INTRODUCTION

Cysticercosis caused by larval stage of the tapeworm *Taenia solium*, is a major public health problem, both in resource-poor as well as western developed countries. It is the single most common cause of epilepsy in the resource-poor endemic regions of the world including most of South and Central America, India, South-east Asia, China and sub-Saharan Africa.1,2

Humans are only definitive host of *T. solium* harbouring the adult tapeworm in the intestine (referred to as, taeniasis). Both humans and pigs act as intermediate hosts and harbour *T. solium* larvae in different internal organs (referred to as, cysticercosis) including the brain (referred to as, neurocysticercosis - NCC). Humans and pigs acquire cysticercosis through ingestion of eggs excreted in faeces of human carriers. *Taenia solium* infection is also being increasingly diagnosed in western, affluent countries because of human migration from, and travel to endemic areas. It is common in communities where pigs roam freely and people consume undercooked pork.3

Neurocysticercosis is central nervous system (CNS) infection with *T. solium*. It is perhaps the commonest parasitic infestation of the CNS, and has received attention in the last two decades because of the availability of MRI and CT scanning in the countries where cysticercosis is endemic.

LIFE-CYCLE OF *TAENIA SOLIUM*

The adult tapeworm resides in the small intestines of humans. Here, it is attached to the intestinal wall by suckers and hooks. A few gravid proglottids are detached from the distal end of the body everyday and passed in faeces. Each proglottid contains thousands of eggs, which are fully embryonated, infective, and resistant to adverse environments. Wandering pigs feed on human faeces containing *T. solium* eggs (Fig. 1). Once in the intestinal tract, the action of bile and pancreatic enzymes helps the eggs lose their coats, liberating oncospheres. These oncospheres cross the intestinal wall, enter the bloodstream, and are carried to the tissues of the host where embryos evolve to form larvae (also known as, cysticerci). In these circumstances, pigs become the intermediate hosts in the life cycle.

Human consumption of inadequately cooked infected pork results in the transmission of viable cysticerci to the human small intestine, where, by the action of bile and digestive enzymes, the scolex of a cysticercus evaginates and attaches to the intestinal wall. Proglottids multiply and the parasite becomes a cestode that can be passed in the faeces as mature proglottids. Humans can also act as intermediate hosts for *T. solium* after ingestion of these eggs. In the given circumstances, human cysticercosis develops. The mechanisms by which eggs cross the intestinal wall and lodge in human tissues are the same as those in pigs. The two main sources from which humans contact cysticercosis are ingestion of food contaminated with taeniid eggs and the faeco-oral route in individuals harbouring the intestinal cestode. Once in the digestive tract, the eggs lose their coat due to action of gastric and pancreatic enzymes and liberate hexacanth embryos or oncospheres. Aided by their hooklets, oncospheres cross the intestinal wall and local venules, enter the systemic circulation and are carried to different organs of the host. Here the oncospheres lose their hooklets, acquire a vesicular shape and evolve into cysticerci by gradual evagination of the proto scolex (invaginated scolex) over a period of several months.4 The life cycle is completed when undercooked pork infested with cysticerci is
eaten. Humans may thus also become intermediate host and develop the larval stage of disease.

**HISTORICAL PERSPECTIVE**

The earliest descriptions of tapeworms were found in 2000 BC in works of ancient Egyptians. The work of Aristotle (384–322 BC) reveals that the infection of pork with tapeworm was known to ancient Greeks. They were also known to Jewish and Muslim physicians and have been accounted as the reason for pork being forbidden by Jewish and Islamic dietary laws. Review of the evolutionary histories of hosts and parasites and DNA evidence reveal that over 10,000 years ago, ancestors of modern humans in Africa were exposed to tapeworms when they scavenged for food or preyed on antelopes and bovid, and later passed the infection on to domestic animals such as pigs.

Rumler (1555) described cysticercosis; however relation between tapeworms and cysticercosis was not known at that time. In 1850, Küchenmeister fed pork containing cysticerci to prisoners awaiting execution and later recovered the developing and adult tapeworms from their intestines during autopsy. By the middle of the 19th century, it was clear that cysticercosis was caused by the ingestion of the eggs of *T. solium*.

**EPIDEMIOLOGY**

The tapeworm is endemic in many parts of the world including Latin America, China, Southeast Asia, India, and sub-Saharan Africa. Literature suggests prevalence of cysticercosis in Mexico is between 3.1 and 3.9 percent. A seroprevalence as high as 20 percent in humans, and 37 percent in pigs has been reported in areas of Guatemala, Bolivia, and Peru. The frequency has decreased in developed countries due to strict eat inspection, better hygiene and sanitary facilities. The distribution of cysticercosis coincides with the distribution of *T. solium*. In Latin America, around 75 million people live in endemic areas and 400,000 people have symptomatic disease. In the United States, the disease is found in immigrants from Mexico, Central and South America.

Unlike Latin America, disease was ignored in most parts of Asia, but over the last two decades there been an increased interest in the disease in Asia. The epidemiological aspects of the disease are poorly worked out in most Asian countries. The disease is prevalent in all states of India, although the prevalence varies between the states (Fig. 2). There are few reports of cysticercosis from Kashmir, which is largely populated by Muslims, and from Kerala, as education and hygienic standards are good in the state. The National Institute of Mental Health and Neuro Sciences (NIMHANS), Bangalore reported a diagnosis of NCC in 2% of unselected series of epilepsy patients. In a study from New Delhi, NCC accounted for 2.5% of all intracranial space occupying lesions. The solitary form of the disease (solitary cysticercus granuloma, SCG) is the commonest presentation, reported in nearly two-thirds of all patients with NCC. Between 26 and 50% of all Indian patients presenting with partial seizures are diagnosed with a SCG on the CT scan (16). Low proportion of pork eaters amongst Indian patients is the other unusual feature of the disease, less than 1-2% of patients with NCC admits eating pork and more than 95% of Indian patients with NCC are vegetarians. Serological assays using the enzyme linked immunotransfer blot (EITB) revealed exposure to the disease in 21.5% of 107 neurological patients attending a hospital in Mumbai.
either definitive or probable diagnostic criteria for NCC.

The single cyst infection (47.7% - 53.4%), is the most common in Indian subcontinent.21 In a study of 156 pathologically proven cases of cysticercosis from Patiala, Punjab, 88% patients presented with solitary lesion.21 In a seroprevalence study in Chandigarh, anti-cysticercus antibodies were found in 17.3% with highest prevalence (24%) reported from slum areas; however only 8% of the seropositives had previous history of seizure.22 In a community-based survey of population of 15,000 in a slum area in Ludhiana, Punjab, 114 cases of active epilepsy were diagnosed and EITB assay was positive in 27 of 106 cases with active epilepsy.23

In a community based study in Vellore district of South India the prevalence of NCC causing active epilepsy was 1.3 per 1000 population. The results revealed high levels of exposure of the population to the parasite and a relatively high prevalence of active infections (4.5% antigen positives) but a low prevalence of NCC causing active epilepsy (0.13%).24 Cysticercosis seroprevalence among the healthy blood donors from Pondicherry was 6.5% using both antigen and antibody detection methods.25 The prevalence of taeniasis ranged from 0.5-2% in hospitalized patients in northern India to 12–15% in labour colonies where pigs are raised.22

**NEUROCYSTICEROSIS: THE CLINICAL DISORDER**

Classifying neurocysticercosis to the anatomic compartment of involvement is advantageous to clinicians, radiologists and the pathologists (Table 1), but it does not take into account the evolutionary stage of neurocysticercosis, which also influences the clinical presentation. In 1985, Sotelo et al., proposed the classification into active and the inactive disease (Table 2).

Morphologically, four stages of development and regression of the cysticercus in the CNS are recognized:

i. Cystic or vesicular stage is viable and comprises of well-defined, fluid-filled membrane containing scolex.

ii. Degenerating, colloid stage; It appears as eosinophilic structure in which components of the bladder and scolex are in various stages of disintegration and tissue around have multinuclear giant cells, foamy macrophages, and neutrophils.

iii. Nodular stage.

iv. The fibrous nodule undergoes mineralization and calcification.

### CLINICAL FEATURES

Neurocysticercosis has been traditionally also classified in to two important types - parenchymal NCC and extraparenchymal NCC.

A. **Solitary cerebral cysticercus granuloma (SCCG)**

Solitary cerebral cysticercus granuloma (SCG) were initially noted on computed tomography (CT) studies performed in Indian patients with seizures, in the late 1970’s and early 1980’s, as a solitary small enhancing lesion. It was initially thought to be an “immature tuberculoma” or “microscopic tuberculoma” and patients with these lesions were treated with antitubercular therapy.26-27 The etiology of the single, small, enhancing CT lesion was revealed only in late 1980s from the pathological studies performed on excised lesions in a series of patients at Vellore, India (Fig. 3).28-30 Solitary granulomas are more frequently reported from India but also from the United States and South and Central America.

Acute symptomatic seizures are the most common manifestation of SCG. According to some experts, partial seizures are more common, while the others report that generalised seizures are more common. Probably partial seizures with secondary generalisation or the generalised seizures are more common than the complex partial seizures. Status epilepticus occurs in less than 1% of patients with single lesions. An important feature is lack of progressive neurological deficit and increased intracranial pressure. Seizures due to NCC can be either acute symptomatic or they may be remote symptomatic seizures. There is no correlation between the NCC bur-
den of the lesions and the severity of epilepsy.

The natural history of SCG varies: the lesion may completely resolve or may resolve by leaving behind a punctuate calcific residue. The risk of seizure recurrence remains high as long as the granuloma is visible on imaging as an enhancing lesion. Seizure outcome improves following resolution of SCG. The majority of SCGs resolve by 1 year.

B. Meningeal Cysticercosis

The meningeal form of neurocysticercosis was first described by Virchow in 1860. Cysticerci located in the brain parenchyma or within the cortical sulci between two cerebral convolutions is described as “cysticercus cellulosae” and those cysticerci located within the basal cisterns as “cysticercus racemosus”. Arachnoiditis caused by cysticercus can cause entrapment of nerves exiting from the brainstem. There can be visual field defects, decreased visual acuity and third nerve entrapment manifesting as diplopia.31-32 Symptoms or signs of increased intracranial pressure or cranial nerve dysfunction can be presenting feature. In a report by Bonametti et al., fever was reported in 74% and neck stiffness was reported in 44% cases.33 Irritation of subjacent cerebral cortex by overlying subarachnoid cysticerci may cause seizures which are probably partial seizures with the secondary generalization.34 Subarachnoid cysticerci of spinal canal cause non-specific clinical picture of radicular pains and motor deficit of subacute onset and progressive course.34-36

C. Heavy multilesional parenchymal cysticercotic syndromes

A small subset of individuals harbour massive infection. Three characteristic forms of multiple neurocysticercosis are described:

Cysticercotic Encephalitis

Its manifestations are due to severe inflammatory response around the dying cysts. Patients present with headache, that intensify rapidly prior to diagnosis and seizures, though these symptoms may have been present earlier for around a period of 18 months, mean of 6 months. Papilledema, secondary optic atrophy, false localising third and sixth nerve palsy, and deep tendon hyperreflexia and Babinski response are main presenting features.

Heavy Non-encephalitic NCC

No inflammatory reaction is seen around the cysts, and all parasites are viable and so do not enhance upon contrast in CT/MRI. It is more common during the third or fourth decade of the life and has no sex predilection. It presents as a mild syndrome. Patients present with seizures and neuropsychological abnormalities.

Disseminated cysticercosis

It was reported as early as 1912 by the British Army medical officers stationed in India.37 In 1961, a review of 450 cases of cysticercosis by Dixon and Lipscomb reported only one case of dissemination.38 Kumar et al.,39 and Wadia et al.,40 reviewed 2 cases each. Involvement of lung and muscles is rare. The clinical features depend on the location of the cyst, the cyst burden and the host reaction. The syndrome is characterized by pseudomuscular hypertrophy (100%), palpable subcutaneous nodules (87%), seizures (78%) and abnormal mentation. There is diffuse symmetrical painful or painless enlargement of all groups of muscles associated with weakness and easy fatigability.

D. Intraventricular neurocysticercosis

The cysticerci are present inside the cerebral ventricular system. The intraventricular cysts become symptomatic at the time of implantation due to obstruction of the CSF flow, with consequent hydrocephalus and signs and symptoms of raised intracranial pressure. Inflammation around dead or dying cysts produces ependymitis, scarring, obstruction and ventriculitis.
Neurocysticercosis – Indian Scenario

Table 3: Clinical and radiologic features consistent with a diagnosis of SCG

A. Clinical features that are supportive of a diagnosis of SCG
   - Focal seizures with or without secondary generalization
   - Note: Seizures may be new-onset or of longer duration; may be generalized at onset; may occur in clusters (2 or more seizures over 2–3 days); may be followed by unilateral or diffuse headaches lasting for a few hours to days; or may be followed by transient and mild postictal neurologic deficits

B. Clinical features that make a diagnosis of SCG unlikely
   - Persistent and severe neurologic deficit
   - Clinical evidence of intracranial hypertension
   - Evidence of neurologic disorder, other systemic disease (e.g., systemic infection such as AIDS) that can account for imaging findings
   - Age <2 years and >60 years

C. CT features compatible with a diagnosis of SCG
   - Single, small (<20 mm), well-defined
   - Contrast-enhancing (closed ring, disc, or nodular type)
   - With or without surrounding edema
   - Associated with minimal mass effect and no midline shift

D. MRI features compatible with a diagnosis of SCG
   - Single, small (<20 mm) lesion with fluid contents
   - T1 sequence: intensity slightly greater than or isointense to CSF
   - T2 sequence: hyperintense or isohypointense with central hyperintensity
   - Ring or nodular type enhancement after contrast
   - Scolex may or may not be visible as an eccentric nodule within the fluid cyst contents
   - (T1 isointense and T2 iso/hypointense)
   - Mild to moderate surrounding edema but no midline shift

DIAGNOSIS

The initial diagnostic criteria for cysticercosis were based on the objective evaluation of clinical, radiological, immunological and epidemiological parameters.46 After 4 years, revised diagnostic criteria were proposed.47 Majority of Indian patients with neurocysticercosis can not satisfy several items even of the new diagnostic criteria, so revised criteria for Indian patients with neurocysticercosis can not satisfy several immunological and epidemiological parameters.46 After 4

MRI is considered the best neuro-imaging tool for the detection of degenerating and innocuous (viable) cysticerci, while CT is the best for calcified lesions.1 The MRI can differentiate the stages of the parasite, which CT fails to do. Gradient echo sequence phase imaging is good for the detection of the scolex in cystic lesions and also the calcified stage of the parasite.1 MRI helps better detection of the active parasites but few calcified parasites may be missed. Once CT demonstrates a single enhancing lesion consistent with a diagnosis of SCG, further evaluation with MRI may not be required

Follow-up imaging (either contrast-enhanced CT or MRI) should be undertaken at 6 months following initial symptomatic presentation in all individuals with SCG. However, earlier CT (e.g., at 3 months) might be useful in order to identify those lesions that enlarge or change morphology, hence suggesting an alternative etiology (e.g., neoplasm, tuberculoma, or fungal granuloma)
PREVENTION AND TREATMENT

Improved animal husbandry and meat inspection procedures have resulted in the successful interruption of transmission of intestinal T. solium in the United States and Western Europe. Tapeworm carriers are good target for the control of cysticercosis/taeniasis. In the developing world, emphasis has been placed on control of the parasite through health education and mass administration of anthelminthic drugs in areas of endemicity in an attempt to remove tapeworm carriers.

VACCINATION

Till date no vaccine has been developed against the T. solium . Vaccinating pigs in endemic region to prevent porcine cysticercosis may be good option prevent taeniasis and consequently human cysticercosis. A protective antigen from Taenia ovis oncosphere-stage was cloned to develop a recombinant vaccine for ovine cysticercosis and this vaccine is available commercially for veterinary use in New Zealand.

TREATMENT

Role of anthelminthic drugs

A meta-analysis and other studies suggest a possible beneficial effect of albendazole in subjects with SCG in the form of improved resolution rates of the granuloma and better seizure control. To make definite conclusions regarding the effect of albendazole in SCG, larger multicentric trials with sound methodology are required. Until such evidence is available, a short course (1–2 weeks) of albendazole (with or without corticosteroids, depending upon the judgment of the treating physician) may be prescribed soon after presentation, i.e., the first seizure.

Role of corticosteroids

While treating individuals with SCG, one can either prescribe a short course of corticosteroids alone (without specific anthelminthic treatment) or antihelminthic drugs (alone or with corticosteroids). The concept of prescribing a short course of corticosteroids alone is in conflict with the practice of administering anthelminthic drugs (alone or with corticosteroids) to individuals with SCG. Large randomized, double-placebo-controlled trial comparing corticosteroids alone, albendazole alone, and albendazole with corticosteroids is required in order to dissect out the benefits accrued due to either agent. Until such evidence is available, definite recommendations regarding the use of corticosteroids alone in the management of SCG cannot be made.

Role of antiepileptic drugs

The risk of seizure recurrence in an individual with SCG is related to the persistence of the enhancing lesion. The currently used AEDs effectively prevent seizure recurrence. It is appropriate to continue AEDs until such time that the lesion (granuloma) is actively degenerating (i.e., appears as an enhancing lesion on imaging studies). The AED may be withdrawn once complete resolution of the granuloma is demonstrated on follow-up imaging studies. The long-term seizure outcome in patients with SCG is generally good. However, the risk of seizure recurrence remains high if the granuloma resolves leaving behind a calcific residue. In the case of resolution with calcification, longer duration of AED should be considered. It is unclear how long AEDs should be administered to individuals with SCG that resolve with calcification. Any AED might be used for much of the period of treatment in individuals with SCG. A newer, non-enzyme-inducing AED might be considered for the period of time that anthelminthic treatment is administered.

REFERENCES

16. Wadia, R.S., Makhale, C.N., Kelkar, A.V., Grant, K.B. Focal epilepsy in India with special reference to lesions showing ring or disc-like enhancement on contrast computed tomography. J Neurol Neurosurg Psychiatry 1987;50:1298./1301.


23. G. Singh Association between Toxocara canis and epilepsy,A collaborative, community prevalence and hospital based incidence case - control study.


58. Tsang V C, Brand J A and Boyer AE. An enzyme-linked immunoelectrotransfer blot assay and glycoprotein antigens for diagnosing human cysticercosis (Taenia solium); J Infect Dis 1989;159:50–59


