NEUROCYSTICERCOSIS

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Agenda

1 Luisa Alviz

1. Epidemiology
2. Physiopathology
3. Clinical Presentation
4. Risk of Calcification

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Diagnosis

1. Neuroimaging
2. Laboratory diagnosis
3. Diagnostic criteria

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Treatment

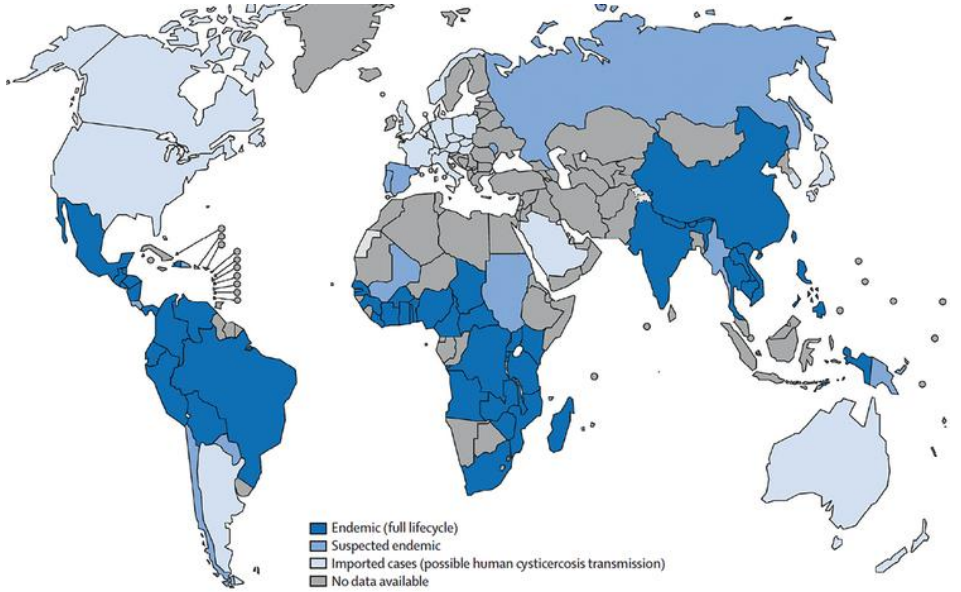
1. Antiparasitic therapies
2. Steroids
3. Antiseizure medication

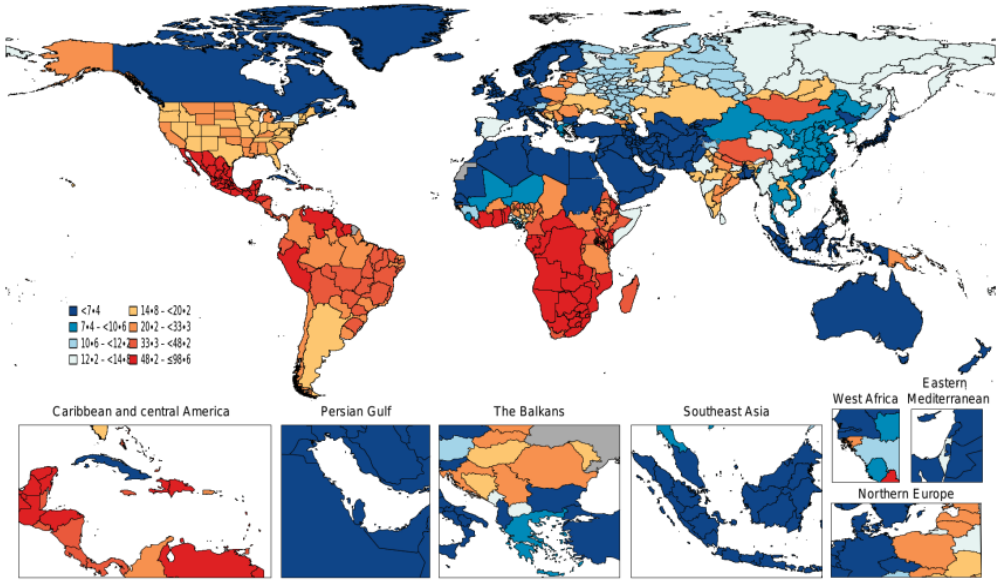
Epidemiology

Endemic in most **Latin American countries, Sub-Saharan Africa, and some regions in Asia**.

NCC is a major cause of epilepsy in developing countries.

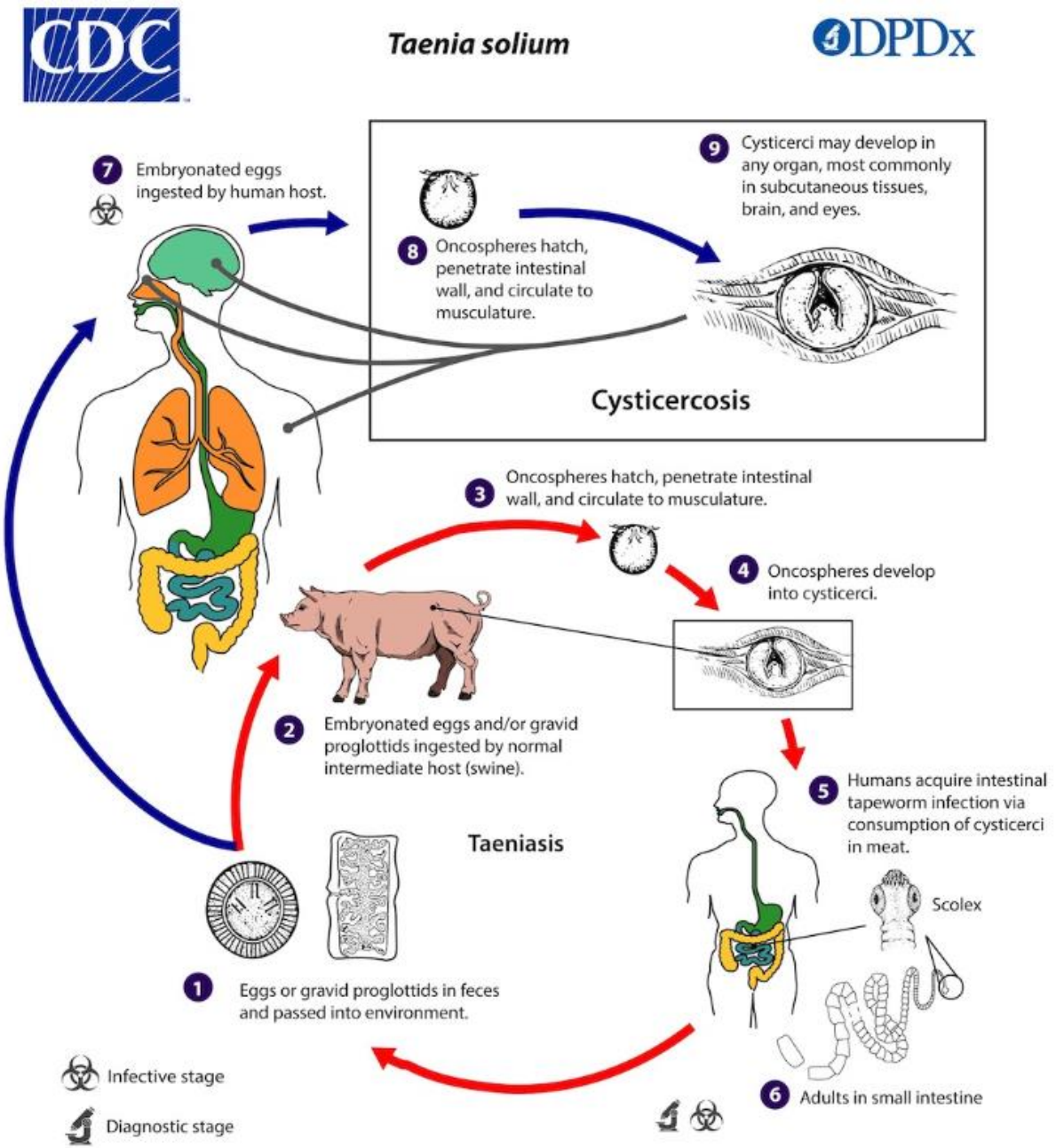
GBD of cysticercosis in 2021: 1.24 million DALYS. In Latin America and the Caribbean= highest burden → 195,000 DALYS.



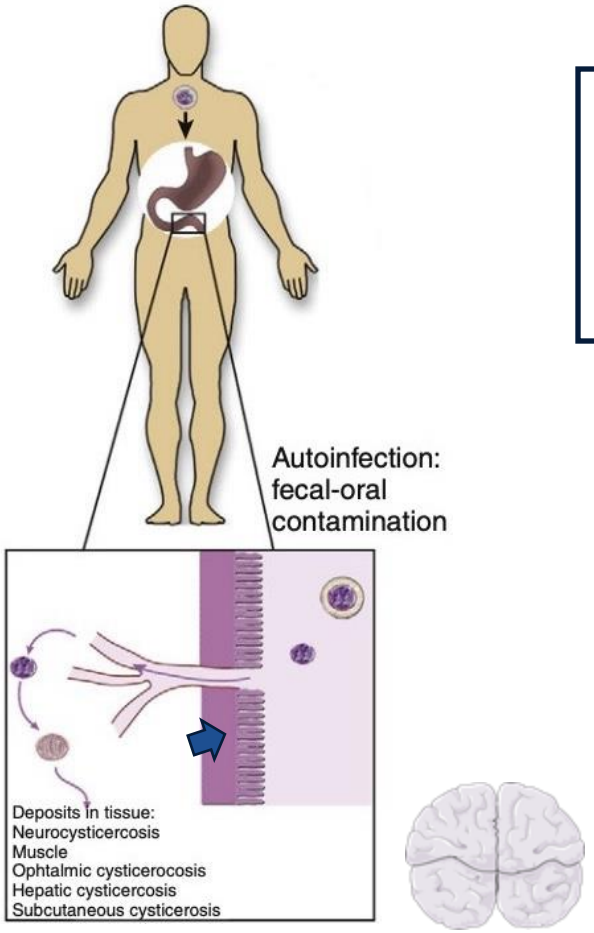


Physiopathology

- **Pigs:** Intermediate
- **Humans:**
  A. Definite: ingestion of infected pork meat.
  B. Intermediate: ingestion of eggs.



CNS invasion



CNS invasion occurs when humans serve as the intermediate host of *T. solium*. In this context, oncospheres penetrate the CNS, where they develop into cysticerci and progress through subsequent stages.

Vesicular

Colloidal

Granular

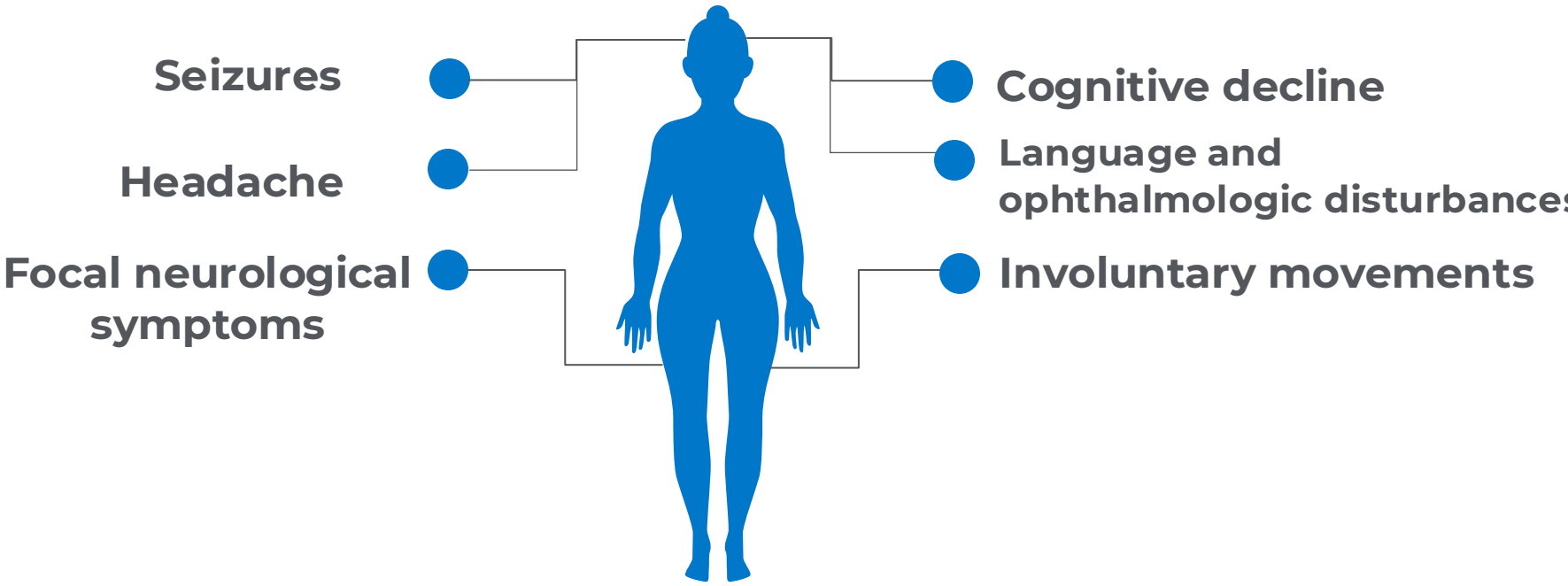
Calcified

Clinical Presentation

Most cases are asymptomatic

Clinical course: subacute or Chronic

Presentation depends on: Location and immune system reaction.



Risk of Calcification

Predictors of calcification:

- Cysts larger than 14 mm
- Edema at baseline
- More than 24 months with seizures
- Mild antibody response
- Increased dose albendazole regime
- Lower doses of dexamethasone
- Not receiving antiparasitic retreatment
- Complete cure

Table 2. Risk Ratios for the Development of Residual Calcifications After Antiparasitic Treatment in Patients With Viable Brain Parenchymal Neurocysticercosis

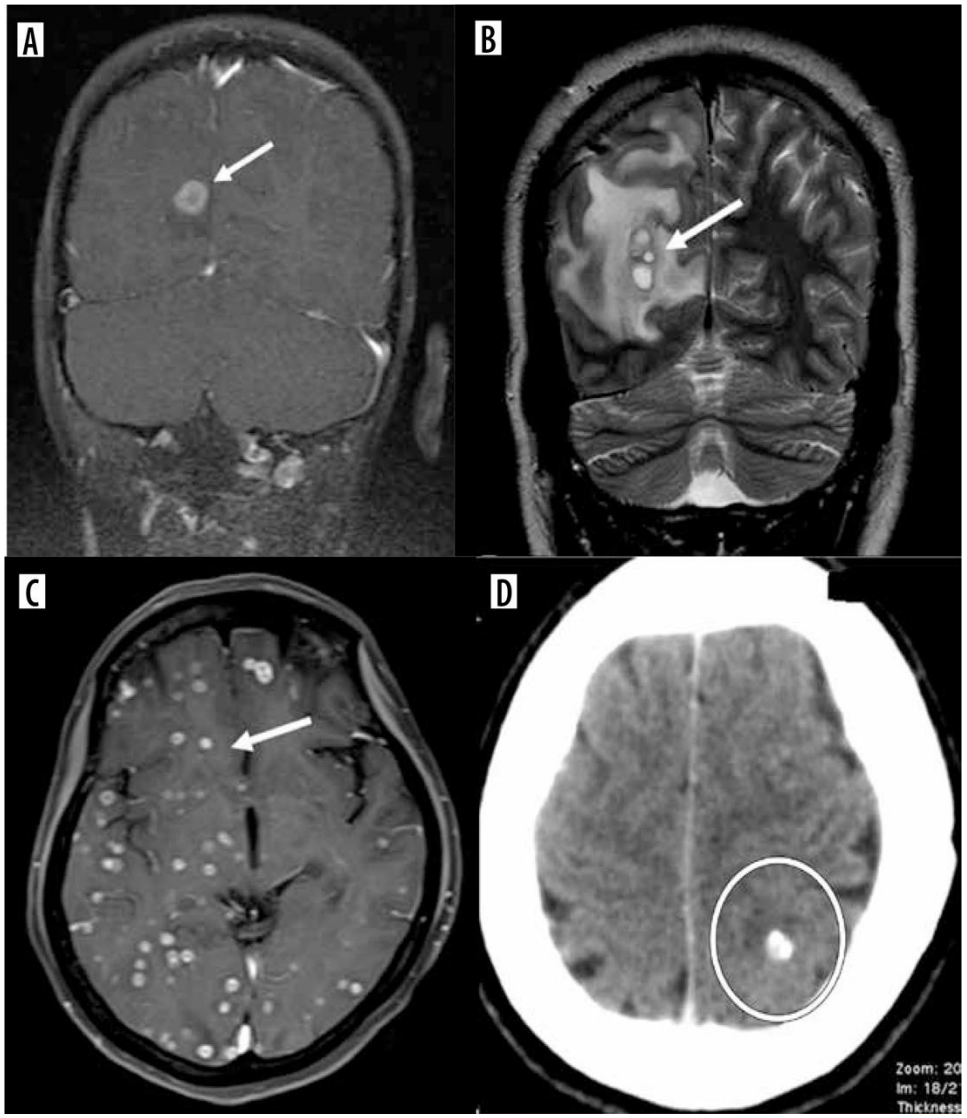
Study Variable	Calcified/Cysts Resolved (%)	Univariate Models RR (95% CI)	*P* Value	Multivariate Model 1[b] RR (95% CI)	*P* Value	Multivariate Model 2[c] RR (95% CI)	*P* Value
Cyst level							
Cyst size, mm							
≤14	166/453 (36.6)	Ref.		Ref.		Ref.	
>14	22/44 (50.0)	1.35 (1.14–1.60)	<.001	1.30 (1.07–1.57)	.007	1.34 (1.02–1.75)	.035
Cyst content							
Clear	158/435 (36.3)	Ref.					
Turbid	30/62 (48.4)	1.30 (.18–2.15)	.313				
Cyst location							
Frontal lobe	67/172 (39.0)	1.02 (.78–1.35)	.866				
Parietal lobe	60/182 (33.0)	.82 (.67–1.00)	.047				
Occipital lobe	27/63 (42.9)	1.13 (.85–1.52)	.402				
Temporal lobe	36/98 (36.7)	.98 (.70–1.38)	.902				
Cyst edema							
No	125/365 (34.3)	Ref.		Ref.		Ref.	
Yes	63/132 (47.7)	1.37 (1.17–1.62)	<.001	1.36 (1.16–1.59)	<.001	1.39 (1.05–1.85)	.023
Patient level							
Age (tertiles), y							
16–25	67/177 (37.9)	Ref.					
26–35	56/156 (35.9)	.98 (.69–1.38)	.899				
>35	65/164 (39.6)	1.03 (.81–1.32)	.796				
Sex							
Female	63/172 (36.6)	Ref.					
Male	125/325 (38.5)	1.04 (.83–1.30)	.733				
Disease time, mos							
≤24	79/229 (34.5)	Ref.				Ref.	
>24	109/268 (40.7)	1.17 (1.13–1.21)	<.001			1.25 (1.08–1.46)	.003
Number of cysts							
1–2	38/78 (48.7)	Ref.		Ref.			
3 or more	150/419 (35.8)	.74 (.44–1.25)	.261				
Number of calcifications at baseline							
None	39/98 (39.8)	Ref.					
1 or more	149/399 (37.3)	.95 (.55–1.69)	.891				
Electroimmunotransfer blot bands							
≥4	140/388 (36.1)	Ref.		Ref.		Ref.	
≤3	48/109 (44.0)	1.21 (1.14–1.28)	<.001			1.14 (1.02–1.27)	.020
Previous APT							
No	173/440 (39.3)	Ref.					
Yes	15/57 (26.3)	.69 (.36–1.30)	.249				
Previous antiepileptic drugs							
No	92/254 (36.2)	Ref.					
Yes	96/243 (39.5)	1.11 (.99–1.23)	.064				
APT scheme							
ABZ + Praziquantel	78/224 (34.8)	Ref.				Ref.	
Standard ABZ	73/190 (38.4)	1.09 (.84–1.41)	.525			1.04 (.71–1.51)	.861
Increased ABZ	37/83 (44.6)	1.27 (1.18–1.36)	<.001			1.26 (1.14–1.39)	<.001
Days with APT							
10	136/361 (37.7)	Ref.	Ref.				
14	52/136 (38.2)	.99 (.88–1.13)	.958				
Dose of DXM, mg/d							
>6.5	71/217 (32.7)	Ref.	Ref.			Ref.	Ref.
≤6.5	117/280 (41.8)	1.26 (1.04–1.52)	.018			1.36 (1.02–1.81)	.037
Days with DXM							
10–12	163/429 (38.0)	Ref.	Ref.				
28	25/68 (36.8)	.95 (.86–1.06)	.366				
Cyst cure and retreatment							
Incomplete cure and retreated	19/66 (28.8)	Ref.	Ref.			Ref.	Ref.
Complete cure and not retreated	111/280 (39.6)	1.41 (1.21–1.63)	<.001			1.48 (1.29–1.71)	<.001
Incomplete cure and not retreated	58/151 (38.4)	1.33 (1.16–1.53)	<.001			1.45 (1.08–1.93)	.012

Diagnosis

- Dx. is still a challenge
- Histological confirmation is not possible in most cases
- Dx. relies on neuroimaging and immunodiagnostic tests
- Poor specificity of neuroimaging
- Suboptimum predictive values of the immunodiagnostic tests in endemic settings

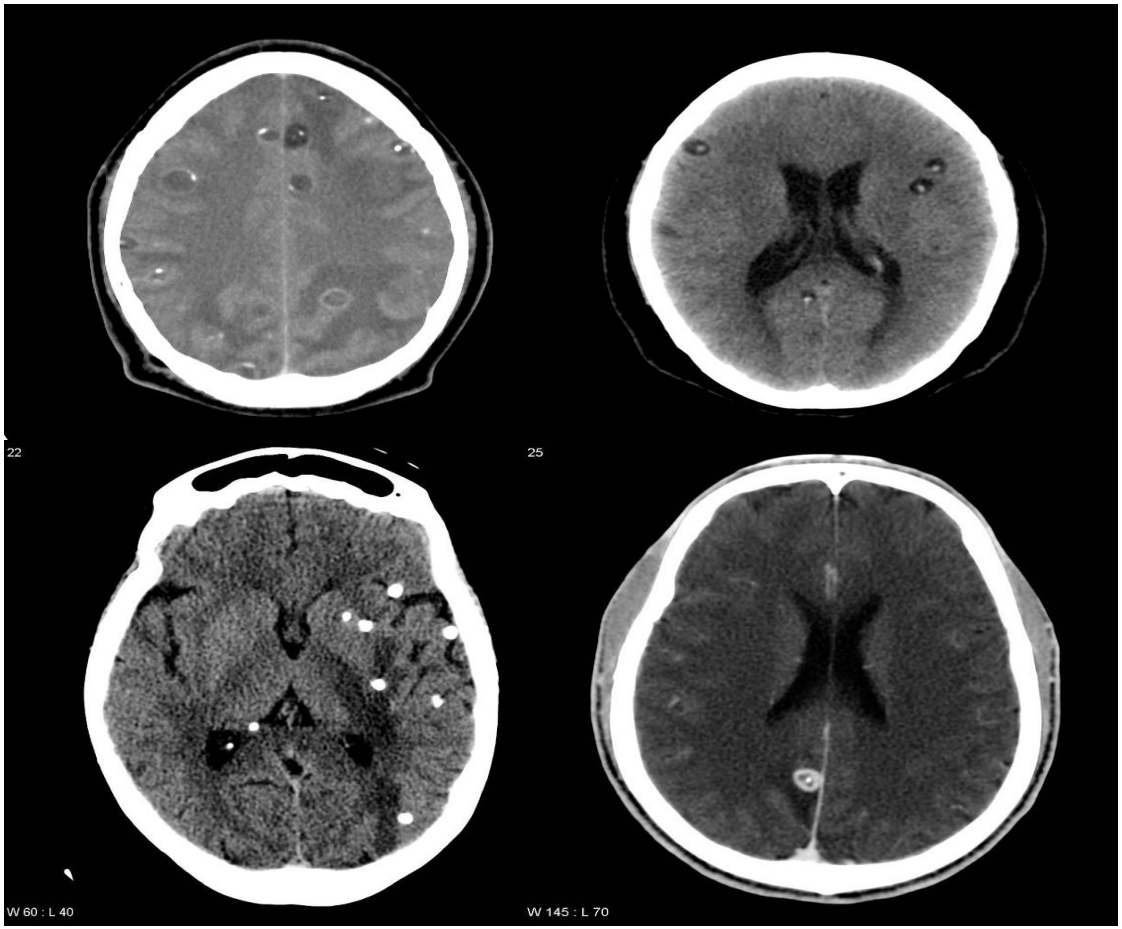
Neuroimaging

- Brain CT and MRI
- Morphology, localization of cysts, number and size, burden of infection, stage of the cysts, the presence of surrounding inflammation
- Collateral alterations, such as hydrocephalus or other signs



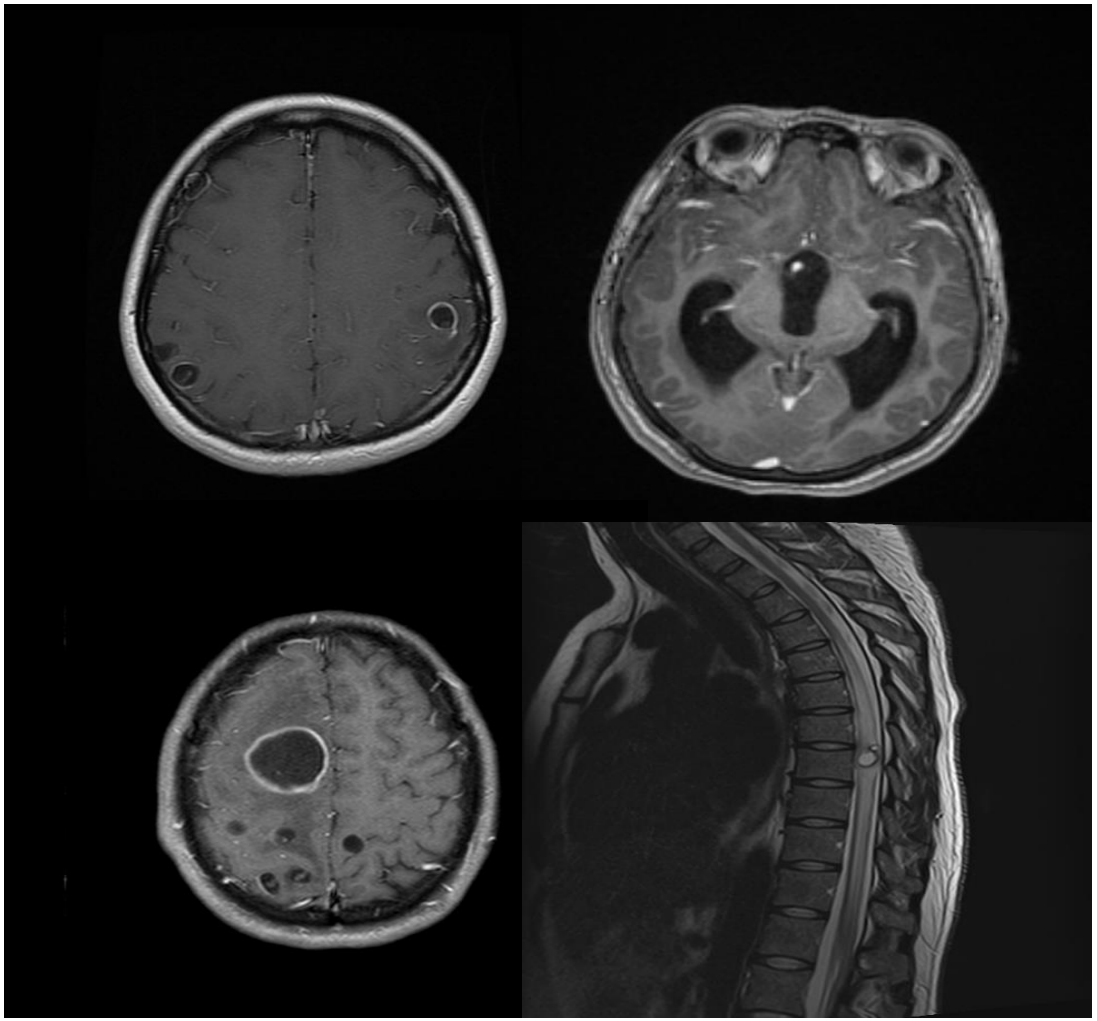
Brain CT Scan

- Best for detecting calcifications



MRI Brain

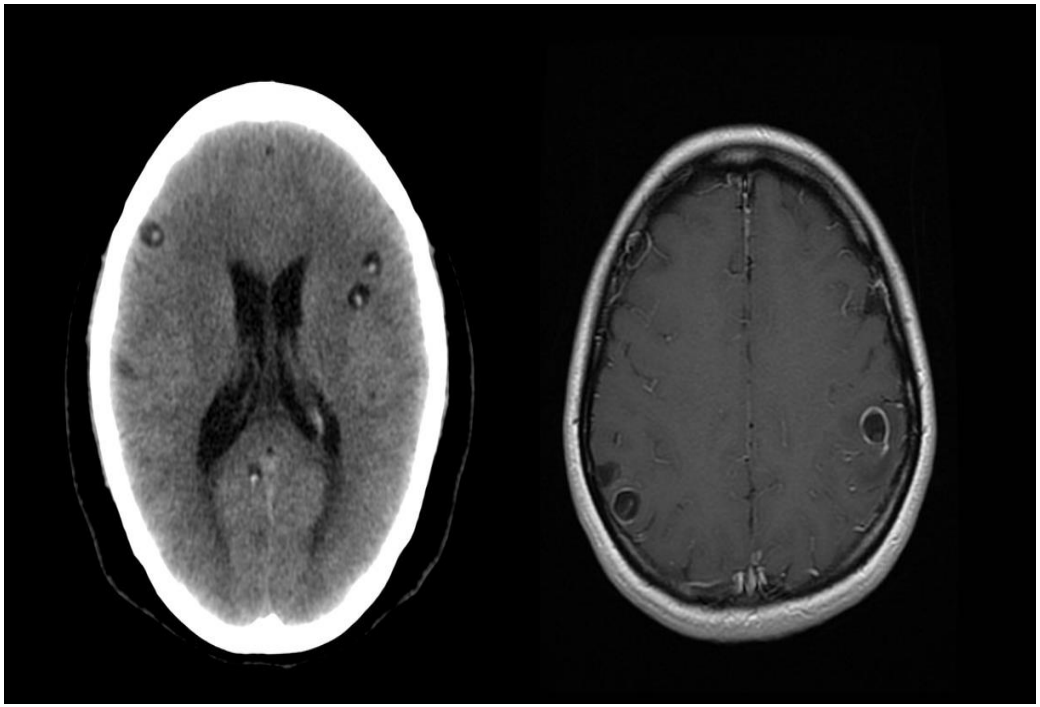
- Superior for intraventricular, subarachnoid, and spinal NCC
- Can identify the cyst wall, scolex, and surrounding inflammation
- Use 3D CISS/FIESTA sequences for ventricular cysts



The evolution of parenchymal cysts

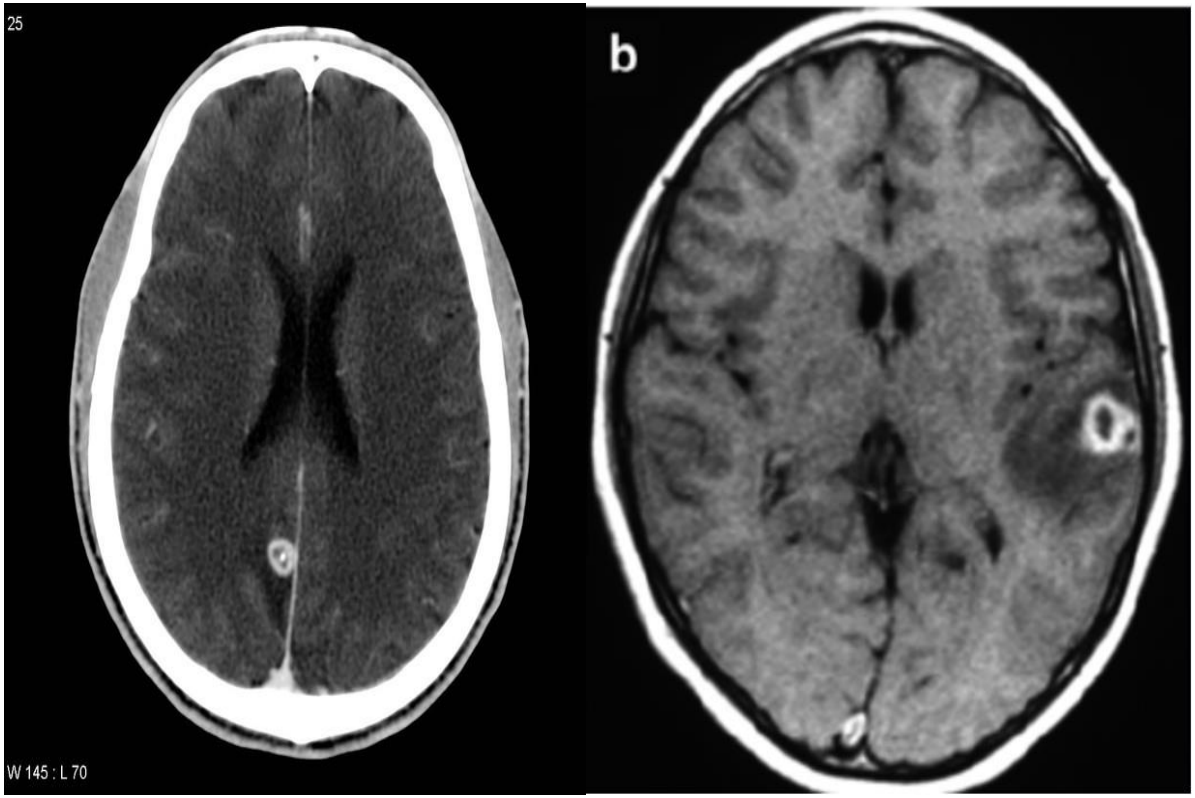
1. Live vesicular cysts

- Small and rounded lesions with little or no pericystic oedema and are not enhanced with contrast
- Frequently show the tapeworm scolex as an internal asymmetric nodule in the cyst (hole-with-dot)
- Spherical hypodense lesion on CT scan and as a CSF-like signal on MRI
- Both CT and MRI can show the invaginated scolex



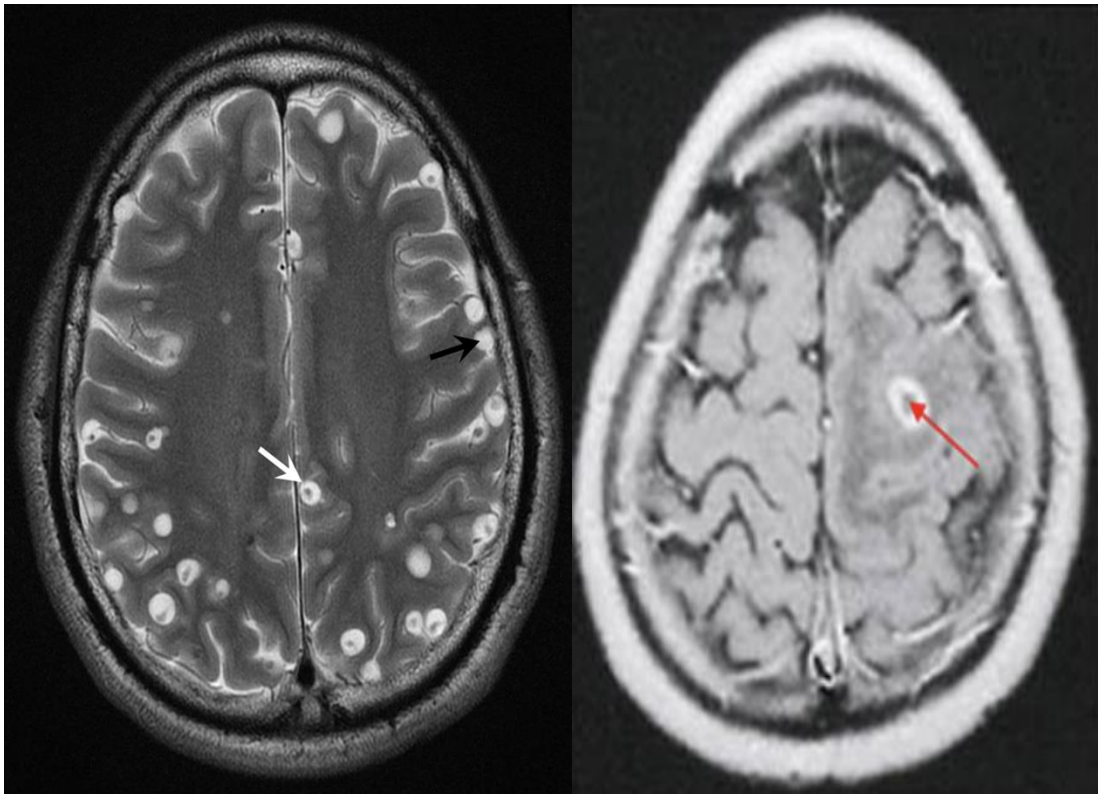
2. Colloidal stage

- Poorly defined borders
- Surrounded by edema
- Marked ring or nodular contrast enhancement
- DWI and ADC map



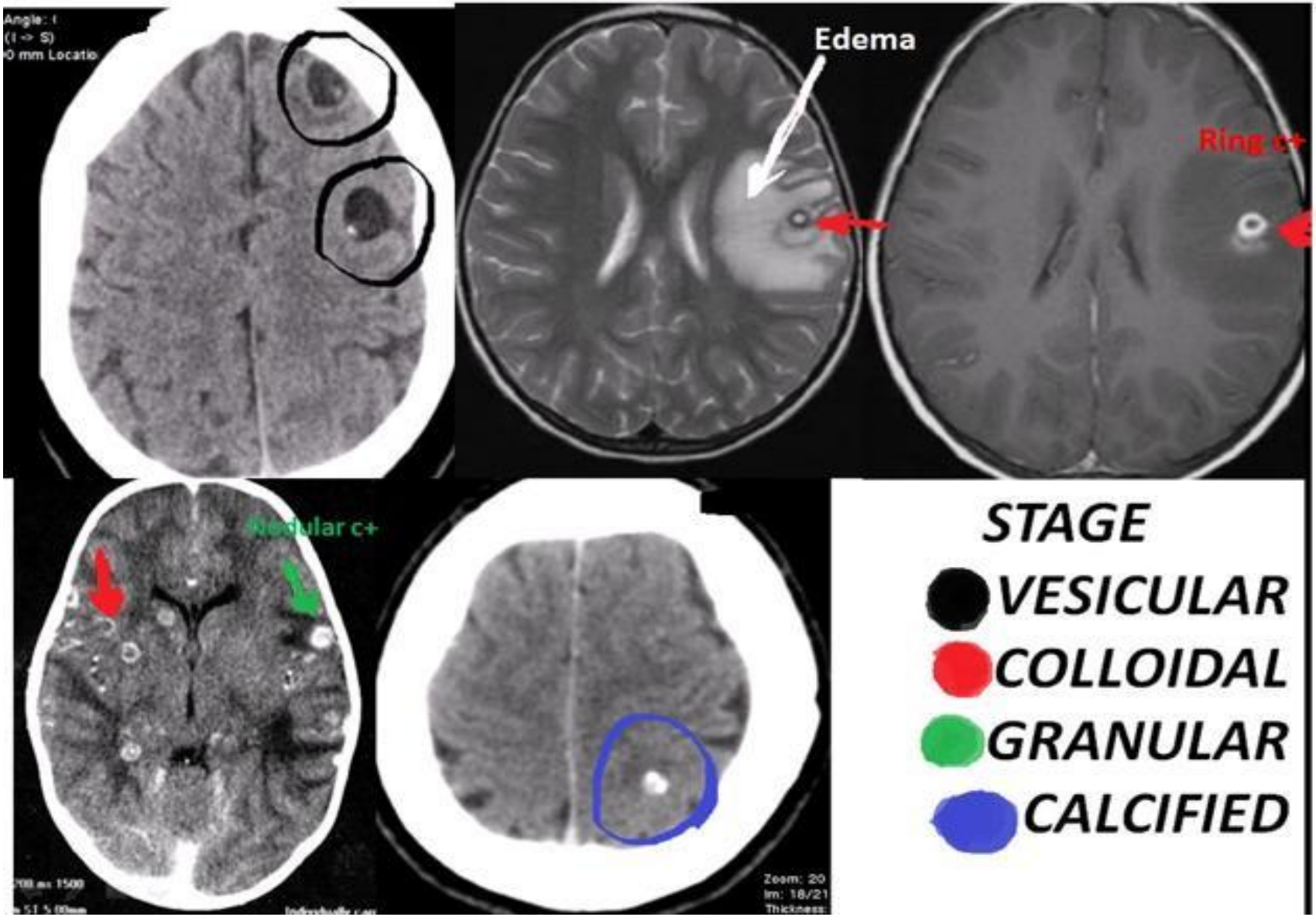
3. Granular stage

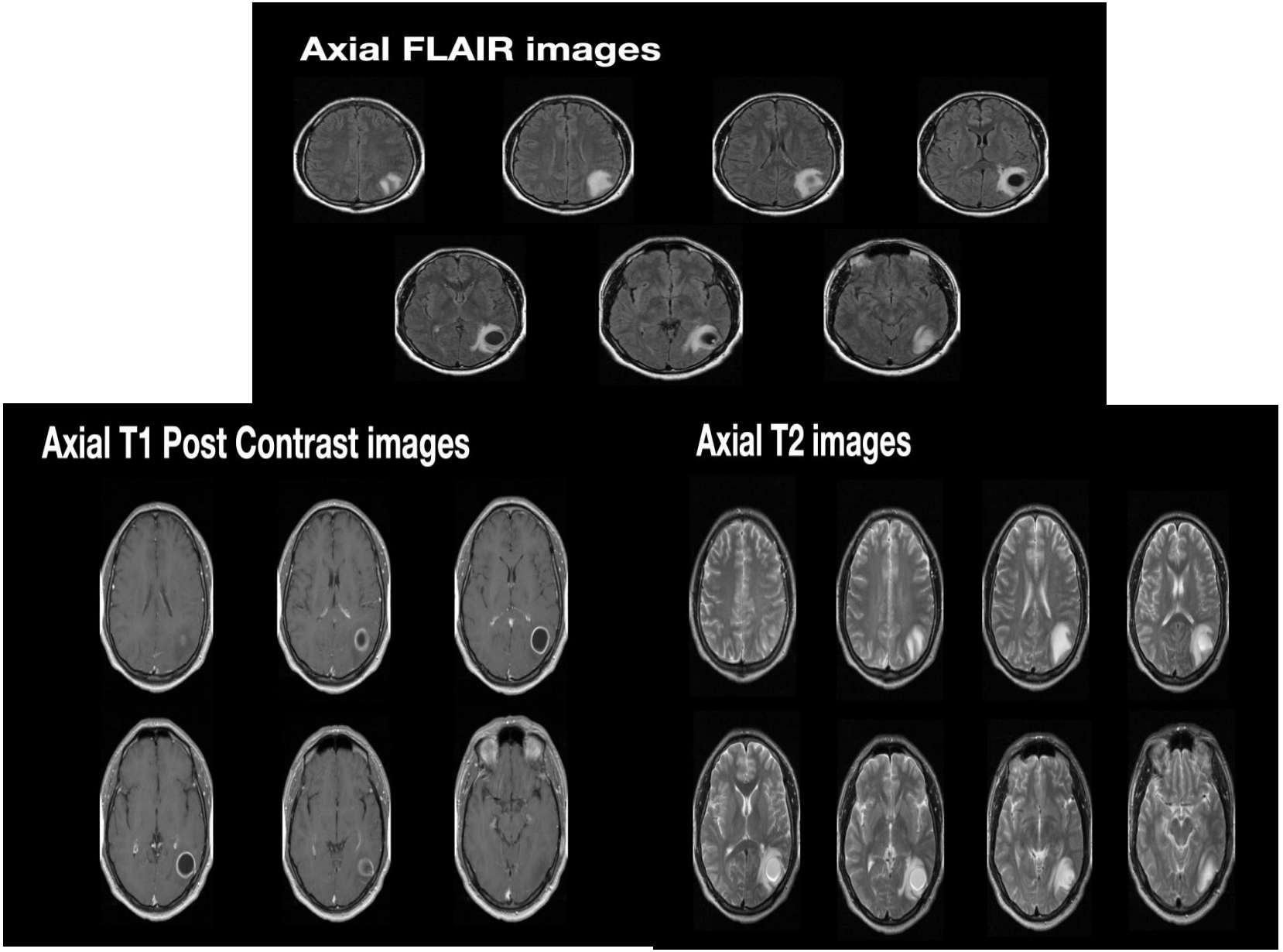
- Begins to be reduced in size
- Walls become thicker
- Mineralization with calcium salts
- Transformed into coarse granules



4. Calcified nodular stage

- Cyst attains complete mineralization
- Visible on CT as non-enhancing hyperdense nodules
- Usually without peripheral oedema
- Susceptibility-weighted image protocols may show

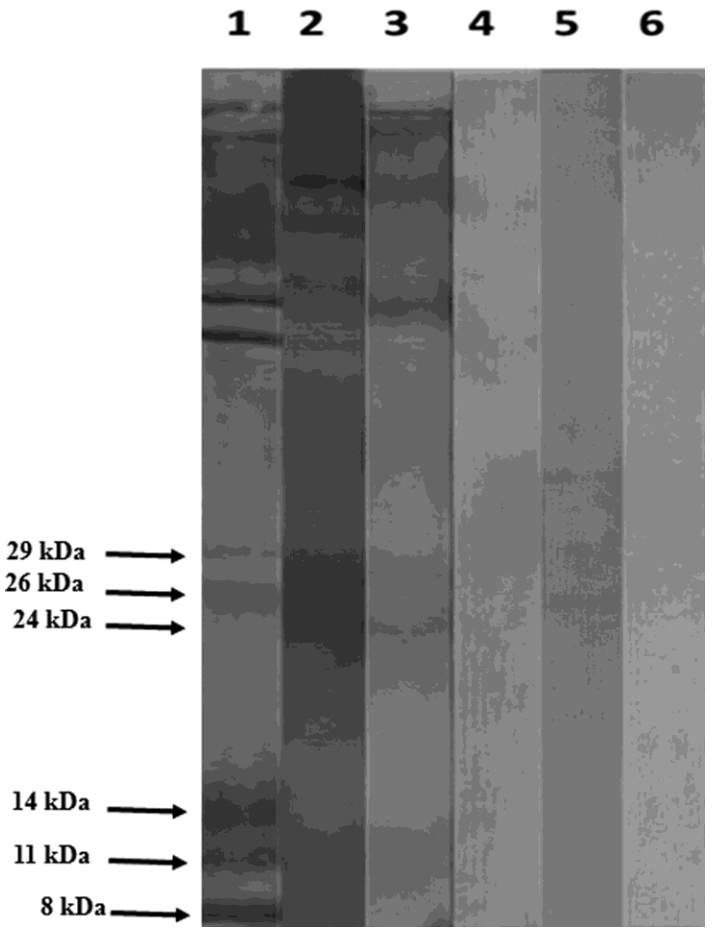

Edema
Ring c+
Nodular c+
STAGE
VESICULAR
COLLOIDAL
GRANULAR
CALCIFIED


Axial FLAIR images
Axial T1 Post Contrast images
Axial T2 images

Laboratory Diagnosis

- ✓ **Enzyme-linked Immunoelectrotransfer blot assay (EITB)**

  - Uses lentil lectin-purified parasite glycoprotein antigen (LLGP)
  - Gold standard, >95% specificity and sensitivity for multiple lesions
  - Sensitivity drops in cases with a single cyst
  - Antibodies can be detected on EITB as early as 5 weeks after infection
  - Not affected by HIV infection or immunosuppressive therapies
  - Complex, longer time of execution, and cost



ELISA

- ✓Can detect an antibody and an antigen
- ✓Antigen detection using a monoclonal antibody-based ELISA can confirm the presence of living parasites and monitor the effect of antiparasitic treatment
- ✓Its sensitivity is lower, and it is frequently negative in patients with one or a few living parasites and calcified disease
- ✓ 89% sensitive and 93% specific for active neurocysticercosis infections in CSF.
- ✓Alternative when the EITB test is unavailable.

CSF analysis

- ✓ Lymphocytic pleocytosis, elevated protein, reduced glucose
- ✓ Eosinophilia (37%)
- ✓ Specific antigens /antibodies detected by ELISA or EITB

Revised Diagnostic Criteria (Del Brutto et al., 2017)

✓ Absolute criteria

- Histological demonstration of the parasite from a 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
  - Multilobulated cystic lesions in the subarachnoid space
  - Typical parenchymal brain calcifications
- ✓ Confirmatory neuroimaging criteria
  - Resolution of cystic lesions after cysticidal drug therapy
  - Spontaneous resolution of single small enhancing lesions
  - Migration of ventricular cysts documented on sequential neuroimaging studies
- ✓ 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
  - Cysticercosis outside the central nervous system
  - Evidence of a household contact with T. solium infection

- ✓ Minor clinical/exposure
  - Clinical manifestations suggestive of neurocysticercosis
  - Individuals coming from or living in an area where cysticercosis is endemic

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

Antiparasitic therapies

- 1-2 viable cysts[1]
  - monotherapy with **Albendazole**: 15 mg/kg/d divided in 2 doses (max 1200mg/d) for 10-14 days
  - Retreat if cystic lesion persists after 6 months
- >2 viable cysts[1]
  - dual therapy with **Albendazole + Praziquantel**: 50 mg/kg/d divided in 3 doses for 10-14 days
- Single enhancing lesion (SEL)[1]: 7 days of Albendazole + steroids vs. symptomatic treatment
- Cysticercotic encephalitis[1]: raised ICP and diffuse edema secondary to multiple degenerating cysts
  - Control intracranial hypertension/hydrocephalus, steroids/surgical approach
  - Avoid antiparasitic drugs
- Calcified lesions[1] do not require antiparasitic therapy

	ABZ + PZQ (n=39)	ABZ 15 mg/kg/d(n=41)	ABZ 22.5 mg/kg/d (n=38)	*P*
Mean cysts Baseline	**9.0**	**6.8**	**7.1**	**0.25**
Mean 180 d	**0.6**	**5.3**	**3.7**	**<.001**
Cysts resolved	**94%**	**21%**	**48%**	**<.001**
Patient cured	**68%**	**5%**	**25%**	**<.001**

Garcia et al Lancet Infect Dis 2014

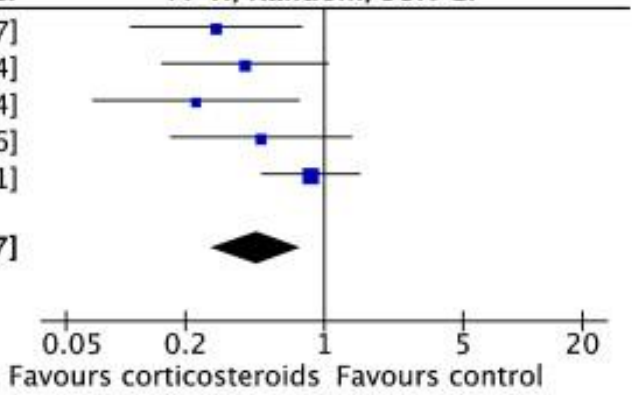
Steroids

Outcome 1: Seizure recurrence

Study or Subgroup	Corticosteroids Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Garg 2006	4	30	14	30	18.2%	0.29 [0.11, 0.77]
Kishore 2007	5	47	12	45	18.9%	0.40 [0.15, 1.04]
Mall 2003	3	49	13	48	14.2%	0.23 [0.07, 0.74]
Prakash 2006	4	25	9	27	16.9%	0.48 [0.17, 1.36]
Singla 2011	16	62	19	63	31.8%	0.86 [0.49, 1.51]
Total (95% CI)		**213**		**213**	**100.0%**	**0.46 [0.27, 0.77]**
Total events	32		67			

Heterogeneity: $Tau^2 = 0.15$; $Chi^2 = 6.75$, df = 4 (P = 0.15); $I^2 = 41\%$

Test for overall effect: Z = 2.91 (P = 0.004)

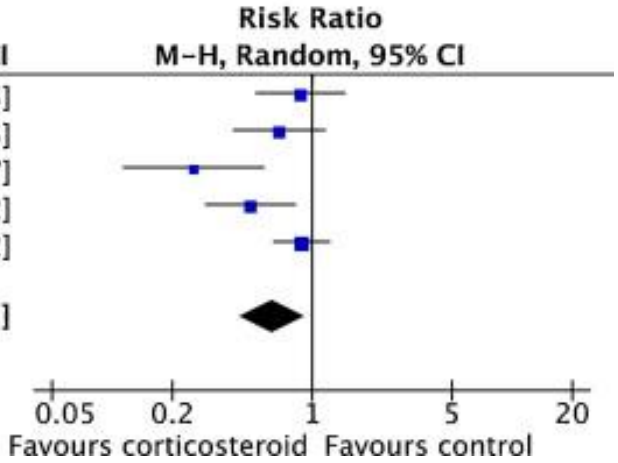


Outcome 2: Lesion persistence in imaging studies

Study or Subgroup	Corticosteroids Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Garg 2006	14	30	16	30	20.4%	0.88 [0.53, 1.45]
Kishore 2007	15	47	21	45	20.0%	0.68 [0.41, 1.15]
Mall 2003	6	49	23	48	13.1%	0.26 [0.11, 0.57]
Prakash 2006	10	25	22	27	20.3%	0.49 [0.29, 0.82]
Singla 2011	31	58	35	58	26.3%	0.89 [0.64, 1.22]
Total (95% CI)		**209**		**208**	**100.0%**	**0.63 [0.43, 0.92]**
Total events	76		117			

Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 11.29$, df = 4 (P = 0.02); $I^2 = 65\%$

Test for overall effect: Z = 2.37 (P = 0.02)



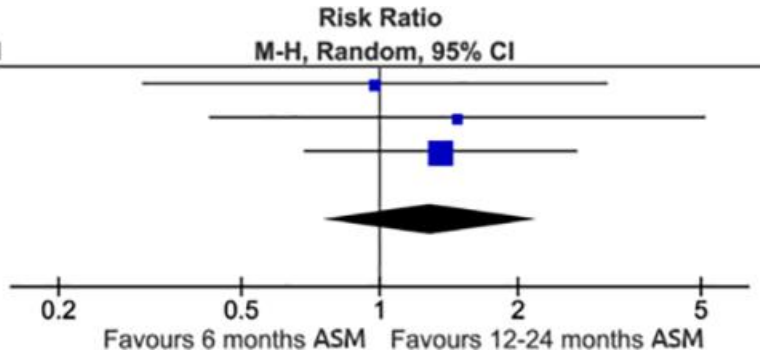
Cuello-Garcia et al. International Journal of Infectious Diseases, 2013

Antiseizure medications

- Phenytoin and Carbamazepine most described in the literature
  - Clobazam vs. Phenytoin[6]
  - Carbamazepine vs. Levetiracetam[7]
  - Lacosamide vs. Oxcarbazepine[8]

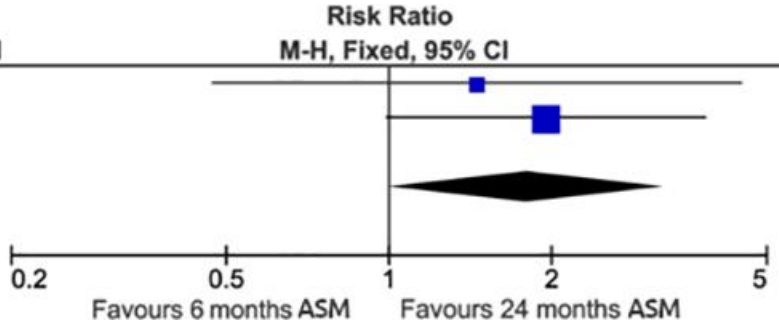
Study or Subgroup	6 months ASM Events	Total	12-24 months ASM Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Gupta et al 2002	5	41	5	40	20.8%	0.98 [0.31, 3.11]
Thussu et al 2002	8	47	3	26	18.3%	1.48 [0.43, 5.08]
Verma et al 2006	16	98	13	108	60.9%	1.36 [0.69, 2.67]
Total (95% CI)		186		174	100.0%	1.29 [0.76, 2.18]
Total events	29		21			

Heterogeneity: Tau² = 0.00; Chi² = 0.29, df = 2 (P = 0.87); I² = 0%
Test for overall effect: Z = 0.93 (P = 0.35)



Study or Subgroup	6-12 months ASM Events	Total	24 months ASM Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Thussu et al 2002	8	22	3	12	31.7%	1.45 [0.47, 4.48]
Verma et al 2006	14	33	10	46	68.3%	1.95 [0.99, 3.84]
Total (95% CI)		55		58	100.0%	1.79 [1.00, 3.20]
Total events	22		13			

Heterogeneity: Chi² = 0.19, df = 1 (P = 0.66); I² = 0%
Test for overall effect: Z = 1.98 (P = 0.05)



Abraham et al. PLoS neglected tropical diseases, 2021

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2 Temesgen Nurye

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2. Revised diagnostic criteria for neurocysticercosis, O H Del Brutto et al
3. Proposed diagnostic criteria for neurocysticercosis, OR Del Brutto et al
4. Current Diagnostic Criteria for Neurocysticercosis, Carolina Guzman et al

3 Anlys Oliveira

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