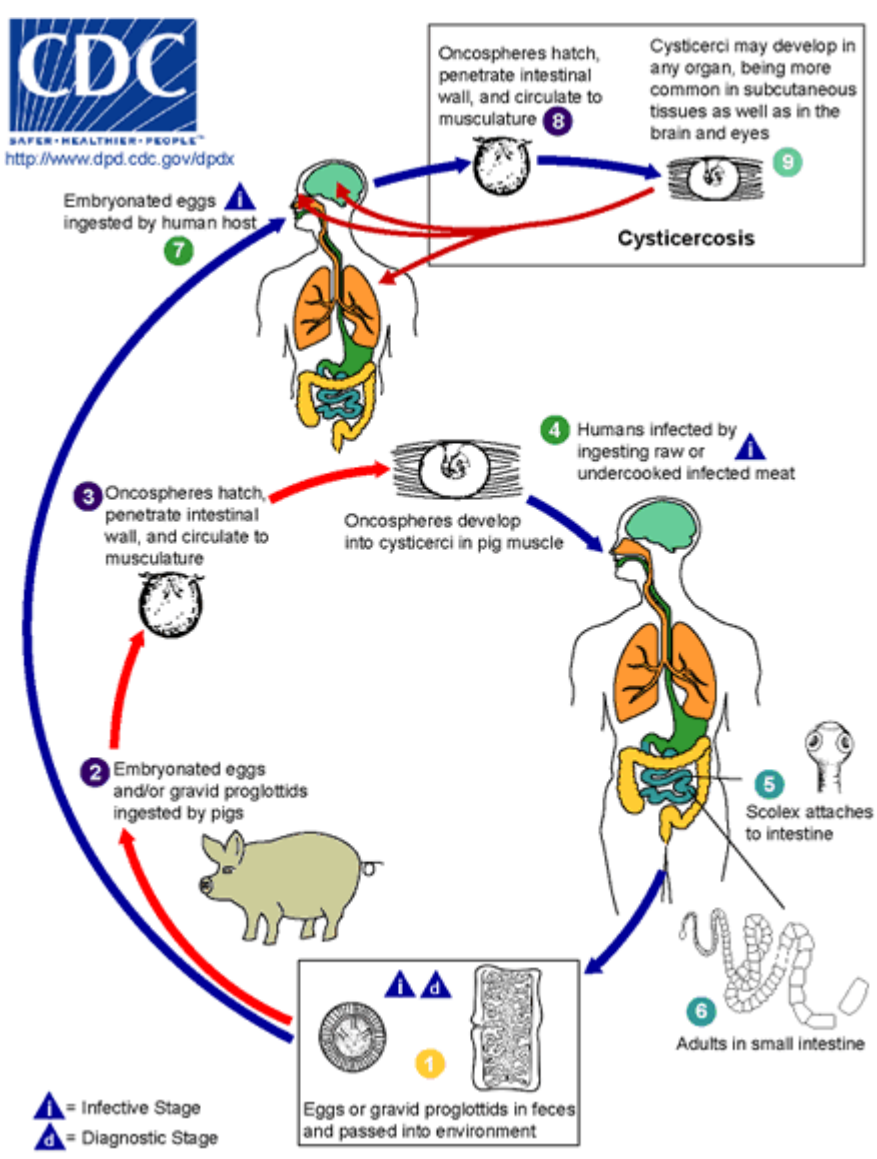
Parasitic Nervous System Infections

Last updated: April 17, 2019

CYSTICERCOSIS

Life cycle of *Taenia solium* (pork tapeworm):
egg in feces
↓
INTERMEDIATE HOST (pigs, humans): **egg** in mouth → **embryos** hatch in duodenum → lymphatics or systemic circulation → embryos mature into **larvae** in tissues
↓
DEFINITIVE HOST (only humans): **larvae** in mouth → larvae mature into **adult** in small bowel → **egg** in feces

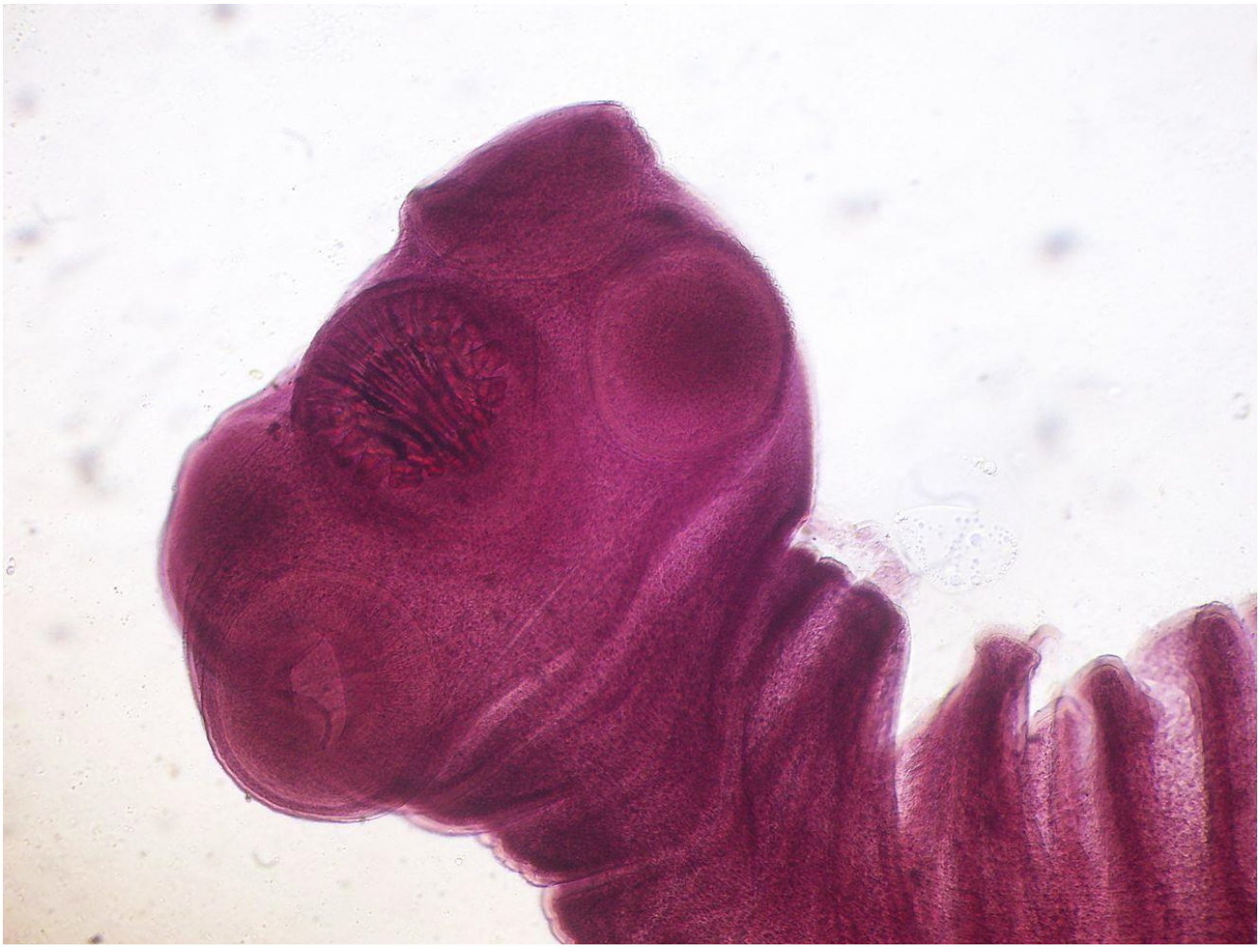


T. solium can infect man in two different ways:

A. Adult worm in human as definitive host: eating undercooked infested (measly) pork → encysted larvae are released in small bowel → larvae mature within intestine into adult over 2 months → **taeniasis (intestinal tapeworm):** scolex (head) of segmented adult worm attaches by means of four suckers and two rows of hooklets to wall of small intestine where worm absorbs food directly through its cuticle.
   - proglottids (mature segments, each containing reproductive organs) produce eggs which are liberally excreted along with gravid proglottid segments in feces.
   - nervous system is not affected!

B. Larva in human as intermediate host: ingesting eggs*:
   **not from eating infested meat* (vegetarians are susceptible too)
   a) **food** (usually vegetables) or water contaminated with human feces containing eggs or gravid proglottids (this is means whereby pigs acquire disease)
   b) **fecal-oral autoinoculation** in individual harboring adult tapeworm
   c) **autoinfection by reverse peristalsis** of gravid proglottids from intestine into stomach during vomiting (unproven theoretical possibility) → swallowing regurgitated eggs.
   - in duodenum shell of ova dissolves → hatched embryos (oncospheres) burrow through small bowel wall → lymphatics or systemic circulation → in tissues embryos develop cyst wall in 2 months (immature cyst) which matures in 4 months to larva → **cysticercosis**:
     a) neurocysticercosis *see below >>*
     b) eye (immunologically privileged, like brain)
     c) skeletal muscle
     d) subcutaneous tissue (palpable nodules)
     e) heart
   - larval cysts are usually rapidly eliminated by immune system; many larvae die naturally within 5-7 yrs or with cysticidal therapy → inflammatory reaction → collapse of cyst (granular nodular stage), these sometimes calcify (nodular calcified stage); in pigs, larva lie dormant in muscle, "waiting" to be eaten.

Scolex (head) of Taenia solium:



NEUROCYSTICERCOSIS (NCC)

Cysticercosis → see p. 289 (3-4)

- intracranial encystment of larva of *Taenia solium*

- most common parasitic CNS infection.
- endemic in South and Central America – seroprevalence up to 11% (esp. in rural areas); 18% in Madagascar.
- in USA government inspection identifies ≈ 10 cases of cysticercosis in 80 million hogs that are slaughtered each year; important sources:
  1) immigrant Hispanics
  2) contact with infected immigrant food preparers (e.g. neurocysticercosis has also been reported in Orthodox Jewish people with no travel outside the USA or exposure to pork products)

PATHOPHYSIOLOGY, CLINICAL FEATURES

- larva has ***marked predilection for neural tissue*** - brain is involved in 60-90 of cases of cysticercosis; spinal cord and peripheral nerve involvement is rare.
- EXTRANEURAL CYSTICERCOSIS may occur in skeletal musculature, conjunctiva or retina, but is rarely present in persons with NCC.

Pathologic stages

Host tolerates worm as long as embryo is alive (vesicular stage)
↓ 2-6 years after infection
Worm dies
↓
Disintegration of parasite triggers vigorous inflammatory tissue reaction → severe symptoms; cyst wall and fluid become infiltrated by mononuclear cells (colloid stage).
↓
Fibrosis with collapse of cyst cavity (granular-nodular stage)
↓
Parasite decays into eosinophilic desiccated material.
↓
Dystrophic calcified nodule (calcific stage)

N.B. latency from ingestion of eggs to symptomatic* neurocysticercosis: 2-6 years (83% cases show symptoms within 7 years of exposure)
*release of T. solium antigens from dying parasite, mass effects → *acute*, *chronic* or *relapsing* clinical picture

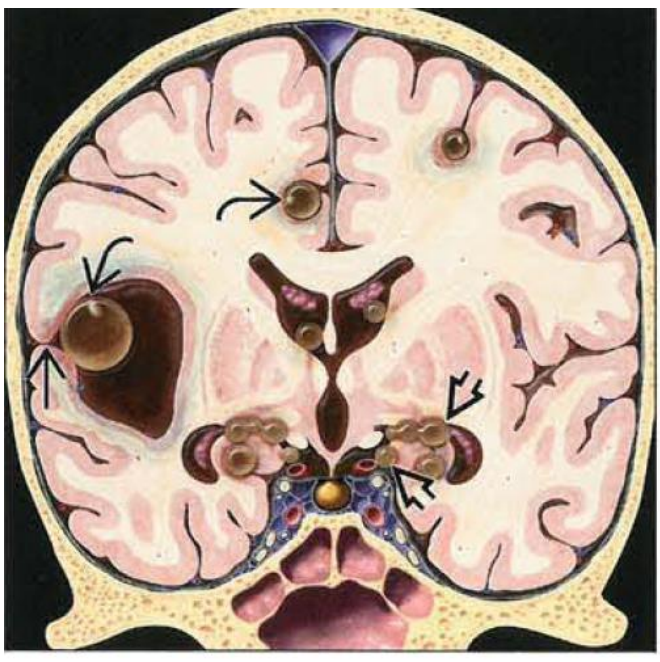
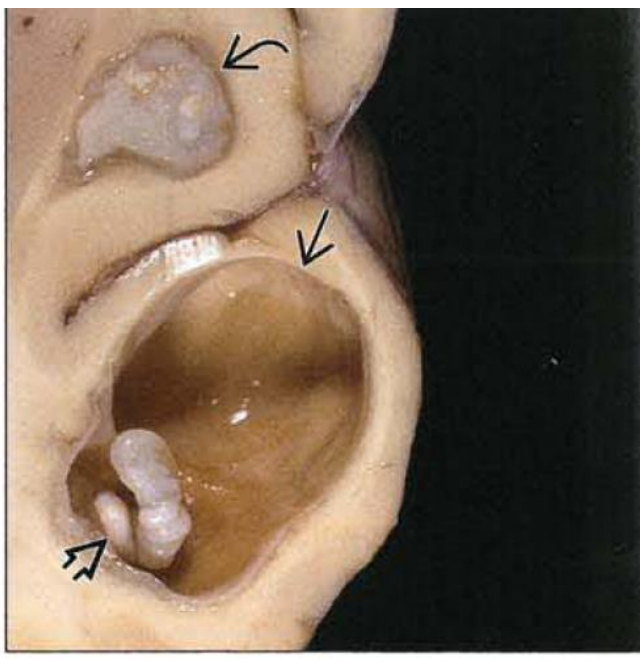
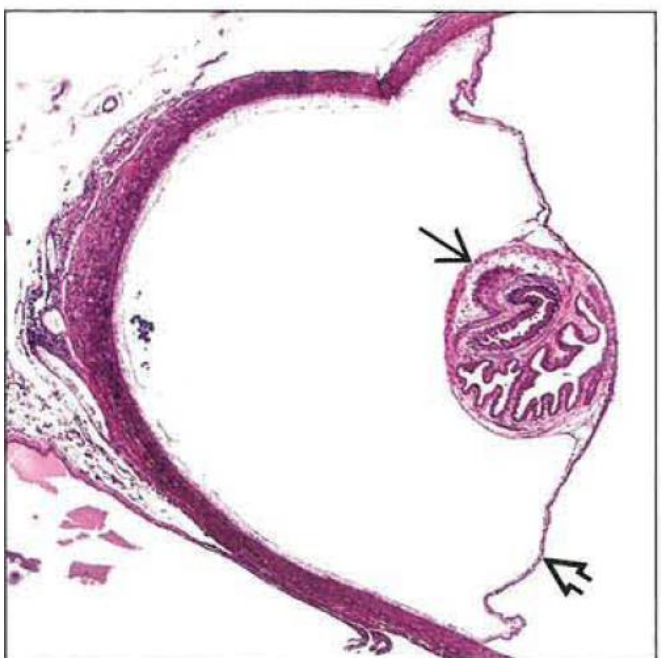
Two types of cysts in brain:

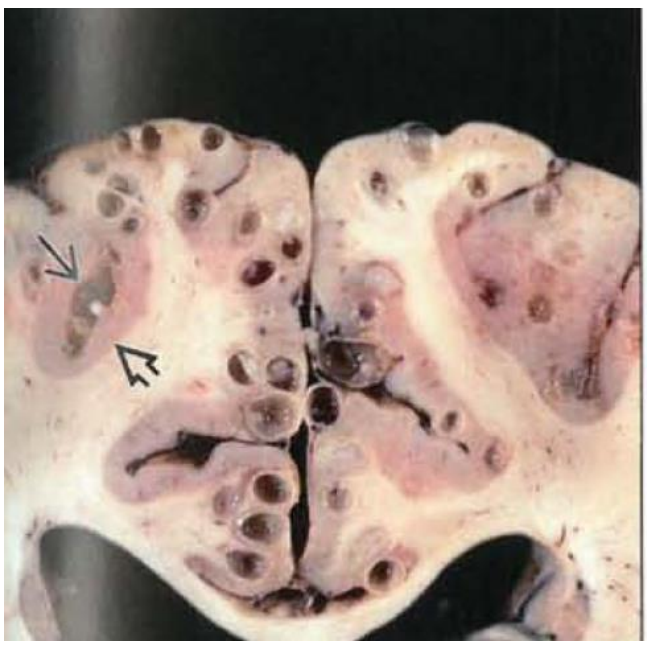
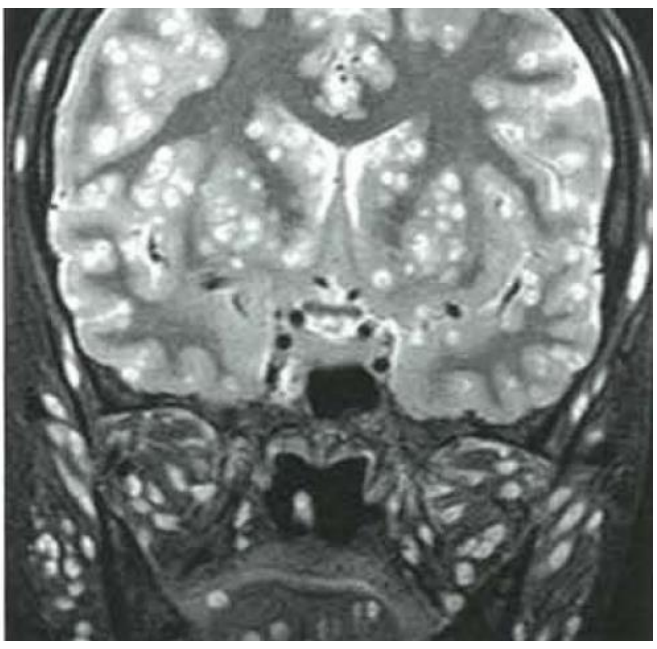
1. ***Cysticercus cellulosae***: regular thin-walled cyst (3-20 mm) in parenchyma or narrow subarachnoid spaces; ***contains larva with scolex***, usually static - produces only mild inflammation during active phase
2. ***Cysticercus racemosus***: large (4-12 cm) cysts ***without larvae***; grows actively producing grape-like clusters in basal subarachnoid spaces and produces intense inflammation; cysts usually degenerate in 2-5 years → capsule thickens and clear cyst contents are replace by whitish gel → calcium deposition with concomitant cyst shrinkage.

Location of cysts:

1. **Parenchymal** (30-63%) → seizures (most common cause of acquired epilepsy in developing countries), other focal deficits (paresis, visual loss); cysticercotic encephalitis (most often seen in young girls and is characterized by numerous intraparenchymal cysts and diffuse cerebral edema) produced by immunologic reaction → dementia, behavioral abnormalities.
2. **Meningeal** (27-56%):
   a) adherent or free-floating ***C. cellulosae*** cysts in *dorsolateral* subarachnoid space causing minimal symptoms
   b) expanding ***C. racemosus*** cysts in *basal* subarachnoid space → chronic basal meningitis (RACEMOSE CYSTICERCOSIS) with meningeal signs; fibrosis can cause cranial neuropathies and strokes, obstruct foramina of Luschka and Magendie (→ obstructive hydrocephalus); *extremely high mortality*.
3. **Ventricular** (12-18%) via choroid plexus; 50% in 4th ventricle; pedunculated or free floating cysts can cause obstructive hydrocephalus with intermittent intracranial hypertension (**BRUN syndrome**); MRI shows adjacent ependymal enhancement (ependymitis).
4. **Spinal cord** (most often – cervical/thoracic) → radiculopathy or myelopathy.

N.B. increased ICP may be due to hydrocephalus or mass effect of giant cysts.

ESCOBAR STAGES

Escobar stage	Pathology	Imaging findings	Treatment
VESICULAR	Larva alive, invaginated, cyst fluid translucent	Smooth thin-walled cyst that is isodense / isointense to CSF; may see small nodule. Edema: 0 Enhancement: 0	Asymptomatic; treatment with anthelmintic ***effective***
COLLOIDAL VESICULAR	Parasite dying; degenerative changes present; cyst fluid jelly-like and white; fibrous capsule develops with perilesional edema	Cyst with thick capsule; fluid signal hyperdense / hyperintense (on T1) to CSF. No DWI restriction. MRS shows succinate, acetate, and lactate peaks. Edema: 3+ Enhancement: 3+ ring-enhancing capsule.	Usually asymptomatic; treatment with anthelmintic ***effective***
GRANULAR NODULAR	Cyst smaller; cyst fluid with coarse granules and pericystic gliosis	Thickened, retracting cyst wall. Edema: 1+ Enhancement: 2+ enhancing nodule.	Symptomatic; treatment with anthelmintic probably ***not necessary***; treat seizures with anticonvulsant
NODULAR CALCIFIED	Complete mineralization of cyst fluid; no host immune response.	Small calcified nodule (bright dots on CT, black dots on MR). HEME sequence may show "blooming" Edema: 0 Enhancement: 0	Symptomatic; treatment with anthelmintic ***not indicated***; treat seizures with anticonvulsant

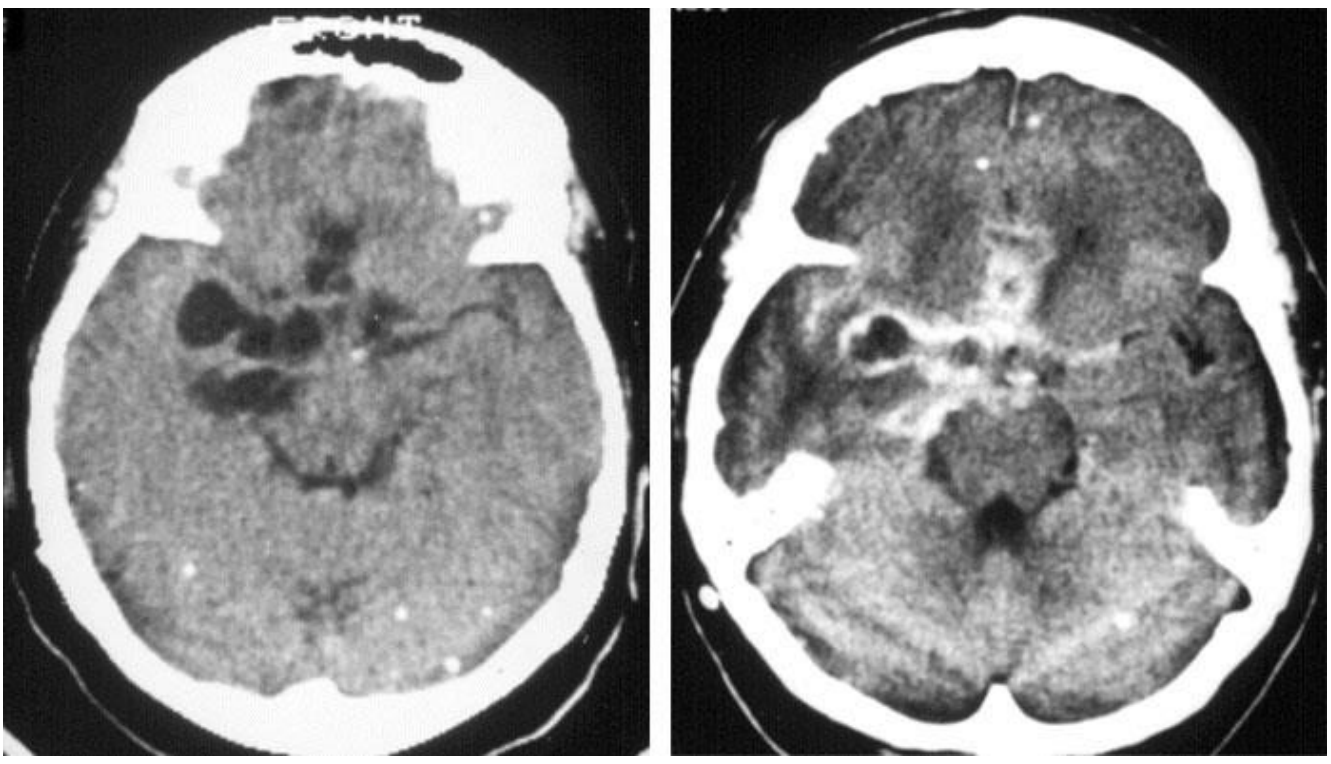
DIAGNOSIS

CT, MRI

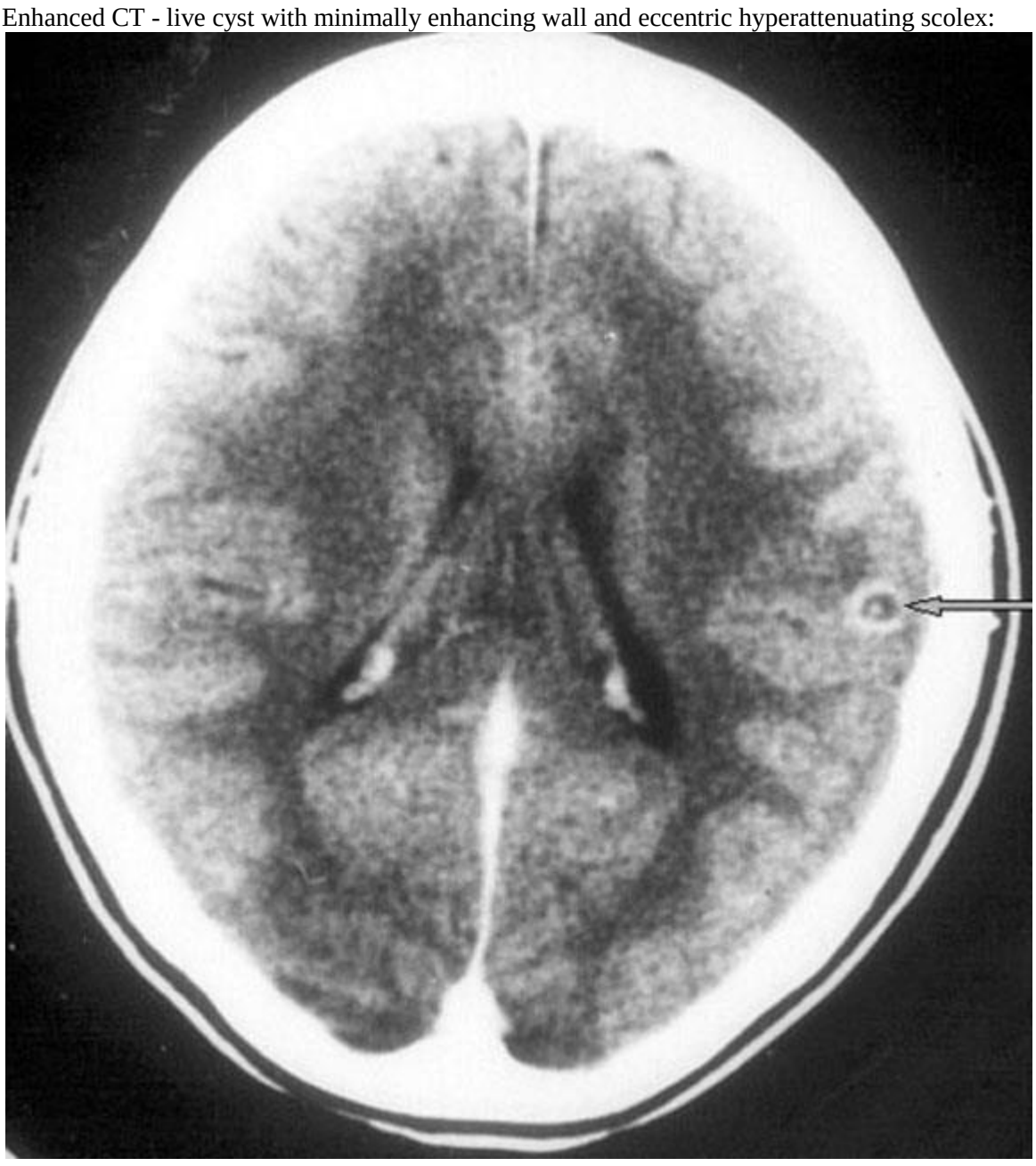
1) ***non-enhancing areas of edema → homogeneous contrast-enhancing lesions →*** SYMPTOMATIC STAGE: low density ***nonenhancing*** cyst(s) with eccentric punctate high density (scolex = tapeworm head); little inflammatory response (edema) occurs as long as larva is alive → low density ***ring enhancing*** cysts (intermediate stage) with inflammatory ***edema → complete resolution*** or oval ***calcifications*** without edema (dead parasites) →.
2) hydrocephalus is common; *intraventricular cysts* may be isointense with CSF (H: CISS MRI or contrast CT ventriculography)

- MRI has higher sensitivity.
- if ***eccentric scolex*** is seen within cyst, NCC may be diagnosed confidently!
- presence of multifocal cigar or rice-like calcifications in *skeletal muscles* is suggestive of cysticercosis, particularly in patients from endemic areas.

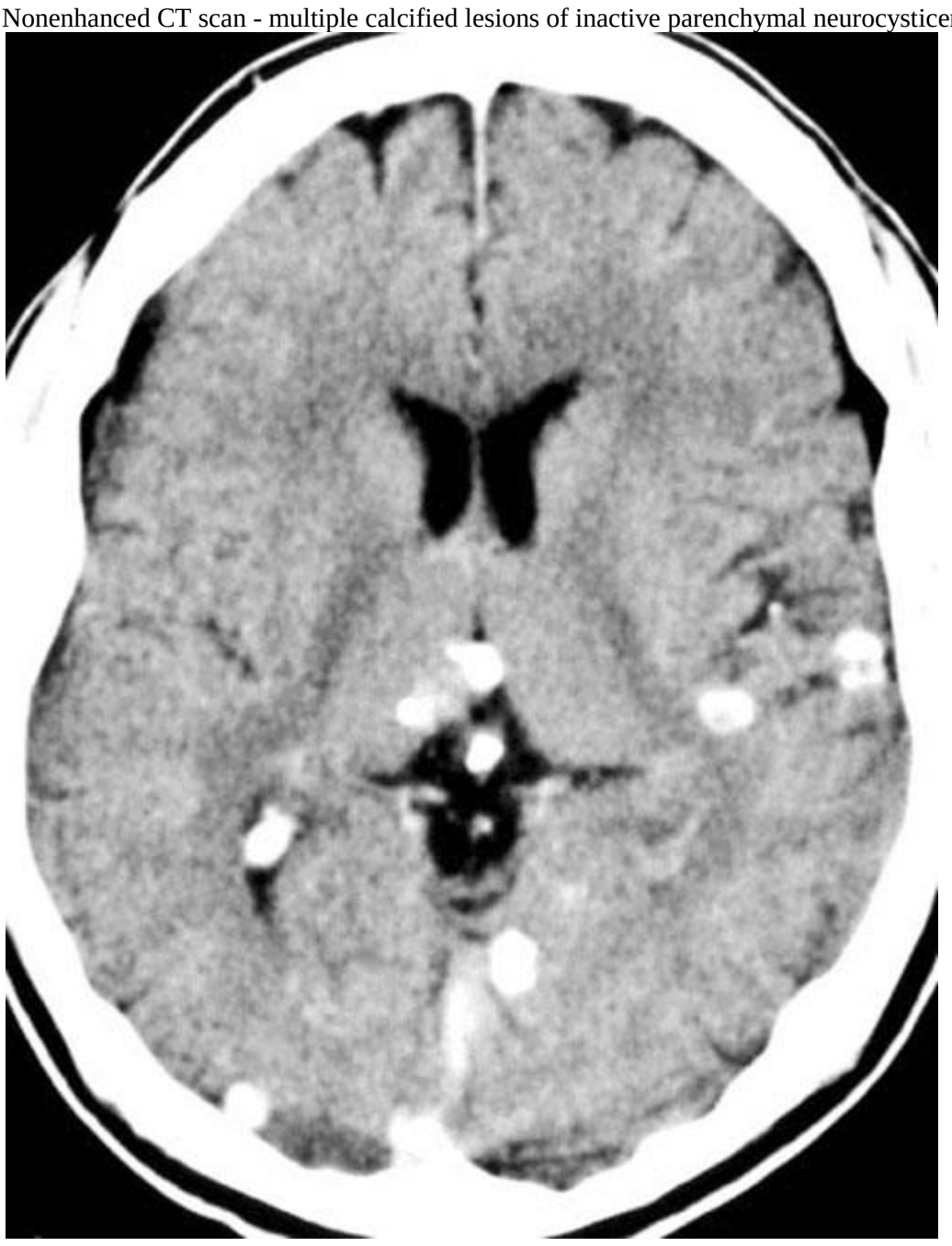
Nonenhanced (left) and enhanced (right) CT -peripheral meningeal enhancement around cysts in suprasellar and right sylvian cisterns:



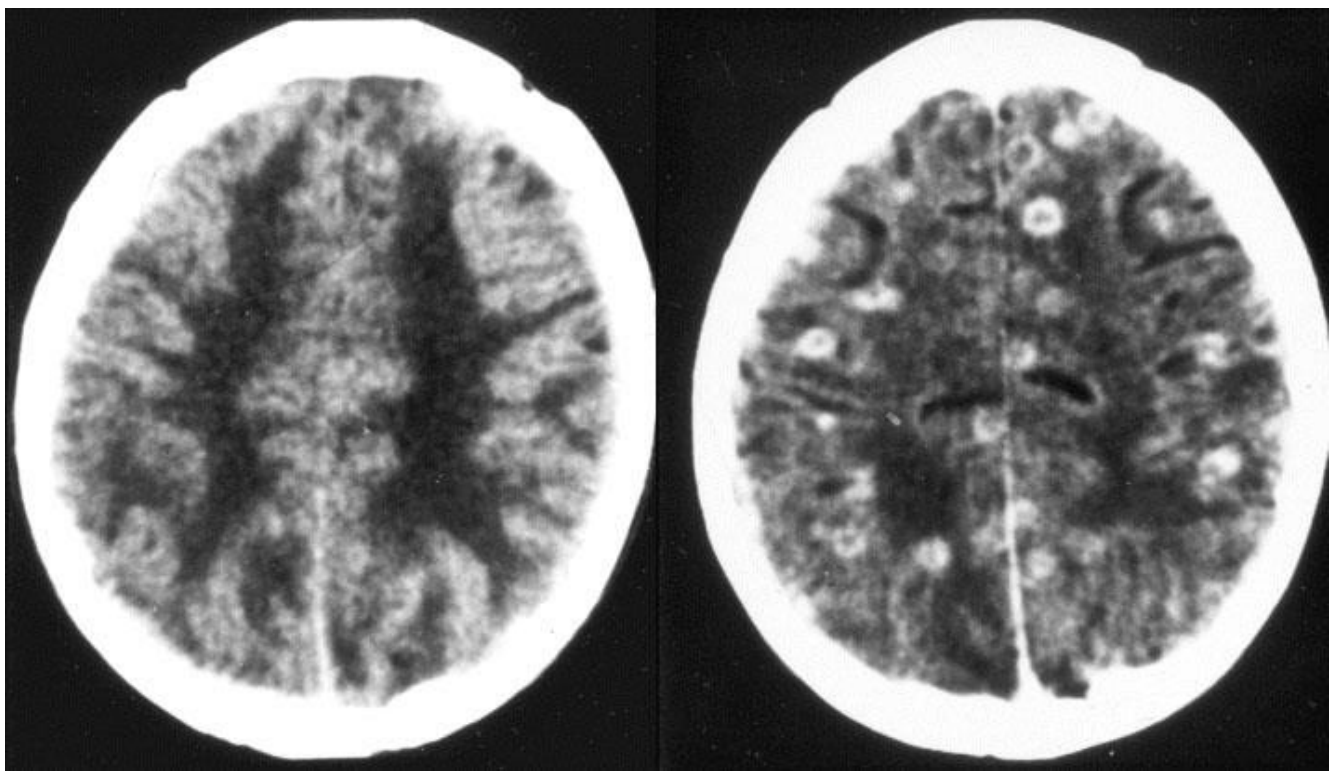
Enhanced CT - live cyst with minimally enhancing wall and eccentric hyperattenuating scolex:



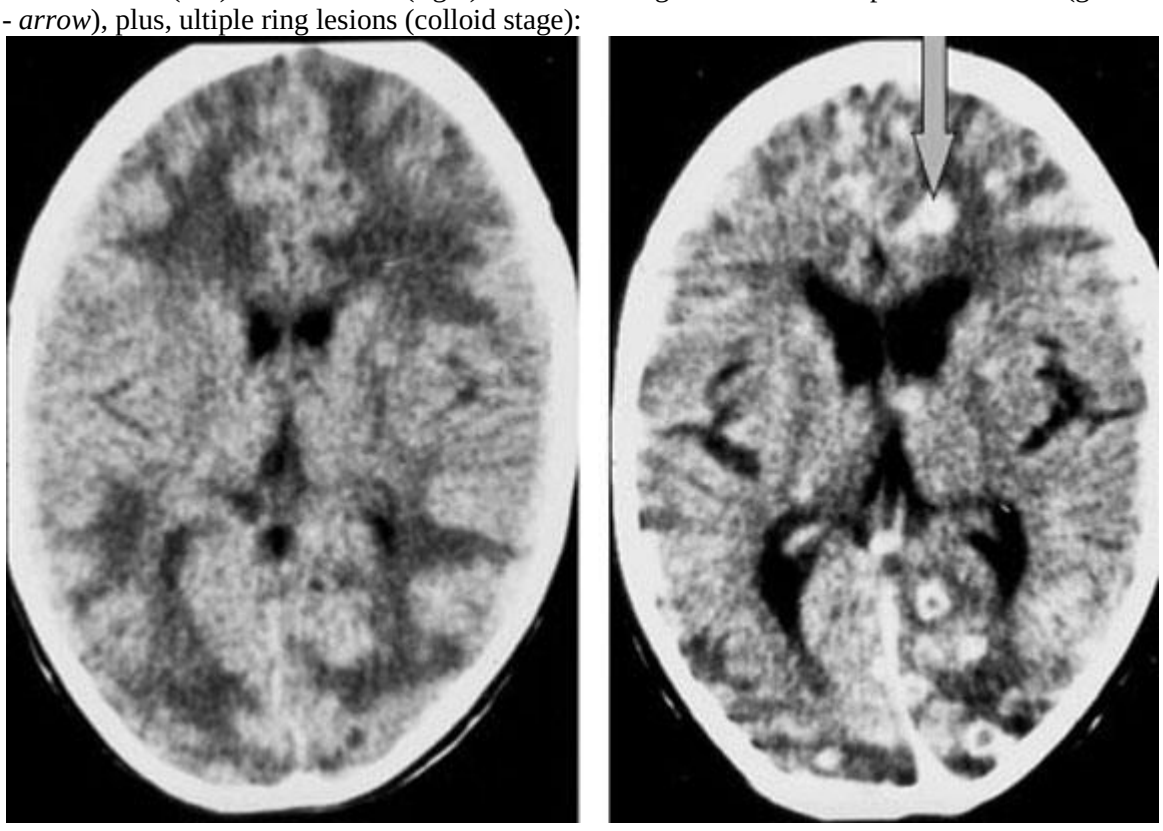
Nonenhanced CT scan - multiple calcified lesions of inactive parenchymal neurocysticercosis:



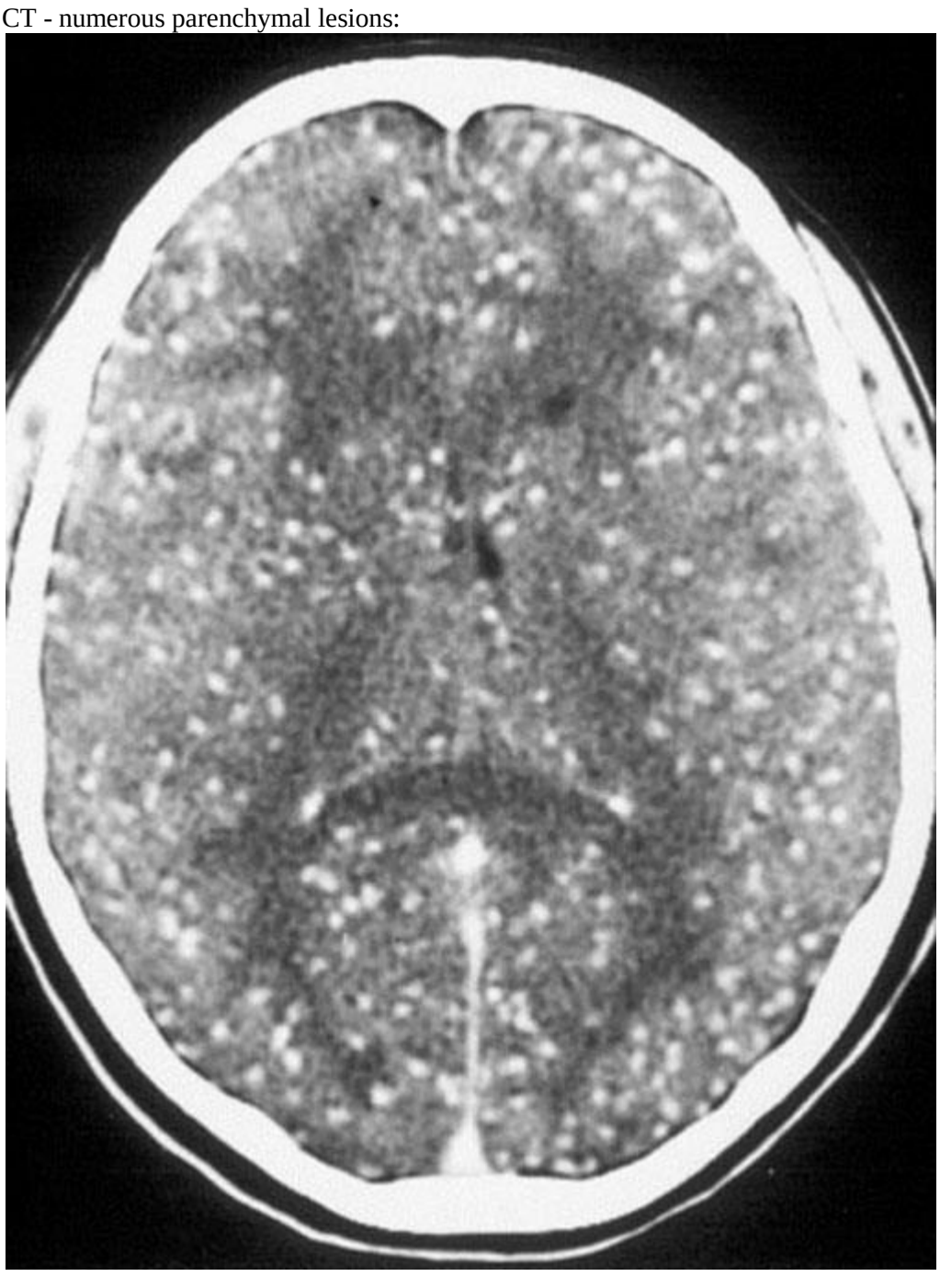
Nonenhanced (left) and enhanced (right) CT - multiple ring-enhancing lesions with perifocal edema:



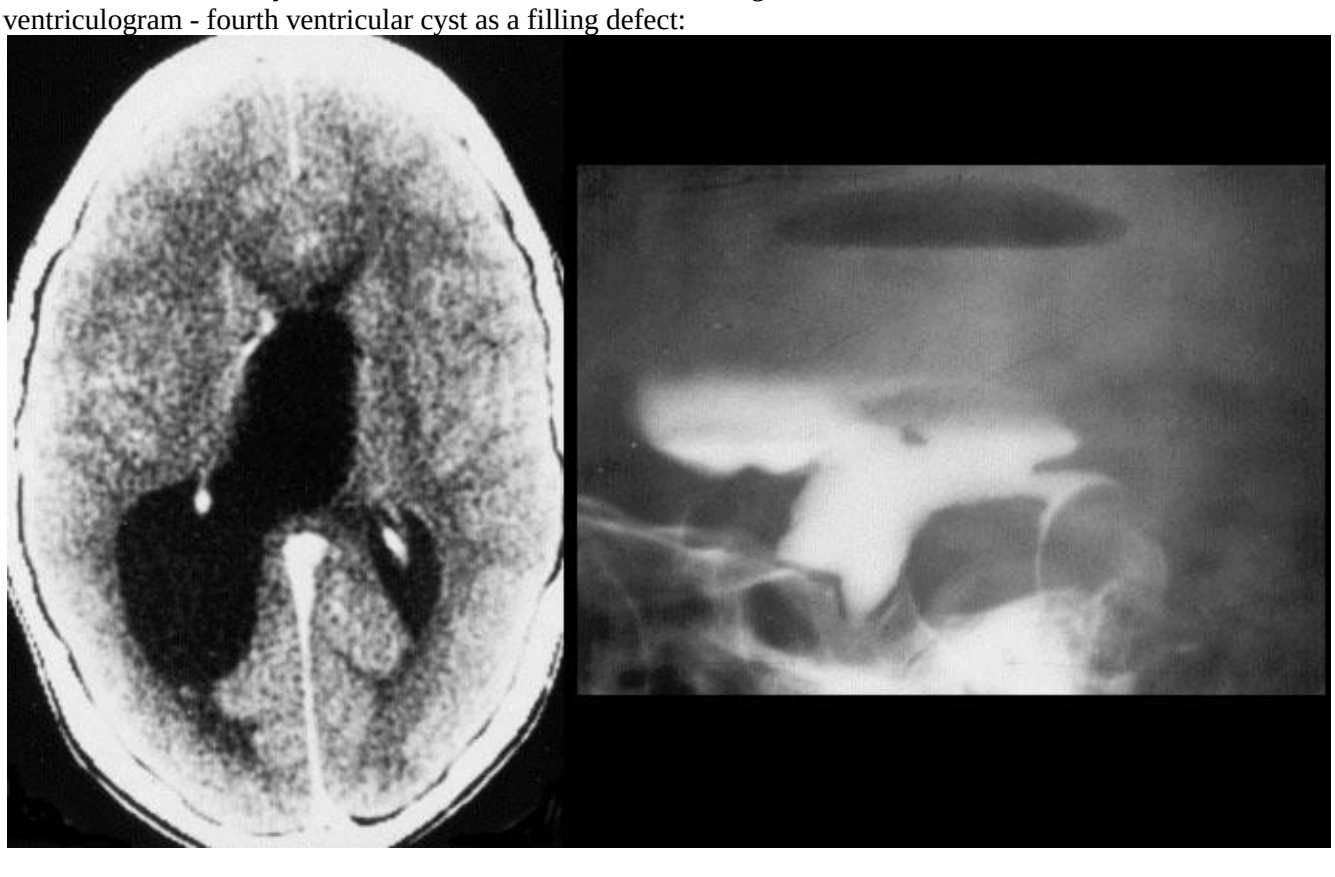
Nonenhanced (left) and enhanced (right) CT - enhancing disk lesion with perifocal edema (granulomatous stage - *arrow*), plus, ultiple ring lesions (colloid stage):



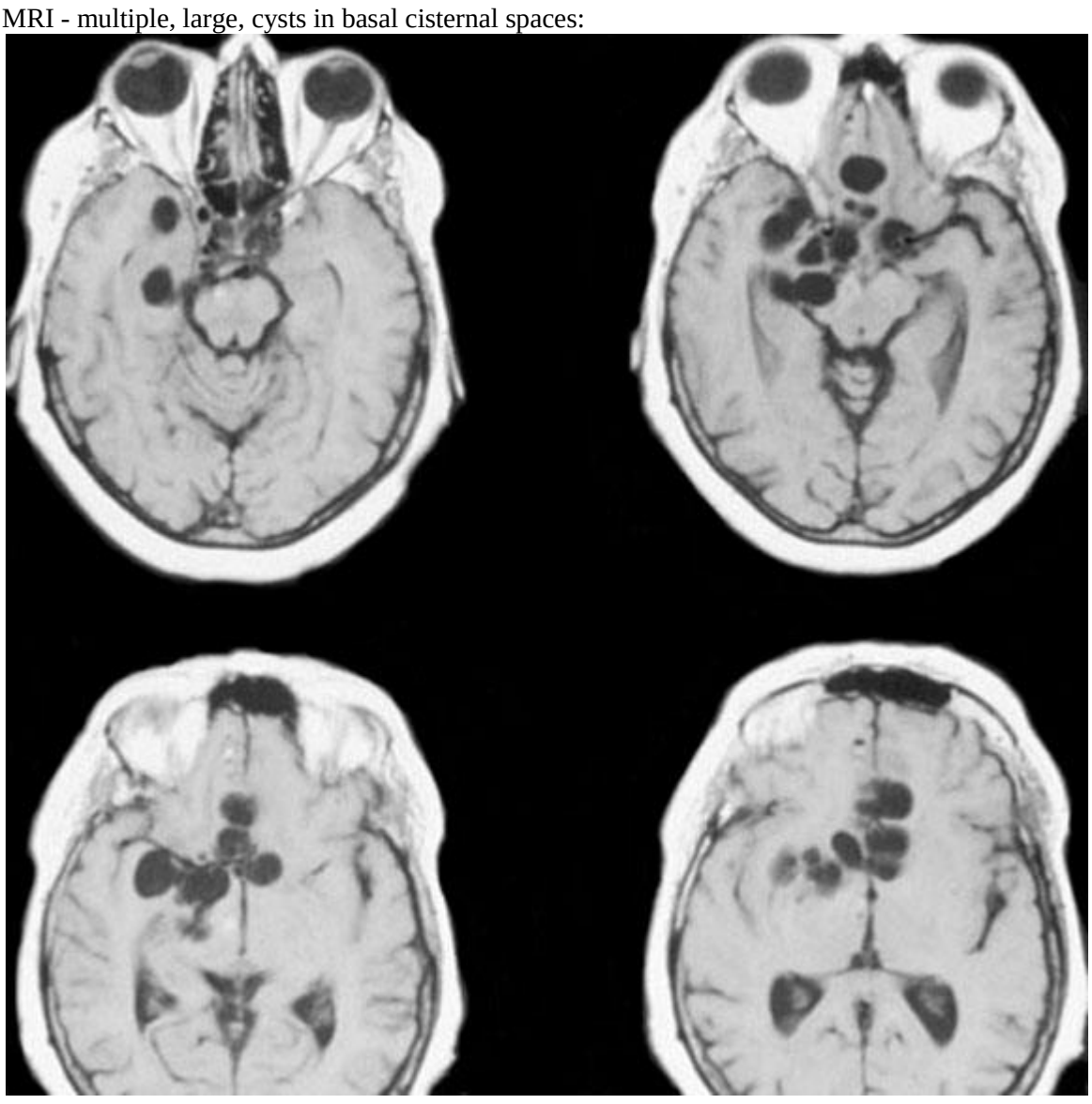
CT - numerous parenchymal lesions:



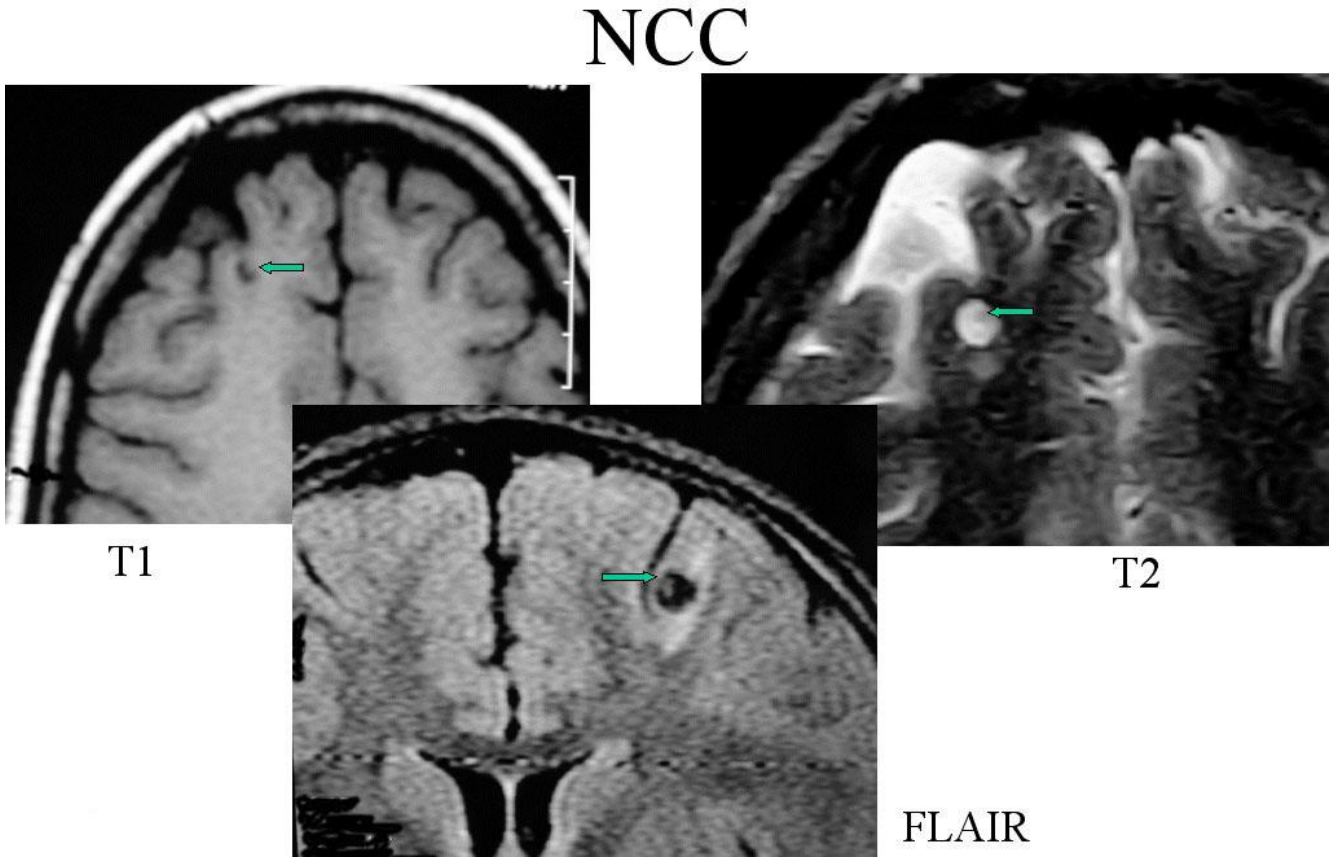
Intraventricular neurocysticercosis: CT - marked dilatation of right lateral ventricle. Contrast-enhanced ventriculogram - fourth ventricular cyst as a filling defect:



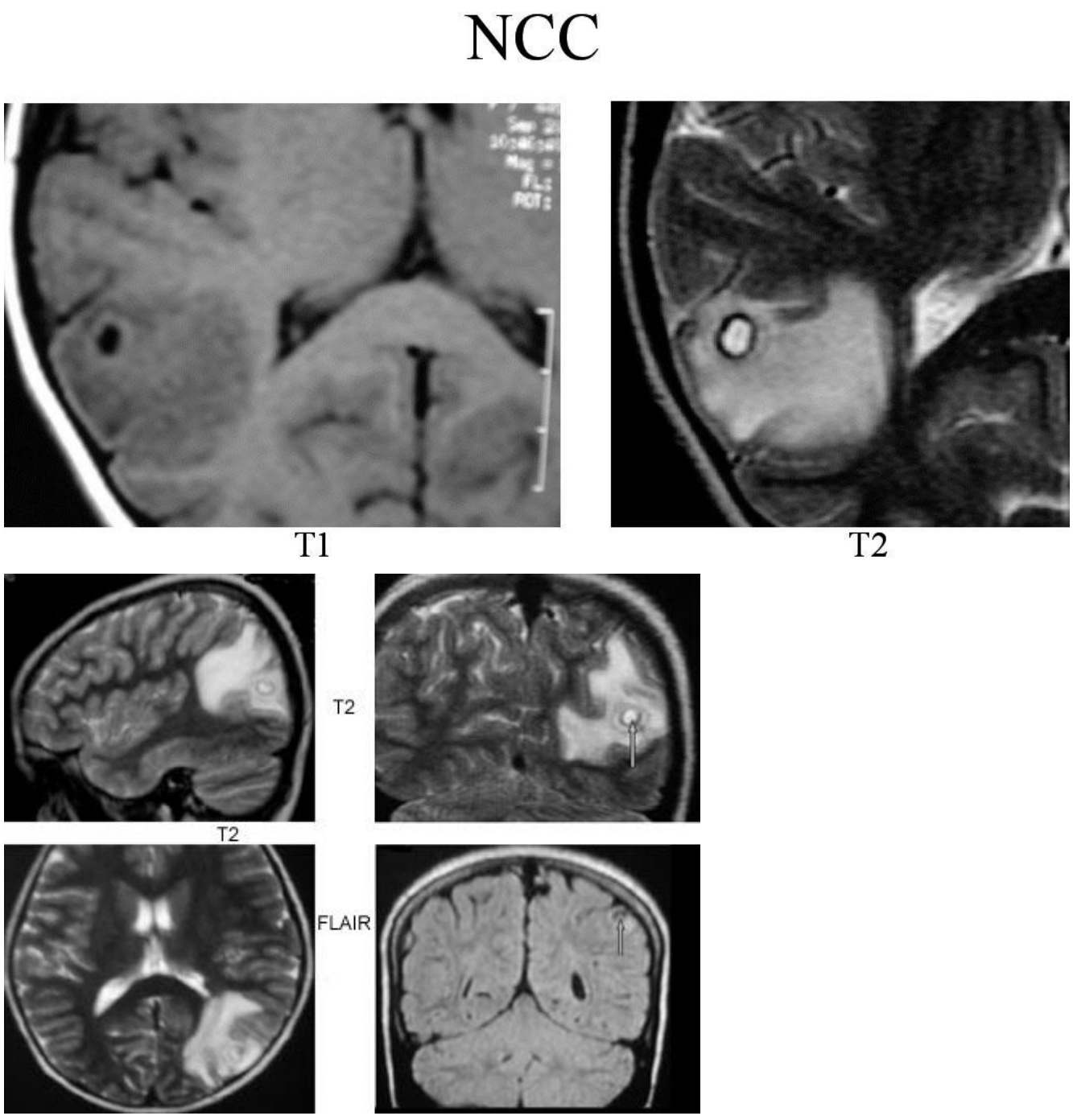
MRI - multiple, large, cysts in basal cisternal spaces:



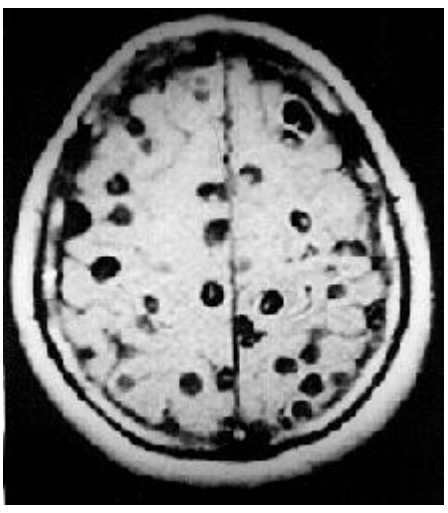
T1, T2, and FLAIR MRIs show cyst with scolex (*arrow*):



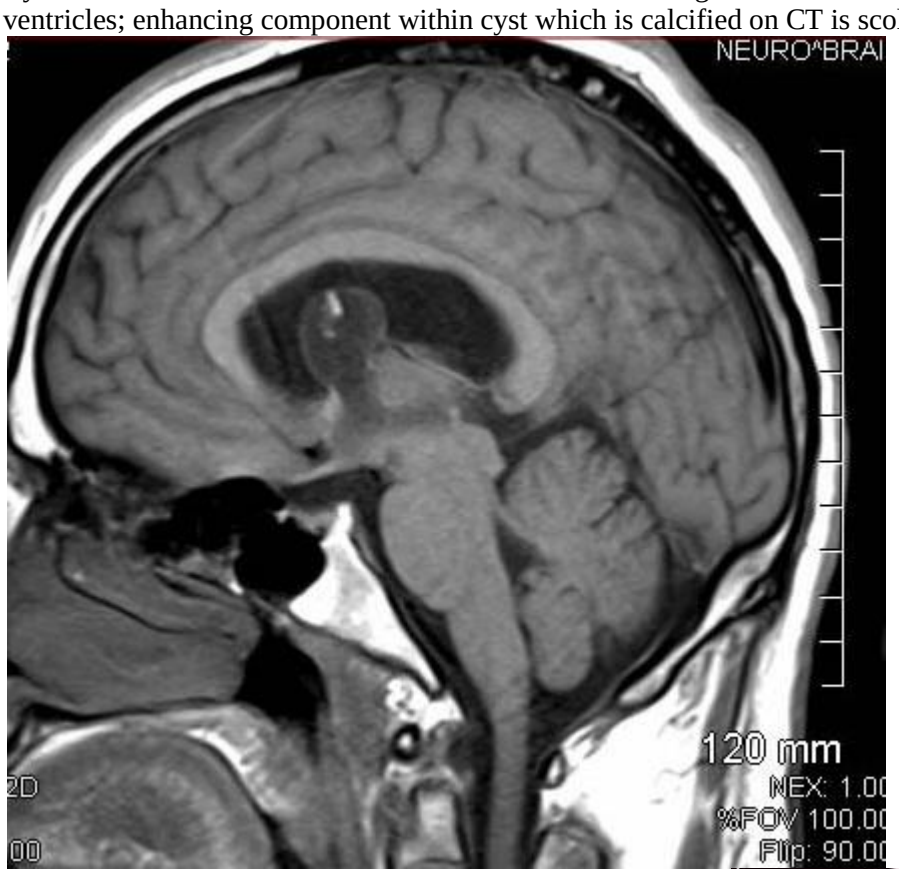
Degenerating cyst with hypointense wall and surrounding edema:

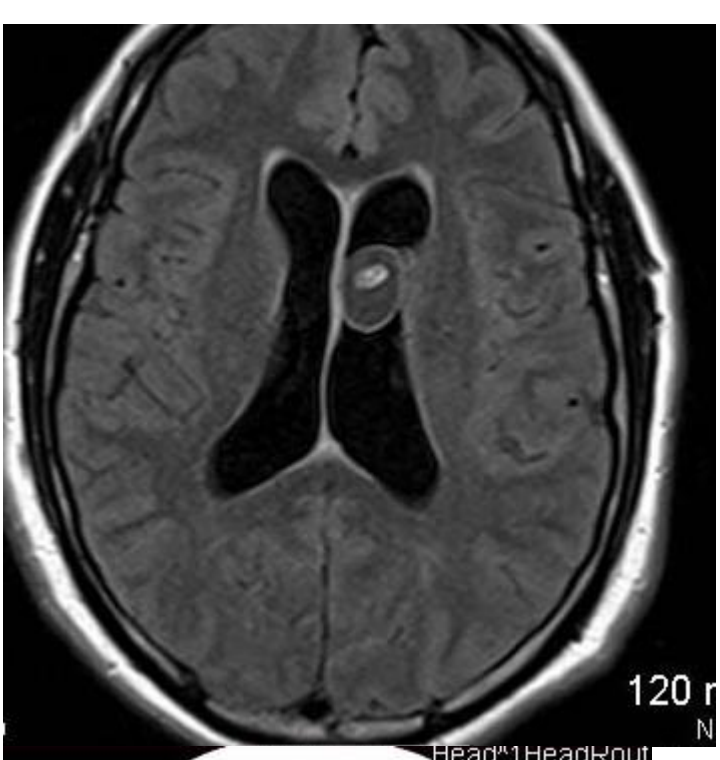


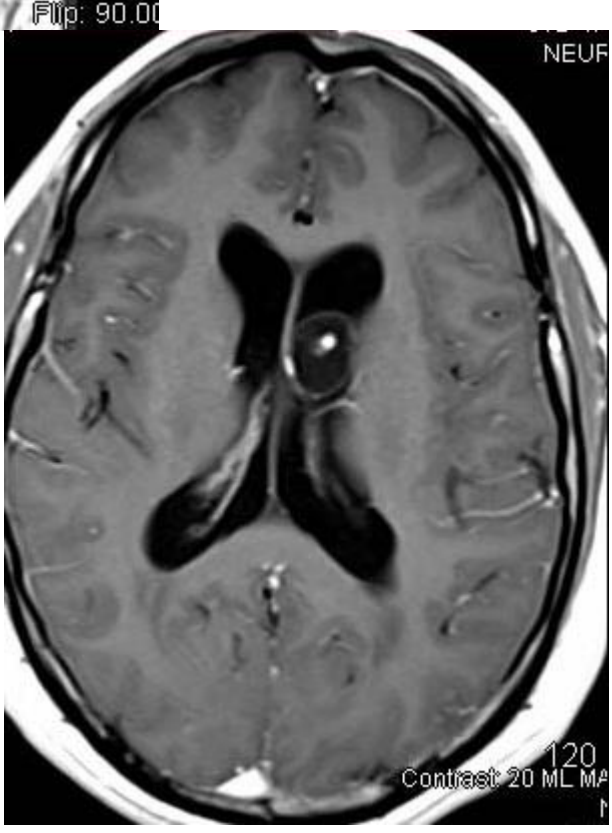
Multiple cysticerci:

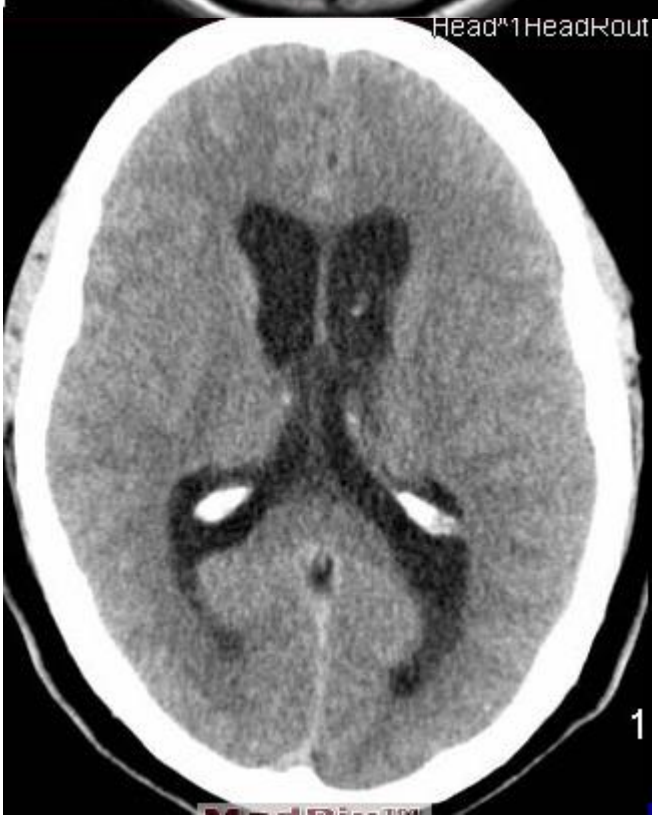


Cystic mass in frontal horn of the lateral ventricle extending into foramen of Monro producing enlarged ventricles; enhancing component within cyst which is calcified on CT is scolex:

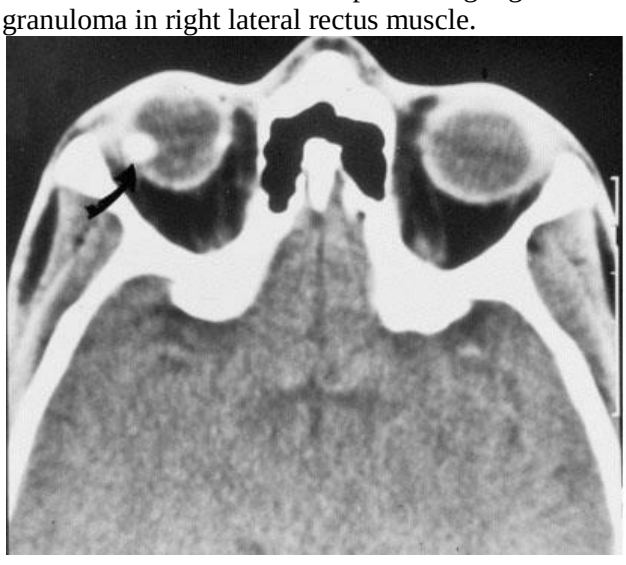


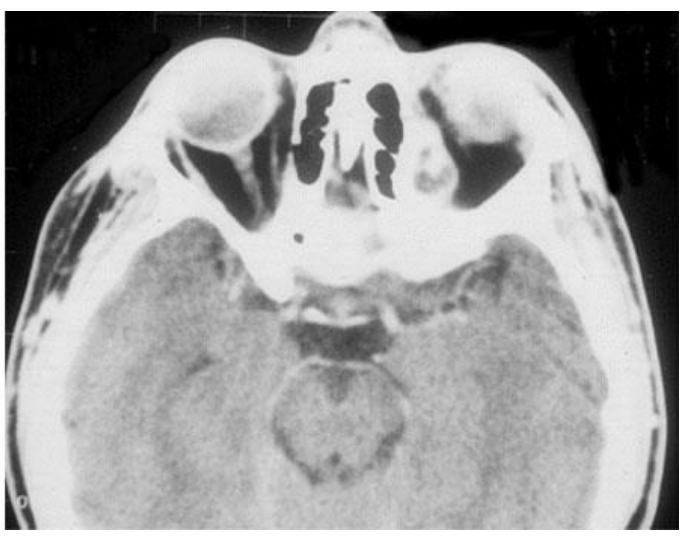






Ocular involvement:
Enhanced CT scan of orbit shows:
calcified lesion in subretinal space of right globe.
granuloma in right lateral rectus muscle.





Serology on ***serum*** or ***CSF***: enzyme-linked immunoelectrotransfer blot (EIBT)* against glycoprotein antigens (100% specific and 70-98% sensitive in asymptomatic stages; but negative in 80% cases with solitary lesion or in calcified stages)

*effectively superseded ELISA (titer is significant at 1:64 in serum, and 1:8 in CSF)

- test of choice is serum EITB

- false negative rates are higher in cases without meningitis.

Biopsy - sometimes needed for diagnosis (no diagnostic test identifies all cases of cysticercosis).

CBC: mild peripheral eosinophilia.

CSF may be normal (or opening pressure↑, pleocytosis with eosinophils, protein↑, glucose↓)

Stool: < 33% of cases have T. solium ova.

TREATMENT

Inactive infection does not require treatment!
Some cases of NCC have lesions that are in ***different stages*** - the most active stage of infection should determine if treatment is necessary!

ANTIHELMINTIC DRUGS

- if cyst is calcified or ring-enhancing, treatment with anthelmintics is probably not necessary.
- start after control of intracranial hypertension (usually after 3 doses of steroids).

  N.B. any cysticercocidal drug may cause irreversible damage when used to treat ocular or spinal cysts, even with corticosteroid use!

  N.B. steroids and aggressive management of hydrocephalus, should be performed prior to administration of anthelmintics!

  1. ALBENDAZOLE – cysticidal agent of choice (more parasiticidal and fewer side effects than praziquantel); 400 mg q12h or 15 mg/kg/day divided in 2-3 doses, taken with fatty meal to enhance absorption (same dose for pediatrics) for 3 months (can be stopped sooner if imaging shows resolution)
  2. PRAZIQUANTEL – also cysticidal
     a) 50 mg/kg/d divided in 3 doses (same dose for pediatrics) for 15 days (doses of 100 mg/kg/d have been recommended because steroids reduce serum concentration by 50%).
     b) 10-100 mg/kg/d x 3-21 days
     c) high dose single day regimen: 25-30 mg/kg q 2 hrs x 3 doses
     d) for intestinal infestation: single oral dose of 5-10 mg/kg
  3. NICLOSAMIDE (Niclocide® and others) given orally for adult tapeworms in GI tract: 1 gm (2 tabs) chewed PO, repeated in 1 hour (total 2 gm).
- there is no consensus on efficacy of medical treatment for intraventricular cysts

STEROIDS

- for all patients concomitantly with anthelmintic (to reduce edema), but may lower plasma level of PRAZIQUANTEL or increase plasma level of ALBENDAZOLE
  - start 2-3 d before antihelmintics (e.g. DEXAMETHASONE 8 mg q 8 hours, on day 3 decrease to 4 mg q 8 hours, on day 6 change to PREDNISONE 0.4 mg/kg/day divided TID)
  - taper after antihelmintics are discontinued

ANTIEPILEPTICS

- to treat seizures (sometimes medically refractory and lifelong)

SURGERY

Indications – symptomatic cases:
- unclear diagnosis → stereotactic biopsy
- hydrocephalus (intraventricular, subarachnoid cysts) → CSF diversion (may become obstructed by granulomatous inflammatory debris), endoscopic resection.
- giant cysts (> 50 mm) when intracranial hypertension persists despite steroids → resection.
- uncontrollable seizures → resection.
- spinal / orbital cysts → resection (inflammation associated with medical treatment may cause worsening of symptoms or loss of vision)

- spinal, intraventricular, subarachnoid cysts are more refractory to medical therapy!
- antihelmintics may be required even after complete surgical removal because of possibility of relapse.

FOLLOW-UP

CT / MRI every 6 months until lesions disappear or calcify.

CONTACTS

- screen patients and their personal contacts for ***tapeworm infection*** → single dose of NICLOSAMIDE or PRAZIQUANTEL.
- screen close contacts of persons with tapeworms for ***cysticercosis*** (medical history and serology); if suggestive of cysticercosis → CT/MRI

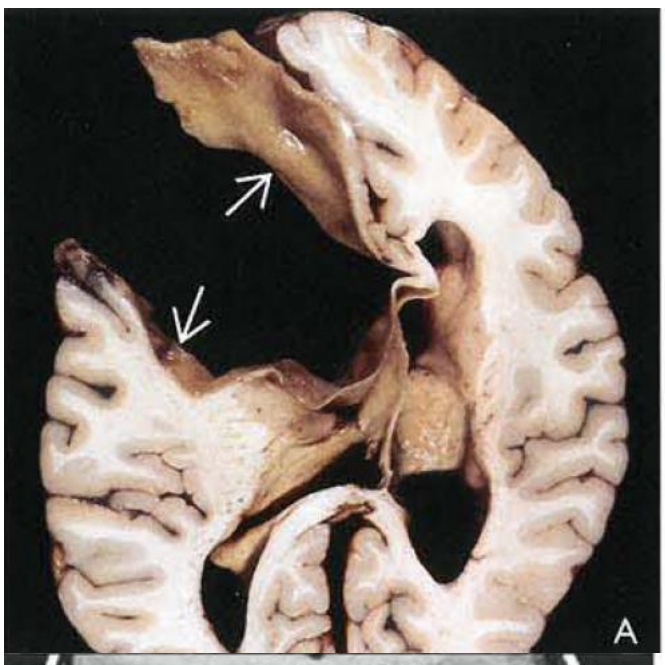
ECHINOCOCCOSIS

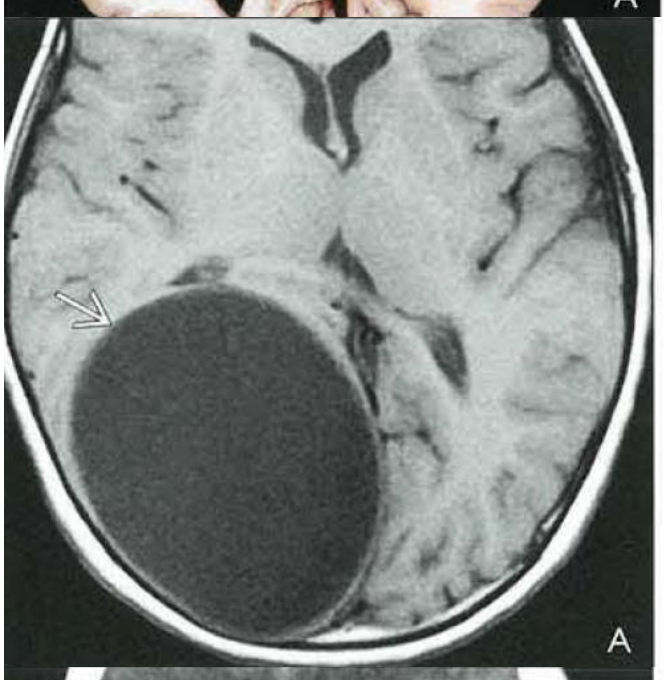
- second most common parasitic CNS infection.

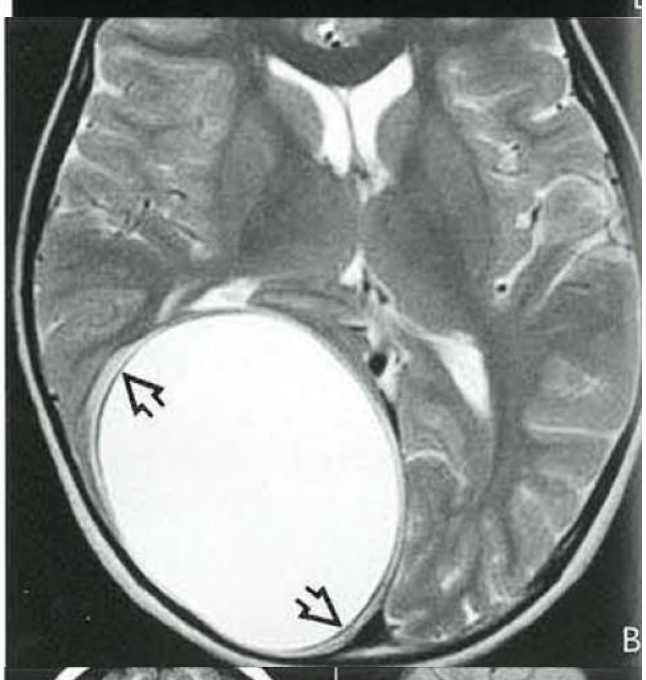
Two species of Echinococcus tapeworms:

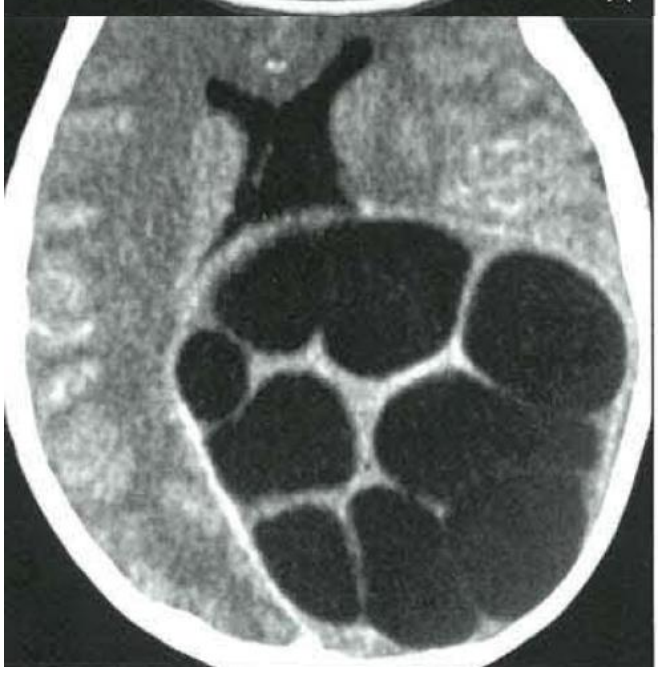
E. GRANULOSUS (EG)

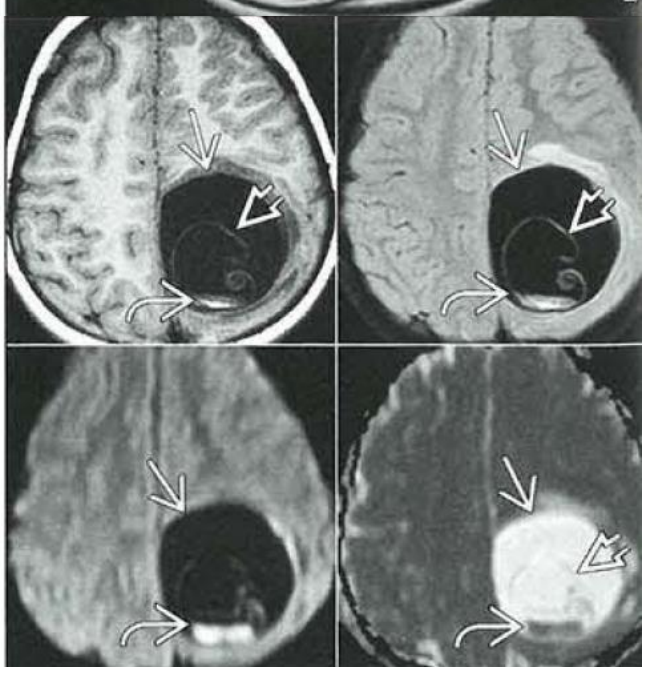
- **hydatid disease** or **hydatid cyst (HC)** – single large thin-walled cyst (but maybe multilocular with "daughter" cysts); no calcification, no edema, no enhancement, fluid isodense / isointense to CSF (sometimes "sand" can be seen in dependent portion of cyst).





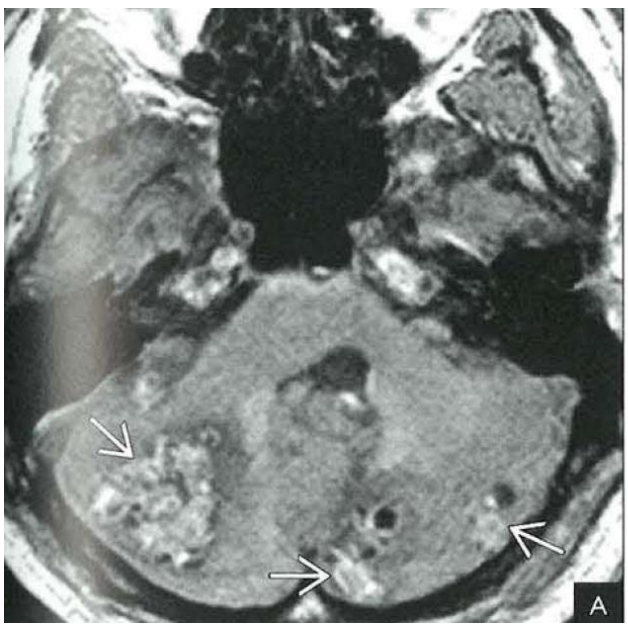


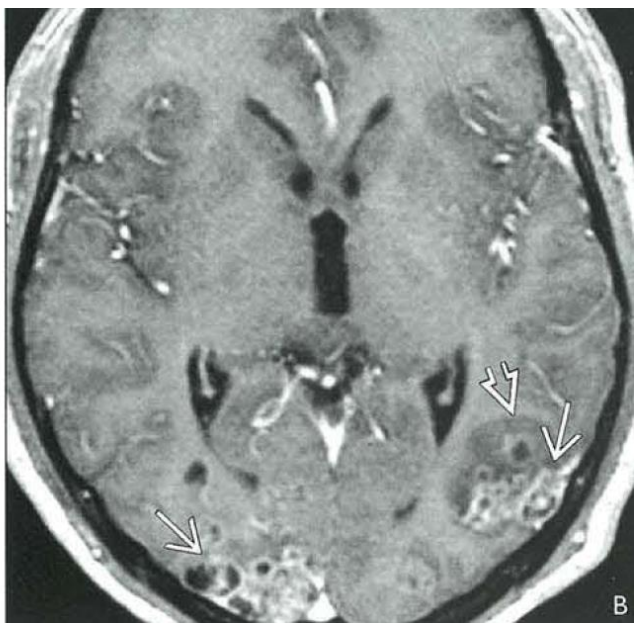




E. MULTILOCULARIS / ALVEOLARIS (EM/EA)

– **alveolar echinococcosis** – multiple irregular cysts that are not sharply demarcated and enhance in ring-like / nodular / cauliflower patterns.



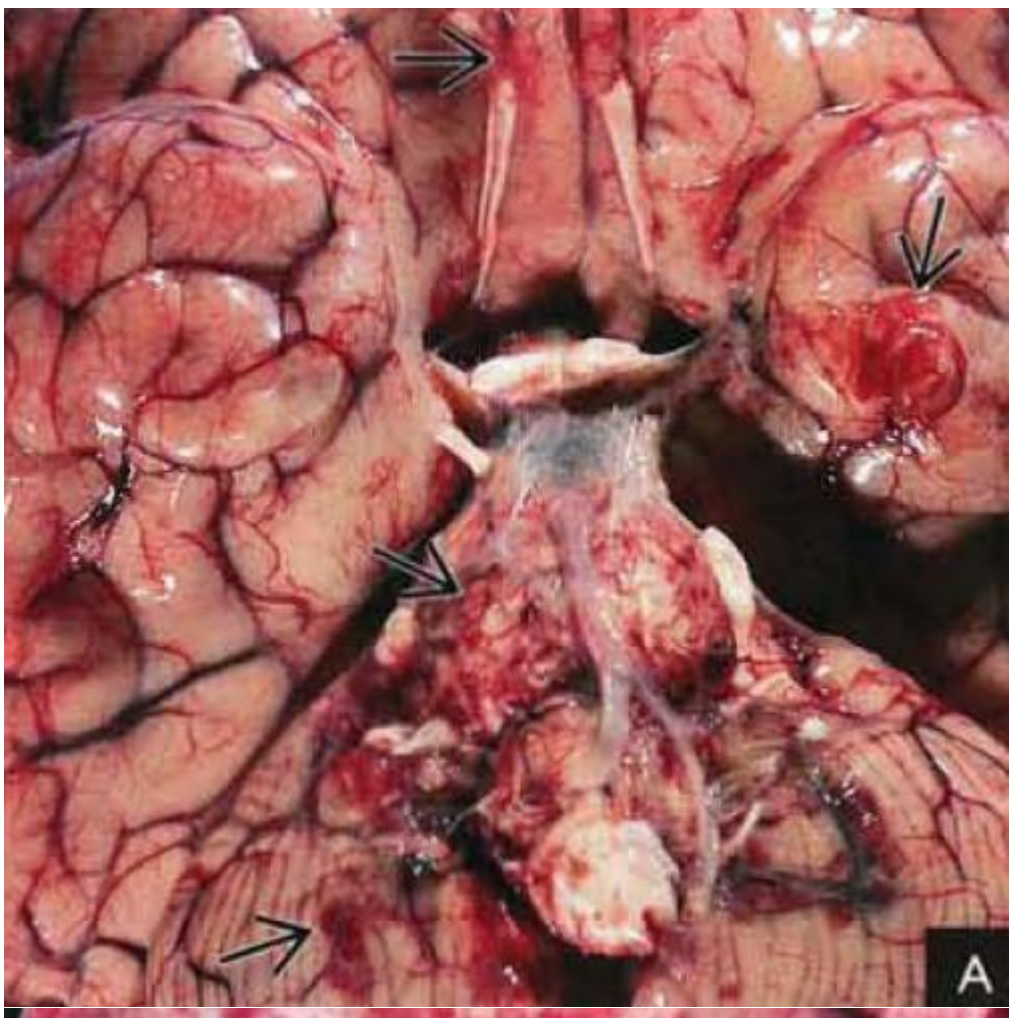


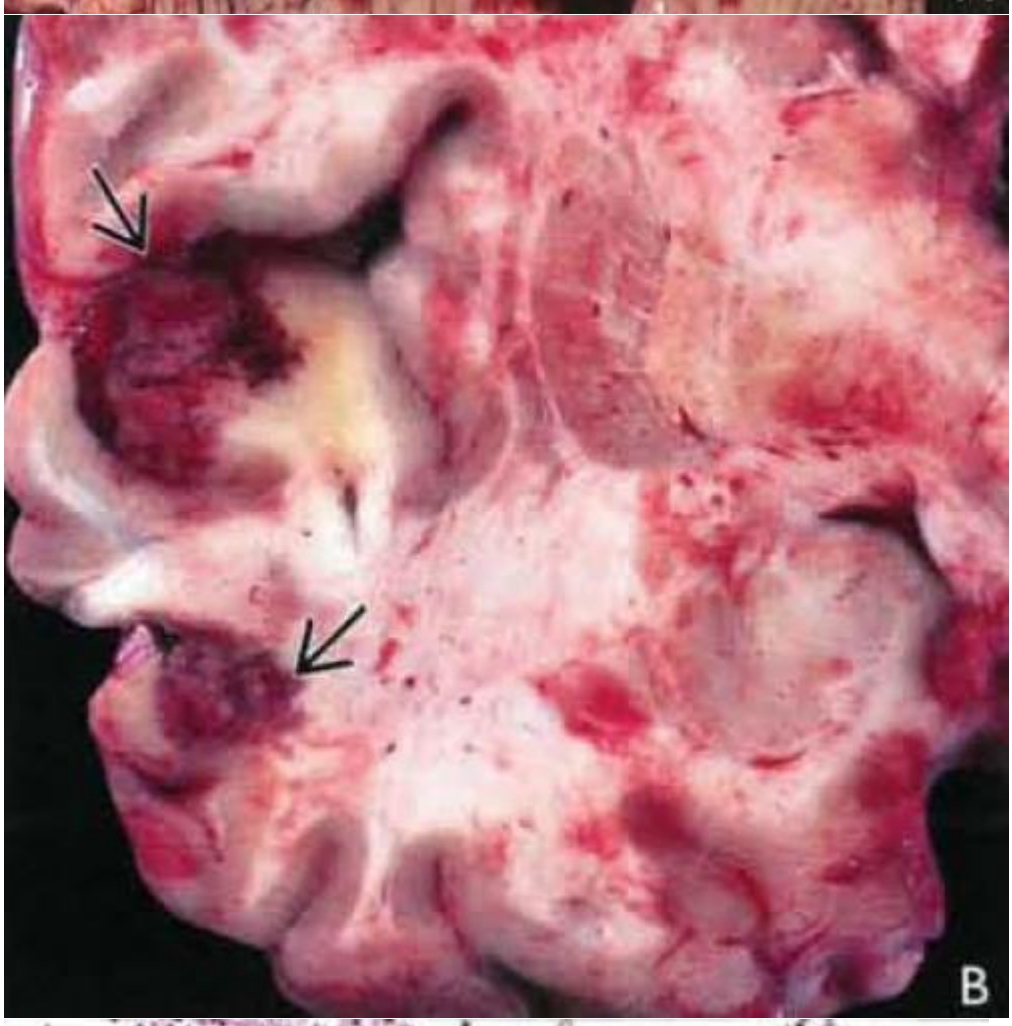
AMEBIASIS

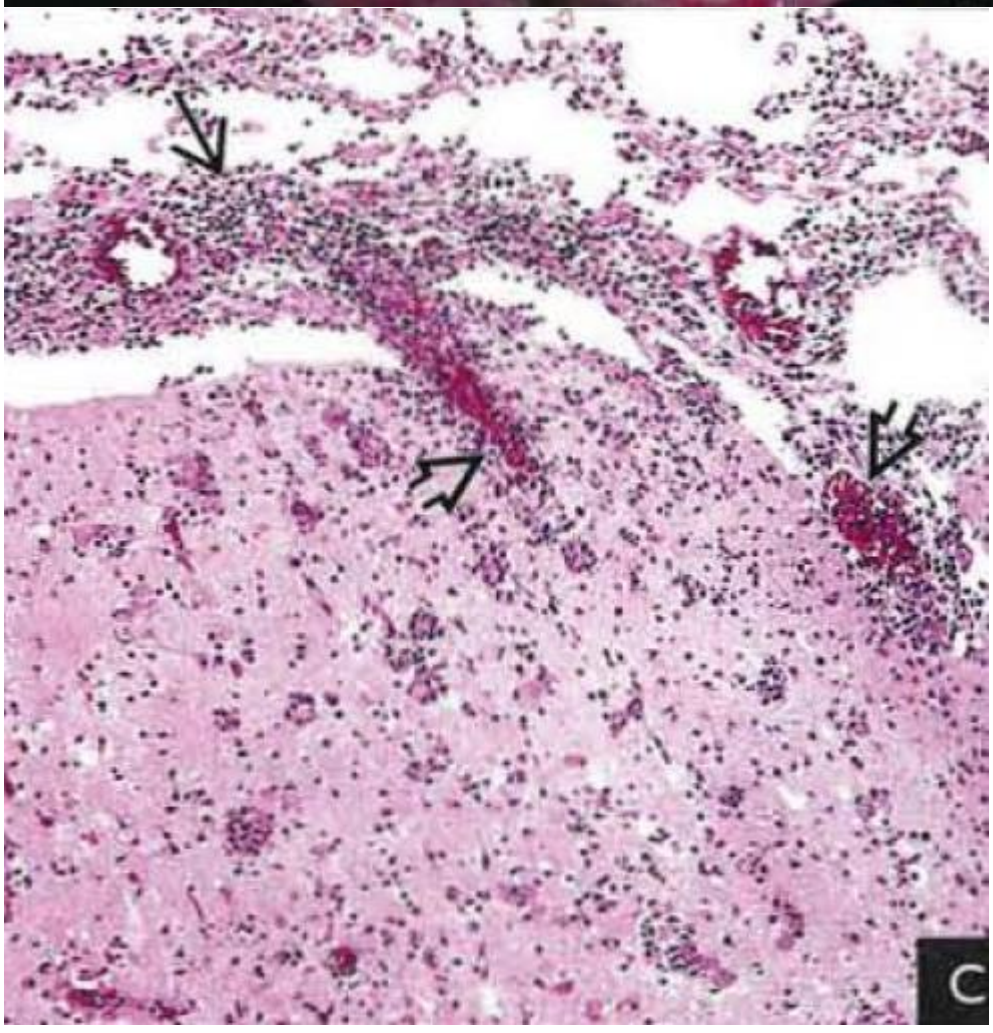
PRIMARY AMEBIC MENINGOENCEPHALITIS (PAM)

- acute, rapidly progressing, necrotizing, hemorrhagic meningoencephalitis and angiitis with focal lesions – numerous trophozoites are present, but no cysts are seen because of disease acuity.

- *N. fowleri* in immunocompetent young adults swimming in warm fresh water during the summer.
- *N. fowleri* invades the olfactory mucosa and enters the brain along the olfactory nerves.
- fatal within 48-72 hours.



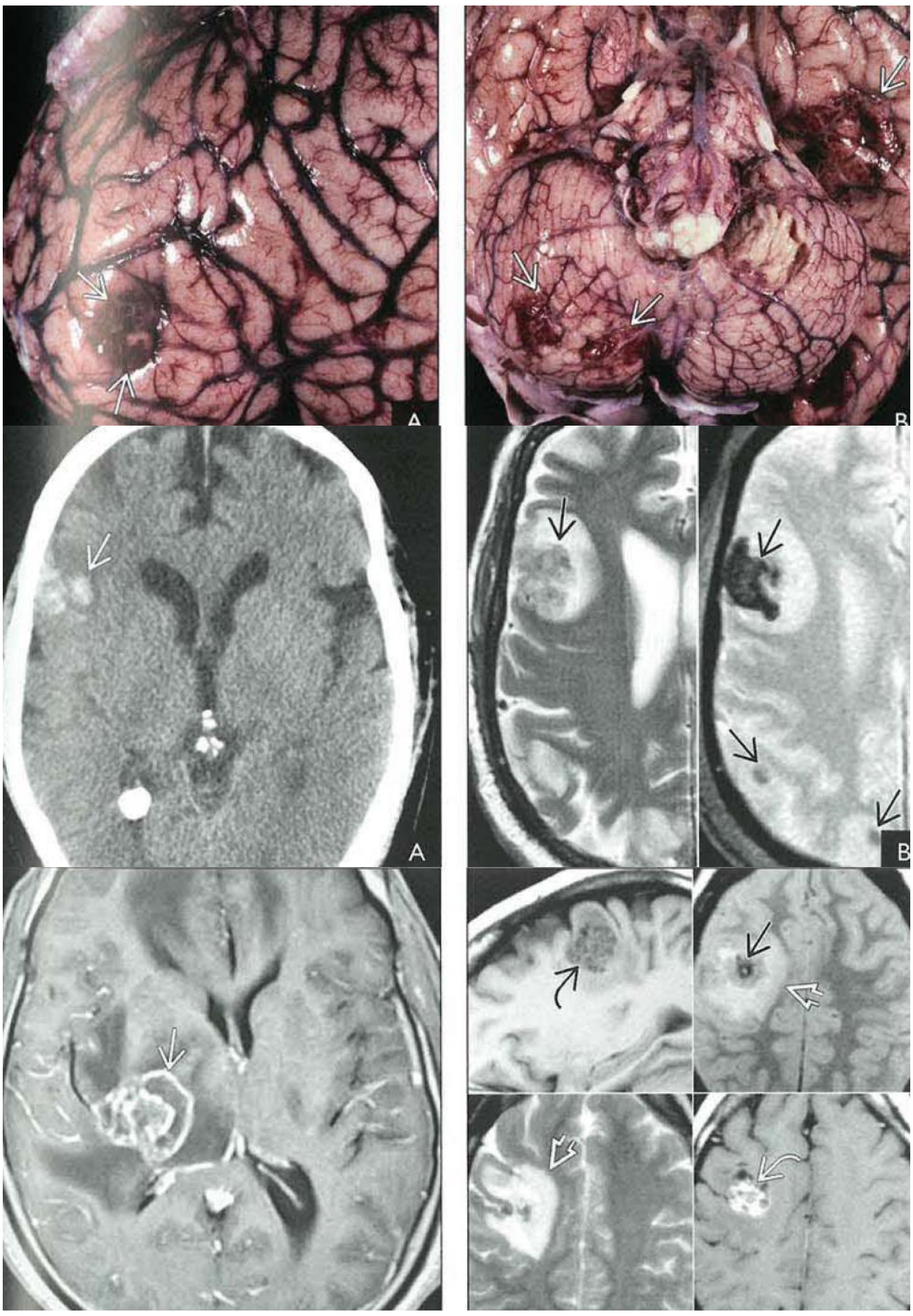




GRANULOMATOUS AMEBIC ENCEPHALITIS (GAE)

- granulomatous inflammation with multinucleated giant cells, trophozoites, and cysts.

- subacute to chronic condition.
- caused by one of six *Acanthamoeba species* or *Balamuthia mandrillaris*.
- no seasonal predilection.
- associated with immunodeficiency (and chronic debilitating conditions.



AMEBIC ABSCESS

- pus with trophozoites at the edge of the lesion.
- caused by E. histolytica.
- most patients have intestinal or liver infection.
- not related to immunodeficiency.

BIBLIOGRAPHY for ch. "Infections of Nervous System" → follow this LINK >>