INTRODUCCIÓN A LAS

NEUROINFECCIONES

Dr. Perfecto Oscar González Vargas

Neurólogo

INNN-HMP MP- MDS- SOMENE

Conceptos

- **Meningitis**. Meninges. Bacteriana, Fímica, Viral, Química
- **Encefalitis**. Encéfalo. Viral.
- Meningoencefalitis. No me agrada. Es un término neuropatológico.

Sintomatología

- **Meningitis.** Signos Meníngeos.
- **Encefalitis**. Signos Encefálicos
- **Neuroinfecciones**. Pobres Datos Focales

Sintomatología

- **Síndrome de Hipertensión Endocraneal**
- **Síndrome Febril**
- **Crisis Convulsivas**
- **Estado Confusional**
- **Ausencia de Focalización**

Signología

- **Síndrome de Hipertensión Endocraneal.**

  Papiledema. Bordes papilares difuminados, pérdida de la excavación fisiológica, drusas, pérdida del pulso venoso…

  Deterioro Rostrocaudal.

  Herniación Cerebral.

Signología

- **Signos Meníngeos**. Rigidez nucal, Kerning, Brudzinsky (cefálico, podálico).

- **Datos Focales**. Escasos. III NC, VI NC

	Non-cirrhotic (n = 573)		Cirrhotic (n = 29)		
	n/total	%	n/total	%	p
Length of disease >4 days	92/566	16	9/28	32	0.029
Mean age (years)	49.6 ± 19		55.8 ± 12		NS
Gender (male)	255/573	44	13/29	44.8	NS
Fever	509/544	93.6	24/26	92	NS
Headache	455/528	86	17/23	73.9	NS
Nuchal rigidity	514/559	91.9	21/28	75	0.008
Vomiting	394/522	75.5	16/27	59	NS
Obtunded-comatose[b]	427/568	75	25/28	89	NS
Hemiparesis	58/567	10	3/28	10.7	NS
Seizures	95/569	16.7	4/26	15	NS
Shock	43/573	7.5	4/29	13.8	NS
Escherichia coli aetiology	7/573	1	5/29	17	0.000
Listeria monocytogenes aetiology	28/573	4.9	5/29	17	0.017
Neisseria meningitidis aetiology	223/573	38.9	6/29	20.6	0.049
Streptococcus pneumoniae aetiology	178/573	31	8/29	27.5	NS
Unknown aetiology	72/573	12.5	1/29	3	NS

Cabellos 2008 *Clin Microbiol Infect* 14:35-40

THE SOCIETY OF NEUROLOGICAL SURGEONS

ICP Management

The Society of Neurological Surgeons Bootcamp

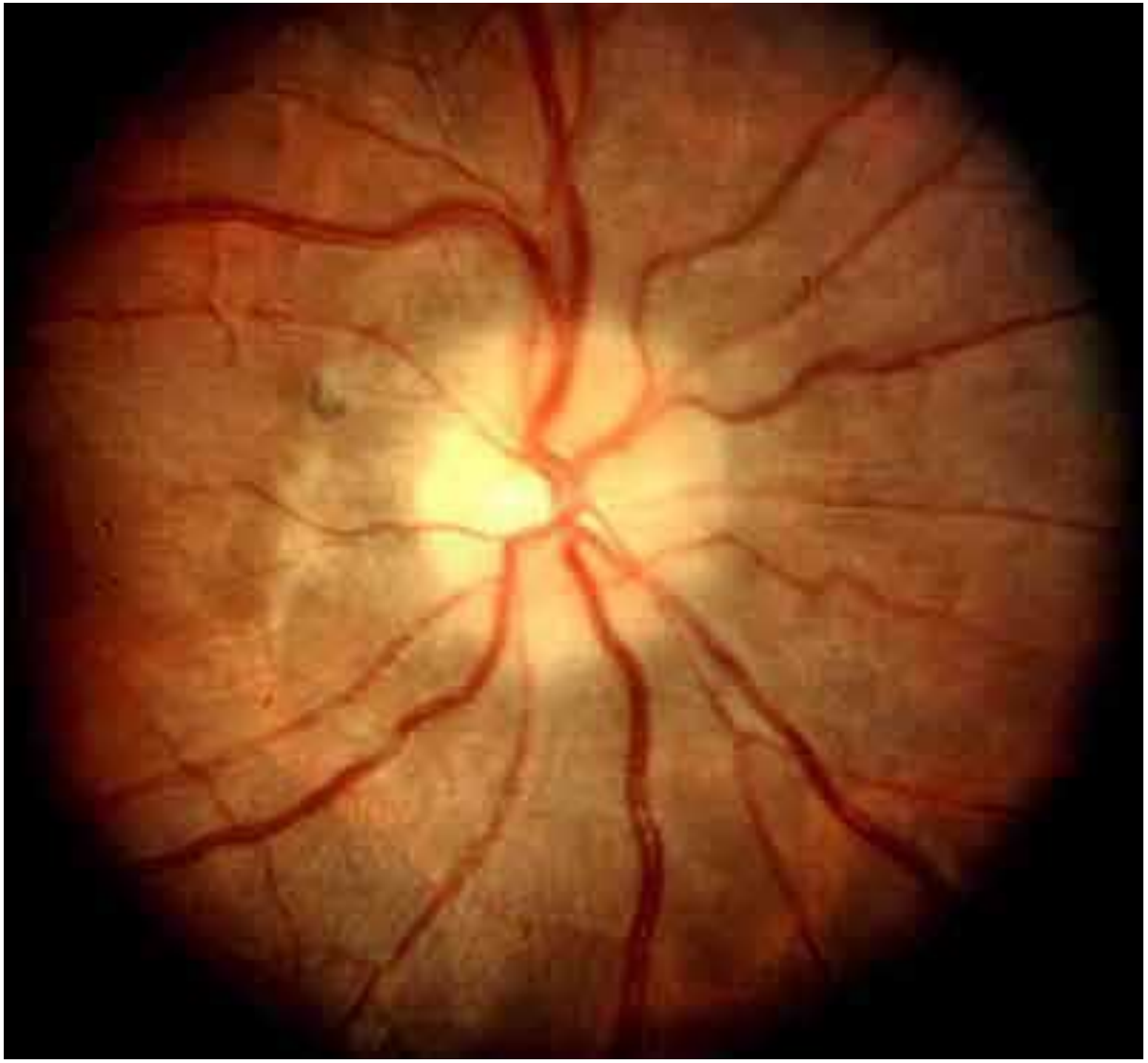
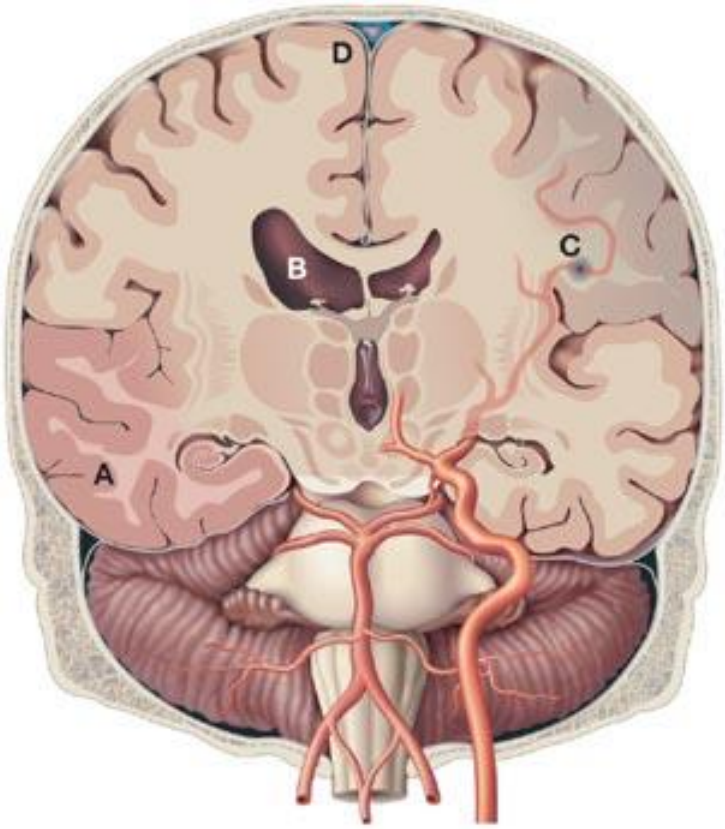


Figure 3 Causes of raised intracranial pressure in a patient with bacterial meningitis



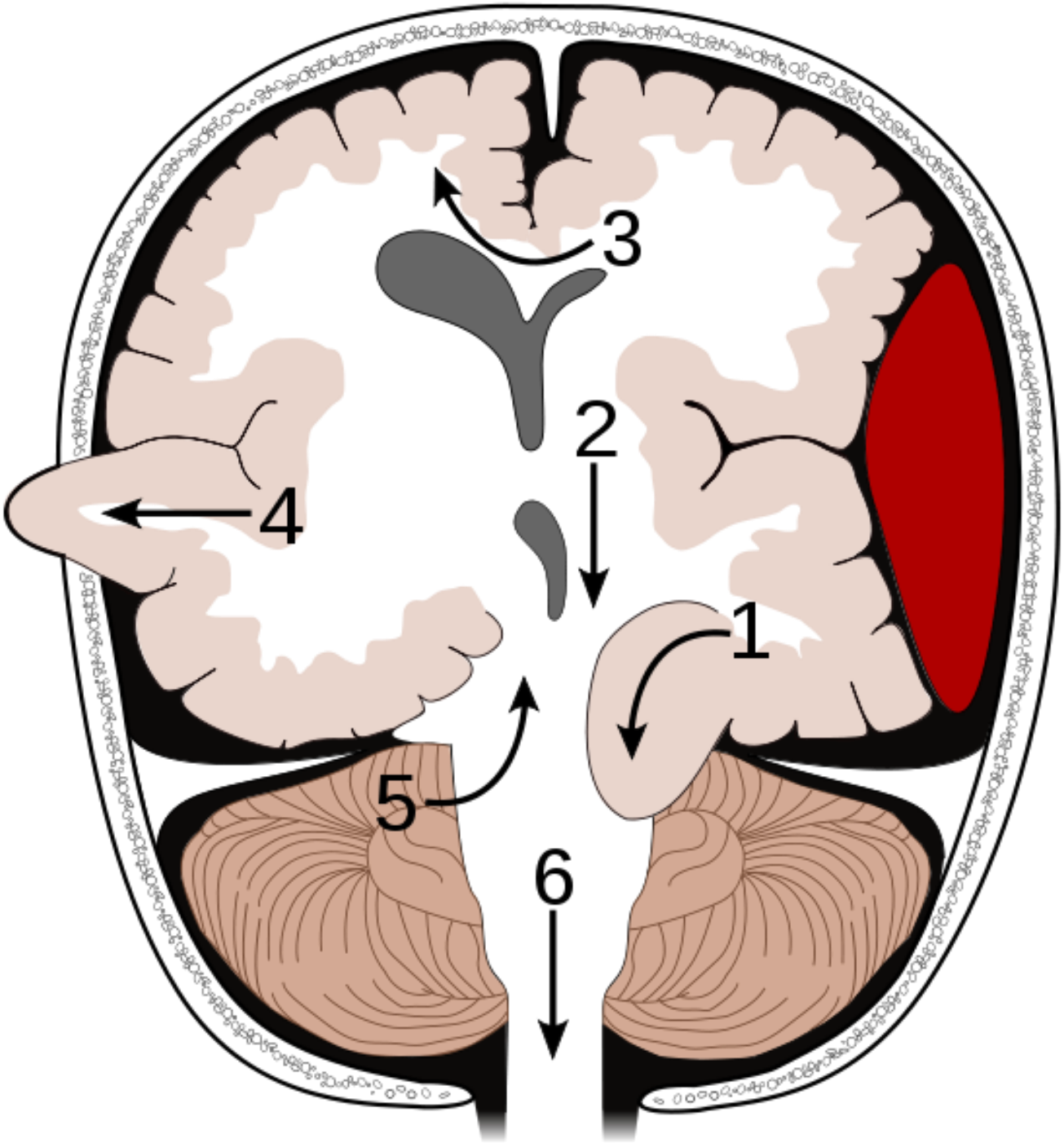
(**A**) Diffuse swelling of the brain.
(**B**) Hydrocephalus results from basal obstruction of the cerebrospinal fluid.
(**C**) Infarcts are caused by inflammatory occlusion of arteries.
(**D**) Thrombosis of the cerebral veins and sinuses.

van de Beek D *et al.* (2006) Drug Insight: adjunctive therapies in adults with bacterial meningitis
Nat Clin Pract Neurol **2:** 504–516 10.1038/ncpneuro0265

nature CLINICAL PRACTICE NEUROLOGY

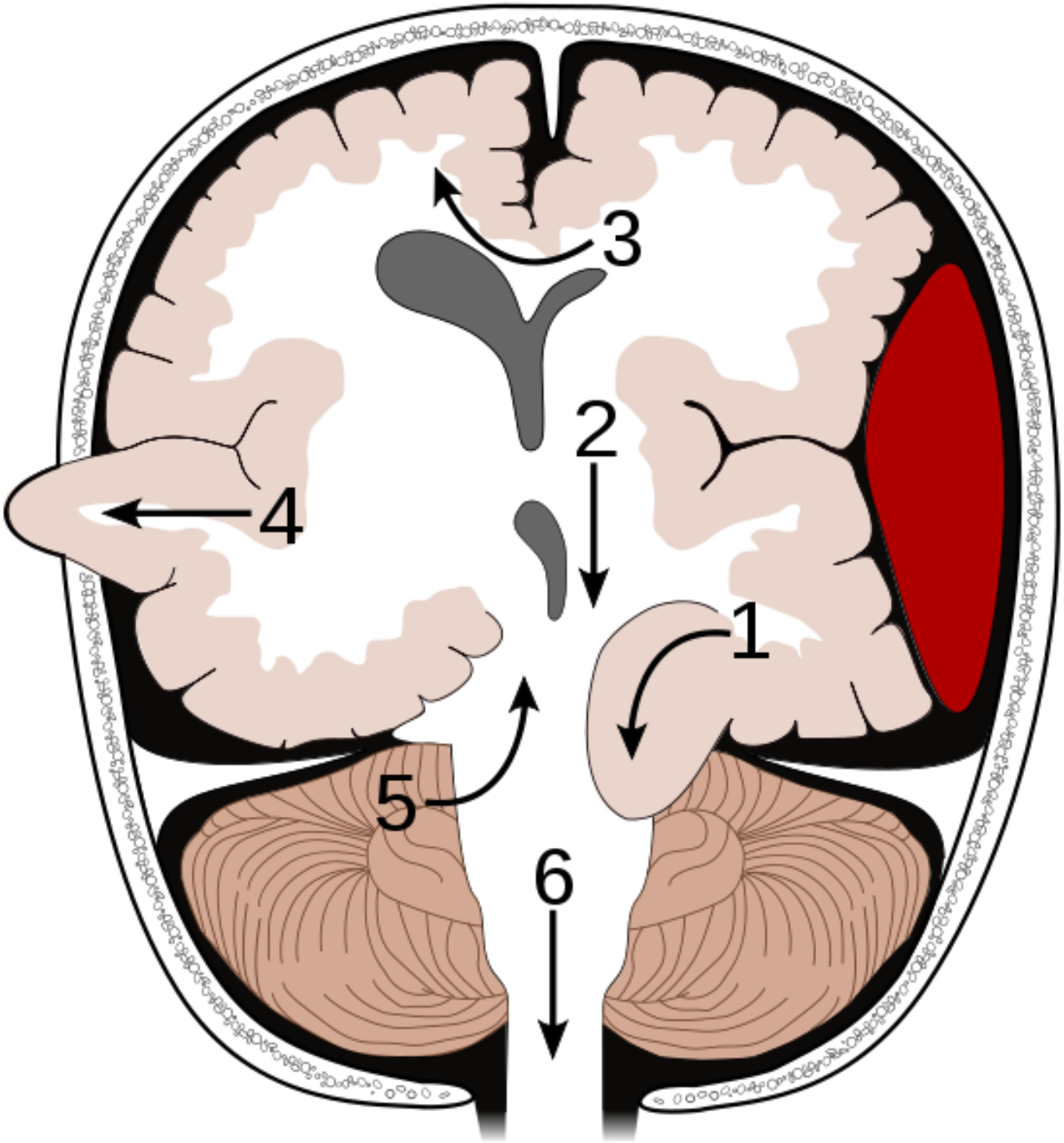
Table 1. Examples of Physiologic Roles of Known Viral Receptors

Virus	Receptor	Abbreviation/Synonym	Function
Measles virus	Membrane cofactor protein	CD46	Regulates complement and prevents activation of complement on autologous cells
Poliovirus	CD155	hPVR/CD155	Expressed on primary human monocytes; supports poliovirus replication in vivo
HSV	Heparan sulfate	None	Cell surface proteoglycans
	Herpesvirus entry mediator A	Hve A, HVEM	TNF receptor superfamily
	Herpesvirus entry mediator B	Hve B, Human nectin-2, or Prr2alpha-Hve B	Participate in organization of epithelial and endothelial junctions
	Herpesvirus entry mediator C	Hve C, nectin1delta, or Prr1-Hve C	Immunoglobulin superfamily
	TNFSF14	hTNFSF14/HVEM-L	TNF receptor superfamily
Rabies virus	Nicotinic AChR (a-bungarotoxin binding site)	AChR	Nicotinic AChR
	NCAM	NCAM, CD56, D2CAM, Leu19, or NKH-1	Cell adhesion glycoprotein of immunoglobulin superfamily
	NGFR	NGFR	NGFR
	p75 neurotrophin receptor (p75NTR)	p75NTR	


3
2
4
1
5
6

Síndromes de Herniación Cerebral

- Uncal. Uncus
- Cíngulo o subfacial. Falx
- Central
- Amigdalina
- Kernohan o Paradójica
- Transcalvaria


3
2
4
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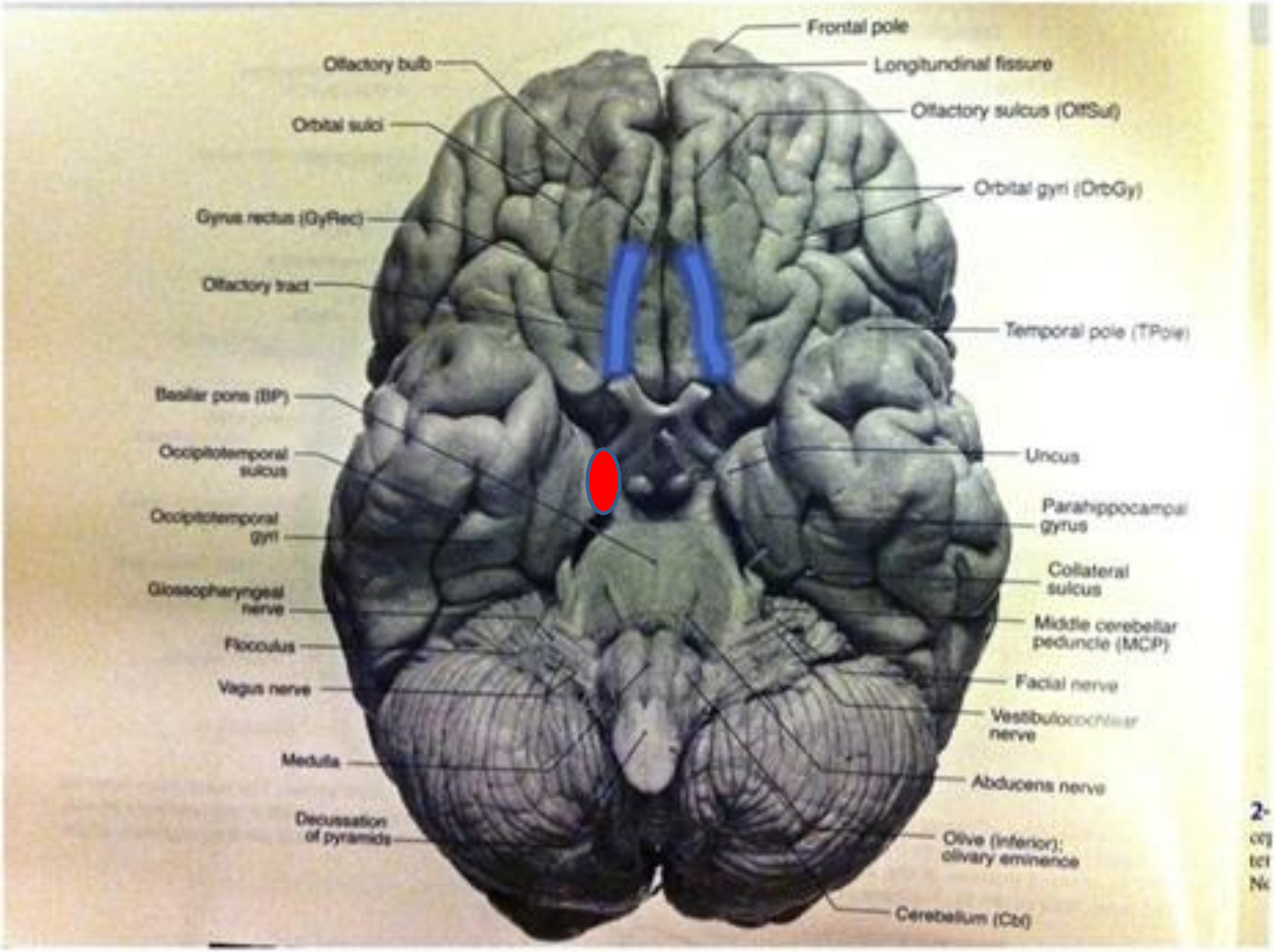
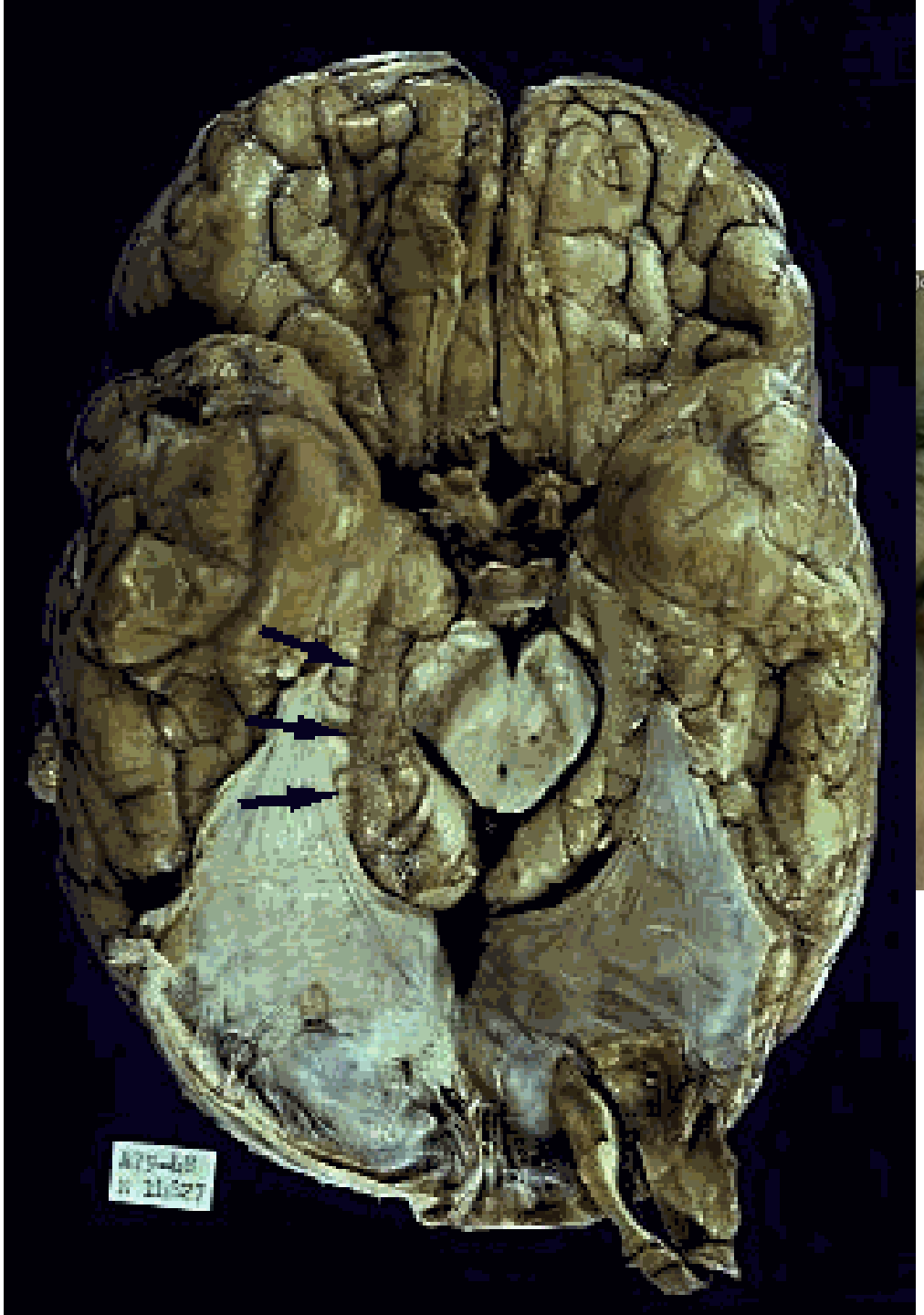

Frontal pole
Olfactory bulb
Longitudinal fissure
Olfactory sulcus (OlfSul)
Orbital sulci
Orbital gyri (OrbGy)
Gyrus rectus (GyRec)
Olfactory tract
Temporal pole (TPole)
Basilar pons (BP)
Occipitotemporal sulcus
Uncus
Occipitotemporal gyri
Parahippocampal gyrus
Collateral sulcus
Glossopharyngeal nerve
Middle cerebellar peduncle (MCP)
Flocculus
Facial nerve
Vagus nerve
Vestibulocochlear nerve
Medulla
Abducens nerve
Decussation of pyramids
Olive (inferior); olivary eminence
Cerebellum (Cbl)

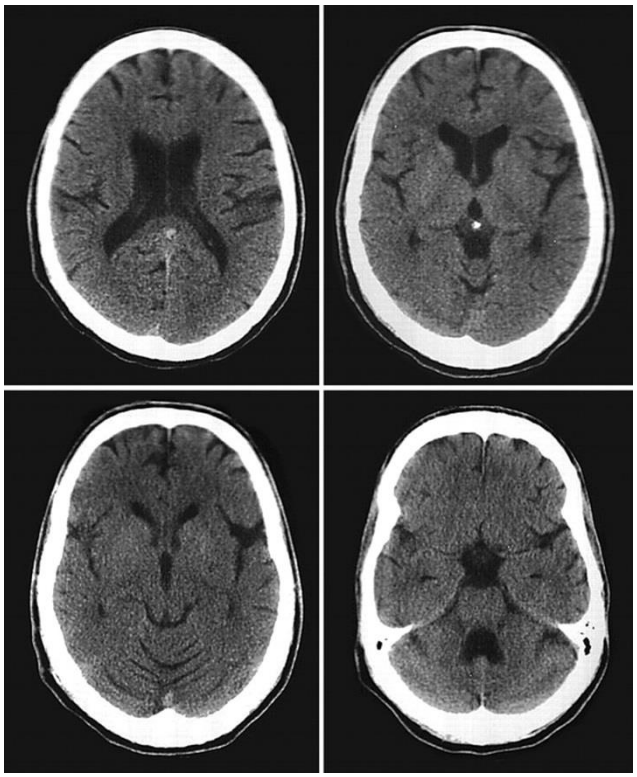



Journal of Ophthalmology - www.onjoph.com

Diagnóstico

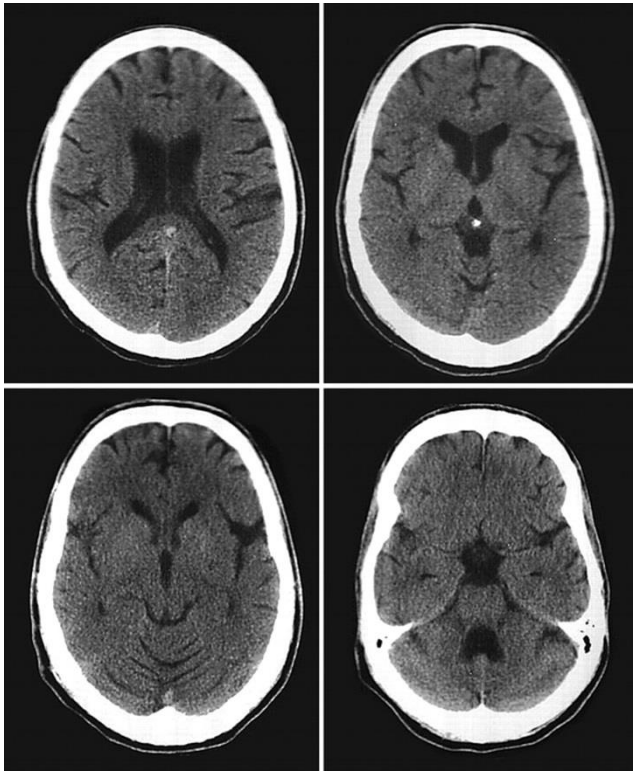
- **Clínico**
- **Imagen**
- **LCR**

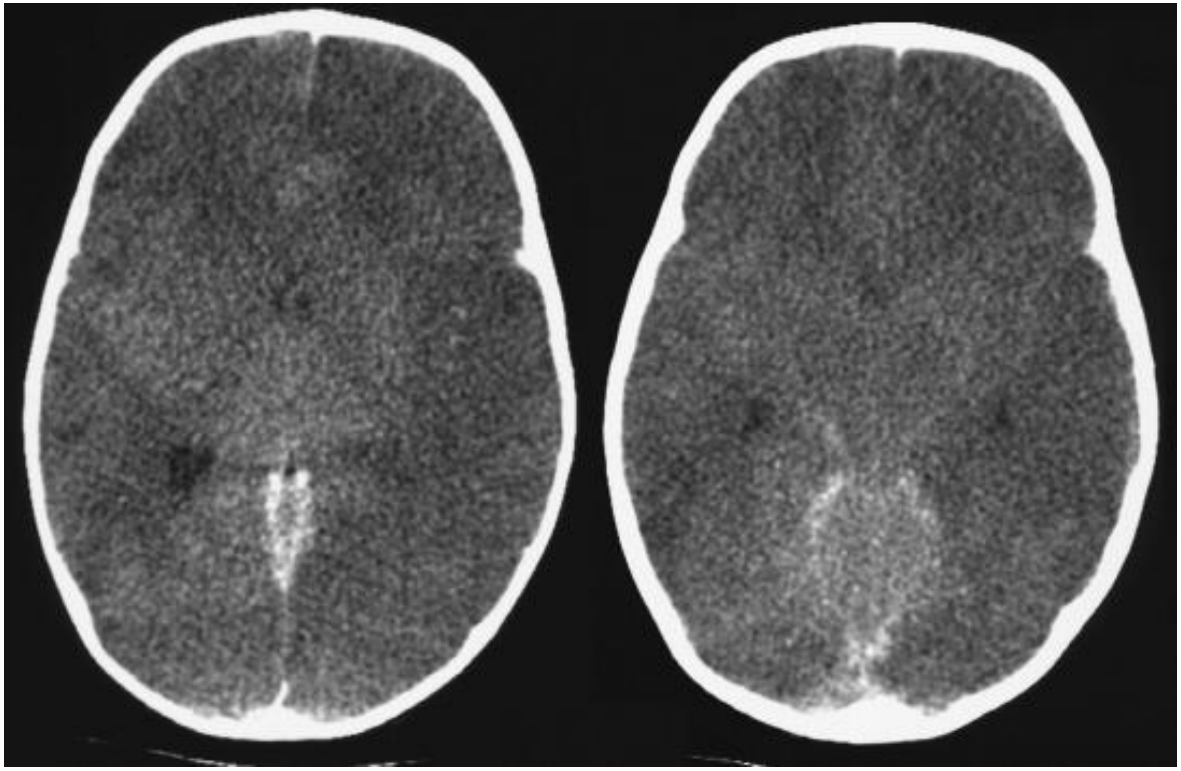
Diagnóstico. Imágen



- Ningún dato específico
- Datos en relación a la Hipertensión Endocraneal: borramiento de lo surcos, ventrículos pequeños, interfase SB/SG mal definida
- Puede obviarse ante falta de datos focales o signos claros de SHEC

Diagnóstico. Imágen



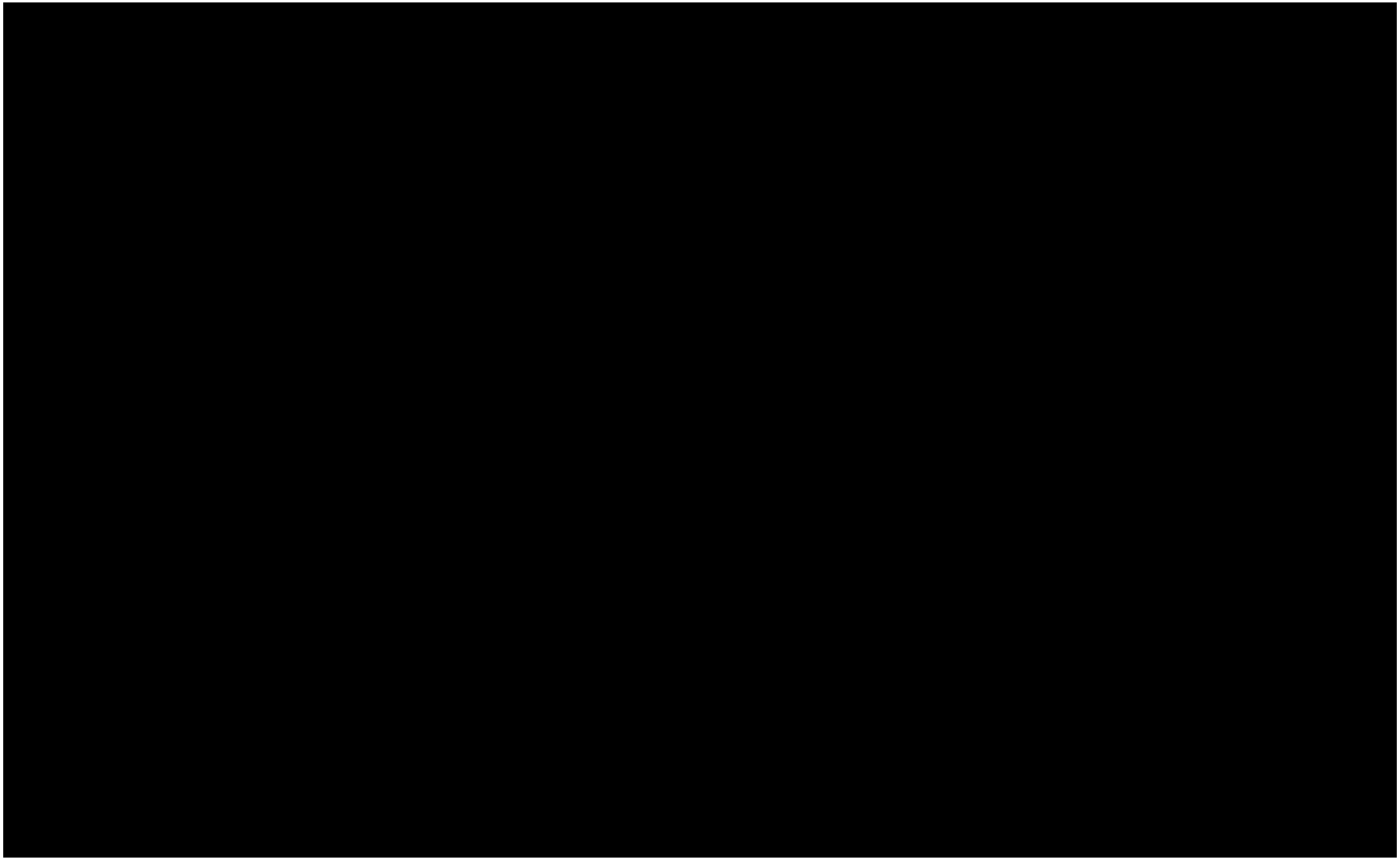


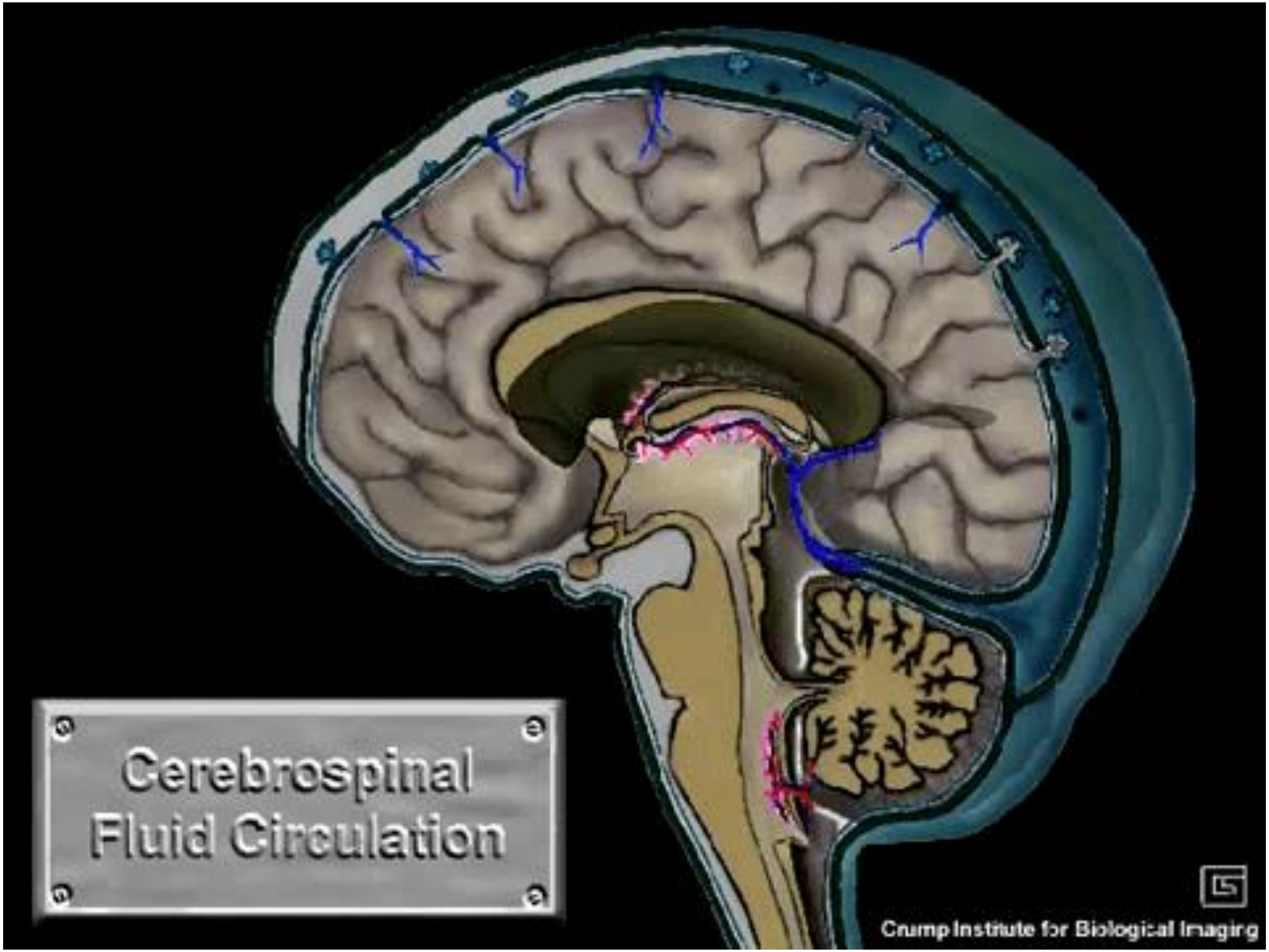
Pero la excepción es esto:

¡Encefalitis Herpética!

Diagnóstico
Valores Normales de LCR

- **Glucorraquia. 1/3 o ½ sérica**
- **Proteínas. 30-40 mcg/dl**
- **Células. Menor de 6-8**




Cerebrospinal
Fluid Circulation
Crump Institute for Biological Imaging

Diagnóstico. LCR

LCR	Bacteriana	Viral	Fímica
Glu	↓ ++	Normal	↓ +
Prot	↑ ++	↑ +	↑ +++
Células	↑ +++	↑ +	↑ ++

Diagnóstico Avanzado

- **Fímico.** PCR en LCR. ADA
- **Bacteriano.** PCR vs antígeno superficie
- **Viral.** PCR

Review Article

Use of Adenosine Deaminase for the Diagnosis of Tuberculosis: A Review

Lakkana Boonyagars, M.D.,
Sasisopin Kiertiburanakul, M.D., MHS

ABSTRACT

The current methods for the diagnosis of tuberculosis (TB) do not provide enough sensitivity and specificity. Adenosine deaminase (ADA) has been developed and widely used for the diagnosis of TB. This article reviews the characteristics, metabolism and clinical uses of ADA for the diagnosis of TB in clinical practices. ADA is an enzyme that increases in TB because of the stimulation of T-cell lymphocytes by mycobacterial antigens. There is sufficient data supporting yield of ADA in various body fluids for the diagnosis of TB. ADA may be used for early diagnosis of TB, especially in case of negative AFB smear from the body specimens. (*J Infect Dis Antimicrob Agents 2010;27:111-8.*)

INTRODUCTION

Tuberculosis (TB) remains one of the health problems in Thailand and worldwide. Although we have many methods for the diagnosis of TB, for example

Characteristics of adenosine deaminase

ADA is an enzyme catalyzing the deamination reaction from adenosine to inosine. It is also an essential enzyme of the purine catabolic pathway. ADA presents

Etiología de las Neuroinfecciones

- **Bacteriana. Meningitis.** Por grupo etáreo. Verificar no esté inmunocomprometido. Revisar si tiene historial de un procedimiento neuroquirúrgico (cambia agente etiológico).

- **Viral. Encefalitis.** Herpes 65% casos.
- **Autoinmune.** (NMDA).

Hay Neuroinfecciones que son fáciles.
Las lesiones dérmicas acusan al agente etiológico

Pero en otras Neuroinfecciones es difícil encontrar al agente etiológico

In Search of Encephalitis Etiologies: Diagnostic Challenges in the California Encephalitis Project, 1998–2000

Carol A. Glaser,[1] Sabrina Gilliam,[1] David Schnurr,[1] Bagher Forghani,[1] Somayeh Honarmand,[1] Nino Khetsuriani,[2] Marc Fischer,[3] Cynthia K. Cossen,[1] and Larry J. Anderson[2]

[1]Viral and Rickettsial Disease Laboratory, California Department of Health Services, Richmond, California; and [2]Respiratory and Enteric Viruses Branch and [3]Meningitis and Special Pathogens Branch, Centers for Disease Control and Prevention, Atlanta, Georgia

62 % no proven cause!!!

25 % with proven microbiology

The Cal ... ize the
clinical ... viruses,
enterovi ... formed
at the Vi ... mation
collected ... ho met
our case ... tis was
found in ... nd in 2
cases (1[9] ... d in 32
cases (1[0] ... uation,
the etiology of 208 cases (62%) remained unexplained.

Tratamiento

- Ser lo más **específico** posible.
- Esquemas contra todo, no recomendable.
- Buscar por todos los medios, LCR.

Tratamiento

- **Bacteriana.** Específico al agente etiológico.
  Cefalosporinas, vancomicina.
- **Viral.** Sólo si es Herpes, aciclovir.
  Si es NMDA, GGB, plasmaféresis
- **Fímico.** Triple esquema.

Preclinical ABs?

PLAIN LANGUAGE SUMMARY

Pre-admission antibiotics for suspected cases of meningococcal disease

Meningococcal disease is a contagious, bacterial disease caused by Neisseria meningitidis (*N. meningitidis*) that often leads rapidly to death. Administering antibiotics as soon as the condition is suspected, and while waiting for the diagnosis to be confirmed, has been advocated as a method of preventing death and the disabling consequences of this disease.

We found no randomised controlled trials that compared pre-admission antibiotics with placebo or no intervention. In the one randomised controlled trial we identified, a single injection of either ceftriaxone (a relatively expensive, newer antibiotic) or a long-acting form of chloramphenicol (an inexpensive antibiotic) were found to be equally effective in preventing death and the disabling consequences in suspected, non-severe cases of meningococcal disease. Due to the serious complications of meningococcal disease, it would be diffic ; soon as the diagnosis is suspe ococcal cases will provide insigh

It would be difficult for ethical reasons … comparing the use of antibiotics, as soon as the diagnosis is suspected, versus no antibiotics.

Cochran Lib 2008

The New England
Journal of Medicine

VOLUME 347 NOVEMBER 14, 2002 NUMBER 20

DEXAMETHASONE IN ADULTS WITH BACTERIAL MENINGITIS

JAN DE GANS, PH.D., AND DIEDERIK VAN DE BEEK, M.D., FOR THE EUROPEAN DEXAMETHASONE IN ADULTHOOD BACTERIAL MENINGITIS STUDY INVESTIGATORS*

Tratamiento
Tiempo

- **Bacteriana.** Hasta LCR normal o bien clínico.
  Habitualmente +/- 12 días.
- **Viral.** Hasta un mes. vo.
- **Fímico.** 6-12 meses.

TABLE 4. GUIDELINES FOR THE DURATION OF ANTIBIOTIC THERAPY.

PATHOGEN	SUGGESTED DURATION OF THERAPY (DAYS)
H. influenzae	7
N. meningitidis	7
S. pneumoniae	10–14
L. monocytogenes	14–21
Group B streptococci	14–21
Gram-negative bacilli (other than *H. influenzae*)	21

Quagliarello et al, 1997 NEJM

Neuroinfecciones
Secuelas

- **Agudas:**
  - Hidrocefalia,
  - Infartos por vasculitis
- **Crónicas:**
  - Hipoacusia o sordera
  - Epilepsia
  - Déficit cognitivo
  - Cefalea. Vascular.

Conclusiones

- Es una Emergencia Neurológica
- El diagnóstico rápido es esencial (bacteriana, fúngica, viral).
- El tratamiento antimicrobiano inmediato reduce la morbilidad y la mortalidad.
- Apegarse a las Guías locales
- “Tiempo es Cerebro”. Y aplica no sólo a EVC

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Edward W. Campion, M.D., *Editor*

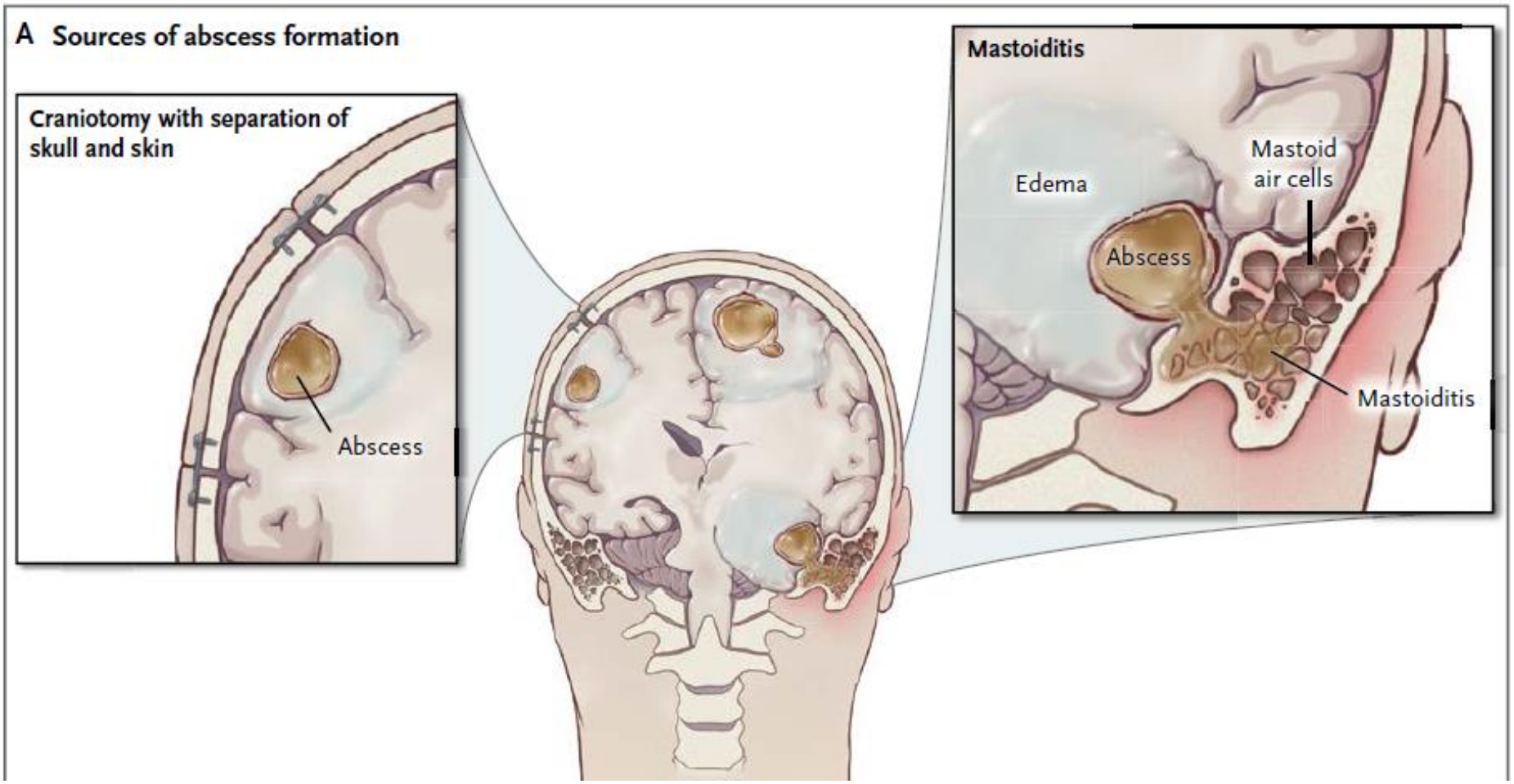
Brain Abscess

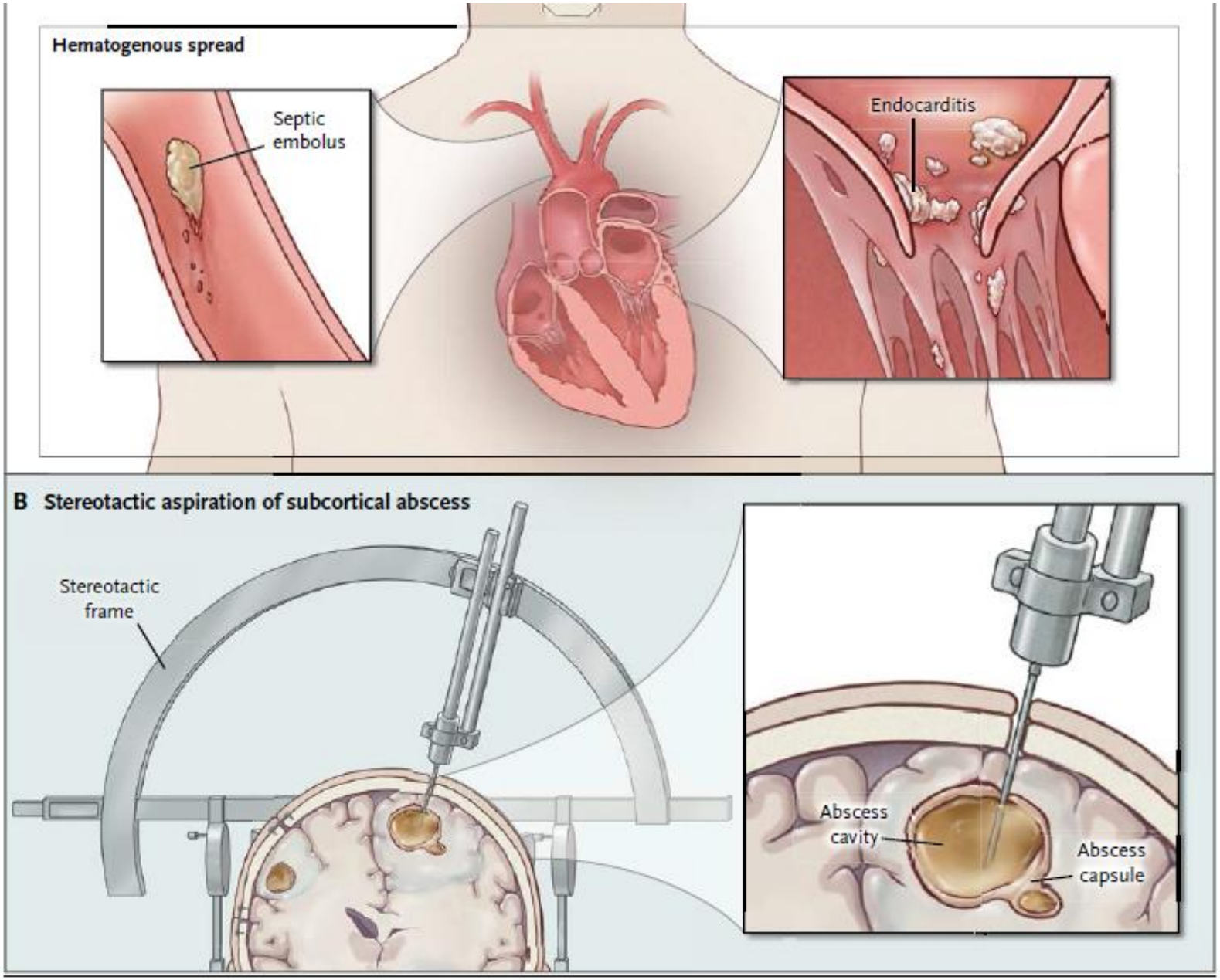
Matthijs C. Brouwer, M.D., Ph.D., Allan R. Tunkel, M.D., Ph.D.,
Guy M. McKhann II, M.D., and Diederik van de Beek, M.D., Ph.D.

N Engl J Med 2014 july;371:447-56.

Brain Abscess

- 0.4 to 0.9 cases per 100,000
- Increased in immunosuppressed patients.
- HIV, immunosuppressive drugs, trauma, mastoiditis, sinusitis, dental infection, endocarditis or bacteremia.
- Contiguous spread 50%. Hematogenous 30% and unknown mechanisms 20%.

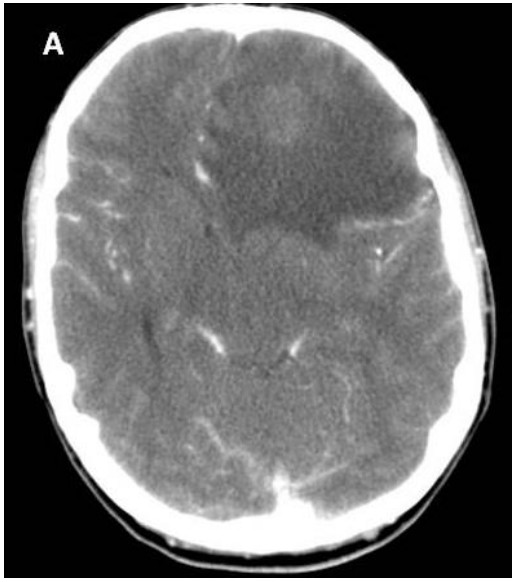

A Sources of abscess formation
Craniotomy with separation of skull and skin
Abscess
Mastoiditis
Edema
Mastoid air cells
Abscess
Mastoiditis


Hematogenous spread
Septic embolus
Endocarditis
B Stereotactic aspiration of subcortical abscess
Stereotactic frame
Abscess cavity
Abscess capsule

Brain Abscess

Pathological Finding

- Lesion evolution (based on experimental animal models):
- Days 1-3: “early cerebritis stage”
- Days 4-9: “late cerebritis stage”
- Days 10-14: “early capsule stage”
- > day14: “late capsule stage”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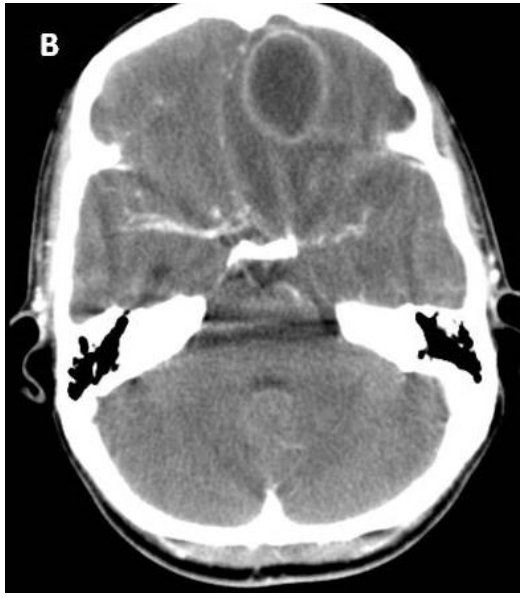
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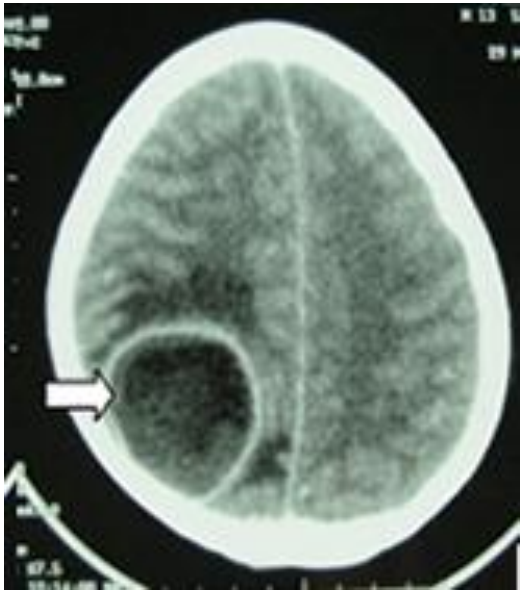


Brain Abscess

Microbiology

- Dependent upon:
  - Site of primary infection, Patient's underlying condition
- Usually streptococci and anaerobes
- 30-60 % are polymicrobial

Brain Abscess

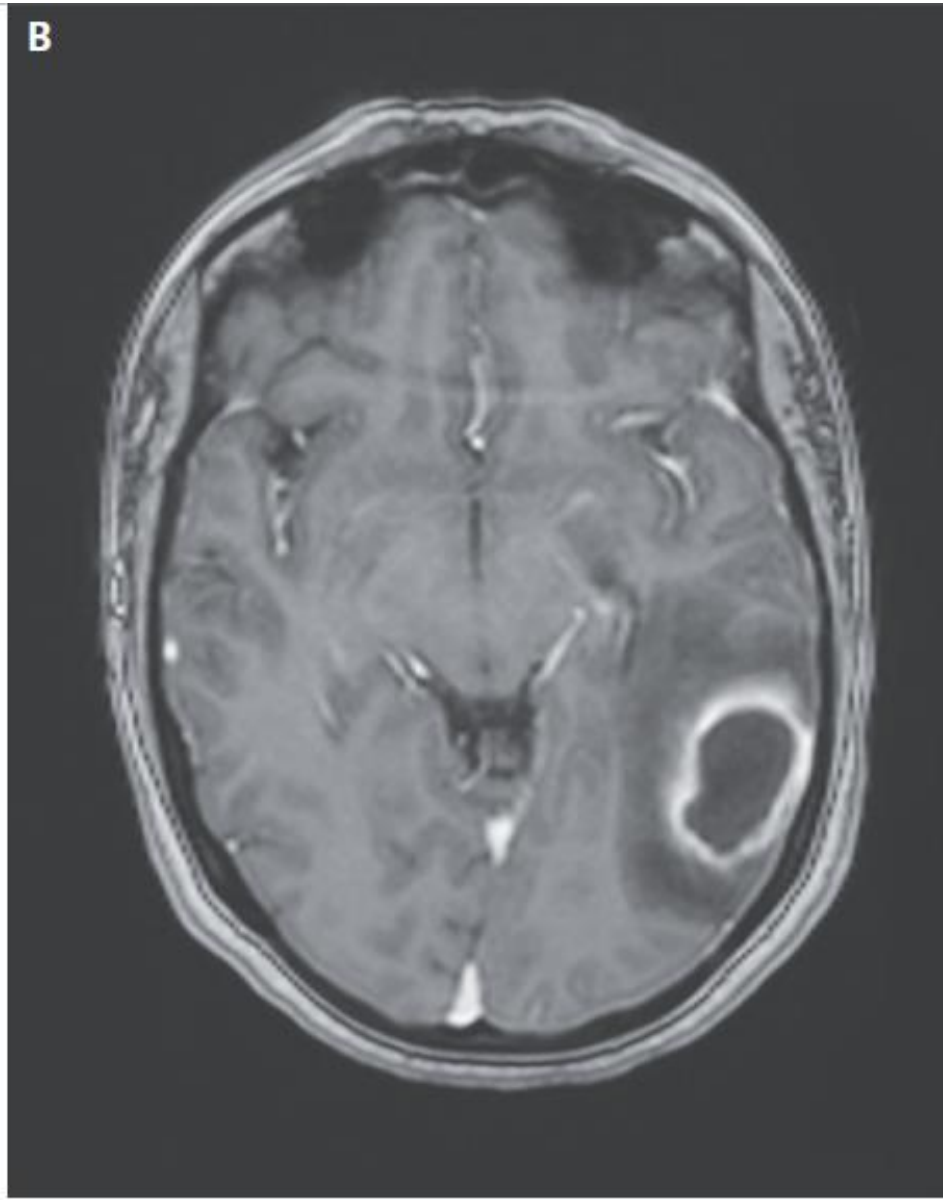
Clinical Manifestation

- The most frequent is headache; fever and altered level of consciousness are frequently absent.
- Neurologic signs depend on the site of the abscess.
- 25% of patients present with seizures

Brain Abscess

Diagnosis Measures

- Cranial imaging



Contrast

Brain Abscess

Treatment

- Neurosurgical.
- Stereotactic aspiration, excision.
- Indication for aspirating the abscess depends on its size and location, the patient's clinical condition
- Antimicrobial therapy

Brain Abscess

Mortality

- Mortality has declined from 40% in 1960 to 15% in the past decade.
- Currently, 70% of patients with brain abscess have a good outcome, with no or minimal neurologic sequelae

NCC

Neurocisticercosis

NCC

- Neurocysticercosis is the result of accidental ingestion of eggs of *Taenia solium* (ie, pork tapeworm), usually due to contamination of food by people with taeniasis. In developing countries, neurocysticercosis is the **most** common parasitic disease of the nervous system and is the main cause of **acquired epilepsy**.
- In the United States, neurocysticercosis is mainly a disease of immigrants.

NCC. Historia

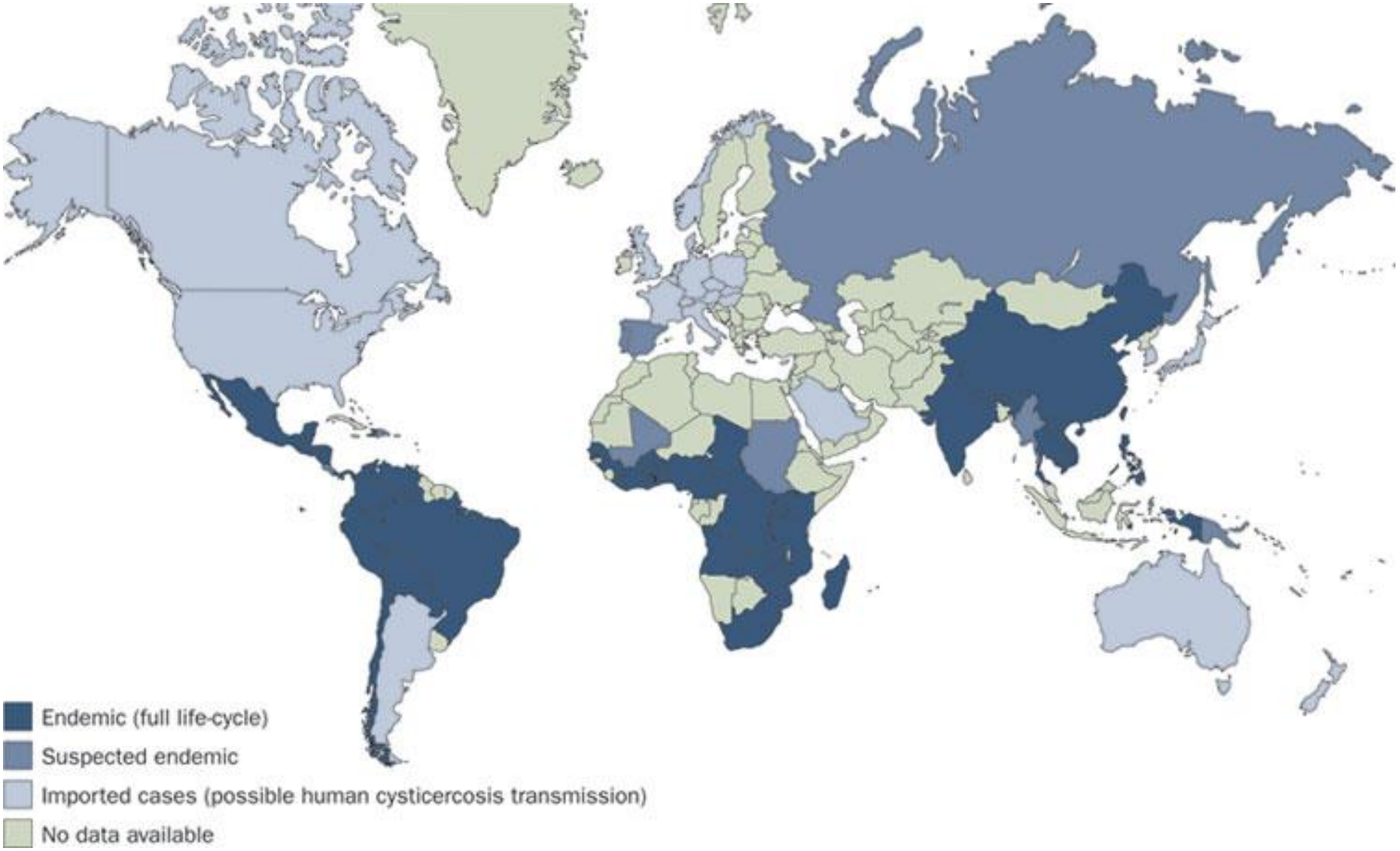
Sotelo J, Guerrero V, Rubio F — Neurocysticercosis: a new classification based in active and inactive forms. A study of 753 cases. Arch Intern Med 145:442, 1985

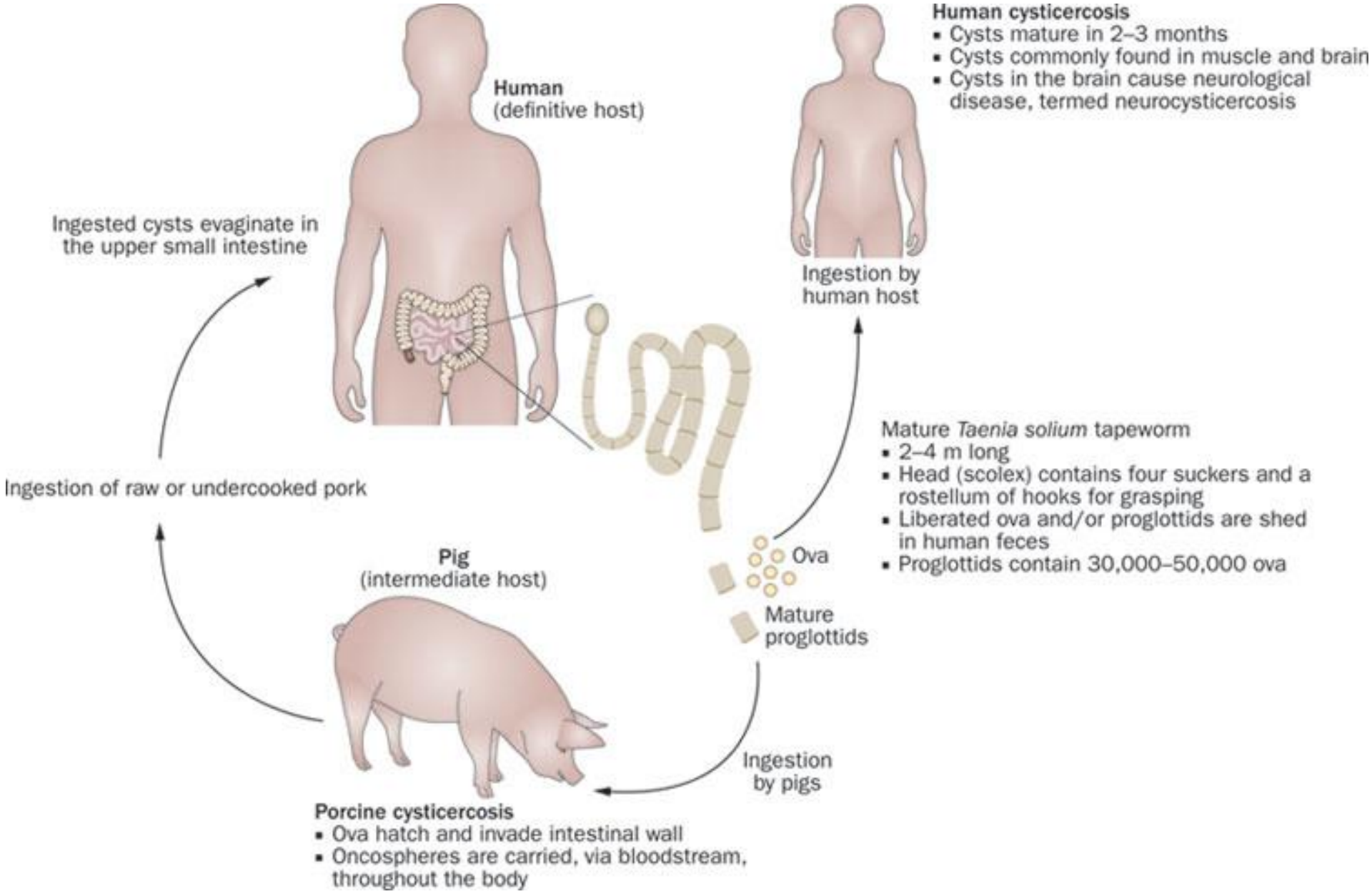
A. Salazar, J. Sotelo, H. Martinez, and F. Escobedo, “Differential diagnosis between ventriculitis and fourth ventricle cyst in neurocysticercosis,” Journal of Neurosurgery, vol. 59, no. 4, pp. 660–663, 1983.

NCC. Historia

F. Barinagarrementeria and C. Cantu, “Frequency of cerebral arteritis in subarachnoid cysticercosis: an angiographic study,” Stroke, vol. 29, no. 1, pp. 123–125, 1998.

O. H. Del Brutto and J. Sotelo, “Neurocysticercosis: an update,” Reviews of Infectious Diseases, vol. 10, no. 6, pp. 1075–1087, 1988.,

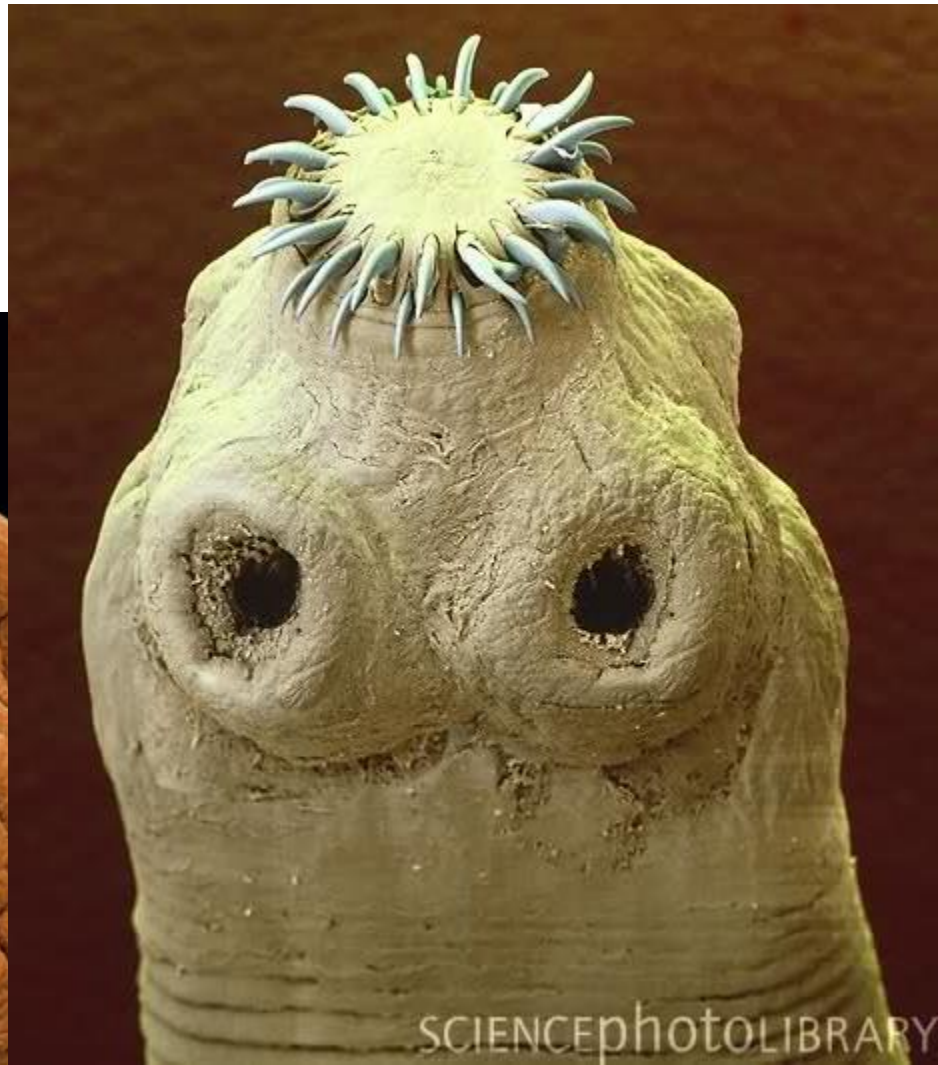

Endemic (full life-cycle)
Suspected endemic
Imported cases (possible human cysticercosis transmission)
No data available


Human
(definitive host)
Human cysticercosis
• Cysts mature in 2–3 months
• Cysts commonly found in muscle and brain
• Cysts in the brain cause neurological disease, termed neurocysticercosis
Ingested cysts evaginate in the upper small intestine
Ingestion by human host
Ingestion of raw or undercooked pork
Mature Taenia solium tapeworm
• 2–4 m long
• Head (scolex) contains four suckers and a rostellum of hooks for grasping
• Liberated ova and/or proglottids are shed in human feces
• Proglottids contain 30,000–50,000 ova
Ova
Mature proglottids
Pig
(intermediate host)
Ingestion by pigs
Porcine cysticercosis
• Ova hatch and invade intestinal wall
• Oncospheres are carried, via bloodstream, throughout the body

PERLAS

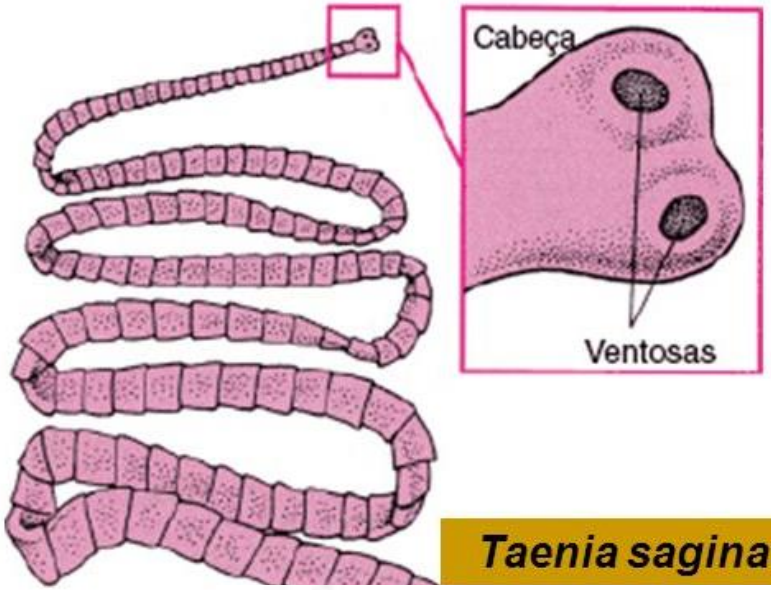
- La ingesta de carne contaminada produce **teniasis**
- La transmisión fecal-oral a humanos produce **cisticercosis**

Tenia

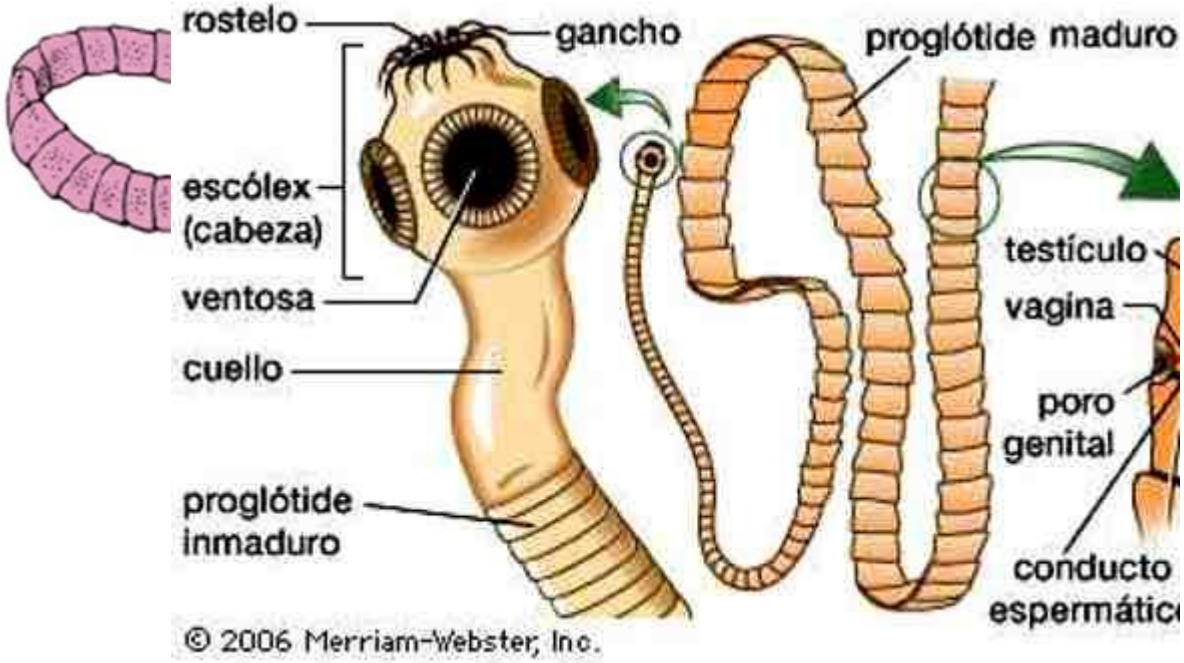


Taenia solium

Uma Tênia Bovina



Taenia saginata



NCC. Signs and symptoms

- Vary with the locations of the lesions, the number of parasites, and the host's immune response.
- Many patients are asymptomatic.
- Symptomatic presentations include the following:

Epilepsy: Most common presentation (70%)
Headache, dizziness
Stroke
Neuropsychiatric dysfunction

Onset of most symptoms is usually subacute to chronic, but seizures present acutely

Views & Reviews

Proposed diagnostic criteria for neurocysticercosis

O. H. Del Brutto, MD, V. Rajshekhar, MCh, A. C. White Jr., MD, V. C. W. Tsang, PhD, T. E. Nash, MD, O. M. Takayanagui, MD, P. M. Schantz, DVM, PhD, C. A. W. Evans, MD, A. Flisser, DSc, D. Correa, DSc, D. Botero, MD, J. C. Allan, PhD, E. Sarti, MD, DSc, A. E. Gonzalez, DVM, PhD, R. H. Gilman, MD and H.H. García, MD

+ SHOW AFFILIATIONS
Address correspondence and reprint requests to Dr. Oscar H. Del Brutto, Air Center 3542, PO Box 522970, Miami, FL 33152-2970; e-mail: odbrutto@telconet.net

doi: 10.1212/WNL.57.2.177
Neurology July 24, 2001 vol. 57 no. 2 177-183

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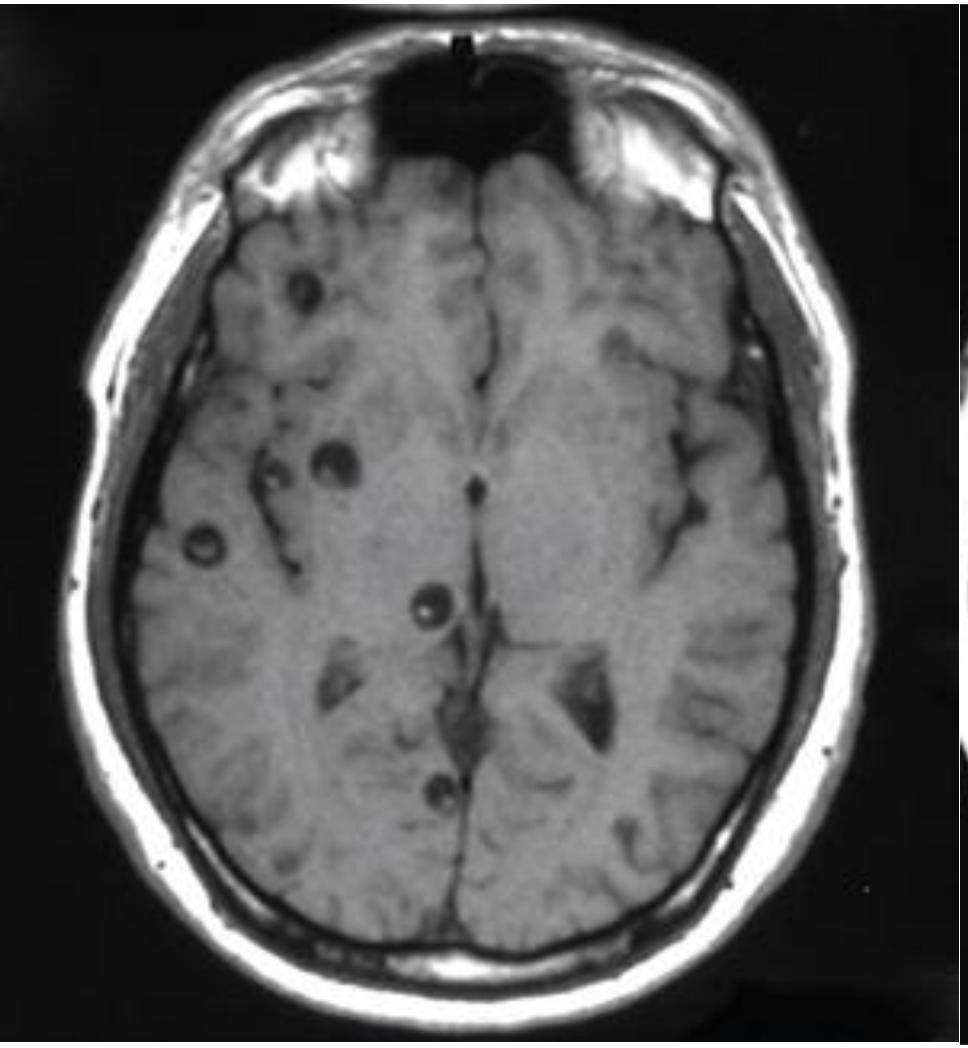
Reply to both Letters to the Editor
Brutto Oscar H Del | Published November 14, 2001

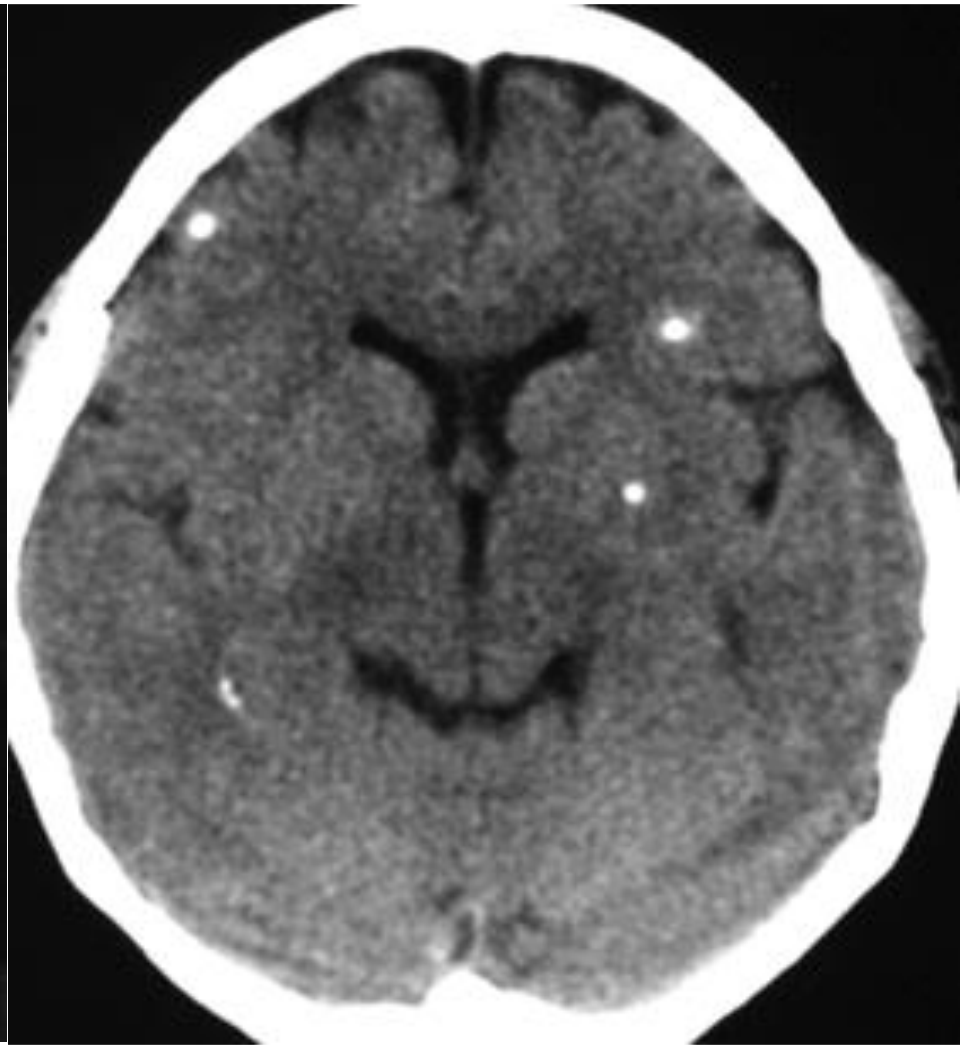
cysticercus granuloma versus tuberculoma
Garg Ravindra Kumar | Published September 17, 2001

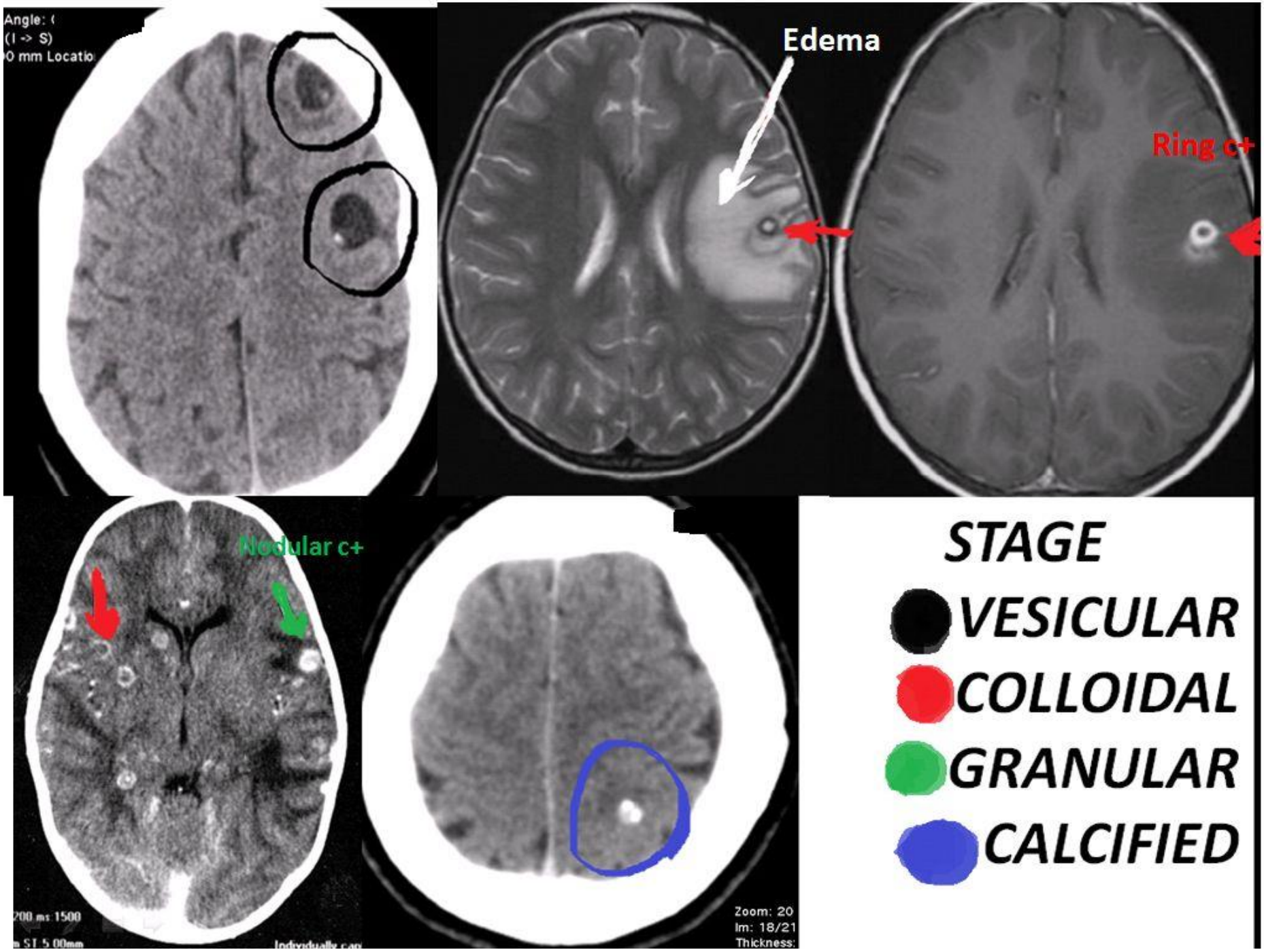
Diagnosis

CT

MRI






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

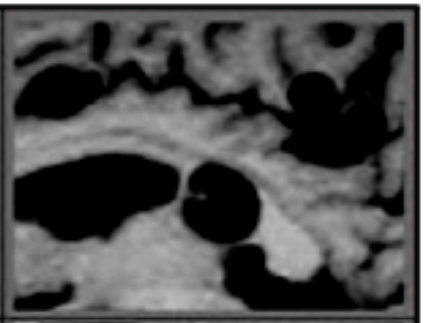
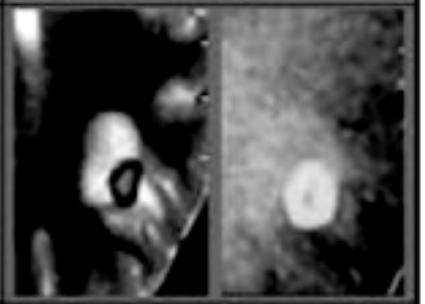
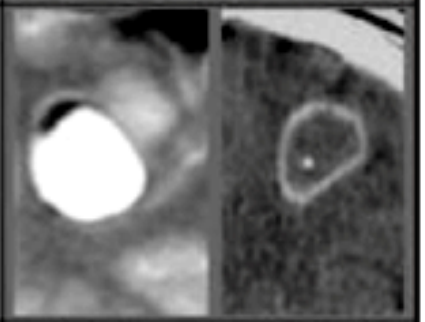
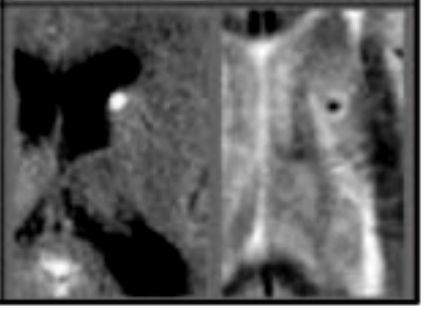
First stage	Vesicular	Cyst + Scolex Non enhancement	
Second stage	Coloidal	Ring enhancement Edema	
Third stage	Granular nodular degeneration	Decreased enhancement and edema Begins calcification	
Fourth stage	Involution	Obvius calcification on CT and MRI (T2*WI)	

Table 1. Stages of cysticerci on MRI.

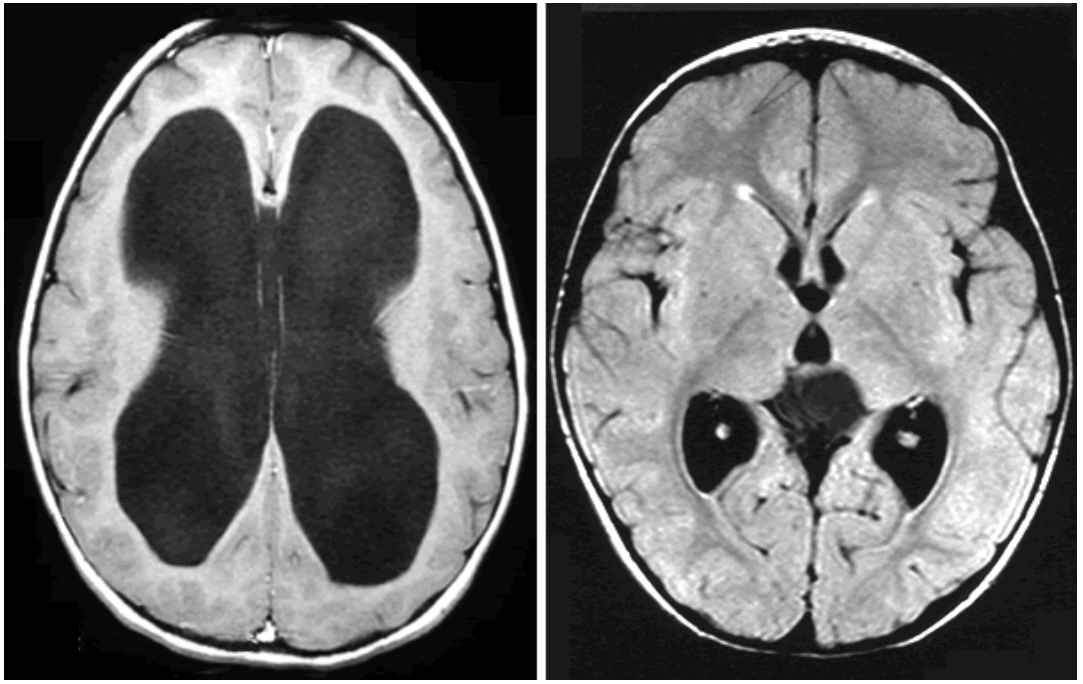
Diagnosis

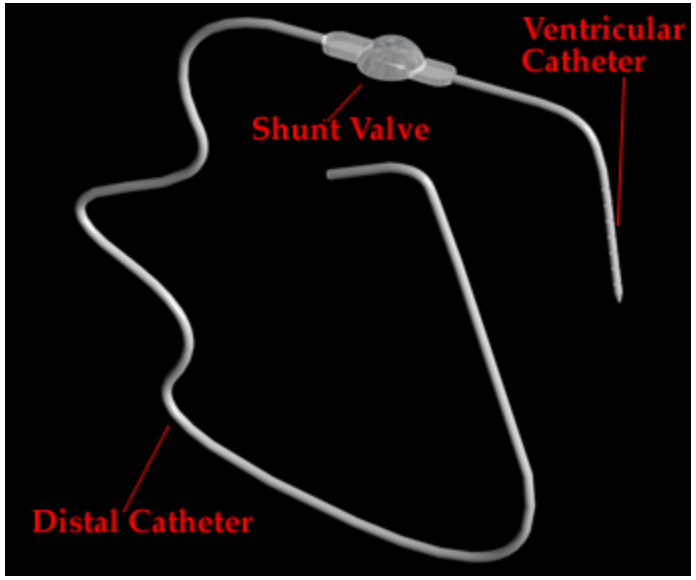
ELISA unspecific

Complications

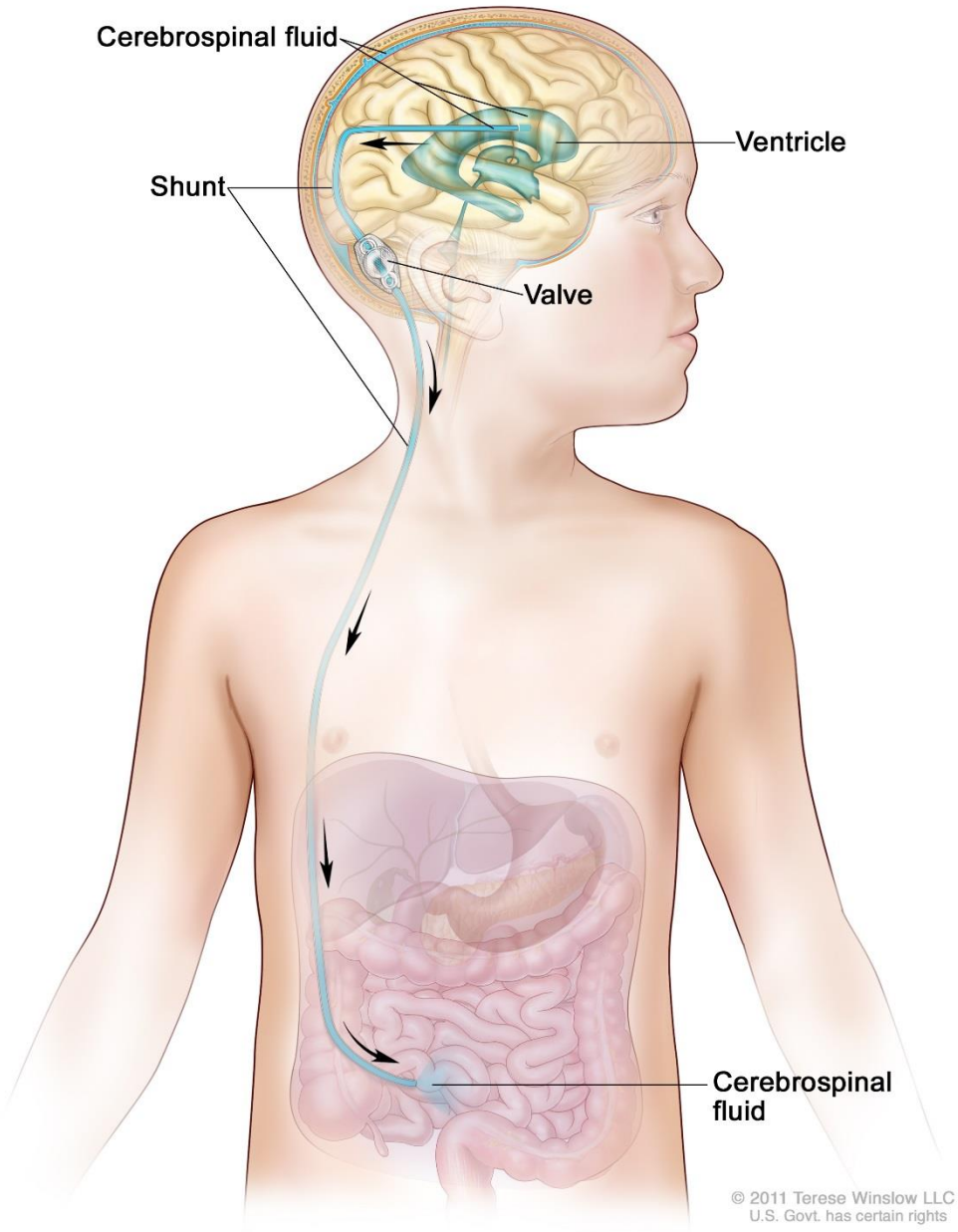
Seizures

Hydrocephalus. Shunt





Cerebrospinal Fluid (CSF) Diversion



Management

Lesion or complications

Active

Inactive. Calcified

Management

Praziquantel. doses of 50mg/kg/day (given every 8 hours) for 15 days was arbitrarily chosen.

Albendazole. at doses of 15 mg/kg/day for 7-30 days

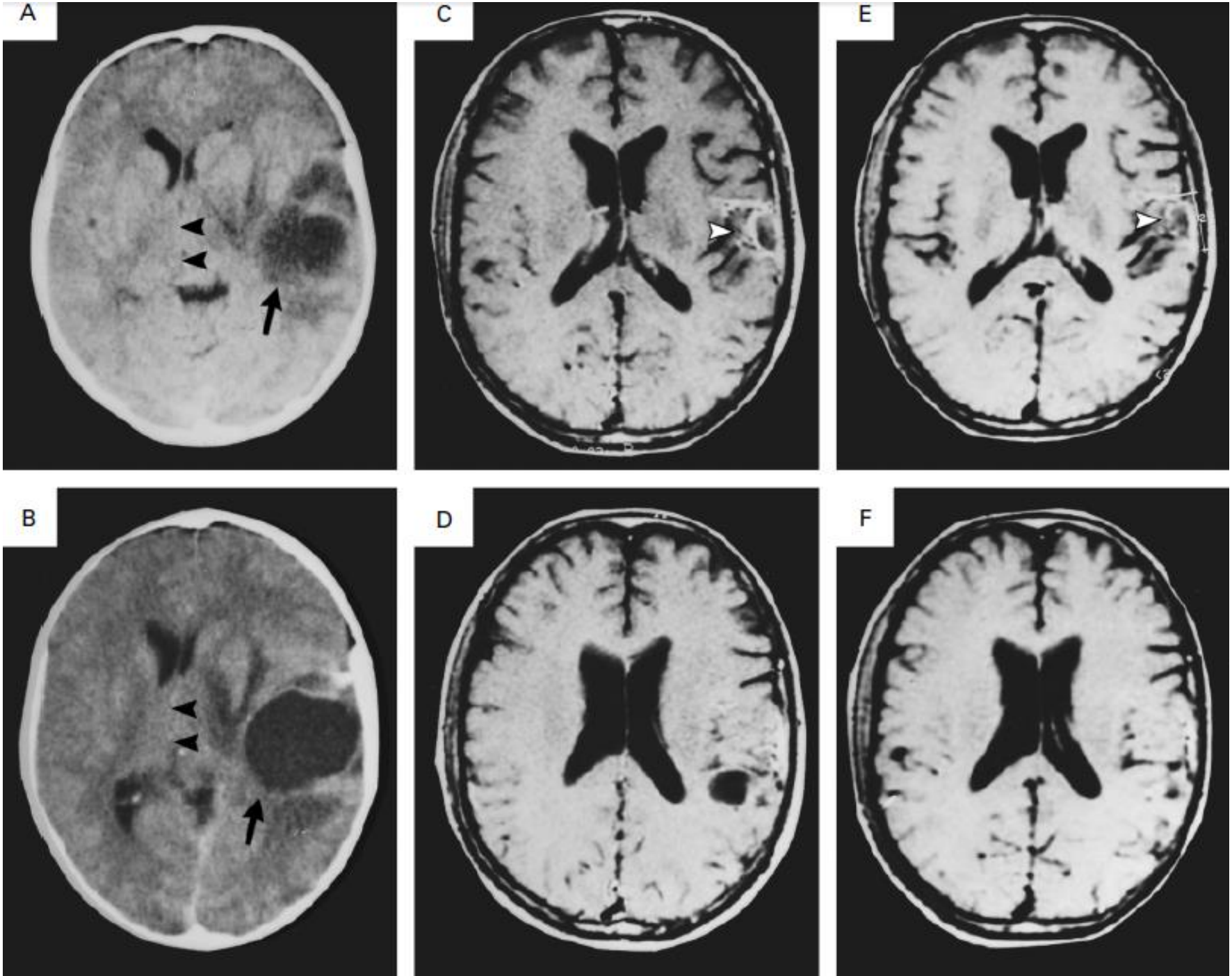
Steroids

The New England Journal of Medicine

MEDICAL TREATMENT FOR NEUROCYSTICERCOSIS CHARACTERIZED BY GIANT SUBARACHNOID CYSTS

JEFFERSON V. PROAÑO, M.D., IGNACIO MADRAZO, M.D., D.SC., FRANCISCO AVELAR, M.D., BLAS LÓPEZ-FÉLIX, M.D., GENARO DÍAZ, M.D., AND ISRAEL GRIJALVA, M.D., D.SC.

N Engl J Med 2001;345:879-85.


A
C
E
B
D
F

World Health Organization

10 facts about neurocysticercosis

1. Pigs become infected with *T. solium* when they come into contact with human faecal waste

2. Neurocysticercosis and taeniasis are two different diseases caused by the same parasite

3. 50 million people are affected by epilepsy. More than 80% live in the developing world

4. T. solium was recently named the food-borne parasite of "greatest global concern"

5. Neurocysticercosis is prevalent mainly in developing countries

World Health Organization

10 facts about neurocysticercosis

6. Neurocysticercosis mainly affects rural farming communities

7. Food handlers can also transmit T. solium

8. Diagnosis of neurocysticercosis is difficult in rural regions

9. Treatment for neurocysticercosis can be long, complicated and costly

10. Eliminating neurocysticercosis requires breaking the life cycle of T. solium