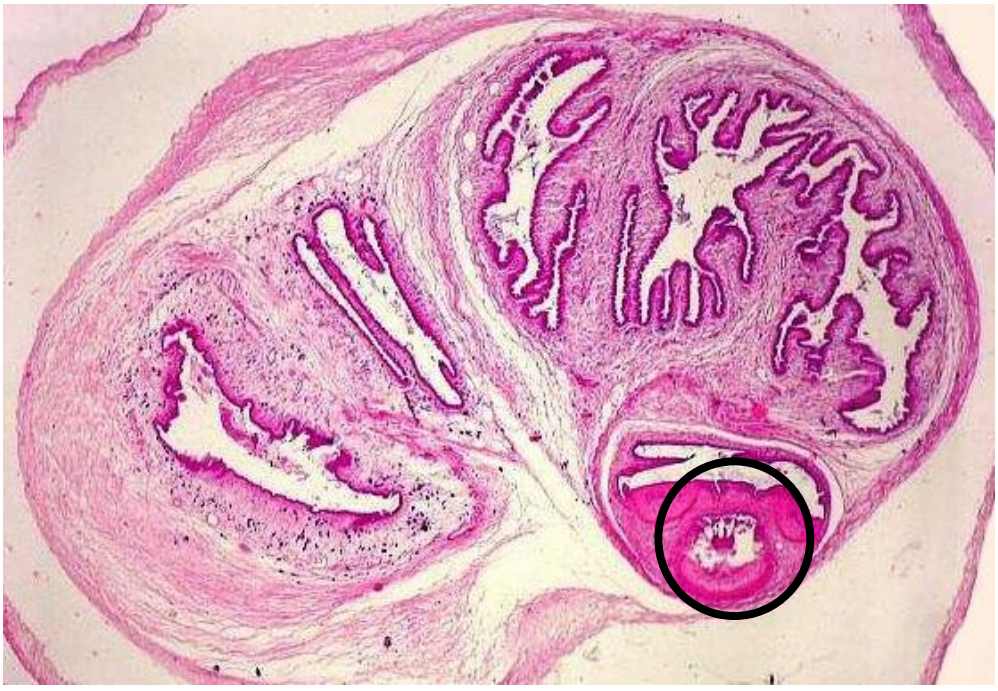
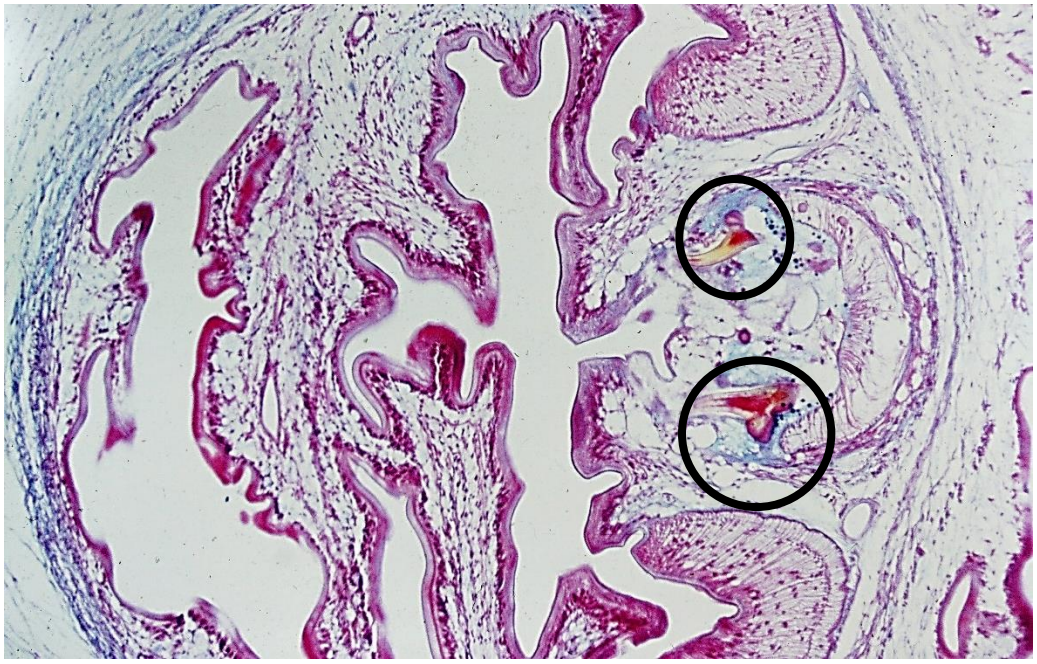
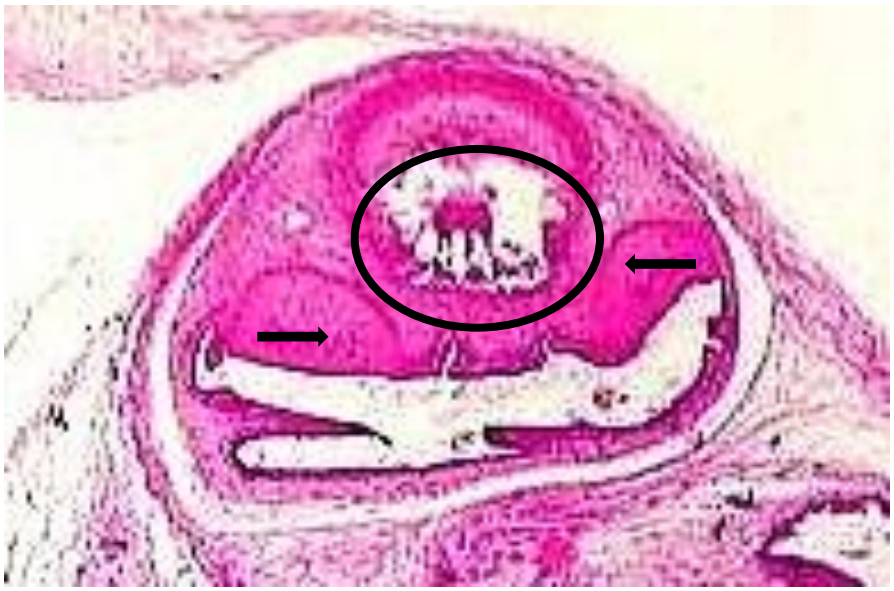
PARASITOLOGY CASE HISTORY 5 (HISTOLOGY)
(Lynne S. Garcia)

A 47 year-old male presented with symptoms that were consistent with possible late adult-onset epilepsy (frequent headaches and occasional seizures). Lesions obtained from the right frontal lobe of the brain revealed the following images.







- Based on these images, what is your diagnosis?

Scroll Down for Answer and Discussion

Answer and Discussion of Histology Quiz #5

This is a case of cysticercosis caused by the larval stage of *Taenia solium*. Cysticercosis infections with *T. solium* larvae are relatively common in certain parts of the world. However, cysticercosis is becoming more common within the United States; the infection is associated with Hispanic ethnicity, immigrant status, exposure to areas where neurocysticercosis is endemic, and the American Southwest.

Upper Image: Single cysticercosis from the brain. Note the sucker and hooklets (circle).

Middle Image: Extensive folding of the spiral canal and hooklets (circles).

Lower Image: Single cysticercus from brain (arrow); (Right) Note the suckers (arrows) and hooklets (circle) (Courtesy of Dr. Luciano S. Queiroz, Dept. of Pathology, School of Medical Sciences, State University of Campinas (UNICAMP), Campinas, Sao Paulo, Brazil.

Cysticercosis is an infection of both humans and pigs with the larval stages of the parasitic cestode, *Taenia solium*. This infection is caused by ingestion of eggs shed in the feces of a human tapeworm carrier. Pigs and humans become infected by ingesting eggs or gravid proglottids. Humans are infected either by ingestion of food contaminated with feces, or by autoinfection. In the latter case, a human infected with adult *T. solium* can ingest eggs produced by that tapeworm, either through fecal contamination or, possibly, from proglottids carried into the stomach by reverse peristalsis. Once eggs are ingested, oncospheres hatch in the intestine, invade the intestinal wall, and migrate to striated muscles, as well as the brain, liver, and other tissues, where they develop into cysticerci. In humans, cysts can cause serious sequelae if they localize in the brain, resulting in neurocysticercosis.

The larval forms of *T. solium* have been recovered from all areas of the body, and symptoms depend on the particular body site involved. The presence of cysticerci in the brain represents the most frequent parasitic infection of the human nervous system and the most common cause of adult-onset epilepsy throughout the world. For unknown reasons, in Latin America it is unusual for both brain and muscle cysticercosis to occur in the same patient, with fewer than 6% of patients having cysticerci in both sites. However, elsewhere in the world, subcutaneous involvement by *T. solium* cysticerci has been detected in as many as 78.5% of patients with cerebral cysticercosis. Possible reasons for such differences may include (i) the immune status of the patient, (ii) the human leukocyte antigen type, (iii) the nutritional status of the patient, (iv) the burden of eggs infecting the patient, and (v) a difference in the strains of *T. solium.* It is also rare for a patient with cysticercosis to harbor adult *T. solium* worms in the intestine. Neurocysticercosis usually affects males and females of all ages, with a peak incidence between 30 and 50 years of age. It has been estimated that 50,000 individuals die annually due to neurocysticercosis.

Neurocysticercosis is the most common parasitic disease of the central nervous system; in some countries the prevalence exceeds 10% and is responsible for up to 50% of late-onset epilepsy cases (13). Factors related to neurocysticercosis pathology include (i) the individual immune response to the presence of the parasite, from tolerance to a severe inflammatory response; (ii) the location of the parasite in the brain; (iii) the number of cysticerci present; and (iv) the stage or age of the lesions (live cysts, inflammatory

exudates, granulomas, calcifications, and residual fibrosis). Estimates of prevalence as defined in Latin American countries (LAC) range between 15% and 38%. Applying these prevalence calculations to the 75 million persons at risk in these geographic areas found in 1993.

In general, the evidence suggests that with properly specific assays, serum performs better than CSF for antibody detection. Unfortunately, in most cases, the sensitivity of antigen detection assays is inferior to that of indirect, antibody-detecting assays.

Antibody test	Identify antigens or epitopes to maintain high sensitivity and specificity compared to native antigens.
	Increase the sensitivity for single brain lesion.
	Identify antigens capable to differentiate exposure from infection.
	Identify antigens capable to differentiate viable and non-viable cysticercosis.
	Produce these antigens or epitopes in recombinant or synthetic way to have an easier and reproducible source of antigen.
	Use these antigens or epitopes to develop a point of care test, to have a primary tool in field settings.
Antigen test	Produce MoAbs or nanobodies against *T. solium* metacestodes in order to increase sensitivity and specificity.
	Standardize a qualitative assay with a better reproducibility and repeatability.
	Produce a test capable of differentiating viable and non-viable cysticercosis, with a high PPV for extraparenchymal NCC.
	Assay needs to perform well in urine samples to avoid invasive and risky sampling

When the larvae are found in the brain, symptoms can result from actual larval invasion of the brain tissue and/or death of the organism, which stimulates tissue reactions around the larvae. It has been recommended that in every case of epilepsy occurring in a patient with no family history of fits and no personal history of fits in childhood, the probability of cysticercosis should be entertained. Although studies indicate the presence of epileptiform seizures in patients with cysticercosis, other symptoms, including abnormal behavior, transient paresis, intermittent obstructive hydrocephalus, disequilibrium,

meningoencephalitis, and visual problems, may also be present. Spinal fluid from patients with cerebral cysticercosis shows possible eosinophilia and pleocytosis (the most common cell type is the lymphocyte), with atypical mononuclear lymphoid cells. The most distinctive features of the infection in the spinal fluid are atypical, reactive lymphoid cells with a mixed cellular population. A study by Sotelo et al. of 753 cases of neurocysticercosis reviewed inactive and active disease, the frequency of signs and symptoms, and cerebrospinal fluid (CSF) findings. More than 50% of all patients exhibit at least two of these clinical presentations.

Larger numbers of cysticerci usually correlate with more serious disease. In general, patients with >20 cysticerci within the parenchyma and the absence of hydrocephalus have a more positive prognosis than do patients who have many basal or ventricular lesions accompanied by hydrocephalus. Also, it is not clear how many asymptomatic patients with intracranial cysticerci eventually develop symptoms or how many symptomatic patients spontaneously recover.

References:

1. **Garcia, LS**, 2016. *Diagnostic Medical Parasitology*, 6th Ed., ASM Press, Washington, DC.

2. **Coyle CM, S Mahanty, JR Zunt, MT Wallin, PT Cantey, AC White Jr, SE O'Neal, JA Serpa, PM Southern, P Wilkins, AE McCarthyu, ES Higgs, TE Nash.** 2012. Neurocysticercosis: Neglected but not forgotten. *PLoS Negl Trop Dis* **6**:e1500.

3. **Medina, M. T., E. Rosas, F. Rubio-Donnadieu, and J. Sotelo.** 1990. Neurocysticercosis as the main cause of late-onset epilepsy in Mexico. *Arch. Intern. Med.* **450:**325–327.

4. **Wallin, M. T., and J. F. Kurtzke**. 2005. Neurocysticercosis in the United States: review of an important emerging infection. *Neurology* 63:1559–1564.

5. **Nash, TE, HH Garcia,** 2011. Diagnosis and treatment of neurocysticercosis. *Nat. Rev. Neurol* 7:584-594.

6. **Garcia, H. H., O. H. Del Brutto, T. E. Nash, A. C. White, Jr., V. C. Tsang, and R. H. Gilman.** 2005. New concepts in the diagnosis and management of neurocysticercosis (*Taenia solium*). *Am. J. Trop. Med. Hyg.* **72:**3–9.