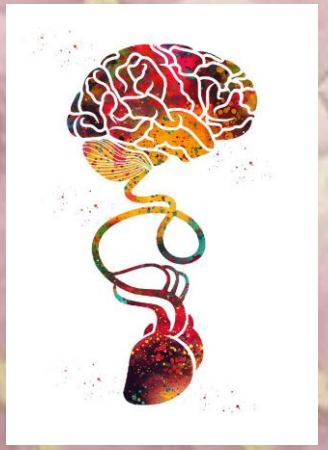
Topic Review – Neurology Resident

Parasitic & Protozoa infection in CNS



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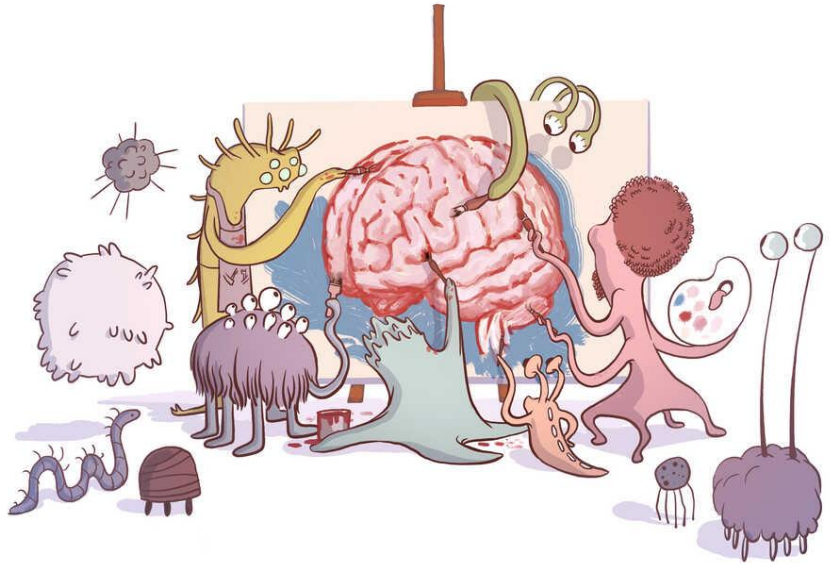
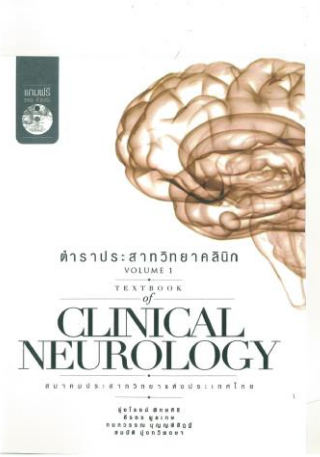
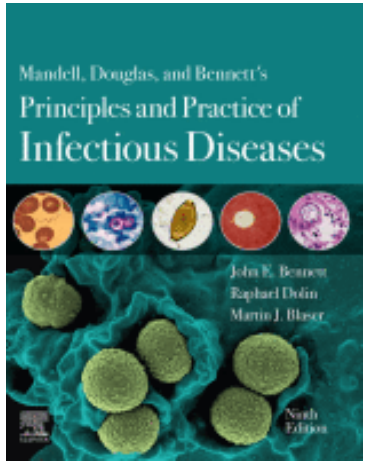
14 Feb 2022 - Academic Year 2021

Scope of talk

- Introduction to Neuroparasitology
- Nematode (Roundworm)
  - Angiostrongyliasis
  - Gnathostomiasis
  - Filariasis
- Trematode (Flatworm – Fluke)
  - Schistosomiasis
  - Paragonimiasis
- Cestode (Flatworm – Tapeworm)
  - Neurocysticercosis
- Protozoa
  - Cerebral Toxoplasmosis
  - Cerebral Malaria
  - Cerebral Amebiasis
    - *Entamoeba histolytica*
  - Primary Amebic meningoencephalitis
    - *Naegleria fowleri*







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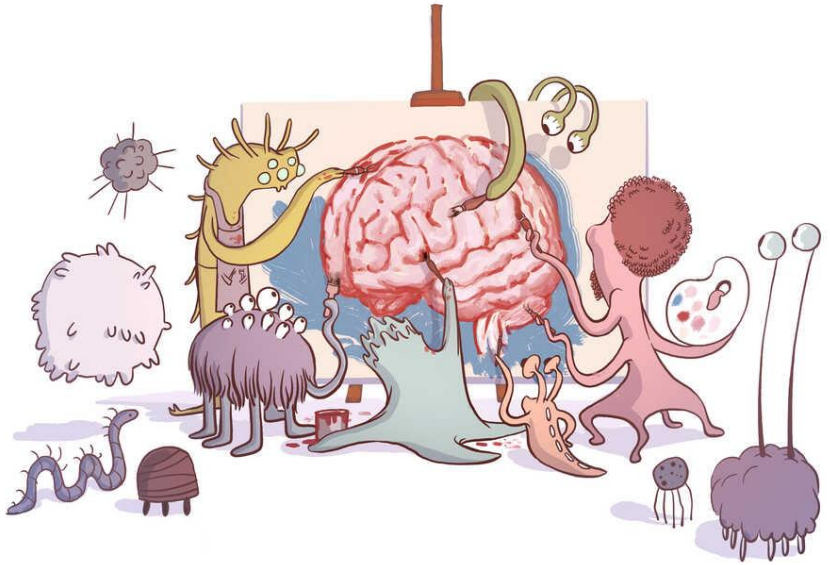

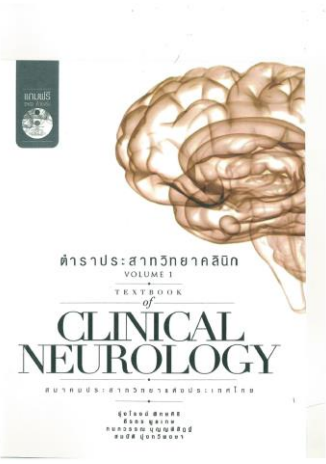

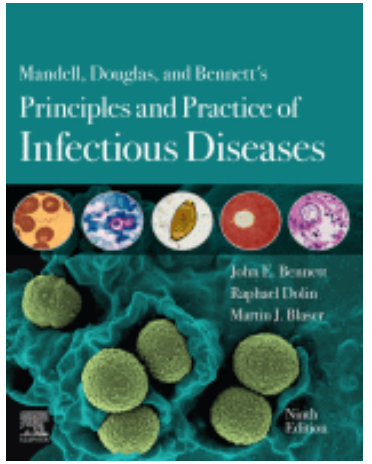

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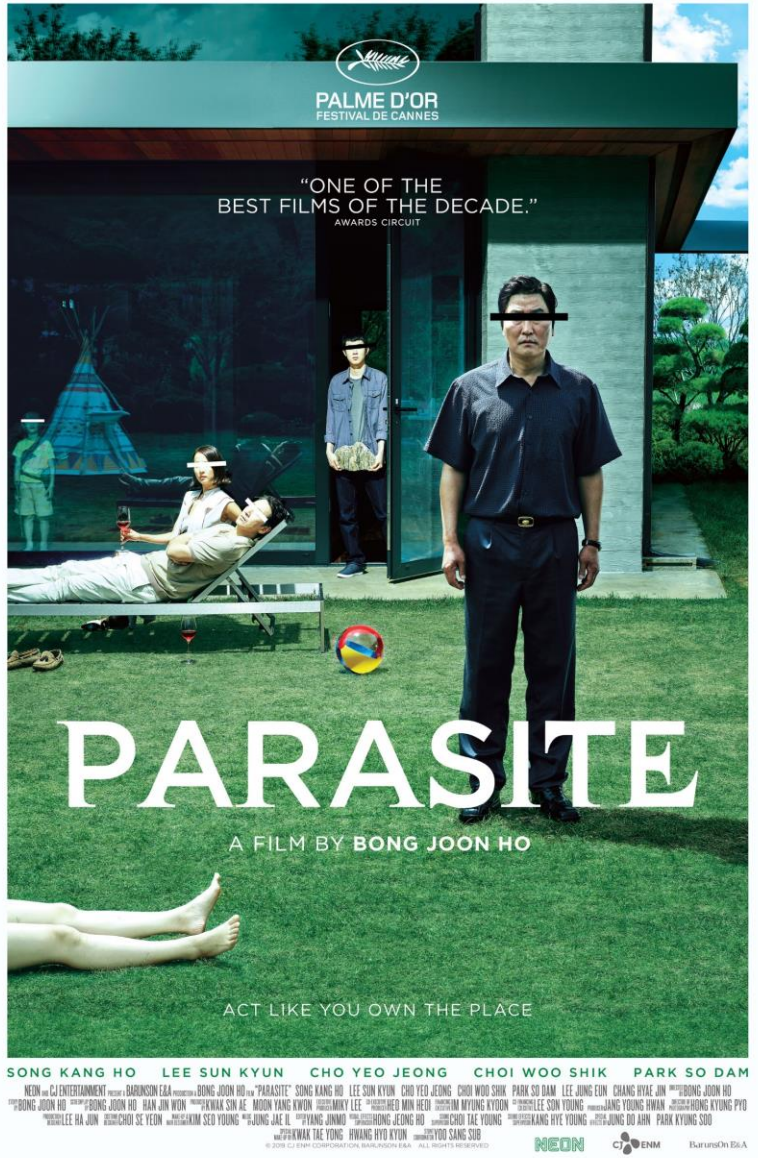
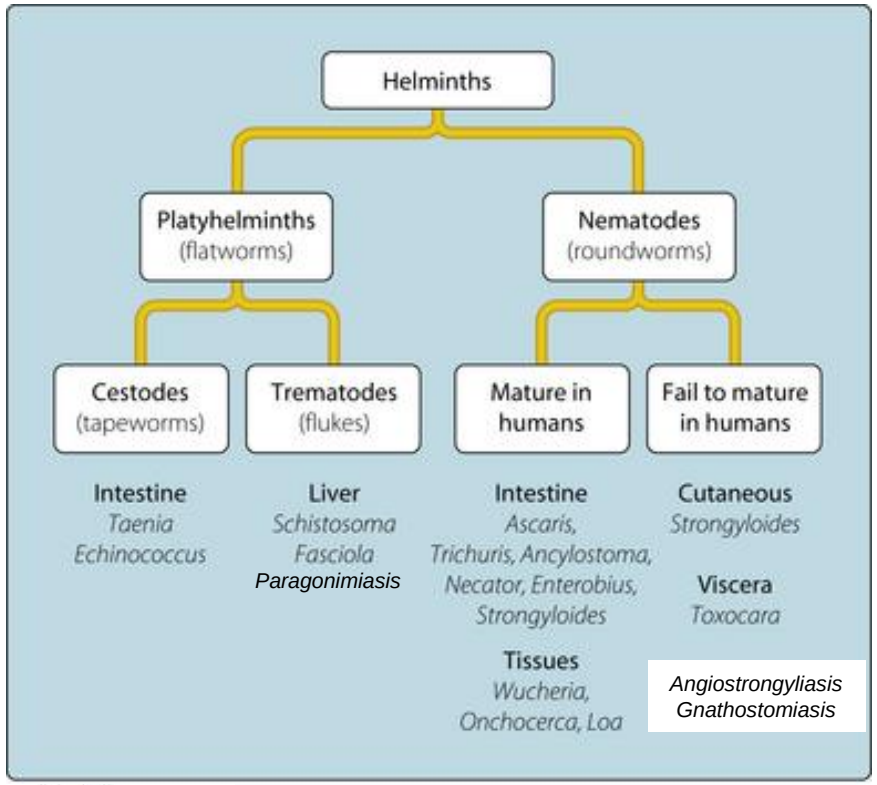
Introduction to Neuro-Parasitology

- **Parasite**
  - an organism that lives on or in another organism from a different species, **taking its nourishment from the host.**
  - **DO NOT** always harm the host, and a typical vertebrate is the host of many species of parasites.
- **Focusing on**
  - Endoparasite (infect inside the body) & CNS infection
  - Public health issue
  - Endemic area!! – mainly in Thailand



Basic Classification

Helminths (multicellular)



Protozoa (unicellular)

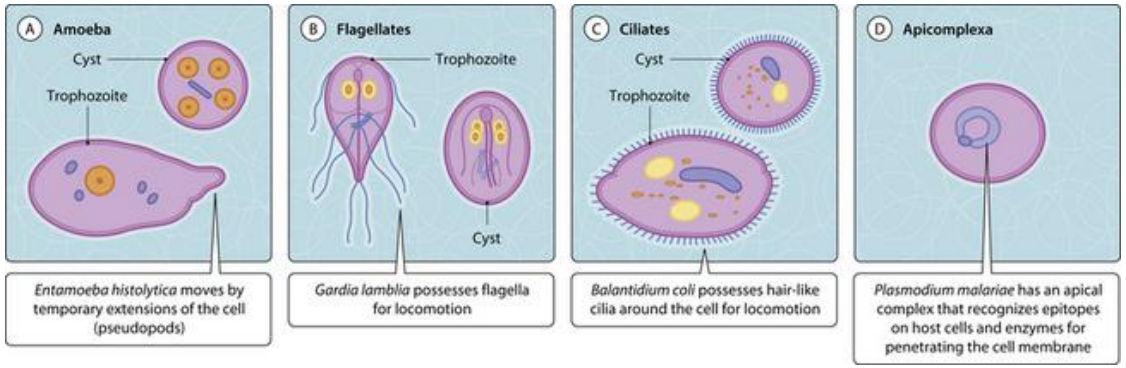


Table 1. Classification of parasitic infections of the central nervous system.

Protozoa	Metazoa		
Malaria	Flatworms	Trematoda	Schistosomiasis
American trypanosomiasis			Paragonimiasis
African trypanosomiasis		Cestoda	Cysticercosis
Toxoplasmosis			Coenurosis
Amebiasis			Hydatidosis
Microsporidiasis			Sparganosis
Leishmaniasis	Roundworms or Nematoda	Gnathostomisasis	
		Angiostrongyliasis	
		Toxocariasis	
		Strongyloidiasis	
		Filariasis	
		Baylisascariasis	
		Dracunculiasis	
		Dicronemiasis	
		Lagochilascariasis	

Life cycle & Host

- **Life cycle**
  - 1) Complete life cycle in **ONE** host
  - 2) Need **TWO** different hosts
- **Host**
  - **Definitive host (primary host / final host)**
    - the one which harbors the adult parasite and where **the parasite reproduces sexually.**
  - **Intermediate host (secondary host)**
    - the host which harbors the **larval stage** or **the asexual forms** of the parasite.
  - **Paratenic host (transfer host / transported host)**
    - a potential or substitute intermediate host that **serves until the appropriate definitive host is reached,** and in which no development of the parasite occurs
    - **** it may or may <u>not</u> be necessary** to the completion of the parasite's life cycle.
  - **Accidental host**
    - one that accidentally harbors an organism that is **<u>NOT</u> ordinarily parasitic in the species**.

Life cycle & Host

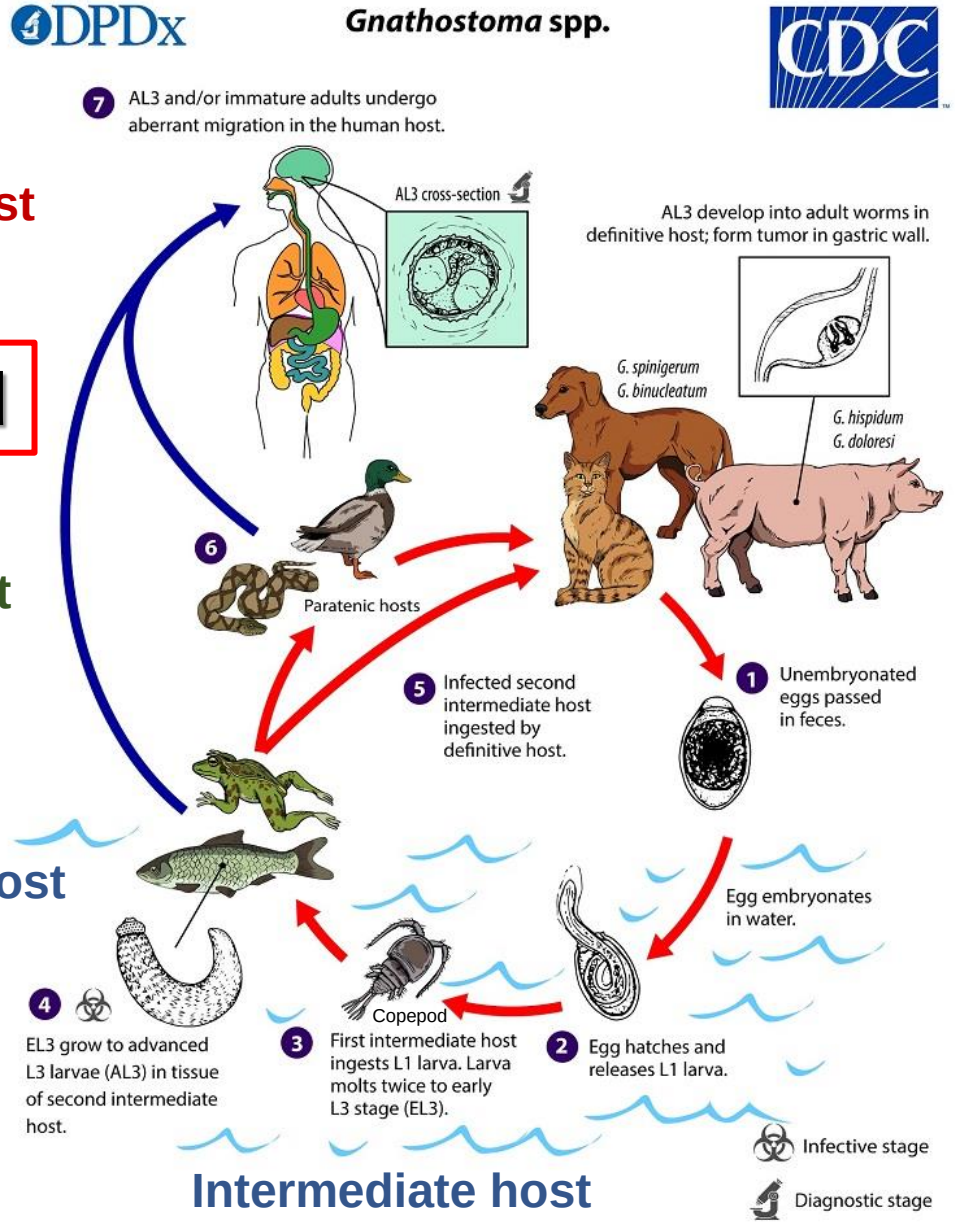
- **Examples**

Accidental host

Incubation period

Paratenic host

Intermediate host



Definitive host

Clinical Manifestation

- **Acute/Subacute/Chronic**
- **Systemic manifestation**
  - Fever
  - **Eosinophilia**
    - Absolute E > 500 cells
    - Count > 7% of total leukocytes
- **CNS manifestation**
  - Seizure
  - Headache
  - Focal neurological deficit – space occupying lesion
  - Encephalitis
  - **Eosinophilic meningitis**
    - Absolute E > 10 cells/ul
    - Count > 10% total CSF leukocyte
- **Extra-CNS manifestation**

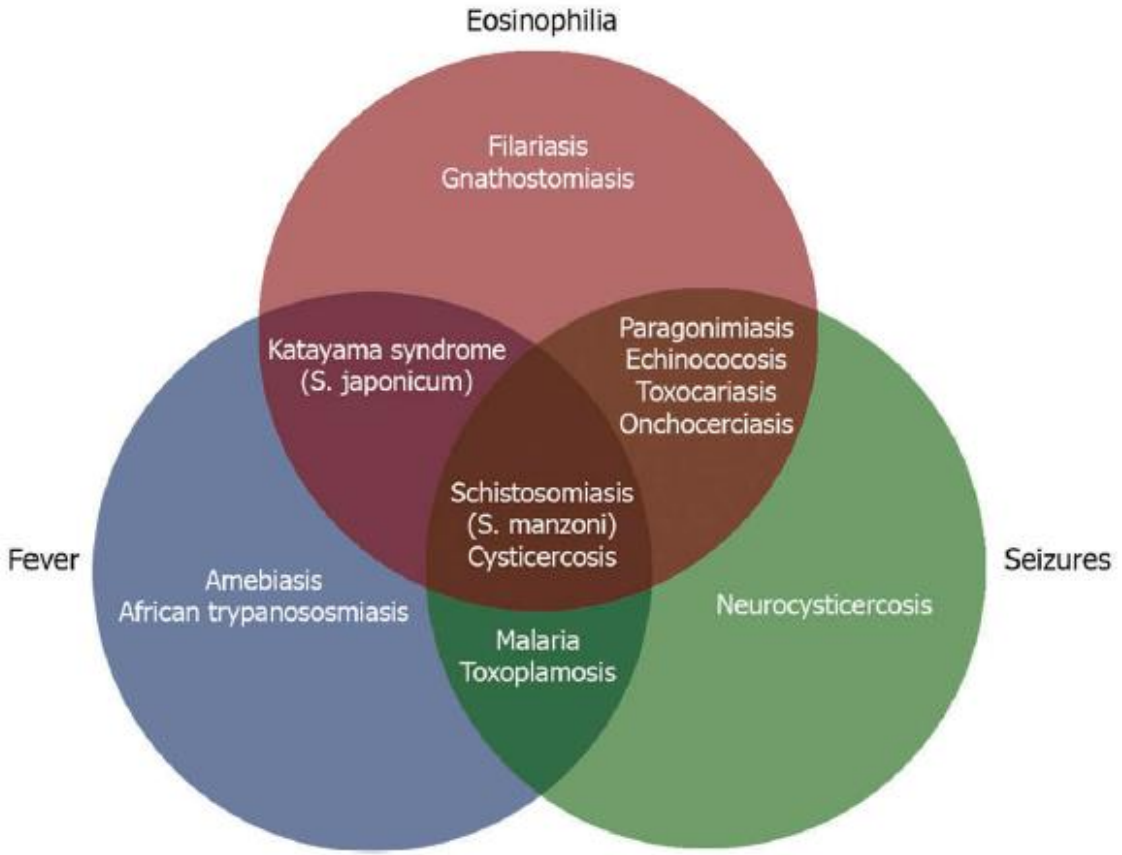
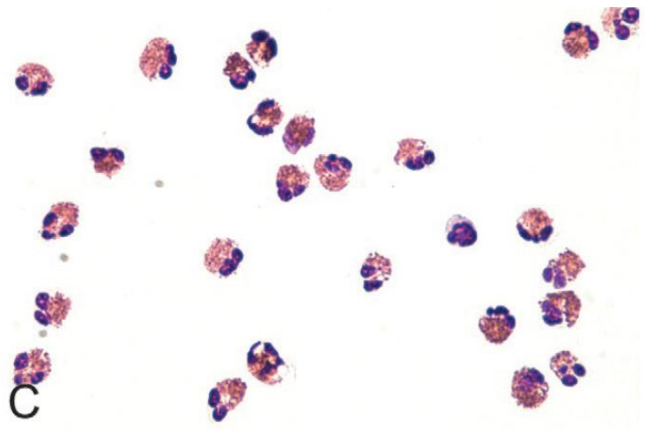


Figure 1. Parasitic diseases of central nervous system according to presentation.

Clinical Manifestation

- **Eosinophilic meningitis**
  - **In practice – HARD TO Dx!**
    - Hard to see in fresh smear >> Request special stain i.e. Wright's stain
    - Easy cell lysis >> Urgent direct examination
  - **D/Dx beyond parasitic infection!**
    - Infectious agents
      - Tuberculous meningitis
      - Granulomatous meningitis
      - Neurosyphilis
    - Idiopathic eosinophilic meningitis
    - Local allergic reaction to foreign material
    - Tumors: Hodgkin lymphoma
    - Drugs



Eosinophils

Causes of eosinophilic meningitis

Infection	Noninfection
Parasites	Malignancy
Angiostrongylus cantonensis	Hodgkin diseases
Gnathostoma spinigerum	Non-Hodgkin lymphoma
Baylisascaris procyonis	Eosinophilic leukemia
Neurocysticercosis (*Taenia solium*)	Drugs
Cerebral paragonimiasis	Ibuprofen
Neurotrichinosis	Ciprofloxacin
Cerebral toxocariasis	Intraventricular gentamicin, vancomycin, iophendylate dye
Cerebral/spinal schistosomiasis	Others
Bacteria	Ventriculoperitoneal shunts
Virus	Hypereosinophilic syndrome
Fungus: *Coccidioides immitis*	

Adapted from Lo Re and Gluckman (2003).

Coconut color

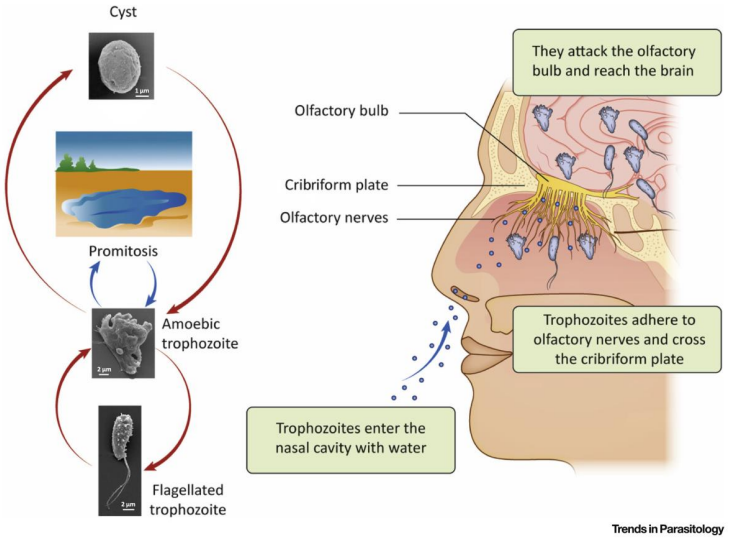
Angiostrongylus cantonensis

Overview of cerebrospinal fluid cytology.
Handbook of Clinical Neurology, Vol. 145 (3rd series). Neuropathology
G.G. Kovacs and I. Alafuzoff, Editors
http://dx.doi.org/10.1016/B978-0-12-802395-2.00035-3

Mechanisms of CNS invasion

- **First line defense**
  - **Skin, mucosa, GI, RS**
- **Normal protection in CNS**
  - Blood-brain barrier
  - Blood-nerve barrier
- **Vulnerable points**
  - Blood vessels in the leptomeninges
  - Others
    - the choroid plexus
    - the brain circumventricular organs (CVOs)
    - peripheral nerve root ganglia

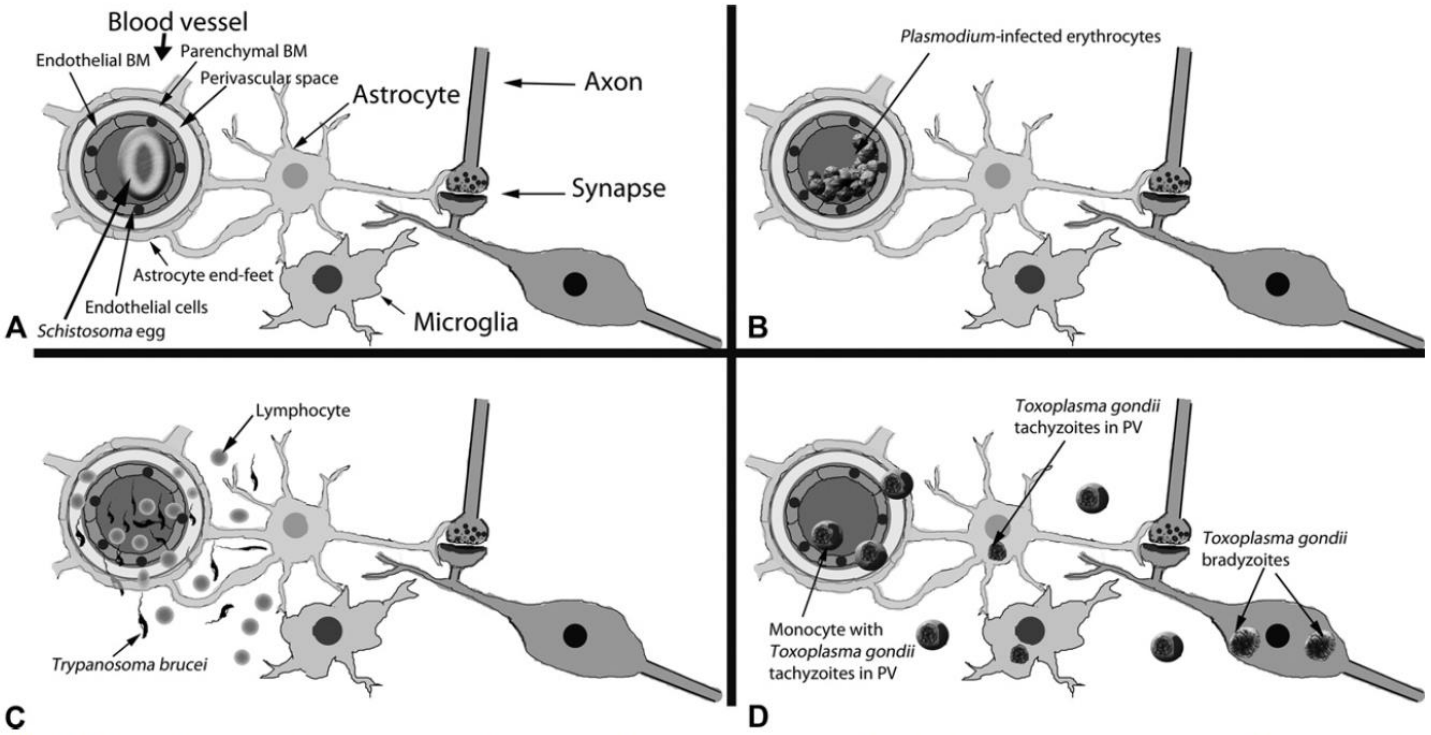
- **CNS invasion routes**
  - Bloodstream
    - free-living or extracellular parasites, by embolization of eggs, or within red or white blood cells when adapted to intracellular life.
  - Target the areas lacking a BBB
  - Olfactory nerve pathway from nasal cavity



Mechanisms of CNS invasion

Vascular route of neuroinvasion

Emboli



Infected RBC

Infected Monocyte

Fig. 2.1. Vascular route of neuroinvasion by parasites. Parasites transported by the bloodstream can interact with or cross the blood–brain barrier into the brain parenchyma. (**A**) The eggs of Schistosoma (e.g., *S. japonicum*) lodge within small vessels as emboli. (**B**) Erythrocytes infested with *Plasmodium* parasites attach to endothelial cells of cerebral vessels and to each other to be sequestered within the vessel. (**C**) The extracellular parasite *Trypanosoma brucei* spp. and T cells cross the endothelial cell layer, the endothelial basement membrane (BM) and the parenchymal BM of postcapillary venules to invade the brain parenchyma. In the absence of IFN-γ-inducible molecules, the parasites and T cells do not penetrate the parenchymal BM efficiently and they accumulate within the perivascular space as cuffs. (**D**) Monocytes carrying *Toxoplasma gondii* tachyzoites inside parasitophorous vacuoles (PV) cross the BBB into the parenchyma. Once inside the brain parenchyma, astrocytes and neurons are infected and the parasites are transformed to slowly replicating bradyzoites.

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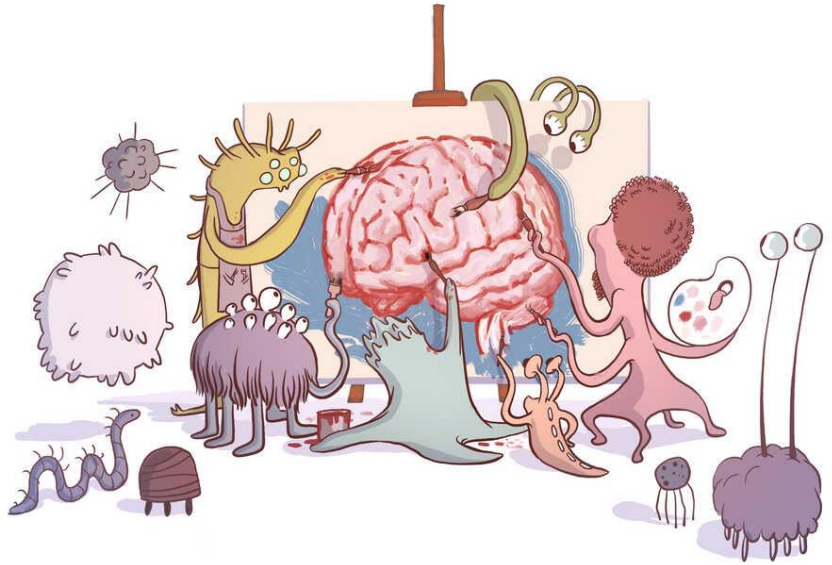

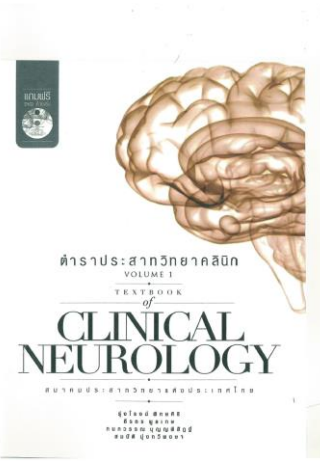

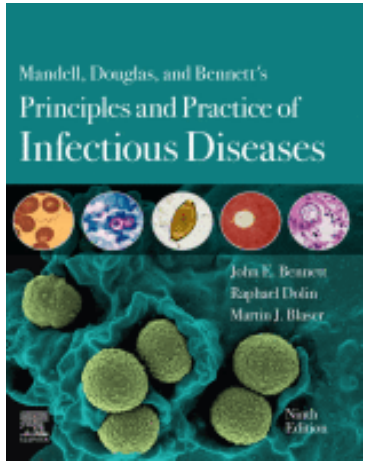

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Angiostrongylus cantonesis (Rat lung worm; พยาธิปอดหนู)

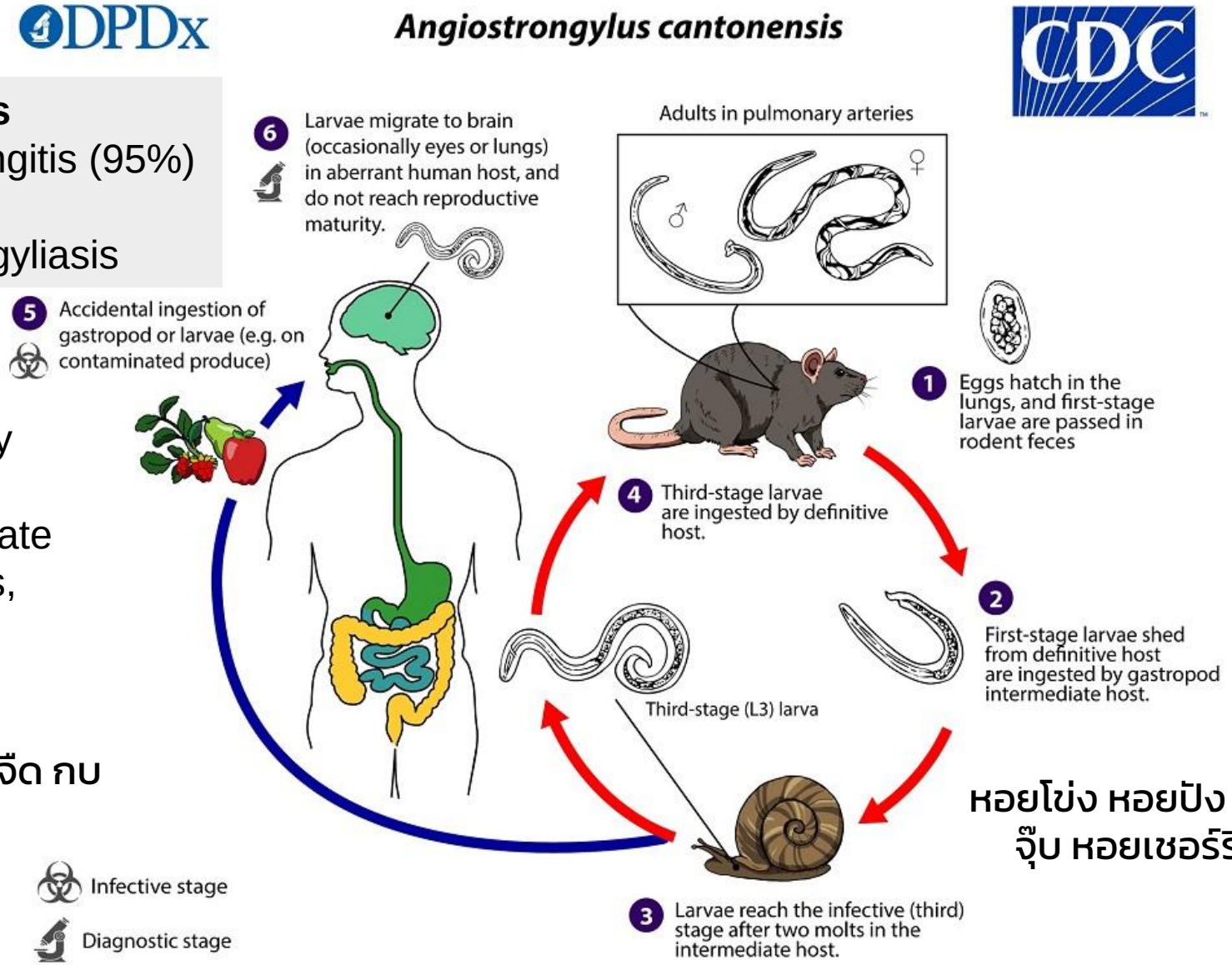
Most common CNS parasitic infection!!

Angiostrongyliasis

Overview

3 Main manifestations

- Eosinophilic meningitis (95%)
- Encephalitis
- Ocular angiostrongyliasis



Humans are infected by eating larvae in undercooked intermediate hosts (e.g. snails, slugs, crabs, or prawns)

หอยต่างๆ
กุ้งเต้น ตับตะกวดดิบ ปูน้ำจืด กบ

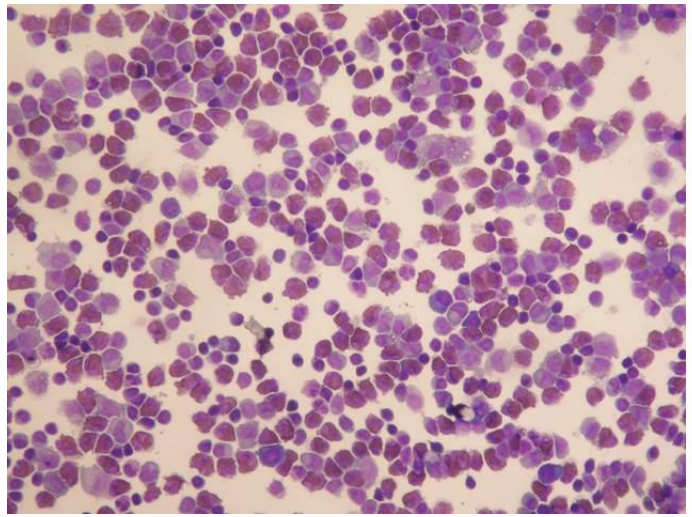
หอยโข่ง หอยปัง หอยขม หอยจุ๊บ หอยเชอร์รี่ หอยทาก

Incubation period
1-3 weeks

Angiostrongyliasis

Clinical manifestation

- **Eosinophilic meningitis**
  - Acute-subacute



H&E stain for CSF

Age (year) mean (range)	33 (15-70)
Sex, male	69%
Incubation, day	18 (1-90)
Signs or symptoms	
Headache Non-specific	100%
Duration, day	7 (1-30)
Vomiting	47%
Stiff neck	54%
Fever (T >38.0OC)	7%
6th cranial nerve palsy	4%
7th cranial nerve palsy	2%
Hyperesthesia Localized	7%
Hearing loss, spine, GI tract - RARE	

Misdiagnosis – Migraine, Tension

50% Normal neurological exam!!

Some patients developed encephalitis esp. elderly >> coma & high mortality!

A Case Report on Eosinophilic Meningitis Caused by *Angiostrongylus cantonensis*. Int J Med Sci. 2011

Angiostrongyliasis

Clinical manifestation

- **Ocular angiostrongyliasis**
  - **Clinical**
    - Visual loss
    - Found parasite at retina or vitreous
    - +/- meningitis

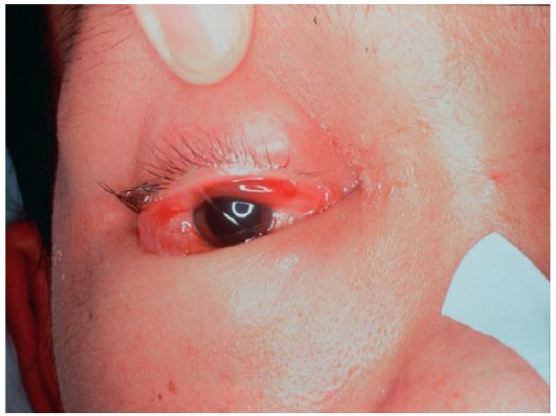


Fig. 15.3. A patient with ocular angiostrongyliasis. Blurred vision with chemosis is presenting symptom.

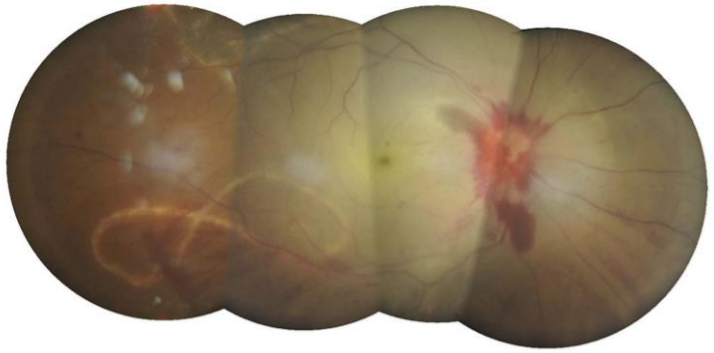


Figure 2 Large subretinal angiostrongyliasis with severe disk hemorrhage and extensive retinal whitening.

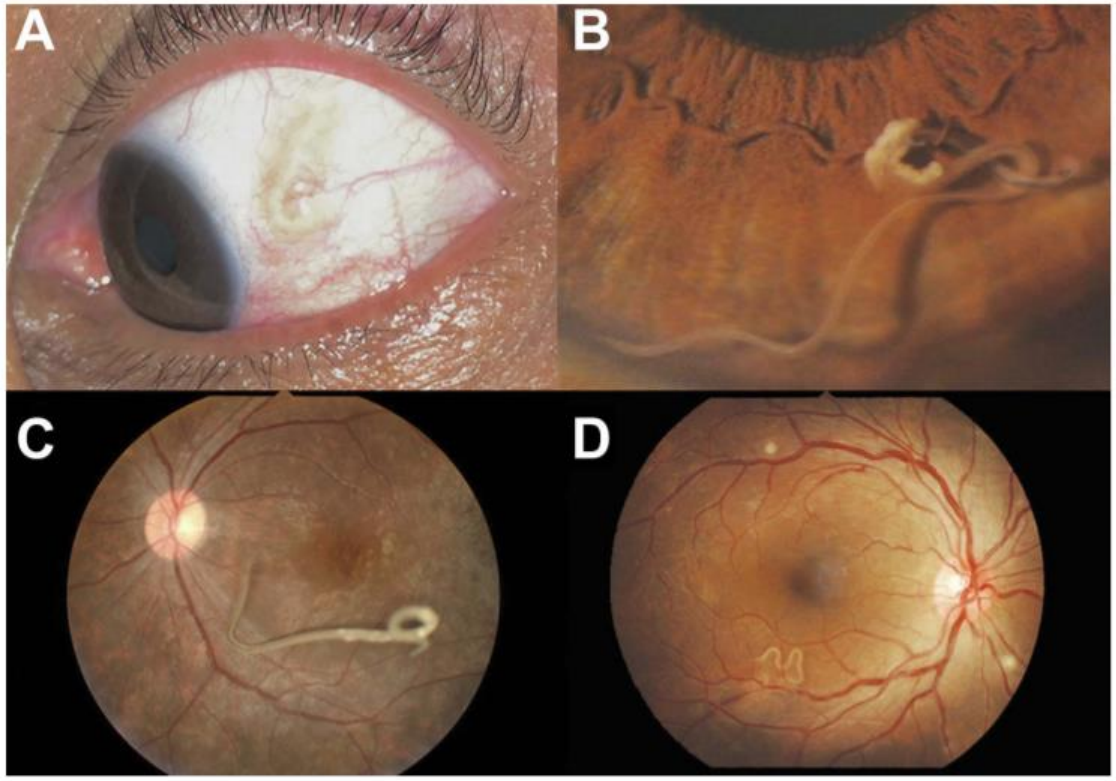


Figure 1 *Angiostrongylus cantonensis* larvae in subtenon space (**A**), aqeous humour (**B**), vitreous cavity (**C**), and subretinal space (**D**).

Sinawat S, et al. Ocular angiostrongyliasis in Thailand: a retrospective analysis over two decades. Clinical ophthalmology. 2019

Angiostrongyliasis

- **CBC** – Eosinophilia ***
- **LP** – confirmed eosinophilic meningitis
  - Rarely found parasite in specimen
- **CT/MRI brain**
  - Done before LP in case of AOC
  - Non-specific
- **Serology**
  - ELISA/Western blot in blood
    - Detect Specific Ab to 29kDa or 31kDa of Ag to parasite
    - Only Available in KKU, MU
    - Sensitivity 50-60%
- **PCR**
  - high specificity; rarely use

Investigation

ตารางที่ 3 การตรวจทางห้องปฏิบัติการ
ในผู้ป่วยเยื่อหุ้มสมองอักเสบชนิดอีโอสิโนฟิลิก

Blood eosinophilia (> 700 cells/mm3)	78%
CSF abnormalities	
High opening pressure (>300 mm H2O)	38%
WBC/mm3	711 (85-5,700)
Eosinophilia, %	45 (10-84)
Protein content, mg/dl	111 (27-574)
Glucose ratio, CSF/blood,	44 (17-100)

high protein
normal/low glucose ratio

Something floating in Coconut juice

(Light reflection from eosinophil granule)
Angiostrongylus cantonensis

Tangwanicharoen T, et al. CSF fluid analysis in Eosinophilic Meningoencephalitis. SEA J Trop Med Public Health. 2001.

Angiostrongyliasis

Investigation

- **CT/MRI – non-specific**
  - Tract-like lesion
  - White matter involvement
  - Nodular enhancement
  - Myelitis

Table 2: Findings at MR imaging and MR spectroscopy

Case No.	Dilated Perivascular Space	Periventricular High Signal	Subcortical Enhancing Lesions	Microcavity with Migratory Track	Small Hemorrhage	MR Spectroscopy Findings
1	+	+	+	−	−	Decrease choline
2	+	+	−	+	−	···
3	+	−	+	−	+	···
4	+	+	+	−	−	···
5	−	+	+	−	−	Normal
6	+	+	+	−	−	Normal

Note.—+ indicates postive; −, negative.

Kanpittaya J, et al. MR Findings of Eosinophilic Meningoencephalitis Attributed to *Angiostrongylus cantonensis*. AJNR. 2000

Angiostrongyliasis

Investigation

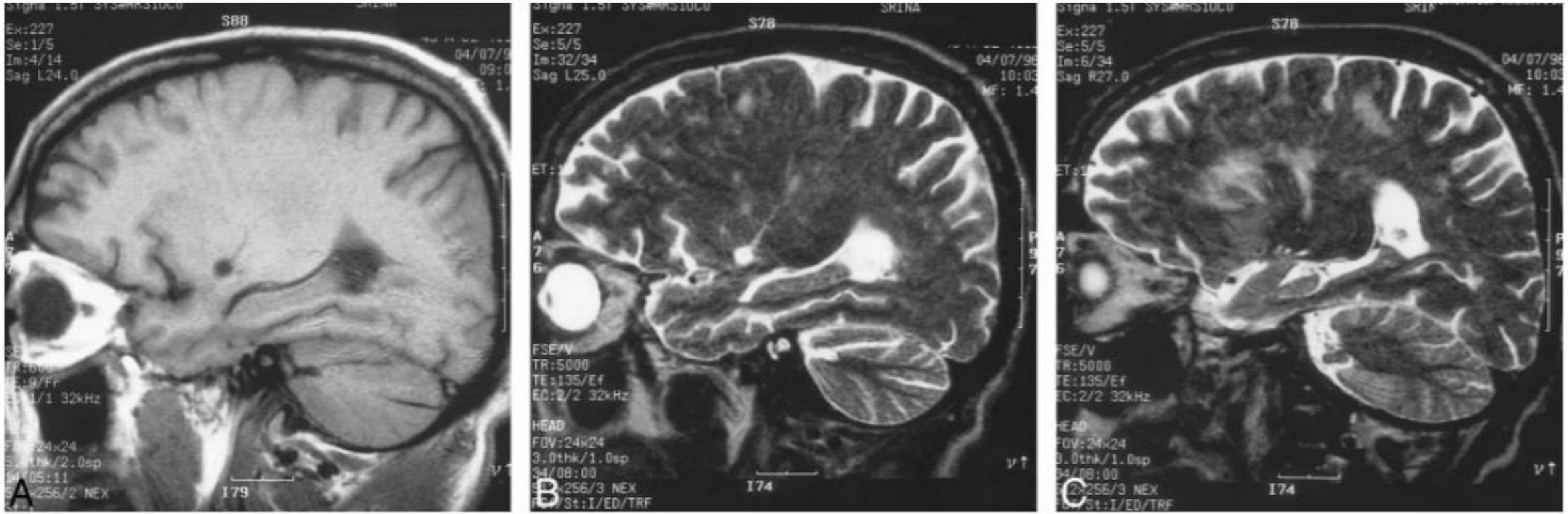


FIG 2. *A* and *B*, 45-year-old man. Sagittal T1-weighted (600/9/2) (*A*) and T2-weighted (5000/135/3) (*B*) MR images show a long track with a cavity in the left putamen (low signal in *A* and high signal in *B*).

C, Sagittal T2-weighted image (5000/135/3) shows abnormally high signal in periventricular, linear, and fuzzy nodular lesions.

Kanpittaya J, et al. MR Findings of Eosinophilic Meningoencephalitis Attributed to *Angiostrongylus cantonensis*. AJNR. 2000

Angiostrongyliasis

Investigation

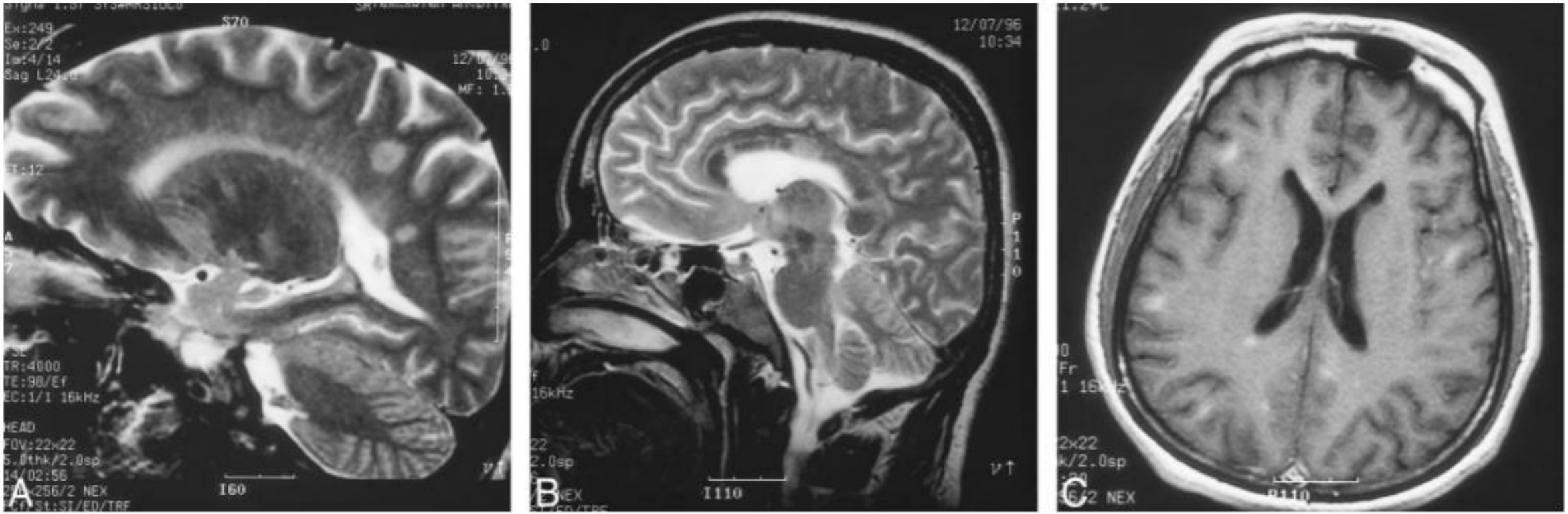


FIG 4. *A* and *B*, 32-year-old man. Sagittal T2-weighted MR images (4000/98/2) reveal nodular and linear high-signal lesions in periventricular white matter in parietooccipital lobe and corpus callosum.

C, Axial contrast-enhanced T1-weighted image (500/9/2) shows multiple enhancing subcortical lesions and right periventricular lesions.

Kanpittaya J, et al. MR Findings of Eosinophilic Meningoencephalitis Attributed to *Angiostrongylus cantonensis*. AJNR. 2000

Angiostrongyliasis

Investigation

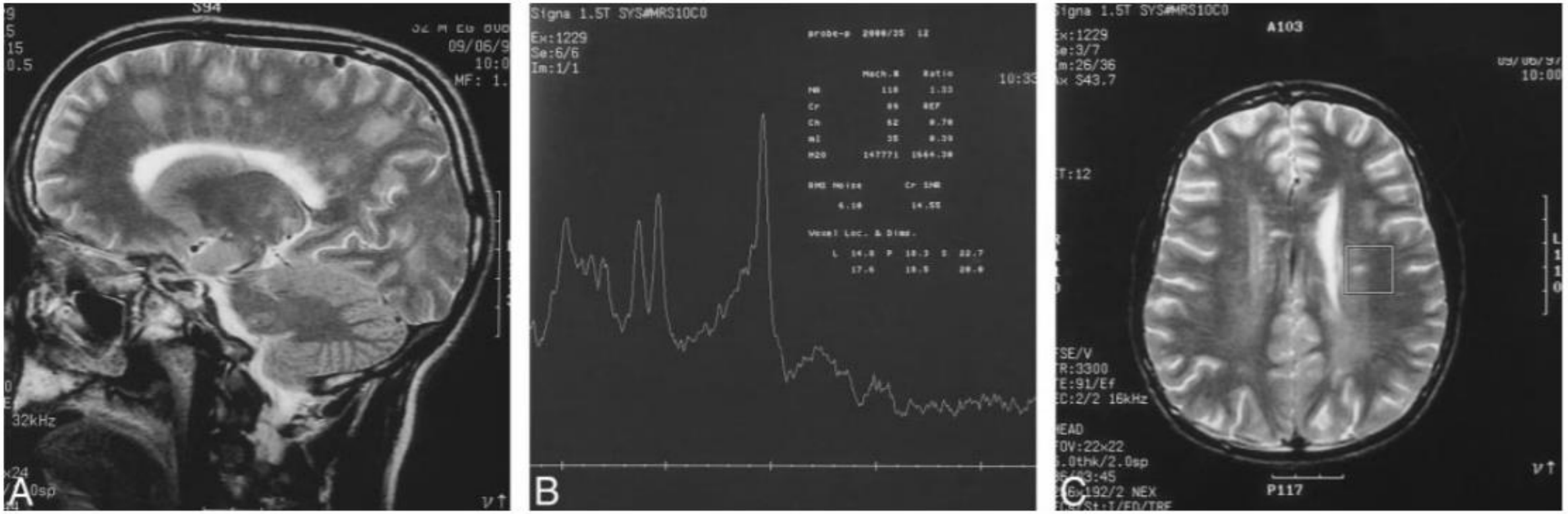


FIG 1. *A*, 32-year-old man. Sagittal T2-weighted MR image (3500/80/3) reveals areas of fuzzy hyperintense signal in the left fronto-parietal region and centrum semiovale.

B and *C*, MR spectrum (*B*) reveals decreased choline (choline/creatine ratio, 0.70) in the left centrum semiovale (voxel indicated by *box* in *C*).

Kanpittaya J, et al. MR Findings of Eosinophilic Meningoencephalitis Attributed to *Angiostrongylus cantonensis*. AJNR. 2000

Angiostrongyliasis

Investigation

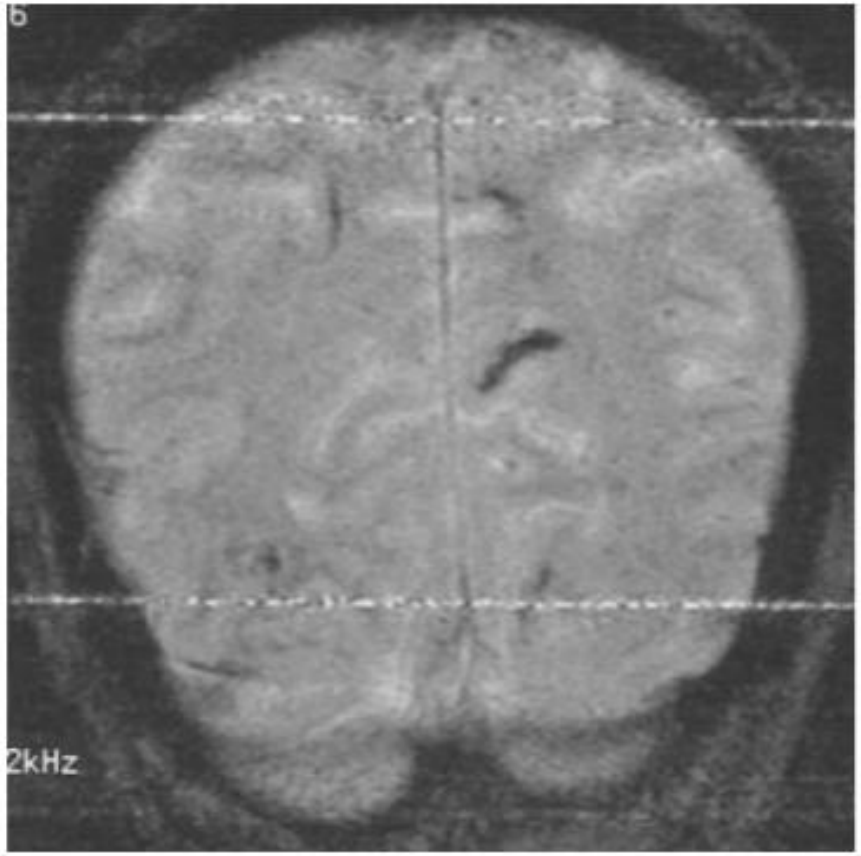


FIG 3. 64-year-old man. Coronal gradient-echo MR image (640/25/2) shows linear hypointense subcortical lesions, which might represent hemorrhagic tracks.

Kanpittaya J, et al. MR Findings of Eosinophilic Meningoencephalitis Attributed to *Angiostrongylus cantonensis*. AJNR. 2000

Angiostrongyliasis

Treatment

- **Meningitis**
  - **Specific treatment –** Might combination both!
    - **Albendazole 15 mg/kg/day divided in bid dose x 2 weeks**
      - Minimize damage from parasite
      - NOT use albendazole alone!
    - **Prednisolone 60 mg/day x 2 weeks**
      - **Main therapy** (more important than albendazole)**
      - Reduce inflammation
      - Decrease headache + pain medication
      - Decrease frequency of LP for releasing pressure
  - **Supportive**
    - Large volume LP releasing pressure 20-40 ml in case of high ICP
  - **Prognosis**
    - Usually, Self-limited with good recovery within 4-6 weeks
    - **Encephalitis - High risk of mortality!!**

Ansdell V, et al. Guidelines for the diagnosis and treatment of neuroangiostrongyliasis: updated recommendations. Parasitology. 2021

Angiostrongyliasis

Treatment

- **Ocular angiostrongyliasis**
  - **Focal laser**
    - eradicate subretinal angiostrongyliasis
  - **Laser treatment prior to surgical removal**
    - eliminate intracameral and intravitreal angiostrongyliasis.
  - **IVMP**
    - may be beneficial in cases of acute optic neuritis.
  - **Anti-helminthic** in case of meningitis
  - The visual prognosis mainly depends on
    - ocular pathology
    - parasitic migration pathway.

Table 1 Patient demographic data, ocular findings, management, and visual outcome

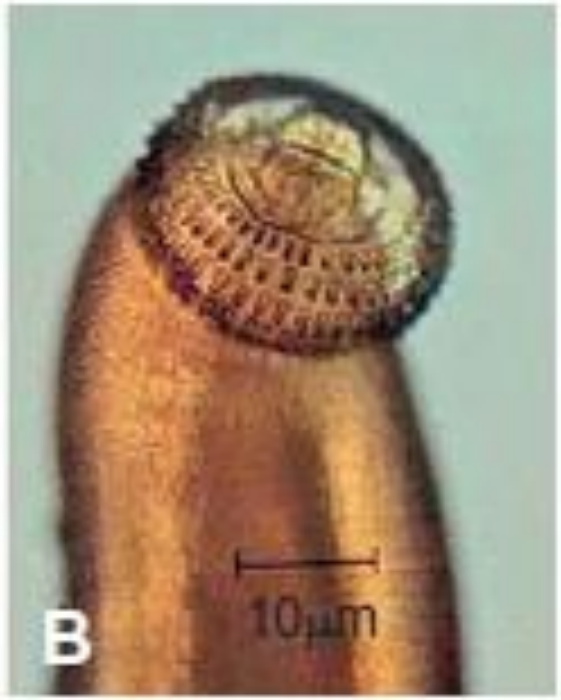
Sex	Age (y)	Meningitis	Duration (weeks)	Ocular exam (initial)					Investigation		Treatment				Final VA
				Eye	Location	VA	RAPD	Ocular findings	Eosinophilia	Stool exam (eggs)	Laser	Antihelminthic	Steroid	PR	
M	27	Preceded	3	Left	Intravitreal	1/60	+	Chorioretinitis, subretinal track	–	NA	+	Albendazole ×7	Topical prednisolone	+	1/60
M	21	Coexisting	1	Left	Intravitreal	2/60	+	RPE alteration	+	NA	+	—	Oral prednisolone	–	2/60
M	47	—	3	Left	Intracameral	CF	+	RPE alteration, disk swelling, intraretinal hge	NA	Sarcocystis Opisthorchis	+	Albendazole ×14	IV, oral, topical prednisolone	+	1/60
F	44	—	0.5	Right	Subretinal	LP	+	Subconjunctival hge subretinal track, serous R.D, macular opacification, peripapillary hge, vitreous hge	NA	Not found	+	Albendazole ×14, ivermectin once	Oral, topical prednisolone	–	no LP
F	36	Preceded	1	Left	Intravitreal	CF	+	RPE alteration, disk swelling	+	NA	+	—	Oral prednisolone	+	CF
F	41	—	4	Left	Subtenon	6/6	–	Conjunctival injection	NA	*Enterobius*, hookworm	–	Albendazole ×7	Topical prednisolone, subconjunctival dexa	+	6/6
M	50	—	2	Left	Subretinal	CF	+	RPE alteration, subretinal track	+	Not found	+	Albendazole ×7	Topical prednisolone	+	CF
M	76	—	2	Right	Intracameral	6/60	–	Corneal scar, fibrin in anterior chamber	NA	Opisthorchis	–	Praziquantel ×7	Topical prednisolone	+	6/36
F	63	—	8	Left	Intracameral	LP	–	Corneal scar, hyphema, vitreous hge, preretinal hge	–	Not found	–	Albendazole ×7	Topical prednisolone, Subconjunctival dexa	+	HM
F	51	—	2	Left	Intravitreal*	HM	–	Focal iris atrophy, choroiditis	+	*Strongyloides* larva	+	Albendazole ×7	Topical prednisolone	–	HM
F	22	—	8	Right	Intravitreal	1/60	+	RPE alteration, disk swelling	–	NA	–	—	Oral prednisolone	+	1/60
F	28	—	0.5	Right	Subretinal	6/24	–	Subretinal track	–	NA	+	—	Oral prednisolone	–	6/24
M	36	—	1	Right	Subretinal	CF	+	Macular edema	NA	Echinostoma	+	Albendazole ×7	Topical prednisolone	+	2/60
M	39	—	1.5	Right	Intravitreal	6/6	–	—	NA	NA	+	—	—	–	6/6
F	33	—	1	Left	Subretinal	1/60	+	RPE alteration	–	NA	+	—	Oral prednisolone	–	5/60
M	27	—	4	Right	Subretinal	CF	+	Subretinal track	NA	NA	+	Albendazole ×7	-	–	CF
M	46	—	3	Right	Intracameral	CF	+	RPE alteration, vitritis	–	NA	+	—	Oral, topical prednisolone	+	CF
M	46	—	1	Right	Intravitreal	CF	+	RPE alteration, vitritis	–	Not found	+	Albendazole ×7	Topical prednisolone	+	6/60

Note: *The parasite migrated from anterior chamber to vitreous cavity.
Abbreviations: VA, visual acuity; CF, counting finger; hge, hemorrhage; HM, hand motion; LP, light perception; PR, parasitic removal; RPE, retinal pigment epithelium; dexa, dexamethasone; RAPD, relative afferent pupillary defect; NA, not available.

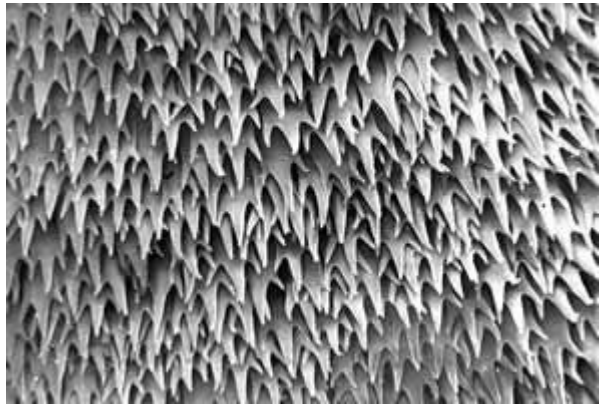
Sinawat S, et al. Ocular angiostrongyliasis in Thailand: a retrospective analysis over two decades. Clinical ophthalmology. 2019

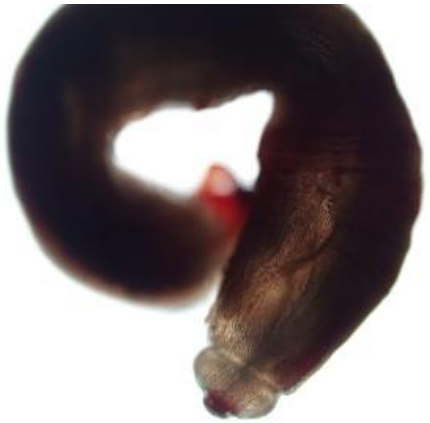
Gnathostoma spinigerum (พยาธิตัวจี๊ด)

Size is <u>larger</u> than *Angiostrongylus spp.*



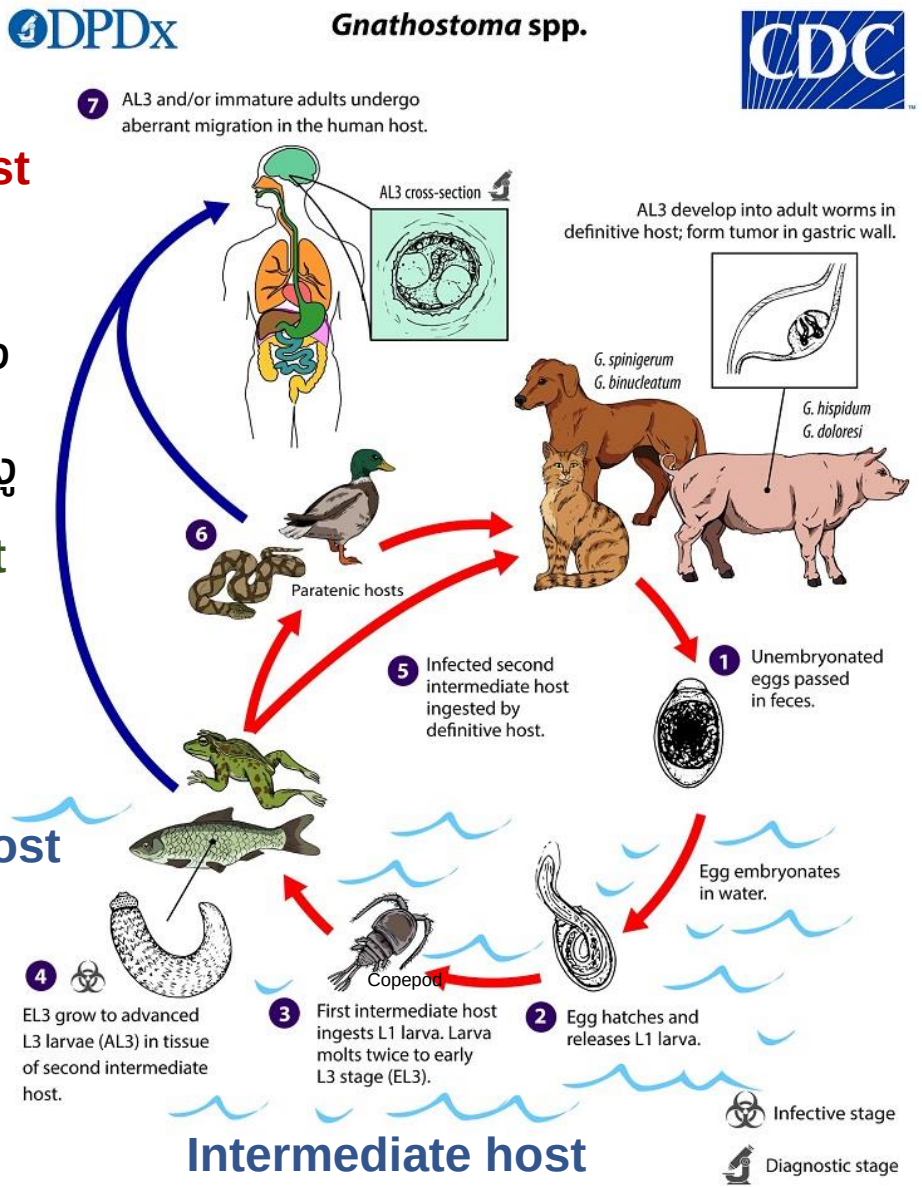
3rd stage larvae





Gnathostomiasis

Overview



Accidental host

กินอาหารที่มี AL3
ปลาส้มฟัก ปลาย่าง
ก้อย
ไก่ เป็ด กบ นก หนู งู

Paratenic host

Definitive host

Intermediate host

Intermediate host

Rare cause
- Skin
- Prenatal

Gnathostomiasis

Overview

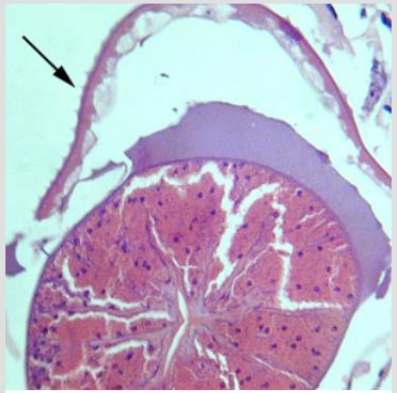


Figure A: Hematoxylin and eosin (H&E)-stained cross section of *Gnathostoma spinigerum*, taken from a subcutaneous nodule above the right breast of a patient, showing the esophagus. Note the presence of cuticular spines (arrow). Image courtesy of Diagnostix Pathology Laboratories LTD, Canossa Hospital, Hong Kong, China.

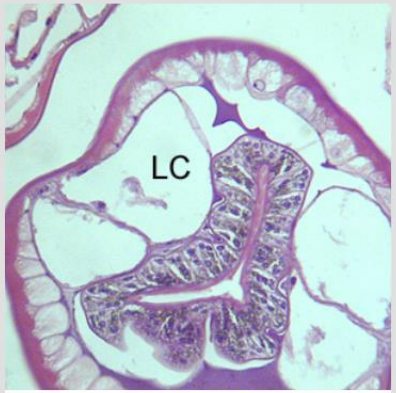


Figure B: Another H&E-stained cross section of *Gnathostoma spinigerum*, taken from the same specimen in Figure A, showing the intestinal cells and characteristic large lateral chords (LC). The multinucleated columnar intestinal cells with from three to five nuclei per cell identify this as *G. spinigerum*. Note also the presence of pigmented granular material in the intestinal cells

Figure C: Cross section of an immature *Gnathostoma spinigerum* adult in a small intestinal wall biopsy specimen, H&E stained. Note the thick cuticle, coelomyarian muscle cells, and well-developed intestine.

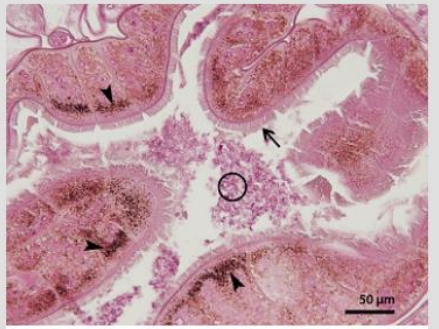


Figure D: Closer view of the intestinal morphology of the *G. spinigerum* specimen shown in Figure C. The multinucleated intestinal cells have a prominent microvillus border (arrow) and contain dark, granular pigment (darts). Ingested host red blood cells (circle) are present in the lumen of the intestine.

Figure E: Cross section of *Gnathostoma hispidum* AL3 larva in a skin biopsy specimen, H&E stained. The intestine (arrow) has rounded to cuboidal cells with single nuclei, an identifying feature of *G. hispidum*. Note also the typical genus-level larval features including low, coelomyarian muscle cells (dart), and spacious lateral chords bisected by a lateral line (asterisks).

CDC

Gnathostomiasis

Clinical manifestation

- **LARGER** than *Angiostrongylus spp.* >> **Migration!!**
- **<u>5 main features</u>**
  - **Nerve root or Radicular pain***
    - Electrical/shock-like pain at one limb
    - Occurs 1-5 days
  - **Myelopathy***
    - Paraplegia/Quadriplegia
      - Rare – Brown-Séquard or Cauda equina syndrome
  - **Intracerebral hemorrhage (ICH)**
    - Acute progressive headache + focal neurological deficit +/- SDH
  - **Subarachnoid hemorrhage (SAH)**
    - Sudden headache + meningism + AOC >> Coma, Seizure
  - **Others – radiculomyelitis, radiculomyeloencephalitis**

Gnathostomiasis

Clinical manifestation

- **Clinical clues for diagnosis**
  - Eating suspected food
  - Skin sign
    - **Intermittent migratory swelling****
      - Itching & Pain (Hallmark); migratory area
      - Average 1-2 wk (range 2-3 d to 1 mo)
    - Creeping eruption (rare)
  - Found parasite in other organs
    - Size around 2-12.5 x 0.4-1.25 mm
    - Eye
    - Opening route – mouth, genitalia, KUB, ear, GI

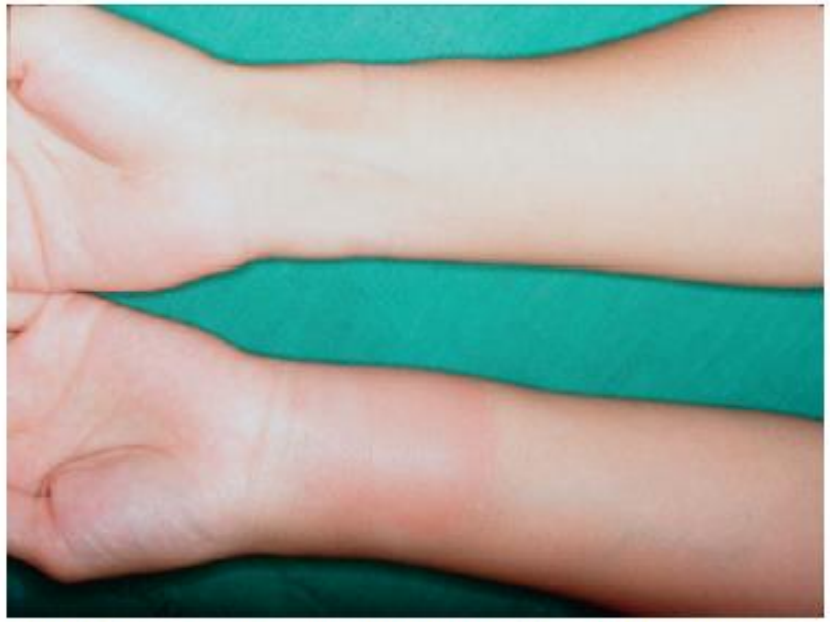


Fig. 15.6. Migratory swelling on left forearm caused by *G. spinigerum*.

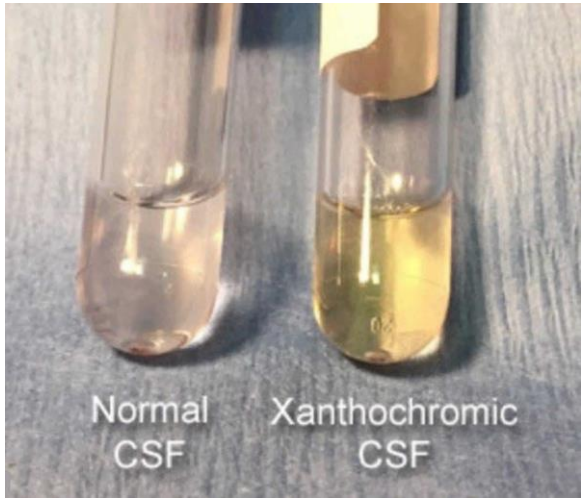
Fig. 15.7. A patient with ocular gnathostomiasis. Ocular swelling is presenting symptom.

Gnathostomiasis

Investigation

- **CBC**
  - Eosinophilia *** (50% of cases)
- **LP** – confirmed eosinophilic meningitis
  - Pressure – normal, high
  - **SAH – bloody CSF or Xanthochrome**
  - WBC < 500 + Eosinophils
  - Slightly elevation of protein
  - Normal sugar
- **Serology**
  - ELISA/Western blot in blood
    - Detect Specific Ab to 21kDa or 24kDa of Ag to parasite

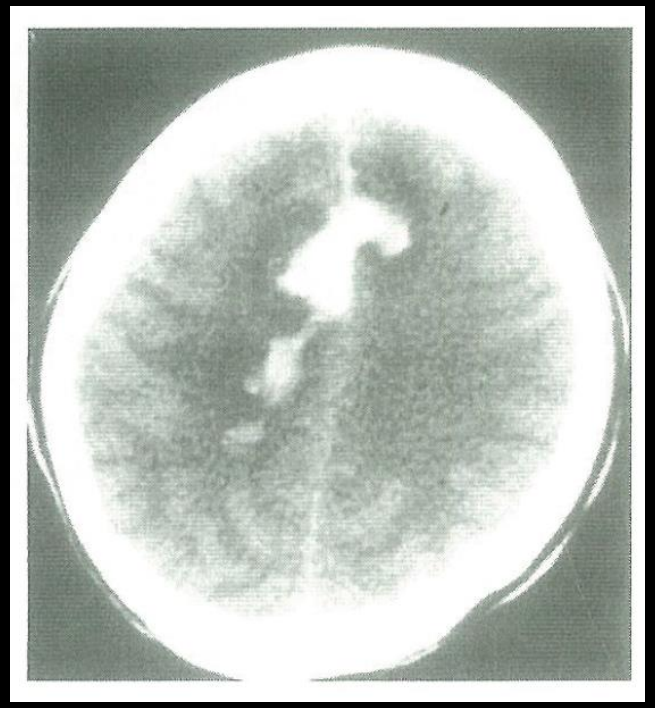
SAH artificial bleeding



Gnathostomiasis

Investigation

- **CT/MRI brain**
  - Hemorrhagic tract lesion – migration of larvae
  - Non-traumatic ICH
  - Non-traumatic SDH
  - Non-traumatic SAH
- **MRI spinal cord**
  - Edema



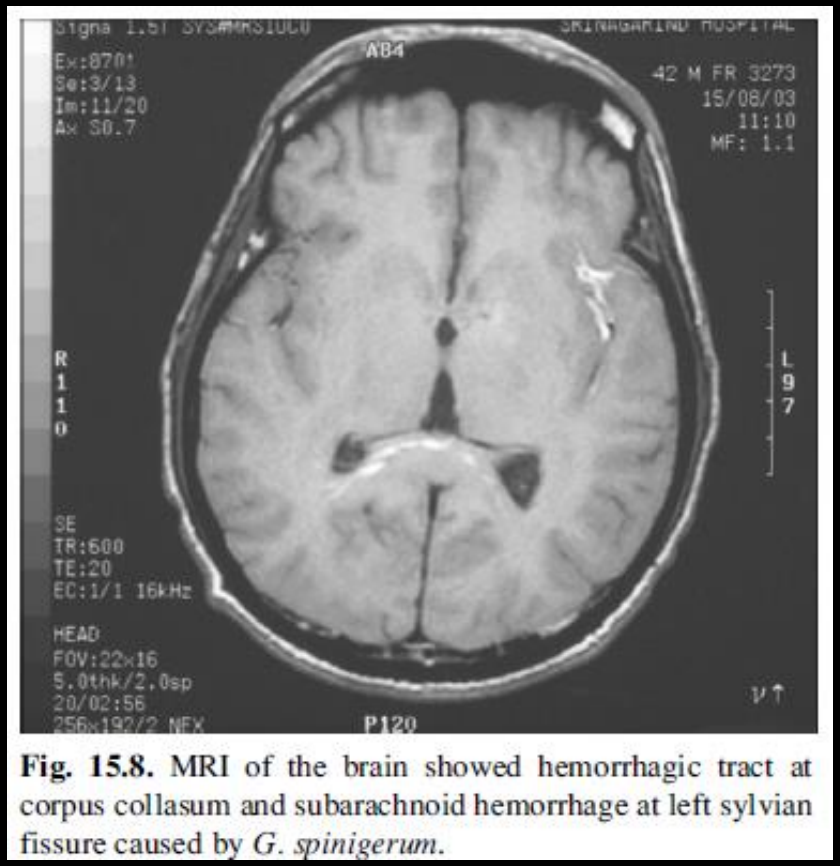
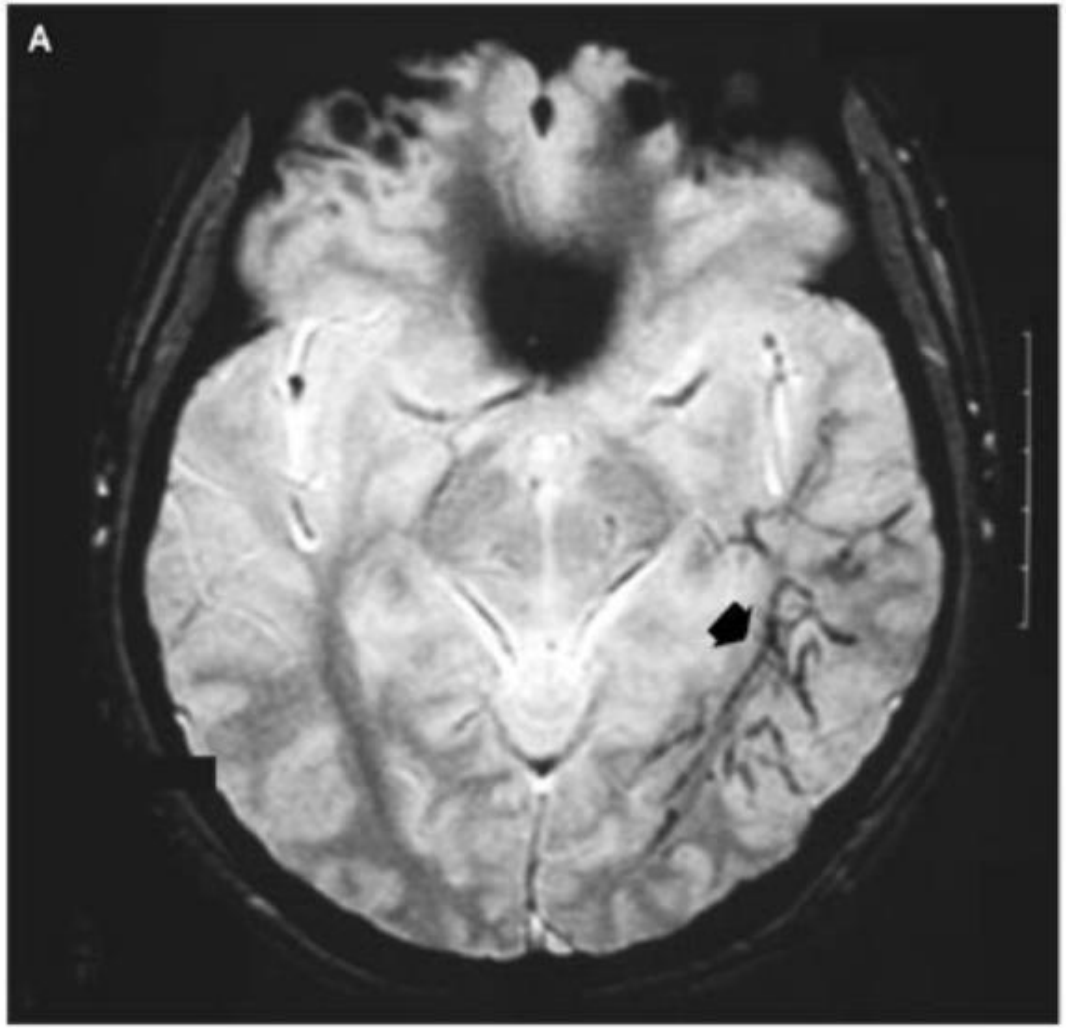
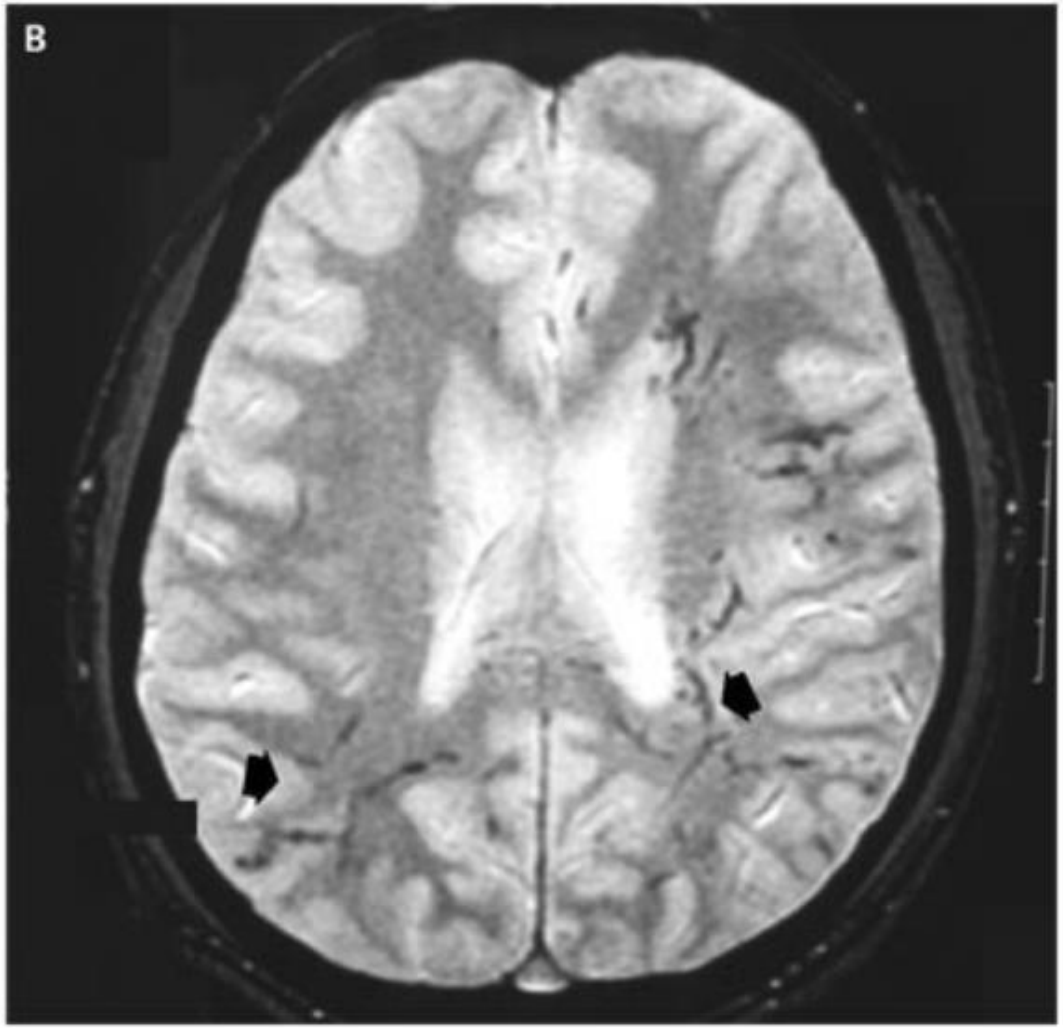


Fig. 15.8. MRI of the brain showed hemorrhagic tract at corpus collasum and subarachnoid hemorrhage at left sylvian fissure caused by *G. spinigerum*.

Gnathostomiasis

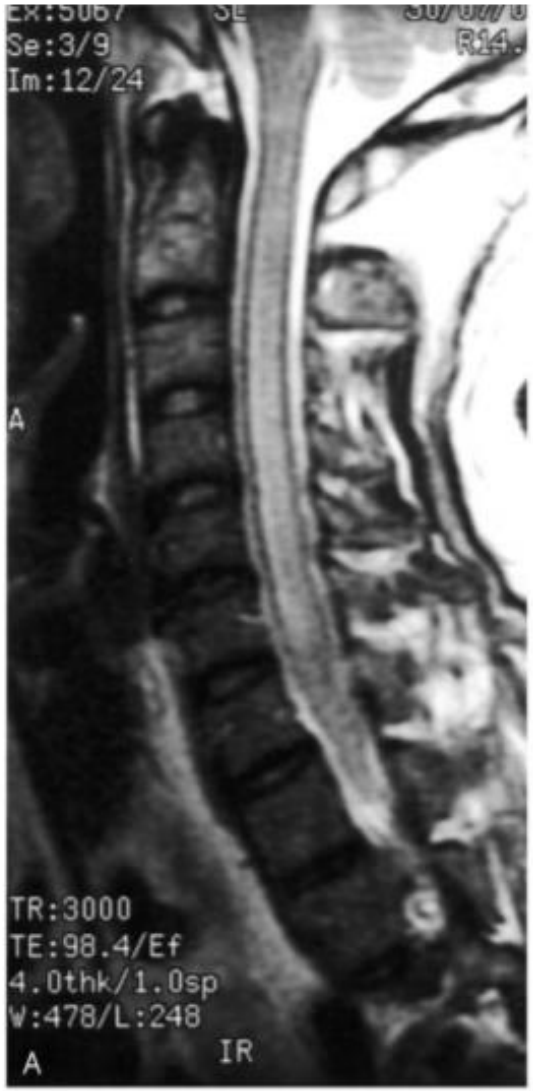
Investigation

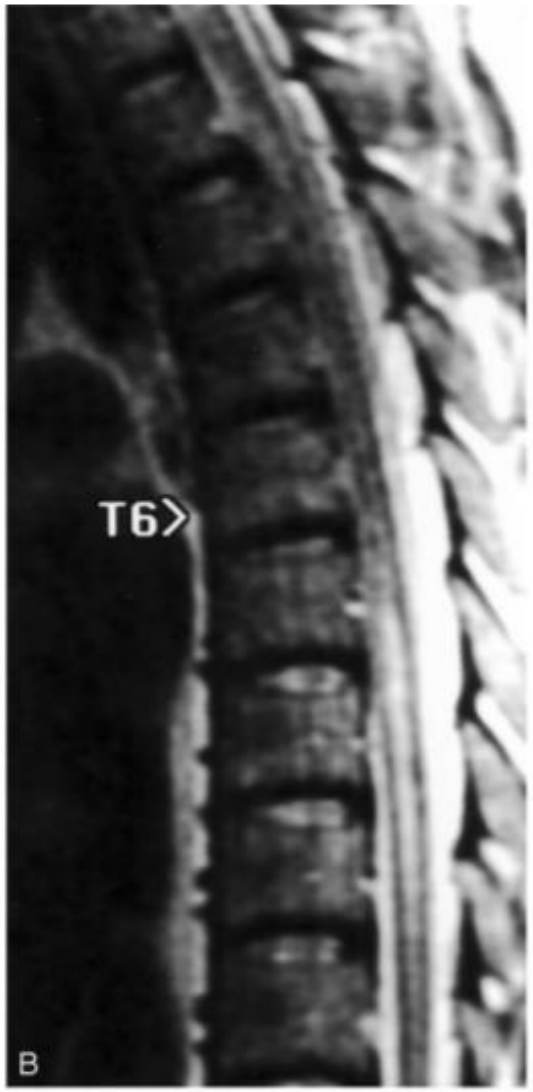




Sithinamsuwan P, Chairangsaris P. Gnathostomiasis — Neuroimaging of Larval Migration. NEJM. 2005

Gnathostomiasis





Investigation

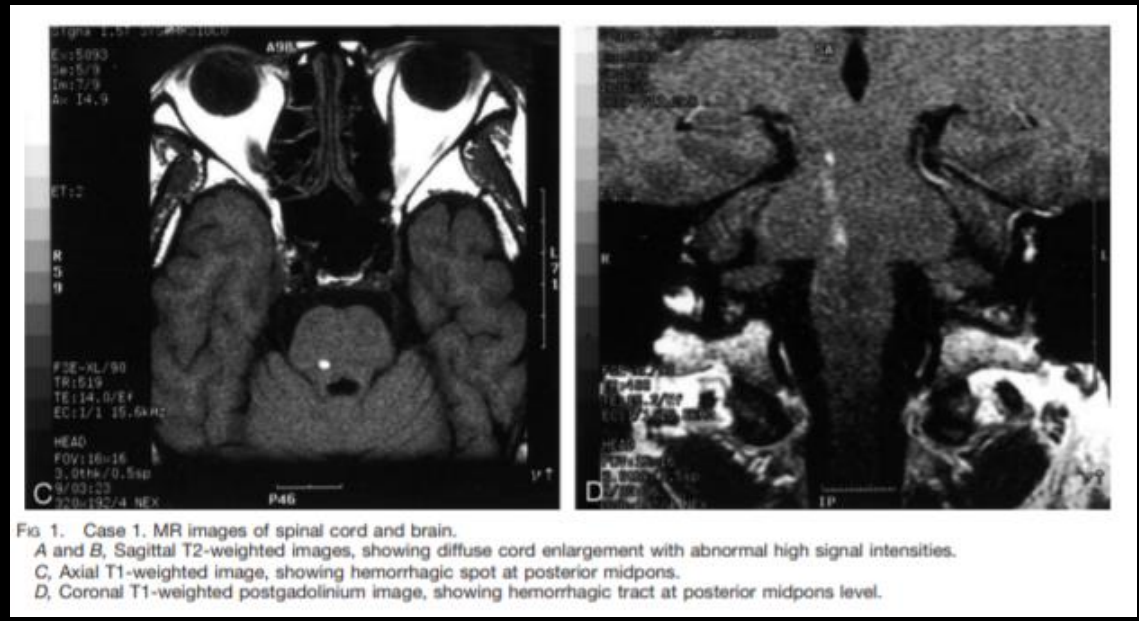


FIG 1. Case 1. MR images of spinal cord and brain.
A and *B*, Sagittal T2-weighted images, showing diffuse cord enlargement with abnormal high signal intensities.
C, Axial T1-weighted image, showing hemorrhagic spot at posterior midpons.
D, Coronal T1-weighted postgadolinium image, showing hemorrhagic tract at posterior midpons level.

Sawanyawisuth K, et al. MR Imaging Findings in Cerebrospinal Gnathostomiasis. AJNR. 2004

Gnathostomiasis

Investigation

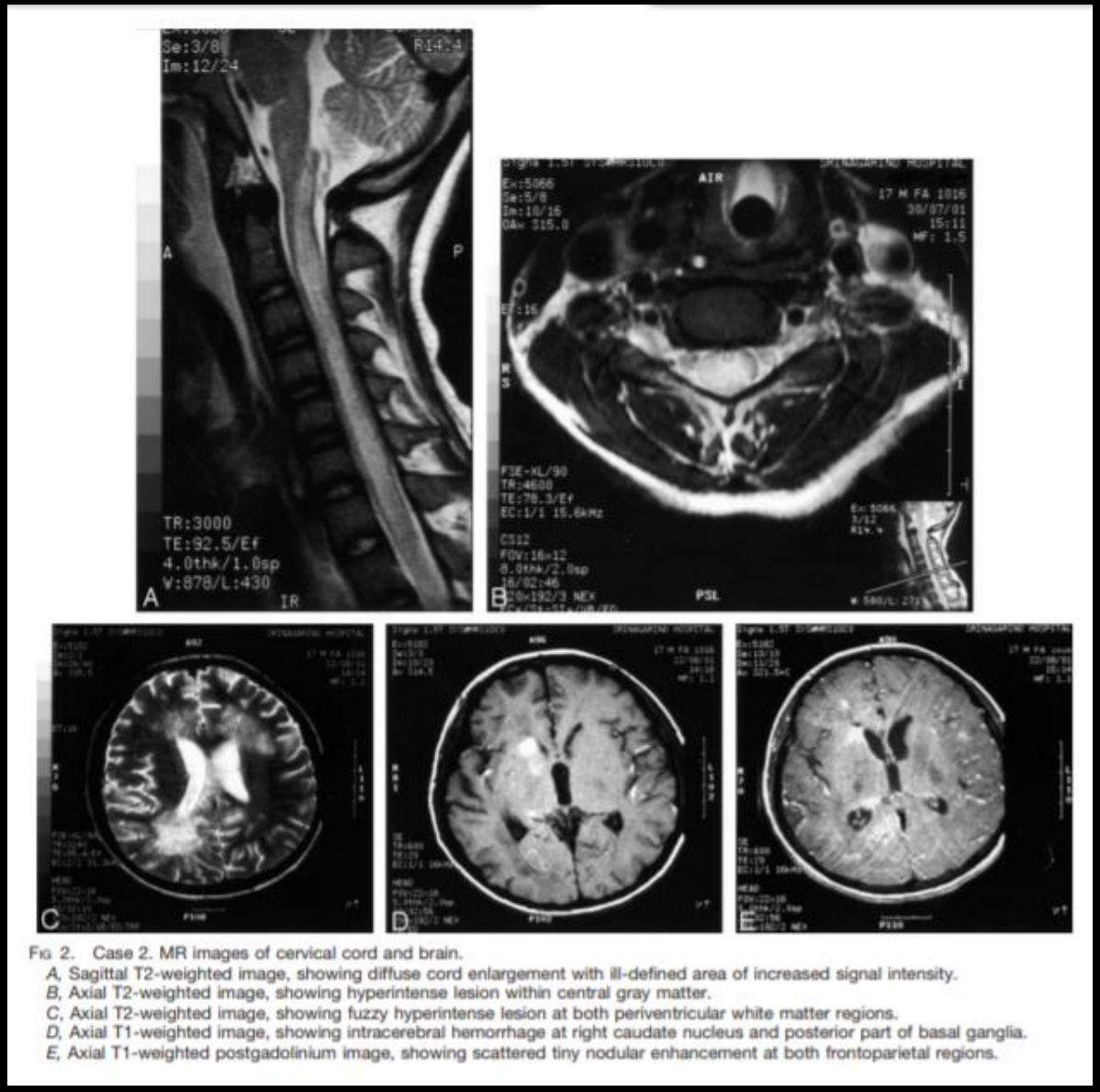


Fig. 2. Case 2. MR images of cervical cord and brain.
A, Sagittal T2-weighted image, showing diffuse cord enlargement with ill-defined area of increased signal intensity.
B, Axial T2-weighted image, showing hyperintense lesion within central gray matter.
C, Axial T2-weighted image, showing fuzzy hyperintense lesion at both periventricular white matter regions.
D, Axial T1-weighted image, showing intracerebral hemorrhage at right caudate nucleus and posterior part of basal ganglia.
E, Axial T1-weighted postgadolinium image, showing scattered tiny nodular enhancement at both frontoparietal regions.

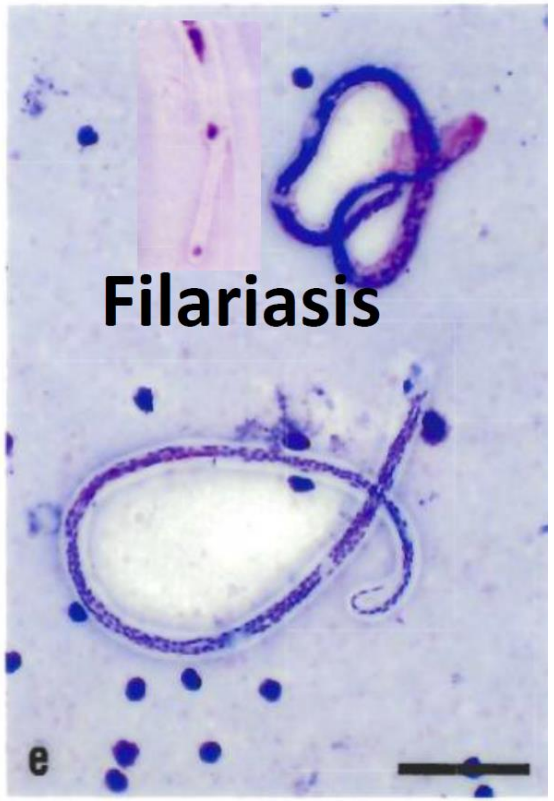
Sawanyawisuth K, et al. MR Imaging Findings in Cerebrospinal Gnathostomiasis. AJNR. 2004

Gnathostomiasis

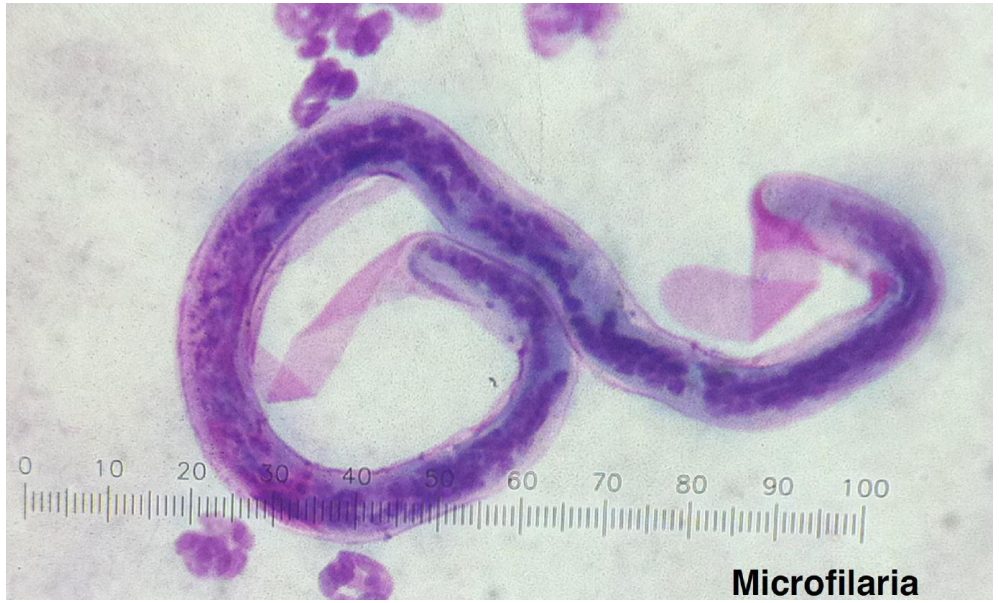
Treatment

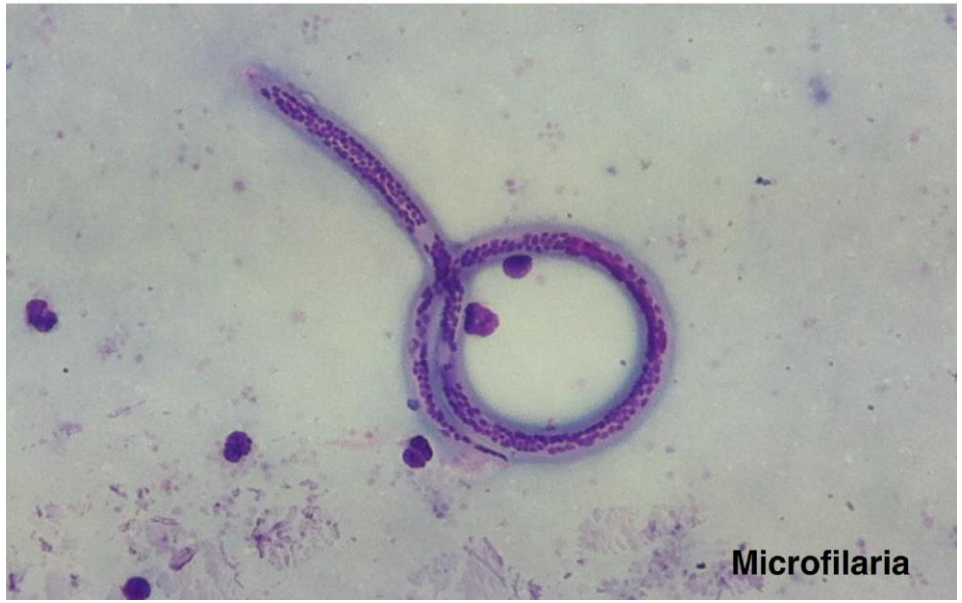
- **Still controversial**
  - **Role Surgical treatment** **>** Medical treatment (lack large studies supported)
- **Specific treatment**
  - **CNS – Limited data, Depends on site (case by case)**
    - **NOT recommended in vulnerable area (thin) – brain, ocular >> prevent further migration before dying**
  - Skin only >> Creeping out of skin
  - **Regimen – Albendazole** 400 mg/day x 21 days OR **Ivermectin** 200 mcg/kg
- **Symptomatic treatment**
  - Pain control – Headache, Root pain
  - PM&R esp. spinal cord involvement
  - **Steroid** – usually recommend in case of using Antiparasitic agents
    - Might developed migration
- **Prognosis**
  - Generally self limited with fully recovery
  - Poor prognosis – severe bleeding + AOC

Filariasis
(พยาธิโรคเท้าช้าง)



B. malayi (upper) and ***W. bancrofti*** (lower) microfilariae in the same field of a Giemsa-stained blood film (e). The pink-stained sheath and the darkly stained, compact column of nuclei identify ***B. malayi*** and distinguish it from ***W. bancrofti***





Filariasis

Overview

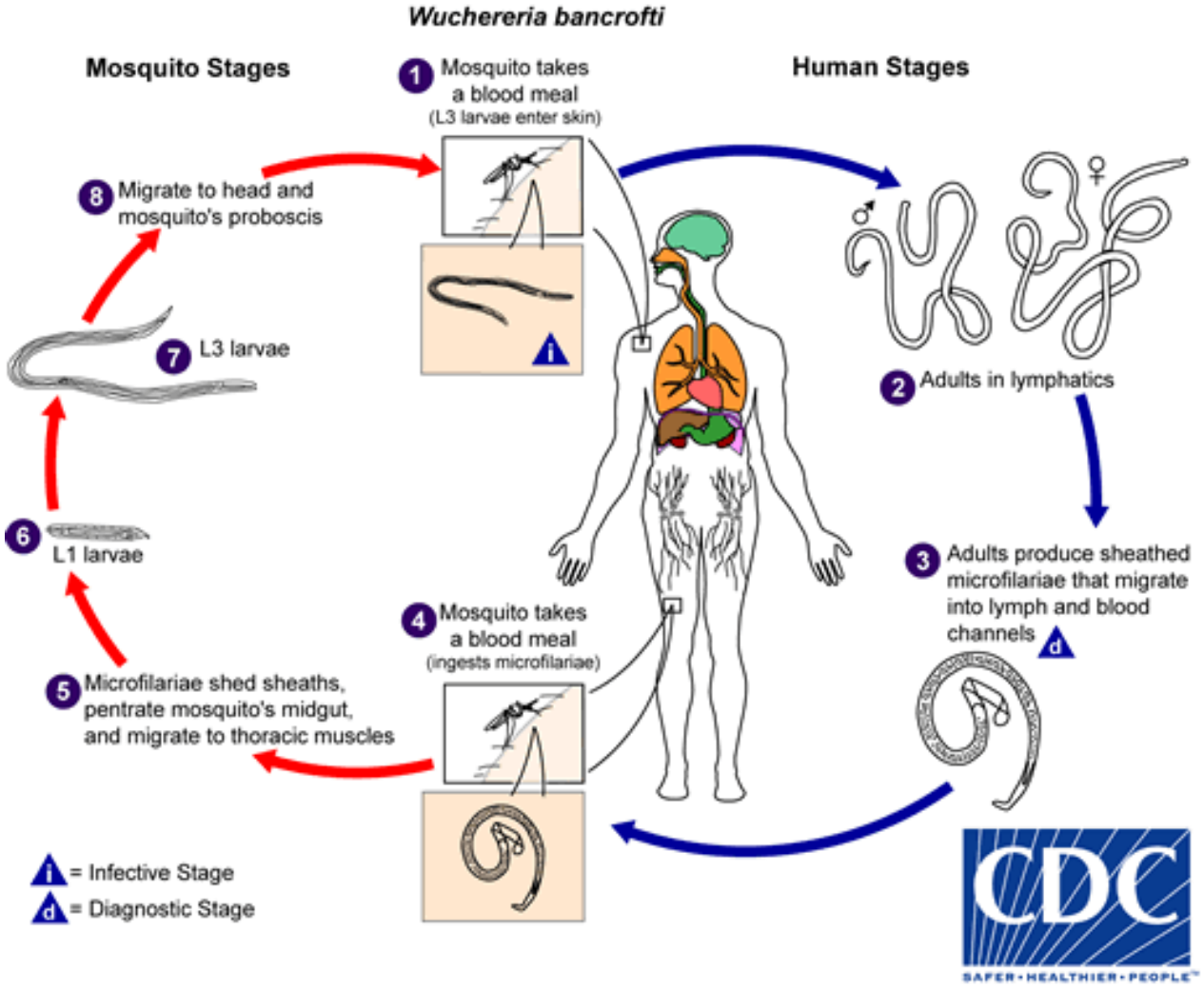
- In Thailand
  - *Wuchereia bancrofti – CNS complication*
  - *Blugia malayi*

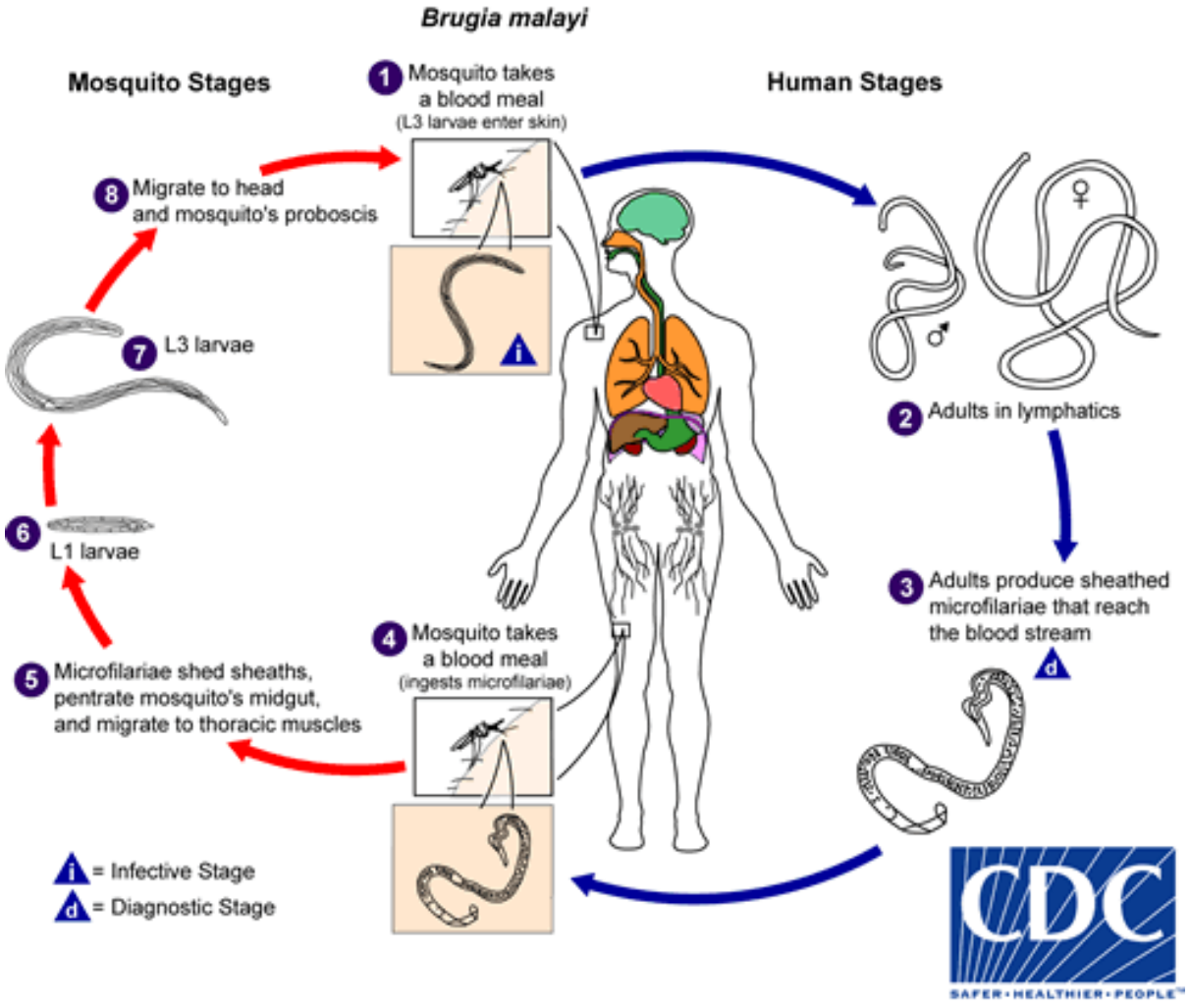
Possible neurological complications of various filariae

Filariae	Microfilariae	Location of adult filariae	Neurological complications
Dracunculiasis medinensis	Subcutaneous	Subcutaneous	Medullar compression
Loa loa	Blood	Subcutaneous	Epilepsy, meningitis
Onchocerca volvulus	Skin	Subcutaneous	Epilepsy
Wuchereria bancrofti	Blood	Lymphatic vessels	Encephalitis
Dipetalonema perstans	Blood	Peritoneal	Headache

Filariasis

Overview





Filariasis

Clinical manifestation

- **Lymphatic filariasis**
  - Lymphedema = Elephantiasis
    - Increased risk of bacterial infection
  - Other swelling areas
    - arms, breasts, genitalia
- **Tropical pulmonary eosinophilia syndrome**
  - shortness of breath, and wheezing
- **CNS manifestation – Encephalitis**
  - **RARE**
    - High load of infection
    - Co-infection with malaria – Mosquito as vector
  - Pathogenesis – complex
    - Mechanical disruption as they migrate through or disrupt tissues or vascular lesion or vascular block of cerebral vessels, or via immune response to infection
  - Degeneration is often followed by granulomas, which can cause fibrosis or mass effects on other tissues or induce disordered inflammatory responses resulting in meningitis, encephalitis, or localized inflammatory responses

Filariasis

Investigation

- **CBC** – Eosinophilia
- **Thick blood smear with Giemsa****

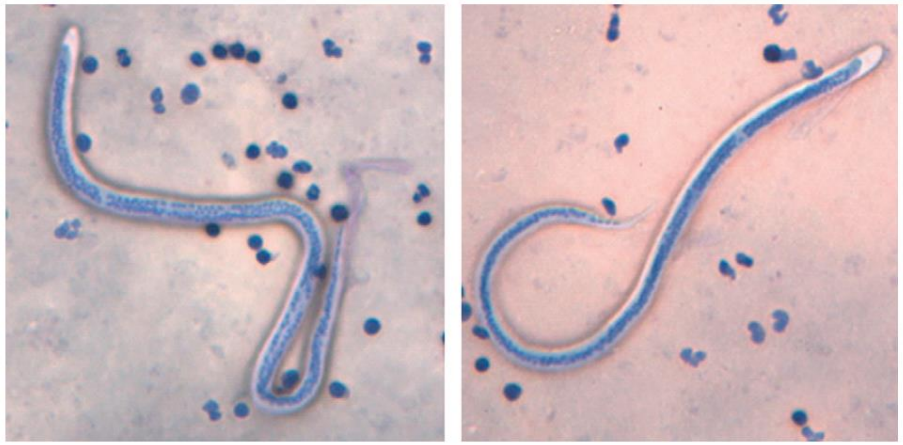
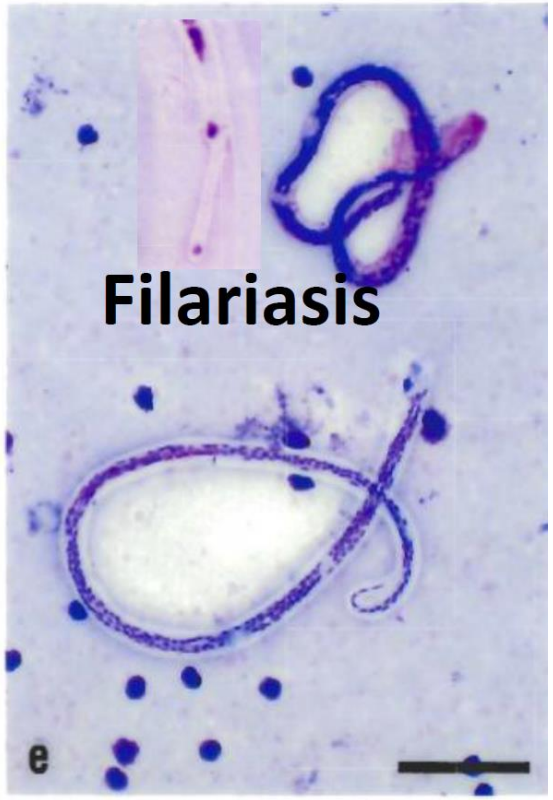


Fig. 18.3. Microfilariae of *W. bancrofti* in thick blood smears stained with Giemsa. (Images courtesy of the O Health Laboratory and Centers for Disease Control and Prevention.)



B. malayi (upper) and ***W. bancrofti*** (lower) microfilariae in the same field of a Giemsa-stained blood film (e). The pink-stained sheath and the darkly stained, compact column of nuclei identify ***B. malayi*** and distinguish it from ***W. bancrofti***

Species	*Wuchereria bancrofti*	*Brugia malayi*
Geographical distribution	Tropics and subtropics worldwide	South-east Asia, Indian subcontinent
Vectors	Mosquitos: *Culex, Aedes, Anopheles, Mansonia*	Mosquitos: *Mansonia, Anopheles, Aedes*
Adult habitat	Lymphatic system	Lymphatic system
Habitat of microfilaria	Blood	Blood
Periodicity	Nocturnal[b]	Nocturnal[b]
Sheath	Present	Present
Length (μm)[a] smears 2% formalin skin snips	244–296 (260) 275–317 (298) —	177–230 (220) 240–298 (270) —
Width (μm)	7.5–10.0	5.0–6.0
Tail	Tapered; anucleate	Tapered; subterminal and terminal nuclei widely separated
Key features of microfilaria	Short head space; dispersed nuclei; sheath unstained in Giemsa; body in smooth curves	Long head space; sheath stains pink in Giemsa; terminal and subterminal nuclei

เก็บเลือดช่วง 0.00 - 2.00 ก็เจอ
หรือมียาให้มันออกมาในเลือดค่อยเจาะ

Specimen collection

- *Loa loa*—midday (10 AM to 2 PM)
- *Brugia or Wuchereria*—at night, after 8 PM
- *Mansonella*—any time
- *Onchocerca*—any time

Filariasis

PostScript

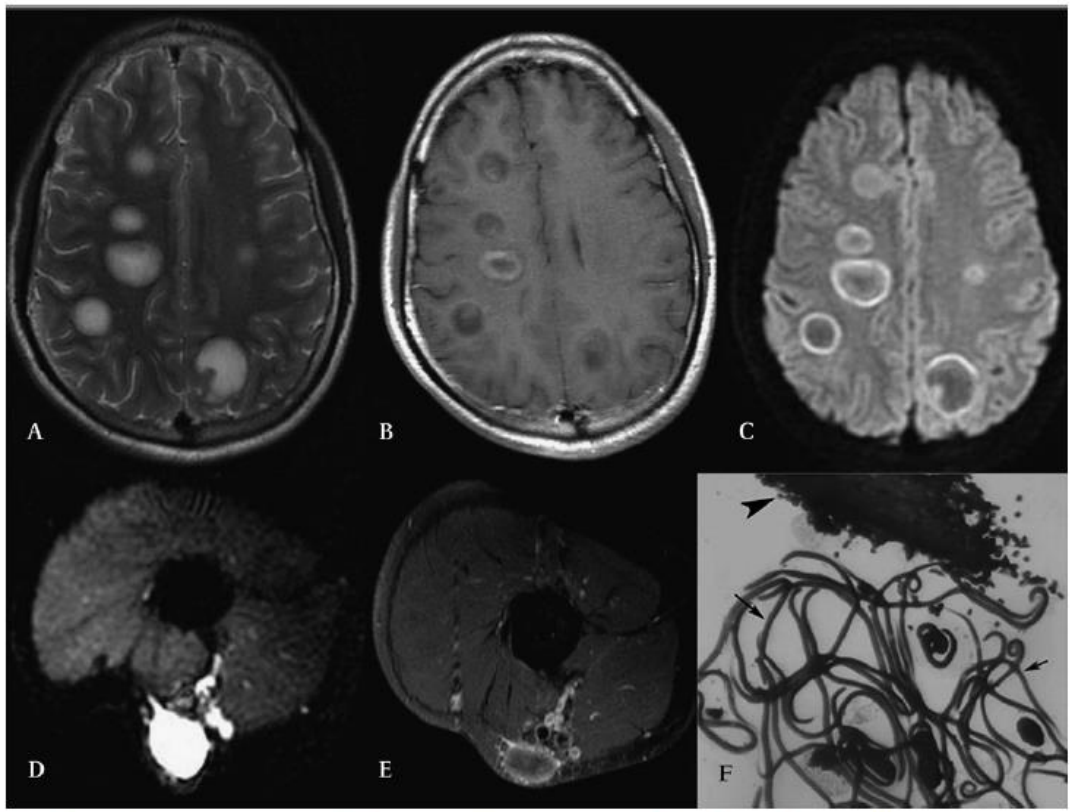


Figure 1 Cranial magnetic resonance images showing multiple bilateral T2 hyperintense lesions (A), which show variable enhancement on post-contrast T1 (B) and peripheral restricted diffusion on diffusion-weighted MRI (C). Axial imaging through the arm shows hyperintense subcutaneous swelling (D) that also shows ring enhancement (E) consistent with infective pathology. Fine needle aspirate of arm swelling (F) shows numerous microfilariae (arrows) of *Wuchereria bancrofti* along with adult female worm (arrow head) (May–Grunwald–Giemsa stain, 40×).

Investigation

A. Shrivastava et al.

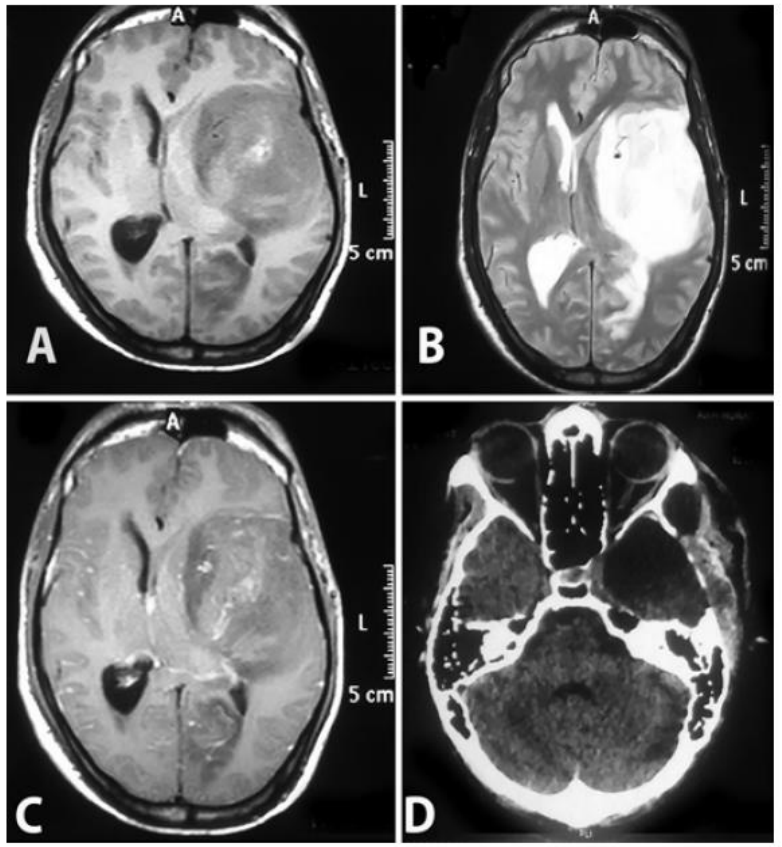
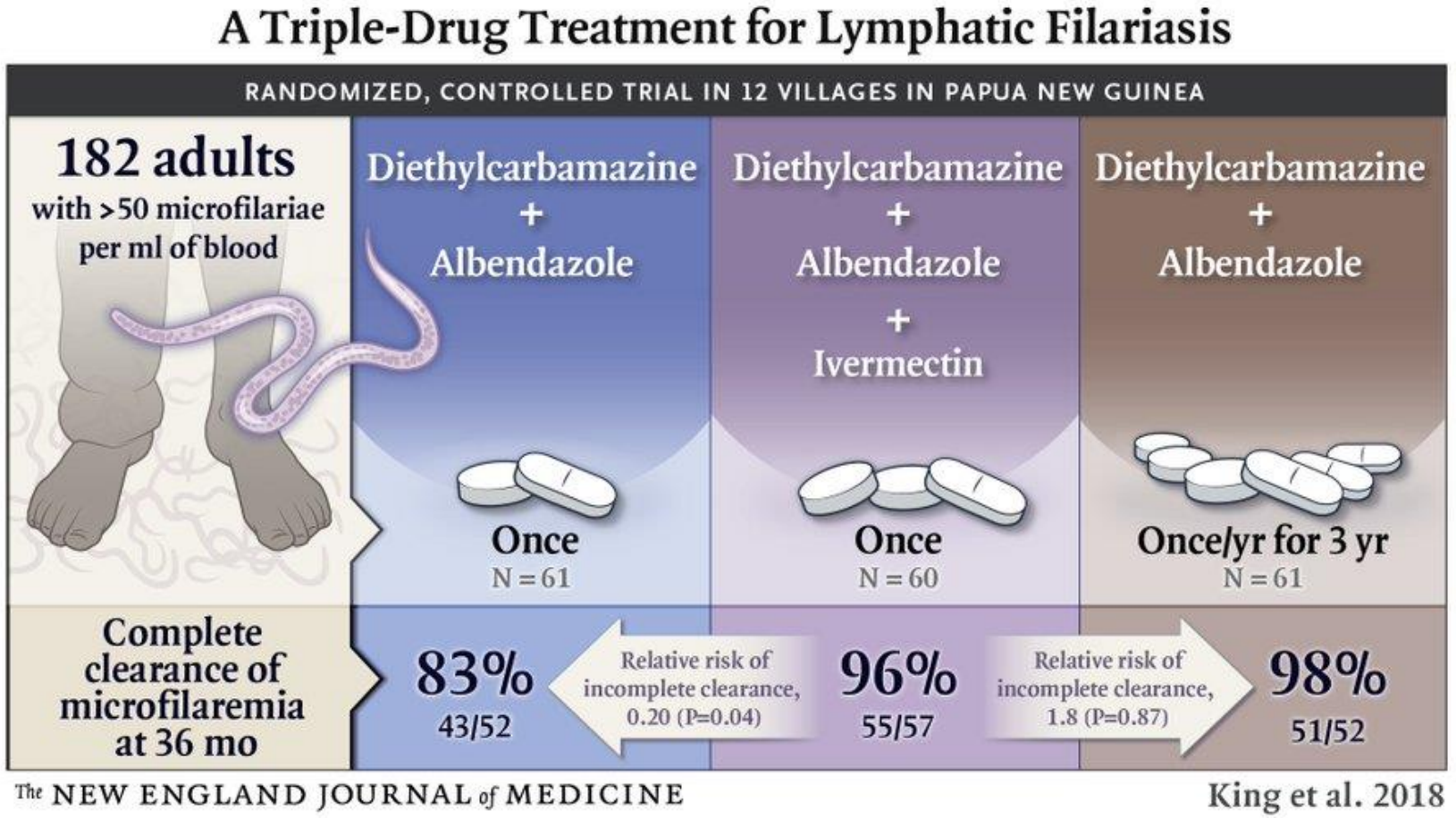


FIG. 1. Preoperative axial T1-weighted (A), T2-weighted (B), and gadolinium-enhanced TI-weighted (C) MR images showing a mass lesion. Postoperative CT scan showing complete resolution of the lesion after surgery and a course of the anthelmintic drug DEC (D).

Filariasis

Treatment

- Diethylcarbamazine citrate (DEC)**

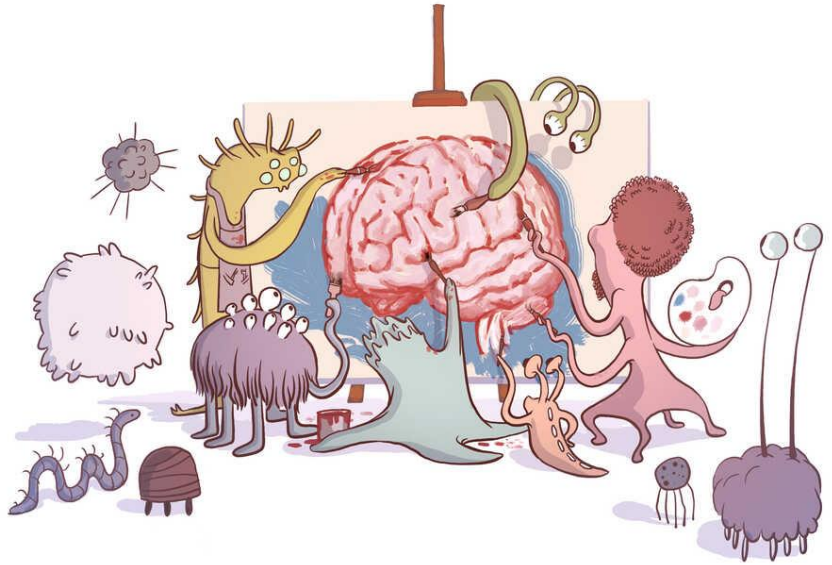


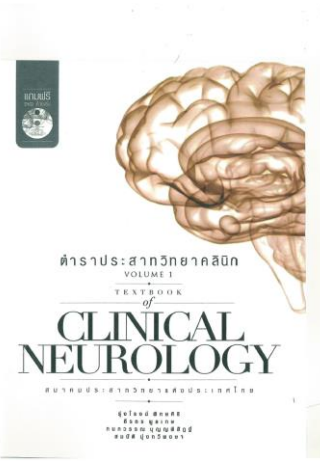
Wuchereia bancrofti

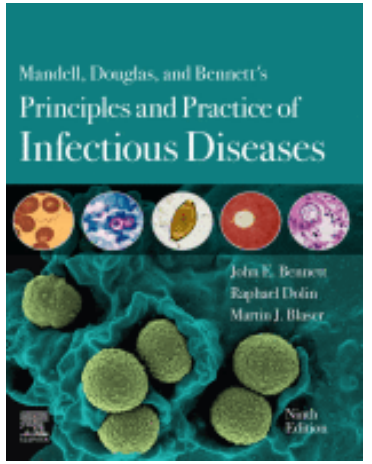
A Trial of a Triple-Drug Treatment for Lymphatic Filariasis. N Engl J Med 2018

Scope of talk

- Introduction to Neuroparasitology
- Nematode (Roundworm)
  - Angiostrongyliasis
  - Gnathostomiasis
  - Filariasis
- Trematode (Flatworm – Fluke)
  - Schistosomiasis
  - Paragonimiasis
- Cestode (Flatworm – Tapeworm)
  - Neurocysticercosis
- Protozoa
  - Cerebral Toxoplasmosis
  - Cerebral Malaria
  - Cerebral Amebiasis
    - *Entamoeba histolytica*
  - Primary Amebic meningoencephalitis
    - *Naegleria fowleri*

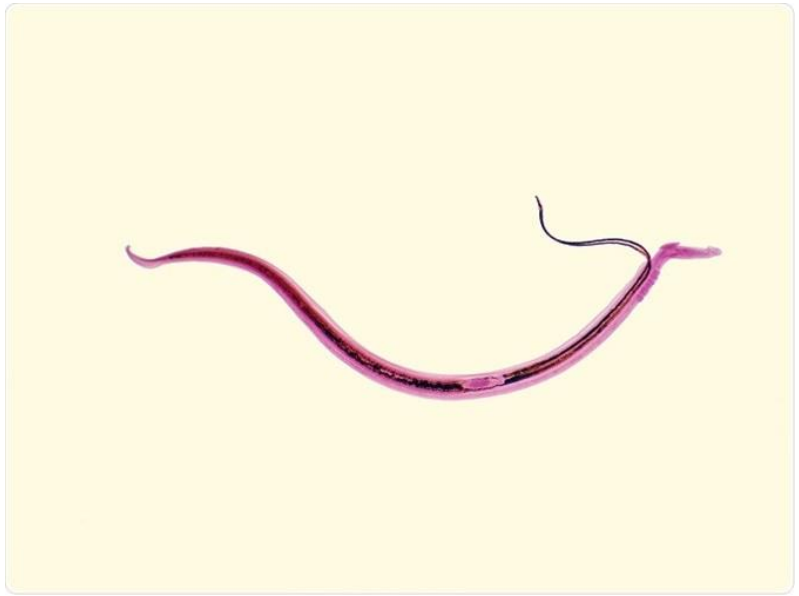


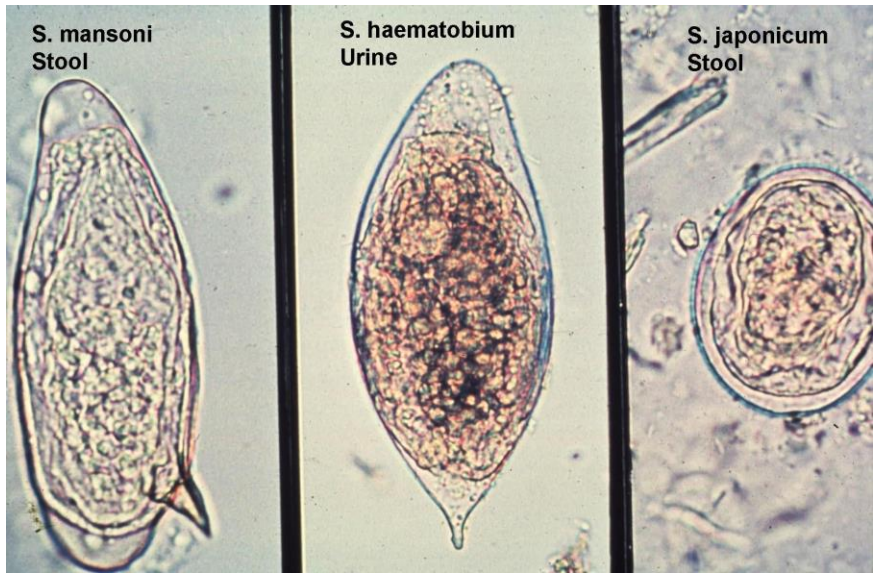




Neuroparasitology and Tropical Neurology Edited by Hector H. Garcia, Herbert B. Tanowitz, Oscar H. Del Brutto Volume 114,Pages 2-414 (2013)
Textbook of Clinical Neurology. Thai Neurological Society. 2014
Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Ninth Edition
CONTINUUM (MINNEAP MINN) 2021;27(4, NEUROINFECTIOUS DISEASE):943–962
Parasitic diseases of the central nervous system: lessons for clinicians and policy makers. EXPERT REVIEW OF NEUROTHERAPEUTICS, 2016.
Centers for Disease Control and Prevention

Schisostomiasis / Bilharziasis (Blood fluke / Snail fever) (พยาธิใบไม้ในเลือด)





Schistosomiasis

Overview

- ***S. mansoni***
  - Distributed throughout Africa: There is risk of infection in freshwater in southern and sub-Saharan Africa–including the great lakes and rivers as well as smaller bodies of water. Transmission also occurs in the Nile River valley in Sudan and Egypt.
  - South America: Including Brazil, Suriname, and Venezuela.
  - Caribbean (risk is very low): Dominican Republic, Guadeloupe, Martinique, and Saint Lucia.
  - Also found in SEA
- ***S. haematobium***
  - Distributed throughout Africa: There is risk of infection in freshwater in southern and sub-Saharan Africa–including the great lakes and rivers as well as smaller bodies of water. Transmission also occurs in the Nile River valley in Egypt and the Mahgreb region of North Africa.
  - Found in areas of the Middle East.
  - A recent focus of ongoing transmission has been identified in Corsica.
  - Also found in SEA
- ***S. japonicum***
  - Found in Indonesia and parts of China and Southeast Asia.
- ***S. mekongi***
  - Found in Cambodia and Laos.
- ***S. intercalatum***
  - Found in parts of Central and West Africa.

Schistosomiasis

Overview

DPDx

Schistosoma spp.

CDC

Incubation period
months to years

5 Free-swimming cercariae released from snail into water

6 Cercariae penetrate skin

4 Sporocysts develop in snail (successive generations)

7 Cercariae lose tails during penetration and become schistosomulae

8 Circulation

3 Miracidia penetrate snail tissue

9 Migration to portal blood in liver and maturation into adults

1 Eggs shed from infected human:
in feces
in urine

2 Eggs hatch and release miracidia

S. mansoni B
S. japonicum *S. mekongi* A
S. haematobium C

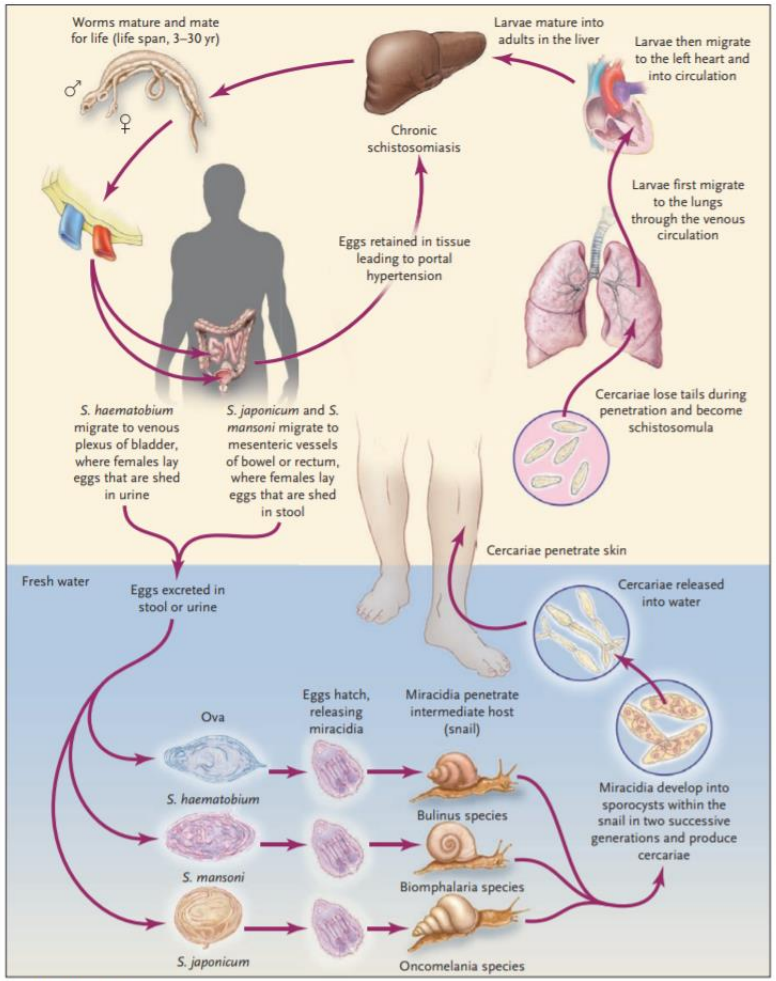
10 Paired adult worms migrate to:

A B Mesenteric venules of bowel/rectum (laying eggs that circulate to the liver and shed in stools)

C Venous plexus of bladder; eggs shed in urine

Infective stage

Diagnostic stage



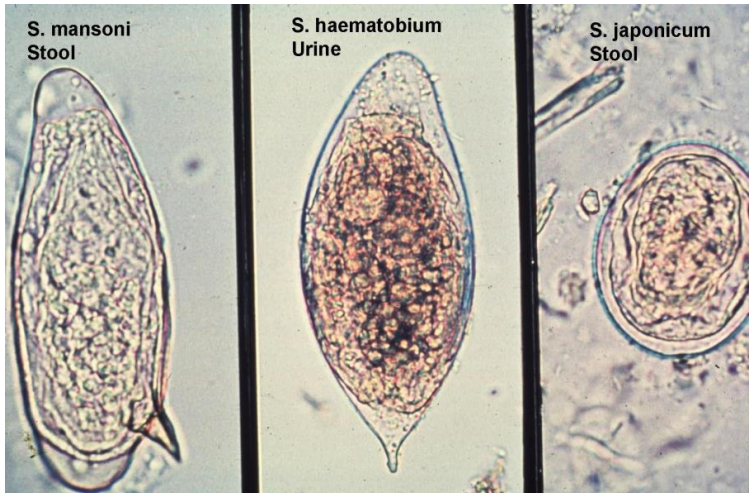
Life Cycle of the Schistosome.
Infection of humans with schistosoma species causes chronic hepatic and intestinal fibrosis or fibrosis, stricturing, and calcification of the urinary tract. Infection follows contact with fresh water harboring larval parasites called cercariae, which penetrate humans' skin, become schistosomula, and enter capillaries and lymphatic vessels. The worms migrate to the portal venous system, where they mature and unite, and then to the superior mesenteric veins, the inferior mesenteric and superior hemorrhoidal veins, or the vesical plexus and veins draining the ureters. Eggs are produced and pass into adjacent tissues; many are shed in feces or urine. The eggs hatch, releasing miracidia that infect freshwater snails, which ultimately release cercariae.

Toward the Elimination of Schistosomiasis. NEJM. 2009

Schistosomiasis

Clinical manifestation

- Schistosomal infection of the CNS (neuroschistosomiasis)
  - **RARE** complication



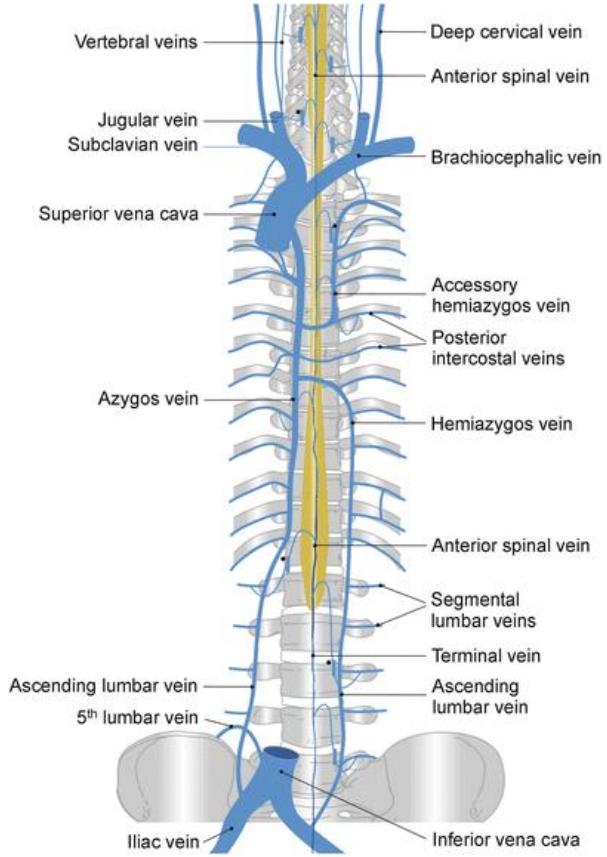
Two forms

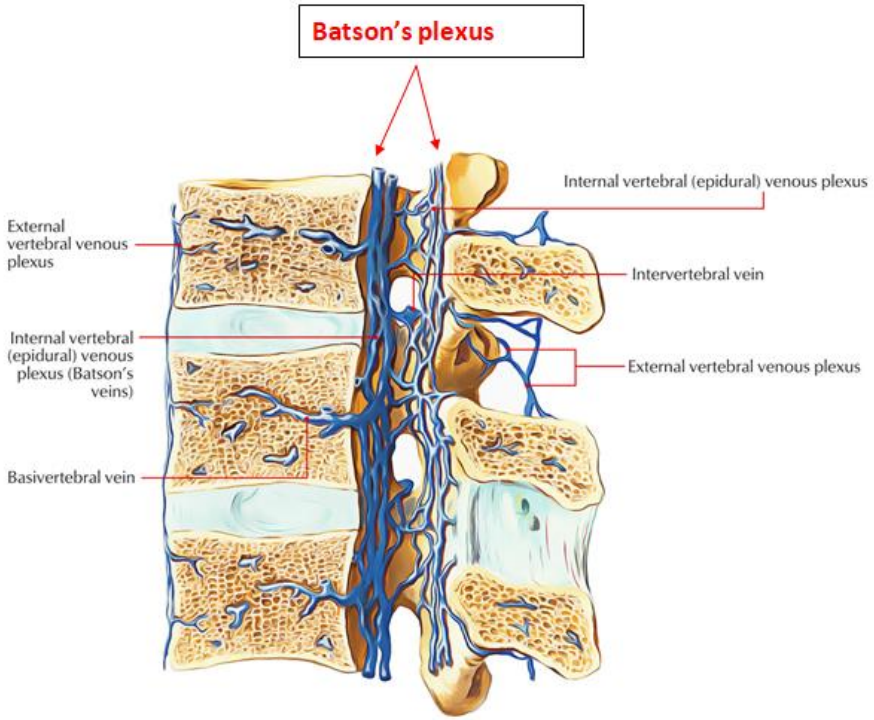
- **Cerebral schistosomiasis**
  - ***S. japonicum*** – smaller egg
- **Myelopathy schistosomiasis – lumbrosacral**
  - ***S. mansoni***, ***S. haematobium*** – larger egg
- **CNS symptoms**
  - Headache
  - Vary depending on the location of the lesion in the brain
    - motor deficits, visual abnormalities, seizures, altered mental status, vertigo, sensory impairment, speech disturbances, cognitive impairment, vomiting, and ataxia
  - Systemic schistosomiasis are typically **ABSENT**

Schistosomiasis

Clinical manifestation

- **Mechanism – mainly via ectopic deposition of eggs**
  - Retrograde flow from the **iliac veins and inferior vena cava** through the **<u>valveless</u> Batson venous plexus** into the spinal cord.

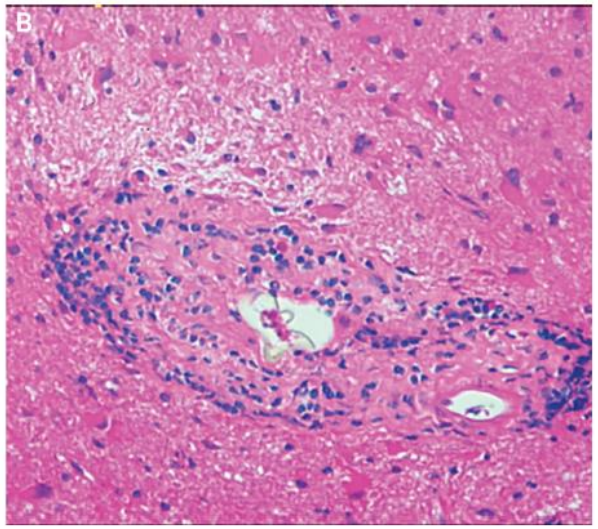




Schistosomiasis

Clinical manifestation

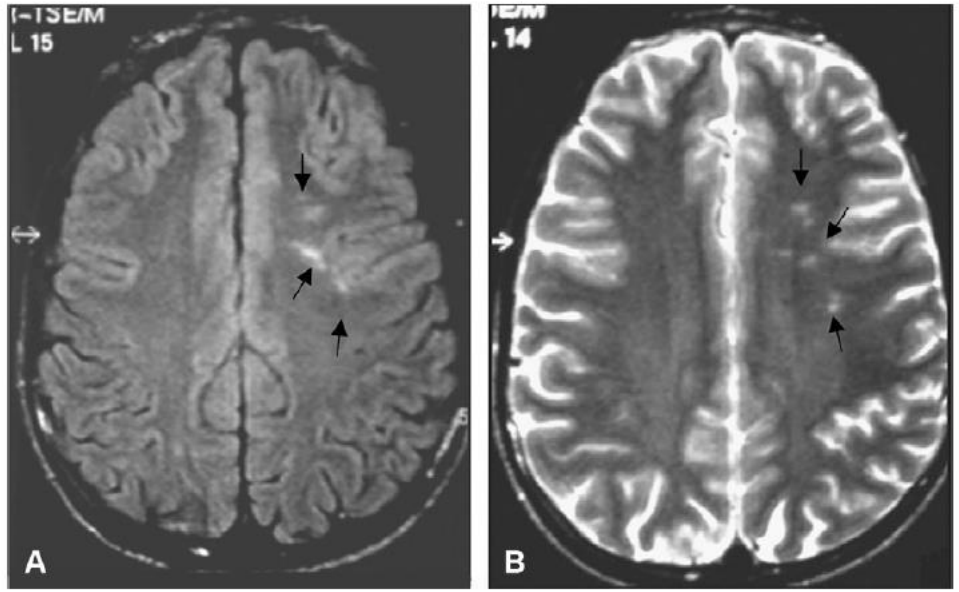
- **Mechanism – mainly via ectopic deposition of eggs**
  - The eggs are **immunogenic** >> host response leads to **granulomatous** inflammation, with local edema, congestion, and varying degrees of fibrosis.
  - Pathology - ***S. mansoni, S. japonicum*** schistosomiasis
    - Various **hepatic complications** from inflammation and granulomatous reactions, and occasional embolic egg **granulomas** in brain or spinal cord.
  - Pathology - ***S. haematobium*** schistosomiasis
    - hematuria, scarring, calcification, squamous cell carcinoma, and occasional embolic egg **granulomas** in brain or spinal cord



Schistosomiasis

Clinical manifestation

- **Cerebral schistosomiasis**
  - ***S. japonicum*** – smaller egg
  - Bleeding - segmental damage of small leptomeningeal or parenchymal blood vessels induced by the parasites
    - ICH
    - SAH
  - Headache
  - Seizure
  - Focal neurological defcit



Schistosomiasis

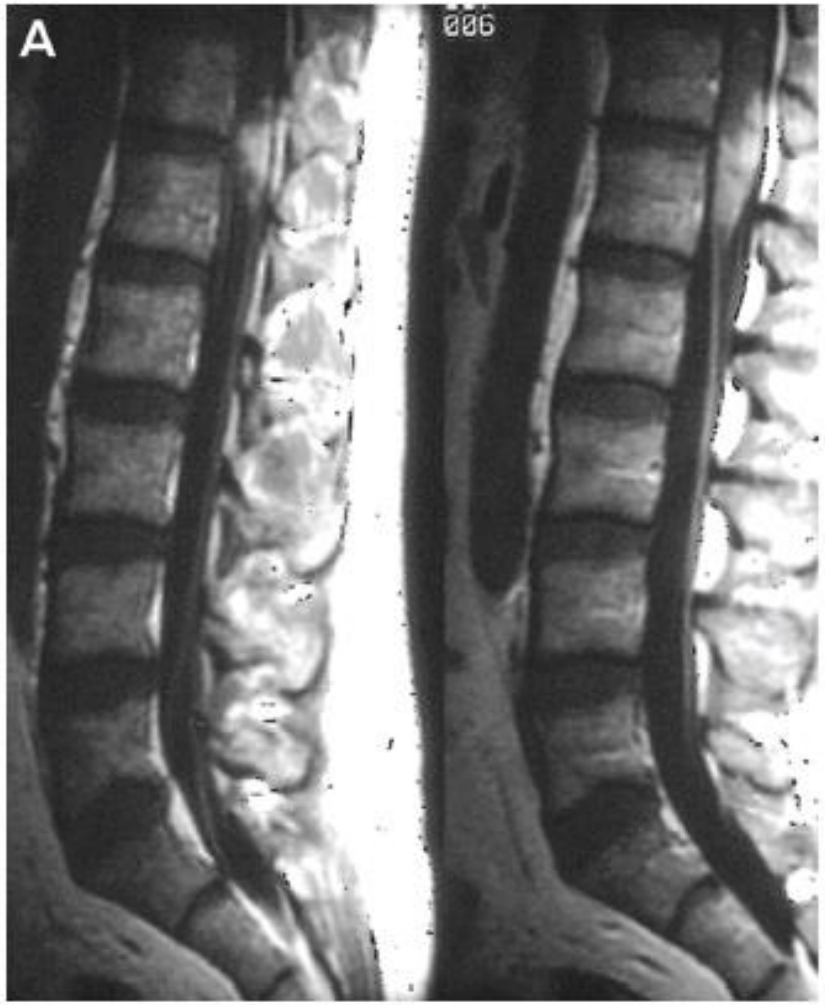
Clinical manifestation

- **Myelopathy schistosomiasis – lumbrosacral**
  - ***S. mansoni*, *S. haematobium*** – larger egg

Transverse myelitis

- granulomatous lesions with inflammatory necrosis of the spinal cord.
- Progress in an acute to subacute (peak 15 days)

- **Sites**
  - spinal cord, nerve roots, or, most commonly, both.
  - **The lower spinal cord (T11 through L1)** possibly because of increased anastomoses between the **Batson venous plexus** with the **portal venous system** at this location.
- **Clinical presentation**
  - Low back pain (79-100%) – most common, initial
  - Pain in the lower limbs, which can be symmetric or asymmetric.
  - Lower spinal cord or cauda equina or conus medullaris involvement is common,
    - weakness of the lower limbs, lower limb sensory disturbance, sphincter dysfunction, sexual dysfunction, and abnormal reflexes.
  - In some patients, acute paraplegia may result from occlusion of the anterior spinal artery by the parasites.

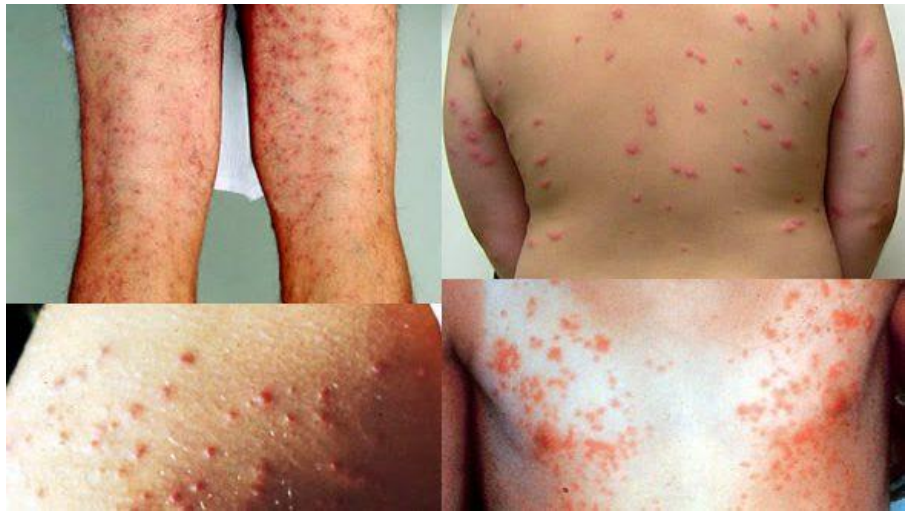


Schistosomiasis

Clinical manifestation

- **Common presentation**
  - Most people have no symptoms when they are first infected
  - Within days – rash, skin reaction
    - A local cutaneous hypersensitivity reaction following **skin penetration by cercariae** may occur and appears as small, itchy maculopapular lesions.

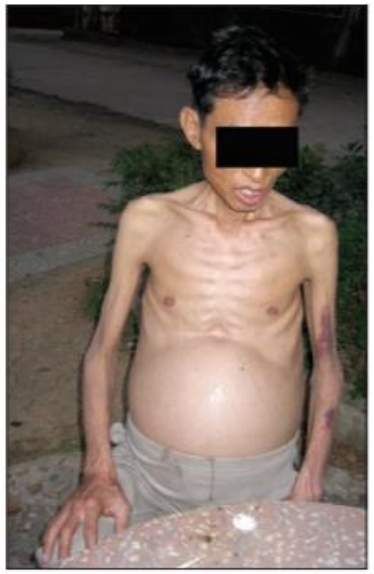
    OR
    - Egg deposition
  - Within 1-2 months of infection – fever, chills, cough, and muscle aches
  - Many infections – asymptomatic



Schistosomiasis

Clinical manifestation

- **Acute schistosomiasis (Katayama fever)**
  - a systemic hypersensitivity reaction that may occur weeks after the initial infection, especially by ***S. mansoni*** **and** ***S. japonicum***.
  - fever, cough, abdominal pain, diarrhea, **hepatosplenomegaly**, eosinophilia.
- **Chronic schistosomiasis**
  - Abdominal pain, enlarged liver
  - Blood in the stool or blood in the urine, and problems passing urine.
  - Increased risk of liver fibrosis or bladder cancer.
  - **CNS**
    - Seizures, paralysis, or spinal cord inflammation.
    - Spinal cord mass
    - Slowly expanding intracranial mass **(pseudotumor)**
      - a solitary mass or multiple mass lesions – parenchymal brain granulomas

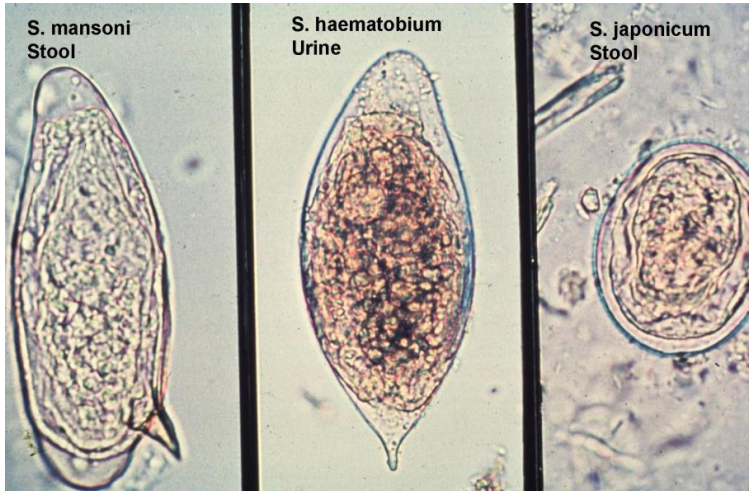


Toward the Elimination of Schistosomiasis. NEJM. 2009

Schistosomiasis

Investigation

- **CSF**
  - WBC – mild mononuclear pleocytosis
  - Protein increased
- **Direct examination** - confirm eggs in …
  - **Stool**
    - ***S. mansoni, S. japonicum***
  - **Urine**
    - ***S. haematobium***



Schistosomiasis

Investigation

- **CT/MRI brain - Cerebral neuroschistosomiasis**
  - Solitary or multiple subcortical mass lesions surrounded by hypodense or T2-hyperintense edema, with heterogeneous contrast enhancement and irregular borders.
  - **The arborized pattern (suggestive, non-specific)**
    - A linear enhancement pattern surrounded by multiple enhancing nodules

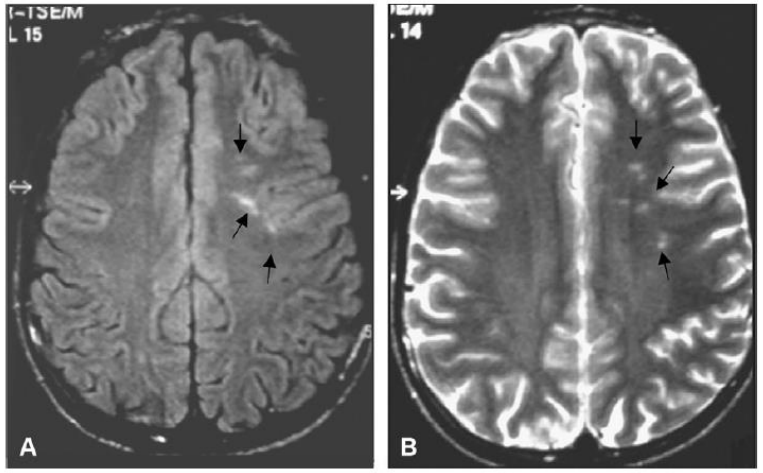


Fig. 22.1. Magnetic resonance images of patient 14, a 15-year-old boy with schistosomiasis mansoni. Axial fluid attenuated inversion recovery (**A**) and TSE-T2WI (**B**) show small focal hyperintensities in the white matter of the frontal lobe (small arrows). From Manzella et al. (2012). Republished with permission of The American Society of Tropical Medicine & Hygiene. Permission conveyed through Copyright Clearance Center, Inc.

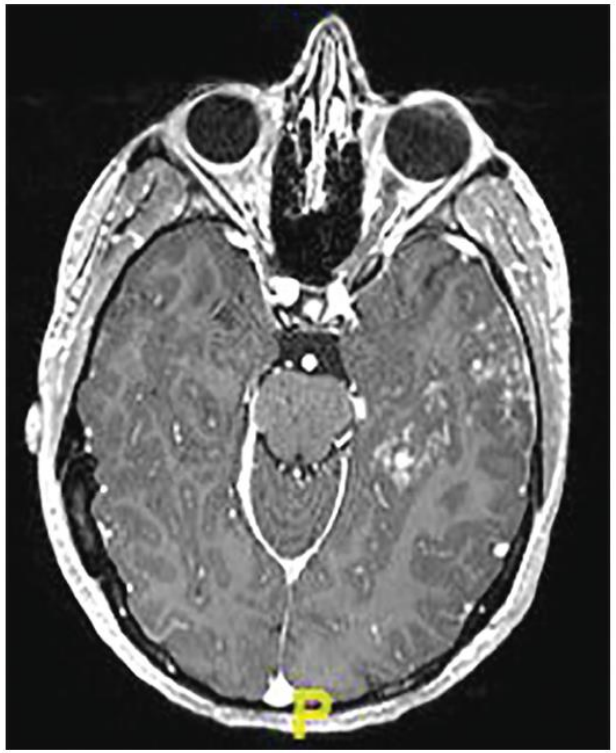


FIGURE 6-9

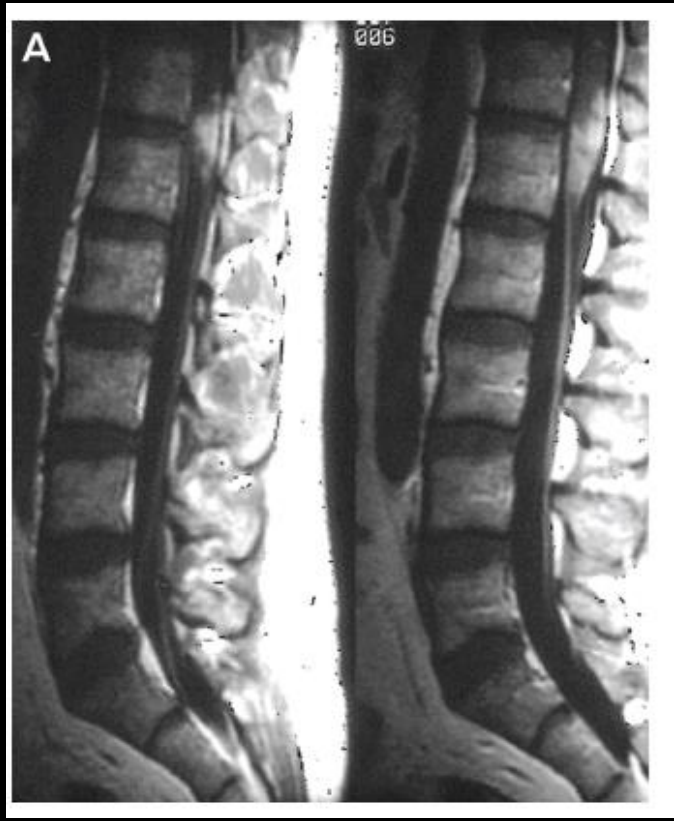
Axial postcontrast T1-weighted MRI shows patchy enhancement in an arborized pattern in the left temporal lobe in cerebral schistosomiasis.

Reprinted with permission from Cho T, Continuum (Minneap Minn).[53] © 2018 American Academy of Neurology.

Schistosomiasis

Investigation

- **MRI spine**
  - enlargement of the lower spinal cord or the conus medullaris on T1-weighted images, signal hyperintensity on T2-weighted images
  - heterogeneous nerve root patterns of contrast enhancement



A 22-year-old man traveled to Malawi. Three months after returning to the United States, he noticed back pain and weakness in both legs that progressively worsened. A spinal MRI demonstrated an intramedullary lesion at the T11-T12 level (FIGURE 6-10A[59]). Serum laboratory evaluation including comprehensive metabolic panel, liver function tests, and complete blood cell count were normal, and no parasite eggs were found in stools or urine. Surgery was performed, and pathologic examination of the excised tissue revealed an inflammatory granuloma around a crenated *Schistosoma* egg (FIGURE 6-10B). Postsurgical evolution was favorable with complete recovery.

CASE 6-4

FIGURE 6-10

Imaging of the patient in CASE 6-4 with spinal schistosomiasis. *A*, Sagittal postcontrast T1-weighted MRI of the spine shows an intramedullary lesion in the lower thoracic spine. *B*, Pathologic (hematoxylin and eosin [H&E]) specimen from the same lesion shows a granuloma around a *Schistosoma* egg.

Images courtesy of Christina Coyle, MD. Reprinted from Coyle CM, Handb Clin Neurol.[59]

Schistosomiasis

Treatment

Systemic + Cerebral CNS

- **Medical**
  - **Praziquantel (PZQ) >> kills adult female worm** [Not good for larvae]
    - 40 mg/kg per day for 3 days ***S. mansoni, S. haematobium*** ***(larger egg – spinal)***
    - 60 mg/kg per day for 6 days ***S. japonicum*** ***(small egg – cerebral)***
    - Re-examined stool/urine 1 month after treatment to assess the efficacy of medical treatment.
    - **!! Releasing of eggs after PZQ**
  - **Steroid – Acute phase sequalae**
    - **Early** treatment (10–15 days post exposure) better than delay
    - **IVMP** (15–20 mg/kg; maximum dose 1 g) over 5–7 days followed by oral prednisone for 2–6 weeks
    - Because the levels of praziquantel are decreased in the setting of steroid administration and immature worms are not susceptible to praziquantel a second course should be given after 6-12 weeks to eradicate surviving parasites
- **Surgery in refractory cases**

Schistosomiasis

Treatment

Systemic + CNS involvement

- **Medical**
  - **Praziquantel (PZQ) >> kills adult female worm** [Not good for larvae]
    - 40 mg/kg per day for 3 days ***S. mansoni, S. haematobium*** ***(larger egg – spinal)***
    - 60 mg/kg per day for 6 days ***S. japonicum*** ***(small egg – cerebral)***
    - Re-examined stool/urine 1 month after treatment to assess the efficacy of medical treatment.
    - **!! Releasing of eggs after PZQ**
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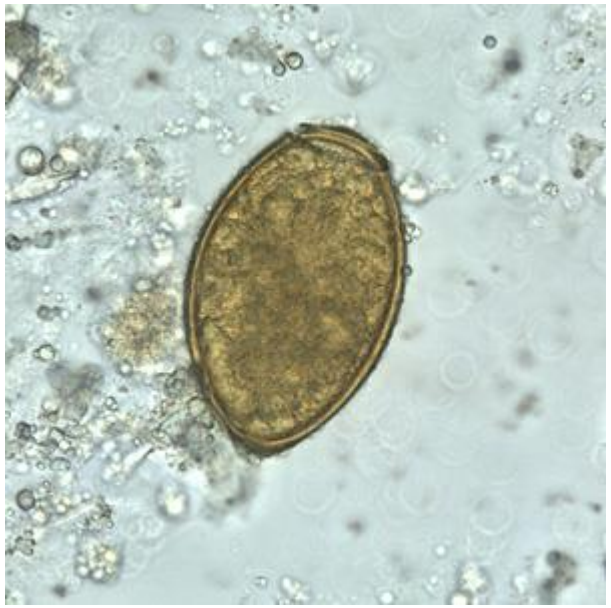
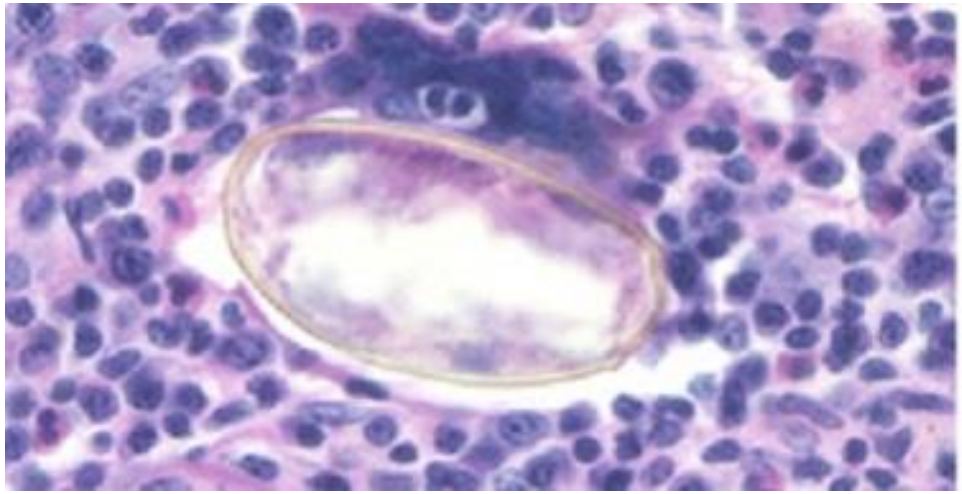
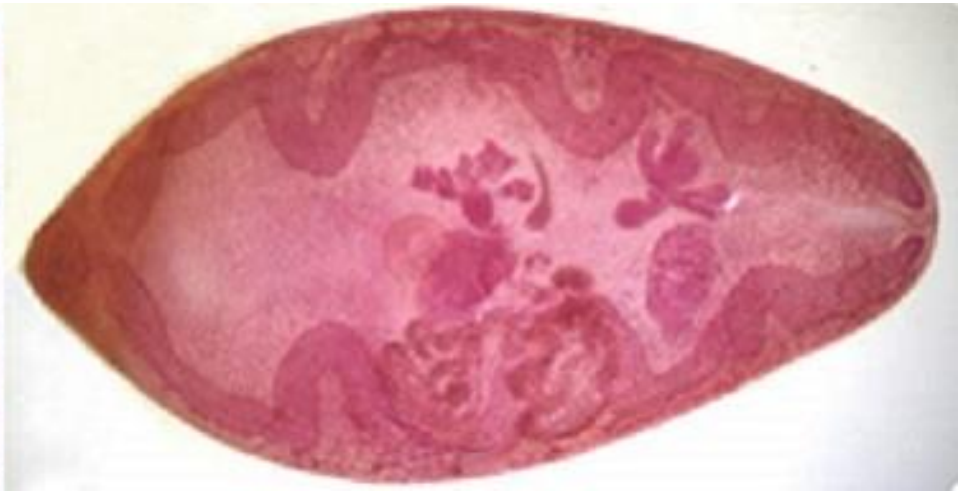
    - **Early** treatment (10–15 days post exposure) better than delay
    - **IVMP** (15–20 mg/kg; maximum dose 1 g) over 5–7 days followed by oral prednisone for 2–6 weeks
    - Because the levels of praziquantel are decreased in the setting of steroid administration and immature worms are not susceptible to praziquantel a second course should be given after 6-12 weeks to eradicate surviving parasites
  - Spinal form – dose varies in studies
- **Surgery in refractory cases**

Paragonimiasis (Lung fluke) (พยาธิใบไม้ในปอด)







Paragonimiasis

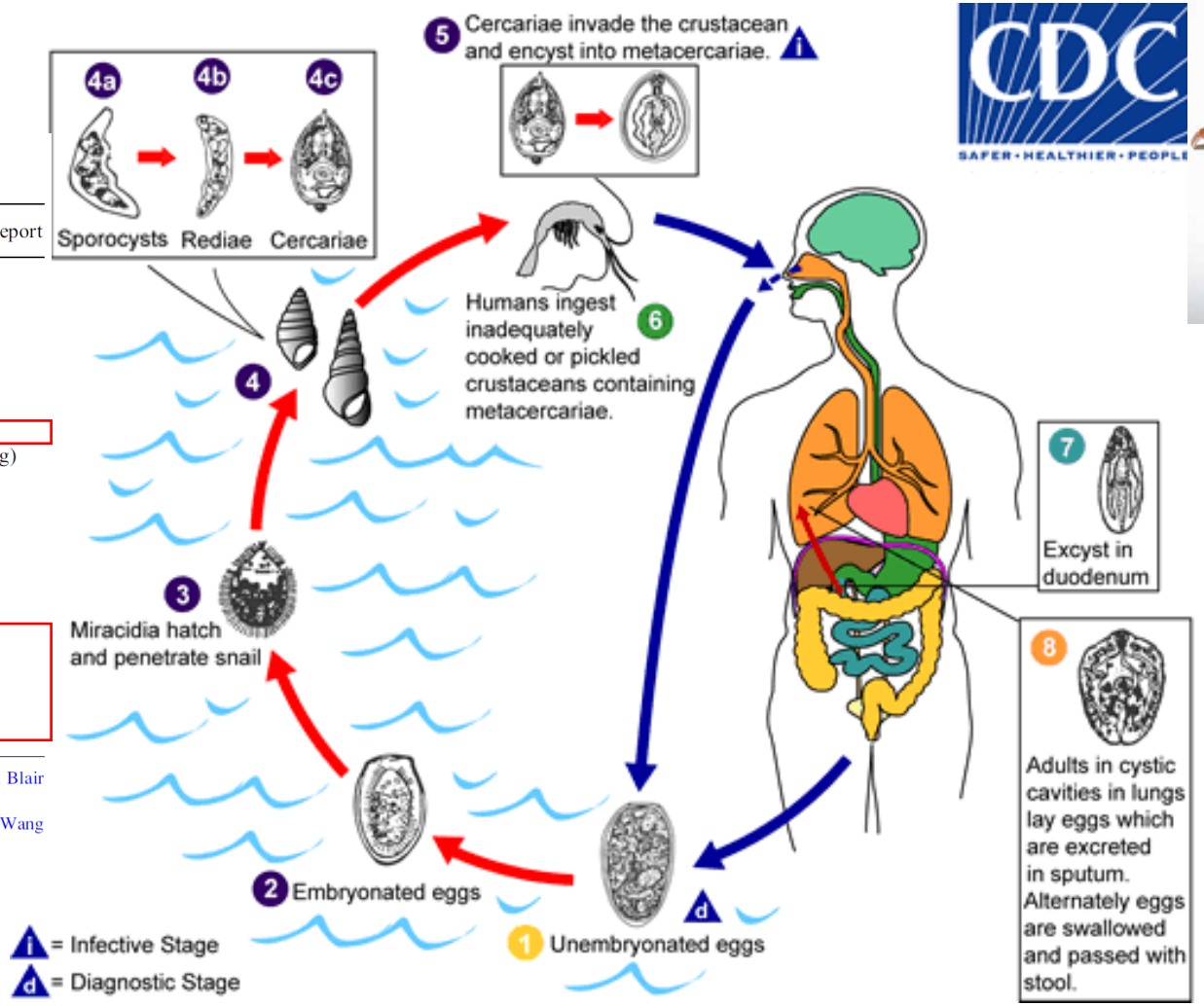
Overview

Table 23.1

***Paragonimus* spp. reported from humans**

Species of Paragonimus	Country of first report
P. africanus	West Cameroon
P. heterotremus (syn. *P. tuanshanensis*)	China (Guangxi)
P. kellicotti	USA (midwest)
P. mexicanus (syn. *P. ecuadoriensis*, *P. peruvianus*)	Mexico
*P. siamensis**	Thailand
P. skrjabini (skrjabini) (syn. *P. hueitungensis*, *P. szechuanensis*, *P. veocularis*)	China (Guangdong)
P. skrjabini miyazakki (syn. *P. miyazakii*)	Japan
P. uterobilateralis	Cameroon
P. westermani (syn. *P. assymetricus*, *P. edwardsi*, *P. filipinus*, *P. macacae*, *P. philippinensis*, *P. pulmonalis*, *P. ringeri*)	India

*The majority of the above information can be obtained from Blair et al. (1999).
This species has been added as a human-infecting species by Wang et al. (2011).



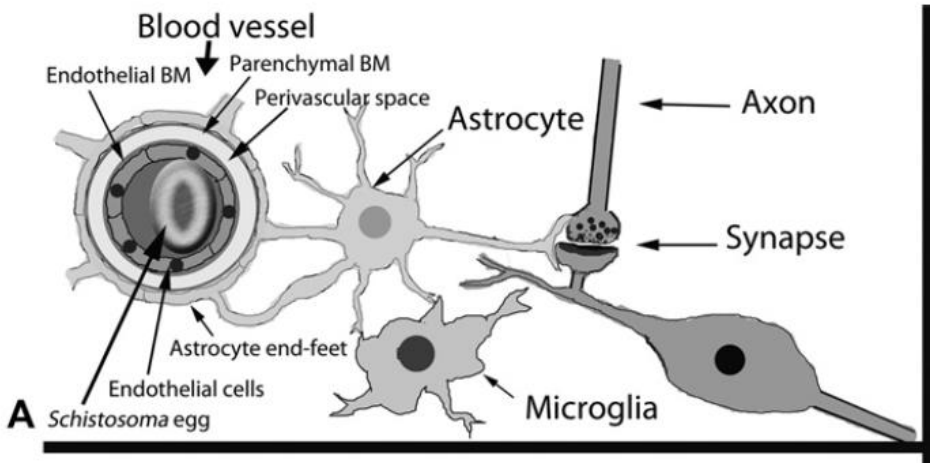
Human infection with
P. westermani occurs by eating
inadequately cooked or
pickled crab (ปูน้ำจืด ปูไข่ดอง) or
crayfish (กุ้งเคย์ฟิช)
that harbor metacercariae of the parasite

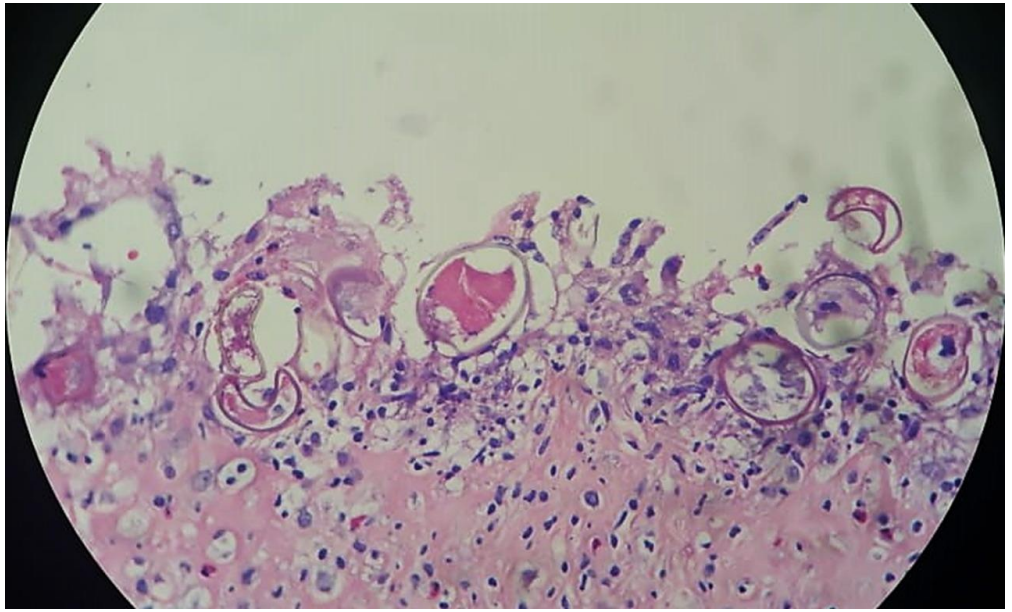
P. siamensis

Paragonimiasis

Clinical manifestation

- **Cerebral paragonimiasis**
  - **General**
    - **RARE (1%)**
    - 45% (30–60%) of all extrapulmonary paragonimiasis
    - Usually accompanied by **pleuropulmonary infection**
      - Chronic cough, rusty-colored sputum (¼ hemoptysis), pleuritic chest pain
    - **Neurovascular invasion** hypothesis
      - larvae migrate through perivascular loose connective tissues around the jugular vein or carotid artery and enter the posterior circulation via the skull base foramina
  - **Pathology**
    - Early **granulomatous** lesion and later mass formation with **calcification and liquefaction**, surrounded by the fibrous capsule
    - Adult worms may disintegrate early, and **only irregularly shaped eggs are often observed in sections of the brain abscess cavity**
  - **Site** – Cerebral cortex (common)
- **Spinal paragonimiasis**
  - Relative **RARE**
- **General symptoms**
  - an acute syndrome with cough, abdominal pain, discomfort, and low-grade fever
  - Incubation 2 to 15 days after infection





Paragonimiasis

Clinical manifestation

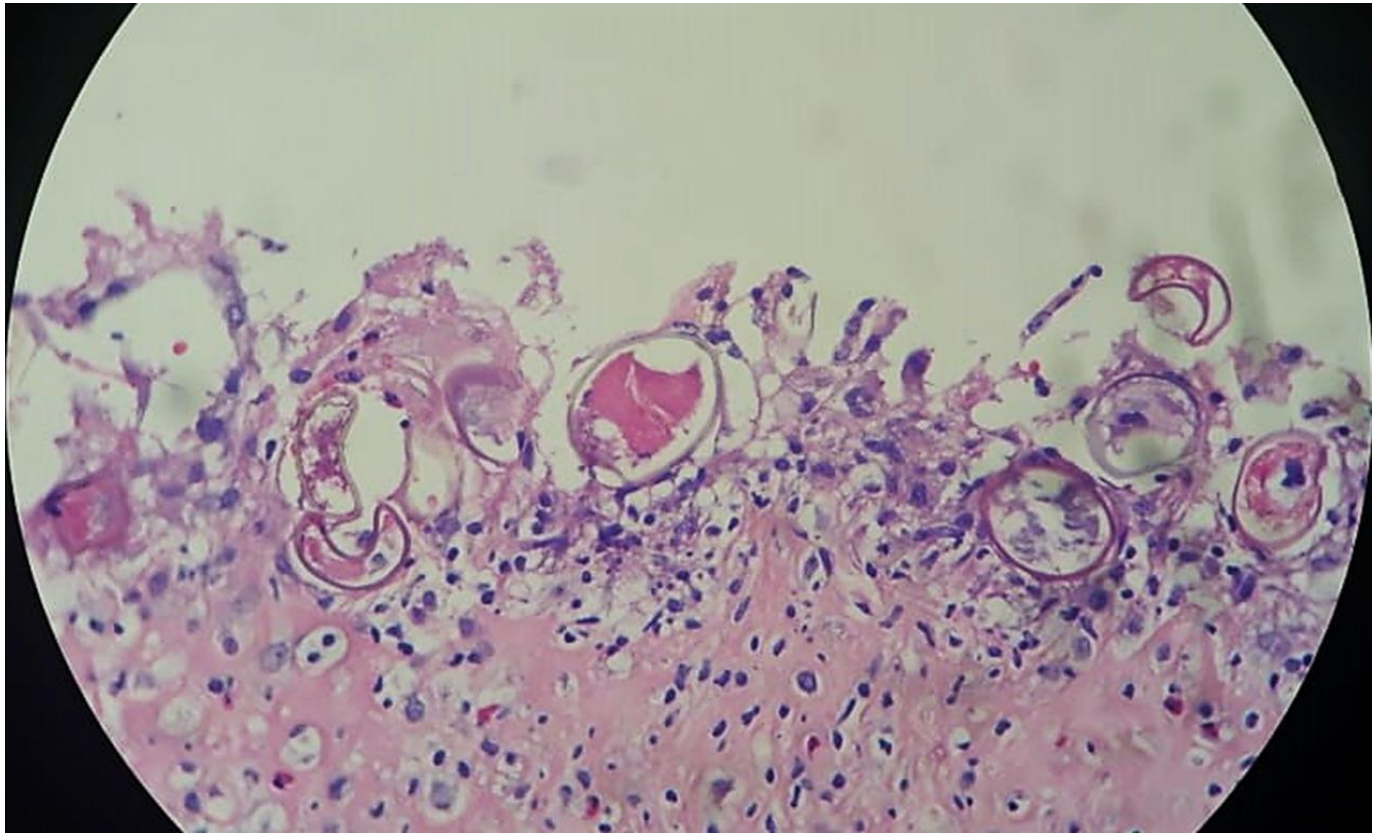
- **Cerebral paragonimiasis**

Table 23.2

Histopathological findings of cerebral paragonimiasis

Stage	Findings
Stage I	Meningo-encephalitic form (representing the exudative and infiltrative phase). In this form, meningitis, encephalitis, and noncapsulated early necrotizing granuloma are the salient features
Stage II	Granulomatous form (representing the localized phase). This stage is histopathologically characterized by the formation of a well-encapsulated granuloma
Stage III	Organization-calcification form (representing the chronic stabilized phase). This stage is characterized by the organization and calcification of the cysts and granuloma and diffuse atrophy in the involved cortex or subcortex

From Oh (1969).



Paragonimiasis

Investigation

- **Imaging**
  - Abscess (ring)
  - Calcification
  - Bleeding

Table 23.3

Four types of intracranial calcifications in plain skull films of cerebral paragonimiasis patients

Type	Findings
Type I	Punctuate and amorphous calcified deposits and occasional formation of trabecular lined calcification
Type II	Round nodular calcifications in spotty arrangement with diameter ranging from 5 to 7 mm, with poor demarcation
Type III	Solitary, round, well-defined cystic calcification with diameter ranging from l0 to 20 mm
Type IV	Congregated, multiple, round or oval, cystic calcifications, the density is greater around the circumference and less in the center; diameter ranging from 7 to 30 mm. Because of clustering of calcified cysts, the appearance resembles "soap bubbles"

From Oh (1968c).

Table 23.4

CT/MRI findings of early and late-stage cerebral paragonimiasis (Procop, 2009)

Stage	Findings
Early	Conglomerated, multiple ring-shaped enhancements with surrounding edema, which appear as a cluster that resembles grapes (some patients may have solitary ring-shaped lesions) Nodules have iso- or hypodense centers with a hyperintense periphery (T1-weighted image) or iso- to hypointense peripheries compared with the center (unenhanced T2-weighted image) Localized hemorrhages
Late	Multiple, round or nodular, densely calcified areas that correlate with the "soap bubble" or type IV calcifications seen on plain skull films Nodules with peripheral low density and central hyperintensity (T1-weighted image) Peripheral regions of low intensity and areas of central high intensity (T2-weighted image) Large low-density areas connected with the calcified areas, and ventricular dilatation and widening of the cortical sulsi

Paragonimiasis

Investigation

- Imaging – **Soap bubble!**

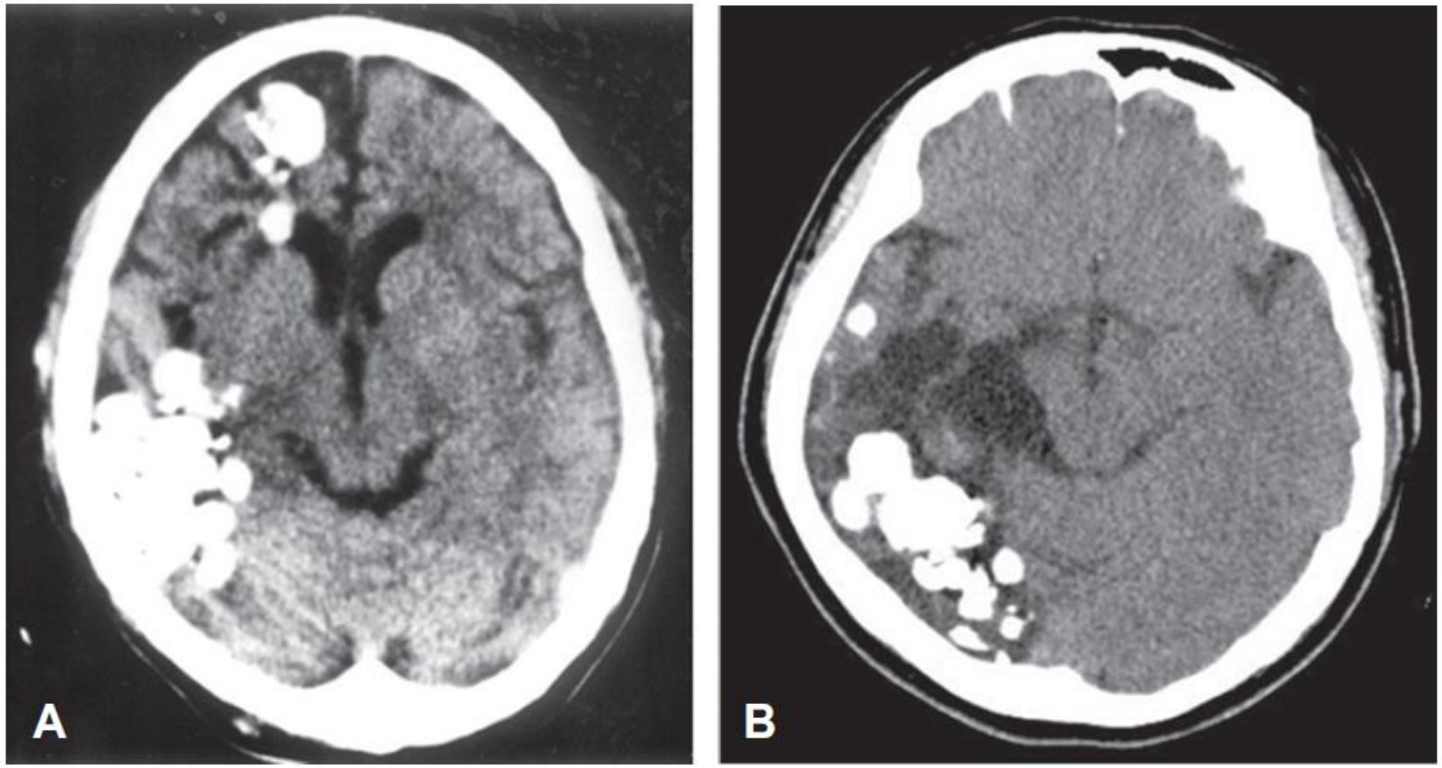


Fig. 23.5. Brain CT findings of chronic cerebral paragonimiasis. (**A**) A case reported by Kang et al. (2000) in Korea. Multiple calcified lesions with high density are seen in the right frontal and temporal areas of the brain. (Kindly provided by Dr. Sung-Jong Hong, Chung-Ang University, Seoul, Korea; this reproduction was permitted by the *Korean Journal of Parasitology*.) (**B**) Another case in Korea showing the typical "soap bubble" appearance in the right temporal areas of the brain.

Paragonimiasis

Investigation

- **Imaging**

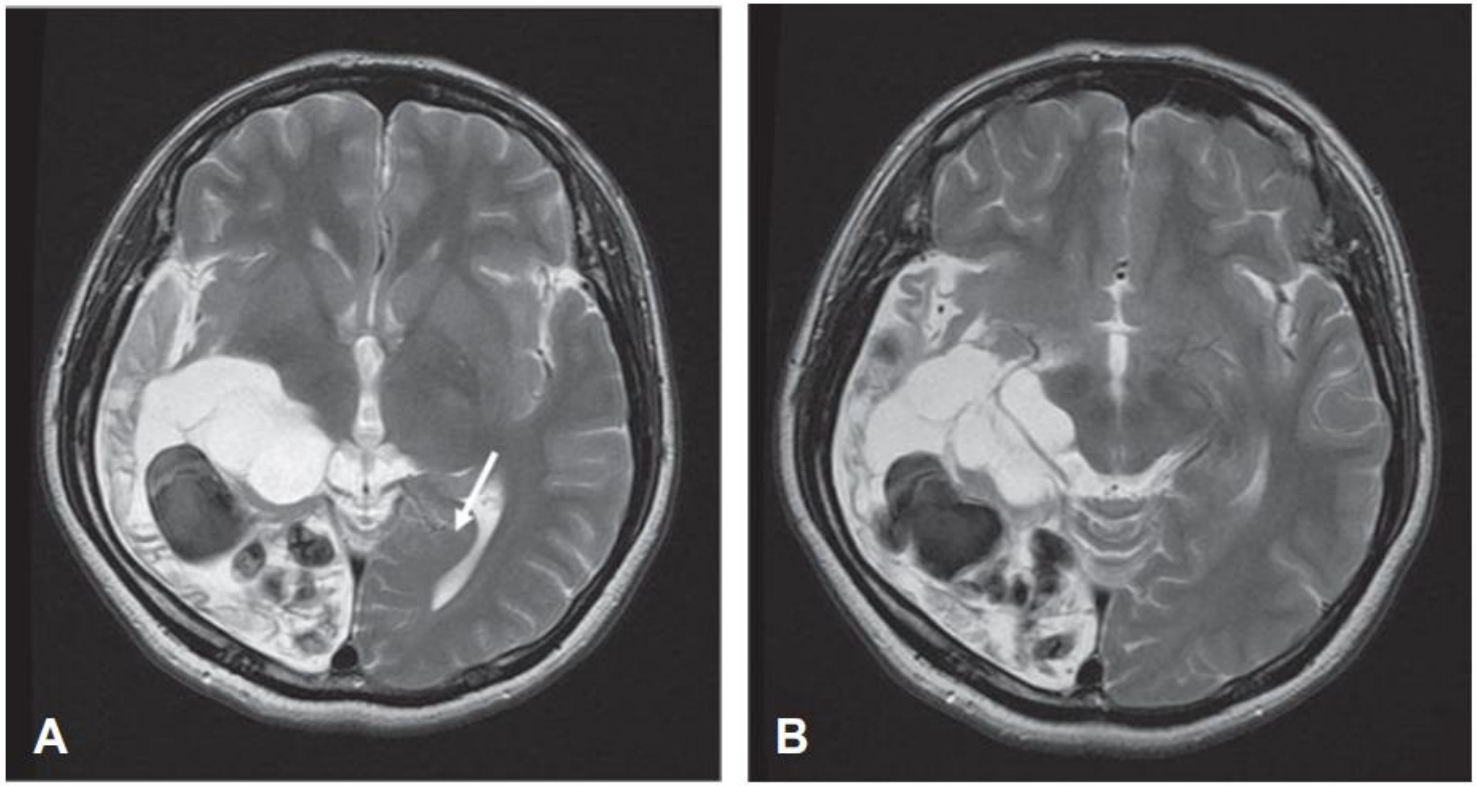


Fig. 23.6. Brain MR images (**A**, **B**) of cerebral paragonimiasis from a chronic case in Korea. T2-weighted axial image shows nodules with peripheral low density and central hyperintensity and inflammatory changes in the surrounding tissues in the right temporal areas.

Paragonimiasis

Investigation

- Imaging

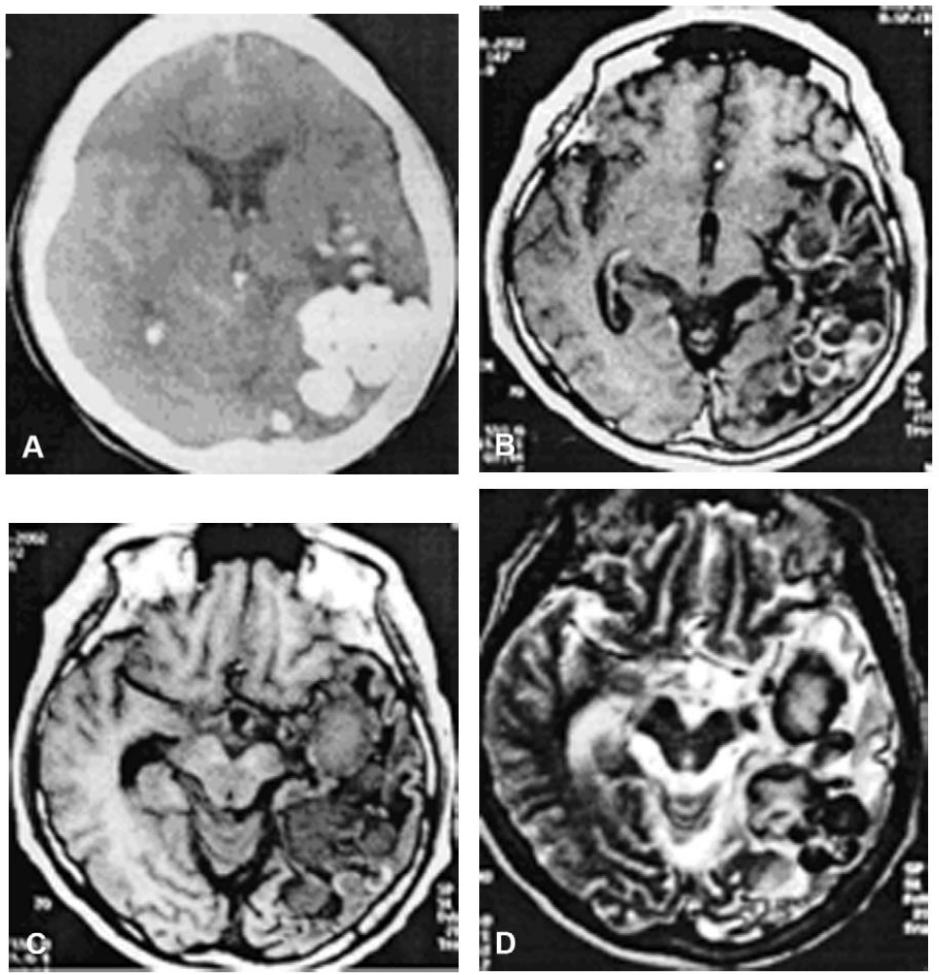


Fig. 4.15. (**A**) Unenhanced axial CT scan showing conglomerated high-density calcified nodules (5 × 5 cm in size) in the left temporo-occipito-parietal region and subarachnoid hemorrhage in the basal cisterns in a patient with paragonimiasis. (**B**) T1W, (**C**) T2W, and (**D**) contrast-enhanced T1W axial images showing conglomerated iso- or low-signal intensity round nodules with peripheral rim enhancement in the left temporo-occipito-parietal area. (With permission from Choo JD, Suh BS, Lee JS et al. (2003). Chronic cerebral paragonimiasis combined with aneurysmal subarachnoid hemorrhage. Am J Trop Med Hyg 69: 466–469.)

Paragonimiasis

Investigation

- Imaging

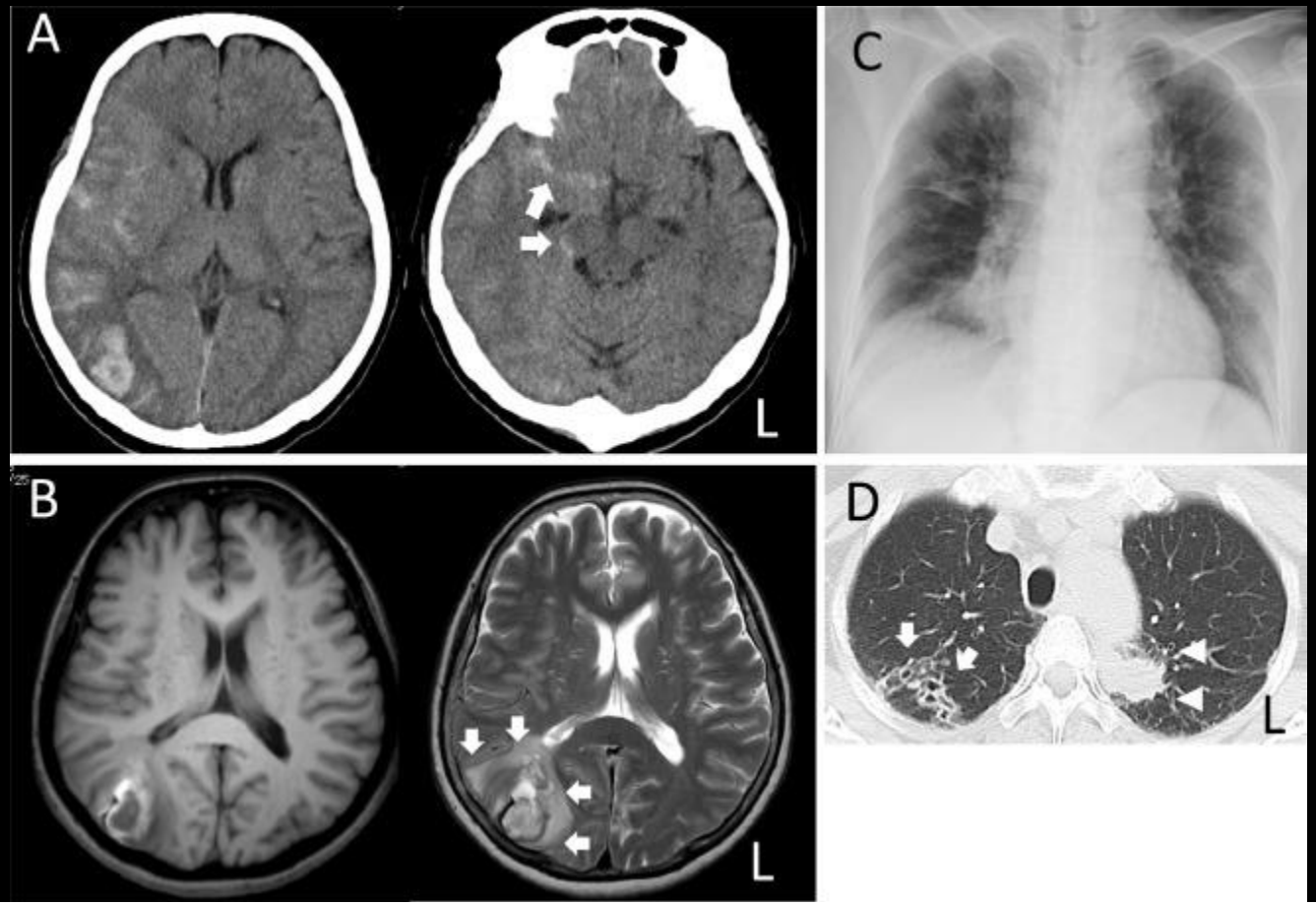


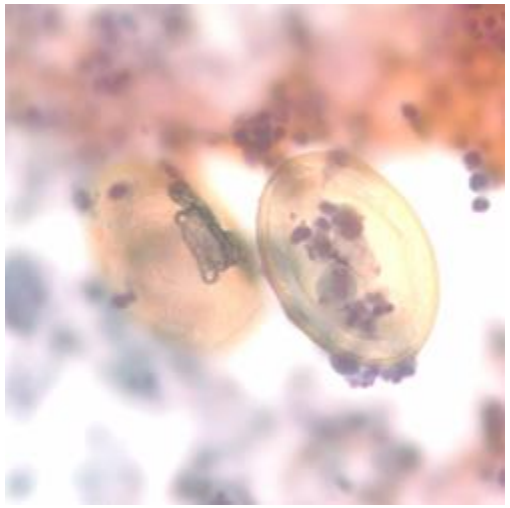
Figure 1 (A) A head CT scan revealed intracerebral and subarachnoid hemorrhage in the right temporal and occipital lobes, and subarachnoid hemorrhage was observed in the right Sylvian fissure and ambient cistern (arrow). (B) An MRI scan revealed low signal intensity with surrounding ring-shaped high signal intensity in T1WI. High signal intensity with peripheral visible circular low signal intensity was observed in T2WI. Unbalanced edema around the lesion was observed (arrow). (C) A chest X-ray film revealed multiple shadows. (D) A chest CT scan revealed conglomerated lesions in the right lung (arrow) and nodular lesions in the left lung (arrow head). CT, computed tomography.

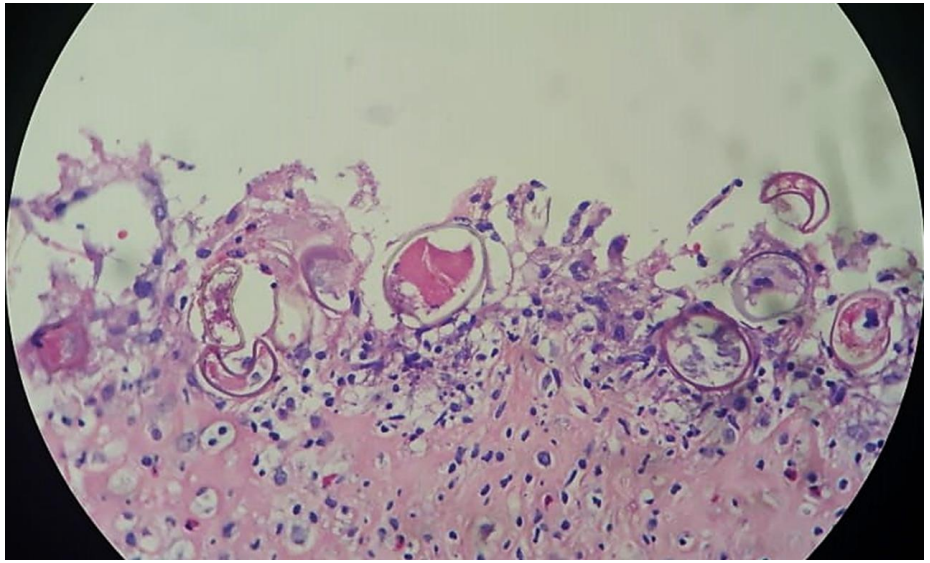
Cerebral Paragonimiasis With Hemorrhagic Stroke in a Developed Country. J Stroke CVD. 2018.

Paragonimiasis

Investigation

- **Direct examination of eggs in …**
  - **Sputum**
  - Stool (coughed-up eggs are swallowed).
- **Tissue biopsy** – looking for eggs
- **Serology**
  - Specific and sensitive antibody tests based on *P. westermani* antigens





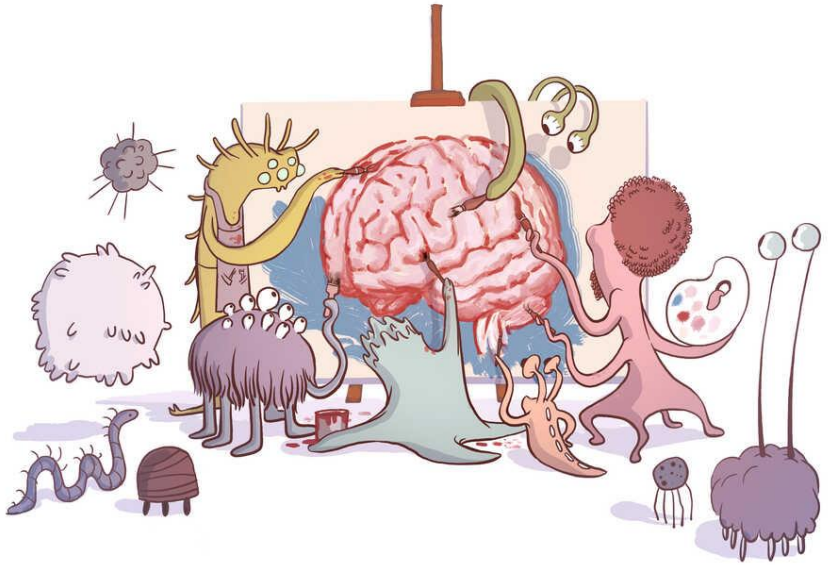
Paragonimiasis

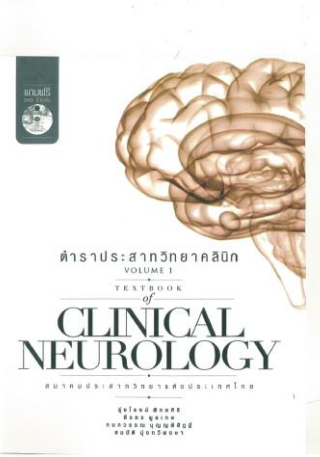
Treatment

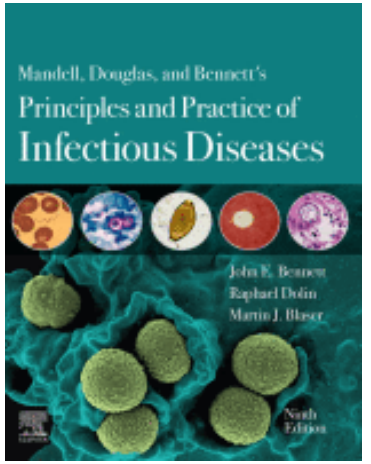
- **Praziquantel**
  - *P. westermani* 25 mg/kg three times daily for 2–3 days
    - high ELISA titer and/or multiple pulmonary lesions >> second dose is considered

Scope of talk

- Introduction to Neuroparasitology
- Nematode (Roundworm)
  - Angiostrongyliasis
  - Gnathostomiasis
  - Filariasis
- Trematode (Flatworm – Fluke)
  - Schistosomiasis
  - Paragonimiasis
- Cestode (Flatworm – Tapeworm)
  - Neurocysticercosis
- Protozoa
  - Cerebral Toxoplasmosis
  - Cerebral Malaria
  - Cerebral Amebiasis
    - *Entamoeba histolytica*
  - Primary Amebic meningoencephalitis
    - *Naegleria fowleri*

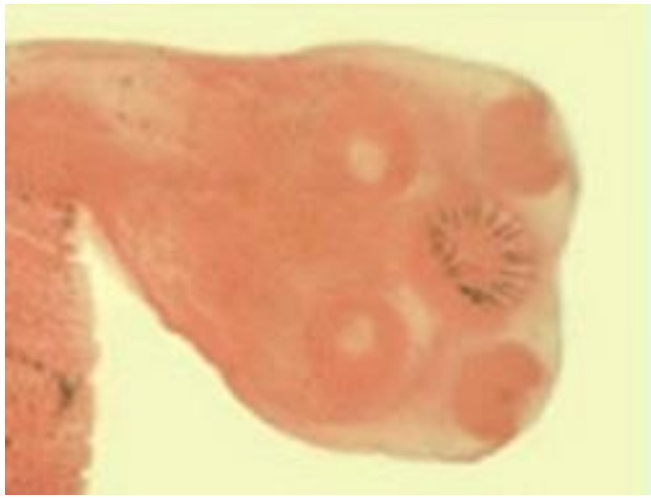


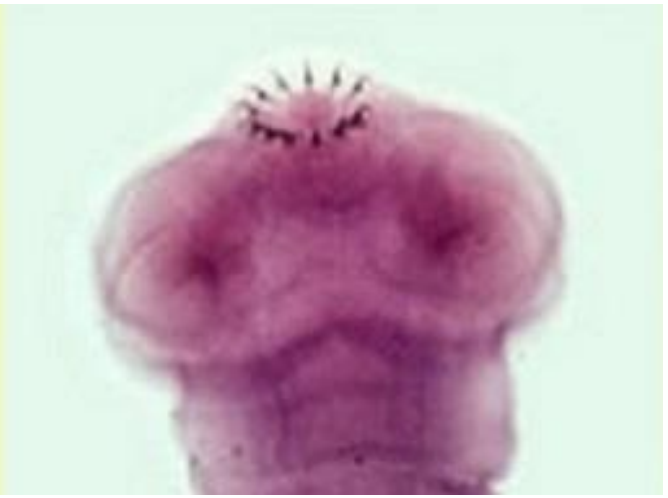


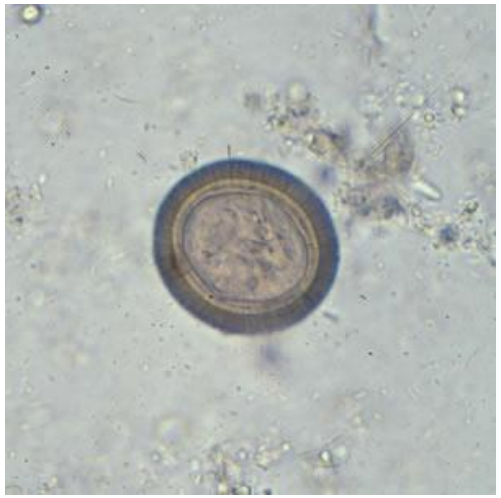


Neuroparasitology and Tropical Neurology Edited by Hector H. Garcia, Herbert B. Tanowitz, Oscar H. Del Brutto Volume 114,Pages 2-414 (2013)
Textbook of Clinical Neurology. Thai Neurological Society. 2014
Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Ninth Edition
CONTINUUM (MINNEAP MINN) 2021;27(4, NEUROINFECTIOUS DISEASE):943–962
Parasitic diseases of the central nervous system: lessons for clinicians and policy makers. EXPERT REVIEW OF NEUROTHERAPEUTICS, 2016.
Centers for Disease Control and Prevention

Neurocysticercosis (Pork tapeworm) (พยาธิตืดหมู)







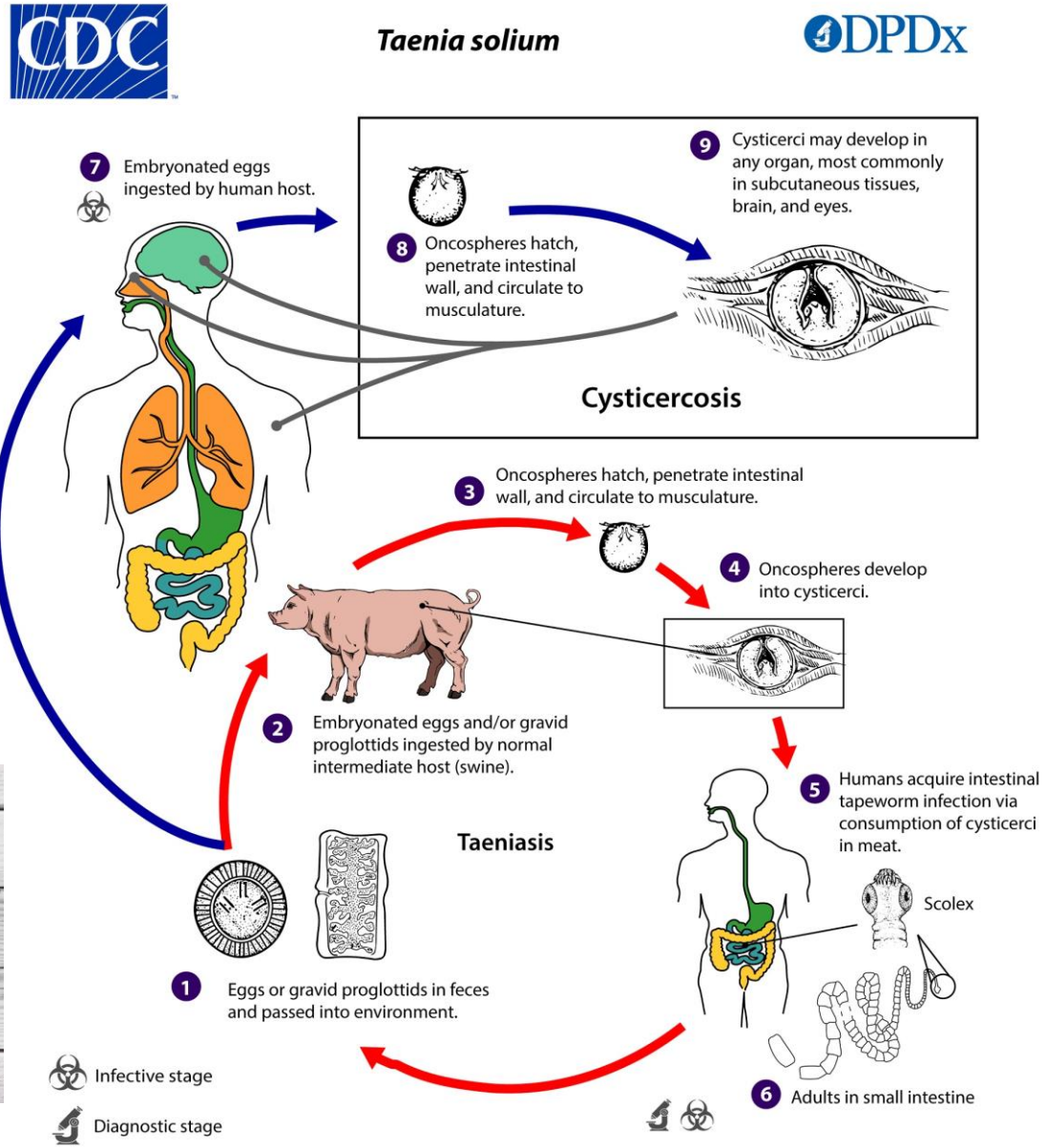
Neurocysticercosis

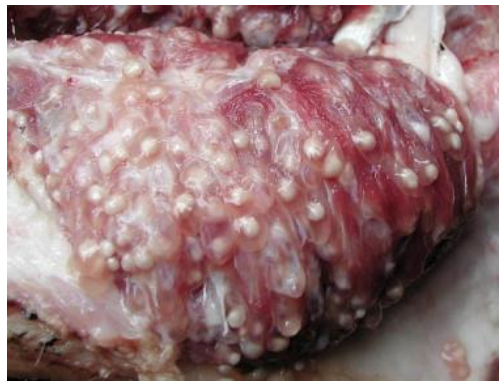
Overview

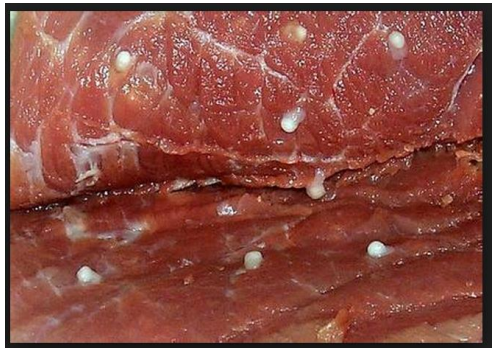
Fig. 15.9. Numerous subcutaneous nodules representing intramuscular cyst of *T. solium*.

Cysticercosis (MSK Neuro)

ผักดิบ







Taeniasis

หมูดิบ/หมูสาคู

Neurocysticercosis

Overview

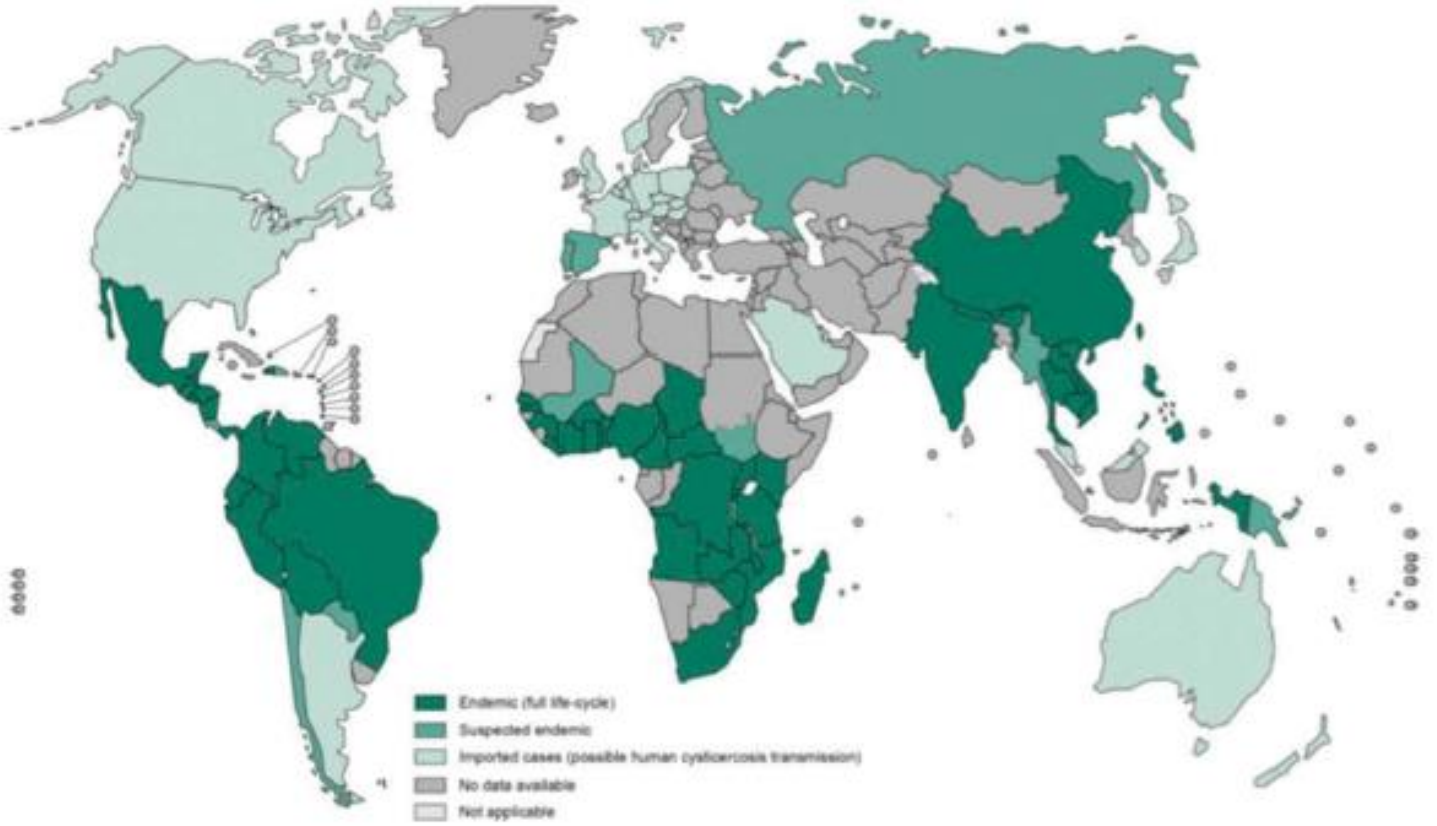


Figure 3. Countries and areas at risk for cysticercosis.
Reprinted from: World Health Organization. Assembling a Framework for Intensified Control of Taeniasis and Neurocysicercosis caused by Taenia solium, 2013. Available at: http://apps.who.int/iris/bitstream/10665/153237/1/9789241508452_eng.pdf?ua=1 [Last accessed 29 December 2015].

Neurocysticercosis

Clinical manifestation

Common clinical presentation – depends on location

- Seizure
- Eosinophilic meningitis (less frequent than nematode)
- Increased intracranial pressure

5 main forms in CNS presentation

- 1) Parenchymatous form
- 2) Meningeal form
- 3) Ventricular form
- 4) Spinal form
- 5) Mixed form

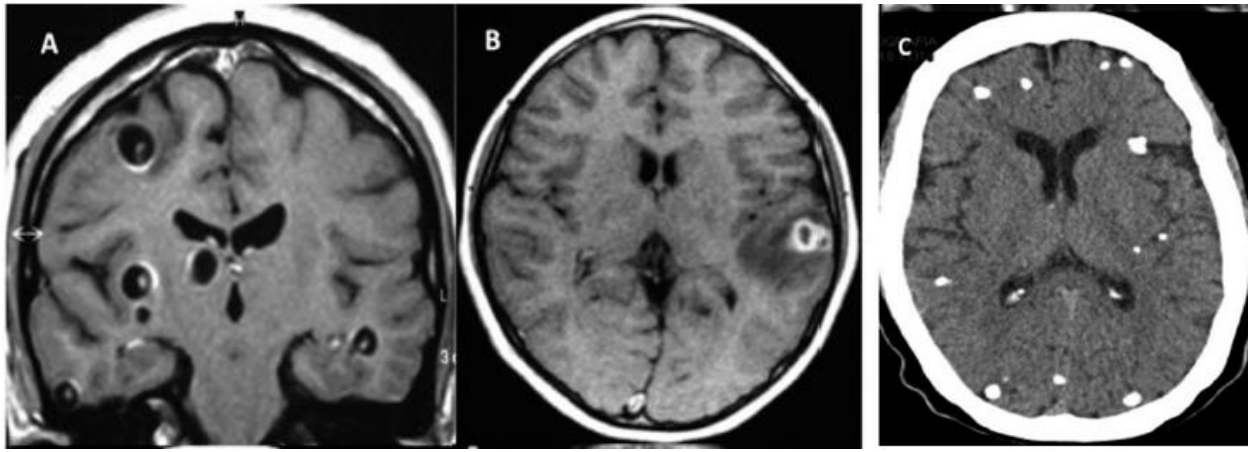
Active form	Inactive form

• **Parenchymal cyst(s)**
  • Reaction varies!
• **Arachnoiditis**
  • Chronic headache
  • Eosinophilic meningitis DDx TB
• **Vasculitis**
  • Posterior circulation – large or small vss
• **Hydrocephalus**
  • **Inflammation** >> CSF abnormal
  • **Intraventricular cyst**
• **Compressive symptoms**
  • Brain or Spinal cord
	• **Parenchymal calcification (M/C)**
	  • CT scan
	• **Hydrocephalus secondary to meningeal fibrosis**
	  • CSF profile >> normal

Neurocysticercosis

Clinical manifestation

- **1) Parenchymatous form**
  - Any area; GW > WM
  - Inflammation & edema >> Gliosis >> Calcification (years)
  - **Evolutive (involutive) stages**
    - **Vesicular stage** – a viable noninflamed cyst; could seen scolex
    - **Colloidal stage** – increased density of its fluid contents, local inflammation with edema, and contrast enhancement
    - **Granular/nodular stage –** parasite is nonviable, a small inflammatory nodule; disappeared
    - **Nodular calcified stage** – reappeared as a calcified scar (30-40%)

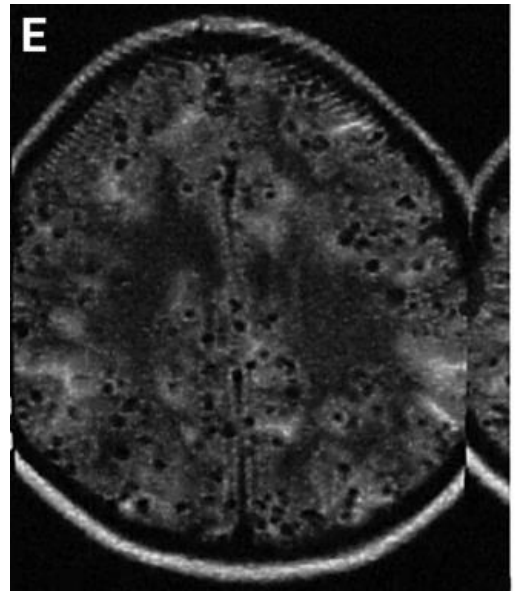


Vesicular cyst with scolex | Colloidal | Calcification

Neurocysticercosis

Clinical manifestation

- **1) Parenchymatous form**
  - Any area; GW > WM
  - Inflammation & edema >> Gliosis >> Calcification (years)
    - Active reaction varies
  - **Presentation**
    - Epilepsy/seizure – in both active & chronic form; focal or generalized
    - Headache – brain edema & increased ICP; +/- papilledema
    - Compressive symptoms – hemiparesis, ataxia, Parinaud's syndrome
    - Alteration of consciousness – encephalitic form
    - Cognitive decline

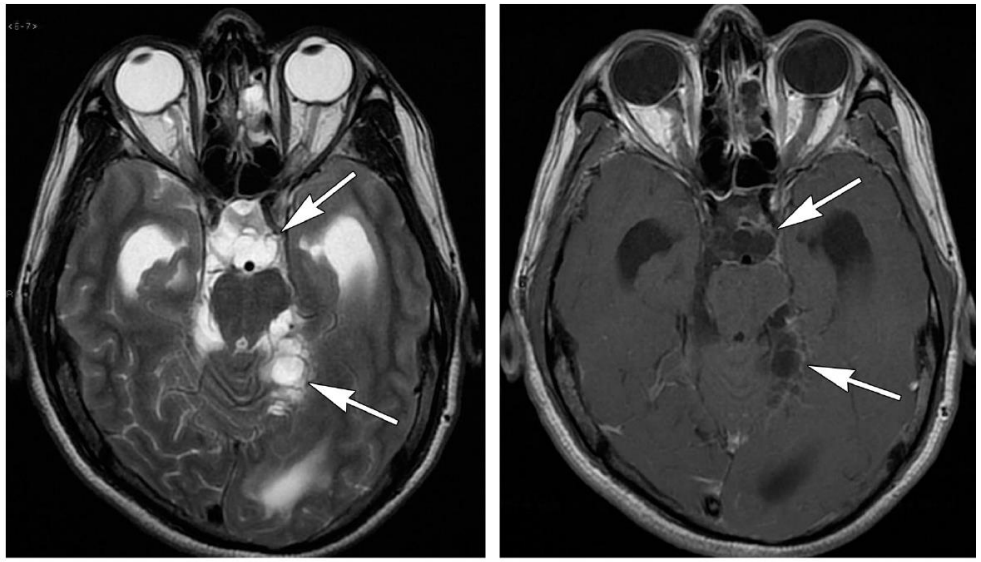


Encephalitis

Neurocysticercosis

Clinical manifestation

- **2) Meningeal form**
  - Only **leptomeningeal**
    - Commonly found at brainstem
    - Yellowish & thickening >> fibrosis
    - Sometimes obstruction of CSF >> hydrocephalus
  - Inflammation of vertebrobasilar system >> Ischemic stroke
  - **Clinical presentation**
    - Meningitis
      - CSF profile
        - Mononuclear + Eosinophil
        - Protein slightly elevation – high 100
        - Sugar normal or low
      - Headache +/- stiff neck
      - Cranial nerve palsy – Basal arachnoiditis/Fibrosis
    - Stroke syndrome



14a. 14b.

Kimura-Hayama ET, et al. Neurocysticercosis: Radiologic-Pathologic Correlation. RSNA. 2010

Neurocysticercosis

Clinical manifestation

- **2) Meningeal form**
  - **“Cysticercus racemosus”**
    - Grape-like appearance
    - Basal cistern, ventricle, subarachnoid

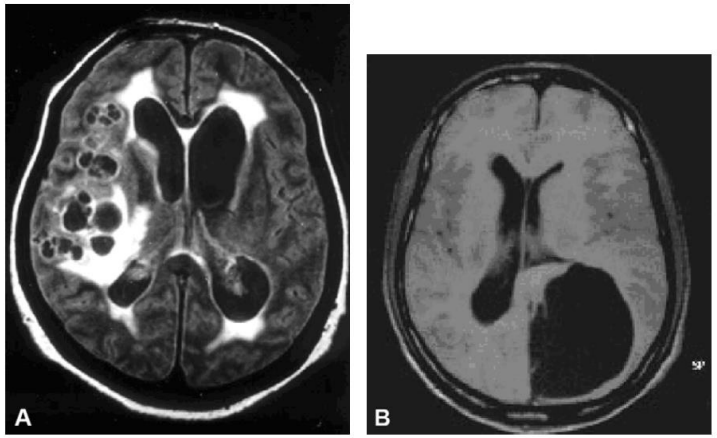
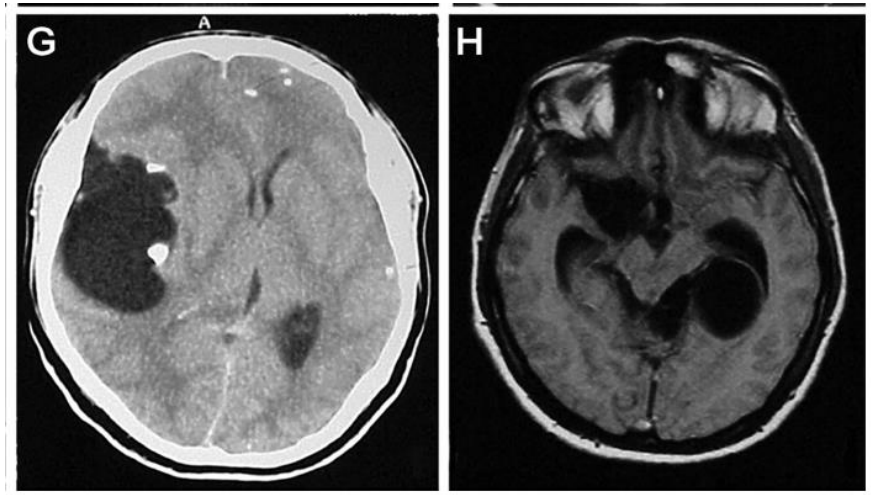


Fig. 4.25. (**A**) Axial FLAIR image at the level of the lateral ventricles shows multiple cysts in the right sylvian cistern. The cyst contents have similar intensity to that of the CSF. The ventricles are dilated. Edema appearing bright is seen in the brain parenchyma adjacent to the cysts and in the periventricular regions. (**B**) Axial T1W image at the level of the lateral ventricles shows a large racemose cyst in the left occipital region displacing the left trigone anteriorly. The content of the cyst has intensity similar to that of the CSF.



Subarachnoid neurocysticercosis

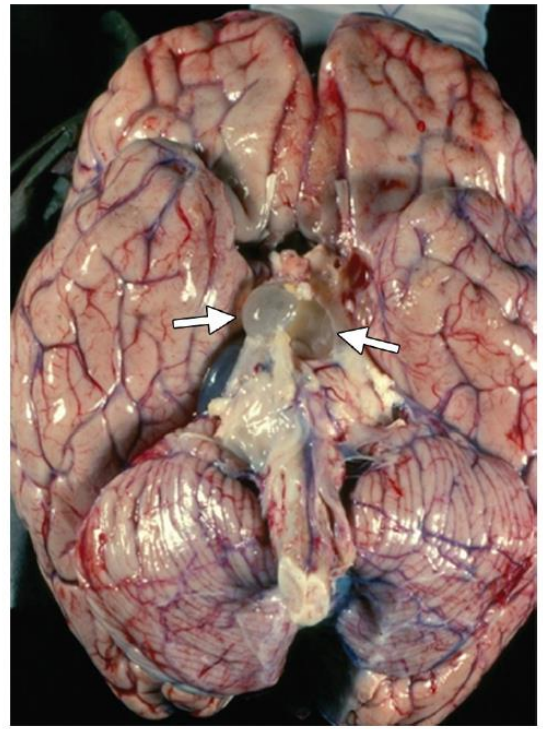


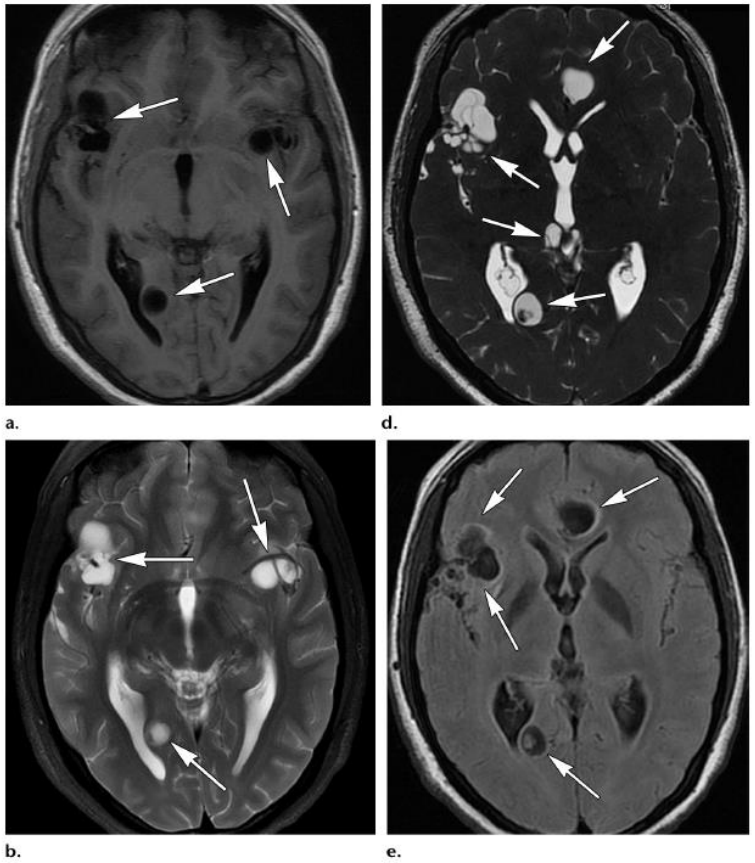
Figure 4. Photograph of a pathologic specimen shows cisternal neurocysticercosis in the prepontine cistern (arrows).

Kimura-Hayama ET, et al. Neurocysticercosis: Radiologic-Pathologic Correlation. RSNA. 2010

Neurocysticercosis

Clinical manifestation

- **2) Meningeal form**
  - **"Cysticercus racemosus"**
    - Grape-like appearance
    - Basal cistern, ventricle, subarachnoid



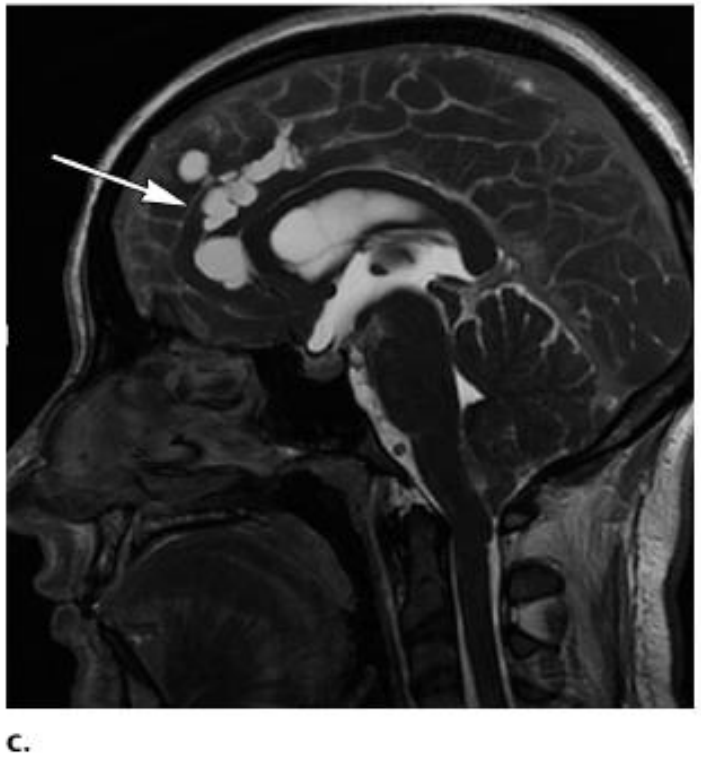


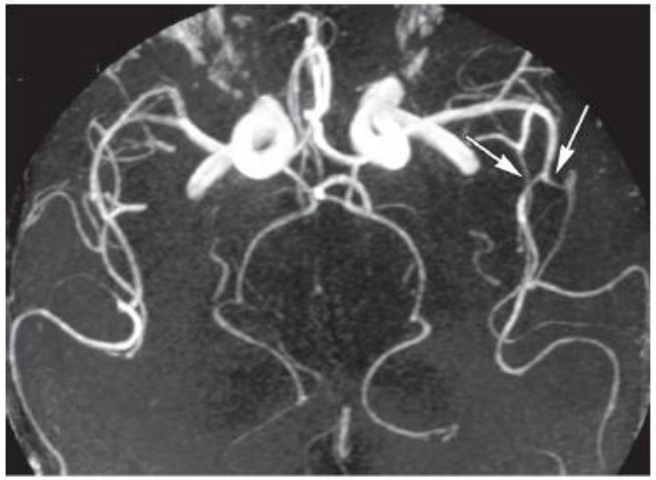
Figure 9. Subarachnoid vesicular neurocysticercosis. Axial T1-weighted (a), axial T2-weighted (b), sagittal T2-weighted (c), axial gradient-echo T2-weighted (d), and fluid-attenuated inversion recovery (e) MR images obtained in a 32-year-old woman with seizures show multiple cysts (arrows), some of which are racemose (ie, appearing like a cluster of grapes), with minimal or no edema. The cystic lesion located next to the right fusiform gyrus and occipital horn of the ventricular system could be classified as parenchymal; the remaining lesions are clearly located within the subarachnoid space.

Kimura-Hayama ET, et al. Neurocysticercosis: Radiologic-Pathologic Correlation. RSNA. 2010

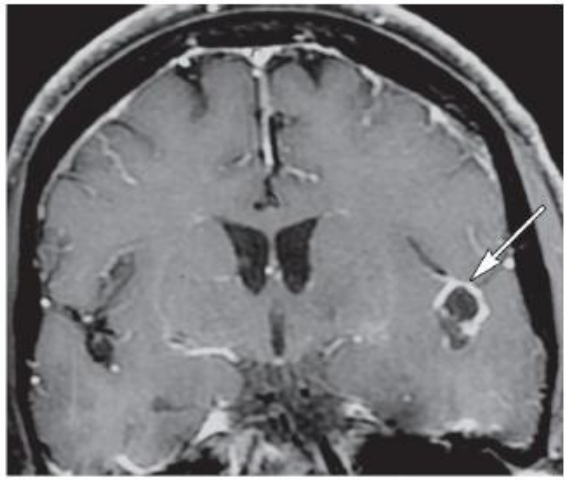
Neurocysticercosis

Clinical manifestation

- **2) Meningeal form**
  - **Vasculitis**



12a.



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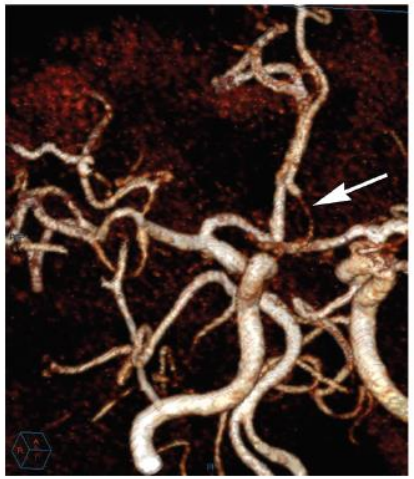

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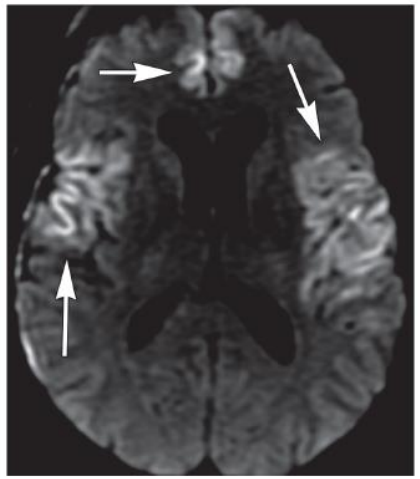
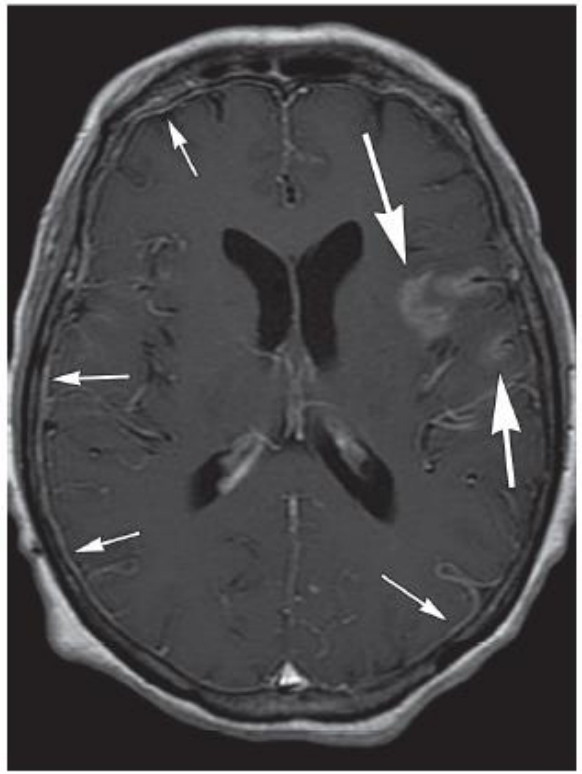


13b.



13c.

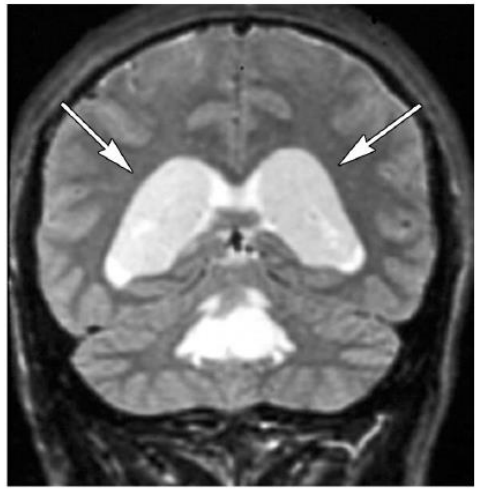
Figures 12, 13. (12) Vasculitis due to subarachnoid colloidal vesicular neurocysticercosis in a 68-year-old man with seizures. (a) Time-of-flight maximum intensity projection image shows focal zones of mild stenosis in the left middle cerebral artery (arrows). (b) Gadolinium-enhanced T1-weighted MR image shows a cystic lesion in the left sylvian fissure with peripheral enhancement (arrow), a finding associated with stenosis. (13) Vasculitis and arachnoiditis due to neurocysticercosis in a 45-year-old man with seizures and headache. (a) Time-of-flight volume-rendered MR image shows a focal zone of stenosis in the left A1 segment (arrow). (b) Diffusion-weighted MR image shows multiple areas of restricted water diffusion (arrows), findings associated with the focal zone of stenosis. (c) Gadolinium-enhanced MR image shows focal zones of enhancement in the left temporal subarachnoid space (large arrows) representing arachnoiditis, as well as diffuse abnormal pachymeningeal enhancement (small arrows). No cysts are evident.

Kimura-Hayama ET, et al. Neurocysticercosis: Radiologic-Pathologic Correlation. RSNA. 2010

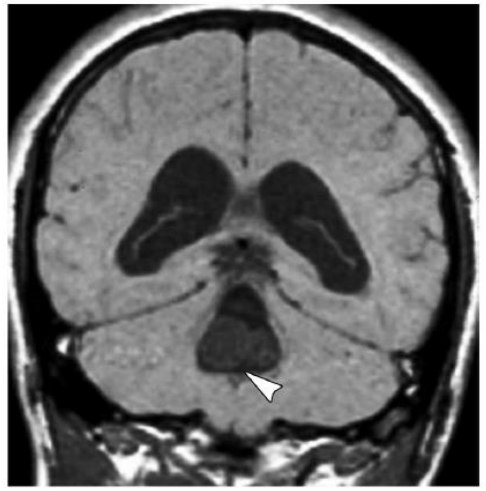
Neurocysticercosis

Clinical manifestation

- **3) Ventricular form**
  - Cyst in ventricle or attached with ependymal layer of ventricle
    - Sometimes pendulums
  - **Clinical presentation**
    - Obstructive hydrocephalus
      - Mimics NPH – chronic progressive dementia, gait, bladder
      - Papilledema
      - Could found in active or inactive form
      - Cause – cyst obstruction cyst pathway or ependymitis
    - Brun's syndrome
      - Episodic and recurrent headache, vertigo, ataxia, sometimes drop attack
      - Cyst floating in CSF and transient obstruction of CSF pathway



15a.



15b.

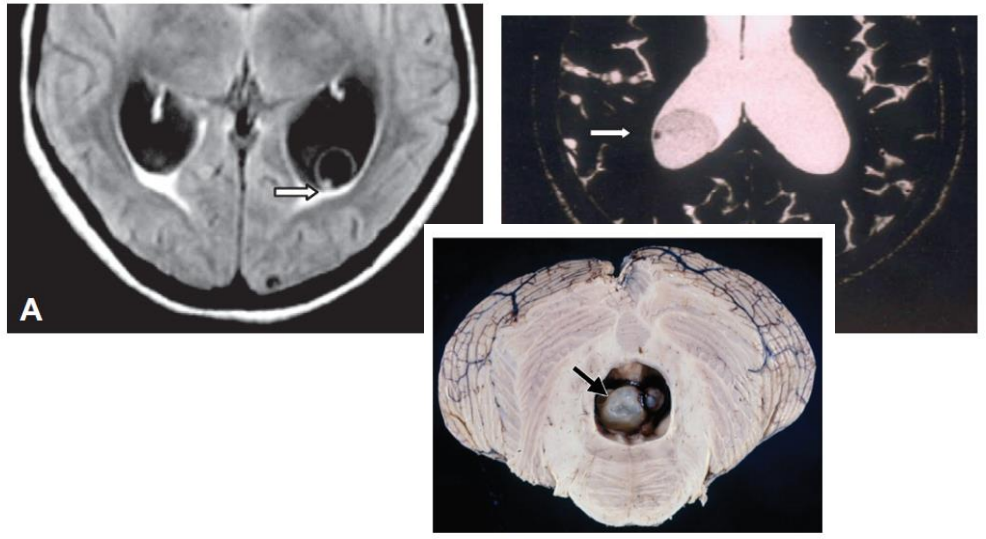


Figure 7. Photograph of a pathologic specimen shows intraventricular neurocysticercosis (arrow).

Kimura-Hayama ET, et al. Neurocysticercosis: Radiologic-Pathologic Correlation. RSNA. 2010

Neurocysticercosis

Clinical manifestation

- **4) Spinal form**
  - Rare
  - Cyst or racemose form intramedullary vs extramedullary
    - Compressive
    - Arachnoiditis
  - Clinical presentation – depends on location
    - Brown-Sequard syndrome
    - Paraparesis/Quadriparesis
    - Radicular pain
    - Cauda equina syndrome

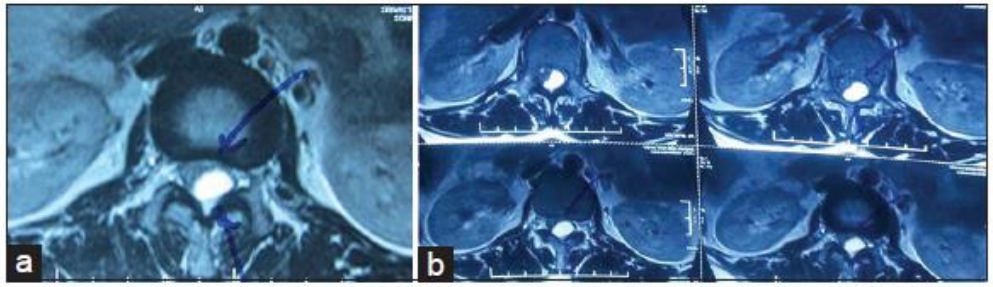
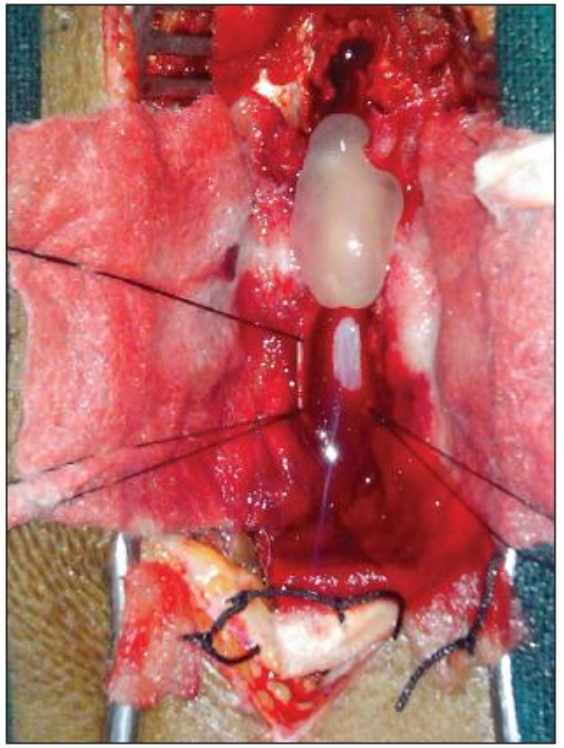


Figure 3: (a and b) Magnetic resonance imaging (sagittal and axial T2 weighted images) at the level of conus showing a thin-walled intramedullary cystic mass expanding the conus with perifocal edema. No obvious solid components identified



Microphotograph showing the intraoperative cyst

Isolated Intradural-Extramedullary Spinal Cysticercosis

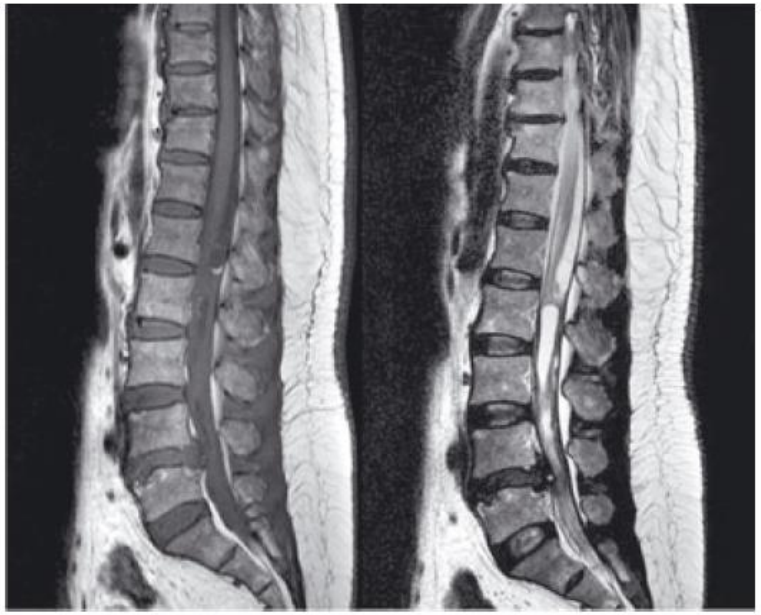


Figure 1 MRI of the lumbar spine. Left: Sagittal T1-weighted image before and after gadolinium administration disclosed the presence of two separate teardrop-shaped cystic structures beginning at level L1 and extended down to L4 with displacement of the roots peripherally. Right: Post-contrast images demonstrated there is peripherally an avid ring of enhancement along the cysts.

Journal of Travel Medicine 2011; Volume 18 (Issue 4): 284–287

Journal of Craniovertebral Junction and Spine / Oct-Dec 2016 / Volume 7 / Issue 4

Neurocysticercosis

Clinical manifestation

- **5) Mixed form**

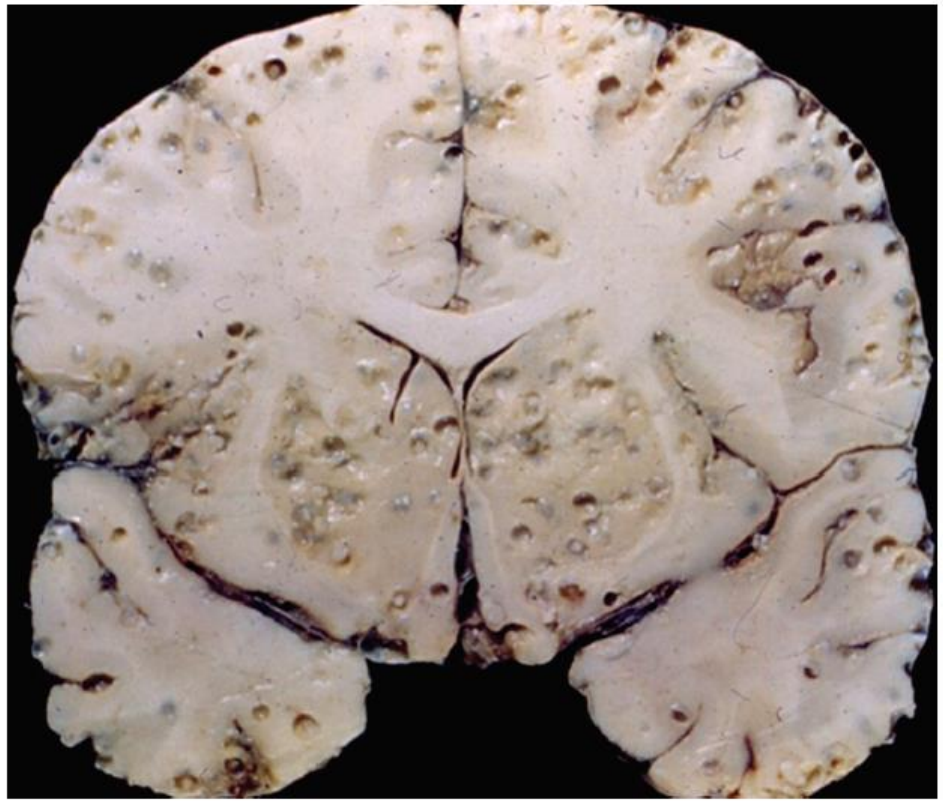
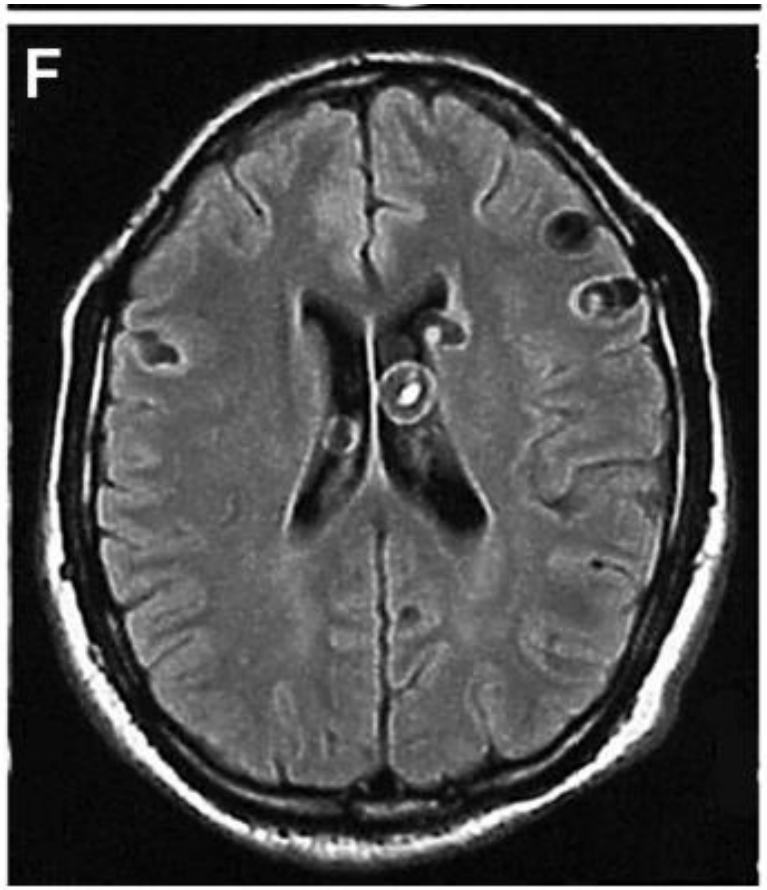


Figure 5. Photograph of a pathologic specimen shows subarachnoid-parenchymal neurocysticercosis.



Kimura-Hayama ET, et al. Neurocysticercosis: Radiologic-Pathologic Correlation. RSNA. 2010

Neurocysticercosis

Clinical manifestation

Revised Diagnostic Criteria and Degrees of Diagnostic Certainty for Neurocysticercosis[a]

Standard diagnostic criteria for neurocysticercosis were first developed in 1996 and last updated in 2017

Diagnostic criteria

- **Absolute criteria**
  - Histologic demonstration of the parasite from biopsy of a brain or spinal cord lesion
  - Visualization of subretinal cysticercus
  - Conclusive demonstration of a scolex within a cystic lesion on neuroimaging studies
- **Neuroimaging criteria**
  - Major neuroimaging criteria
    - Cystic lesions without a discernible scolex
    - Enhancing lesions[b]
    - Multilobulated cystic lesions in the subarachnoid space
    - Typical parenchymal brain calcifications[b]
  - Confirmative neuroimaging criteria
    - Resolution of cystic lesions after cysticidal drug therapy
    - Spontaneous resolution of single small enhancing lesions[c]
    - Migration of ventricular cysts documented on sequential neuroimaging studies[b]
  - 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[b]
    - Cysticercosis outside the central nervous system[b]
    - Evidence of a household contact with *Taenia solium* infection.
  - Minor clinical/exposure
    - Clinical manifestations suggestive of neurocysticercosis[b]
    - Individuals coming from or living in an area where cysticercosis is endemic[b]

Degree of diagnostic certainty

- **Definitive diagnosis**
  - One absolute criterion
  - Two major neuroimaging criteria plus any clinical/exposure criteria
  - One major and one confirmative neuroimaging criterion plus any clinical/exposure criteria
  - One major neuroimaging criterion plus two clinical/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 criterion plus any two clinical/exposure criteria
  - One minor neuroimaging criterion plus at least one major clinical/exposure criterion

[a] Reprinted with permission from Del Brutto OH, et al, J Neurol Sci.[44] © 1996 Elsevier Science B.V.

[b] Operational definitions. Cystic lesions: rounded, well-defined lesions with liquid contents of signal similar to that of CSF on CT or MRI; enhancing lesions: single or multiple, ring- or nodular-enhancing lesions of 10 mm to 20 mm in diameter, with or without surrounding edema, but not displacing midline structures; typical parenchymal brain calcifications: single or multiple, solid, and most usually <10 mm in diameter; migration of ventricular cyst: demonstration of a different location of ventricular cystic lesions on sequential CTs or MRIs; well-standardized immunodiagnostic tests: so far, antibody detection by enzyme-linked immunoelectrotransfer blot assay using lentil lectin-purified *T. solium* antigens, and detection of cysticercal antigens by monoclonal antibody-based enzyme-linked immunosorbent assay (ELISA); cysticercosis outside the central nervous system: demonstration of cysticerci from biopsy of subcutaneous nodules, x-ray films or CT showing cigar-shaped calcifications in soft tissues, or visualization of the parasite in the anterior chamber of the eye; suggestive clinical manifestations: mainly seizures (often starting in individuals aged 20 to 49 years; the diagnosis of seizures in this context is not excluded if patients are outside of the typical age range), but other manifestations include chronic headaches, focal neurologic deficits, intracranial hypertension and cognitive decline; cysticercosis-endemic area: a place where active transmission is documented.

[c] The use of corticosteroids makes this criterion invalid.

Neurocysticercosis

Investigation

- **Tissue biopsy/diagnosis**
- **Cysticercosis in other organs**
  - Skin/muscle
  - Subretinal cysticercus

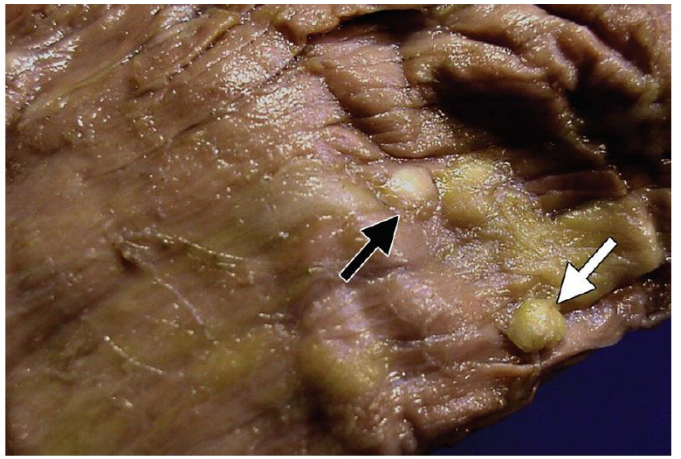
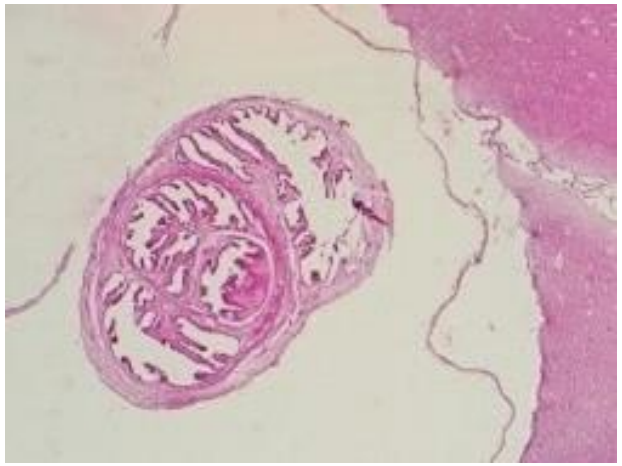
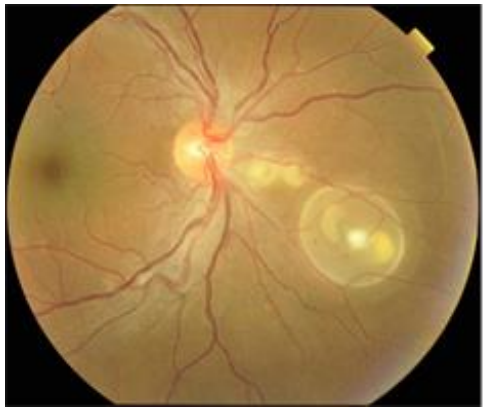
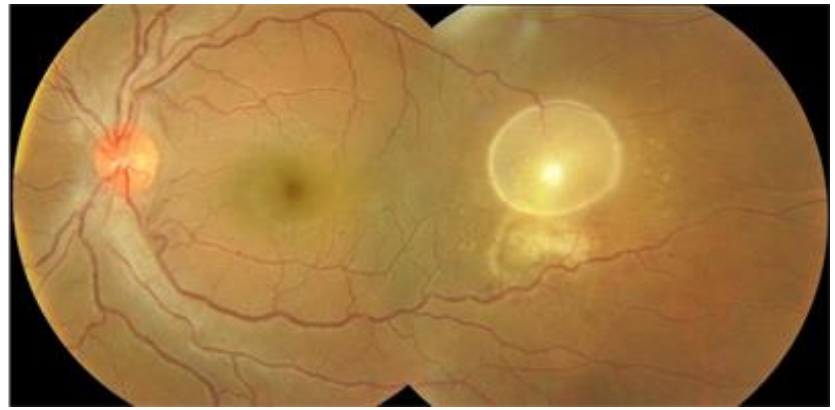


Fig. 15.9. Numerous subcutaneous nodules representing intramuscular cyst of *T. solium*.



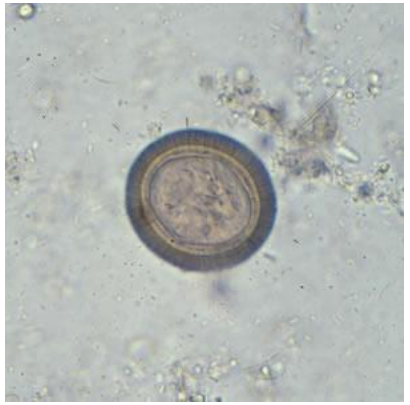




Neurocysticercosis

Investigation

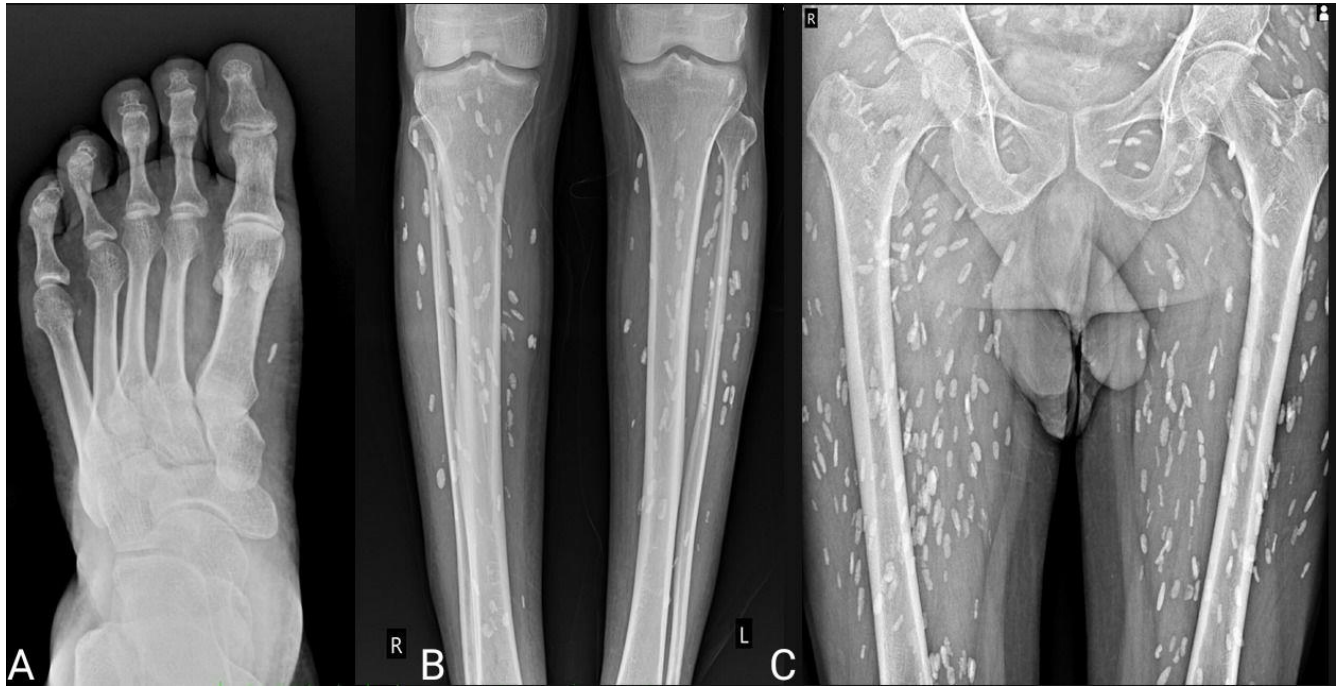
- **CBC**
  - Eosinophilia (0-37%)
- **CSF** – depend on stage (active vs inactive); cyst intraventricular
  - Increased ICP
  - Pleocytosis usually < 100 cell (sometimes > 1000)
    - Monocyte predominate
    - Eosinophils (50%)
  - Protein elevation < 100 mg/dl (rare > 300)
  - Normal sugar (low sugar ratio 25%)
  - ** DDx TB/Cryptococcal meningitis
- **Stool**
  - Usually **normal** in cysticercosis condition; Found in taeniasis



Neurocysticercosis

Investigation

- **Serology**
  - EITB (Enzyme immunotransfer blot) – serum or CSF
  - ELISA
- **Plain film**
  - Calcification of cyst intramuscular (most common at thigh)



Neurocysticercosis

Investigation

- **CT/MRI**

CT and MR Imaging Findings of Various Stages of Neurocysticercosis

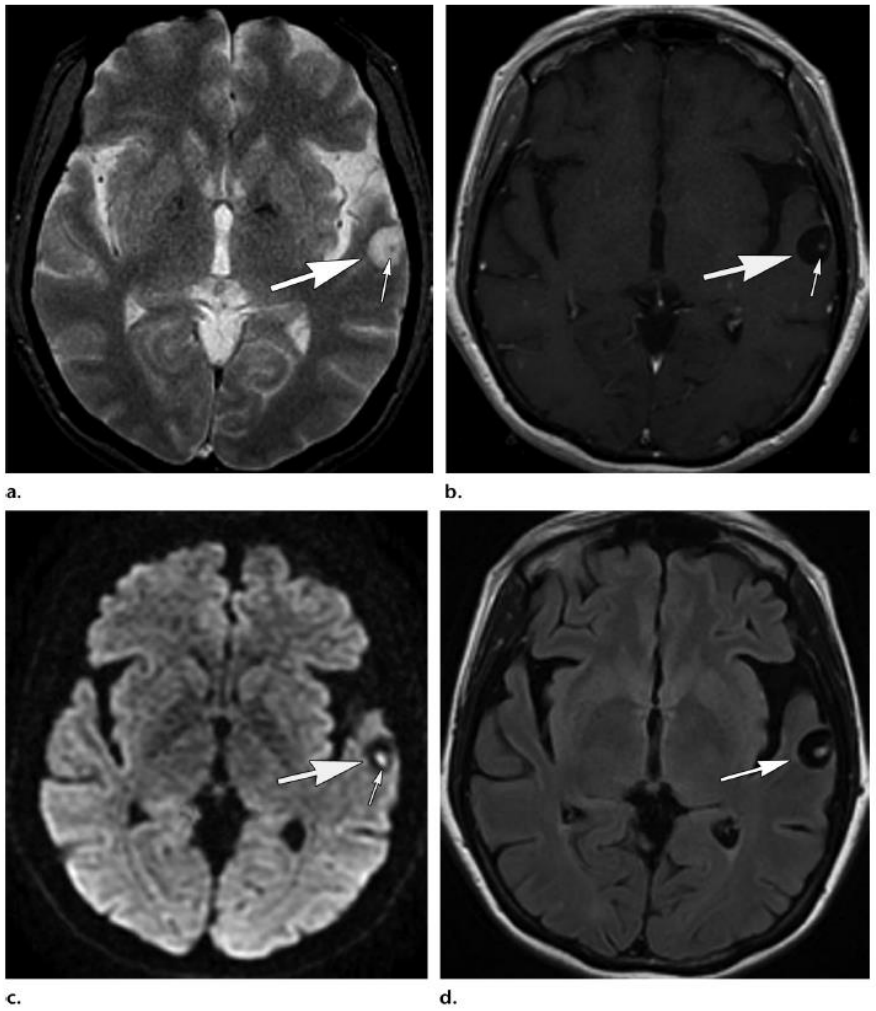
Stage	CT Findings	MR Imaging Findings
Noncystic	Often invisible	Often invisible
Vesicular*	10–20-mm cyst with fluid attenuation; cyst wall is thin and smooth; little or no pericystic edema or contrast enhancement; scolex appears as a small, round, isoattenuating structure (hole with dot appearance)	Cyst signal intensity similar to that of CSF on T1- and T2-weighted images; cyst wall is well defined and thin, with little or no enhancement on gadolinium-enhanced images; scolex (hole with dot appearance); iso- or hypointense relative to white matter on T1-weighted images; iso- to hyperintense relative to white matter on T2-weighted images; best seen on proton-density–weighted images
Colloidal vesicular†	Cyst may be hyperattenuating, pericystic enhancement on contrast-enhanced images, edema may be seen	Cyst contents hyperintense on T1- and T2-weighted images (proteinaceous fluid), cyst wall is thick and hypointense, pericystic edema (best seen on fluid-attenuated inversion recovery images), pericystic enhancement on gadolinium-enhanced images
Granular nodular	Similar to colloidal vesicular stage but with more edema, thicker ring enhancement	Similar to colloidal vesicular stage but with more edema, thicker ring enhancement
Calcified nodular	Hyperattenuating calcific nodules, no edema, no enhancement	Hypointense nodules, no edema, no enhancement

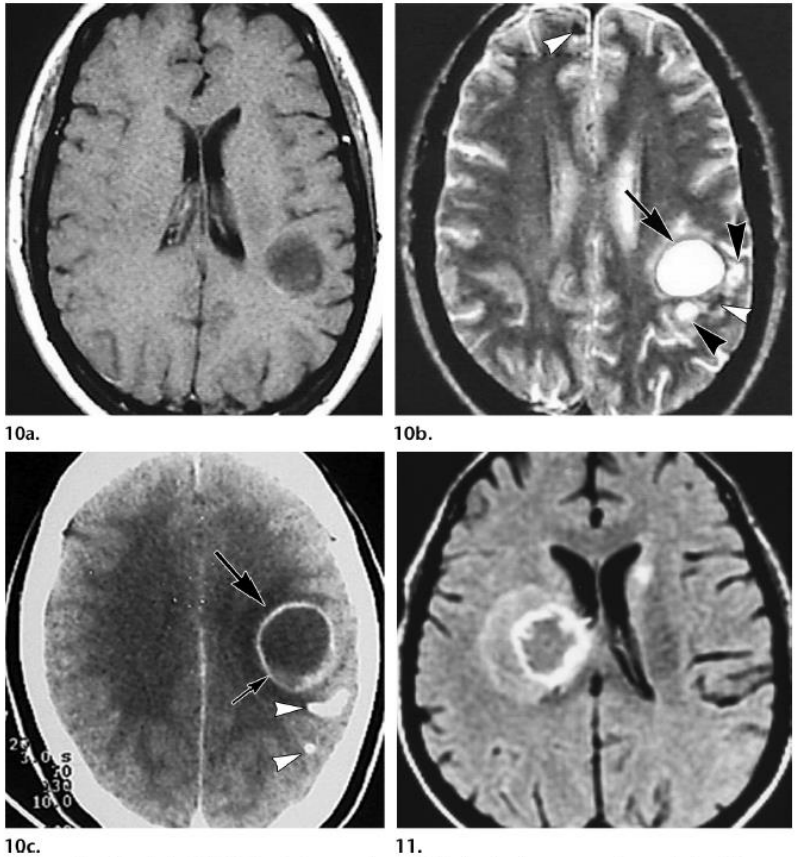
*In racemose neurocysticercosis, the scolex may not be seen.
†So-called encephalitic phase of neurocysticercosis.

Kimura-Hayama ET, et al. Neurocysticercosis: Radiologic-Pathologic Correlation. RSNA. 2010

Neurocysticercosis

Investigation





Figures 10, 11. (10) Calcified and degenerating colloidal vesicular neurocysticercosis in a 52-year-old woman with seizures. (a) T1-weighted MR image shows a cystic lesion in the left precentral gyrus. (b) T2-weighted MR image shows the lesion surrounded by edema (arrow), as well as two satellite cysts (black arrowheads). Calcified lesions are also seen (white arrowheads). (c) Contrast material–enhanced CT scan shows the lesion with marked ring enhancement (arrows). Arrowheads indicate calcified lesions. (11) Colloidal vesicular neurocysticercosis in a 35-year-old woman with seizures and headache. Gadolinium-enhanced T1-weighted MR image shows a large cystic mass with rim enhancement and peripheral edema exerting a mass effect on the right ventricle, a finding that represents colloidal vesicular neurocysticercosis. However, the differential diagnosis should include tumors and other infections such as tuberculoma or toxoplasmosis, and clinical correlation is mandatory in these cases.

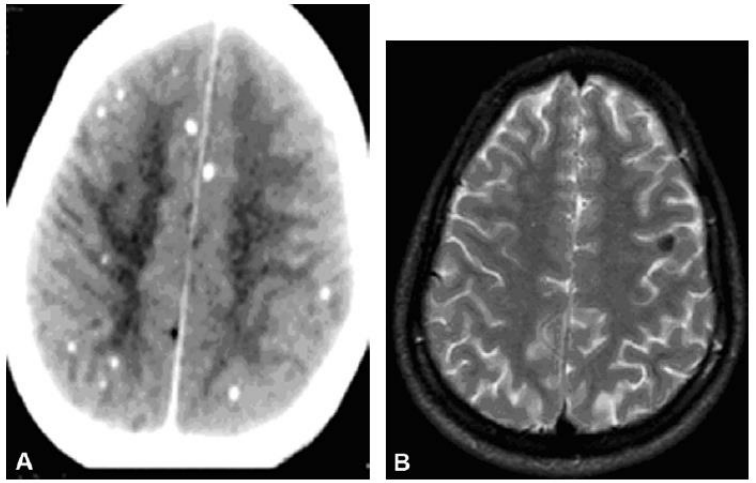
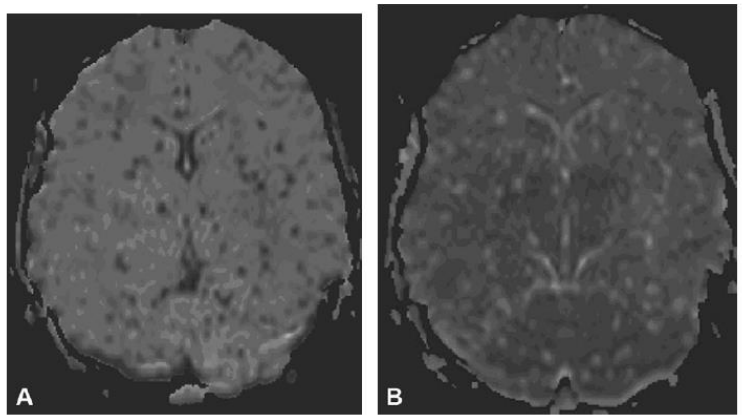


Fig. 4.22. Nonenhanced CT scan (**A**) showing multiple calcified cysticercal cysts in both the cerebral hemispheres. T2W MRI scan (**B**) shows a calcified cyst in the left frontal lobe. There is no evidence of perilesional edema.



Kimura-Hayama ET, et al. Neurocysticercosis: Radiologic-Pathologic Correlation. RSNA. 2010

Neurocysticercosis

Treatment

- **Combination of management**
  - **Antiparasitic drugs** (often with steroids) **if viable or degenerating cysts** are present.
    - may temporarily **worsen neurologic symptoms** – inflammation around a damaged cyst.
    - **Contraindication** – uncontrolled elevated ICP

    Single parenchymal cyst – choose ONE antiparasitic
    - **Albendazole** 15 mg/kg/day x 7-15 days divided in 2-3 times **(Continuum 2021)**
    - **Praziquantel** 100 mg/kg/day x 4 wks divided in 3 times (Textbook of clinical neurology TH)

    Multiple parenchymal cyst – choose combination therapy (Continuum 2021)
    - **Albendazole** 15 mg/kg/day x 7-15 days divided in 2-3 times
      - Longer duration (extended to 1 month) if large or several number of cysts

    PLUS
    - **Praziquantel** at 50 mg/kg/d for 10 days
  - **Steroid**
    - Decreasing brain edema and reducing pressure esp. high burden and high reaction

    Indication
    - Developed high ICP during antiparasitic Rx
    - Encephalitis form – priming with steroid + delayed antiparasitic drug
      - Repeat CT brain + closed monitoring

Follow-up imaging in parenchymal form

Repeat CT brain after 3 months of complete treatment >>
see stage change + confirm Dx

Neuroparasitology and Tropical Neurology Edited by Hector H. Garcia, Herbert B. Tanowitz, Oscar H. Del Brutto Volume 114,Pages 2-414 (2013)
Textbook of Clinical Neurology. Thai Neurological Society. 2014
CONTINUUM (MINNEAP MINN) 2021;27(4, NEUROINFECTIOUS DISEASE):943–962

Neurocysticercosis

Treatment

- **Combination of management**
  - **Anti-seizure drug**
    - Active form – consider during initial treatment of antiparasitic >> could cessation later
    - Calcification – Rx as epilepsy patient
  - **Elevated intracranial pressure, if present**
  - **Surgery**
    - Large parenchymal cyst >> removal
    - Ventricle and spinal cyst refractory to treatment >> removal
    - Ventricular shunt in case of hydrocephalus
- **Prognosis**
  - Active parenchymal form – usually good response to treatment
    - Observe seizure in long term due to calcification
  - High load of cyst >> poor prognosis
  - Hydrocephalus response to surgery

Neuroparasitology and Tropical Neurology Edited by Hector H. Garcia, Herbert B. Tanowitz, Oscar H. Del Brutto Volume 114,Pages 2-414 (2013)
Textbook of Clinical Neurology. Thai Neurological Society. 2014
CONTINUUM (MINNEAP MINN) 2021;27(4, NEUROINFECTIOUS DISEASE):943–962

Neurocysticercosis

Treatment

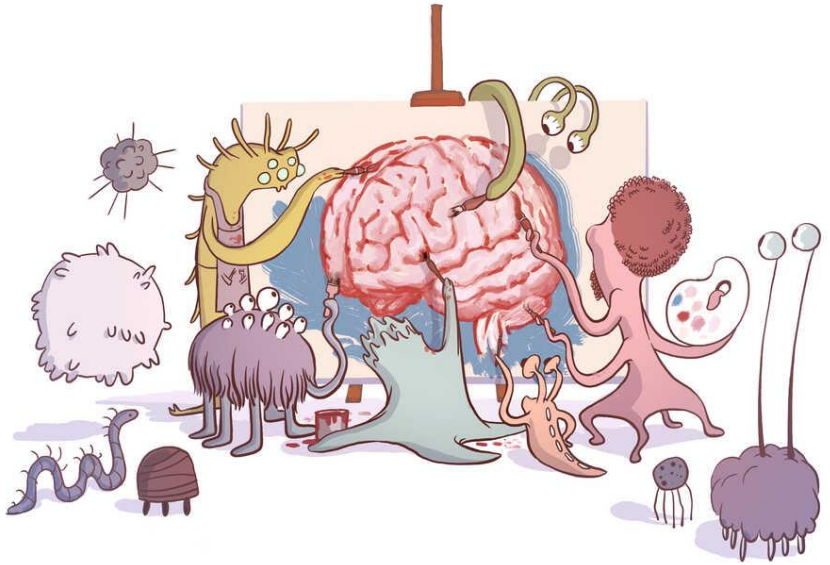
ตารางที่ 4 แสดงการรักษา neurocyticercosis

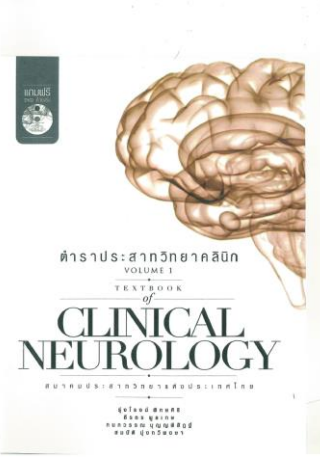
ลักษณะของโรค	การรักษา
Active disease	
Parenchymal cyst ขนาดเล็ก	ยาฆ่าพยาธิ
Parenchymal cyst ขนาดใหญ่	ยาฆ่าพยาธิ หรือ การผ่าตัดเอา cyst ออก
Meningitis/arachnoiditis without hydrocephalus	ยาฆ่าพยาธิและเฝ้าระวังการเกิด hydrocephalus
Meningitis/arachnoiditis with hydrocephalus	ยาฆ่าพยาธิร่วมกับ ventricular shunt
Intraventricular cyst	การผ่าตัดเอา cyst ออก หรือยาฆ่าพยาธิร่วมกับ ventricular shunt ถ้ามี hydrocephalus ร่วมด้วย
Spinal cord cyst	ยาฆ่าพยาธิ หรือ การผ่าตัดเอา cyst ออก
Inactive disease	
Calcified granuloma	รักษาตามอาการ เช่น ยากันชัก
Hydrocephalus without meningitis/arachnoiditis	Ventricular shunt

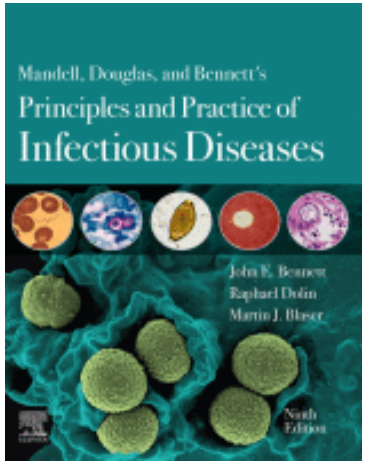
Textbook of Clinical Neurology. Thai Neurological Society. 2014

Scope of talk

- Introduction to Neuroparasitology
- Nematode (Roundworm)
  - Angiostrongyliasis
  - Gnathostomiasis
  - Filariasis
- Trematode (Flatworm – Fluke)
  - Schistosomiasis
  - Paragonimiasis
- Cestode (Flatworm – Tapeworm)
  - Neurocysticercosis
- Protozoa
  - Cerebral Toxoplasmosis
  - Cerebral Malaria
  - Cerebral Amebiasis
    - *Entamoeba histolytica*
  - Primary Amebic meningoencephalitis
    - *Naegleria fowleri*

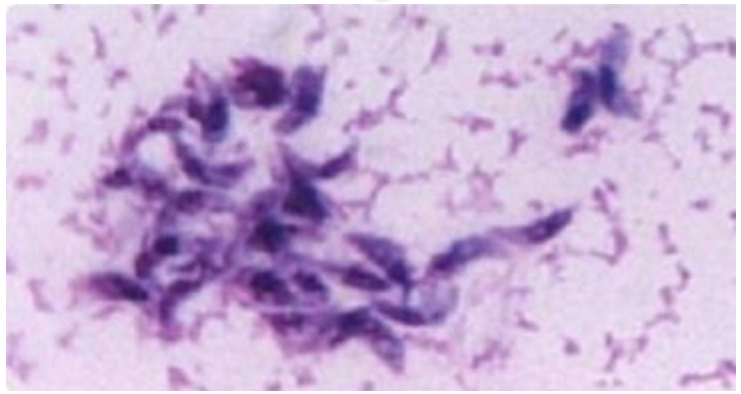




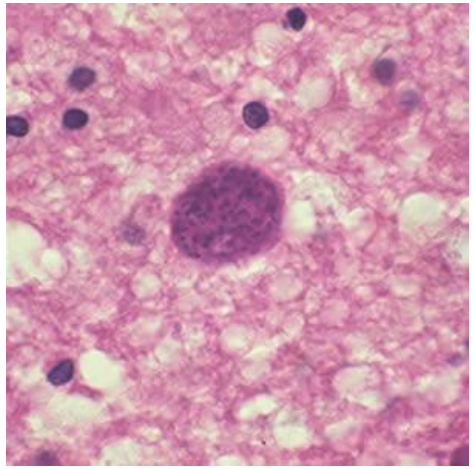


Neuroparasitology and Tropical Neurology Edited by Hector H. Garcia, Herbert B. Tanowitz, Oscar H. Del Brutto Volume 114,Pages 2-414 (2013)
Textbook of Clinical Neurology. Thai Neurological Society. 2014
Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Ninth Edition
CONTINUUM (MINNEAP MINN) 2021;27(4, NEUROINFECTIOUS DISEASE):943–962
Parasitic diseases of the central nervous system: lessons for clinicians and policy makers. EXPERT REVIEW OF NEUROTHERAPEUTICS, 2016.
Centers for Disease Control and Prevention

Cerebral toxoplasmosis (Toxoplasma gondii)

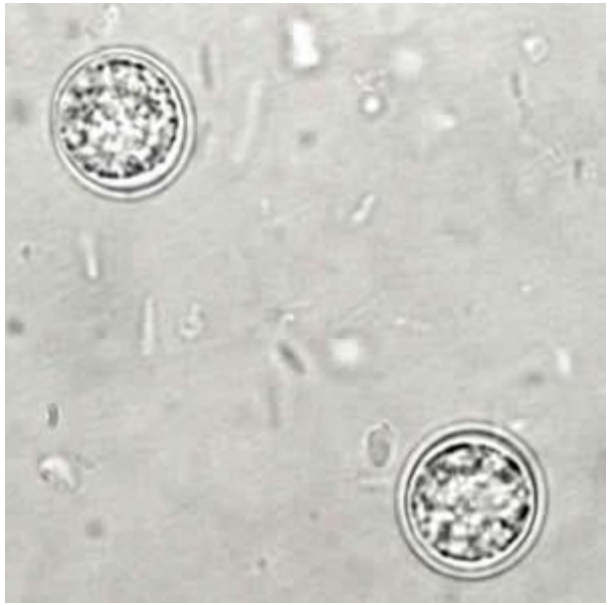


Tachyzoites



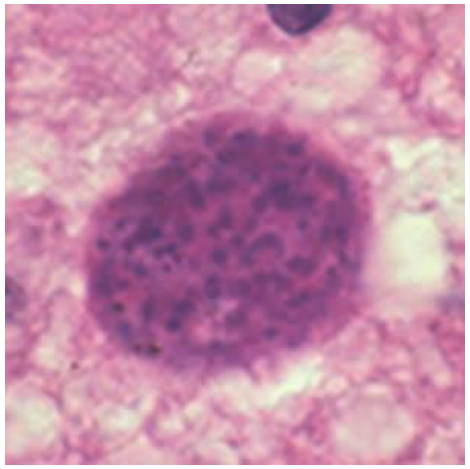
Cyst in tissue

Most common CNS OI in HIV <u>CD4 < 100</u>
Most common parasitic infection of the human CNS
1/3 are asymptomatic worldwide



Oocyst in feline feces

Cerebral toxoplasmosis



Tissue cysts

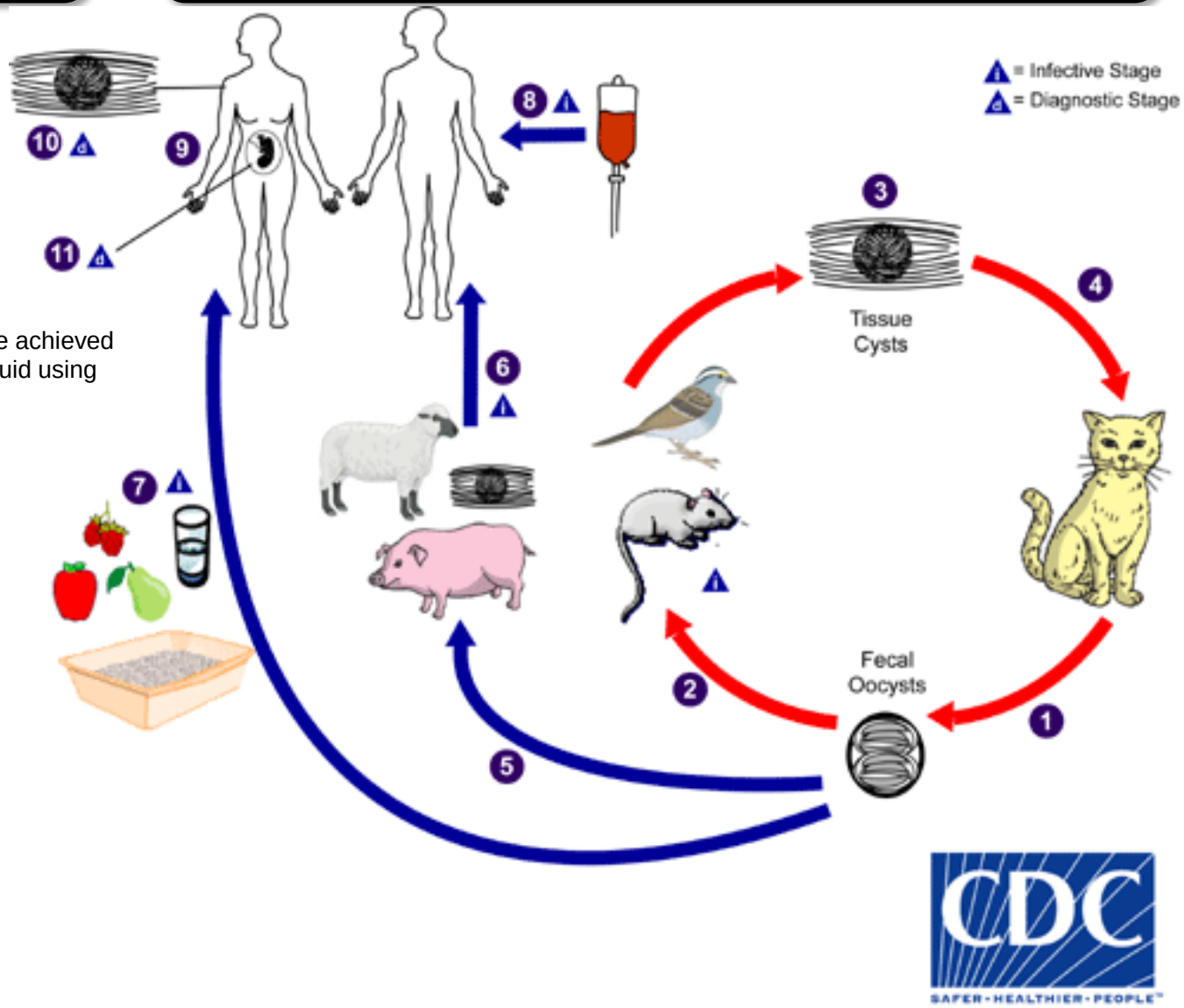
- **Brain, Eye**
- Heart, **Skeletal Muscle**
- Lung, Marrow, Liver
- Rare – spinal cord, skin

Diagnosis of congenital infections can be achieved by detecting *T. gondii* DNA in amniotic fluid using molecular methods such as PCR

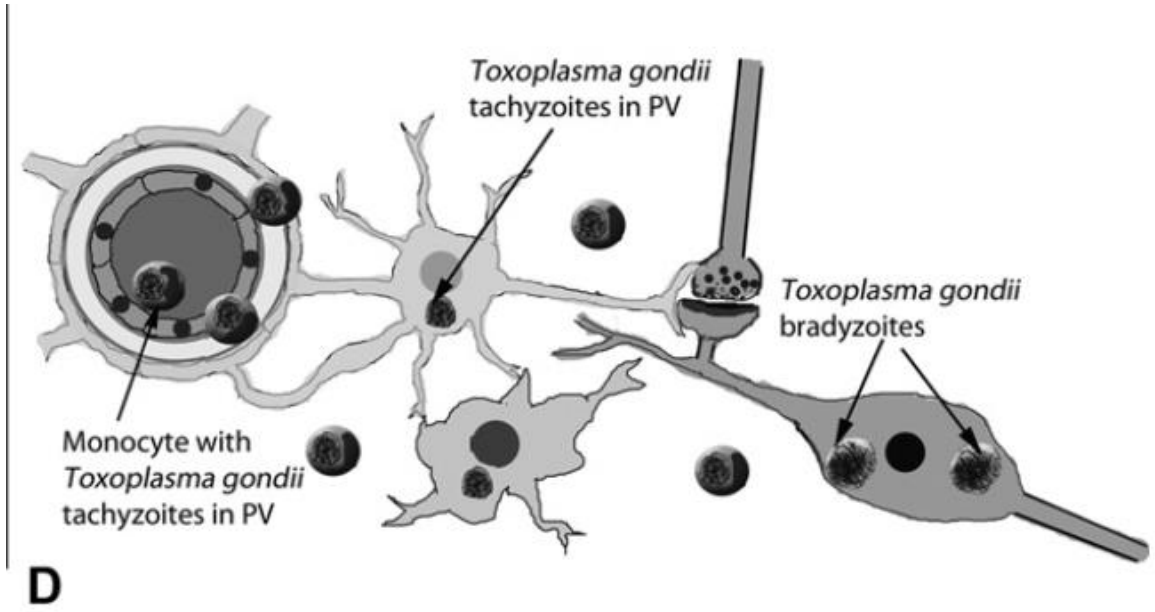
Several entry routes

- Eating undercooked meat of animals harboring tissue cysts (6)
- Consuming food or water contaminated with cat feces or by contaminated environmental samples (such as fecal-contaminated soil or changing the litter box of a pet cat) (7)
- Blood transfusion or organ transplantation (8)
- Transplacentally from mother to fetus (9)

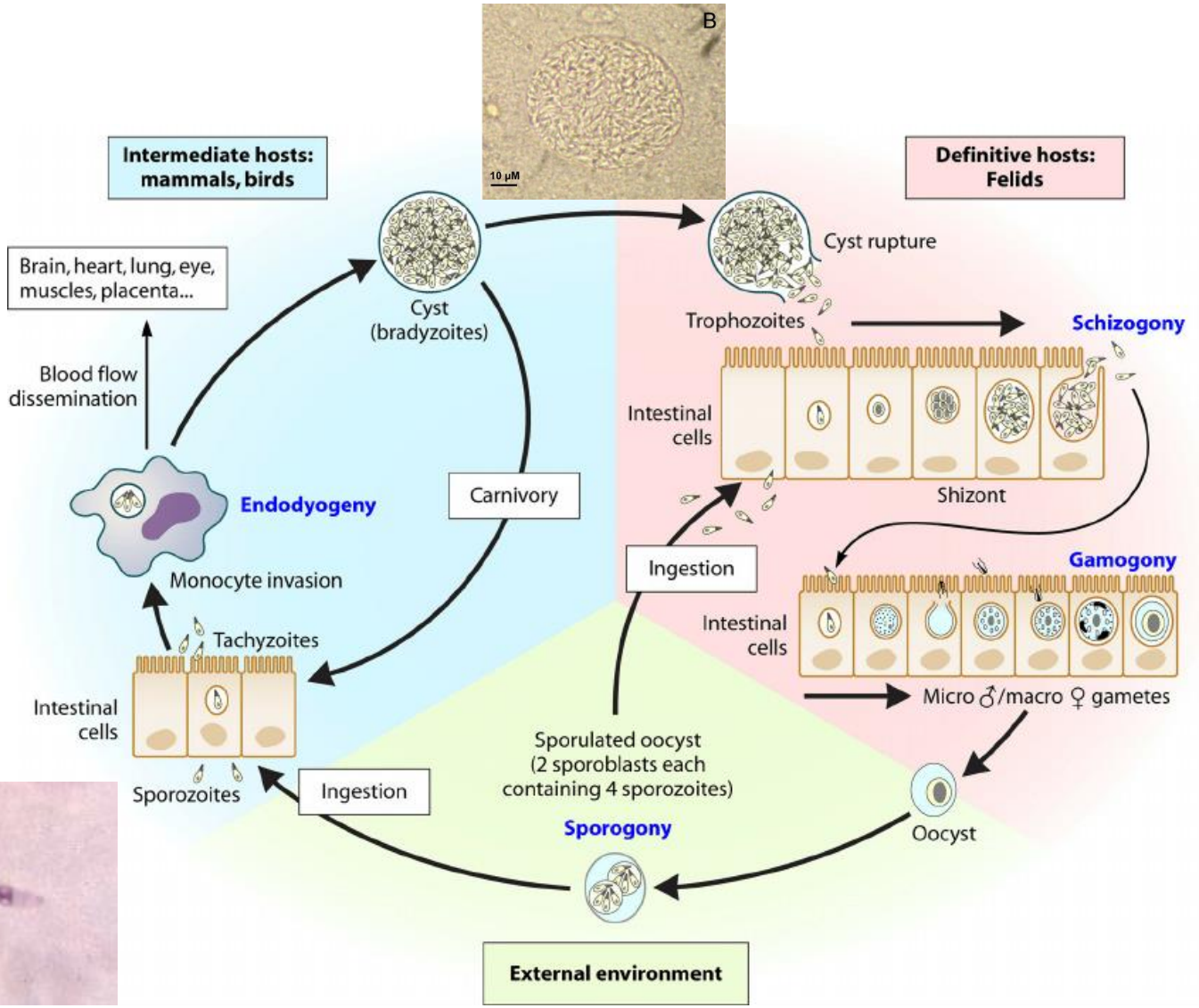
Overview

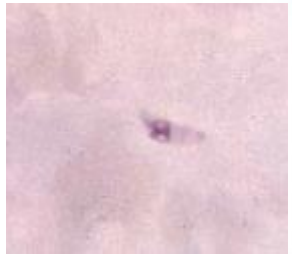


Cerebral toxoplasmosis



Overview





Epidemiology of and Diagnostic Strategies for Toxoplasmosis. Clinical Microbiology Reviews. 2012

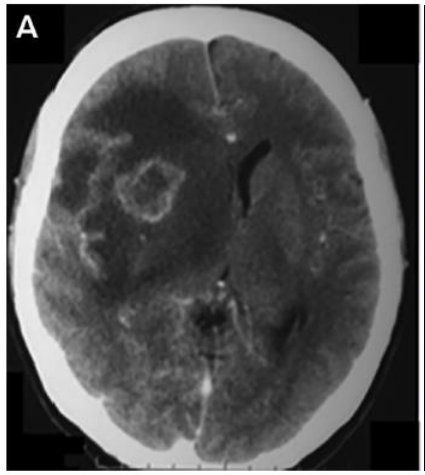
Cerebral toxoplasmosis

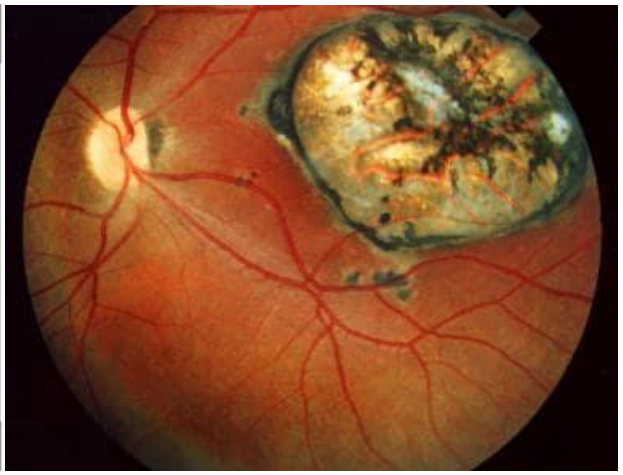
Clinical manifestation

- **Immunocompetent**
  - Asymptomatic; latent brain infection
  - Very rarely develop an acute diffuse encephalitis due to overwhelming primary infection >> undiagnosed immunodeficiency.
- **Immunocompromised esp. HIV CD4 < 100**
  - Reactivation!! >> symptomatic infection
- **Clinical manifestation**
  - Subacute onset
  - Depend on the topography and number of lesions
  - Main symptoms
    - Fever & Headache (increased ICP)
    - Seizures, focal deficits, confusion/alteration of consciousness, lethargy
    - Visual alterations related to retinal toxoplasmosis
  - Less frequent symptoms
    - Persistent cognitive impairment and movement disorders

ตารางที่ 1 ลักษณะทางคลินิกของ cerebral toxoplasmosis ในผู้ป่วยเอดส์จำนวน 166 คนที่โรงพยาบาลมหาราชนครเชียงใหม่ ระหว่างปี พศ. 2533-2537

ลักษณะทางคลินิก	ร้อยละ
ปวดศีรษะ	96
ไข้	84
คอแข็ง (stiffness of neck)	48
อัมพฤกษ์ครึ่งซีก (hemiparesis)	44.4
ระดับความรู้สึกตัว	
Drowsy	42.91
Stupor	3.85
ความผิดปกติของเส้นประสาทศีรษะ	42.31
ชัก	39

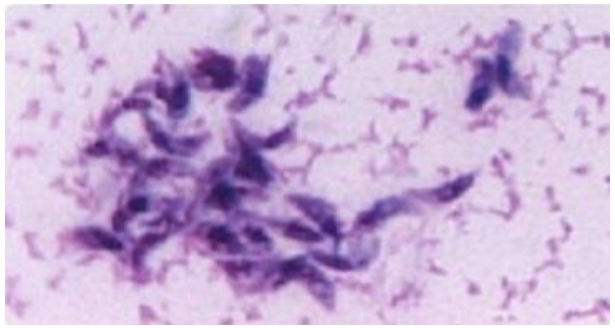


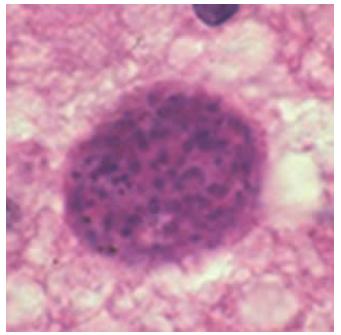


Cerebral toxoplasmosis

Investigation

- **Therapeutic diagnosis!**
  - Within 14 days of specific treatment, a good clinical and neuroimaging response is expected.
- **Biopsy (gold standard)**
  - In case of uncertain diagnosis
- **CSF (** Careful LP **)**
  - Mild pleocytosis with mononuclear
  - Mild protein elevation
  - tachyzoite from spun CSF (Giemsa stain) – hard to found
- **CSF PCR for toxoplasma gondii**
  - High specificity (96-100%) but low sensitivity (50-60%)

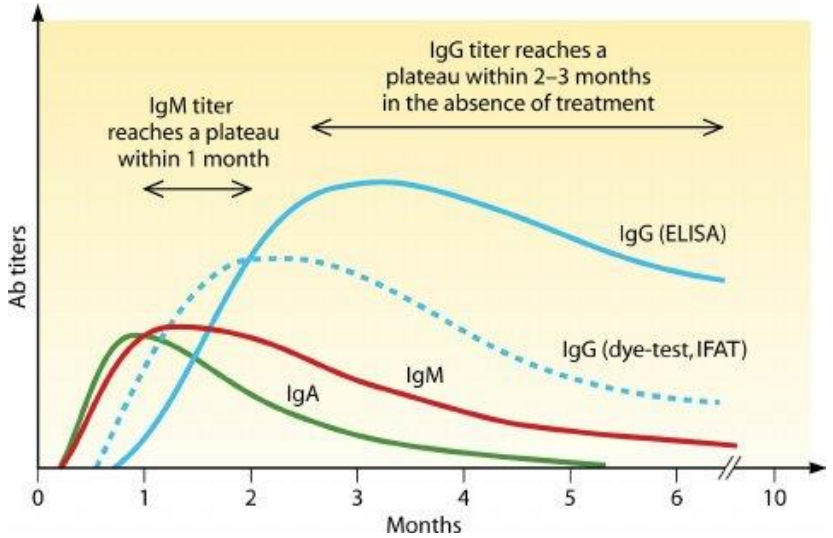




Cerebral toxoplasmosis

Investigation

- **Serology = Serum Anti-toxoplasma Ab (IgM/IgG)**
  - Acutely rising serum IgG antibodies OR a positive IgM – favor acute infection
  - **Limitation**
    - IgM serology is less specific as it may cross-react with other protozoa and may be positive in patients with autoimmune disease.
    - **In low-income countries, the majority has specific antibodies (IgG)** [high-income 10-50%]
    - **Negative serology** BUT clinical suspected >> NOT rule out toxoplasmosis
    - **Negative serology** >> NOT exclude latent infection and risk of reactivation in IRIS



Epidemiology of and Diagnostic Strategies for Toxoplasmosis. Clinical Microbiology Reviews. 2012

CONTINUUM (MINNEAP MINN) 2021;27(4, NEUROINFECTIOUS DISEASE):943–962

Textbook of Clinical Neurology. Thai Neurological Society. 2014

Cerebral toxoplasmosis

Investigation

- **Imaging – CT/MRI**
  - In AIDs patients
    - DDx CNS lymphoma, PML, TB, Cryptococcosis, bacterial abscess
    - PET & SPECT – lymphoma
  - **unifocal or multifocal**
  - Common sites – **basal ganglia**, cortical, or subcortical white matter
  - **CT**
    - hypodense **ring-enhancing** lesions with **significant perilesional edema**
  - **MRI**
    - T1-hypointense
    - T2-hyperintense lesions with ring enhancement
    - May have small hemorrhagic foci

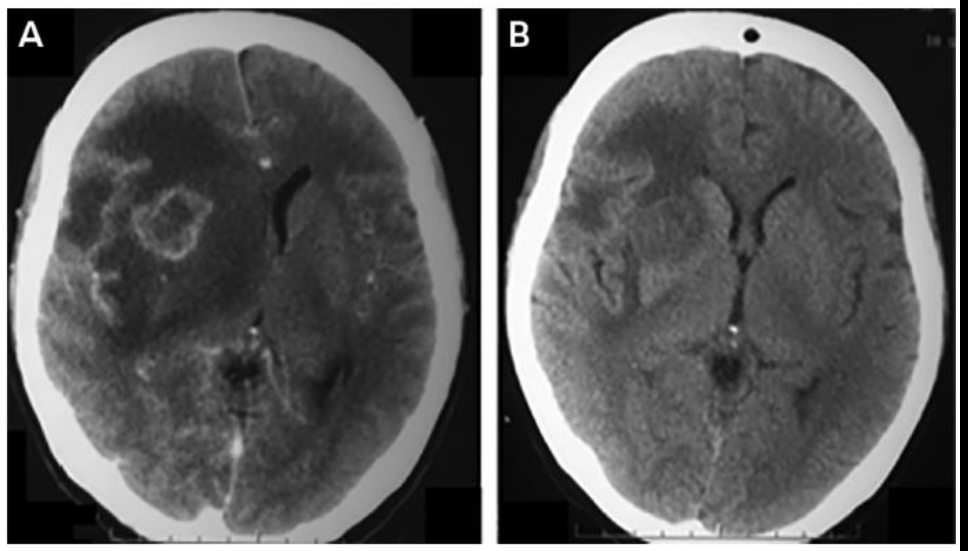


FIGURE 6-4

Imaging of the patient in CASE 6-1. Axial CT shows a large rim-enhancing lesion in the right basal ganglia associated with perilesional edema and midline shift (*A*) with marked improvement seen after 2 weeks of anti-*Toxoplasma* treatment (*B*).

Images courtesy of Jose Vidal, MD.

Cerebral toxoplasmosis

Investigation

- **Imaging – CT/MRI**

  Specific sign

  - **Eccentric target sign**
    - a ring-shaped zone of peripheral enhancement with a small eccentric nodule along the wall
    - <30% of cases
  - **Concentric target sign**
    - concentric alternating zones of hypointensity and hyperintensity seen on T2-weighted MRI
  - **Target sign (TB)**
    - central nidus of calcification or central enhancement surrounded by a ring of enhancement

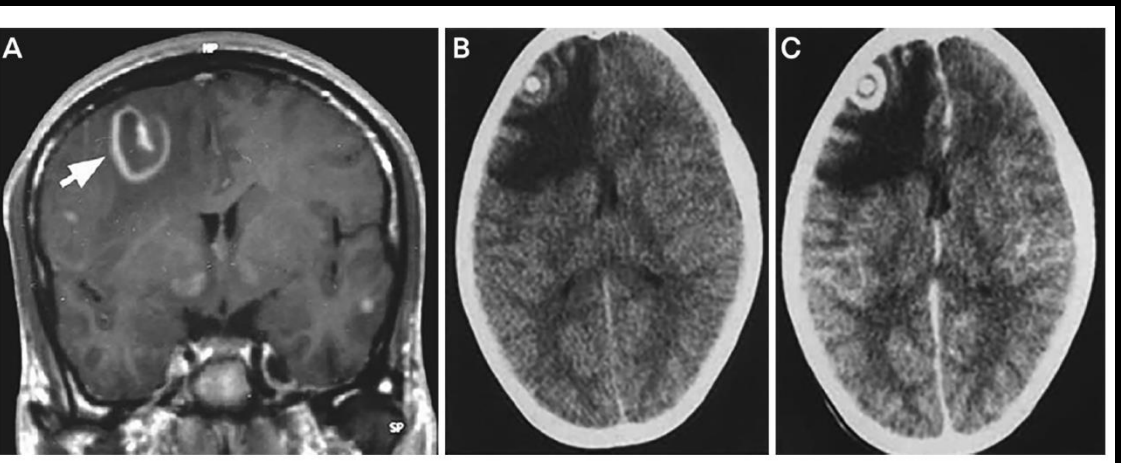
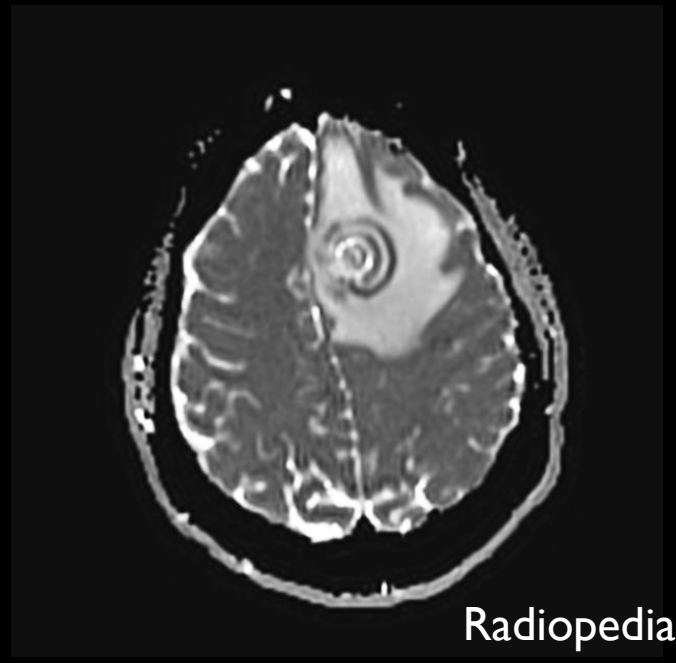
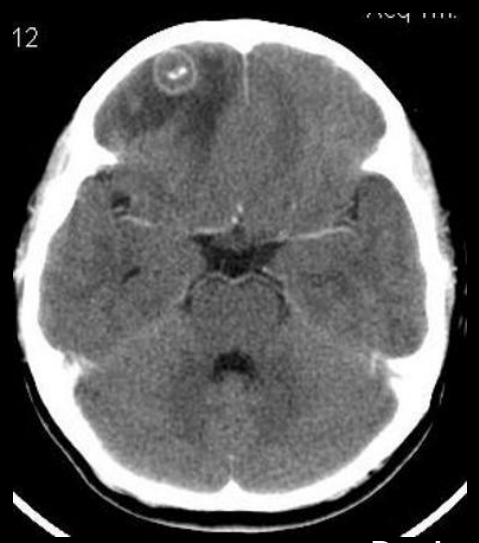


FIGURE 6-5
Eccentric target sign. The eccentric target sign (*A, arrow*) in neurotoxoplasmosis shown in coronal postcontrast T1-weighted MRI (*A*) and the target sign caused by tuberculoma shown in axial CT before (*B*) and after (C) contrast.
Panel A reprinted with permission from Kumar GG, et al, J Magn Reson Imaging.[27] © 2010 Wiley-Liss, Inc.
Panels B and C reprinted with permission from Van Dyk A, Neuroradiology.[28] © 1988 Springer Nature.





Cerebral toxoplasmosis

Treatment

- **Acute phase – at least 6 weeks**
  - **Steroid in brain edema**
    - **Dexamethasone 4 mg IV q 6 h (or oral) then tapering**

Any of both main regimens
Generally good response clinical and radiologic improvement in 80% to 90%

Pyrimethamine-based treatment

- **Pyrimethamine** 100-200 mg single dose then 50-100 mg/day
- **Sulfadiazine** 1-2 g q 6 h
  - Alternative drug (if sulfa allergy) – any one of the followings
    - Clindamycin 300-450 mg po q 6 h OR 600-1200 mg IV q 6 h
    - Atovaquone 750 mg 4 times/day
    - Azithromycin 1200-1500 mg/day oral
    - Clarithromycin 1 g bid oral
- **Folinic acid** 10 mg/day

Trimethoprim-sulfamethoxazole regimen

- **TMP** 10 mg/kg/day + **SMZ** 50 mg/kg/day

- lower pill burden and less-frequent dosing
- the availability of IV formulations (important for patients who are critically ill)
- the availability of multiple generic formulations with the consequent impact on cost
- increased accessibility in poor regions.
- prevents Pneumocystis jirovecii pneumonia, other bacterial infections, and malaria
- simplifies the early initiation of combination antiretroviral therapy

CONTINUUM (MINNEAP MINN) 2021;27(4, NEUROINFECTIOUS DISEASE):943–962
Textbook of Clinical Neurology. Thai Neurological Society. 2014

Cerebral toxoplasmosis

Treatment

- **Secondary prophylaxis**

Main regimen

- **Pyrimethamine** 25-50 mg/day
- **Sulfadiazine** 0.5-1 g 4 times per day
- **Folinic acid** 10-25 mg/day

Alternative regimen 1

- **Pyrimethamine** 25-50 mg/day OD dose
- **Clindamycin** 600 mg po q 8 h
- **Folinic acid** 10-25 mg/day

Alternative regimen 2

- **Atovaquone** 750 mg po q 6-12 h
- **+/- Pyrimethamine** 25-50 mg/day OD dose
- **+/- Folinic acid** 10-25 mg/day

CONTINUUM (MINNEAP MINN) 2021;27(4, NEUROINFECTIOUS DISEASE):943–962
Textbook of Clinical Neurology. Thai Neurological Society. 2014

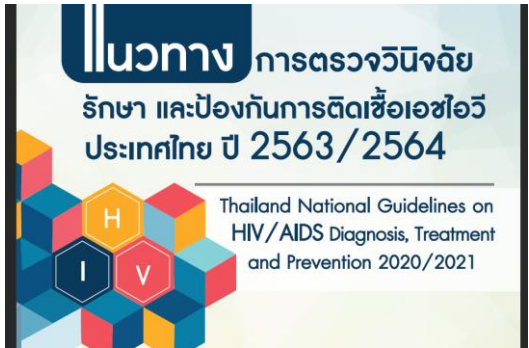
Cerebral toxoplasmosis

Treatment

ตารางที่ 5.9 ขนาดยาที่ใช้ในการป้องกัน การรักษาโรคติดเชื้อฉวยโอกาส และการป้องกันการกลับเป็นซ้ำในผู้ใหญ่ (ต่อ)

โรค	Primary prophylaxis		การรักษา		Secondary prophylaxis	
	แนะนำ	ทางเลือก	แนะนำ	ทางเลือก	แนะนำ	ทางเลือก
Toxoplasmosis	co-trimoxazole (80/400) 2 เม็ด วันละครั้ง	• co-trimoxazole (80/400) 1 เม็ด วันละครั้ง หรือ 2 เม็ด สัปดาห์ละ 3 วัน • Dapsone 50 มก./วัน ร่วมกับ pyrimethamine 50 มก./สัปดาห์ ร่วมกับ folinic acid 25 มก./สัปดาห์ • Dapsone 200 มก. ร่วมกับ pyrimethamine 75 มก./สัปดาห์ ร่วมกับ folinic acid 25 มก./สัปดาห์	• Co-trimoxazole (TMP 5-10 มก./กก./วัน หรือ SMX 25-20 มก./กก/วัน) ทางหลอดเลือดดำ หรือ กินวันละ 2 ครั้ง นาน 6 สัปดาห์ • Pyrimethamine 200 มก. 1 ครั้ง ตามด้วย 50 มก./วัน (นน. ≤ 60 กก.) หรือ 75 มก./วัน (นน. > 60 กก.) + sulfadiazine 1,000 มก. (นน. ≤ 60 กก.) หรือ 1,500 มก. (นน. > 60 กก.) วันละ 4 ครั้ง + folinic acid 10-25 มก./วัน อย่างน้อย 6 สัปดาห์	• Pyrimethamine ตามขนาดในยาหลัก + clindamycin 600 มก. ทุก 6 ชั่วโมง • Pyrimethamine ตามขนาดในยาหลัก + azithromycin 1,000-1,250 มก./วัน • Atovaquone 1,500 มก. กินวันละ 2 ครั้ง	Pyrimethamine 25-50 มก./วัน + sulfadiazine 500-1,000 มก. วันละ 4 ครั้ง + folinic acid 10-25 มก./วัน	• Pyrimethamine 25-50 มก./วัน + clindamycin 600 มก. ทุก 8 ชม. + folinic acid 10-25 มก./วัน • Co-trimoxazole SS 2 เม็ด วันละครั้ง

HIV positive + CD4 < 100 + Ab to Toxoplasma +ve



Cerebral toxoplasmosis

ตารางที่ 5.10 สรุปเกณฑ์ CD4 ในการหยุด primary และ secondary prophylaxis ของโรคติดเชื้อฉวยโอกาสในผู้ใหญ่

Opportunistic infections	Primary prophylaxis	Secondary prophylaxis
PCP	• CD4 > 200 cells/mm^3 นานกว่า 3 เดือน • CD4 100-200 cells/mm^3 แต่มี VL undetectable นานกว่า 3-6 เดือน	• CD4 > 200 cells/mm^3 นานกว่า 3 เดือน • CD4 100-200 cells/ mm^3 แต่มี VL undetectable วัดไม่ได้นานกว่า 3-6 เดือน
Cryptococcosis	หยุดยาได้เมื่อเริ่มรักษาด้วยยาต้านเอชไอวี	• ได้รับ secondary prophylaxis อย่างน้อย 1 ปี และ CD4 ≥ 100 cells/mm^3 นานกว่า 3 เดือน และ VL undetectable
Candidiasis	-	ได้รับยาต้านเอชไอวีจนมีจำนวน CD4 > 200 cells/mm^3
Toxoplasmosis	• CD4 > 200 cells/mm^3 นานกว่า 3 เดือน • CD4 100-200 cells/mm^3 แต่มี VL undetectable นานอย่างน้อย 3-6 เดือน	CD4 > 200 cells/mm^3 นานกว่า 6 เดือน
Talaromycosis/ Histoplasmosis	หยุดยาได้เมื่อเริ่มรักษาด้วยยาต้านเอชไอวี	• CD4 > 100 cells/mm^3 (สำหรับ talaromycosis) และ > 150 cells/mm^3 (สำหรับ histoplasmosis) นานกว่า 6 เดือน • HIV VL undectable นานกว่า 6 เดือน

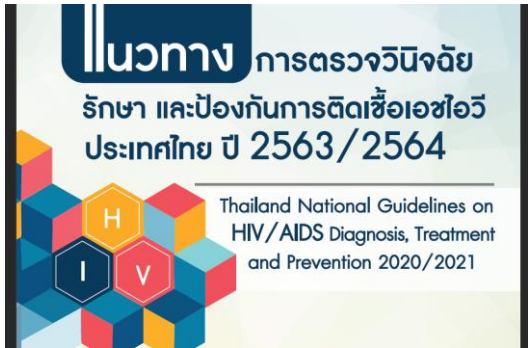
Treatment

โรคติดเชื้อฉวยโอกาส

- เริ่มยาต้านเอชไอวีในผู้ป่วยที่มีโรคติดเชื้อฉวยโอกาสทุกรายเมื่อผู้ป่วยพร้อมและสามารถทนต่อยาที่รักษาโรคติดเชื้อฉวยโอกาส

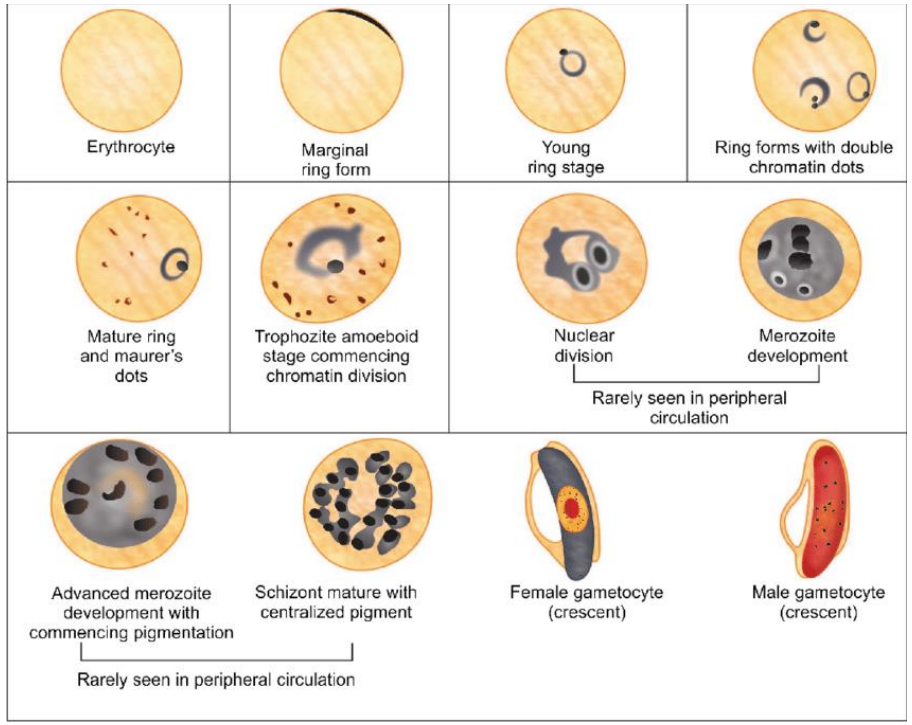
ตารางที่ 2.7 ระยะเวลาเริ่มยาต้านเอชไอวีภายหลังรักษาโรคติดเชื้อฉวยโอกาส

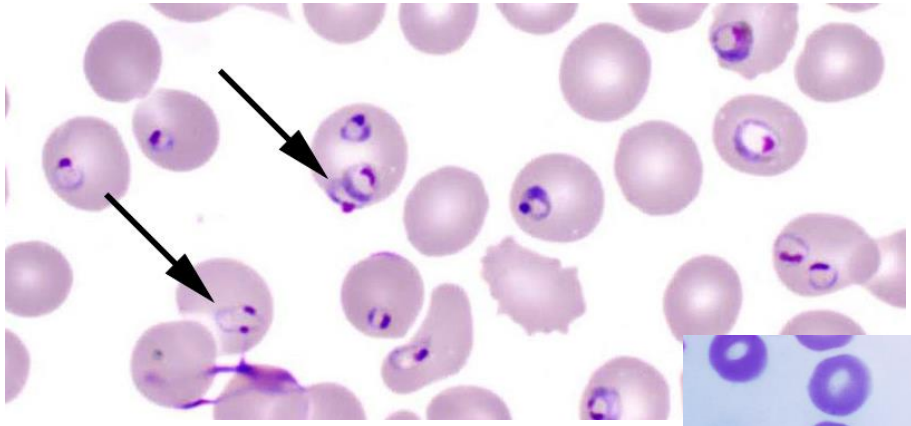
	ระยะเวลาเริ่มยาต้านเอชไอวี	
วัณโรค	< 50 cells/mm^3	เริ่มภายใน 2 สัปดาห์ อย่างช้าไม่เกิน 4 สัปดาห์
	≥ 50 cells/mm^3	เริ่มภายใน 8 สัปดาห์
	วัณโรคในระบบประสาท	เริ่มยาต้านเอชไอวีหลังรักษาวัณโรคแล้วอย่างน้อย 2 สัปดาห์ อย่างช้าไม่เกิน 8 สัปดาห์
Cryptococcal meningitis		ระหว่าง 4-6 สัปดาห์
Non-CNS Cryptococcosis		ระหว่าง 2-4 สัปดาห์
Cerebral toxoplasmosis		ระหว่าง 2-4 สัปดาห์
โรคติดเชื้อ cytomegalovirus		ชะลอการเริ่มยาต้านเอชไอวีได้ 2 สัปดาห์ โดยเฉพาะผู้ป่วยที่มี chorioretinitis และ encephalitis
โรคติดเชื้อฉวยโอกาสอื่น ๆ		เร็วที่สุดภายใน 2 สัปดาห์

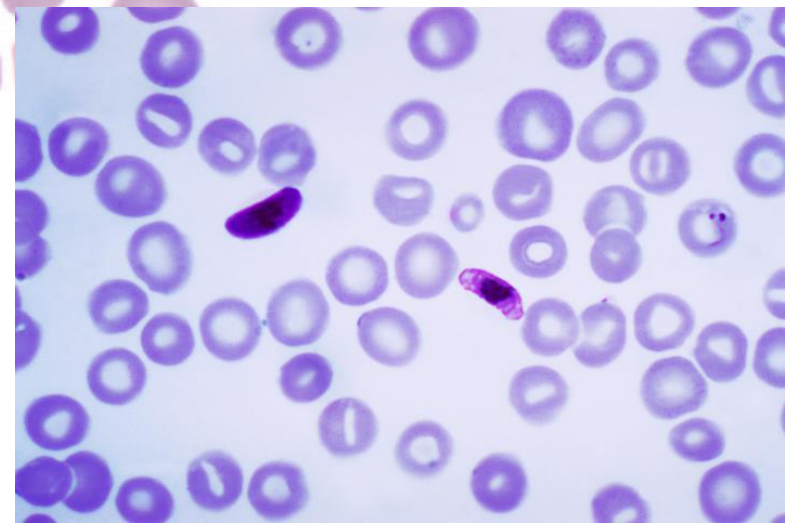


Cerebral malaria

ONLY *Plasmodium falciparum* affects the CNS!!
The most common non-traumatic encephalopathy!







Cerebral Malaria

Overview

Anopheles ยุงก้นปล่อง

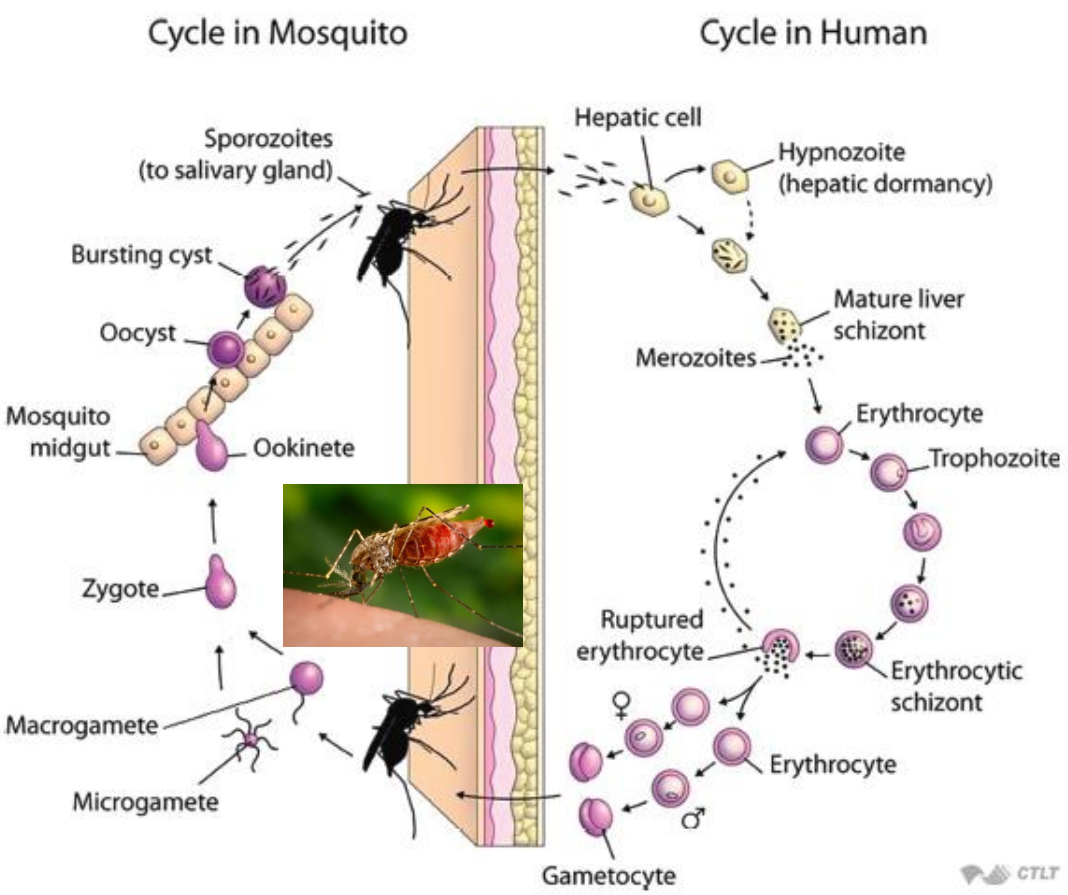
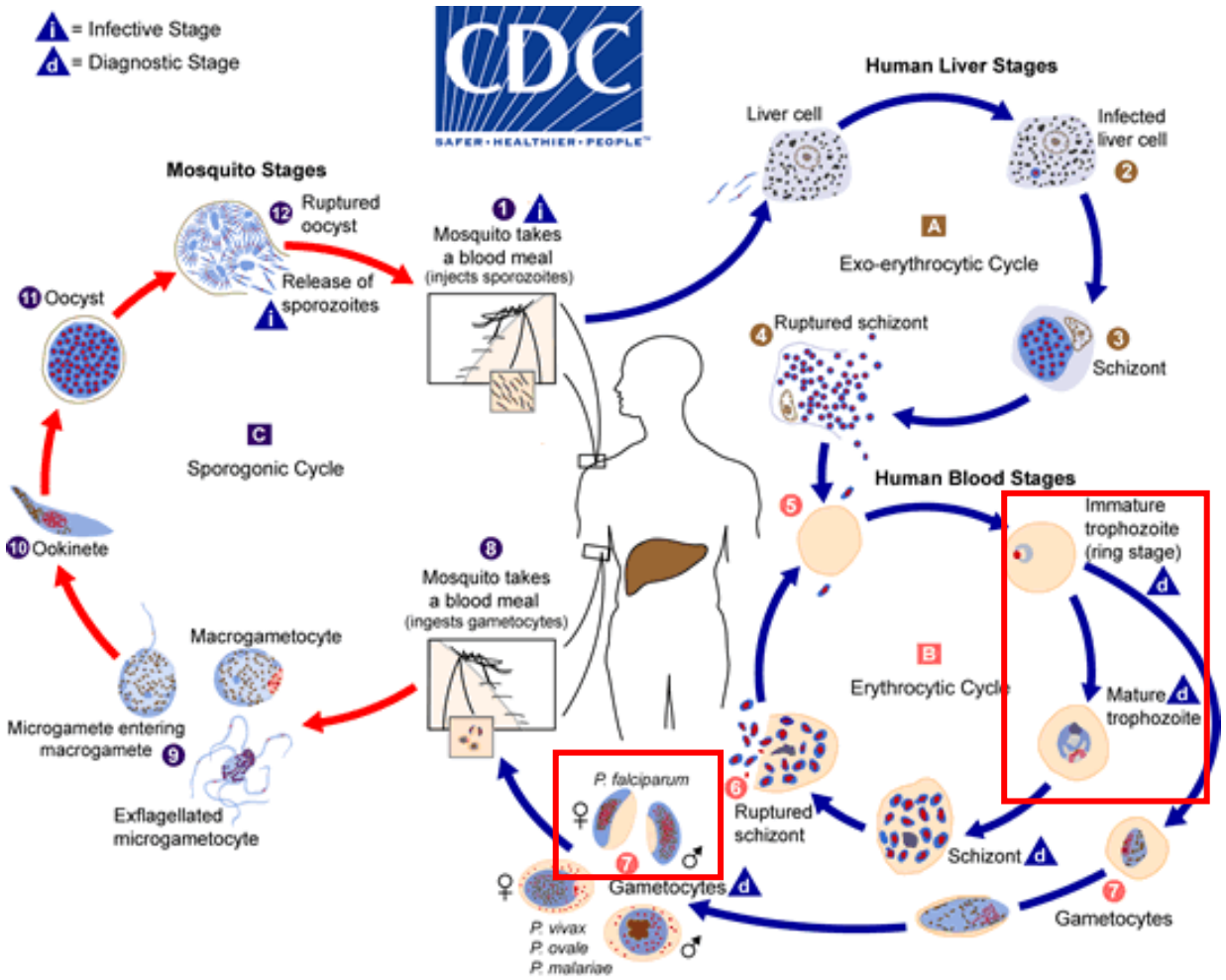


FIGURE 6-1
Life cycle of the malaria parasite.
Modified from JHSPH Open Courseware.[8] © 2021 Johns Hopkins Bloomberg School of Public Health.



Cerebral Malaria

Clinical manifestation

- **Clinical presentation**
  - Systemic – cyclical fever and malaise
  - Asymptomatic parasitemia, endemic regions
- **Severe malaria** (one or mole of the following)
  - Impaired consciousness
  - Prostration
    - inability to perform a previously-acquired motor function, such as standing, sitting or, in very young children
  - Multiple seizures
  - Circulatory collapse or shock
  - Low systolic blood pressure
  - Acute kidney injury
  - Clinical jaundice plus evidence of other vital organs dysfunction
  - Abnormal bleeding

Cerebral Malaria

Clinical manifestation

- **Cerebral malaria**
  - In children (6 mo – 5 y old)
    - Initial non-specific – fever, cough, vomiting
    - Febrile encephalopathy >> Coma
    - Seizure (> 70%)
  - In adult (esp. nonimmune traveler)
    - Progression to coma is gradual
    - Seizure (15-20%)
    - Multiorgan system failure
  - Systemic
    - Severe anemia
    - ARDS

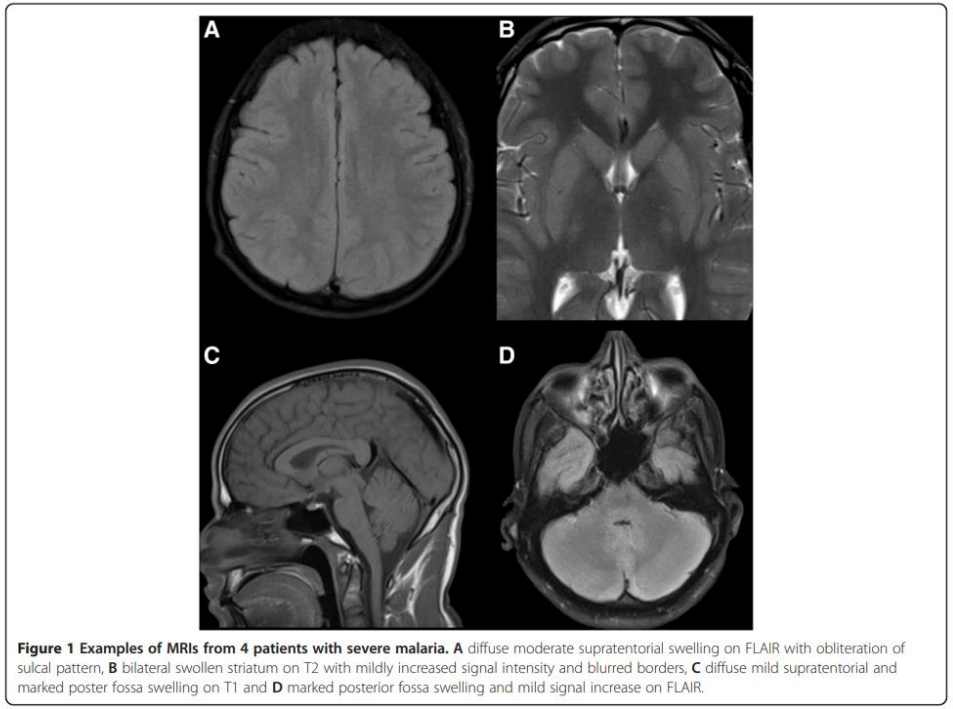


Figure 1 Examples of MRIs from 4 patients with severe malaria. A diffuse moderate supratentorial swelling on FLAIR with obliteration of sulcal pattern, **B** bilateral swollen striatum on T2 with mildly increased signal intensity and blurred borders, **C** diffuse mild supratentorial and marked poster fossa swelling on T1 and **D** marked posterior fossa swelling and mild signal increase on FLAIR.

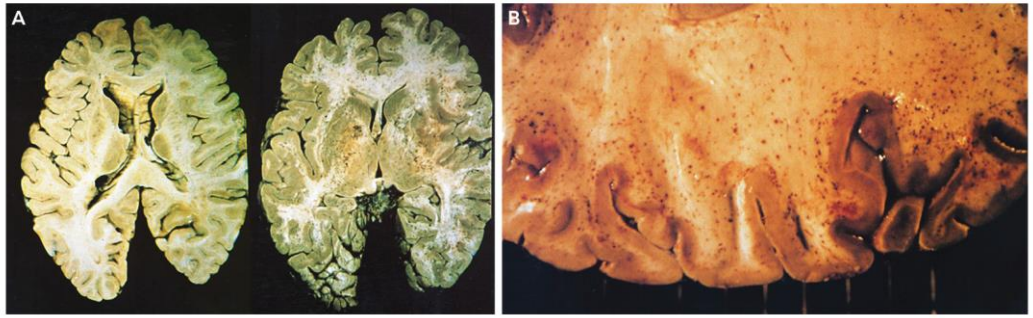


FIGURE 6-2
Pathology of cerebral malaria. *A*, Macroscopic pathology of cerebral malaria (*right*) compared to a normal brain (*left*). *B*, Close-up view of the brain demonstrating the typical "flea-bitten" appearance resulting from multiple ring hemorrhages in the white matter.
Reprinted with permission from Román GC, J Neurol Sci.[14] © 1991 Elsevier Inc.

Maude, R.J., Barkhof, F., Hassan, M.U. *et al.* Magnetic resonance imaging of the brain in adults with severe falciparum malaria. *Malar J* **13,** 177 (2014).

Cerebral Malaria

Clinical manifestation

- **Cerebral malaria**
  - **Prognosis**
    - Untreated >> death!
    - Appropriate care
      - Short-term mortality 15-30%
      - Long term neurologic sequelae (30%)
        - Epilepsy, cognitive & behavior disorders, or neurological deficits
        - Adult fewer neurologic complications BUT can rarely develop postmalaria neurologic syndrome (PMNS)
  - **PMNS**
    - Myriad neuropsychiatric manifestation (mild-severe) 3 forms
      - a mild form characterized by isolated cerebellar ataxia or postural tremor;
      - a diffuse, relatively mild encephalopathic form, associated with acute confusion or seizures
      - a severe encephalopathy typified by motor aphasia, generalized myoclonus, postural tremor, and cerebellar ataxia.
    - One form of ADEM
    - Rare BUT Self-limiting

Yadava SK, Laleker A, Fazili T. Post-malaria neurological syndrome: a rare neurological complication of malaria. *Infection*. 2019;47(2):183-193. doi:10.1007/s15010-019-01267-9

Cerebral Malaria

Clinical manifestation

- **Cerebral malaria**
  - Pathogenesis – not completely understood
  - The obstruction of blood vessels caused **by intravascular sequestration of infected red blood cells** leading to
    - cytokine release
    - blood-brain barrier disruption
    - brain edema
    - metabolic alterations

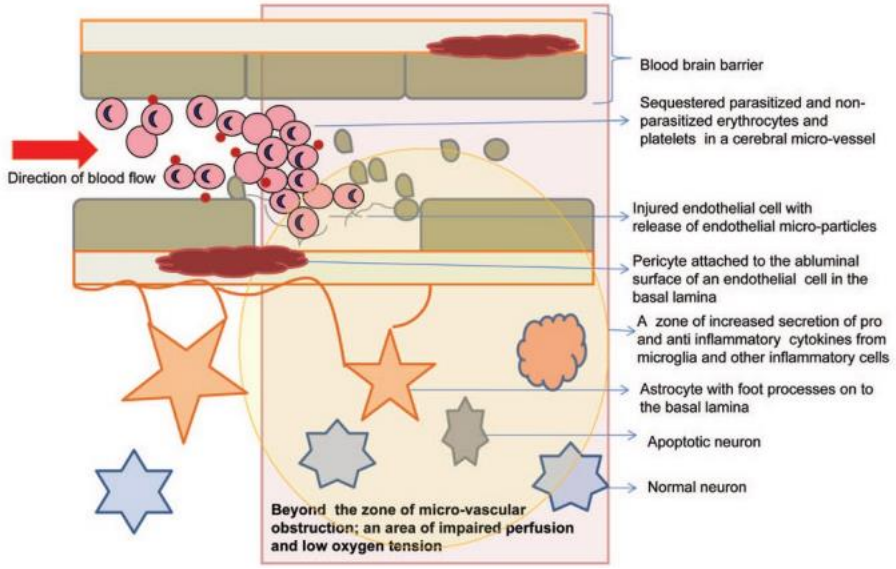


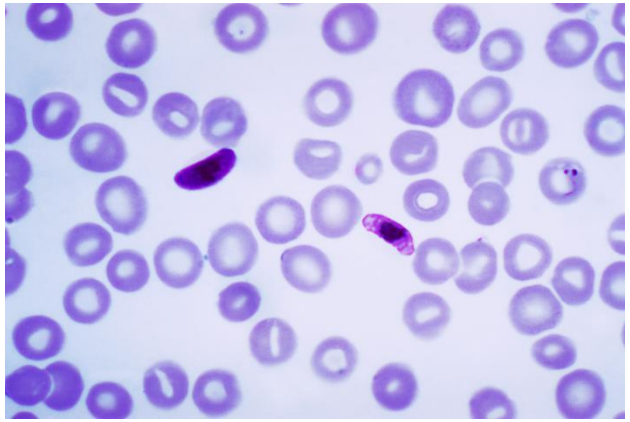
Figure 1. Changes in and around a cerebral microvessel with sequestered *Plasmodium falciparum* parasites. A schematic diagram showing changes in and around a cerebral vessel with sequestration of pRBCs. Cytoadherence of parasitized erythrocytes to the endothelial cell lining and sequestration of parasitized and non-parasitized cells in the cerebral capillary or postcapillary venule initiates an inflammatory process, endothelial activation, release of EMPs, and apoptosis in the exposed area. At the site of cytoadherence, the BBB is possibly disrupted, and there is an increased inflammatory response in the perivascular area with an increased release of proinflammatory cytokines.

Idro R, et al. Cerebral Malaria: Mechanisms of Brain Injury and Strategies for Improved Neurocognitive Outcome. 2010

Cerebral Malaria

Investigation

- **Thin blood smear***
  - Ring-form trophozoites
    - Double chromatin dots
    - Double infection
  - Gametocyte
    - Banana shape
  - Endemic area
    - ! Co-existence in case of asymptomatic parasitemia



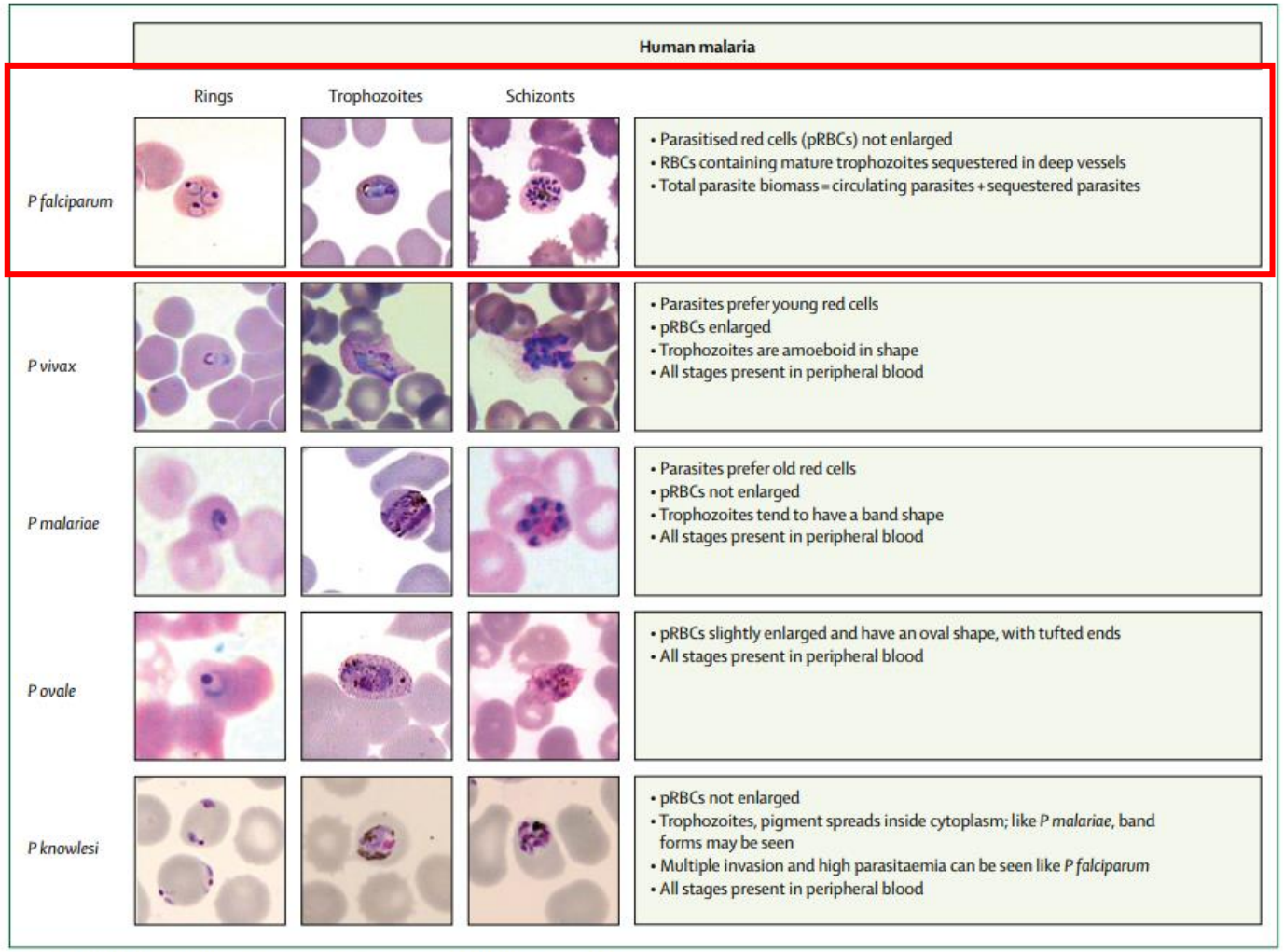


***Figure 2:* Blood films showing microscopic appearance of the human malarias**
All parasite stages are visible in peripheral blood except *P falciparum* RBCs containing mature trophozoites where the vast majority are sequestered in deep vessels. Thin blood films were prepared from specimens taken from patients with clinical malaria, stained with modified Field's stain and examined by light microscopy under oil immersion at x1000 magnification. P=*Plasmodium*.

Malaria. Lancet. 2018

Cerebral Malaria

Investigation

- **Fundoscopy exam**
  - Malaria retinopathy
    - Retinal whitening, retinal hemorrhages, papilledema, and vascular changes
    - Sensitivity 95% Specificity 90% esp. children in coma
- **CSF profile**
  - **Usually, normal**
  - Exclude other causes
  - Could perform in clinically stable patient despite evidence of brain edema

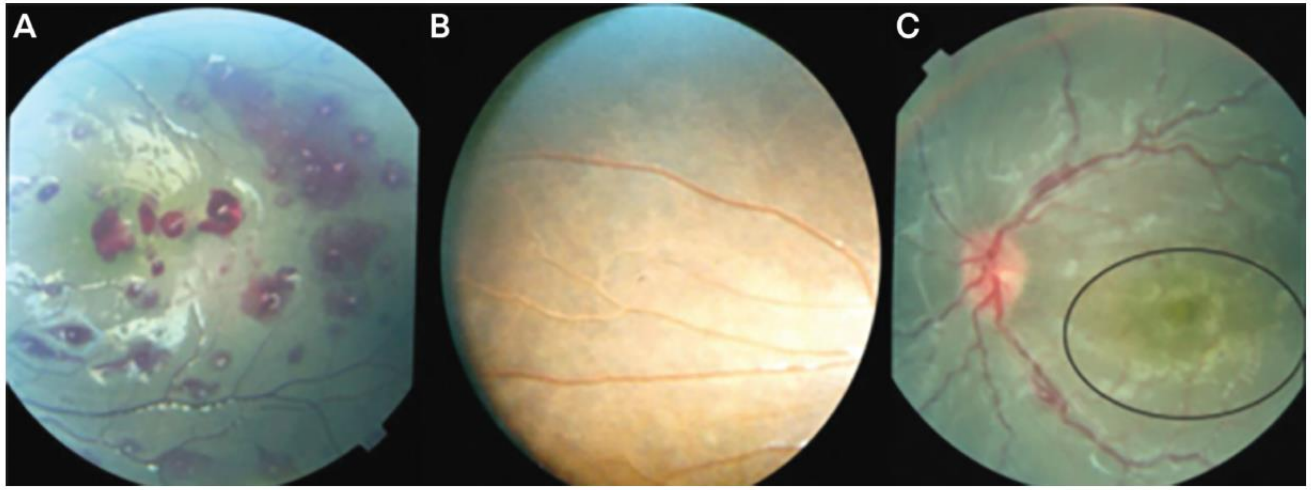


FIGURE 6-3

Malarial retinopathy in pediatric patients from Malawi showing white-centered hemorrhages (*A*), vessel discoloration (*B*), and perimacular whitening (*C*, *circle*).

Reprinted with permission from Taylor TT and Molyneux ME, Ann NY Acad Sci.[11] © 2015 New York Academy of Sciences.

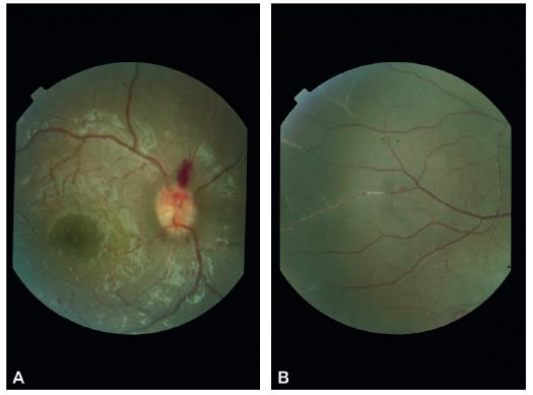
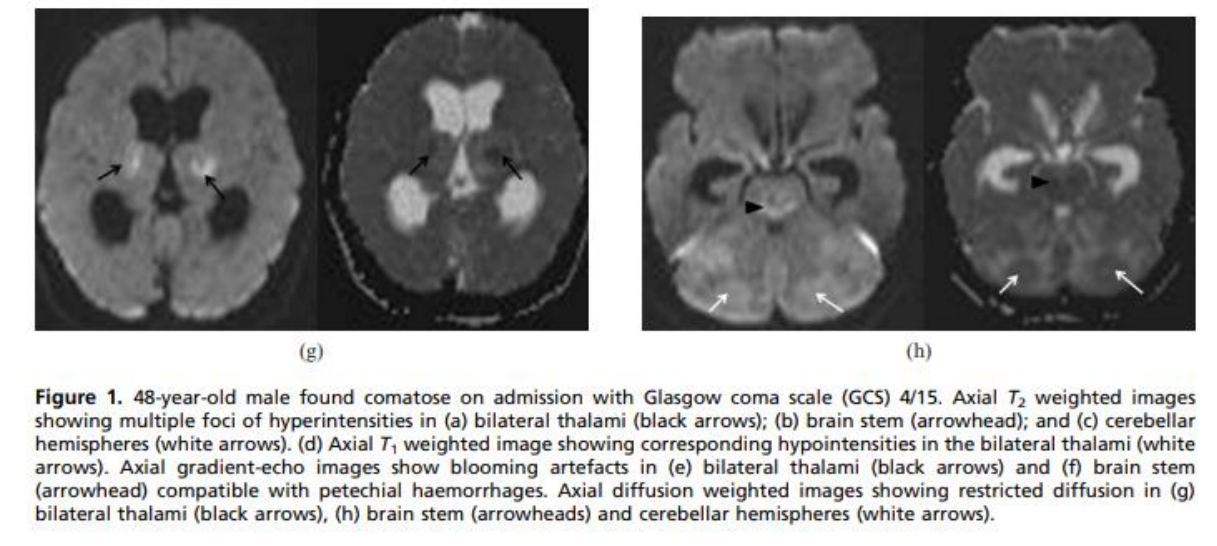


Fig. 6.3. (**A**) Ocular fundus of child with CM reveals typical findings of malarial retinopathy including retinal whitening, flame hemorrhages, and papilledema. (Photo courtesy of Dr. Simon Glover, Queen Elizabeth Central Hospital, Blantyre, Malawi). (**B**) Fundus photograph of child with CM showing orange and white retinal vessels, typical of malarial retinopathy. (Image courtesy of Dr. Simon Glover, Queen Elizabeth Central Hospital, Blantyre, Malawi.)

Cerebral Malaria

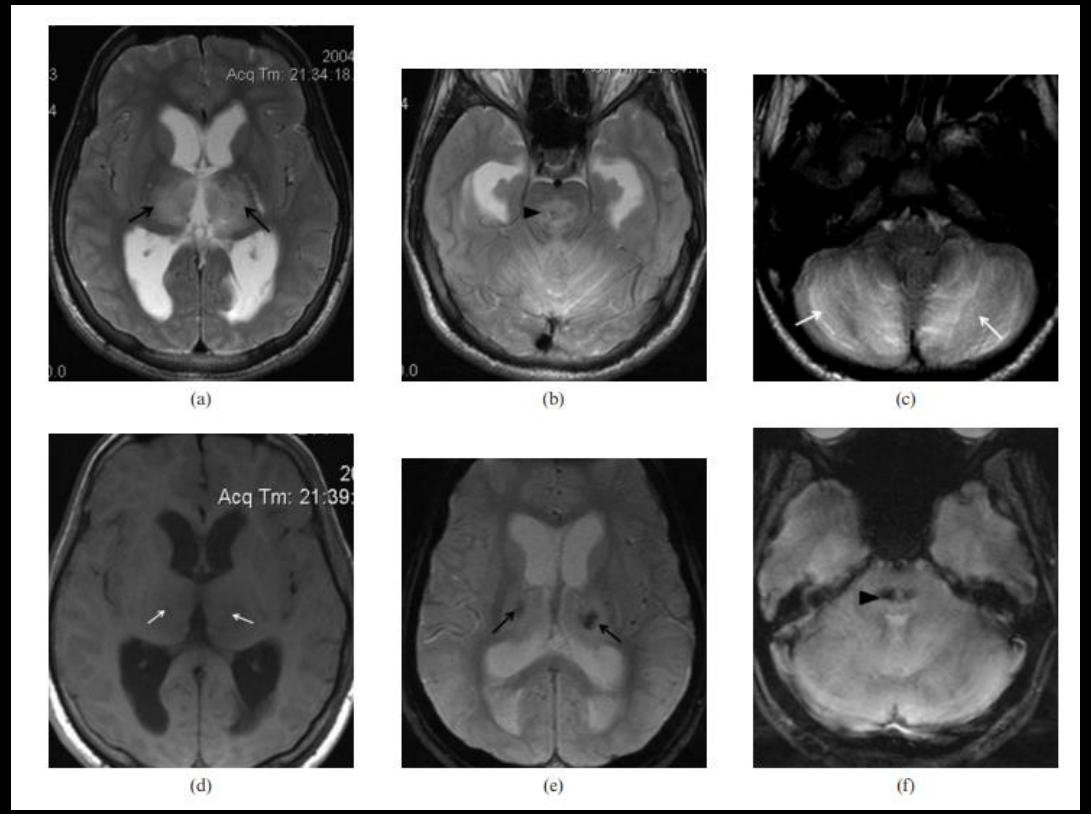
Investigation

- **Imaging – limited data & non-specific**
  - Cerebral edema
  - Abnormal T2 and DWI in cortical, deep grey (esp. thalamus), white matter
  - Hemorrhage!
  - Brainstem & cerebellum involvement
    - Poor prognosis



(g) (h)

Figure 1. 48-year-old male found comatose on admission with Glasgow coma scale (GCS) 4/15. Axial T_2 weighted images showing multiple foci of hyperintensities in (a) bilateral thalami (black arrows); (b) brain stem (arrowhead); and (c) cerebellar hemispheres (white arrows). (d) Axial T_1 weighted image showing corresponding hypointensities in the bilateral thalami (white arrows). Axial gradient-echo images show blooming artefacts in (e) bilateral thalami (black arrows) and (f) brain stem (arrowhead) compatible with petechial haemorrhages. Axial diffusion weighted images showing restricted diffusion in (g) bilateral thalami (black arrows), (h) brain stem (arrowheads) and cerebellar hemispheres (white arrows).



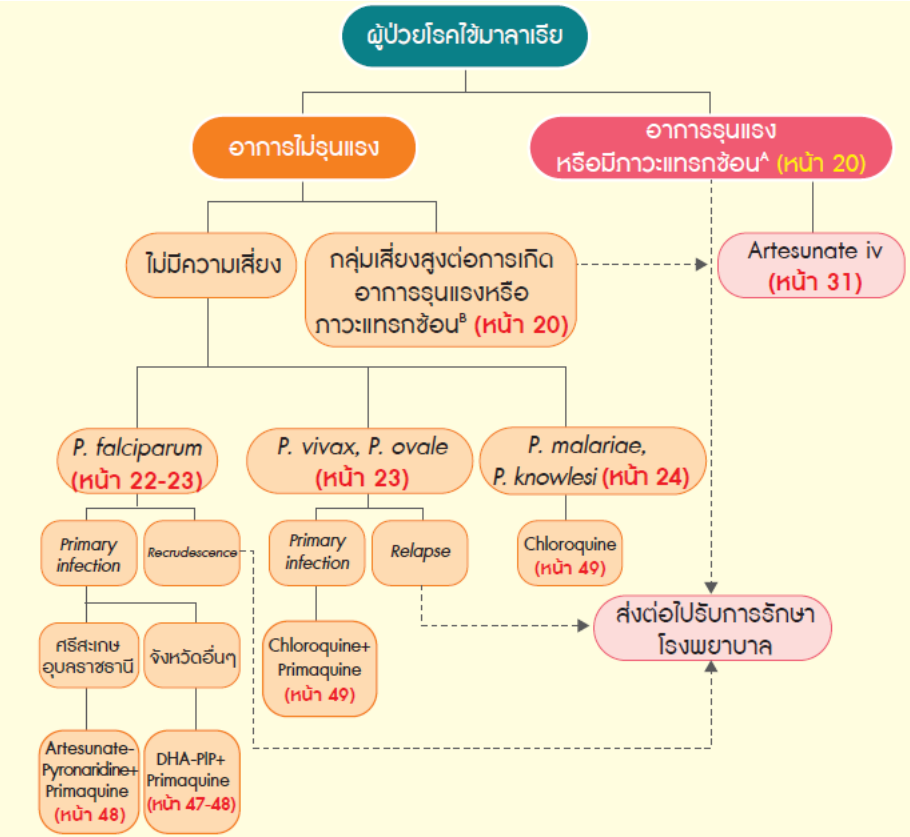
Rasalkar DD, Paunipagar BK, Sanghvi D, Sonawane BD, Loniker P. Magnetic resonance imaging in cerebral malaria: a report of four cases. *Br J Radiol.* 2011;84(1000):380-385. doi:10.1259/bjr/85759874

Cerebral Malaria

Treatment

- **Regimen for cerebral malaria/severe malaria**
  - **Artesunate IV**

    2.4 mg/kg IV bolus then
    2.4 mg/kg at 12 h, 24 h then
    2.4 mg/kg OD



A ผู้ป่วยโรคไข้มาลาเรียที่มีภาวะแทรกซ้อนหรืออาการรุนแรง

- มีระดับสติสัมปชัญญะลดลงหรือหมดสติ
- อ่อนเพลียมาก จนไม่สามารถนั่ง เดิน หรือยืนเองได้
- ชัก
- หอบเหนื่อย หายใจเร็ว
- ตัวเหลืองตาเหลือง ระดับ Bilirubin สูงร่วมกับจำนวนเชื้อมาลาเรียในเลือดมากกว่า 100,000/µl
- มีภาวะโลหิตจาง ร่วมกับจำนวนเชื้อมาลาเรียในเลือดมากกว่า 100,000/µl
- มีภาวะช็อค
- ปัสสาวะออกน้อย หรือไม่มีปัสสาวะภายใน 4 ชั่วโมง หรือมีภาวะไตวาย
- เลือดออกผิดปกติ เช่น เหงือก จมูก อาเจียนหรือถ่ายเป็นเลือด
- ระดับน้ำตาลในเลือดต่ำ
- ภาวะเลือดเป็นกรด ระดับแลคเตทสูงหรือระดับไบคาร์บอเนตต่ำ
- ปัสสาวะสีเข้ม (Hemoglobinuria)
- มีภาวะน้ำท่วมปอด

B กลุ่มเสี่ยงสูงต่อการเกิดภาวะแทรกซ้อนหรืออาการรุนแรง

- เด็กอายุน้อยกว่า 1 ปี หรือน้ำหนักน้อยกว่า 11 กิโลกรัม
- เด็กอายุต่ำกว่า 5 ปีที่มีไข้สูงเกิน 39 องศาเซลเซียส
- หญิงมีครรภ์ หรือขาดประจำเดือนสงสัยว่าตั้งครรภ์
- ผู้ที่มีภาวะพร่องเอนไซม์ G6PD
- ผู้ป่วยที่สงสัยว่ามีการติดเชื้อ *P. knowlesi*
- ผู้ป่วยที่มีโรคประจำตัว เช่น โรคอ้วน, โรคพิษสุราเรื้อรัง, โรคตับ, โรคไต, โรคเบาหวาน, ความดันโลหิตสูง, โรคเลือด, โรคภูมิคุ้มกันผิดปกติ เป็นต้น
- ผู้ป่วยที่ไม่สามารถรับประทานยาเม็ดได้ หรือรับประทาน แล้วอาเจียน และยังอาเจียนอีกเมื่อรับประทานยาซ้ำใน 1 ชั่วโมง
- ผู้ที่มีประวัติแพ้ยาต้านมาลาเรีย
- ผู้ที่ตรวจพบเชื้อมาลาเรียมากกว่า 2,500 เซลล์ต่อเม็ดเลือดขาว 200 เซลล์ หรือ 100,000/µl ในกรณีที่ตรวจด้วยฟิล์มเลือดหนา หรือพบระยะแบ่งตัว (Schizont)

ขนาดยาที่ใช้รักษาผู้ป่วยโรคไข้มาลาเรียมีอาการรุนแรง

- **แนะนำให้เลือกใช้ยาฉีด Artesunate มากกว่า Quinine Hydrochloride** เนื่องจาก Artesunate สามารถลดอัตราการตายในผู้ป่วยมาลาเรียรุนแรงได้มากกว่า Quinine Hydrochloride
- **ยาขนานแรก:** Artesunate 2.4 มก./กก. เข้าหลอดเลือดดำแบบ Bolus injection ทันที ตามด้วย 2.4 มก./กก. ที่ 12 และ 24 ชั่วโมง (ในกรณีผู้ป่วยน้ำหนักน้อยกว่า 20 กก. ให้ Artesunate ขนาด 3 มก./กก.) จากนั้นฉีดวันละครั้ง จนกว่าผู้ป่วยรับประทานยาได้ จึงเปลี่ยนเป็น Artemisinin-based Combination Therapy (ACT) รับประทานนาน 3 วัน
- **ยาขนานที่สอง (กรณี ไม่มียาฉีด Artesunate):** Quinine Hydrochloride ขนาด 20 มก./กก. Intravenous drip ใน 4 ชั่วโมง ตามด้วย 10 มก./กก. Intravenous drip เข้าหลอดเลือดดำใน 2 - 4 ชั่วโมง ทุก 8 ชั่วโมง เมื่อรับประทานยาได้ จึงเปลี่ยนเป็น Artemisinin-based Combination Therapy (ACT) รับประทาน นาน 3 วัน หรือ Quinine Sulphate ร่วมกับ Doxycycline หรือ Quinine Sulphate ร่วมกับ Clindamycin หรือ Artesunate ร่วมกับ Doxycycline หรือ Artesunate ร่วมกับ Clindamycin ชนิดรับประทาน 7 วัน

  หมายเหตุ Artemisinin-based Combination Therapy (ACT) หมายถึงยาผสมซึ่งมียาในกลุ่ม Artemisinin เป็นส่วนประกอบ ร่วมกับยาต้านเชื้อมาลาเรียอื่นๆ
- ในกรณีที่ผู้ป่วยมีภาวะตับทำงานผิดปกติ หรือไตวาย หรืออาการทั่วไปเลวลง
  - ไม่จำเป็น ต้องปรับลดขนาดยา Artesunate
  - หากให้ Quinine Hydrochloride ต้องปรับขนาดยาในวันที่ 3 โดยลดเหลือ 2/3 หรือ ครึ่งหนึ่งของ Maintenance dose
- ห้ามให้ Doxycycline ในหญิงมีครรภ์ หญิงให้นมบุตร และเด็กอายุน้อยกว่า 8 ปี
- การให้ยารับประทานในขณะผู้ป่วยมีไข้สูง ผู้ป่วยอาจอาเจียนทำให้ได้รับยาไม่เต็มขนาด ควรลดไข้ให้ผู้ป่วยก่อน เช่น รับประทานยาพาราเซตามอล หรือเช็ดตัว
- ให้วินิจฉัยหาสาเหตุร่วมอื่น ๆ และ Co-infection ร่วมด้วยหากมีข้อบ่งชี้

Thai Malaria Guideline 2564

Cerebral Malaria

Treatment

Drug-resistant Malaria – ACT (artemisinin-based combination) failure

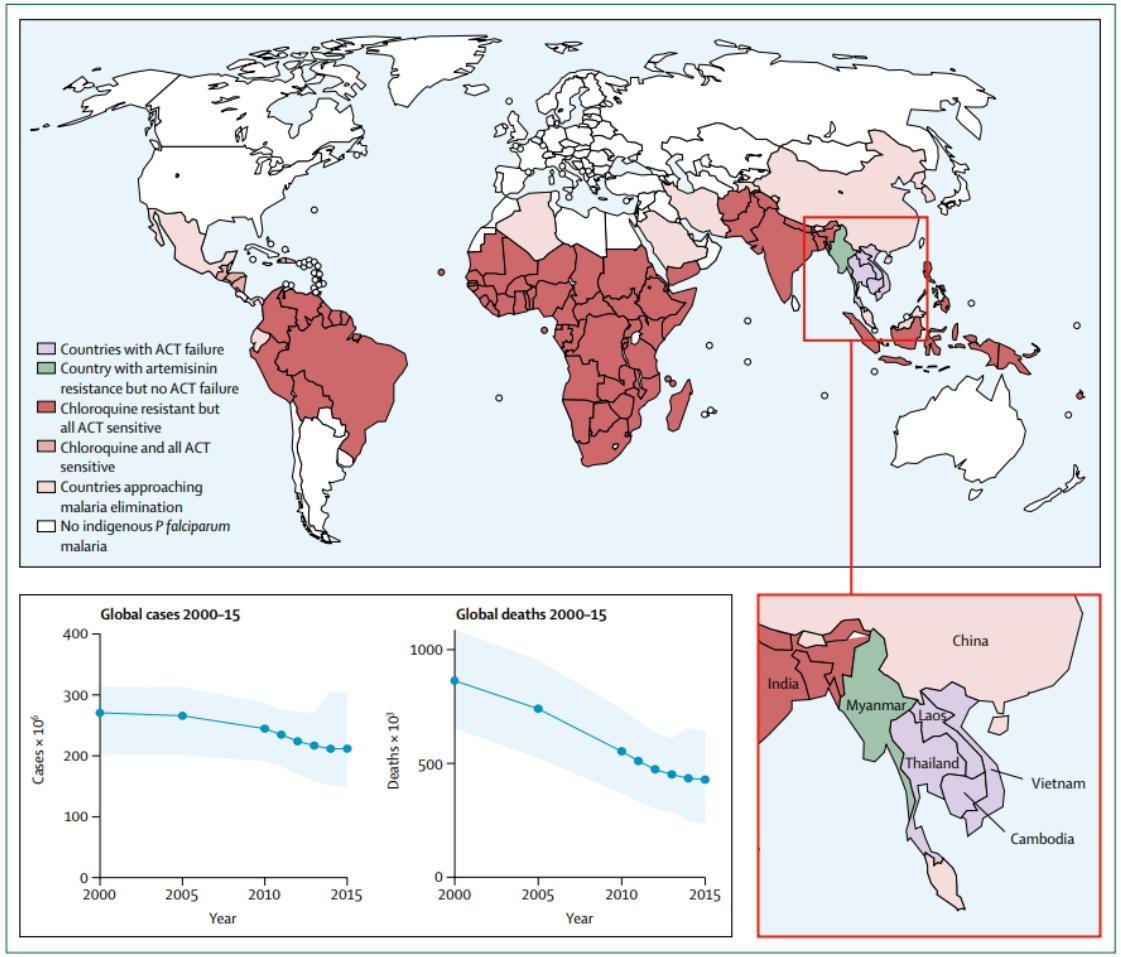
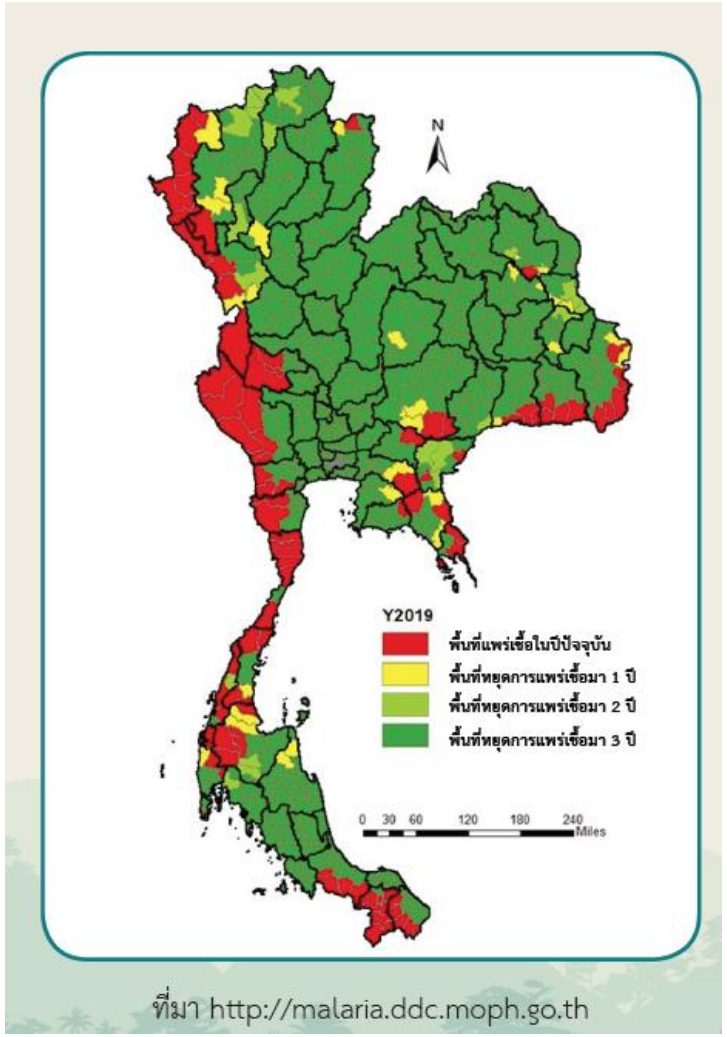


Figure 3*: Global distribution of drug-resistant *Plasmodium falciparum
Countries are shown according to the level of resistance of local *P falciparum*; the 13 countries approaching elimination (as defined in the World Malaria Report 2016) are also shown. The inset graphs show WHO estimates of global annual malaria case numbers and deaths from 2000 to 2015 (with 95% upper and lower uncertainty intervals).[58] ACT=artemisinin-based combination therapy. Created with mapchart.net ©.



Thai Malaria Guideline 2564
Malaria. Lancet. 2018

Cerebral Malaria

Treatment

- Drug-resistant Malaria – ACT (artemisinin-based combination) failure
  - Please following guideline

การให้ยารักษาผู้ป่วยโรคไข้มาลาเรียกลุ่มการรักษาล้มเหลว

การรักษาล้มเหลว หมายถึง หลังจากให้การรักษาด้วยยาตามสูตรต่าง ๆ แล้ว ตรวจพบข้อใดข้อหนึ่ง ต่อไปนี้

1. มีอาการทางคลินิกเลวลงในวันใดก็ตาม และตรวจพบเชื้อชนิดเดิมซ้ำในฟิล์มเลือด
2. มีอาการ/อาการแสดงกลับซ้ำขึ้นมาใหม่ แต่อาการไม่รุนแรง
3. ไม่มีอาการ/อาการแสดงแล้ว แต่ตรวจพบเชื้อชนิดเดิมซ้ำในฟิล์มเลือด ภายในวันที่ 28 หลังเริ่มได้ยา

การดูแลรักษาผู้ป่วยโรคไข้มาลาเรียที่รักษาล้มเหลวนี้ ให้การรักษาโดยการใช้ยาขนานที่สอง (Second Line Treatment) และเจ้าหน้าที่สาธารณสุขจะส่งต่อผู้ป่วยกลุ่มนี้มารับการรักษาที่โรงพยาบาล

1. การรักษาผู้ป่วยโรคไข้มาลาเรียที่รักษาล้มเหลวชนิดฟัลซิปารัม

1.1 กลุ่มที่มีอาการเลวลงในวันใดก็ตาม และตรวจพบเชื้อเดิมซ้ำในฟิล์มเลือด

ให้ทำการรักษาเช่นเดียวกับผู้ป่วยโรคไข้มาลาเรียที่มีอาการรุนแรง และเมื่อผู้ป่วยสามารถรับประทานได้ ให้เปลี่ยนเป็นยารับประทานสูตรใดสูตรหนึ่งที่แตกต่างจากยาขนานแรก ต่อไปนี้

A. Artesunate - Pyronaridine

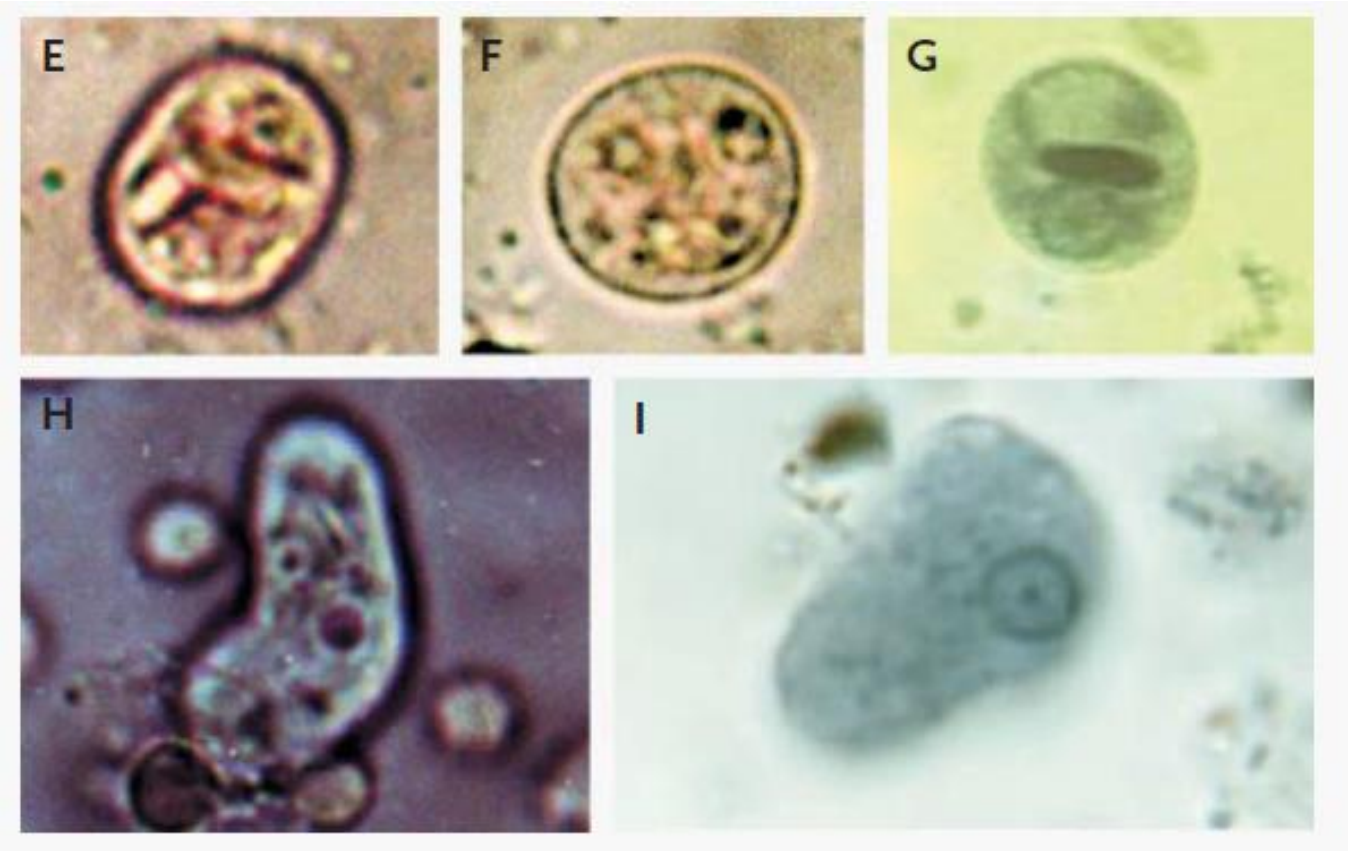
B. Artemether - Lumefantrine

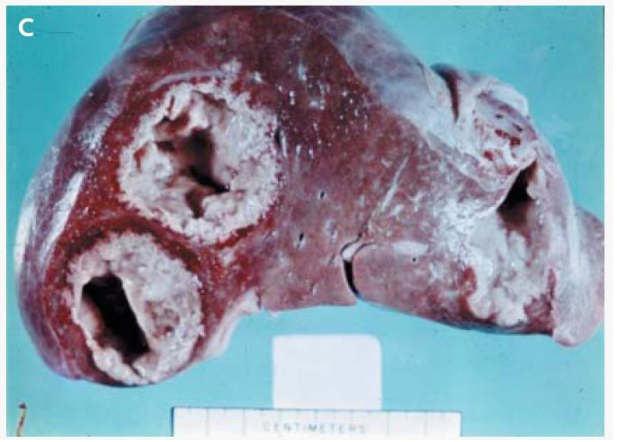
C. Quinine Sulfate ร่วมกับ Clindamycin หรือ Doxycycline หรือ Tetracycline

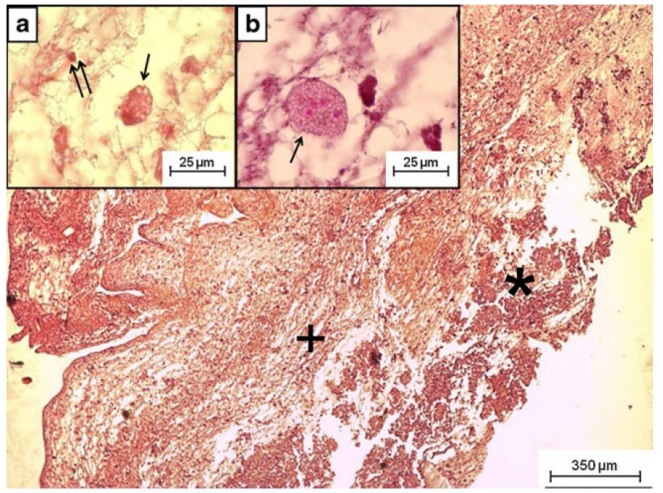
D. Atovaquone - proguanil

Thai Malaria Guideline 2564

Cerebral amebiasis (Entamoeba histolytica infection)







Anchovy paste

Cerebral amebiasis

Overview

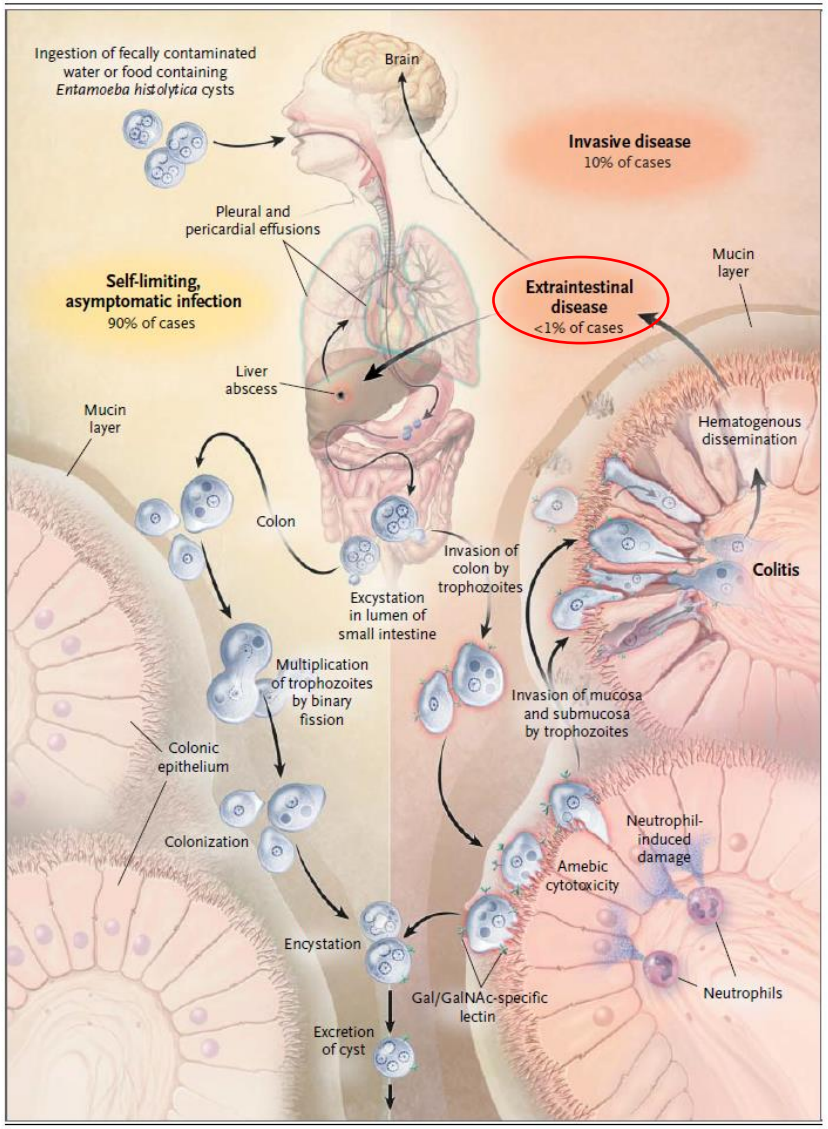


Figure 1 (facing page). Life Cycle of *Entamoeba histolytica*.

Infection is normally initiated by the ingestion of fecally contaminated water or food containing *E. histolytica* cysts. The infective cyst form of the parasite survives passage through the stomach and small intestine. Excystation occurs in the bowel lumen, where motile and potentially invasive trophozoites are formed. In most infections the trophozoites aggregate in the intestinal mucin layer and form new cysts, resulting in a self-limited and asymptomatic infection. In some cases, however, adherence to and lysis of the colonic epithelium, mediated by the galactose and *N*-acetyl-D-galactosamine (Gal/GalNAc)–specific lectin, initiates invasion of the colon by trophozoites. Neutrophils responding to the invasion contribute to cellular damage at the site of invasion. Once the intestinal epithelium is invaded, extraintestinal spread to the peritoneum, liver, and other sites may follow. Factors controlling invasion, as opposed to encystation, most likely include parasite "quorum sensing" signaled by the Gal/GalNAc-specific lectin, interactions of amebae with the bacterial flora of the intestine, and innate and acquired immune responses of the host.

Amebiasis. NEJM. 2003

Cerebral amebiasis

Clinical manifestation

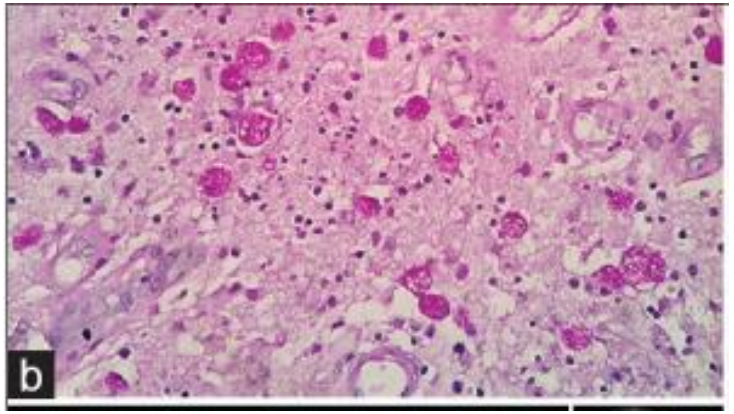
- **Clinical Manifestation**
  - Intestinal infection
    - Amebic colitis
      - a several week history of cramping abdominal pain, weight loss, and watery or less commonly bloody diarrhea.
  - Extraintestinal
    - Liver abscess
      - fever, cough, and a constant, dull, aching abdominal pain
    - Brain abscess = Cerebral amebiasis
      - Rare and commonly concomitant with liver abscess
- **Cerebral amebiasis**
  - Many patients do not have a prior history of amebic dysentery and few have intestinal amebiasis at the time of diagnosis of brain abscess
  - Presentation
    - commonly meningeal signs, facial nerve (VII) palsy, motor paralysis, and seizure.

Cerebral amebiasis

Investigation

- **Biopsy (gold standard)**
- **CSF**
  - Abnormal CSF profile without specific feature
- **PCR in CSF or brain tissue**

- **Indirect evidence from Stool**
  - Stool direct exam
  - Stool Ag detection
  - Stool PCR for *E. histolytica*



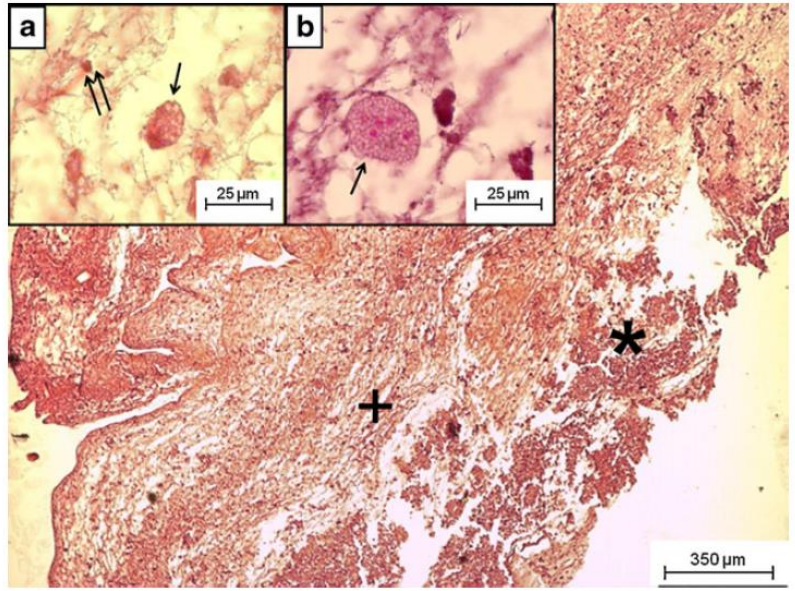


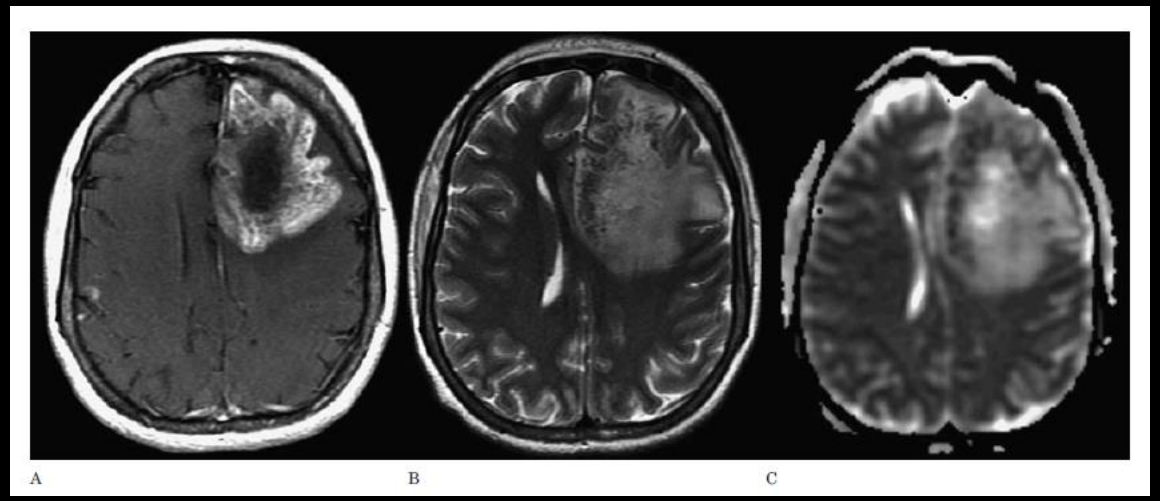
Fig. 1 Panoramic view of an amebic brain abscess with extensive necrotic (*cross*) and abscessed areas (*asterisk*) in the tissue. *a* Magnification of the necrotic area is shown with ameboid cellular structures that have clear microvacuoles in their cytoplasm (*arrow*) and with normal glial cells in the near vicinity (*double arrow*). *b* Trophozoite with ingested fragmented erythrocytes (*arrow*) is shown in the necrotic area

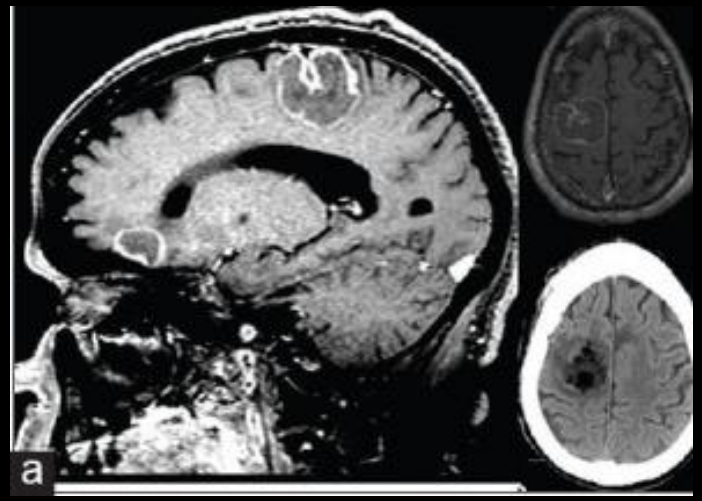
Maldonado-Barrera CA, Campos-Esparza Mdel R, Muñoz-Fernández L, et al. Clinical case of cerebral amebiasis caused by E. histolytica. *Parasitol Res.* 2012;110(3):1291-1296. doi:10.1007/s00436-011-2617-8

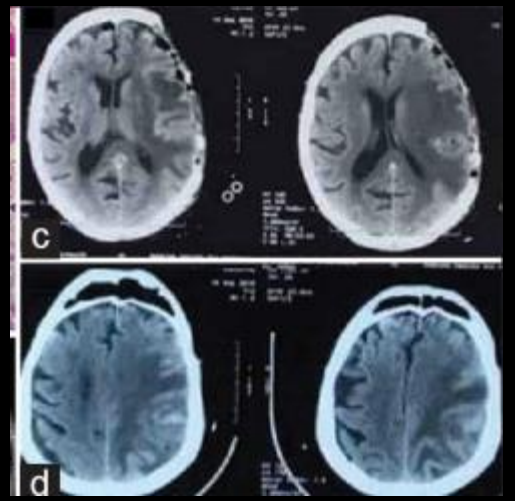
Cerebral amebiasis

Investigation

- **Imaging**
  - **Non-specific; Could mimics bacterial abscess**







Celik H, Karaosmanoglu DA, Gultekin S, Tokgoz N, Tali TE. Cerebral Amebiasis: MRI, DWI, Perfusion and MRS Features. Rivista di Neuroradiologia. 2005;18(5-6):559-563. doi:10.1177/197140090501800506

Varghese V, Kansal A, Bhardwaj S, Sharma A. Cerebral Amebiasis: An Uncommon Cerebral Abscess. *Ann Indian Acad Neurol*. 2021;24(3):445-447. doi:10.4103/aian.AIAN_583_20

Cerebral amebiasis

Treatment

Limited data in CNS

Table 2. Drug Therapy for the Treatment of Amebiasis.*

Drug	Adult Dosage	Pediatric Dosage	Side Effects
Amebic liver abscess			
		give	
Metronidazole	750 mg orally 3 times a day for 7–10 days	35–50 mg/kg of body weight/day in 3 divided doses for 7–10 days	Primarily gastrointestinal: anorexia, nausea, vomiting, diarrhea, abdominal discomfort, or unpleasant metallic taste; disulfuram-like intolerance reaction with alcohol; rarely, neurotoxicity, including seizures, peripheral neuropathy, dizziness, confusion, irritability
		or	
Tinidazole†	800 mg orally 3 times a day for 5 days	60 mg/kg/day (maximum, 2 g) for 5 days	Primarily gastrointestinal and disulfuram-like intolerance reaction as for metronidazole
		followed by a luminal agent	
Paromomycin	25–35 mg/kg/day in 3 divided doses for 7 days	25–35 mg/kg/day in 3 divided doses for 7 days	Primarily gastrointestinal: diarrhea, gastrointestinal upset
		or second-line agent	
Diloxanide furoate‡	500 mg orally 3 times a day for 10 days	20 mg/kg/day in 3 divided doses for 10 days	Primarily gastrointestinal: flatulence, nausea, vomiting, pruritus, urticaria
Amebic colitis			
		give	
Metronidazole	750 mg orally 3 times a day for 7–10 days	35–50 mg/kg/day in 3 divided doses for 7–10 days	As for amebic liver abscess
		followed by a luminal agent (as for amebic liver abscess)	
Asymptomatic intestinal colonization			
		give	
Paromomycin	25–35 mg/kg/day in 3 divided doses for 7 days	25–35 mg/kg/day in 3 divided doses for 7 days	Primarily gastrointestinal: diarrhea, gastrointestinal upset
		or second-line agent	
Diloxanide furoate‡	500 mg orally 3 times a day for 10 days	20 mg/kg/day in 3 divided doses for 10 days	Primarily gastrointestinal: flatulence, nausea, vomiting, pruritus, urticaria

* The information is updated annually by the *Medical Letter on Drugs and Therapeutics* at http://www.medletter.com/html/prm.htm#Parasitic.
† This drug is not yet available in the United States.
‡ This drug is not available in the United States.

Amebiasis. NEJM. 2003

Primary Amebic Meningoencephalitis (PAM) (Naegleria fowleri; brain eating amoeba)

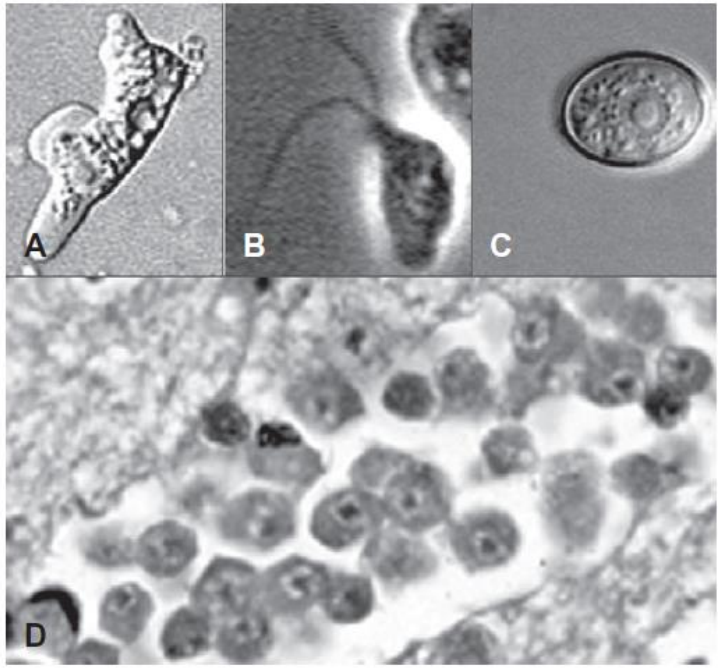
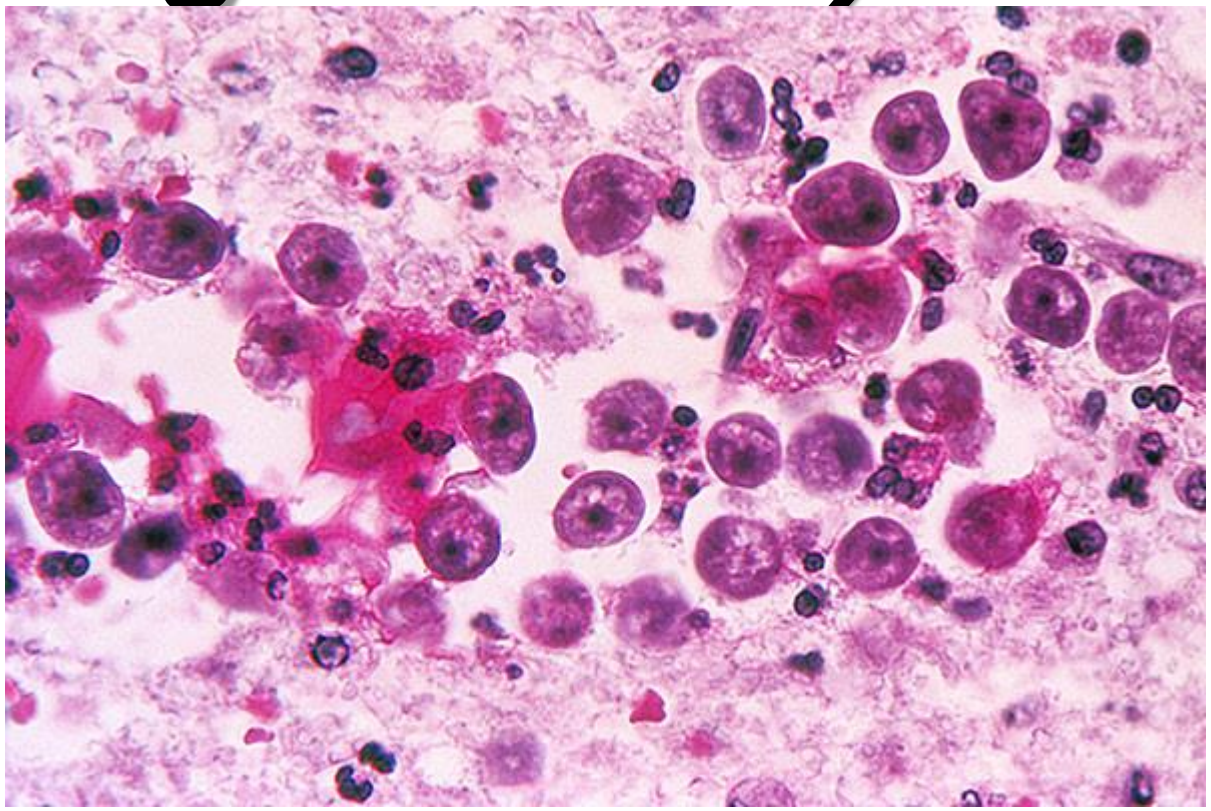


Fig. 10.3. *Naegleria fowleri* trophozoite (**A**); flagellate (**B**); and cyst (**C**) from culture. Phase contrast. X 1,000. D. *N. fowleri* trophozoite in a brain section stained with H&E. X 400.



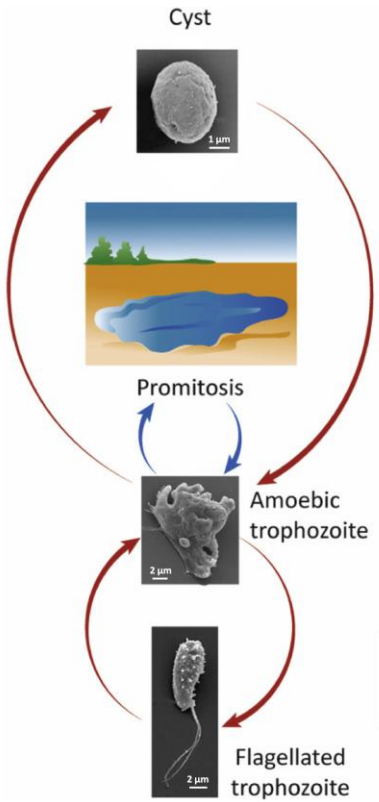
PAM

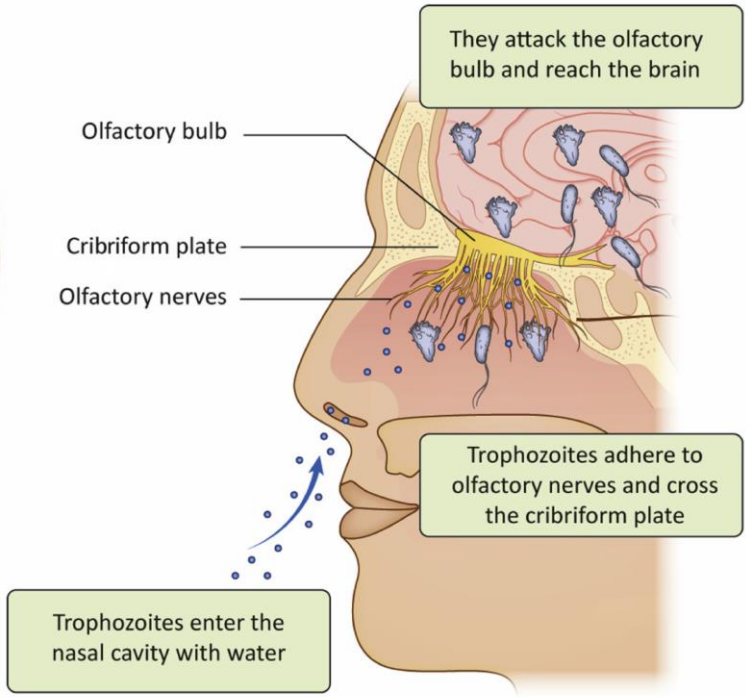
Overview

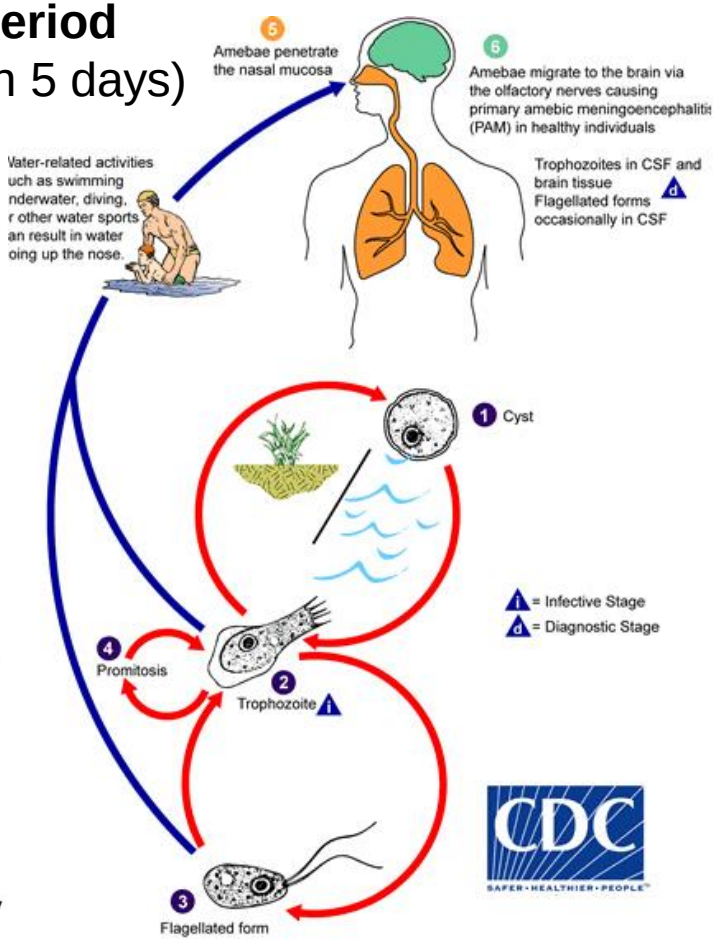
warm freshwater (e.g. lakes, rivers, hot springs), soil, poorly maintained swimming pool

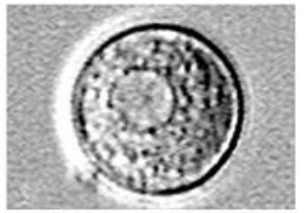
Invasion of olfactory bulb via nasal mucosa

Incubation period
1-9 days (median 5 days)



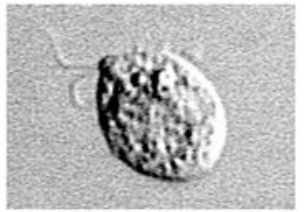






Cyst stage

Trophozoite stage



Flagellated stage

heat-loving (thermophilic) organism

Trends in Parasitology. 2019.

PAM

Clinical manifestation

- **Acute and fulminant course!**
  - Clinical – mimics bacterial meningitis & hard to diagnosis
  - The brain damage leads to brain haemorrhage and death occurs within 3–7 days in undiagnosed cases and maltreated cases.
  - **High mortality rate**
- **Stage 1**
  - Severe frontal headache
  - Fever
  - Nausea
  - Vomiting
- **Stage 2**
  - Stiff neck
  - Seizures
  - Altered mental status
  - Hallucinations
  - Coma

Table 2

Clinical Manifestations on Admission in 12 Cases With PAM

Clinical Manifestations	Number of Patients (%)
Fever	12 (100%)
Headache	12 (100%)
Impaired consciousness	12 (100%)
Stiff neck	12 (100%)
Vomiting	3 (25.0%)
Convulsion	2 (16.7%)
Running nose	1 (8.3%)
Blurred vision	1 (8.3%)
Intermittent abdominal pain	1 (8.3%)
Deviated gait	1 (8.3%)

Wiwanitkit V. Review of clinical presentations in Thai patients with primary amoebic meningoencephalitis. *MedGenMed*. 2004;6(1):2. Published 2004 Mar 8.

PAM

- **CSF profile**
  - PMN pleomorphic
  - hypoglycorhachia pattern
  - **mobile amoebic organism**
  - Special C/S for amoeba
- **Direct visulaization**
  - Fresh smear, Giemsa-Wright or a modified trichrome stain
- **Antigen detection**
  - immunohistochemistry [IHC], indirect immunofluorescence [IIF]
- **PCR**

Investigation

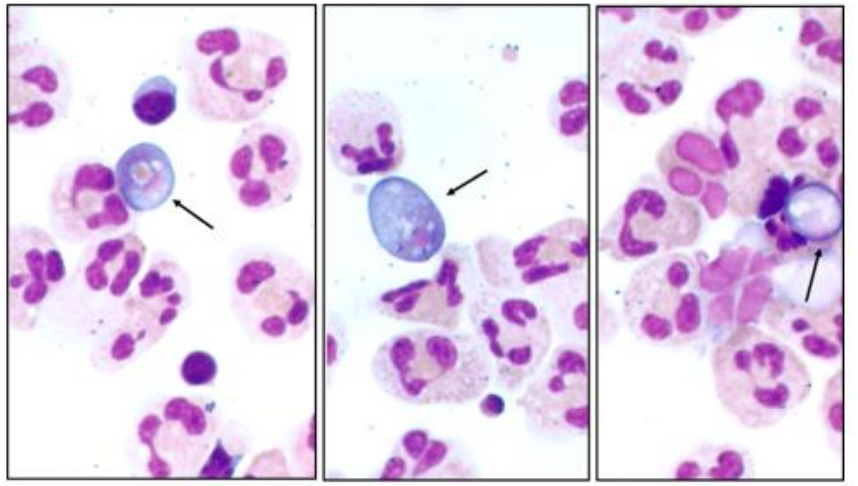
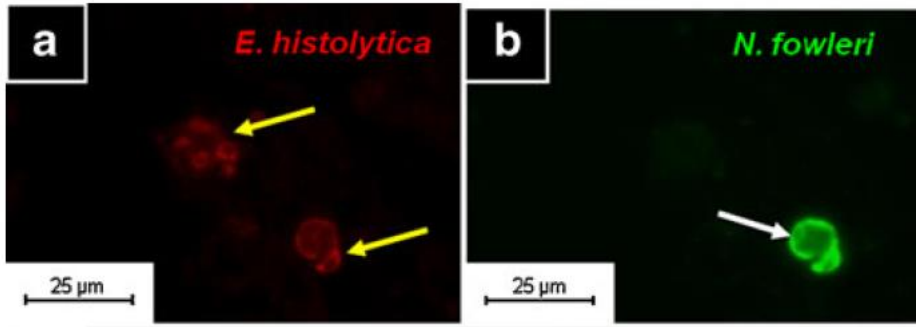


Figure 1. Images of *Naegleria fowleri* on Wright–Giemsa stained CSF cytospin slides (1000×, oil immersion). Black arrows point to *Naegleria* trophozoites with a background of neutrophils.



Pugh JJ, Levy RA. Naegleria fowleri: Diagnosis, Pathophysiology of Brain Inflammation, and Antimicrobial Treatments. ACS Chem Neurosci. 2016;7(9):1178-1179. doi:10.1021/acschemneuro.6b00232

PAM

Investigation

- Imaging
  - nonspecific
  - may be normal early in the disease, with evidence of brain edema and basilar meningeal enhancement subsequently
  - Sometimes – hydrocephalus, cerebral infarction

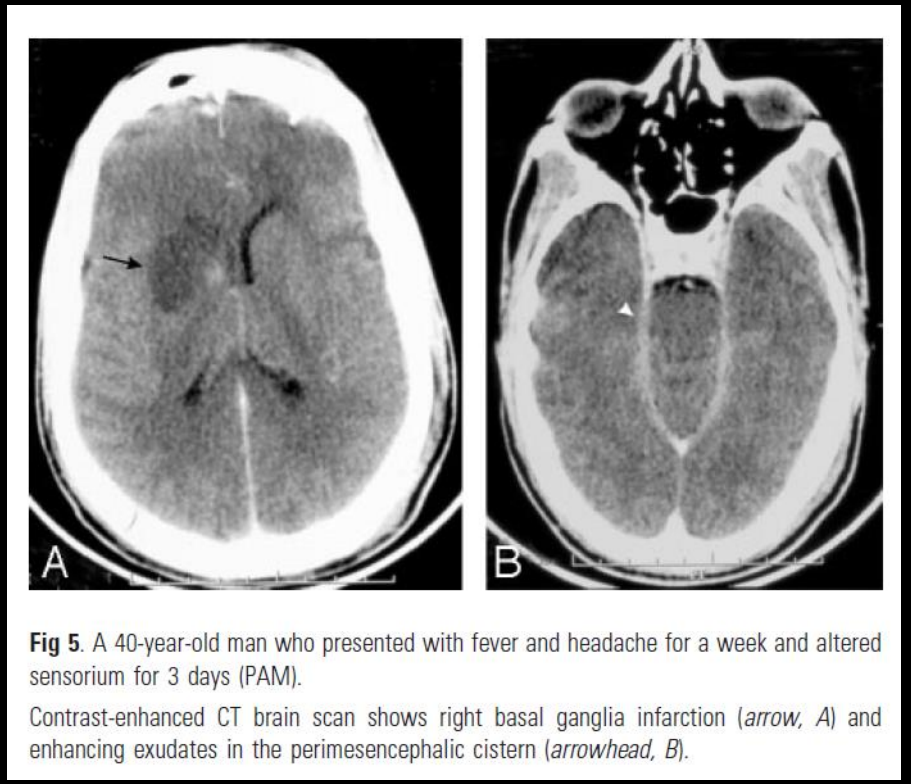


Fig 5. A 40-year-old man who presented with fever and headache for a week and altered sensorium for 3 days (PAM).

Contrast-enhanced CT brain scan shows right basal ganglia infarction (*arrow, A*) and enhancing exudates in the perimesencephalic cistern (*arrowhead, B*).

Amebic Meningoencephalitis: Spectrum of Imaging Findings. AJNR. 2006

PAM

Treatment

- an acute and fulminating infection resulting in death within a short period of time only a few patients have survived
  - One of these survivors, a Californian girl, was aggressively treated with intravenous and intrathecal amphotericin B, intravenous and intrathecal miconazole, and oral rifampin (Seidel et al., 1982)
- **Lack of evidence…**
- **Potential treatment**
  - **Amphotericin B**
    - Survival rate still 5%
  - **Azithromycin**
  - **Rifampicin**

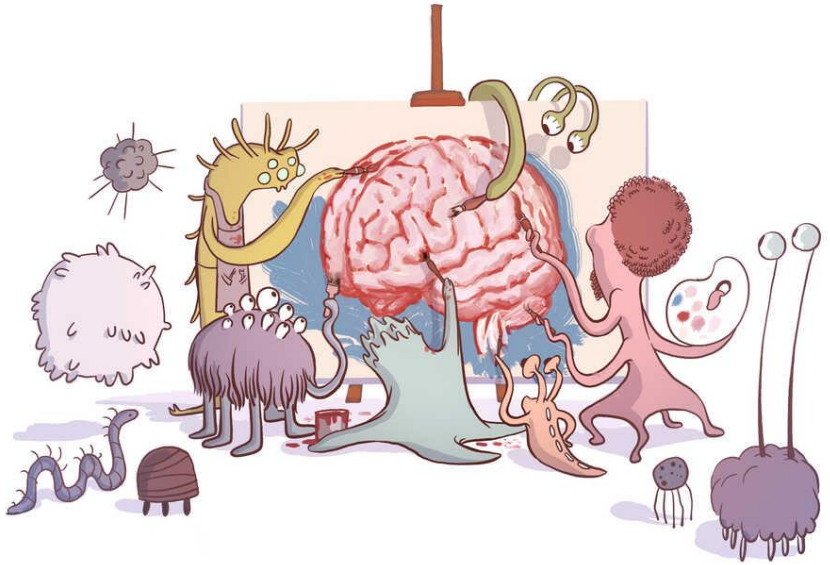
TABLE 2 PAM survivors with different treatment regimen

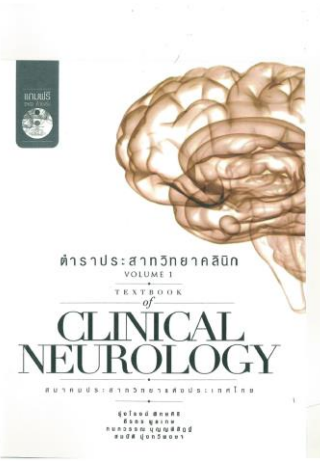
PAM survivor	Year	Treatment description	References
26-y-old female	2002	Rifampicin, amphotericin B, imidazole, treatment was continued for 3 wk	102
10-y-old boy	2005	Intravenous (iv) dexamethasone, amphotericin B, fluconazole, and oral rifampicin	103
8-mo-old infant	2008	Amphotericin B, chloramphenicol and rifampicin for 3 wk	104
12-y-old girl	2013	Amphotericin B, fluconazole, rifampin, azithromycin, dexamethasone, miltefosine	77
8-y-old Hispanic boy	2013	Amphotericin B, rifampin, fluconazole, azithromycin, miltefosine, dexamethasone	20
40-y-old male	2015	Amphotericin B, Metronidazole, Rifampicin	12
16-y-old boy	2016	Amphotericin, rifampin, azithromycin, fluconazole, dexamethasone, and miltefosine	74
12-y-old Caucasian girl	2016	Amphotericin, rifampin, azithromycin, fluconazole, dexamethasone, and miltefosine	105

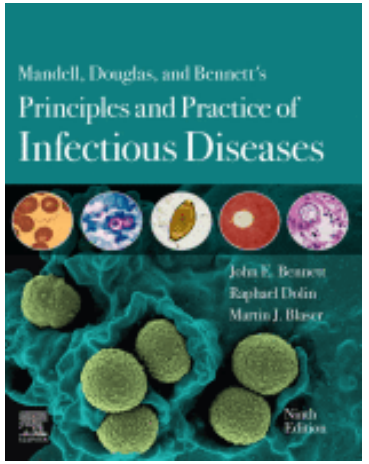
Jahangeer M, Mahmood Z, Munir N, et al. Naegleria fowleri: Sources of infection, pathophysiology, diagnosis, and management; a review. *Clin Exp Pharmacol Physiol*. 2020;47(2):199-212. doi:10.1111/1440-1681.13192

Scope of talk

- Introduction to Neuroparasitology
- Nematode (Roundworm)
  - **Angiostrongyliasis**
  - **Gnathostomiasis**
  - Filariasis
- Trematode (Flatworm – Fluke)
  - Schistosomiasis
  - Paragonimiasis
- Cestode (Flatworm – Tapeworm)
  - **Neurocysticercosis**
- Protozoa
  - **Cerebral Toxoplasmosis**
  - **Cerebral Malaria**
  - Cerebral Amebiasis
    - *Entamoeba histolytica*
  - Primary Amebic meningoencephalitis
    - *Naegleria fowleri*







Neuroparasitology and Tropical Neurology Edited by Hector H. Garcia, Herbert B. Tanowitz, Oscar H. Del Brutto Volume 114,Pages 2-414 (2013)
Textbook of Clinical Neurology. Thai Neurological Society. 2014
Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Ninth Edition
CONTINUUM (MINNEAP MINN) 2021;27(4, NEUROINFECTIOUS DISEASE):943–962
Parasitic diseases of the central nervous system: lessons for clinicians and policy makers. EXPERT REVIEW OF NEUROTHERAPEUTICS, 2016.
Centers for Disease Control and Prevention

Summary of clinical manifestation

Table 2. Characteristics of main parasitic infections of the central nervous system.

Parasite disease	Causative organism	Vector/intermediate host	Mode of transmission	Endemic regions
Taeniasis/Cysticercosis	*Taenia solium*	Pigs, humans	Fecal–oral, ingestion of eggs from human feces (ingestion of larval cyst from pig muscle leads to taeniasis)	Widespread throughout rural areas, with poor sanitation, where humans and pigs cohabitate: Latin America, Africa, Asia
Toxoplasmosis	*Toxoplasma gondii*	Cats, intermediate hosts in nature (including birds and rodents)	Ingestion of oocysts (cat feces) or tissue cysts (undercooked meats), blood transfusion, transplacentally from mother to fetus	Worldwide, greatest burden in Sub-Saharan Africa and Asia
Echinococcosis (Hydatidosis)	*Echinococcus granulosus, Echinococcus multilocularis*	EG: Sheep, goats, cattle, pigs, yaks or other farm animals EM: Small mammals (rodents and lagomorphs)	Ingestion of contaminated soil, water or food, contact with infected animals	Middle East, Europe, Pacific, Latin America; Inuit populations in North America
Schistosomiasis	*Schistosoma japonicum, mansoni*, and *haematobium*	Fresh water snail	Penetration of skin by cercariae in freshwater	Tropical and subtropical areas of Sub-Saharan Africa, Latin America and Asia
Paragonimiasis	*Paragonimus westermani*	Freshwater snails, crustacean-eating mammals	Fecal–oral, raw, undercooked freshwater crustaceans	East and Southeast Asia, West and Central Africa, Central and South America
Malaria	*Plasmodium falciparum*	Vector borne, *Anopheles* mosquito	Insect bite	Tropics from Sub-Saharan Africa, Latin America, Asia and Oceania
Toxocariasis	*Toxocara canis, Toxocara cati*	Cats, humans	Fecal–oral, contaminated soil	Worldwide
Onchocerciasis	*Onchocerca volvulus*	Blackfly (Similium)	Insect bite	West and Central Africa, as well as parts of Central and South America
Chagas disease	*Trypanosoma cruzi*	Triatomine bug	Insect bite	Latin America
African trypanosomiasis	*Trypanosoma brucei gambiense, Trypanosoma brucei rhodesiense*	Tsetse fly	Insect bite	Africa

Summary of mechanism of CNS invasion

Table 2.1

Portals of entry into the host, cell invasion, and routes for spread to the CNS of selected human parasites

Parasite	Mode of entry	Host cell interaction	Route of spread to CNS	BBB interaction
Schistosoma spp.	Skin, larval penetration	Extracellular worms	Bloodstream as migrating worms or seeding of eggs	Egg embolization
Plasmodium spp.	Skin, mosquito bite	Traversal: macrophages, hepatocytes PV: erythrocytes, hepatocytes	Bloodstream in erythrocytes	Infected erythrocytes attach to endothelia
Babesia	Skin, tick bite	Erythrocytes	Bloodstream	Infected erythrocytes attach to endothelia
Taenia solium	Intestine, larval penetration	Extracellular larvae	Bloodstream	Lodge in small cerebral vessels
Toxocara canis	Intestine	Extracellular larvae	Bloodstream	Choroid plexus Cross BBB
Angiostrongylus cantonensis	Intestine	Extracellular larvae	Bloodstream	Cross BBB
Gnathostoma spinigerum	Intestine	Extracellular larvae	Along peripheral nerve roots	Unclear
Acanthamoeba	Respiratory tract, skin	Free-living ameba	Bloodstream	Cross BBB
Balamuthia mandrillaris	Respiratory tract, skin	Free-living ameba	Bloodstream	Degrade and cross BBB
Trypanosoma brucei	Skin, tsetse fly bite	Extracellular parasites	Bloodstream	Choroid plexus, CVOs Cross BBB similar to T cells
Toxoplasma gondii	Intestinal epithelia	PV: all karyotic cells	Bloodstream in monocytes	Cross in infected monocytes
Trypanosoma cruzi	Skin, bug bite	Escape from PV to cytosol: various cells incl. muscle, autonomic neurons, macrophages, glia	Bloodstream	Cross BBB, probably within monocytes
Encephalitozoon cuniculi	Respiratory, intestinal tracts	PV: various cells incl. macrophages, glia	Bloodstream	Unclear
Naegleria fowleri	Nasal cavity	Free-living ameba	Olfactory route	None

PV, parasitophorous vacuole.

Summary of treatment

Table 3. Currently available antiparasitic drug regimens for parasitic infections of the CNS.

Neurocysticercosis	• Albendazole with corticosteroids • Praziquantel (alternative to albendazole) with corticosteroids • Combined albendazole/praziquantel with corticosteroids if >2 active parenchymal cysts
Toxoplasmosis	• Sulfadiazine + pyrimethamine with leucovorin • Clindamycin (or atovaquone) + pyrimethamine with leucovorin (alternative) • Trimethoprim-sulfamethoxazole (alternative)
Echinococcosis	• Albendazole or mebendazole (alone or with surgery)
Schistosomiasis	• Praziquantel (after starting corticosteroid treatment)
Paragonimiasis	• Praziquantel • Triclabendazole
Cerebral malaria	Severe falciparum malaria • IV artesunate • IV quinine dihydrochloride or quinidine gluconate ◦ + doxycycline, tetracycline, or clindamycin
Toxocariasis	• Albendazole with corticosteroids • Mebendazole (alternative to albendazole) with corticosteroids
Onchocerciasis	• Ivermectin • Doxycycline
American trypanosomiasis	Acute or chronic infection • Benznidazole • Nifurtimox
African trypanosomiasis	Early infection • *Trypanosoma brucei gambiense* ◦ Pentamidine ◦ Suramin (alternative) • *Trypanosoma brucei rhodesiense* ◦ Suramin Late infection • *Trypanosoma brucei gambiense* ◦ Eflornithine + nifurtimox ◦ Eflornithine monotherapy ◦ Melarsoprol (alternative) with corticosteroids • *Trypanosoma brucei rhodesiense* • Melarsoprol
Angiostrongyliasis	• None (corticosteroids and symptomatic treatment only)

Take Home Massage

- Parasitic infection needs high clinical suspected
  - Combination – Host + Risk factors
  - Understanding life cycle/mode of transmission
- Diagnosis is a challenging! >> appropriate test is needed
- Appropriate treatment
  - Some are self-limited
  - Antiparasitic agent (specific dose & duration)
  - Might consider role of steroid
  - Surgery?

THANK YOU FOR YOUR ATTENTION