University of Nebraska Medical Center
Nebraska Medicine

Neurocysticercosis Diagnosis and Management Workflow

Background

Cysticercosis is a disease caused by infection with the parasite *Taenia solium* that can cause neurologic and extraneural disease. Infection involving the central nervous system (CNS) is called neurocysticercosis and can involve any portion of the CNS. It is endemic throughout the southern hemisphere and Asia, although it is also found in the U.S. When disease is detected, it should be followed by ID consult and careful image-based staging to support guideline-driven management. Efficiency can be gained in structuring assessment, both from radiologic evaluation and bedside management standpoints. This can address the following challenges:

- Appearance on neuroimaging can be varied and affect many neuroanatomical structures
- Differentiation from other clinical entities challenging, symptomatically & radiographically
- Under-recognition due to rarity in our region (~2,000 cases in the U.S. annually):
    - No incidence data exist for the state of Nebraska specifically (though several cases per year are seen at UNMC alone); and,
    - A 2015 study categorized U.S. NCC cases requiring hospitalization & stratified by regional prevalence; it found that the Midwest accounted for 9.8% of such cases[1]

Clinical Presentation

Most patients with *Taenia solium* infection are asymptomatic and identified due to incidental identification of typical cystic lesions after undergoing neuroimaging for other reasons. The approach to NCC varies by the location and distribution of cysticerci within the CNS, as detailed in the 2017 updated guidelines from IDSA (Infectious Diseases Society of America) & ASTMH (American Society of Tropical Medicine & Hygiene).[2,3]

Table 1: Potential Clinical Presentations of Neurocysticercosis

The most common presentation is asymptomatic with imaging findings only

Parenchymal	Ventricular	Subarachnoid
Seizures, headache	Obstructive hydrocephalus symptoms (headache, nausea/emesis, balance/gait abnormalities, vision changes, urinary incontinence)	Obstructive hydrocephalus symptoms, meningitis, hemorrhagic stroke, focal neurologic deficit (FND)

Patients may present with acute or chronic disease:

- Acute: seizures (most common), acute headache, new neurologic deficits can occur
- Chronic: asymptomatic (incidentally found on imaging), seizures, chronic focal deficits

Table 2: Clinical Workflow

May enter workflow from any point (concerning symptom, incidental imaging finding, etc.)

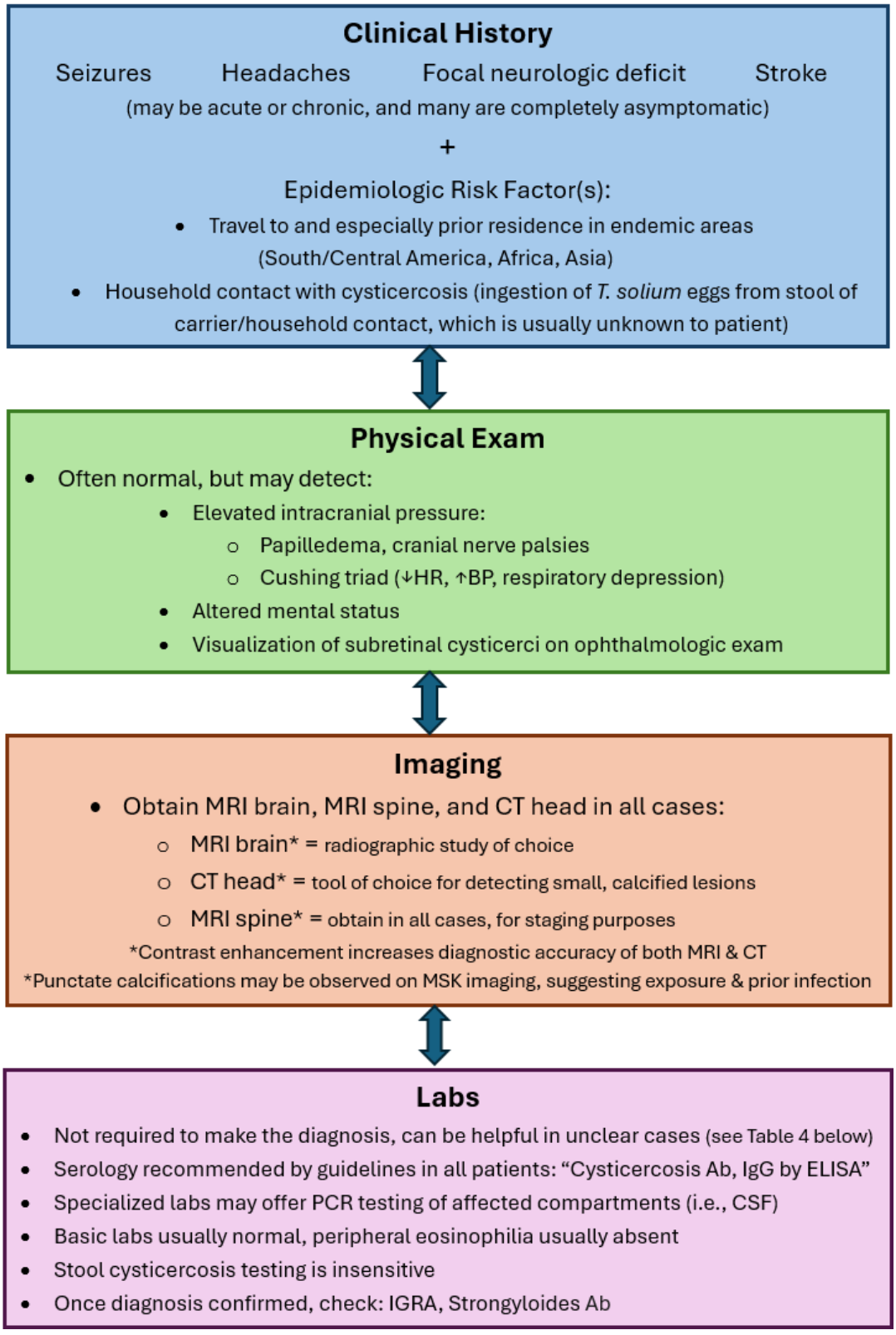


Table 3: Radiographic Categorization and Treatment of Disease

Location	NCC Form	Neuroimaging Findings (MRI = imaging modality of choice[2])	Treatment[+] (antiepileptic therapy not addressed here)
Parenchymal	Nonviable calcified	Calcified nodule (**Major radiographic criteria**) with or without surrounding edema and/or contrast enhancement	-Treatment generally not indicated -Antiparasitics NOT recommended -Manage elevated ICP[#]; if refractory epilepsy, surgical removal of seizure foci
	Viable parenchymal (typical cyst 0.1-2 cm diameter)	Vesicular lesions (round, hypodense) (**Major radiographic criteria**), often with evidence of associated contrast enhancement and/or surrounding edema. Visible scolex = pathognomonic (**Absolute radiographic criteria**), though beware visual mimics	<u>Increased Intracranial Pressure (ICP)</u>: -Manage elevated ICP[#] +/- steroids^ -Avoid antiparasitics until elevated ICP is managed[n#] <u>No Increased ICP</u>: -Single enhancing lesions (SEL): steroids^, then Albendazole[n] -2+ viable cysts: steroids^, then Albendazole and Praziquantel[n]
	Cysticercal encephalitis	Diffuse cerebral edema (excluding perilesional edema associated w/ calcified disease)	-Steroids^, avoid antiparasitics until elevated ICP is managed[n#]
Extra-parenchymal	Intraventricular (typical cyst 1-2 cm diameter)	Cysticerci within the ventricles (**Major radiographic criteria**), obstructive hydrocephalus (**Minor radiographic criteria**), or loculated hydrocephalus with disproportionate dilatation of the ventricles (suggestive of a cysticercus) *Important to note in which ventricle the cysts are located, as surgical approach varies between lateral/3rd vs. 4th ventricles*	<u>No adherent cysts/surgical contraindications</u>: -Lateral/3rd Ventricle: consult neurosurgery (eval for minimally invasive/neuroendoscopic surgery) -4th Ventricle: consult neurosurgery (eval for microsurgery vs endoscopic cystectomy) <u>Cyst adherent to ventricular wall (or other surgical contraindication)</u>: -VP shunt and concomitant steroids^, then antiparasitics[n]
	Subarachnoid* (typical cyst 4+ cm diameter)	Cysticerci in Sylvian fissure, basilar cisterns, or interhemispheric spaces (**Major radiographic criteria**). Strokes (incl. hemorrhagic) or meningitis with evidence of cysticercosis +/- discrete cysts	-Steroids^, then antiparasitics[n] (prolonged courses recommended, up to 1-2 years for racemose form)
	Spinal	Cysticerci within the spinal subarachnoid space (**Major radiographic criteria**) +/- evidence of inflammation/diffuse spinal arachnoiditis. Intramedullary cysticerci within the spinal cord (**Major radiographic criteria**).	-Steroids^, then antiparasitics[n] (prolonged courses recommended); mechanical intervention indicated in some cases

[+]Pursue VP shunt/surgical CSF diversion if hydrocephalus is detected at any stage of NCC.

[#]Management of elevated ICP (removal of obstructing cysticercus, placement of ventricular drain/shunt, ventriculostomy).

^Optimal steroid dosing not well-defined. Prednisone 1 mg/kg/day (or equivalent) is a recommended baseline, up to 2.5 mg/kg/day (or equivalent) used acutely in subarachnoid disease. Consider steroid-sparing therapy (methotrexate) if prolonged therapy needed.

[n]Prior to starting antiparasitics: start steroids at least 1 day prior, all patients need a fundoscopic exam, and ID consult is recommended in all cases; antiparasitic medication dosing/duration/other details outlined below.

[*]Subarachnoid NCC strongly associated w/ asymptomatic spinal disease; obtain spine MRI in all cases[3].

See Table 1 in citation 5 below for complete diagnostic criteria and degrees of diagnostic certainty for NCC.

Table 4: Detailed Lab Testing Outline

Diagnostic Workup	CNS Histopathology	Other Considerations
Laboratory studies aid diagnosis and, critically, allow investigation of the differential diagnosis. **Guidelines recommend:** ● Serology/antibody testing = Cysticercosis IgG (ELISA)* ○ Send-out test to ARUP ○ Test code: 0055284 ○ CPT: 86682 *Serology Interpretation Caveats*: - Specific: positive serology is helpful in confirming suspected NCC based on imaging/symptoms - Variable sensitivity: negative serology does not rule out NCC **Guidelines DO NOT recommend the following, as negative results do not exclude diagnosis:** ● Antigen testing ● Next-generation sequencing ● Molecular/PCR testing (CSF, blood) ○ CSF PCR anecdotally used in some extraparenchymal cases (spinal, subarachnoid, cysticercal encephalitis) for diagnosis & monitoring response to treatment, not routinely recommended, avoid LP until elevated ICP ruled out ● Stool O&P (can be used to identify *Cysticercosis* carriers)	Though not necessary for diagnosis, if brain/spinal tissue sent for pathology & shows any of the following, consider NCC: ● Calcified granulomas +/- surrounding inflammation or fibrinous sheath ● **Visible scolex or parenchymal parasite** (+/- surrounding inflammation or cyst fluid) **= an absolute diagnostic criteria** ● Subarachnoid tissue with arachnoiditis/ vasculitis, may see clusters of cysts with proliferating membranes (racemose form)	Broad differential diagnosis, consider testing for: ● TB ● Toxoplasma ● Chagoma ● HIV If NCC is diagnosed, tests to order prior to starting steroids/ immunosuppression (if indicated): ● IGRA (rule out latent TB) ● Strongyloides antibody (screen vs treat empirically)

*Enzyme-linked immunoelectrotransfer blot (EITB) has better sensitivity and specificity than ELISA and was previously offered by CDC, but has been discontinued. ELISA has poor sensitivity in the setting of a single lesion or only calcified lesions and has a high degree of cross-reactivity with other cestodes, especially *Echinococcus*.

Multidisciplinary Management Considerations:

- If potentially acquired NCC in non-endemic area, screen household members for tapeworm carriage via stool O&P (coordinate with public health department)
- Ophthalmologic evaluation: Recommended for all patients (**visualization of subretinal cysticercus = an absolute diagnostic criteria**)
- Infectious Diseases: Consult in all cases, for treatment/antiparasitic recommendations (agents expensive and non-formulary), longitudinal care, & evaluation for cure
- Neurosurgery: Engage for elevated ICP/surgical management questions or if biopsy is being considered to rule out other diagnoses (i.e. malignancy)
- Neurology: Consider consult in all cases, strongly recommended when seizure present
- To contact CDC for additional expertise in complex cases, call 1-800-232-4636 or visit the CDC's Division of Parasitic Diseases and Malaria.

Table 5: Antiparasitic Medications

Medication	Route	Dose	Duration	Cost
Albendazole	PO	• 15 mg/kg/day (up to daily maximum of 1200 mg)* • Divided into 2 daily doses • 200 mg tabs	7-14 days (repeat treatment course if lesions persist on 6-month re-imaging)	~$50
Praziquantel	PO	• 50 mg/kg/day • Divided into 3 daily doses • 600 mg tabs (can be cut in 150 mg increments)	7-14 days (repeat treatment course if lesions persist on 6-month re-imaging)	~$200

*Higher doses (up to 30 mg/kg/day) recommended in some cases (subarachnoid cysts)
Antiparasitics should always be given in conjunction with corticosteroids. Both agents are non-formulary and must be ordered using non-formulary medication order.

Table 6: Follow-Up/Monitoring

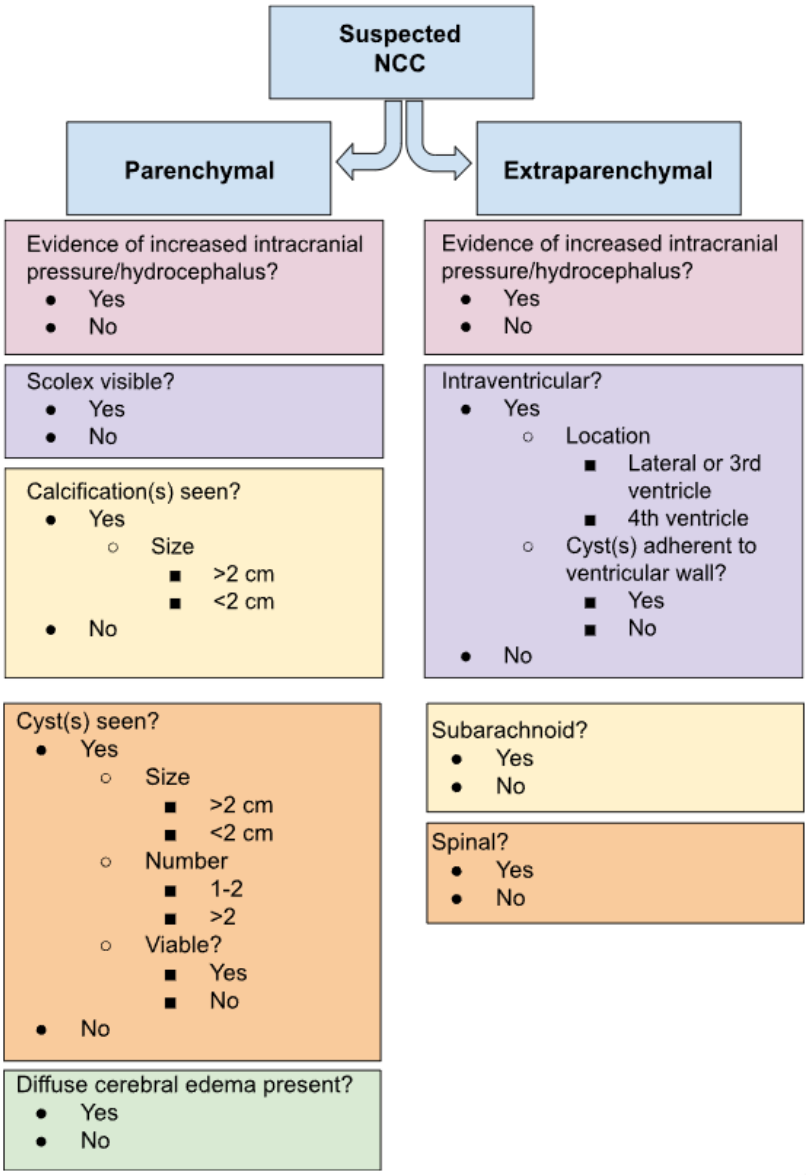
Clinical	Imaging	Labs
• Follow up visit 2-4 weeks after diagnosis to evaluate for new/recurrent seizures or other symptoms • Symptoms/seizures may take weeks to improve, particularly in high-burden disease	• MRI brain +/- spine q6 months until resolution of cystic lesions (retreatment recommended if persistent lesions) • Re-image sooner if new/ concerning symptoms	• For patients on Albendazole: no lab monitoring necessary for ≤2wk courses. For extended courses, CBC and CMP every 2-4wks# • For patients on prolonged steroids: blood glucose monitoring • No utility in repeating or trending ELISA Ab test

#Hepatotoxicity and leukopenia are known side effects of Albendazole; AST or ALT >5x ULN and/or absolute neutropenia are relative contraindications to its continued use[3].

Table 7: Neuroradiology Workflow/Elements to Consider Including in Report (to Help Guide Key Management Decisions)

What features noted on neuroimaging should trigger radiology team to consider NCC?:

- Calcification or cystic lesion + clinical risk factor(s)
- Hydrocephalus + clinical risk factor(s)
    - Calcifications and hydrocephalus have broad radiographic differential diagnoses, so either of these findings in the absence of other/clinical concerns would not necessarily trigger a full NCC evaluation in every case but may instead warrant further exploration of exposure history, collaboration with ordering provider, and/or consider expert consultation
- Visible scolex/parasitic organism
- Any combination of the above findings
- Clinical concern/suspicion from ordering provider



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Reviewed By: UNMC Stewardship Committee

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