected swine, treatment with albendazole (15 mg/kg) for 2 weeks was found 94% and 100% effective to kill the cysticerci in the brain and muscles, respectively (Singh et al. 2015a, b).

## 7.14 Conclusions

*T. solium* infection (taeniasis and cysticercosis/NCC) is a serious public health issue worldwide, particularly in developing nations including India. Swine cysticercosis is an economic loss to the pig farmers. Pig health and management would produce benefits to pig farmers. Avoidance of open defaecation and practice of using latrines may prevent roaming pigs or piglets from infection. Proper porcine meat inspection in slaughterhouses and other measures such as health education, availability of health-care services, elimination of *T. solium* carriers by mass treatment and control on sale of cysticerci infected pork may help in decreasing the infection rate in the endemic areas.

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