Neurocysticercosis: an update

Arturo Carpio

Taeniosis and cysticercosis, diseases caused by the parasitic tapeworm *Taenia solium*, are distributed worldwide where pigs are eaten and sanitation is poor, and also in the more developed countries as a result of increasing migration. Neurocysticercosis is the commonest parasitic disease of the human nervous system. Immunological assays detect positivity for human cysticercosis in 8–12% of people in some endemic regions, which indicates the presence of antibodies against the parasite but not necessarily active or central-nervous-system infection. The only reliable tool for diagnosis of neurocysticercosis is imaging by CT or MRI. The presence of viable cysts with a mural nodule, associated with degenerative cysts and calcifications, is typical. Classification of neurocysticercosis into active, transitional, and inactive forms gives a good clinical-imaging correlation and facilitates medical and surgical treatment. The main clinical manifestations of neurocysticercosis are seizures, headache, and focal neurological deficits, and it can have such sequelae as epilepsy, hydrocephalus, and dementia. Treatment should be individually fitted for each patient, with antiepileptic drugs, analgesics, corticosteroids, or a combination of these. Anthelmintic drugs (praziquantel and albendazole) are used routinely, but so far no controlled clinical trial has established specific indications or definitive doses of treatment. Parenchymal forms of neurocysticercosis have a good prognosis in terms of clinical remission. The most effective approach to taeniosis and cysticercosis is prevention, which should be a primary public-health focus for less developed countries.


In an era of advanced technology and great health improvements, taeniosis and cysticercosis remain a global public-health problem. These parasitic diseases are related to poverty and poor sanitation; they are considered a biological marker of socioeconomic underdevelopment. Taeniosis and cysticercosis disappeared from most European countries about a century ago, thanks to progress in health systems and general sanitation, but they continue as an endemic disease in many less developed countries. Moreover, the disease is spreading back to the more developed countries through increasing migration.

Neurocysticercosis, the nervous-system form of cysticercosis caused by larvae of the tapeworm *Taenia solium*, is commonly associated with seizures, headache, and focal neurological deficits and can have long-term neurological sequelae such as epilepsy and hydrocephalus. Although important advances in the diagnosis, immunology, and pathophysiology of neurocysticercosis have been achieved in the past two decades, much of the natural history of the parasite infestation, its epidemiology, and clinical features remains uncertain.
Many studies on neurocysticercosis have been published worldwide. However, most of the available clinical information has come from retrospective studies, case series, and anecdotal reports from neurological hospitals, which bias the results and confound interpretation and conclusions. There are very few reports on neurocysticercosis based on prospective, systematically collected information, and virtually no controlled studies of treatment strategies have been done. This review critically analyses the available information on the most controversial features of neurocysticercosis.

**Causative agent**

The term taeniosis is used for infection with the parasite *T solium*. Cysticercosis denotes infection with the larval or metacestode stage (cysticercus) of *T solium*. Development from the larva into a mature, adult tapeworm that is capable of producing eggs takes about 2 months. The adult is 2–4 m in length and lives in the human small intestine. The tapeworm consists of a scolex and a strobila. The scolex is the holdfast organ, armed with four suckers and a rostellum with 22–32 hooks. The strobila consists of 700–1000 segments (proglottids). The gravid segments located towards the distal end of the strobila are passed in the faeces. Each gravid proglottid contains about 40 000 eggs. The *T solium* egg is a small embryo covered by an embryophore, which can be disseminated in the external environment. The embryophore has a thick striated cover and contains an oncosphere with six typical embryonic hooklets (hexacanth embryo). *T solium* can shed up to 300 000 eggs daily.

Eggs that are shed into faeces can serve as a source of external infection of people in close contact with the carrier. However, most eggs are disseminated in the environment, though their fate has not been adequately studied. In regions that lack an adequate sanitary infrastructure, free-ranging pigs feed on indiscriminately deposited human faecal matter. Egg survival is adversely affected by extremes of temperature and desiccation. Conversely, humidity and temperatures between 10°C and room temperature favour egg survival. Agents such as wind and water and some invertebrates and birds are believed to aid in egg dispersal.

The mature oncosphere is a globular larva, 30 μm in diameter. Luminal factors such as bile salts are thought to be involved in the liberation and activation of mature oncospheres in the gut. Within 2 h of liberation, oncospheres enter submucosal blood or lymphatic vessels and migrate to internal organs. Why oncospheres have a predilection for certain sites such as muscle, brain, and subcutaneous tissue is not clear.

The postoncospheral development of the larva occurs within the intermediate host, the pig. The oncosphere quickly changes from a solid larva into a bladder form filled with fluid; it has a group of cells that differentiate further into an invaginated scolex. The metacestode reaches its full size of 5–8 mm×3–6 mm within 60–70 days. The cysticercus is an ovoid bladder stage. It is filled with an opalescent fluid and contains an invaginated scolex. Any change in osmotic pressure, such as occurs when the cysticercus reaches the human intestine, causes the scolex to become everted and the bladder wall is lost. The adult tapeworm develops from behind the scolex of the cysticercus. The survival time of a cysticercus is limited to a few years.

**Life cycle, biology, and transmission**

The natural biological cycle of *T solium* zoonosis consists of two hosts and the environment. Human beings, the final host, harbour the adult tapeworm, which produces several thousand eggs daily for years. The eggs are disseminated to the environment through faeces. The pig, the intermediate host, ingests some of these eggs, which develop into cysticerci. When a human being eats contaminated pork containing cysticerci, these develop into an adult worm inhabiting the human intestine (figure 1). However, human beings can also be infected by *T solium* eggs through internal and external autoinfection. External autoinfection implies faecal-oral infection with *T solium* eggs in an individual with intestinal taeniosis. Neglect of hygiene, such as handwashing after defecation and before meals, is the main reason for external autoinfection, which is an established route of self-infection. Internal autoinfection implies infection with eggs through reverse peristalsis. This process seems unlikely, because eggs have to pass through a brief period of peptic digestion for disintegration of the embryophore before they can invade human tissue. Heteroinfection occurs when *T solium* eggs are ingested in contaminated food, as occurs in areas where water for drinking and irrigation carries faeces or when taenia carriers handle food.

Between 5% and 40% of adult carriers of *T solium* develop cysticercosis. The high rates of cysticercosis in individuals with intestinal taeniosis and their family members confirm that faecal-oral self-infection and cross-infection are common. There is a theoretical possibility of an outbreak of cysticercosis around carriers of *T solium* in schools, closed institutions, and public eating facilities, though this possibility has never been adequately confirmed.

In addition to the biological cycle of *T solium*, several economic factors sustain the life cycle in less developed countries. Many rural households rear pigs in small numbers; the animals constitute an important source not only of meat but also of immediate income. The rearing of free-ranging animals requires little investment for the rural poor. In the absence of a sanitary infrastructure, people use open areas and fields for defecation. Free-ranging pigs thus have access to human faeces, which perpetuates transmission of the parasite from human being to pig. Rural pork producers are not motivated to pass pork through meat inspection because of the threat of condemnation. Furthermore, local culinary habits facilitate the consumption of raw or partly cooked meat. These factors lead to transmission of the cysticercus from pig to human being in endemic areas.
Epidemiology

*T. solium* infection is widely endemic in less developed countries, in highlands or tropical areas, in Central and South America, and non-Muslim populations of Asia and Africa (figure 2). The occurrence of cysticercosis in countries in Asia and Africa is mainly related to the sociocultural system. Taeniosis and cysticercosis are endemic in areas where pork is consumed, such as most of sub-Saharan Africa, China, India, and most countries of southeast Asia. Of the American countries, only Canada, the USA, and possibly Argentina and Uruguay appear to be free of transmission in the pig-human cycle; however, Argentina and Uruguay are observing an increase in imported and introduced infections related to immigration of people from neighbouring countries where *T. solium* infection is endemic. *T. solium* has largely disappeared from Europe as a result of improvements in sanitation and hygiene; however, locally acquired infections are still occasionally reported from Spain, northern Portugal, southern Italy, and Poland, indicating persisting foci of transmission in some regions.

Cysticercosis is classified as an emerging infectious disease in some more developed countries; people who have never left the USA as well as visitors to disease-endemic regions are at risk. The disease accounts for up to 2% of neurological and neurosurgical admissions in southern California, and more than 1000 cases per year in the USA. Further away from disease-endemic regions, an outbreak of cysticercosis among orthodox Jews living in New York was reported after food was contaminated with *T. solium* eggs by immigrant cooks infected with the pork tapeworm. These carriers may have been completely unaware of their infection.

Until recently, the only available data on the frequency of neurocysticercosis from any country were collected from clinic-based patients or at autopsy. Neurocysticercosis was found, for example, at 2.8–3.6% of autopsies in Mexico City and high background rates of putatively inactive brain lesions. Some studies, but not all, have found an association between seizures and seropositivity. Although the proportion of EITB-positive individuals has been found to be higher among patients with epilepsy than among those without epilepsy, the proportion of seropositivity in epileptic patients is similar to that reported in the general population in the same areas. There is also a discrepancy between EITB positivity and CT findings; more than 30% of individuals diagnosed as having neurocysticercosis by CT were seronegative. A recent epidemiological study found that people in household contact with patients with neurocysticercosis had a three times higher risk of positive serology for cysticercosis than the general population. Although these findings are consistent with a common environmental source of infection with *T. solium* eggs, they also suggest a potential role for direct human-to-human contamination.

The discordance between the high prevalence of antibodies to *T. solium* in disease-endemic populations, relatively few symptomatic cases of neurocysticercosis, and high background rates of putatively inactive brain lesions in seronegative controls has been attributed to transient antibodies. People with transient antibodies may have been exposed to, but did not develop, a viable infection of *T. solium*, or they may have had cysticercosis that resolved spontaneously. Similarly, people who are currently seronegative may have been seropositive previously.

![Figure 2. Estimated geographical distribution of taeniosis/cysticercosis. Adapted from Roman and colleagues.](http://infection.thelancet.com)
Immune response
Several studies have investigated the mechanisms of the immune response elicited against the *T solium* cysticercus, such as the heterogeneity of the humoral immune response, the existence of immune-evasive mechanisms, and the fact that the immune response can both protect and harm the host.30–32 Living cysticerci can cause an asymptomatic infection through active evasion and suppression of immunity. Histological studies have shown that in both human beings and pigs viable cysticerci show little or no surrounding inflammation.3 Cysticerci can persist in the human host for long periods, in many cases for years, without eliciting a surrounding inflammatory reaction. By contrast, the immune-mediated inflammation around one or more degenerating cysts can precipitate symptomatic disease.

The host immunological response to cysticerci can be divided into humoral and cellular components. The humoral immune response to antigens of *T solium* cysticerci is evident from the number of immunodiagnostic assays that have been developed with different types of antigens.33 Several immunoglobulin classes are produced as specific antibodies against the parasite. The most frequent is IgG, which can be detected in serum, cerebrospinal fluid (CSF), and saliva and suggests that infection is of long duration.34–36 The immune response against *T solium* cysticerci has both Th1 and Th2 components, although the underlying mechanisms are yet to be clarified.3 The parasite is probably killed by eosinophils that are attracted to the site by lymphoid cells. This specific response is assumed to be mediated by Th2 cytokines.37 The inflammatory reaction that leads to destruction of the parasite and resolution with fibrosis seems to be mediated by Th1 cytokines. Some studies have also addressed molecular components in the CSF, serum, and the granuloma itself. High concentrations of interleukins 1 and 6 have been reported in CSF of patients with neurocysticercosis.38

The depressed immunity in patients with neurocysticercosis may be the cause of the reported association of this parasitic disease with conditions resulting from immunological disturbances, such as haematological malignant diseases and conditions leading to the development of cerebral tumours.39–41 This hypothesis should be clarified by further studies.

The evasion of host immune responses by the parasite is an interesting immunological process. A host-parasite equilibrium is maintained, as a result of which the parasite is able to survive in the host for long periods.32 The site where *T solium* oncospheres settle and the nature of their relation to the encapsulating host may contribute to sequestration of the parasites from immune attack. The unequal distribution of cysticerci throughout body tissues could result from selective invasion by the parasite or differential survival of larvae in immunologically privileged sites.42 Some experimental studies suggest that cysticerci develop or persist better in the eye and the brain than in other tissues or organs. A concomitant immunity mechanism has also been proposed, pertaining to protection conferred by already established parasites against newly invading parasites of the same species in a given host.33 This idea implies that previous infection protects against new infection. Though not adequately proven, molecular mimicry (synthesis of host-like antigens by the parasite) may be one of the mechanisms involved in immune evasion.43

Pathophysiology and imaging correlation
The natural history of the cysticerci in the CNS is not entirely understood. CT and MRI have been useful to study the evolution of the cysticercus within the brain parenchyma.44–48 Once the oncosphere has passed into the parenchyma, it grows and evolves through vesicular, colloidal, granular-nodular, and calcified phases (figures 3 and 4).44 So far, there is no experimental evidence that confirms this sequence, but CT or MRI can identify the four phases. In the vesicular phase, the host tends to show immune tolerance, and in most cases there is no surrounding parenchymal reaction; the larva lives inside a translucent liquid-filled cystic structure surrounded by a thin membrane, where it can remain viable for a few months to several years.44–46 When the larva is viable, the CT scan depicts circumscribed, rounded, hypodense areas, varying in size and number, without enhancement by contrast media (figure 5).44–47 The average diameter of the cyst is 8–10 mm, but the range is 4–20 mm or more. Larger cysts are identified in the ventricles. On MRI, the vesicular larva appears with a CSF-like intensity signal on all sequences (figure 5), with no surrounding high signal on T2-weighted images.44–46 Both MRI and CT can show a high-intensity, 2–3 mm mural nodule, depicting the scolex, in the interior of some parenchymal vesicular cysts (figure 5).44

As the cyst degenerates, it goes through a transitional stage: the contrast-enhanced CT scan shows an annular (colloidal phase) or nodular (nodular phase) enhancement surrounded by irregular perilesional oedema (figures 5 and 6).44 At this stage, the fluid content gives slightly higher

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**Figure 3. Parenchymatous cysticercosis.** The cysticerci in the vesicular and colloidal stage are scattered in both the grey and white matter, including right and left thalamus. Reproduced with permission from Enrique Hermida.
signal than CSF and in some cases is isodense with the parenchyma on T1-weighted or proton-density-weighted MRI and shows high signal on T2 images. The capsule shows higher signal than the adjacent brain with thick ring enhancement on T1 images, whereas on T2 images there is a low ring signal surrounded by high signal lesion, due mostly to oedema.46–48 Although these pathological changes are the cause of the clinical manifestations, in most cases consisting of seizures and headache, the reaction can cause no symptoms at all. Finally, when the cyst dies, it can disappear or become an inactive calcified nodule of homogeneous high density on CT43 or low intensity on proton-weighted MRI (figure 5).

One form of neurocysticercosis that has different clinical and radiological characteristics from those described above is cysticercotic encephalitis, which occurs mainly in children and young women.49 The non-contrast CT image shows diffuse and intense cerebral oedema and small or collapsed ventricles; with contrast media, many small, hyperdense, nodular or annular images are visible, disseminated throughout the cerebral parenchyma.43

When the parasites are located in the subarachnoid space or inside the ventricular system, the process of evolution also differs from the usual course. Surgical studies have established that the parasites in these parts of the brain generally remain in the vesicle stage.50,51 Being immersed in a CSF-rich environment, the cysticerci can evolve into a racemose form,44 which constitutes a hydropic change that leads to large or even giant vesicles generally without a scolex; the parasite vanishes during the oedematous process. This type of cyst is most frequently located either in the basal cisterns or inside the sylvian valley; they can reach 100 mm in diameter.44,45 CT depicts a hypodense image in the subarachnoid or ventricular space; the cysts deform the surrounding structures, and non-communicating hydrocephalus can occur.12,13 MRI shows the cyst more precisely as a hypointense CSF-like image in all phases (proton-weighted or T2-weighted), and it permits direct visualisation of intraventricular cysticercosis by identifying the cyst wall, scolex, or both (figure 5). There is no information about the natural history of the parasite inside the ventricular system or the subarachnoid space, and evidence of calcifications in these locations is scarce.

When the parasite is located in the subarachnoid space, it can also cause a meningeal inflammatory process, with pleocytosis and increased protein in the CSF.44 The parasite degenerates to a hyaline mass and remains trapped inside the thickened leptomeninges, where the residue is surrounded by a granulomatous lesion with many multinucleate giant macrophages.46 As a sequel to the chronic intense inflammatory process, fibrosis and thickening of the leptomeninges can lead to chronic hydrocephalus. There may be vasculitis with secondary ischaemic lesions.1 Gadolinium-enhanced MRI and contrast-enhanced CT depict clearly the leptomeningeal thickening along the basal cisterns and sylvian valley.51,52 If there are also parenchymal calcified nodules, the diagnosis is indirectly reinforced.44

**Classification of neurocysticercosis**

Before the advent of CT, several groups of researchers published classifications of neurocysticercosis based on varied clinical and anatomical criteria. Classifications based on the prognosis of the illness as malignant or benign seem...
uncontrolled studies, historical case series, and anecdotal reports collected mainly from neurological hospital settings. Prospective and properly designed studies are needed to elucidate the natural history of the disease and the true distribution of clinical manifestations.

One of the most intriguing features of neurocysticercosis is that a high proportion of individuals harbouring parasites in the CNS remain free of symptoms. In some patients, clinical manifestations develop many years after the parasite lodges in the CNS, by either inflammation around the parasite or mass effect. Among those with symptoms, the only clinical manifestation is seizures in most patients with parenchymal neurocysticercosis, and the neurological status is normal in most. Focal neurological deficits, when present, are generally transient, over a period of a few days, weeks, or months, with periods of remission and relapse, probably due to different evolutionary stages of the parasite. Headache and increased intracranial pressure are frequent in patients with extraparenchymal location of parasites. This location occurs in about a third of patients. Acute hydrocephalus related to intraventricular cysts, or chronic hydrocephalus due to arachnoiditis or ependymitis, is the most frequent cause of this syndrome. Increased intracranial pressure also occurs in patients with the racemose form of neurocysticercosis and in those with cysticercotic encephalitis. Spinal-cord cysticercosis is rare. Patients experience non-specific clinical manifestations, such as nerve-root pain or spinal-cord compression syndromes, according to the level of the lesion. Massive cysticercal infection of striated muscles occasionally produces a clinical picture of generalised weakness associated with muscle pseudohypertrophy.

Neurocysticercosis predominantly affects adults in their third or fourth decade of life; it is uncommon in children and elderly people. Reports of cysticercosis are very unlikely in children younger than 2 years because the incubation period of \( T \) \( s o l i u m \) is long. The disease is recognised mainly in children older than 7 years, owing to this incubation period. Epidemiological data also indicate that EITB seropositivity rates are lower in children than the average prevalence rates for the community. Most children with the disease show a single transitional cyst that resolves spontaneously over a few months and do not require any treatment apart from symptomatic relief and antiseizure drugs (figure 7). However, severe forms of neurocysticercosis can exceptionally occur, including cysticercotic encephalitis, which result in permanent neurological sequelae, such as amaurosis. Hydrocephalus and intraventricular neurocysticercosis are extremely rare in children.

Neurocysticercosis and epilepsy

Seizures are widely reported to be the most common symptom of neurocysticercosis, occurring in 70–90% of patients. There is no consistency in the reported distribution of seizure types. Some investigators report a higher proportion of partial seizures, others that generalised seizures are more frequent. Generalised seizures or partial seizures with secondary generalisation seem to be most

Disease manifestations

The clinical manifestations of neurocysticercosis are varied and probably depend on the number and location of cysts, as well as the host immune response to the parasite. Many syndromes have been described, such as manifestations of brainstem dysfunction, cerebellar ataxia, sensory deficits, involuntary movements, stroke-like symptoms, extrapyramidal signs, and dementia. Other rare clinical manifestations, for instance intrasellar cysticercosis and pseudotumour cerebri, have been reported. However, most of this information is retrospective and based on

My colleagues and I \(^{11} \) proposed a widely accepted classification based on the viability and location of the parasite in the CNS of the host: active, when the parasite is alive; transitional, if it is in the degenerative phase; and inactive, if there is evidence of its death. Each viability category was subdivided into parenchymal and extraparenchymal forms. The viability criterion is very important, because it allows us to analyse the natural history of the parasite and, according to the parasite’s evolutionary stage, the production of pathophysiological changes in the host’s CNS. On the basis of this classification, clinical manifestations and therapeutic procedures can be related to each category. For example, seizures are the main symptom in the transitional parenchymal form owing to the inflammatory reaction in the brain, whereas cranial-nerve abnormalities and intracranial hypertension syndromes are more frequent in the subarachnoid and intraventricular forms. Another advantage of this classification is that it permits a proper relation with CT or MRI.

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Seizures associated with neurocysticercosis can be classified as either acute symptomatic or remote symptomatic seizures. Patients with cysticerci in the transitional form or degenerative phase develop acute symptomatic seizures due to the acute inflammatory reaction in the vicinity of cysts located in the cortex or subcortex. Patients with chronic recurrent seizures, whose imaging studies show several parenchymal calcifications, should be classified as having remote symptomatic unprovoked seizures. In the active form, seizures have been attributed to mechanical compression of the brain by cysticercal cysts. Seizures in the inactive or calcified form have been attributed to residual perilesional gliosis that results in chronic epileptogenic foci. These theories require further confirmatory studies. Some researchers have suggested that mild inflammation, visible on contrast-enhanced MRI or CT, can persist in the calcified stage of neurocysticercosis and may be associated with an increased risk of continuing seizures. These researchers speculate that the perilesional oedema surrounding the calcified lesions is a persistent host inflammatory response provoked by antigens released from the lesions. However, in patients with many calcifications, why only some of the calcified lesions would induce inflammation is not clear.

Comparison of the results of studies of epilepsy due to neurocysticercosis is extremely difficult. The studies are few, and many are targeted at all seizures, rather than epilepsy alone. The term seizures is used indiscriminately in some studies. All people with epilepsy experience seizures, but not all individuals with seizures have epilepsy. Almost all the studies are prevalent case series, which are not useful for identification of the cause of seizures. Studies of highly selected patients with epilepsy (or seizures) in neurological departments of hospitals from some Latin American countries report neurocysticercosis as the main cause of epilepsy, accounting for 30–50% of patients. Surprisingly, the proportion of epilepsy cases associated with cysticercosis, with an immunoserological test as a diagnostic tool, is much lower than the proportion of neurocysticercosis diagnosed by CT. Only 12% of epileptic patients attending an outpatient clinic in Peru had serological evidence of *T solium* as shown by the EITB. In a prospective cohort study among patients with newly diagnosed epilepsy seen at the five main hospitals in the three major cities of Ecuador, the ratio of idiopathic or cryptogenic (63%) to symptomatic epilepsy (37%) is similar to the ratio in studies from more developed countries.

Although neurocysticercosis is one of the most frequent antecedents (8.3%) among the symptomatic group, this disease is not the main cause of epilepsy, as has been suggested previously. There are clinical inconsistencies in the link between epilepsy and neurocysticercosis. Parasite location can be remote from the apparent epileptogenic region. There is also no correlation between the neurocysticercosis burden of lesions and the severity of the epilepsy. Some patients with severe refractory seizures have only one calcified lesion; by contrast, other patients have many cysts or calcifications but no epilepsy. Neurocysticercosis and epilepsy are common diseases in most less developed countries. Because of their high prevalence, there could be a causal as well as fortuitous relation between the two disorders.

**Single enhancing lesion and seizures**

A single enhancing lesion on CT or hyperintense lesion on MRI is a common finding in patients with newly identified seizures in less developed countries. In most cases, the lesion is small, 5–10 mm, well defined, annular or nodular contrast-enhancing, cortical or subcortical, generally associated with perilesional oedema and little mass effect, without any midline shift. Most of the patients, mainly children and young adults, have some benign and transitory clinical manifestations, predominantly partial seizures alone or with secondary generalisation, and, in some, Todd’s paresis or focal neurological deficits. These lesions have been attributed mainly to cysticercosis or tuberculosis; however, similar lesions have been reported in other...
Neurocysticercosis

Inflammatory disorders such as pyogenic abscess, histoplasmosis, blastomycosis and sarcoidosis, and postinfectious vasculitis, and in primary and metastatic brain tumours.

The natural history of these lesions generally takes one of two forms: it becomes isodense on CT or isointense on MRI then either resolves entirely or leaves a punctuate calcification as a residue. The time to resolution of the lesion varies from a few weeks to more than a year. Some clinicians empirically administer cysticidal therapy, assuming that such drugs will accelerate the resolution of the parasite. On the basis of results from a controlled clinical trial, Padma and colleagues concluded that albendazole therapy was unnecessary. A single enhancing lesion on CT is benign and tends to resolve spontaneously, without anticycticeral drugs or surgery, since the parasite is already in the degenerative phase and will eventually disappear or become calcified. Treatment should be limited to that required to control the acute symptoms, such as epilepsy (figure 7).

Diagnosis

Diagnosis of neurocysticercosis on clinical grounds is difficult, because signs and symptoms are non-specific. Some neuroimaging findings are not pathognomonic either, and the serological tests have low sensitivity and specificity. The only truly reliable gold standard is pathologival confirmation through biopsy or autopsy. These procedures have obvious limitations.

Although to date there are no trustworthy data on the specificity and sensitivity of neuroimaging diagnostic studies, CT and MRI are the main tools in neurocysticercosis diagnosis and can be taken as a gold standard. Demonstration of viable cystic lesions with a mural nodule (ie, the invaginated scolex), associated with transitional or degenerative cysts and calcifications is a typical image of cysticercosis (figure 5). However, this typical image is not necessarily the most common. Single enhancing lesions are probably more common, especially in children, though in these cases some other aetiologies should be considered in the differential diagnosis to avoid unnecessary neurosurgical interventions. MRI is superior for showing intraventricular or subarachnoid cysts, but CT is better for showing the calcification of inactive lesions.

Other laboratory studies are useful to complement neurocysticercosis diagnoses. Inflammatory changes in the CSF are largely related to an extraparenchymal location, especially with arachnoiditis. The most consistent finding is moderate mononuclear pleocytosis, not exceeding 0.2–0.3 × 10^6/L in most cases. Protein concentrations are also higher than normal, to within the range of 0.5–2.0 g/L. CSF glucose concentrations are normal or moderately low. The CSF abnormalities, including signs and symptoms of arachnoiditis or chronic meningitis, are difficult to distinguish from those of granulomatous infections, such as tuberculous meningitis.

Electroencephalographic (EEG) findings show little relation to symptoms and CT lesions in patients with neurocysticercosis. EEG was abnormal in 30–50% of patients with seizures due to neurocysticercosis in one study. A positive relation between CT lesions and localising or lateralising EEG abnormalities has been reported for only 15–30% of patients. Similarly, the correlation between seizure type and EEG abnormalities ranges from around 7% to 20%. Since the epileptogenicity of cysticercotic lesions is probably low for residual calcifications, some investigators consider any association between the EEG focus and lesion to be a chance finding.

Clinicians from more developed countries should consider epidemiological information, such as place of birth, residence, and travel to endemic countries, in diagnosis of neurocysticercosis. They should also be aware that the disorder can be acquired from a tapeworm carrier and can therefore be diagnosed in individuals born in non-endemic countries who have never travelled to endemic regions. In that case, a search for a contact with a tapeworm infection is advisable. This finding will support the diagnosis of neurocysticercosis in a patient with suggestive imaging and immunological criteria. A recent report proposed a series of diagnostic criteria for neurocysticercosis, with a combination of clinical, radiological, serological, and epidemiological factors. This system has been criticised for its complexity and for difficulties in clinical and epidemiological application. The proposed criteria must be properly validated, and a satisfactory consensus is yet to be reached.

Immunodiagnosis of cysticercosis

Immunodiagnostic methods are available to detect antibodies that indicate present or past infection, as well as circulating antigens that indicate current infection. Complement fixation, indirect haemagglutination, ELISA, and EITB are among the types of immunodiagnostic assays

Figure 8. Probability of seizure recurrence (Kaplan-Meier curve) after a first seizure in patients with neurocysticercosis as a function of anthelmintic treatment.
Neurocysticercosis

that have been developed. Nowadays, the EITB and ELISA are the tests most frequently used for diagnosis of human cysticercosis. Although EITB is accepted as the best immunological diagnostic test available today, ELISA continues to be used extensively for epidemiological surveys, mainly because it is technically simpler than the EITB. However, many ELISAs have high false-positive and false-negative rates, with a sensitivity of 50% and a specificity of 65% for neurocysticercosis, so results should be interpreted with caution. Some studies have found that serum EITB is highly sensitive (more than 90%) and specific for the diagnosis of human cysticercosis, but in patients with a single brain cyst the sensitivity was only 25%. An EITB is less likely to show a positive result in a patient with calcified lesions than in one with active or transitional cysts. Furthermore, the EITB may become negative after the cysticercus dies. A weakness of this test for diagnosis of neurocysticercosis is that it can be positive in patients with taeniosis. A positive EITB result is of less diagnostic value in patients from areas where cysticercosis is endemic. Conversely, a negative EITB result does not exclude a diagnosis of neurocysticercosis in patients with a single cyst or in those with brain calcifications as the only evidence of the disease.

Another limitation of antibody-based tests is that the presence of antibodies may indicate only previous exposure to or infection with the parasite and not necessarily current viable infection. Furthermore, two-thirds of seropositive individuals have no lesion identifiable on CT. Thus, the presence of antibodies does not constitute direct evidence of a living parasite within the host. To overcome these limitations, several attempts have been made to develop antigen-based assays in the belief that the detection of antigens should indicate the presence of live and active cysticerci. These tests include antigen detection assays based on polyclonal and monoclonal antibodies. Preliminary evidence suggests that differentiation between *T solium* infection due to adult and to metacestode forms may be possible, as may distinction of live and dying-degenerating stages of cysticercosis. This possibility needs further confirmation. PCR assays for the detection of *T solium* eggs, proglottids, and larval material from human and porcine tissues have also been explored. These methods still need to be evaluated in comparison with conventional parasitological methods in both clinical and epidemiological settings.

**Diagnosis of taeniosis**

Definitive diagnosis of tapeworm carriage is achieved by demonstration of ova, proglottids, or both in stool samples. However, because eggs are excreted intermittently, this method underestimates the prevalence of taeniosis. Although microscopic parasitological techniques are simple and inexpensive, they lack sensitivity and specificity. A serological assay has been developed for detection of human taeniosis; it is an immunoblot assay, EITB-T, which uses coproantigens of adult *T solium* tapeworms. Studies with coproantigen detection have shown that these assays are more sensitive than microscopy.

**Treatment**

The treatment of neurocysticercosis should be based on the pathogenesis and natural history of the disease in each individual patient. Therapy in most cases is limited to symptomatic treatment with antiepileptic drugs for seizures. Mannitol or oral glycerol is used if high intracranial pressure is a feature, because such treatment is justified with many other intracranial mass lesions. Suitable analgesics should be given for relief of headache. Corticosteroids are commonly administered in neurocysticercosis on the premise that they reduce inflammation and oedema around dying parenchymal cysts and are also recommended for treatment of large subarachnoid cysts, arachnoiditis, and cysticercotic encephalitis. However, the dose, duration, form, mode, and, most importantly, timing of administration of corticosteroids are not clear. Neurosurgical intervention should be considered for hydrocephalus requiring ventriculoperitoneal shunt, accessible racemose cysts in the basal cisterns, or a cyst in an intraventricular location. Transitional or degenerative cysts, of any size or location (figure 6), should not be sampled or removed because the parasite is dead and will disappear or be calcified spontaneously.

There are no guidelines on the time for which antiepileptic drugs should be continued after an acute episode of neurocysticercosis. The risk of seizures is substantial as long as there is an active process, as shown by persistence of oedema around the degenerating lesion. CT or MRI are useful for treatment decisions. Seizures in the context of oedema and a degenerative lesion should be considered acute symptomatic seizures even if they occur many months after presentation. After resolution of the acute lesion, antiepileptic drugs can be discontinued. Seizures occurring after resolution of oedema or calcification of the degenerating cyst should be considered unprovoked, and long-term antiepileptic drugs are warranted (figure 7). Some researchers suggest that antiepileptic drugs can safely be withdrawn once the follow-up CT shows resolution of the lesion. Seizure recurrence occurred in about 20% of patients with cyst resolution—a proportion in accord with studies on the risk of unprovoked seizures among individuals with structural brain abnormalities and acute symptomatic seizures.

**Controversies in anthelmintic drug treatment**

Although the first reports on treatment of neurocysticercosis with cysticidal or anthelmintic drugs, such as praziquantel and albendazole, were published more than 15 years ago, controversies persist about their use in neurocysticercosis. Many authors have criticised publications on this topic and have concluded that no adequate studies of efficacy have been reported. Others have warned that this therapy might be harmful in some patients, particularly with subarachnoid cysts, because the drugs might lead to the development of arachnoiditis and arteritis, and consequently hydrocephalus.

A systematic review by the Cochrane Collaboration aimed to assess the effect of drug treatment in human neurocysticercosis in relation to survival, cyst resolution on imaging studies, subsequent seizures, and hydrocephalus. It included randomised or quasi-randomised trials that...
compared an anthelmintic drug with placebo or a control group receiving symptomatic therapy in patients with neurocysticercosis. Only four studies, involving 305 people, met the inclusion criteria. A difference just approaching significance was detected between anthelmintic therapy and placebo in relation to cyst persistence up to 6 months (relative risk 0.83 [95% CI 0.70–0.99]). Two trials reported on seizures after 1–2 years of follow-up and found no difference (relative risk 0.95 [0.59–1.51]). In our study, no difference was detected for hydrocephalus (relative risk 2.19 [0.29–16.55]).

The systematic review concluded that there was insufficient evidence to assess whether treatment with anthelmintic drugs is associated with beneficial results in neurocysticercosis. The authors emphasised that clinicians should be aware of the lack of evidence either to support or to refute the use of anthelmintic drugs in neurocysticercosis. This lack of evidence, added to the potential harm recognised with treatment, means that the clinicians have to weigh the benefits and risks of AHD (anthelmintic drugs) very carefully in each individual patient. Two randomised, placebo-controlled, double-blind clinical trials are under way in Ecuador (http://www.cysti.org) and Peru to assess whether albendazole added to symptomatic treatment influences resolution of lesions and long-term clinical outcome. The results of these studies are eagerly awaited.

A recent review by Singhal and Salinas analysed the controversies in the drug treatment of neurocysticercosis. The authors concluded that duration and dose schedule of therapy with praziquantel and albendazole also remain uncertain, and they recommended more double-blind controlled studies to assess the efficacy of these drugs with different dose and duration schedules.

Garcia and colleagues in a recent report proposed guidelines for treatment of neurocysticercosis. They summarised the guidelines using levels of recommendation and quality of evidence. There was only one type of neurocysticercosis (enhancing lesion or degenerating cysts) that they categorise as evidence class I and for which they recommend no antiparasitic treatment. All other types of neurocysticercosis were categorised as levels of evidence class II or III, for which they recommended antiparasitic treatment. However, according to standards of evidence-based clinical practice, evidence of class I is provided only by prospective, randomised, controlled clinical trials with masked outcome assessment, in a representative population.

Therefore, this report confirms the conclusions of the Cochrane systematic review in the sense that there is insufficient evidence to assess whether treatment with anthelmintic drugs is associated with beneficial results in neurocysticercosis.

**Prognosis**

In the landmark papers on cysticercosis in British troops stationed in India, Dixon and Lipscomb observed that “many patients improved spontaneously, and the prognosis is much better than has hitherto been thought”. In fact, parenchymal forms of neurocysticercosis have a good prognosis in terms of remission of clinical signs. However, the prognosis for extraparenchymal forms is unfavourable, especially for patients with hydrocephalus due to arachnoiditis.

Some authors report that neurocysticercosis with acute symptomatic seizures has a good prognosis in terms of remission of seizures; others report that most patients have a high risk of seizure recurrence and suggest that prognosis improves after anthelmintic treatment.

Our recent prospective cohort study assessed the risk of seizure recurrence after a first seizure due to neurocysticercosis and evaluated risk factors for seizure recurrence, including the influence of anthelmintic treatment. Seventy-seven patients were prospectively followed up for longer than 7 years. Thirty-one patients experienced seizure recurrence. The Kaplan-Meier estimated risk of recurrence was 22% at 6 months, 32% at 12 months, 39% at 24 months, and 49% at 48 months and 84 months. Treatment with albendazole did not influence risk of recurrence. There were no significant differences in the Kaplan-Meier curves of recurrence when treatment groups were compared (figure 8).

We concluded that the risk of seizure recurrence is high after a first acute symptomatic seizure due to neurocysticercosis, but the risk seems related to persistence of active brain lesions. The risk is low, and similar to that after other brain insults leading to a static encephalopathy, in patients whose neurocysticercosis lesion clears.

**Vaccination**

Vaccination against taeniosis is not immunologically or logistically feasible at present, because the occult nature of the infection makes tapeworm carriers difficult to detect, and the minor morbidity associated with intestinal infection also makes taeniosis a poor candidate for human vaccine development.

Human protective or therapeutic vaccinations to prevent cysticercosis have not been widely considered as an appropriate intervention in endemic regions because little is known about the immunology of human cysticercosis. There is no evidence of protective immunity against cysticercosis in human beings and little prospect of human vaccination against this parasite in the foreseeable future.

Vaccination of pigs is an appealing strategy to break the parasite's life cycle. Much progress has been made in this endeavour. Field trials have already shown the usefulness of vaccines derived from cysterceral extracts, and recombinant vaccines are probably effective under controlled conditions. Rapid progress with the sequencing and comparison of antigens from *T solium* and related parasites makes the development of more effective *T solium* vaccines likely.
Neurocysticercosis

Prevention

The most effective approach to the eradication of taeniosis and cysticercosis is prevention, which should be a primary public-health focus worldwide.1,13 Neurocysticercosis is associated with enormous costs for antiseizure medication, medical resources, and lost production; a group of investigators has therefore proposed that it should be declared an international reportable disease.14 Human taeniosis and cysticercosis can be controlled by provision of sanitation and improvement of public-health systems. Prevention by enforcing meat inspection and adequate freezing or cooking of pork can break the parasite’s life cycle. Preventing pigs from roaming free might help to prevent porcine cysticercosis, which would scale-large commercial pig rearing that denies the animals access to human faces. Anthelmintic treatment will not eradicate neurocysticercosis, unless the health system and sanitary infrastructure improves.

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Conflicts of interest

I have no conflicts of interest to declare.

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