Neurocysticercosis
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Introduction

This article includes discussion of neurocysticercosis and “mealy” pork disease. The foregoing terms may include synonyms, similar disorders, variations in usage, and abbreviations.

Overview

Neurocysticercosis continues to be the most common CNS parasite and is becoming increasingly identified in the United States. Most patients in the United States present with seizures (focal or generalized) or headaches and have come from Mexico or Latin America. A new set of diagnostic criteria have been published. There are now 3 serological methods of diagnosing neurocysticercosis. A serum or CSF antibody assay, especially an enzyme-linked immunotransfer blot assay, is quite sensitive and specific, and is widely available. A new PCR-based assay to detect T. solium nucleic acid is more specific and is becoming more available. The third assay detects cysticercus antigen. This assay is the most valuable in diagnosing extraparenchymal neurocysticercosis in the ventricle or meninges and can be utilized to follow patient response to treatment. It appears that the cysticercus cyst releases specific proteins that induce an anti-inflammatory host response to prevent the host from destroying viable cerebral cysts. Although some controversy continues regarding the necessity of treating single neurocysticercosis cysts in developing countries, studies, including a 2013 guideline published in Neurology and a meta-analysis report, find that albendazole treatment significantly hastens the disappearance of cysts and reduces the incidence of seizures with generalization.

Key points

• Neurocysticercosis is the most common CNS parasite, with most U.S. cases coming from immigrants from Mexico and Latin America.
• Neurocysticercosis comes from eating viable cysts from human feces of individuals infected with the pork tapeworm and not from eating undercooked infected pork meat.
• So long as organisms remain viable in the brain, the patient is usually asymptomatic due to the parasite cyst producing proteins that prevent the host from initiating an inflammatory response to destroy the cyst.
• Seizures are the most common clinical manifestation, and headaches are the second most common.
• Diagnosis is usually made by demonstration of typical cysts on MRI or CT scan plus presence of cysticercosis enzyme-linked immunoelectrotransfer blot antibody assay in serum or CSF.
• Treatment of parenchymal cysts using albendazole with or without corticosteroids hastens disappearance of parenchymal cysts and reduces rate of seizure recurrence, but treatment of extraparenchymal cysts in meninges or ventricles is difficult and often requires ventricular shunting and repeated courses of albendazole and long-term steroids.

Historical note and terminology

Cysticercosis is a zoonotic infection involving pigs and man and has an ancient history (Del Brutto and Garcia 2015). Tapeworms have been found in 3000 B.C. Egyptian mummies. Human tapeworms were recognized by Hippocrates, and “mealy” pork containing cysticerci were described by Aristotle. Cysticercosis likely was recognized early on as dangerous to humans in that the ancient Hebrew Bible forbid consumption of pork and the ancient Koran also forbid pork consumption.
**Clinical manifestations**

**Presentation and course**

Neurocysticercosis is clinically a pleomorphic disease that may be asymptomatic or manifest a variety of nonspecific mild to severe neurologic syndromes. Clinical signs in neurocysticercosis depend on the number, size, and stage of cysts, CNS location, and severity of inflammatory response against the parasites (see Table 1). In general, cysticerci do not produce clinical symptomatology until the cyst begins to die. The inflammatory reaction triggered by the cyst degeneration produces clinical symptoms such as seizures, headaches, altered mental status, and focal neurologic signs like hemiparesis, visual loss, and paraparesis.

**Table 1. Presenting Signs and Symptoms in Patients with Neurocysticercosis**

<table>
<thead>
<tr>
<th>Signs and symptoms*</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Seizures</td>
<td>75%</td>
</tr>
<tr>
<td>• Headaches</td>
<td>35%</td>
</tr>
<tr>
<td>• Altered mental status (confusion, dementia, stupor)</td>
<td>15%</td>
</tr>
<tr>
<td>• Focal neurologic signs (hemiparesis, visual loss, paraparesis)</td>
<td>10%</td>
</tr>
<tr>
<td>• Signs of elevated intracranial pressure</td>
<td>10%</td>
</tr>
<tr>
<td>• Signs of meningitis</td>
<td>8%</td>
</tr>
<tr>
<td>• Asymptomatic and incidental</td>
<td>20%</td>
</tr>
</tbody>
</table>

Patients may present with more than 1 sign. Estimated from author's personal experience and the following references (Dixon and Lipscomb 1961; Tasker and Plotkin 1979; Loo and Braude 1982; McCormick 1985; Earnest et al 1987; Shandra et al 1994; Carabin et al 2011; Serpa et al 2011; Gonzales et al 2016).

Seizures, either focal or generalized, are the most common presenting complaint and occur in up to 75% of patients (Del Brutto et al 1992; Carabin et al 2011; Serpa et al 2011). Most patients have a normal neurologic examination. However, a study from Brazil reported dementia in 13% of patients (Ciampi de Andrade et al 2010). Longitudinal studies suggest that cognition improves with treatment (Wallin et al 2012).

Headaches are the second most common clinical manifestation. The headache has several causes and may come from intracranial hypertension. The intracranial hypertension has several etiologies, but often is related to obstructive hydrocephalus from meningeal cysts causing chronic arachnoiditis or from ventricular cysts producing ependymitis or directly blocking CSF pathways. Obstructive hydrocephalus should be considered a neurosurgical emergency. Occasional patients develop focal neurologic signs from a lacunar stroke due to vasculitis (Del Brutto 1992).

Headaches with or without meningismus from chronic meningitis occur in about 20% to 35% of patients. In many of these patients, the cysticercus is located in the meninges and can produce hydrocephalus (Mahale et al 2015). Children younger than 15 years of age tend to present with more seizures and less headaches than adults with neurocysticercosis (Saenz et al 2006).

Patients with 1 or 2 cysts may never develop clinical symptoms. However, those that do tend to have seizures. The rare patient who is infested with hundreds of brain cysts will develop early clinical symptomatology, beginning weeks to months after the original infestation. Their brains may show many areas of intense inflammation with marked cerebral edema (Rangel et al 1987; Jain et al 2014). These patients often develop focal neurologic signs and signs of increased intracranial pressure.

Individuals with a concomitant *T. solium* tapeworm are at higher risk of autoinfection and have been shown to have a much higher number of brain cysticerci than individuals without a tapeworm (Gilman et al 2000). However, most individuals with CNS cysts lack gastrointestinal parasites. Individuals with only calcified cysts seldom have new neurologic signs and symptoms, but may have continued seizures.

**Prognosis and complications**

Most patients with only parenchymal neurocysticercosis have an excellent prognosis. Many remain asymptomatic throughout the entire infection. However, those with intraparenchymal cysts often develop transient acute symptoms during cyst degeneration, but these often resolve within months to 2 years. Some patients develop epilepsy with either
focal or generalized seizures. Usually these seizures respond well to anticonvulsant therapy. The rare patient with large numbers of CNS cysts does poorly and may die from the overwhelming CNS infection (Jain et al 2014). Patients who develop chronic meningitis also may do poorly. Thirty percent to 60% of patients with active meningeal cisticercosis will develop obstructive hydrocephalus (Figueroa et al 2011). These patients, if untreated, may experience brain herniation and death (Keane 1984). The occasional patient with a cyst in the spinal cord may be left with paraparesis or quadriplegia (Akiguchi et al 1979). Patients who develop intraocular cysts may lose vision in the affected eye.

Clinical vignette

An 18-year-old high school exchange student visiting the United States from rural Mexico developed a generalized seizure. Several days later she experienced a second generalized seizure. Her general physical and neurologic exams were normal. Her CSF had a normal opening pressure without a pleocytosis or elevated protein. The MRI scan demonstrated 2 cystic lesions characteristic of neurocysticercosis. Serum cysticercosis enzyme-linked immunoelectrotransfer blot assay was positive. She was treated with albendazole and dexamethasone for 2 weeks and daily phenytoin. She had no further seizures, and follow-up CT scan 2 years later showed no cysts, at which time the phenytoin was discontinued.

Biological basis

Etiology and pathogenesis

Neurocysticercosis is caused by CNS infection of Taenia solium larva. In neurocysticercosis, humans are the intermediate host in which cysts develop in the brain parenchyma, meninges, or ventricular spaces.

The life cycle of T. solium involves pigs and humans. Humans may be the definitive host and become infected with tapeworm or be the intermediate host and become infected with the cysticercus (Mahanty and Garcia 2010).

Man as the definitive host with intestinal tapeworm. People become definitive hosts when they ingest insufficiently cooked pork that contains viable larvae of T. solium or larval cyst. Following ingestion of a living cysticercus, the cysticercus larva develops in the small intestine into a tapeworm 1 to 8 m in length. The tapeworm causes few clinical symptoms but can release terminal proglottids bearing up to 50,000 eggs per proglottid or 100,000 eggs per day. Terminal proglottids are passed into the stool liberating viable ova (Lawson and Gemmell 1983; Gripper and Welburn 2017).

If these ova are eaten by pigs through contact with contaminated human stools, the life cycle of the tapeworm continues with pigs as the intermediate hosts. The ova hatch and liberate the embryos or oncospheres that cross the intestinal wall, enter the bloodstream, and are carried into the tissues (especially muscle) where they lodge and develop into larval cysts. The mature infectious 5 to 15 mm diameter transparent cyst develops in about 2 months. The life cycle continues when humans eat undercooked “mealy” pork that contains the viable cysticercus.

Man as intermediate host with neurocysticercosis. Neurocysticercosis develops when humans become the intermediate host. In about 95%, this infection occurs when the individual accidentally ingests ova from a close contact with a tapeworm carrier who failed to wash his hands after defecation. Transmission from ingestion of uncooked vegetables irrigated by water contaminated with human feces occurs less often (Garcia et al 2003a; Garcia et al 2003b). In the remaining 5% to 15%, the patients have an intestinal tapeworm, and the patient becomes self-infected via the fecal-oral route (Loo and Braude 1982; McCormick et al 1982; Gilman et al 2000).

The ingested T. solium ova are partially digested in the stomach, releasing oncospheres that penetrate the stomach and intestinal mucosa to reach the bloodstream. These oncospheres may lodge in any body tissue in humans but show a predilection for the brain. Less common sites include the eye, heart, skeletal muscle, and subcutaneous tissue. In the brain, the oncospheres commonly lodge in small cerebral blood vessels located between the gray and white matter. The oncosphere then appears to burrow through the vessel wall into the adjacent brain or into the leptomeninges, often deep within the sulcus (Thomas et al 1989). Oncospheres may also lodge in the meninges, ependyma, and choroid plexus of the ventricles. Cysts involving the spinal cord are unusual (McCormick et al 1982), but have been reported to be present in patients with extraparenchymal cysticercosis (Nash and Garcia 2011).
Beginning weeks after ova ingestion, the larva creates a small edematous lesion in the brain. Several weeks later, the larva develops into a cyst with a protoscolex surrounded by a bladder wall. At this early stage, the cyst is tiny (1 to 3 mm in diameter). Little adjacent inflammation is present. The cyst continues to expand and becomes mature about 2 months after ova ingestion. The cyst has a protoscolex and a clear fluid filled bladder that is 3 to 18 mm in diameter (Escobar 1983). The viable cyst is often called the vesicular cyst stage. The living cyst evokes only a minimal surrounding inflammation and remains viable from 2 to more than 10 years. The mechanisms employed by helminths, including cysticercosis to prevent aggressive host inflammation against the parasite, are poorly understood. There is evidence that helminth glycans can induce an anti-inflammatory milieu via toll-like receptor 4-dependent mechanisms, which modulate host cytokine responses (Verma et al 2011).

Over years, the osmotic barrier of the cyst wall breaks down. At this time the clear cyst fluid thickens and becomes more opaque, the cyst wall thickens, and hyaline degeneration and mineralization begin. The cyst wall begins to leak cysticercosis antigens, eliciting an intense inflammatory reaction in the adjacent brain that produces adjacent cerebral edema. The immune response is both humoral and cell mediated, including eosinophils and mast cells (Rolfs et al 1995). In response to the inflammation, fibroblasts may form a capsule-like structure surrounding the cyst. The degenerating cysts are often called colloid cyst stage. The colloid cyst stage may persist for months to 1 to 2 years. At this stage, patients typically develop clinical symptoms. The inflammation often is sufficient to trigger seizures.

When the cysticercus dies, the bladder wall collapses to form a small granuloma. Months to years later some of these dead cysts become calcified into 1 to 6 mm nodules (called the calcified phase or nodular calcified stage); more often the lesion disappears on neuroimaging. When the cyst calcifies, some cysts develop an active perilesional gliosis, which predisposes to chronic seizures and can be detected by dynamic contrast-enhanced MRI (de Souza et al 2011; Gupta et al 2012).

At least 5% to 15% of cysticerci lodge in the meninges or ventricular spaces. These patients usually develop clinical symptoms requiring hospitalization. It is now recognized that although less common than parenchymal cysts, extraparenchymal neurocysticercosis is presenting clinically more commonly than previously recognized (Figueroa et al 2011; Serpa et al 2011; Kelesidis and Tsiodras 2012). In the subarachnoid space, some cysticerci grow to over 5 cm in diameter. These giant cysticerci often produce focal neurologic signs and increased intracranial pressure with headaches and papiledema (Del Brutto et al 1992; Proano et al 2001; Bazan et al 2016). Other cysticerci in the subarachnoid space or ventricles never develop a protoscolex and produce a grape-like or racemose structure (Bickerstaff et al 1952; Mahale et al 2015). These nonviable cysts frequently leak foreign antigens into the CSF, producing ventriculitis, ependymitis, chronic meningitis, or arachnoiditis. Over time, the arachnoiditis may obstruct CSF pathways, particularly at the level of the basal cisterns. Occasional lateral ventricular cysts may dislodge and travel until they reach the aqueduct of Sylvius, where they obstruct the CSF pathway, producing acute obstructive hydrocephalus (Figueroa et al 2011). Patients with basal subarachnoid neurocysticercosis may also have spinal cysticercosis (Callacando et al 2012).

In a large series of neurocysticercosis, the incidence of strokes ranged from 4% to 12% (Marquez and Arauz 2012). Most strokes occurred secondary to meningeal inflammation, causing vasculitis in adjacent blood vessels leading to vessel thrombosis. Lacunar strokes in the basal ganglia and brainstem are the most common and have often occurred due to thrombosis of branches of the lenticulostriate artery or penetrating basilar artery branches (Del Brutto 1992). Intramedullary cysticercosis of the spinal cord is quite uncommon. A literature review reported that most patients had a single cyst located in the thoracic spinal cord and presented as a subacute or chronic transverse myelopathy (Del Brutto and Garcia 2015). The MRI demonstrates a cyst surrounded by edema with a ring-like pattern of abnormal enhancement. Some patients were treated medically but others required surgical cyst removal. Many patients made a good recovery. Meningeal cysts also can develop in the spinal meninges.

In summary, the clinical features of neurocysticercosis develop from the cyst producing inflammation (most important), mass effect, and mechanical obstruction of CSF pathways.

**Epidemiology**

Cysticercosis is the most common parasitic infection of the human CNS. The World Health Organization estimated that cysticercosis has the highest global and regional disease burdens in 2010 for foodborne parasitic diseases (Torgerson et al 2015). Most cases of cysticercosis occur in the countries of Latin America, Africa, East Asia, India, and China.
Progress is being made in the development of a vaccine to prevent cysticercosis in pigs; the vaccine could prevent developing either the tapeworm or neurocysticercosis unless they visit rural areas.

In rural Latin America, the prevalence of neurocysticercosis can be high. One study reported a 3% prevalence, with about 6% of the inhabitants giving a history of passing tapeworm proglottids in their feces (Bern et al 1999). Towns in rural Peru have reported prevalence rates as high as 36% (Moyano et al 2016). Two autopsy series from Brazil found a prevalence rates of 2.4% and 0.8% (Lino-Junior Rde et al 2007; de Almeida and Torres 2011). In Peru, a study reported a marked economic burden on that country’s individuals with neurocysticercosis. Patients were found to have a 54% loss of annual minimum wage salary during the first year after diagnosis, with drug costs representing 27% of the burden. Two thirds of wage earners lost their jobs, and only 61% were about to re-engage in wage-earning activities (Rajotia et al 2007). On the positive side, reports from Mexico suggest the prevalence of neurocysticercosis is falling due to the better public health of its citizens (Flisser and Correa 2010).

The actual number of individuals who have been infected with cysticercosis is unknown because patients often lose serum antibody positivity following resolution of their solitary cyst. Thus, the actual prevalence is likely higher than reported.

Neurocysticercosis is a growing public health problem in the United States (Montano et al 2005). There has been an increase in the immigration of individuals from Mexico and Latin America into the United States. This immigration has resulted in an increased prevalence of neurocysticercosis in the United States, particularly in the Southwest, where it accounts for up to 10% of emergency room visits for seizures. In geographically diverse emergency rooms in the U.S., 13.5% of Hispanic patients presenting with seizures have neurocysticercosis (Ong et al 2002). A survey of a Hispanic residential community and 2 farm camps in Southern California found a cysticercosis antibody prevalence of 1.8%, a frequency approaching some endemic areas in Latin America (DeGiorgio et al 2005). Neurocysticercosis is now recognized in all states (Ong et al 2002). The prevalence of neurocysticercosis ranges from 0.2 to 0.6 per 100,000 inhabitants in some western U.S. states (Coyle et al 2012). Neurocysticercosis rarely develops in American tourists visiting Mexico or Latin America (McCormick 1985) or in tourists from Israel visiting endemic countries (Leshem et al 2011). However, occasional cases are seen in U.S. citizens who have never traveled to endemic countries (McCormick et al 1982). In Houston Texas, 18% of 114 patients with neurocysticercosis were born in the United States (Schantz et al 1992; del la Garza et al 2005). A literature review of U.S. cases from 1954 to 2005 found only 78 cases, with the likely source of exposure being household members or close personal contacts in 21% (Sorvillo et al 2011). This may be a low estimate because tapeworms usually persist in the intestine only a few years. However, their contacts consuming the ova may not develop degenerating cysts for many years, so searching for ova in the stools of household members may not yield the source (Gonzales et al 2016).

The cost of hospitalization for neurocysticercosis is considerable. United States data from 2003 to 2012 estimated 23,266 hospitalizations with a mean hospital stay of 6 days and a cost of $1,149,000 (O'Neal and Flecker 2015). Seizures, obstructive hydrocephalus, and headaches were the most common reasons for hospitalization. An analysis of treatment costs in Mexico City, Mexico reported the average direct costs were U.S. $503 for outpatient care and U.S. $2506 when hospitalization was necessary (Bhattarai et al 2015).

Patients with neurocysticercosis in the endemic country can be of any age, from early childhood to elderly, but the majority of cases are in older children and young adults. Most cases in the U.S. are discovered in those immigrating to the U.S. and are young adults, with a mean age of 27 years (Serpa et al 2011; Croker et al 2012).

Prevention

To prevent development of the intestinal tapeworm, all pork should be thoroughly cooked prior to eating (Biagi et al 1963). Freezing pork to -20°C for several days will also inactivate cysticerci (Sotelo et al 1986). Smoked or dried pork may still contain viable cysticerci. Prevention of neurocysticercosis is accomplished by avoiding ova-contaminated food and water. In endemic areas, consumption of raw vegetables should be avoided because they may be contaminated with human fertilizer. Heating food above 60°C or freezing below -30°C is usually sufficient to kill ova (Lawson and Gemmell 1983). Restaurant workers from endemic areas should have their stools routinely checked for the presence of tapeworm ova. However, American tourists visiting Mexican and South American countries appear to be at little risk of developing either the tapeworm or neurocysticercosis unless they visit rural areas.

Progress is being made in the development of a vaccine to prevent cysticercosis in pigs; the vaccine could prevent
transmission of the pig tape worm to humans if widely used in Latin American countries (Lightowlers 2006). However, the vaccine cost to a poor farmer will be a problem for widespread usage.

**Differential diagnosis**

The differential diagnosis of neurocysticercosis depends on the type of clinical presentation. If cysts are identified on CT or MRI scan, major diagnoses to be considered include tuberculoma, brain abscess, syphilitic gumma, arteriovenous malformation, metastatic tumor, small primary tumor, or other parasitic cysts, such as schistosomes or amoebas. Tuberculomas tend to be larger than 20 mm in diameter, have an irregular outline, cause more mass effect, and have a progressive focal neurologic deficit, whereas T. solium cysts tend to be less than 20 mm in diameter, have smooth regular outline, and seldom cause progressive focal neurologic deficits (Sotelo et al 1986). Diffusion-weighted imaging typically shows hyperintense brain abscesses with low apparent diffusion coefficient values compared to non-brain abscess lesions such as neurocysticercosis (Reddy et al 2006). At times, neuroimaging of cysticercosis resembles malignancy, but it can often be distinguished using 18F-FDG PET/MRI (Jolepalem and Wong 2014). A review on ocular parasitic disease nicely discusses the differential diagnosis of ocular parasites (Das et al 2016).

If the patient presents with a subacute or chronic meningitis or obstructive hydrocephalus, tuberculomas meningitis, fungal meningitis, cerebrovascular syphilis, neurosarcoidosis, meningeal carcinomatosis, and CNS vasculitis need to be considered. The presence of CSF eosinophils above 10% increases the probability of meningeal cysticercosis but is uncommonly present.

**Diagnostic workup**

The diagnosis of neurocysticercosis should be considered, especially in young adults from countries endemic for cysticercosis who present with the new onset of focal or generalized seizures, unexplained subacute meningitis, obstructive hydrocephalus, unexplained strokes, or CNS cystic masses. The clinical diagnosis is established if the CT or MRI demonstrates intraparenchymal cysts showing the protoscolex, or a typical cystic lesion in a patient who has anticysticercus antibodies in CSF or serum.

Neuroimaging with CT or MRI is extremely helpful (Davis 2005). The MRI is more sensitive than CT for detection of cysts, and the delayed gadolinium-enhanced T1 sequence is the most sensitive (by about 9 minutes) (Lucato et al 2007). There are 2 excellent reviews of neuroimaging in the stages of neurocysticercosis (Hernandez et al 2014; Venkat et al 2016). MRI sequences called Fast Imaging Employing Steady-sTate Acquisition (FIESTA), T2 Star-Weighted ANgiography (SWAN), and SPOiled Gradient Recalled echo (SPGR) are detecting the cyst scolex in 83% compared to 45% by routine sequences (Kumar et al 2016). This is a huge advantage in distinguishing tuberculomas from neurocysticercosis. CT is more sensitive than MRI for detecting calcified inactive cysts.

Early in the infection, CT scans usually show small homogeneous contrast enhancing lesions that are somewhat ill defined. As the cyst matures, 3 to 18 mm noncontrast enhancing cysts will be seen without significant adjacent edema. These cysts are typically scattered throughout the brain parenchyma often near the gray-white matter junctions. As the cyst begins to degenerate, neuroimaging demonstrates a ring-contrast-enhancing cyst with adjacent edema. MRI scan with the administration of gadolinium demonstrates ring enhancement on T1-weighted images. Occasionally, giant cysts are seen measuring several centimeters in diameter. After the cyst has degenerated, the cyst walls collapse and the cyst becomes isodense to brain parenchyma on CT scan. Over months to years, some cysts will calcify and be identified as calcific nodules 2 to 6 mm in diameter. These calcific nodules are often difficult to identify by MRI (Zee et al 2000). Contrast enhancement and perilesional edema and gliosis may be seen around old calcifications in association with symptoms such as seizures (Nash and Patronas 1999; Zee et al 2000; Nash et al 2001; Poeschl et al 2006). Some patients may have both living cysts and calcified nodules due to repeat infections or delayed deaths of some cysts. In patients from endemic areas who often become repeated-infected, it is common to see patients whose CT scan shows both living cysts and calcified nodules. In developing countries, distinction between a tuberculoma and cyst from neurocysticercosis can be challenging. Identification of a protoscolex within the cyst diagnoses cysticercosis. In its absence, diffusion weighted MRI typically shows higher apparent diffusion coefficients in cysticercosis than tuberculomas (Gupta et al 2005). New advanced MRI sequences such as diffuse-weighted imaging (DWI/DTI), susceptibility-weighted imaging (SWI), 3-dimensional constructive interference in steady state (CISS), perfusion MR imaging, and magnetic resonance spectroscopy (MRS) can be helpful in diagnosing difficult
brain cysts (Venkat et al 2016).

Identification of cysts within the ventricles or meninges is often difficult and may have a varied presentation (Rodacki et al 1989; Figueroa et al 2011). The cyst fluid is usually isodense with CSF and may not enhance with contrast on CT. A study reported that use of intrathecal gadodiamide improves identification of subarachnoid and ventricular cysts even when cysts are not shown by conventional neuroimaging (Higuera-Calleja et al 2015). The cyst may be detected on the basis of distortion or disproportionate enlargement of the third or fourth ventricles. Use of nonionic contrast CT ventriculography may outline the cyst (Woody et al 1984; Suss et al 1986). However, in general the cysts are best detected by MRI. T2-weighted MRI images often do not detect viable intraventricular cysts but they can be distinguished from CSF on proton density images (Ginier and Poirier 1992; Figueroa et al 2011). T1-weighted images often demonstrate a thin bladder wall with a protoscolex within the CSF-isointense cystic fluid.

Results of blood hemograms, including the number of eosinophils, are usually normal. Table 2 outlines the common CSF findings in patients with neurocysticercosis. A CSF pleocytosis can result from a colloid intraparenchymal cyst located near the meninges leaking mononuclear cells into the CSF or from meningeal cisticercosis.

**Table 2. CSF in Neurocysticercosis**

<table>
<thead>
<tr>
<th>CSF finding</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated opening pressure (&gt;200 mm H20)</td>
<td>25%</td>
</tr>
<tr>
<td>Pleocytosis (&gt;10 WBC/mm3)</td>
<td>45%</td>
</tr>
<tr>
<td>Eosinophils in CSF (&gt;15%)</td>
<td>5%</td>
</tr>
<tr>
<td>Elevated protein (&lt;60 mg/dL)</td>
<td>40%</td>
</tr>
<tr>
<td>Increased IgG synthesis</td>
<td>75%</td>
</tr>
<tr>
<td>Oligoclonal bands</td>
<td>30%</td>
</tr>
<tr>
<td>Low glucose (&lt;40 mg/dL)</td>
<td>15%</td>
</tr>
<tr>
<td>Normal CSF</td>
<td>50%</td>
</tr>
<tr>
<td>Positive cisticercosis antibody test</td>
<td>95%</td>
</tr>
<tr>
<td>Pleocytosis and multiple cysts/normal CSF and solitary cyst or calcified cyst</td>
<td>30%</td>
</tr>
</tbody>
</table>

Adapted from (Davis 2005).

Serologic tests for cisticercosis have improved. Currently, the most sensitive and specific diagnostic test is an enzyme-linked immunoelectrotransfer blot assay that was initially developed by the Centers for Disease Control and Prevention (Tsang et al 1989). Studies have shown serum testing is highly sensitive (95%) and specific (98%) for patients with multiple cysts but less sensitive in detecting solitary cysts (28% to 70%) (Wilson et al 1991; Garcia et al 1994; Gekeler et al 2002). After the cisticercus dies, the patient's cisticercus antibody titer persists for a long time but eventually falls to undetectable levels. Thus, patients with only calcified cysts have a positive test ranging up to 88% for patients with multiple calcified cysts to as low as 10% for solitary calcified cysts. In general, the serum enzyme linked immunoelectrotransfer blot assay is as sensitive and specific as the test done on CSF (Rodriguez et al 2009).

Older serologic tests use unfractionated cisticercus antigens and include the enzyme-linked immunosorbent assay and complement fixation assay. These tests are cheaper but are associated with high rates of false positive and false negative reactions, giving the tests a sensitivity and specificity of about 70%. The sensitivity and specificity of these tests improves when CSF rather than serum is assayed.

An IgG monoclonal antibody based antigen detection enzyme-linked immunosorbent assay (Ag-ELISA) has been developed. The test is sensitive (up to 86%) for detection of cisticercus antigen in CSF, especially in meningeal cisticercosis. The antigen test may be helpful to diagnose atypical cisticercosis lesions and could be used to follow response to albendazole treatment (Bobes et al 2006; Rodriguez et al 2009; Abraham et al 2010; Fleury et al 2013). The test is less sensitive in serum, especially when only calcified lesions are present. A new polymerase chain reaction assay to detect T. solium DNA in CSF has shown a sensitivity of 67% if unconcentrated CSF is used but a sensitivity of 96.7% when the CSF is concentrated. This test is becoming more available, and it can also be used to follow clearance of the parasite in patients with meningeal cisticercosis. A modification of the antigen detection assay has been successfully used on urine in developing countries where rural patients were reluctant to have their blood or CSF drawn (Castillo et al 2009). However, the urine assays are less sensitive than serum or CSF assays.
Coming in the near future are global DNA screening platforms to detect specific DNA sequences from many infectious organisms simultaneously, using ribosomal RNA (rRNA) genes sequencing. A case report using this technology identified 2 biopsied space occupying brain masses as due to cysticercosis when standard histology of the tissue could not (Harrington et al 2009). Whether global DNA screening platforms are sensitive enough to detect cysticercosis in CSF in patients with chronic meningitis is currently unclear.

Table 3 compares the relative sensitivity of serological neurocysticercosis tests performed on CSF from patients with proven neurocysticercosis.

Table 3. Relative Sensitivity of CSF Neurocysticercosis Serological Tests*

<table>
<thead>
<tr>
<th>Cyst location by neuroimaging</th>
<th>Antibody test#</th>
<th>Antigen test+</th>
<th>PCR assayα</th>
</tr>
</thead>
<tbody>
<tr>
<td>All CSF samples</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Brain parenchymal vesicular</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Brain parenchymal colloidal</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Brain parenchymal calcified</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Ventricular or meningeal cysts</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
</tbody>
</table>

* Adapted from study using all 3 assays on 121 CSF samples with neurocysticercosis (Michelet et al 2011; Carpio et al 2017)

# Antibody assays were performed using enzyme-linked immunosorbent assay (ELISA) and enzyme-linked immunoelectrotransfer blotting (EITB) methods

+ Antigen test was detection of HP10 parasite antigen (in house assay)

α Polymerase chain reaction (PCR) assay detected the pTsol9 element of the genome

+++ assay score had sensitivity above 81%

++ assay score had sensitivity from 51% to 80%

+ assay score had sensitivity below 50%

In 2017, international cysticercosis experts published a revised diagnostic criteria for neurocysticercosis (see Table 4) (Del Brutto et al 2017). The new criteria updated current diagnostic criteria and emphasized neuroimaging studies as an important criteria.

Table 4. Revised Diagnostic Criteria for Neurocysticercosis*

**Absolute criteria:**
- Histologic demonstration of parasite from biopsy of brain or spinal cord lesion.
- Visualization of subretinal cysticercus.
- Conclusive demonstration of a scolex within a cystic lesion on neuroimaging.

**Neuroimaging criteria:**

**Major neuroimaging criteria:**
- Cystic lesions without a discernible scolex.
- Enhancing lesions.
- Multilobulated cystic lesions in the subarachnoid space.

**Confirmative neuroimaging criteria:**
- Resolution of cystic lesions after cysticidal drug therapy.
- Spontaneous resolution of single small enhancing lesions.
- Migration of ventricular cysts documented on sequential neuroimaging studies.

**Minor neuroimaging criteria:**
- Obstructive hydrocephalus (symmetric or asymmetric) or abnormal enhancement of basal leptomeninges.

**Clinical/exposure criteria:**

**Major clinical exposure:**
• Detection of specific anticysticercal antibodies or cysticercal antigens by well-standardized immunodiagnostic tests.
• Cysticercosis outside the central nervous system.
• Evidence of a household contact with *T. solium* infection.

**Minor clinical exposure:**
• Clinical manifestations suggestive of neurocysticercosis.
• Individuals coming from or living in an area where cysticercosis is endemic.

**Degrees of diagnostic certainty**

**Definitive diagnosis:**
• One absolute criterion.
• Two major neuroimaging criteria plus any clinical or exposure criteria.
• One major and one confirmative neuroimaging criteria plus any clinical or exposure criteria.
• One major neuroimaging criteria plus two clinical or exposure criteria (including at least one major clinical/exposure criterion) together with the exclusion of other pathologies producing similar neuroimaging findings.

**Probable diagnosis:**
• One major neuroimaging criteria plus any two clinical or exposure criteria.
• One minor neuroimaging criteria plus at least one major clinical or exposure criteria.

* Del Brutto and colleagues provide excellent examples and illustrations of these criteria ([Del Brutto et al 2017](#)). An independent group using the new diagnostic criteria found a sensitivity of 93.6% and a specificity of 81.1% for neurocysticercosis versus no neurocysticercosis. For CNS parenchymal neurocysticercosis, the sensitivity was 89.8% and specificity was 80.7%. For extraparenchymal NCC the sensitivity was 65.9% and specificity was 94.9% ([Carpio et al 2016](#)).

**Management**

The management of neurocysticercosis is usually medical with antihelminthic drugs, corticosteroids, and anticonvulsants. The main indications for surgery include cysts exhibiting local compression of brain or cranial nerves, hydrocephalus, intraventricular cysticercosis, spinal cysticercosis with root or cord compression, and ocular cysts ([Sinha and Sharma 2009](#)). Optimal management depends on the number, location, and viability of the cysts. Table 5 lists the current treatment recommendations based on the literature ([Sinha and Sharma 2009](#); [Ramaratnam and Ranganathan 2010](#); [Garcia et al 2011](#); [Baird et al 2013](#); [Del Brutto 2014](#); [Garcia et al 2014a](#)) as modified by my personal experience in treating patients in the United States.

**Table 5. Treatment Recommendations for Symptomatic Neurocysticercosis**

<table>
<thead>
<tr>
<th>Type of neurocysticercosis</th>
<th>Recommendations*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenchymal cysts</td>
<td></td>
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<tr>
<td>• Viable vesicular cysts</td>
<td></td>
</tr>
<tr>
<td>- 1 to 3 cysts on neuroimaging</td>
<td>Antihelminthic drugs ± steroids</td>
</tr>
<tr>
<td>- 4 + cysts on neuroimaging</td>
<td>Antihelminthic drugs + steroids</td>
</tr>
<tr>
<td>• Degenerating colloid cysts</td>
<td></td>
</tr>
<tr>
<td>- 1 to 3 cysts on neuroimaging</td>
<td>Antihelminthic drugs ± steroids</td>
</tr>
<tr>
<td>- 4 + cysts on neuroimaging</td>
<td>Antihelminthic drugs + steroid</td>
</tr>
<tr>
<td>• Dead calcified cysts (asymptomatic)</td>
<td>No antihelminthic treatment</td>
</tr>
<tr>
<td>• Calcified cysts with seizures</td>
<td>Albendazole, steroids, and anticonvulsants</td>
</tr>
<tr>
<td>Cysticercotic encephalitis</td>
<td>High dose steroids without antihelminthic drugs</td>
</tr>
<tr>
<td>Giant cysts</td>
<td>Albendazole with steroids; CSF shunting if hydrocephalus develops</td>
</tr>
<tr>
<td>Meningeal cysts</td>
<td></td>
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</tbody>
</table>
With hydrocephalus
CSF shunting, albendazole with steroids often in high dosage repeatedly for years, careful monitoring of patient for shunt malfunction

Without hydrocephalus
Albendazole in 1 to 2 courses plus steroids with careful monitoring of patient for possible hydrocephalus

Intraventricular cysts
- With hydrocephalus
  CSF shunting, careful monitoring of patient for shunt malfunction, albendazole with steroids; surgical removal of cyst when possible, especially via endoscope
- Without hydrocephalus
  Surgical removal of cyst when possible, especially via endoscope; plus albendazole and steroids

Spinal cysts
Surgical cyst removal with steroids, or albendazole with steroids, when possible

Ophthalmic cysts
- Cyst in globe
  Surgical cyst removal
- Cyst outside globe
  Antihelminthic drug with steroids or surgical cyst removal, when possible

*Patients should be given anticonvulsants as needed for seizures. Modified from (Garcia et al 2002; Sinha and Sharma 2009; Del Brutto 2014; Garcia et al 2014a).

Albendazole and praziquantel are FDA-approved for treatment of neurocysticercosis. Albendazole is moderately well-absorbed by oral administration especially when given with a fatty meal. The drug is rapidly metabolized in first passage by the liver to its active sulfoxide metabolite (Sotelo and Jung 1998), of which 70% is bound to protein. The sulfoxide plasma half-life is between 8 and 14 hours, and it is eliminated in urine with an elimination half-life of 8.5 hours (Sotelo and Jung 1998). The drug readily crosses the blood-brain and blood-CSF barriers to achieve concentrations in CSF that are higher than corresponding serum concentrations and higher than that achieved by praziquantel. However, the sulfoxide concentration in cyst fluid is lower than that of plasma levels but is sufficient to kill the cyst. Albendazole is well-tolerated with minimal adverse effects that include dizziness, gastrointestinal distress, rashes, leukopenia, and elevated serum liver enzymes. Albendazole has been shown to cause teratogenic effects in rats and rabbits and should be avoided in pregnancy. The mechanism by which the cyst dies is incompletely understood but the drug seems to cause degeneration of parasite cytoplasmic microtubules impairing glucose intake, which leads to energy depletion and parasite starvation (Del Brutto 2014). The dose of albendazole is usually 15 mg/kg per day divided into 2 doses for 8 to 14 days (Sotelo and Jung 1998; Del Brutto 2014), but other regiments have been published. For extraparenchymal neurocysticercosis, treatment with 30 mg/kg/day was reported to be superior to 15 mg/kg/day (Gongora-Rivera et al 2006). Concomitant administration of corticosteroids has been shown to increase serum albendazole concentration by 50% (Overbosch et al 1987). Administration of anticonvulsants or other medications does not affect the serum drug concentration.

Praziquantel is well absorbed orally and undergoes extensive first passage hepatic metabolism with the metabolites being inactive (Sotelo and Jung 1998). Peak plasma levels occur 1.5 to 2 hours after administration. About 80% of praziquantel is bound to plasma, but free praziquantel rapidly is distributed in body tissue due to its high lipid solubility. Praziquantel traverses the blood-brain and blood-CSF barriers to achieve therapeutic concentrations in CSF and within cyst fluid (Overbosch et al 1987; Sotelo and Jung 1998). Praziquantel has a plasma and elimination half-life of 1.5 to 2.5 hours. The drug is well-tolerated with few side effects that include gastrointestinal distress, dizziness, fever, headache, and occasionally a diminished sense of well-being (King and Mahmoud 1989). Praziquantel has not been shown to be teratogenic in animals. The mechanism of action of praziquantel is poorly understood but the drug appears to affect calcium channels on the surface of the parasite, causing muscle contractions producing spastic paralysis of the parasite (Vazquez et al 1987; Sinha and Sharma 2009; Del Brutto 2014). A new in vitro assay reported that exposure to praziquantel caused reduced cyst size and inhibition of evagination (Mahanty et al 2011). However, the drug may not kill the racemose form of neurocysticercosis, which lacks a protoscolex. The usual dose of praziquantel is 50 mg/kg per day divided into 3 doses for 15 days (Sotelo et al 1984). Unlike albendazole, concomitant administration of corticosteroids, phenytoin, or carbamazepine will decrease serum and CSF levels of praziquantel (Sotelo et al 1984; Bittencourt et al 1992). Concomitant administration of praziquantel with cimetidine or a high fat or
high carbohydrate diet elevates serum praziquantel levels (Castro et al 2000).

Although both albendazole and praziquantel are effective and equally safe against the cerebral parasite, 2 meta-analyses of comparative trials reported that albendazole is slightly more effective in reducing the cyst burden and controlling seizures (Del Brutto et al 2006; Matthaiou et al 2008). Garcia and colleagues have reported that for patients with many cysts, a combination of both albendazole and praziquantel together was superior in eliminating the cysts at 6 months than either alone without producing any increase in side effects (Garcia et al 2014b; Garcia et al 2016). However, an older reference did not find benefit in children treated with both drugs (Kaur et al 2009).

Corticosteroid administration along with the antihelminthic drug is often indicated to minimize transient worsening of clinical symptoms that may occur early in the treatment. Both antihelminthic drugs rapidly kill the viable cyst releasing antigenic material into the surrounding brain or CSF. As a consequence, there can be a marked increase in inflammation and cerebral edema that can produce new or increased clinical signs that include: increased intracranial pressure (with headaches, lethargy, nausea and vomiting), seizures, and focal neurologic signs such as hemiparesis, ataxia or visual loss. The symptoms often begin on day 2 to day 3 of treatment and last 3 to 5 days (Sotelo and Jung 1998). When albendazole is used, the corticosteroids should be given simultaneously and continued until day 5 or longer if there is a large parasite burden or a severe reaction develops. Dexamethasone, 8 to 24 mg per day in 4 divided doses orally, intramuscularly, or intravenously or prednisone 1 mg/kg per day orally are usually given (Sotelo and Jung 1998; Del Brutto 2014). When praziquantel is administered, the corticosteroids are often withheld for 1 to 2 days or longer if possible because steroids decrease serum praziquantel levels by 50% (Castro et al 2000). If increased symptoms develop, steroids are then administered intramuscularly or intravenously for rapid effect and continued as long as necessary.

Although there is currently controversy as to whether treatment with antihelminthic drugs improves resolution of seizures in patients having only 1 or 2 intraparenchymal cysts, a 2013 guideline review found that most studies favored albendazole treatment. A 2010 Cochrane collaboration reported that for adults, no difference was detected for albendazole compared with no treatment for recurrence of seizures, but fewer participants with albendazole had lesions at follow up (Ramaratnam and Ranganathan 2010). The argument for antihelminthic treatment is based on shortening the time to cyst disappearance on CT and MRI and killing all cysts simultaneously, preventing prolongation of brain inflammation due to multiple cysts degenerating at different times (Davis 2002). A double-blind, placebo-controlled study of 120 Peruvian patients with seizures and neurocysticercosis lesions identified by neuroimaging reported a significant 67% reduction in seizures with generalization following treatment with albendazole. There was also a trend for reduction of partial seizures (Garcia et al 2004). A meta-analysis also concluded that cysticidal drug therapy results in better resolution of colloidal and vesicular cysticerci, lower risk of recurrence of seizures in patients with colloidal cysticerci, and a reduction in the rate of generalized seizures in patients with vesicular cysticerci (Del Brutto et al 2006). In the United States, most patients with cysticercosis receive antihelminthic treatment.

Anticonvulsants should be administered to all seizure patients. Anticonvulsants should be continued for 1 year to 2 years or until the active cysts have disappeared on neuroimaging and the brain irritation has subsided (Carpio and Hauser 2002). Commonly prescribed anticonvulsants are phenytoin, valproate, and carbamazepine (Garcia et al 2011). About 80% of patients do not subsequently develop seizures after the anticonvulsants are discontinued. Patients with subsequent seizures should be considered to have epilepsy from unprovoked seizures and restarted on long-term anticonvulsants (Carpio and Hauser 2002). One study reported a higher rate of long-term seizures in patients whose cysts calcified rather than just degenerated (Goel et al 2010). The long-term clinical outcome of parenchymal neurocysticercosis from India in 500 children found that single lesions have a favorable outcome with few seizure recurrences (Singhi et al 2017).

The optimal duration of antihelminthic treatment for extraparenchymal neurocysticercosis is unknown, but probably of longer duration than for parenchymal disease (Garcia et al 2002). Despite apparent disappearance of viable parasites, chronic inflammation around undetected parasitic membranes may ensue with disease continuation or progression. A specific antigen detection ELISA assay that detects cysticercosis antigens has been developed (Garcia et al 1998; Fleury et al 2007). Monitoring CSF or serum antigen levels may help evaluate efficacy and duration of antiparasitic and steroid therapy. There is some evidence that detection of cysticercus antigen in CSF may help diagnose meningial extraparenchymal neurocysticercosis in patients with chronic meningitis (Parija et al 2007).

It is common for patients with extraparenchymal cysticercosis to fail their first course of albendazole or praziquantel treatment (Figueroa et al 2011). Typically, there is continued CSF inflammation, and the Ag-ELISA assay demonstrated
persistent cysticercosis antigen in the CSF and serum. A second course of antihelminthic drugs is usually given, often with a switch to the other drug because the drugs kill by different mechanisms. Disappearance of cysticercosis antigen from CSF usually indicates the parasite has been eradicated.

Patients who develop obstructive hydrocephalus from a chronic arachnoiditis or blockage of intraventricular CSF pathways require placement of a ventriculoperitoneal shunt. Unfortunately, it often is difficult to maintain shunt patency as inflammatory debris or cyst debris may occlude the shunts. Patients with meningeal or ventricular cysts appear to be better treated with albendazole than praziquantel because albendazole achieves higher CSF concentrations and may have a slightly better success rate. Death may occur from shunt malfunction or from vasculitis of brainstem blood vessels resulting in brainstem or thalamic infarction (Del Brutto 1992). Intraventricular vesicular cysts often can be removed surgically, often by endoscopic surgery (Husain 2007; Rajshekhar 2010). However, if the cyst is degenerating and producing a ventriculitis, the cyst is often firmly attached to ependyma or choroid plexus and difficult to surgically remove. Small viable cysts in the lateral ventricle have successfully been treated with albendazole. Because both drugs act by killing the cysticercus, the drugs are not useful in treatment of patients with dead calcified cysts.

Eliminating neurocysticercosis from developing countries remains a challenge, especially when rural individuals raise pigs on their property. However, pilot studies using a highly effective pig cysticercosis vaccine have shown that interruption of pig to human transmission is feasible (Garcia et al 2014a). Unfortunately, the cost of widespread use of the pig vaccine is currently too high to use widely.

**Special considerations**

**Pregnancy**

Oncospheres that reach the blood could potentially lodge in the placenta but will not cross the placenta. Therefore, the fetus should not be infected, and most pregnancies proceed normally. No experience with praziquantel usage during pregnancy has been published but animal studies have not found teratogenic effects. Albendazole has been shown to cause teratogenic effects in animals and, therefore, should be avoided during pregnancy (Albendazole Drug Monographs 1993).

**Anesthesia**

Neurocysticercosis normally is not affected by administration of anesthesia. However, patients with increased intracranial pressure from the neurocysticercosis may be more sensitive to anesthesia. Anesthetic drugs that do not increase intracranial pressure should be preferentially used.

**References cited**


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Rajsher V. Surgical management of neurocysticercosis. Int J Surg 2010;8:100-4. PMID 20045747


Vazquez ML, Jung H, Sotelo J. Plasma levels of praziquantel decrease when dexamethasone is given simultaneously. Neurology 1987;37:1561-2. PMID 3627459


**References especially recommended by the author or editor for general reading.
ICD and OMIM codes

ICD codes

ICD-9:
Neurocysticercosis: 123.1

ICD-10:
Cysticercosis of central nervous system: B69.0

Profile

Age range of presentation

01-23 months
02-05 years
06-12 years
13-18 years
19-44 years
45-64 years
65+ years

Sex preponderance

male>female

Family history

none

Heredity

none

Population groups selectively affected

Latin Americans, but cases occur often in India and Asia

Occupation groups selectively affected

Farmers

Differential diagnosis list

tuberculoma
brain abscess
syphilitic gumma
arteriovenous malformation
metastatic tumor
small primary tumor
parasitic cysts
schistosomes
amebic cyst
tuberculous meningitis
fungal meningitis
cerebrovascular syphilis
neurosarcoïdosis
meningeal carcinomatosis
CNS vasculitis

Other topics to consider

Headache associated with meningitis, encephalitis, and brain abscess
Molecular diagnosis of CNS infections
Prednisone
Seizures associated with eclampsia
Treatment of epilepsy in developing countries