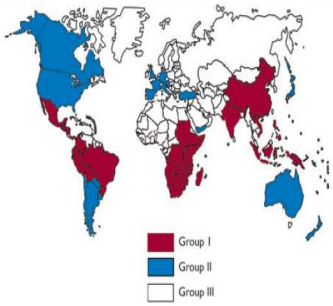
neurocysticercosis

Dr Manesh Pillay
Neurologist
Steve Biko Academic Hospital

Introduction

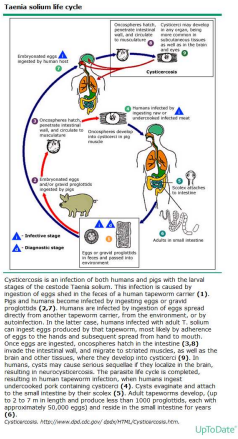
- Neurocysticercosis is not a new disease
- Improved diagnosis and treatment
- Endemic in low income countries
- Acquired epilepsy
- Potentially eradicable

Global distribution of NCC



Life cycle of *Taenia solium*

- Pig intermediate host of tapeworm *Taenia solium*
- Human cysticercosis - eggs, which are excreted in the faeces of an individual carrying the parasite, are ingested.
- Ingestion of infected pork only causes adult tapeworm infestation (taeniasis).
- Ingestion of vegetables irrigated with water contaminated by faeces



Cysticercosis is an infection of both humans and pigs with the larval stages of the cestode Taenia solium. This infection is caused by ingestion of eggs shed in the feces of a human tapeworm carrier (1). Pigs and humans become infected by ingesting eggs or gravid proglottids (2,7). Humans are infected by ingestion of eggs spread directly from another tapeworm carrier, from the environment, or by autoinfection. In the latter case, humans infected with adult T. solium can ingest eggs produced by that tapeworm, most likely by adherence of eggs to the hands and subsequent spread from hand to mouth. Once eggs are ingested, oncospheres hatch in the intestine (3,8) invade the intestinal wall, and migrate to striated muscles, as well as the brain and other tissues, where they develop into cysticerci (9). In humans, cysts may cause serious sequellae if they localize in the brain, resulting in neurocysticercosis. The parasite life cycle is completed, resulting in human tapeworm infection, when humans ingest undercooked pork containing cysticerci (4). Cysts evaginate and attach to the small intestine by their scolex (5). Adult tapeworms develop, (up to 2 to 7 m in length and produce less than 1000 proglottids, each with approximately 50,000 eggs) and reside in the small intestine for years (6).

Cysticercosis. http://www.dpd.cdc.gov/ dpdx/HTML/Cysticercosis.htm.

UpToDate®

Life cycle of *Taenia solium*

- Common source of infective eggs is a symptom-free tapeworm carrier in the household.
- Individuals no history of pork consumption or travel to endemic areas can also develop NCC
- Cysticercosis should be seen as a disease mostly transmitted from person to person, whereas the role of infected pigs is to perpetuate the infection.

NATURAL HISTORY

- Pigs - cysts maximum size in 2–3 months,while alive they trigger little perilesional inflammation.
- Evidence against symptoms appearing at the time of initial exposure
- Humans initial seizure 2–5 years suggesting a long latent stage

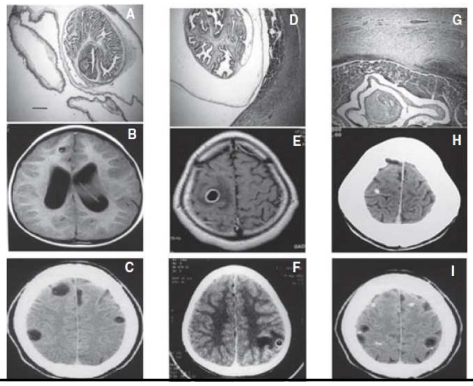
Stages of NCC

- Taenia parasites have sophisticated means of evading destruction.
- Metacestodes elaborate a variety of substances, including taeniaestatin (a parasite serine proteinase inhibitor), paramyosin, sulfated polysaccharides, and secretory proteases, that inhibit or divert host inflammatory responses

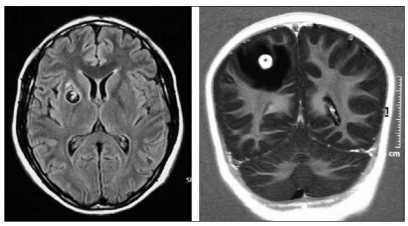
Stages of NCC

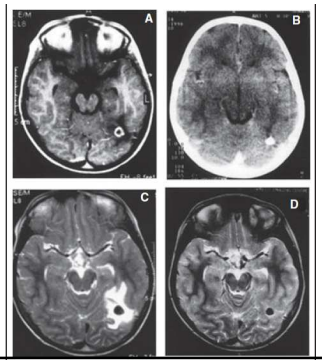
- Eventually (after a variable number of years) the cysts degenerate and lose their ability to modulate the host immune response
- Immune and inflammatory cells attack the cysticercus - edema and/or enhancement on imaging studies.
- Inflammatory response associated with seizures.
- Cystic lesions either resolve or form a calcified granuloma.
- Calcifications are associated with recurrent seizures

Stages of neurocysticercosis



Stages of neurocysticercosis





Clinical syndromes

- Neurocysticercosis (NCC) and extraneural cysticercosis.
- Neurocysticercosis, in turn, is divided into parenchymal and extraparenchymal forms.
- Extraparenchymal forms include intraventricular, subarachnoid, intraocular, and spinal disease

Clinical Description

- Late-onset epilepsy
- Intracranial hypertension - focal or diffuse
- Number, stage, and localisation of the parasites within the nervous system, as well as the severity of the host's immune response against the parasites
- Signs usually follow a subacute or chronic course

CLINICAL MANIFESTATIONS

- **Parenchymal**
- Encephalitis
- Intraventricular
- Subarachnoid - arachnoiditis
- Racemose cysticercosis - proliferating lobulated cysts without scolices, which are usually found in the subarachnoid space. resembling bunches of grapes.
- Spinal cysticercosis

Extraneural cysticercosis

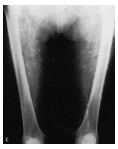
- Ocular cysticercosis - subretinal space, vitreous humor, anterior chamber, conjunctiva or extraocular muscles.
- Symptoms may include impaired vision, recurrent eye pain and diplopia.
- Ocular cysticercosis should be excluded by an ophthalmologic examination in all patients with NCC prior to initiating therapy

Extraneural cysticercosis

- Cardiac cysts. Depending on their location, asymptomatic or arrhythmias and/or conduction abnormalities.
- Subcutaneous and intramuscular cysticercosis .
- Patients may notice subcutaneous nodules 0.5 to 2.0 cm in diameter; cysticerci at these sites are usually asymptomatic but may cause discomfort when inflamed.

PERUVIAN STUDY

- 25 patients w/ calcified intraparenchymal brain lesions underwent non-contrast CT scan of thighs
  - 13 (52%) had 1 or more muscle calcifications consistent with extraneural cysticercosis
    - These patients had plain x-rays of thighs.
      - Only 6 of 13 had visible calcifications on x-ray



Many presentations

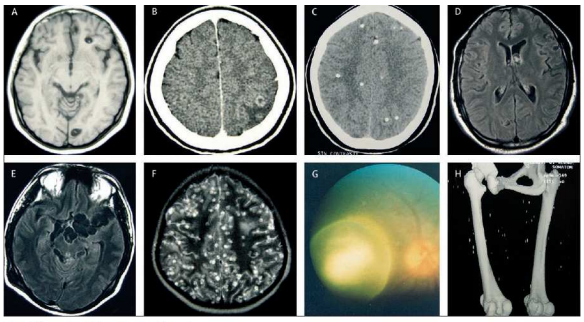


Figure 2: Diverse presentations of neurocysticercosis

Diagnosis

- Neuroimaging studies and confirmatory serological analysis.
- CT vs MRI
- Immunoelectrotransfer blot (EITB) with purified glycoprotein antigens (western blot
- 30% of patients with a single brain parasite may test negative

Diagnosis of cysticercosis

Revised diagnostic criteria for neurocysticercosis

Categories of criteria	Criteria
Absolute	Histologic demonstration of the parasite from biopsy of a brain or spinal cord lesion
	Cystic lesions showing the scolex on CT or MRI
	Direct visualization of subretinal parasites by funduscopic examination
Major	Lesions highly suggestive of neurocysticercosis on neuroimaging studies*
	Positive serum EITB+ for the detection of anticysticercal antibodies
	Resolution of intracranial cystic lesions after therapy with albendazole or praziquantel
	Spontaneous resolution of small single enhancing lesions‡
Minor	Lesions compatible with neurocysticercosis on neuroimaging studies§
	Clinical manifestations suggestive of neurocysticercosis‖
	Positive CSF ELISA for detection of anticysticercal antibodies or cysticercal antigens
	Cysticercosis outside the CNS¶
Epidemiologic	Evidence of a household contact with *Taenia solium* infection
	Individuals coming from or living in an area where cysticercosis is endemic
	History of frequent travel to disease-endemic areas

Revised degrees of certainty for the diagnosis of neurocysticercosis

Diagnostic certainty	Criteria
Definitive	Presence of one absolute criterion
	Presence of two major plus one minor and one epidemiologic criterion
Probable	Presence of one major plus two minor criteria
	Presence of one major plus one minor and one epidemiologic criterion
	Presence of three minor plus one epidemiologic criterion

The presence of two different lesions highly suggestive of neurocysticercosis on neuroimaging studies (the presence of at least one major diagnostic criteria. The most sensitive results from separate types of antibody detection tests should be interpreted only on the basis of the test falling in the highest category of diagnostic criteria.

ELISA: enzyme-linked immunosorbent assay.
* CT or MRI showing cystic lesions without scolex, enhancing lesions, or typical parenchymal brain calcifications.
† Enzyme-linked immunoelectrotransfer blot assay using purified extracts of *Taenia solium* antigens, as developed by the Centers for Disease Control and Prevention (Atlanta, GA).
Δ Solitary ring-enhancing lesions measuring less than 20 mm in diameter in patients presenting with seizures, a normal neurologic examination, and no evidence of an active systemic disease.
◇ CT or MRI showing hydrocephalus or abnormal enhancement of the leptomeninges, and myelograms showing complete or partial filling defects of the subarachnoid space.
§ Seizures, focal neurologic signs, intracranial hypertension, and dementia.
‖ Histologically confirmed subcutaneous or muscular cysticercosis, plain X-ray films showing "cigarshaped" soft-tissue calcifications, or direct visualization of cysticerci in the anterior chamber of the eye.
¶ Intraventricular, subarachnoid, or racemose cysticercosis.
Reproduced with permission from: Del Brutto OH, Rajshekhar V, White AC, et al. Proposed diagnostic criteria for neurocysticercosis. Neurology 2001; 57:177. Copyright © 2001 Lippincott Williams & Wilkins.

UpToDate®

Treatment

- Tailored according to the type and stage of neurocysticercosis .
- Combination of symptomatic and antiparasitic measures, including analgesics, antiepileptic drugs (AEDs), cysticidal drugs, surgical resection of lesions, and placement of ventricular shunts

Progress in treatment

- No longer use praziquantel
- Albendezole 1 week
- Treatment associated parasite death does not leads to worsening.
- Evidence that killing the parasites would lead to fewer seizures during follow-up.

TREATMENT

Parenchymal neurocysticercosis	
Vesicular cysts	
Single	Albendazole 15 mg/kg/day for 1 week, steroids used only if side-effects occur; or praziquantel 100 mg/kg in three equal doses
Moderate infections	Albendazole 15 mg/kg/day for 1 week, with simultaneous use of steroids.
Heavy infections (100 or more cysts)	Albendazole 15 mg/kg/day for 1 week with high doses of steroids
Degenerating (colloidal) cysts	
Single lesions	Albendazole 15 mg/kg/day for 1 week, steroids used only if side-effects occur; or no antiparasitic treatment
Moderate infections	Albendazole 15 mg/kg/day for 1 week with steroids
Heavy infections (encephalitis)	No antiparasitic treatment, high doses of steroids, osmotic diuretics (mannitol)
Calcifications	
Single or multiple	No antiparasitic treatment

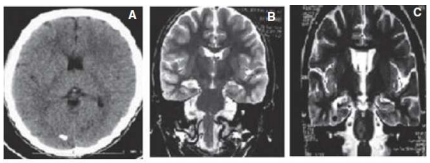
Treatment

Extraparenchymal neurocysticercosis	
Subarachnoid neurocysticercosis	
Giant cyst (usually in Sylvian fissure)	Albendazole 15 mg/kg/day for >1 month, with high doses of steroids; or surgical excision
Basal subarachnoid (racemose)	Albendazole 15 mg/kg/day for >1 month, with high doses of steroids.
Ventricular cysts	Endoscopic aspiration or surgical resection, use of antiparasitic drugs is controversial
Hydrocephalus	No antiparasitic treatment, ventricular shunt
Arachnoiditis, angiitis	No antiparasitic treatment, high doses of steroids for >1 month
Ependymitis	No antiparasitic treatment, ventricular shunt if indicated, high doses of steroids

Seizures

- Seizures may result from inflammation, perhaps from intermittent antigen release, or from scarring .
- Changes in brain plasticity and scarring (eg, hippocampal sclerosis) may result in epileptogenic foci .
- Matrix metalloproteinases in the pathogenesis of seizures in neurocysticercosis - calcified lesions

Association between NCC and hippocampal sclerosis



Anti Epileptic treatment

- Single first-line AED results in seizure control
- Optimum duration of antiepileptic drug therapy not settled.
- Factors associated seizure recurrence - parenchymal brain calcifications, recurrent seizures and multiple brain cysts before the institution of therapy

Corticosteroids

- Cysticercotic encephalitis, angiitis, and chronic meningitis that causes progressive entrapment of cranial nerves .
- Secondary effects of headache and vomiting that may occur during cysticidal drug therapy.
- Giant subarachnoid cysticerci, ventricular cysts, spinal cysts, and multiple parenchymal brain cysts- given before, during,and after the course of cysticidal drugs to avoid the risk of cerebral infarcts, acute hydrocephalus, spinal-cord swelling, or massive brain oedema

Epidemiology and control

Neurocysticercosis is potentially eradicable.

- Mass human chemotherapy to eliminate the tapeworm .
- Slaughterhouse control
- Health education
- Pig corralling
- Improving living conditions
- Treatment of pigs with oxfendazole,Vaccine
- Meat processing

Problems in control

- Major obstacles include the lack of basic sanitary facilities in endemic areas, the extent of domestic pig raising, the costs of the interventions, and most importantly, their cultural acceptability

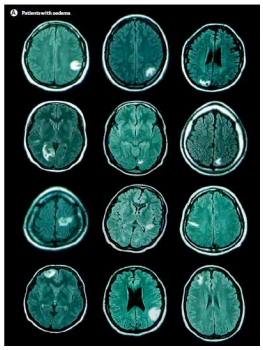
Future research

Perilesional brain oedema and seizure activity in patients with calcified neurocysticercosis: a prospective cohort and nested case-control study

Theodore E Nash, E Javier Pretell, Andres G Lescano, Javier A Bustos, Robert H Gilman, Armando E Gonzalez, Hector H Garcia, for The Cysticercosis Working Group in Peru

Summary

Background Cysticercosis due to *Taenia solium* is a cause of adult-acquired seizures and epilepsy even in patients with only calcified larval cysts. Transient perilesional brain oedema is seen around the calcified foci but its importance, Lancet Neurol 2008; 7:1099-105



FUTURE RESEARCH

- Treatment depending on stages: the living larva, the degenerating larva, a reactive thickening of the cyst membrane, and calcification.
- Neurocysticercosis can be intraventricular or intraocular or involves the subarachnoid space. Different treatment strategies

FUTURE RESEARCH

- HIV coinfection
- Studies focus on clinical outcomes rather than surrogate CT outcomes
- Use and timing of administration of adjuvant corticosteroids OR combination cysticidal therapy

Key problems in diagnosis and control

- Diagnosis of cysticercosis in the field greater challenge than diagnosis in hospital basis.
- Neither neuroimaging studies, serological assays, nor combination - detects every case of neurocysticercosis

Key problems in diagnosis and control

- Seronegative - positive CT imaging but no neurological evidence of the disease - asymptomatic infection, or may have false positive neuroimaging
- Seropositivity and seizures, is considerably weaker than expected (odds ratio 2–3).

THE END