ABX

- CEPHALOSPORINS and CARBAPENEMS can safely be used in patients with an allergic reaction to penicillins that is not type 1 reaction (e.g. anaphylaxis, urticaria, bronchospasm) or exfoliative dermatitis (Stevens-Johnson syndrome, toxic epidermal necrolysis).
- chlorhexidine is contraindicated at age < 2 months (use Betadine).

INFECTION

1. **ENCEPHALITIS** – **viral** invasion of brain parenchyma; often *diffuse*.
2. **CEREBRITIS** – *focal* **bacterial** invasion of brain parenchyma; no capsule or pus.

DIAGNOSIS

- **CT / MRI** is indicated in any patient with syndrome compatible with CNS infection!
- **CSF** is indicated in any patient (after exclusion of intracranial mass).
- **CBC with differential**, **ESR, CRP, procalcitonin**.
  procalcitonin norm [0.1 ng/mL]; > 0.25 ng/mL can indicate infection
- 2-3 **blood cultures** should be obtained from all patients (even when antimicrobial therapy has already been administered).
- **search of infection source** – chest X-ray (!), echocardiography, UA, cultures of other body fluids, bone scans.
- **brain biopsy** is still standard of diagnosis in some specific CNS infections.

FUNGI

– opportunistic organisms – infect only ***immunosuppressed*** individuals.
(except few pathogenic fungi – *Histoplasma**, *Blastomyces**, *Coccidioides**, *Paracoccidioides*** – may infect ***normal*** hosts).

*endemic to some areas of North America
**endemic to some areas of Central-South America

MENINGITIS

MENINGITIS - inflammation of meninges (inflammatory response is generally confined to *arachnoid*, *subarachnoid space* and *pia* – i.e. **LEPTOMENINGITIS**).

meningism (pseudomeningitis) – headache and meningeal irritation in child or young adult with acute febrile illness; CSF pressure↑ but normal in other respects.

Argyll Robertson pupil – small irregular pupil, reacts to convergence, but not to light – basilar luetic meningitis.

HEUBNER arteritis – arteritis of *circle of Willis* due to basal meningitis (syphilis, tbc, fungi).

ETIOLOGY

skull base fracture with CSF leak - *Str. pneumoniae*

S. aureus and coagulase-negative staphylococci - predominant organisms in *CSF shunts*

Viral meningitis – most commonly *enteroviruses*
Fungal meningitis (occurs only in *immunosuppressed hosts*, esp. lymphoma & leukemia, AIDS) – most commonly *Cryptococcus neoformans* (basal ganglia lacunes)

TBC, syphilis - exudate tends to pool in ***basilar cisterns***

DIAGNOSIS

LUMBAR PUNCTURE ASAP - gold standard for diagnosis
glucose↓ - most specific (esp. in bacterial, tuberculous, cryptococcal meningitis; normal in viral meningitis)
VDRL is test of choice in CSF for neurosyphilis

- post-treatment CSF examination is not meaningful criterion of recovery (i.e. CSF need not be re-examined if patient is clinically well!).

Imaging

a) **severe acute meningitis**:
   1) striking *pial and ependymal enhancement* (superficially looks like SAH, but seen only in contrast-enhanced CT; vs. SAH)

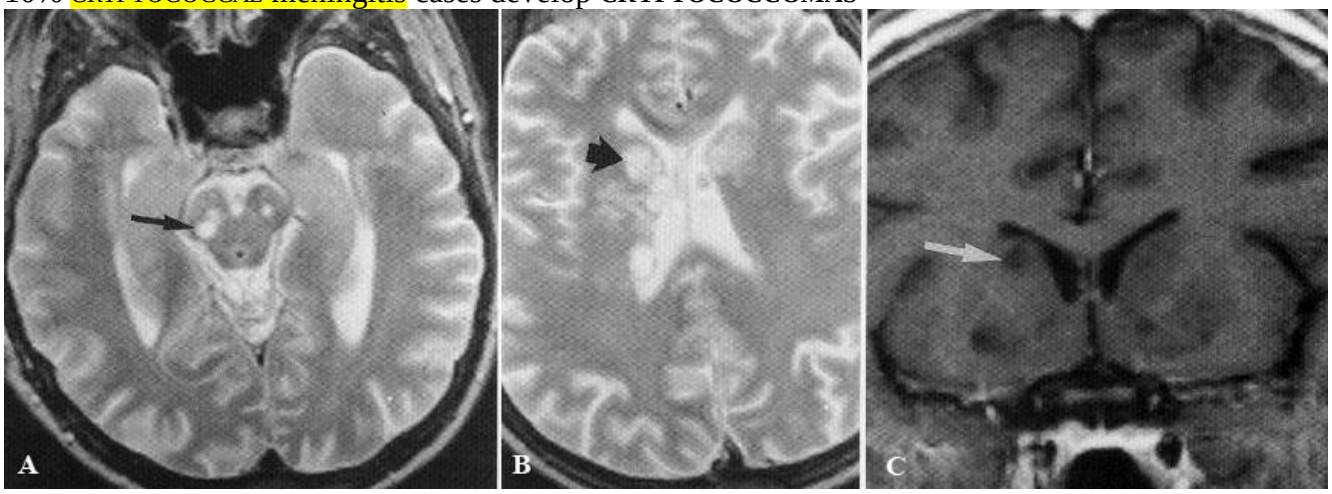
      contrast enhancement of leptomeninges is always abnormal except after *recent neurosurgical procedure*.

   2) brain edema.
   3) complications of meningitis (subdural collections, hydrocephalus, cerebral infarction).

b) **chronic meningitis** – may be *no imaging findings* or merely minimal ventricular enlargement.

Etiologic diagnosis in ***chronic meningitis*** may require meningeal biopsy

10% *CRYPTOCOCCAL* meningitis cases develop **CRYPTOCOCCOMAS**



TREATMENT

- in CSF, humoral defense mechanisms (Ig and complement activity) are virtually absent; opsonic activity is often undetectable even in infected CSF (phagocytosis of encapsulated bacterial pathogens is inefficient) - bacteria commonly reach very high densities in CSF - use of ***bactericidal agents*** is mandatory part of therapy!
- two ***blood samples are drawn*** for culturing → ***empirical antimicrobial therapy*** is started

DEXAMETHASONE **10q6** IV to abolish destructive inflammatory / immune-mediated response (vasogenic and cytotoxic brain edema - decrease rates of hearing loss and neurological complications) - for 4 days of bacterial meningitis (3 weeks in TBC)

First dose of DEXAMETHASONE should be administered 20 min before first antimicrobial dose.
N.B. **VANCOMYCIN** effect may be adversely affected (since meningeal inflammation improves VANCOMYCIN penetration into CSF); H: use **higher doses** of VANCOMYCIN (15 mg/kg q6h) or **intrathecal** VANCOMYCIN.

Antimicrobial therapy: (must be bactericidal in CSF – i.e. maximum tolerated doses!)

- will not significantly alter CSF profile (WBC count, glucose & lactate concentration, antigen test results) for at least 2-3 days.
- will decrease sensitivity of Gram's stain & culture (window of *2-3 hours after giving parenteral antibiotics* when CSF cultures are not adversely affected).

Gram's stain and culture ***should be negative*** in CSF obtained 24 hours after initiation of IV antimicrobial therapy, if organism is sensitive to that antibiotic.

Crucial step is to initiate ANTIMICROBIAL THERAPY immediately!!!!!!!!!!

If suspect meningococcus, give PENICILLIN G before transporting to hospital!

CEFEPIME* 2 g q8h + VANCOMYCIN 15mg/kg q12h (goal trough: 15 – 20 mg/L) for 14 days

*for type I penicillin hypersensitivity (i.e. anaphylaxis) substitute with AZTREONAM 2 g q6h or CIPROFLOXACIN 400 mg q8h

N.B. only 3rd or 4th generation cephalosporins are used.

+ **RIFAMPIN** **CHEMOPROPHYLAXIS** for family members / intimate contacts of child with meningococcal or *H. influenzae* infection.

Treatment of *CRYPTOCOCCAL* meningitis – **AMPHOTERICIN B** + **FLUCYTOSINE** for 2 weeks → **FLUCONAZOLE** for 8 weeks ÷ lifelong.

- often develop ***symptomatic intracranial hypertension***.
  - ventriculomegaly (hydrocephalus) is not always present
  - most patients do well with serial lumbar punctures combined with antifungal therapy.
  - in one case series (50 patients), only 26% patients needed permanent shunting.
  - shunting during active fungal infection is not an issue if antifungal therapy has been started prior to implantation.
    - no cases of shunt infection.
    - no cases of cryptococcal peritonitis after shunting.

MORTALITY ≤ 10-20% (many deaths occur during *first 48 hours of hospitalization*); 50-90%* in untreated cases.

*almost 100% in pneumococcal meningitis!

Austrian syndrome (triad of pneumococcal meningitis, pneumonia, and endocarditis) has particularly high fatality rate.

COMPLICATIONS

Seizures
Stroke
Hearing loss
Mental retardation - bacterial meningitis is one of most preventable causes of mental retardation
Brain abscess, subdural empyema
Subdural effusions - usually in infants as self-limited process (as inflammatory process subsides, subdural fluid is reabsorbed);

Treatment – *repeated daily* ***needle aspirations*** through coronal sutures;

- *indications*: infected fluid (prolonged fever), increased ICP, rapidly enlarging head circumference in child, focal neurological findings (seizures).
- *no more than 20 mL/d of CSF should be removed from one side* (to prevent sudden shifts in intracranial contents).
- if effusion persists after 3-4 wk of taps → surgical exploration for possible excision of subdural membrane is indicated.

Hydrocephalus

- large numbers of leukocytes in subarachnoid space contribute to purulent exudate and impair CSF absorption by arachnoid villi → *COMMUNICATING HYDROCEPHALUS*.
- pia-arachnoid becomes thickened → adhesions → interfere with CSF flow from 4th ventricle → *OBSTRUCTIVE HYDROCEPHALUS*.
- ventriculitis is nearly uniformly present.
- H: EVD until CSF sterility is achieved

Purulent ventriculitis - in severe ventriculitis, EVD/lumbar drain is not efficient enough, especially when CSF contains pus/flakes (niduses of infection adherent to the choroid plexus and ependymal lining) - act as continuous source of infection – consider **endoscopic lavage**:

- clamp EVD ~12 hours.
- insert ***rigid endoscope*** ~4–5 cm lateral to midline and ~1–2 cm anterior to coronal suture.
- copious ***irrigation with Ringer lactate***.
- ***pus is aspirated***;
- after ipsilateral ventricle is cleansed, a generous ***septostomy*** is performed, opposite ventricle entered, and all the purulent material is removed in a similar fashion.

SPINAL MENINGITIS (ARACHNOIDITIS)

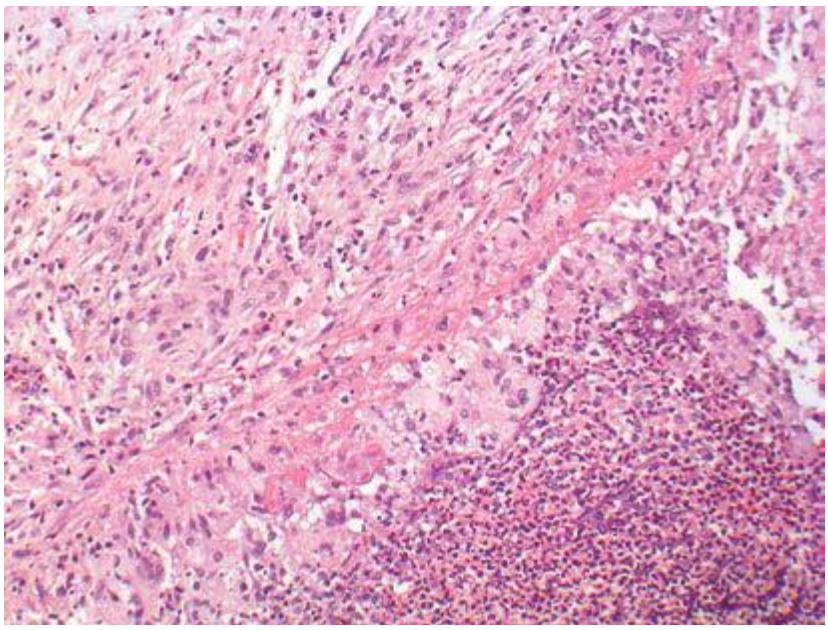
- *injury to roots* (as they traverse subarachnoid space; permanent intradural adhesions) → **multiple radiculopathies**: radicular pain, sensory loss, motor weakness, sphincter dysfunction.

BRAIN ABSCESS

ETIOLOGY

— HIV - Toxoplasma gondii, Mycobacterium tuberculosis.
— solid-organ transplants - fungi (90%).

a) *direct spread* from **CONTIGUOUS CRANIAL SITE** (40-50%): *otitis media*, *sinusitis*
N.B. brain abscess in child < 2 years suggests associated bacillary meningitis
b) *hematogenous spread* from **REMOTE INFECTION SITE** (30%): *pulmonary infection, endocarditis*



1) **streptococci** - 50-70% brain abscesses.
2) **anaerobic bacteria** - common in ***chronic otitis media*** or ***pulmonary disease***.
3) *Staphylococcus aureus* and Gr- rods - common after ***cranial penetration*** from surgery or trauma.

N.B. pneumococci, meningococci, Haemophilus influenzae (major causes of bacterial meningitis) are rarely recovered from brain abscess!

4) fungi are common in ***immunosuppressed***
5) parasites are common in ***immunosuppressed***.

- intact brain parenchyma is relatively resistant to infection - in order for brain abscesses to form, there must be *pre-existing compromised area* (*ischemia, necrosis, hypoxia*) in brain tissue.

Hematogenous spread – following characteristics:
1) multiple* brain abscesses (although solitary lesions may also occur)
2) distribution of MCA - parietal lobe predominates (highest blood flow).
3) initial location at *gray matter-white matter junction*.

*another cause of multiple abscesses – **immunosuppression**.

CLINICAL

- ***subacute*** expanding infectious mass:

1) ICP↑ - prominent headache, AMS, vomiting, papilledema (rare finding in meningitis!).
2) focal neurological deficit - seizures are particularly prominent!
3) infection – *fever* < 50% (i.e. may be minimal or absent!!!)

Abrupt neurologic deterioration:

a) *abscess rupture* into ventricular system → **ventriculitis & hydrocephalus, shock & death**
b) *abscess rupture* into subarachnoid space → **meningitis**
c) *brain herniation*
d) *spontaneous hemorrhage*

- encapsulation is more complete (more mesenchymal cells → tougher capsule) on cortical side (than on ventricular side) - *propensity of abscesses to extend and rupture into ventricular system*.

DIAGNOSIS

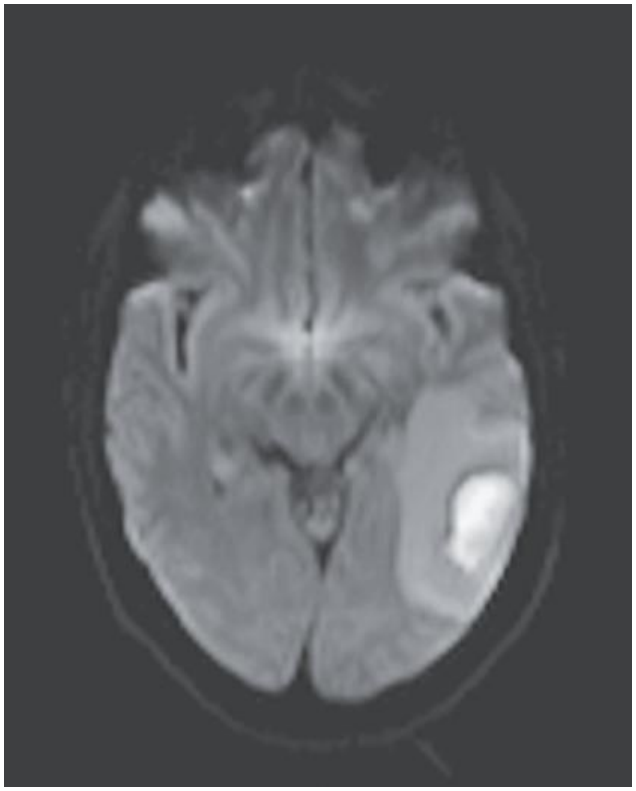
Lumbar puncture is contraindicated - risk of herniation!

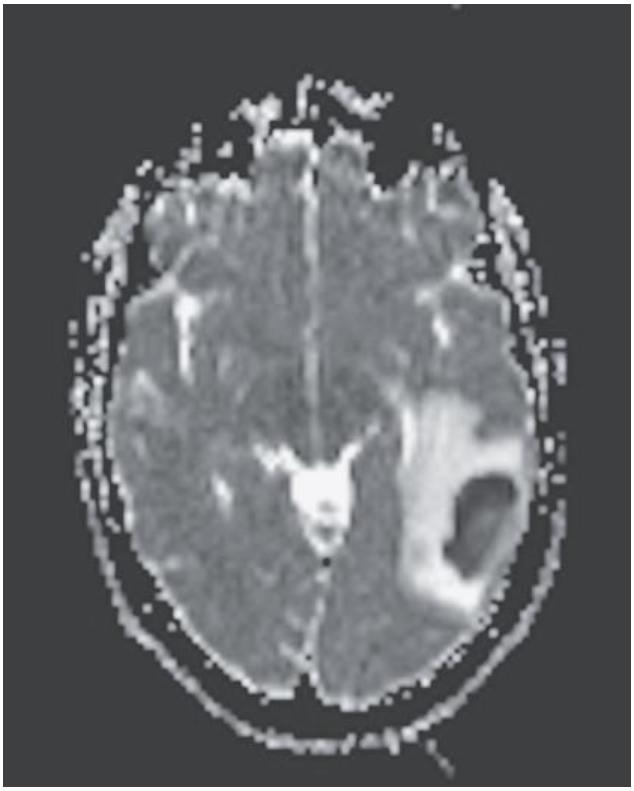
CSF - **aseptic meningeal reaction** (pressure↑, 0-1000 PMNs, protein slightly↑, normal sugar)

MRI w/wo is study of choice - initial detection and subsequent monitoring.
DWI has specificity 96% for differentiation from brain tumors.

Abscess, stroke, and lymphoma (high cellularity) have ***diffusion restriction*** (bright on DWI, dark on ADC), whereas gliomas and metastases do not restrict diffusion!
Same as epidermoid cyst (bright DWI) vs. arachnoid cyst (normal DWI)

Encapsulated stage: *low T1 intensity* (*T2 hyperintense*) lesion with *diffusion restriction* surrounded by *edema*.

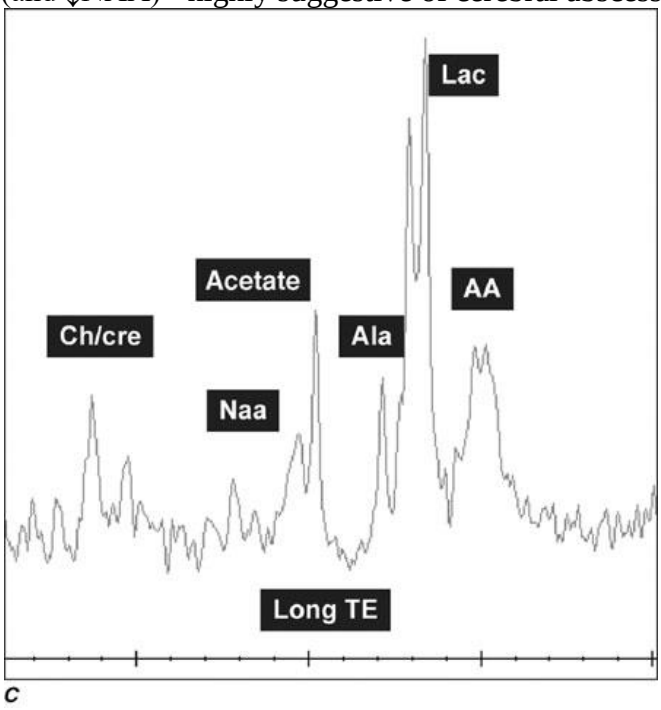




Uniform* *ring of contrast enhancement* surrounded by hypodense region of *edema*.

*markedly irregular wall suggests tumor!

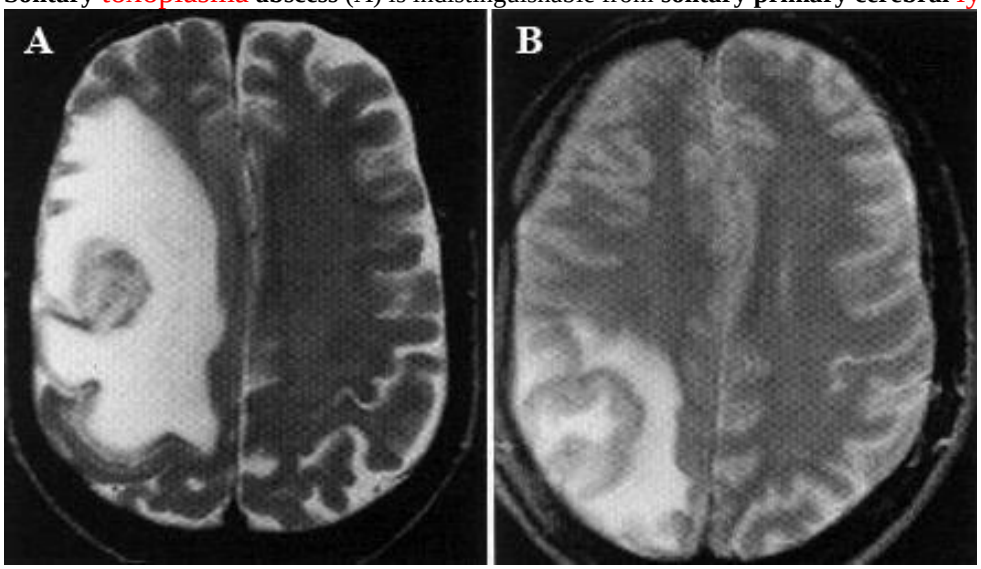
MRS – ↑*lactate* (and ↓NAA) - highly suggestive of cerebral abscess (adds little value to DWI)



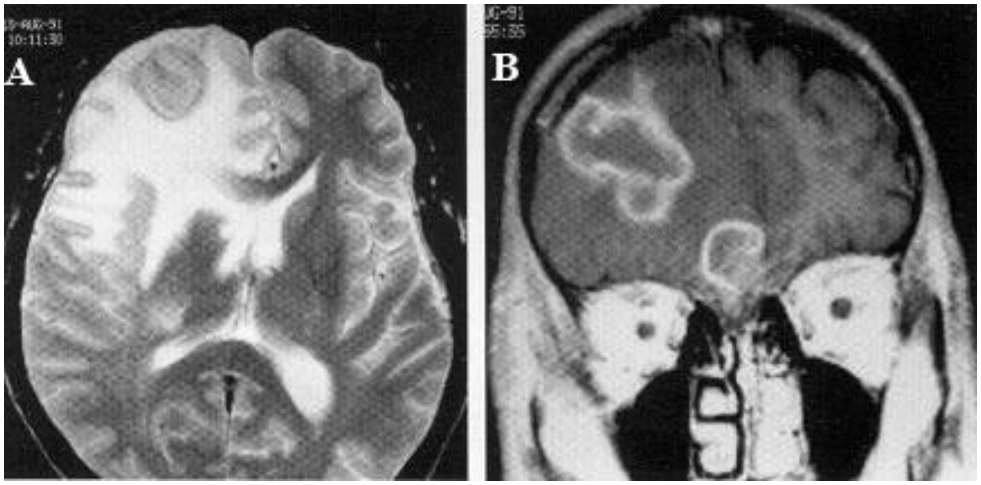
EEG - focal slowing.

Hematogenous source:
a) ESR, CRP, procalcitonin
b) **CXR**, **ECG**, **cardioECHO**
c) **blood cultures** (positive in ≈ 10% cases).
d) serum should be sent for ***antitoxoplasma IgG*** (in patients with AIDS).

Solitary toxoplasma **abscess** (A) is indistinguishable from **solitary primary cerebral** lymphoma (B):



Toxoplasma **abscess**:



TREATMENT

a/b: Blood cx and biopsy first!!!

- neurosurgical patient: **VANCOMYCIN** + **CEFEPIME** + **METRONIDAZOLE** for 6-8 weeks (→ oral for additional 4-8 weeks) - until abscess cavity resolves completely (neovascularity persists!)
  - alternative to CEFEPIME + METRONIDAZOLE - **MEROPENEM**
- empirical therapy for AIDS patient with intraparenchymal lesion:
  A) > 1 enhancing lesion *OR* positive toxoplasma serology = presumptive diagnosis of *TOXOPLASMA ENCEPHALITIS* → 1-2 week **trial of antitoxoplasma therapy** (objective response must be seen on imaging): **PYRIMETHAMINE** (+ **LEUCOVORIN**) + **SULFADIAZINE**
  B) 1 enhancing lesion *AND* negative toxoplasma serology → brain biopsy.

Response to antibiotics is best monitored by **serial MRI**

Even lesions with thick, well-developed ring enhancement may disappear with medical management!

Neurosurgery:

Abscess > 2.5-3.0 cm should go to OR! Must be mature (symptoms > 7-14 days) – avoid operating on cerebritis!
Practically, every patient needs at least biopsy for culture & stain (Gram, acid-fast, fungal)!!!

a) stereotactic **abscess aspiration** ± catheter drainage - procedure of choice (etiological diagnosis and treatment); requirement - abscess > 1 cm showing central cavity*
   *aspiration *during cerebritis stage* → hemorrhage
   N.B. enhancing ring may appear at late cerebritis stage before true capsule has been formed! H: DELAYED SCAN (obtained 30 min. after IV contrast) - *contrast diffusion into low-density center of abscess* (vs. stage of formed true capsule - no inward diffusion of contrast).
   – leaving continuous drainage catheter is not recommended.
   – if organism is known, indications for just decompression:
      1) proximity **to ventricles** (risk of catastrophic rupture → ventriculitis → hydrocephalus)
      2) significant **mass effect** (mostly if abscess > 2.5 cm)
      3) **failure** to demonstrate abscess **shrinkage** in 4 weeks (antibiotic failure)

b) **complete abscess extirpation** – for accessible mature abscess - rapid decompression, abx duration↓; may cause damage to brain parenchyma (→ risk of seizures); indications:
   1) **gas** within abscess cavity
   2) **fungi**, **tbc**, **branching bacteria** (esp. *Actinomyces, Nocardia* species)
   3) retained **foreign bodies** (incl. bone fragments)
   4) **large** (> 3 cm), **multiloculated**, **& readily accessible**

5) **posterior fossa** (potential of brain stem compression)
6) **resistant** to treatment (getting bigger in 2 weeks, no decrease in 4 weeks)

± prophylactic AED for at least 1 year (risk of seizure disorder in 80-90% patients!)
± **corticosteroids** (only for profound cerebral edema with impending herniation!; may decrease penetration of antibiotics! - discontinue when edema and mass effect improve)

Mortality 5-20% (if untreated ≈ 100%).

SPINAL CORD ABSCESS

– particular high risk factor – IV drug abuse.

TREATMENT

1. **Antibiotics** – minimum 4 weeks following surgery.
2. **Steroids** (**DEXAMETHASONE** 4-10 mg q6h during entire course of treatment) – to reduce spinal cord swelling.
3. Surgical drainage of abscess cavity - LAMINECTOMY:
   - ***abscess aspiration*** for culture & stain (Gram, India ink).
   - **myelotomy** over length of abscess.
   - ***irrigate*** (wound and abscess cavity) with antibiotic solution.
   - ***closure*** in anatomical layers.

SUBDURAL EMPYEMA (CRANIAL AND SPINAL)

- empyema *evolution is remarkably rapid* (along falx and over convexities).
- subdural empyema may breach arachnoid (arachnoid is not very strong barrier) → meningitis.
- septic thrombophlebitis extends from dural sinuses to cortical veins → cortical venous infarction of gray and white matter drained by thrombosed vessels → brain abscess (25% patients!).

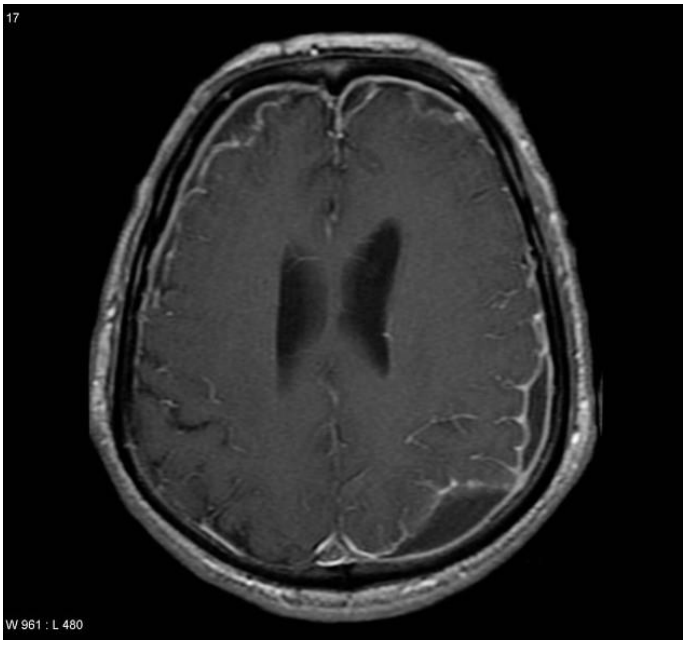
Patient is acutely ill

Spinal subdural empyema - fever with rapidly progressive spinal cord compression.

- **backache** is not as characteristic as in spinal epidural abscess.
- tenderness along spine is often absent (vs. spinal epidural abscess).

MRI (procedure of choice) – T1 *hypointense crescent,* diffusion restriction

– *intense contrast enhancement* of empyema margin (fine line).
– mass effect.



TREATMENT

- surgical emergency!
- **anticonvulsants** should be administered prophylactically.

Intravenous antibiotic therapy (same as for brain abscess)

Immediate surgical drainage:

A. **CRANIAL** – start with **multiple burr holes → craniotomy** PRN.
   - do not try to remove material adherent to cortex (→ infarction)
   - ***drains*** are left in subdural space.
   - postoperatively, repeat CT / MRI scans – ***reoperation*** (drainage of loculated pockets) is typically necessary.

B. **SPINAL** – **laminectomy** → dural incision → drainage.

- mortality 10-40% (almost fatal if untreated).
- in 8-46% patients **chronic epilepsy** results.

CRANIAL EPIDURAL ABSCESS

– almost always associated with *overlying infection in cranial bones* (e.g. penetration from chronic sinusitis or mastoiditis; most common cause is craniotomy complicated by wound infection).

- slowly growing mass (*does not produce sudden major neurologic deficits* unless complicated by deep extension)
- ***rim of contrast enhancement*** (thicker and more irregular than with subdural empyema)

TREATMENT

Same as for subdural empyema except: **craniectomy (debridement of infected bone)** may be needed

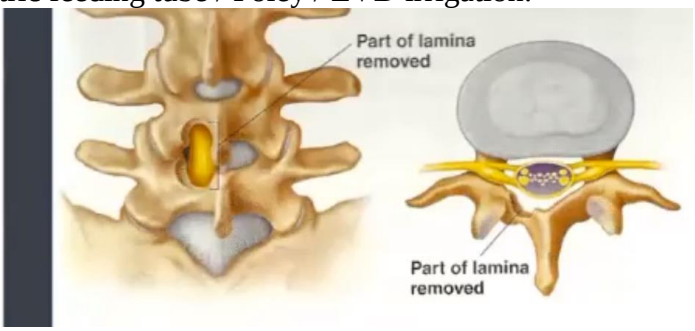
SPINAL EPIDURAL ABSCESS

- any infectious phlegmon involving epidural space, even without demonstrable contained pus.
- most common ETIOLOGY (vs. cranial epidural abscess) - **HEMATOGENOUS SPREAD** from remote site
- also **EXTENSION FROM VERTEBRAL** *osteomyelitis / discitis*

Back pain & tenderness (on percussion & movement) → radiculopathy, myelopathy

Immediate surgery: **laminectomy** - **surgical debridement** of epidural space.

- long abscesses - skip laminotomies and pediatric feeding tube / Foley / EVD irrigation:



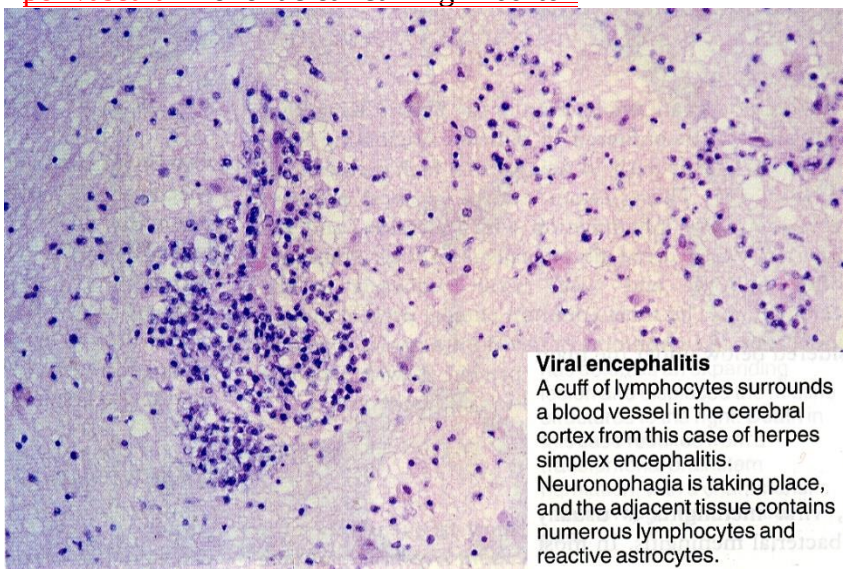
Antibiotics: 4-6 weeks IV → 2-3 months oral.

paralysis 36 hours duration → < 50% will show some return of motor function.

- in *tuberculous epidural abscess* motor recovery has been reported even after paralysis lasting for weeks.

ENCEPHALITIS

- perivascular mononuclear cuffing in ***cortex***



Viral encephalitis
A cuff of lymphocytes surrounds a blood vessel in the cerebral cortex from this case of herpes simplex encephalitis. Neuronophagia is taking place, and the adjacent tissue contains numerous lymphocytes and reactive astrocytes.

PANENCEPHALITIS = **leukoencephalitis** (i.e. myelinoclastic) + **polioencephalitis** (i.e. polioclastic)

- viral encephalitis is polioclastic, vs. postinfectious encephalitis – myelinoclastic
- encephalitis is almost invariably associated with *meningeal inflammation* (**MENINGOENCEPHALITIS**) and sometimes with simultaneous *involvement of spinal cord* (**ENCEPHALOMYELITIS**).
- necrotizing vasculitis with focal (petechial) hemorrhages.

- severe vasogenic edema → ICP↑.

prodromal viral illness → dramatic ENCEPHALOPATHY: **AMS**, **psychiatric symptoms, seizures** (> 50%), **paralysis**

CSF should be examined in all patients!!! (unless contraindicated by ICP↑↑↑).

Characteristic CSF profile ≈ viral meningitis

1) lymphocytic pleocytosis 5-500
2) normal glucose
3) protein↑
4) **PCR** - diagnostic procedure of choice!!! - sensitivity (95-100%) and specificity (< 100%) exceeds brain biopsy (thus, role of **brain biopsy** has declined greatly*)

*still diagnostic criterion standard for *rabies*

EEG - *diffuse slowing*

Neuroimaging – focal or diffuse encephalitic process (*low density with mass effect* predominantly in white matter – i.e. vasogenic edema).

- occasional *intracerebral hemorrhages* within lesion.

Major diagnostic impetus is to distinguish HSV from other viruses!

Other viruses → **supportive measures** (in ICU initially)

MORTALITY depends to etiology (may be up to 75%*).

*100% in *rabies* or *VZV in immunosuppressed patients*

HERPES SIMPLEX

- focal* encephalitis with intense necrosis + petechial hemorrhages, with RBCs in CSF; inferomedial frontotemporal regions:

1) temporal lobe seizures (EEG – *paroxysmal features in temporal lobe* - paroxysmal lateral epileptiform discharges PLEDs)
2) olfactory / gustatory hallucinations, anosmia
3) bizarre behavior / personality alterations, memory disturbance

*tropism for TEMPORAL, ORBITAL-FRONTAL CORTEX, LIMBIC STRUCTURES and PONS!

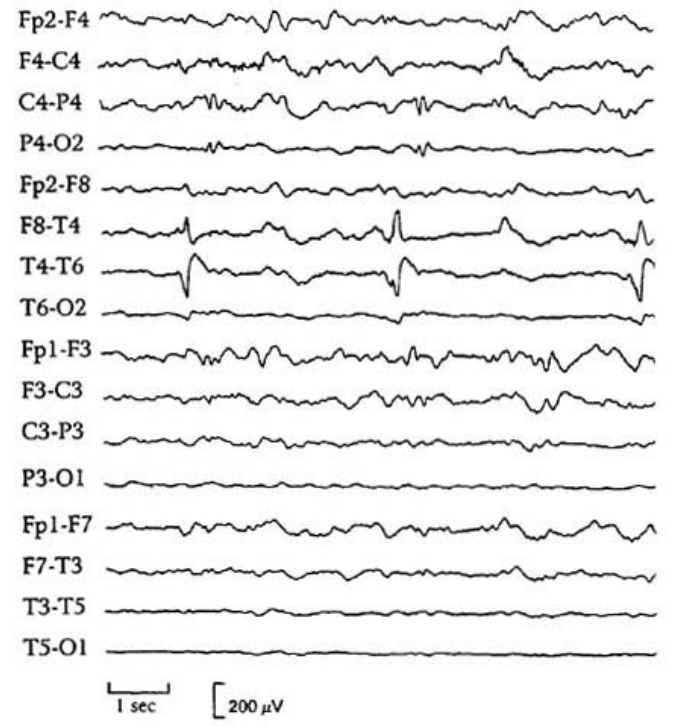
N.B. clinical criteria alone are not reliable in differentiating HSV and non-HSV encephalitis!

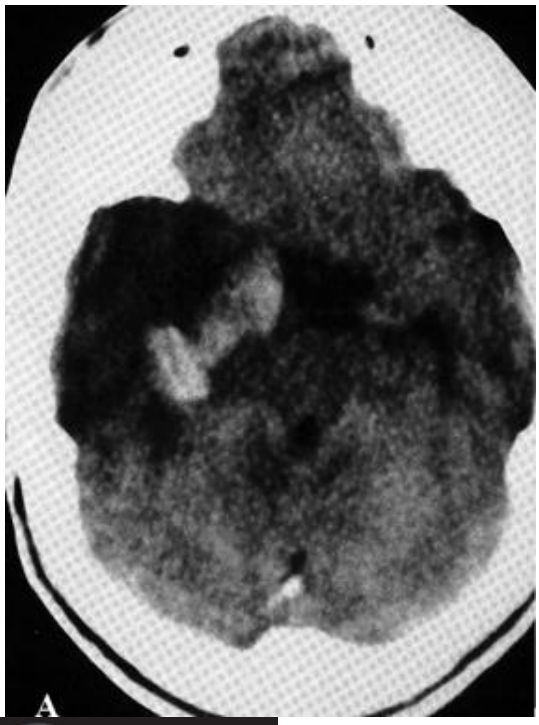
Neurologic disease has been associated with all herpesviruses but HHV-7

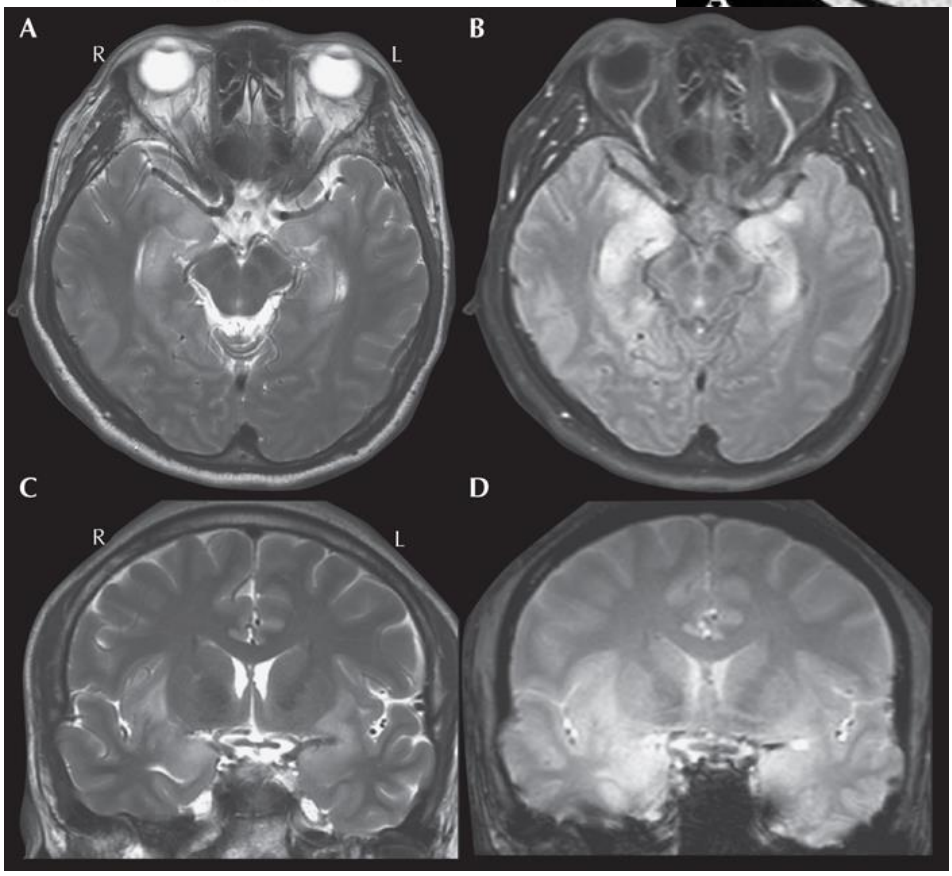
1) herpes simplex virus type 1- most common cause of *sporadic encephalitis*!
2) herpes simplex virus type 2 (encephalitis in neonates)
3) varicella-zoster virus
4) Epstein-Barr virus
5) cytomegalovirus

- not related to immunosuppression.

- ***virus reactivation*** lying dormant in trigeminal ganglia (i.e. virus spreads to CNS transneuronally along CN5)
- often high fever (104-105°F) initially.
- herpetic skin lesions are seen in only few cases.
- characteristically AGGRESSIVE COURSE; more indolent in *immune-compromised persons* (indicates role of immune system in destructive nature of herpes encephalitis).







HSV → urgent ACYCLOVIR 10-15 mg/kg IV q8hr for 10-21 days (also useful in ***selected severe cases*** of EBV or VZV).

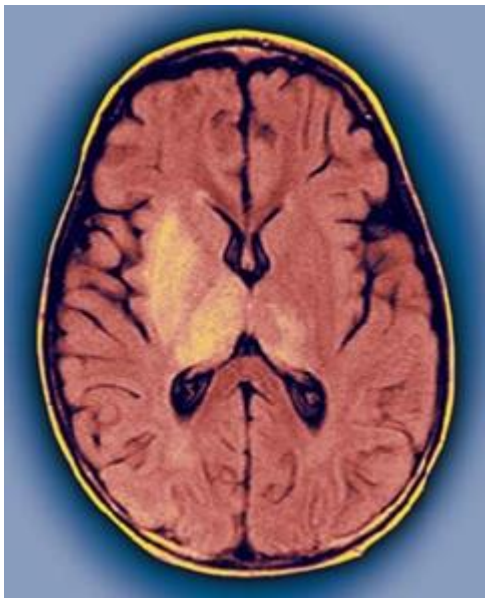
Initiating treatment *before definitive diagnosis* of HSV encephalitis is now common practice!

- discontinue if PCR is found negative.
- if clinical deterioration occurs over next 48-72 hours with ACYCLOVIR → ***brain biopsy***.
- ***decompressive operation*** may be necessary if **steroids** (and other measures) are inadequate to control severe ICP elevations.

ARBOVIRUS

- most common causes of *endemic encephalitis*!

A) *mosquito-borne*
B) *tick-borne* - does not occur in America; **MRI** - *increased T2 signal* in basal ganglia and thalami



ENTEROVIRUS

outbreaks during *warm weather*

SYPHILIS – very long rod cells
RABIES – Negri bodies in cerebellum

HIV

Neuroinvasion occurs in practically every patient

HIV - *neurotropic virus*

N.B. in nervous system, *virus is detected only in* ***microglial*** *cells*; virus is not found in neurons or glia!

Clinical syndromes - neurological disease at any anatomic level:

1) **cognitive dysfunction** → AIDS-dementia complex → coma.
2) **seizures** (focal or generalized)
3) various **focal deficits**
4) **aseptic meningitis**
   most common acute bacterial meningitis - *L. monocytogenes*
5) **myelopathy**
6) **peripheral neuropathies** - autoimmune ***demyelination*** and/or ***axonal degeneration***
7) **myopathy**

Painful neuropathy is often most functionally disabling manifestation of AIDS!

Secondary disorders - result from other identifiable causes:

A. Opportunistic infections:
   1) toxoplasma encephalitis - most common cause of intracranial mass lesion in AIDS!!!
   2) cryptococcal, tbc meningitis
   3) CMV encephalitis / polyradiculopathy
   4) progressive multifocal leukoencephalopathy (PML) – JC virus

B. Neoplasms:
   1) primary CNS lymphoma - EBV genetinė medžiaga (PCR) aptinkama ≈ 100% atvejų!!!
   2) metastatic

C. Drug complications

D. Metabolic-nutritional disorders

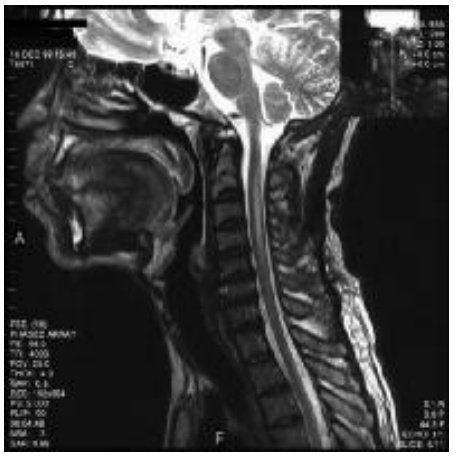
E. Cerebrovascular complications - AIDS is additional risk factor for stroke (ischemic and hemorrhagic)

VACUOLAR MYELOPATHY

- diagnosis of exclusion.

Imaging - normal or *spinal cord atrophy*.

- T2-MRI - *nonenhancing high-signal areas* (extensive vacuolation) confined to posterior columns or diffuse.



CSF - usually normal.

Although no specific treatment is approved / effective, viral control is important.

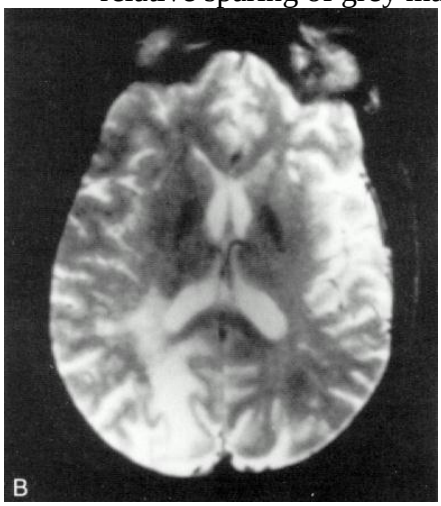
CNS–Immune Reconstitution Inflammatory Syndrome (IRIS)

- develops ***after the initiation of HAART*** in the setting of HIV-related severe immunosuppression (anergic state).
- **intense inflammatory reaction** to dead or latent organisms or to self-antigens.
- clinical range: mild (self-limiting mild symptoms and eventual immune restoration) to fulminant death.
- diagnosis of exclusion
- responds to **steroids**.

Progressive Multifocal Leukoencephalopathy (PML)

- JC virus reactivation in cellular immunodeficiency states.

- focal parieto-occipital demyelination:
  - no mass effect;
  - no contrast enhancement with gadolinium.
  - relative sparing of grey matter!



Definitive diagnosis: **PCR** in CSF → **Brain biopsy**
No specific treatment = high mortality rate

PRIONS

- fatal **TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES** (noninflammatory neurodegenerative disorders)

PRION - infectious protein (**prion protein** PrP)

- **PrP gene** (termed *PRNP*) - single copy is located on short arm of chromosome 20 - PrP^{C} (normal cellular isoform of PrP) is normal cell surface glycoprotein

Prion diseases are result of PrP^{Sc} (abnormal isoform of PrP^{C}; ^{S} for "scrapie").
  - PrP^{C} exists as α-helical structure.
  - PrP^{Sc} exists as β-pleated sheets (arise from post-translational changes in PrP^{C} conformation) - resists proteolytic digestion → spontaneously aggregates to rodlike or fibrillary particles (***PRION RODS***).

- PrP^{Sc} facilitates, in cooperative fashion, comparable transformation of other PrP^{C} molecules - PrP^{Sc} acts as template that promotes cascading PrP^{C} conversion - ability to replicate! (infectious nature of PrP^{Sc} molecules).
- *intracytoplasmic vacuoles* in cortical neurons and glia → vacuolated areas coalesce into cystlike spaces ("status spongiosus").
- severe neuron loss → reactive astrocytic gliosis → **cortical atrophy** without white matter changes.

Clinical
- ***long incubation*** (several months ÷ several years).
- ***protracted course*** generally ending in death.
- visada apima CNS (ir tik CNS):
  1) progressive dementia
  2) motor deficits
  3) seizures

Diagnosis confirmation – **brain biopsy**.

Treatment - supportive (e.g. suppression of myoclonus or seizures).

Chirurginiams instrumentams: N.B. irradiation is ineffective!

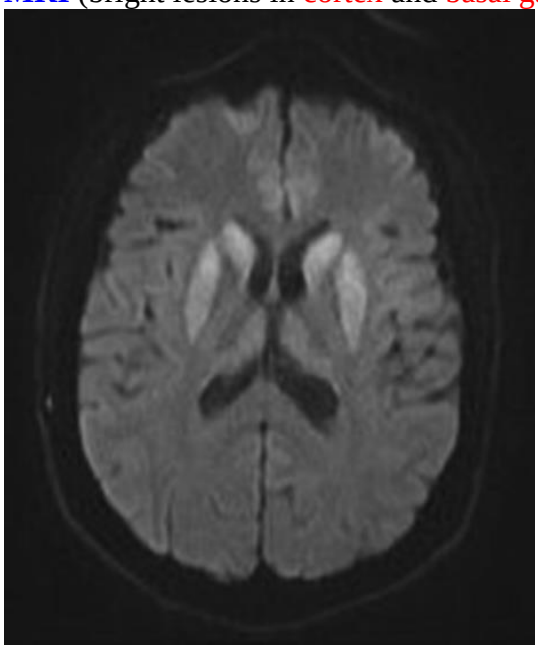
a) autoklavavimas 60 min. 134°C.
b) immersion in 1 *N* NaOH for 1 hour.

CREUTZFELDT-JAKOB DISEASE (CJD)

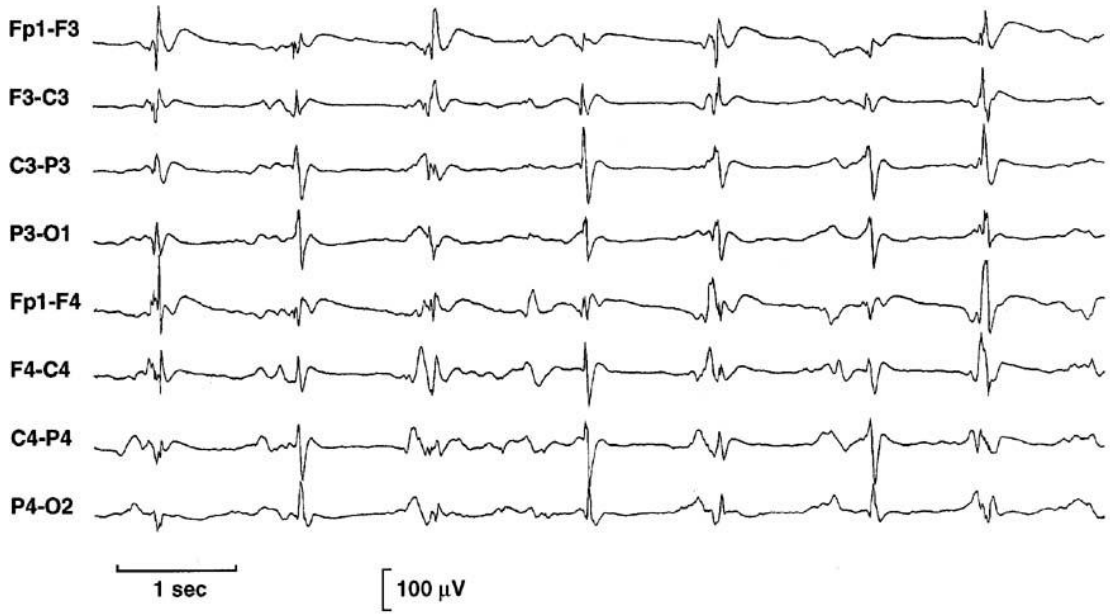
– most common prion disease!
Sporadic CJD (90%)
Infectious CJD (rare) – transmission: ***human-to-human parenteral*** or ***ingestion of beef***

1. Rapidly progressive **dementia** → mutism & global dementia.
2. **Involuntary movements** (esp. ***myoclonus*** provoked by sensory stimuli - startle myoclonus)

MRI (bright lesions in cortex and basal ganglia+pulvinar):



EEG - pathognomonic - generalized bilaterally synchronous **periodic** **triphasic spiking** activity (resembles ECG).



CSF immunoassay for protein 14-3-3 – high sensitivity and specificity (90-92%) for CJD
- more specific/sensitive test for Prion disease - RT-Quic test.

Brain biopsy with immunostaining for PrP^{Sc} is gold standard for establishing diagnosis (almost never necessary).

> 90% miršta per 1 metus!

CRANIAL OSTEOMYELITIS

Look for postop bone flap absorption on CT!

GRADENIGO'S syndrome – ***apical petrositis*** (osteomyelitis) involving **CN5 & CN6**.

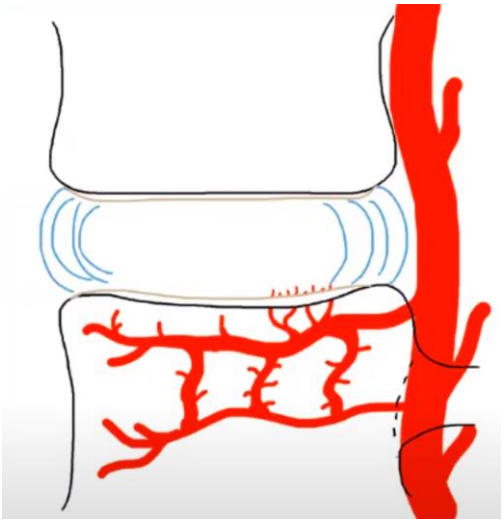
1. **Surgical debridement** (removal of infected bone)
   - adequate margin of normal bone is removed to minimize risk of recurrence.
   - *after at least 1 year* with no evidence of inflammation, **cranioplasty** may be performed.
2. **Antibiotics**
   - MRSA is treated with 6 weeks of VANCOMYCIN
   - if hardware is present (e.g. cranial mesh), add RIFAMPIN.

VERTEBRAL OSTEOMYELITIS

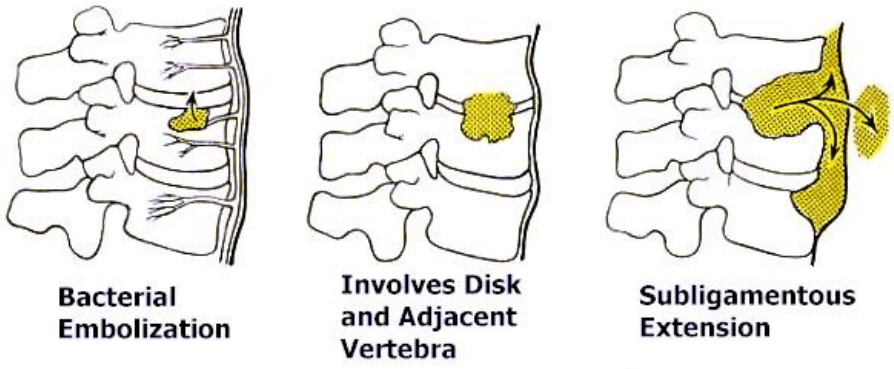
- destructive **disco-vertebral lesion**.

Infections usually involve disk space (vs. malignant lesions!)

- hematogenous spread to metaphyses:



- well-recognized risk factor - IV drug use.
- complications - *paraspinal extension* - paraspinal abscess, psoas abscess, anterior epidural abscess;
  - paraspinal masses are large in indolent infections (such as tuberculosis).



1. **Spine tenderness, Deep back pain** - exacerbated by motion + unrelieved by rest.
2. **Fever** (25%).

N.B. all signs of infection may be absent and course may be indolent!

Neurological involvement – (in 40% of cases caused by tuberculosis!):

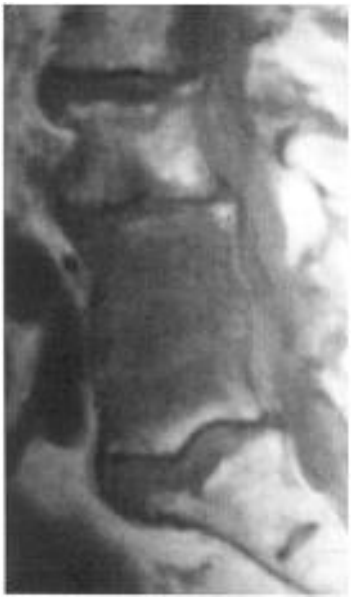
a) epidural extension
b) spine instability and fractures

Blood culture x2 ASAP before starting antibiotics! (else may need **IR biopsy**)

CT - punched-out erosions of bone adjacent to involved disc ("moth-eaten" endplates)

MRI (diagnostic method of choice – highly sensitive and specific!:

1) edema - low T1 signal (high signal on T2) throughout disc and in adjacent vertebral bodies.
2) thinning and eventual loss of dark line of vertebral end-plates.
3) diffuse enhancement.



N.B. in *degenerative disk disease*, changes are less uniform, disk is desiccated and bone destruction is absent, no paravertebral soft-tissue masses.

TREATMENT

1. Infection control
   - MRSA is treated with 6 weeks of VANCOMYCIN; if hardware is present, add RIFAMPIN.
2. Pain comfort and prevention of further deformity (**brace**)
3. **Operative debridement** – limited indications:
   a) epidural extension as abscess with progressive neuro deficits
   b) progressive spinal deformity / instability
   c) recurrent/persistent bacteremia
   d) worsening pain despite appropriate antimicrobial therapy
   - just pain, including radicular pain (tends to get better with abx) are not surgical indications.
   - **instrumentation***, **discectomy** up to **corpectomy** for instability / kyphosis.
     **modern instrumentation* is titanium – does not need to be isolated from site of infection.
   - when infection is controlled, disc space will eventually spontaneous fusion.

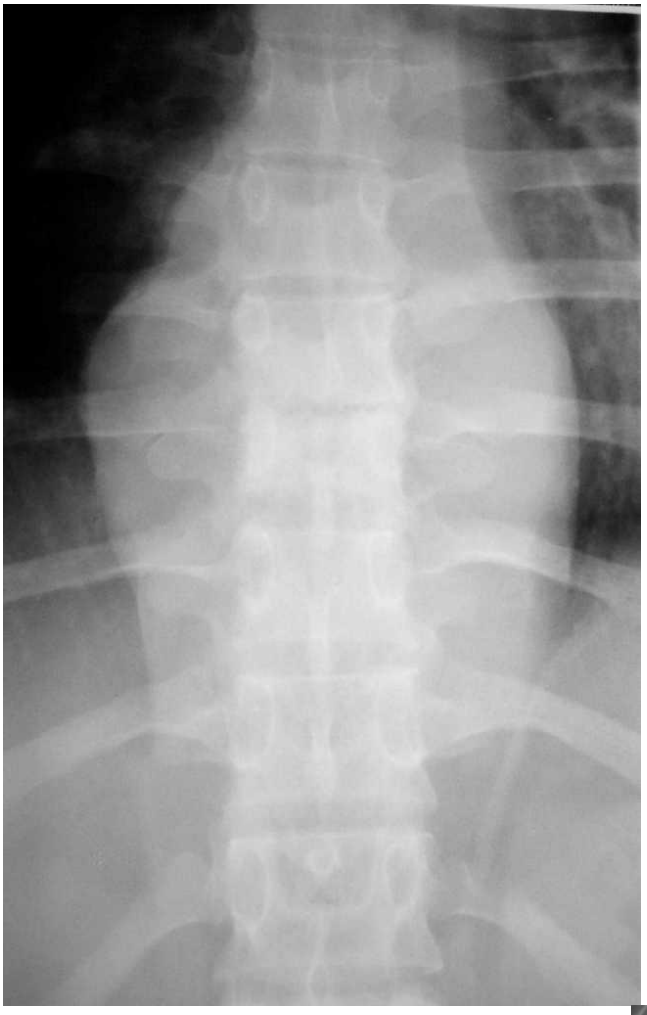
POTT'S DISEASE

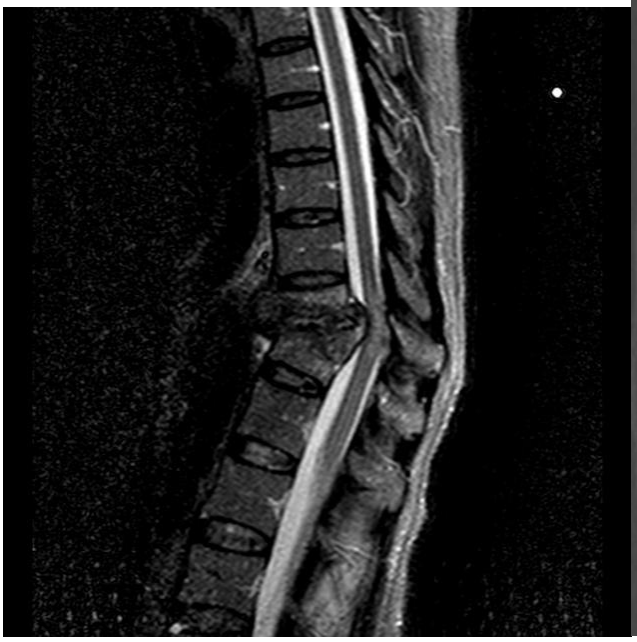
M. tuberculosis

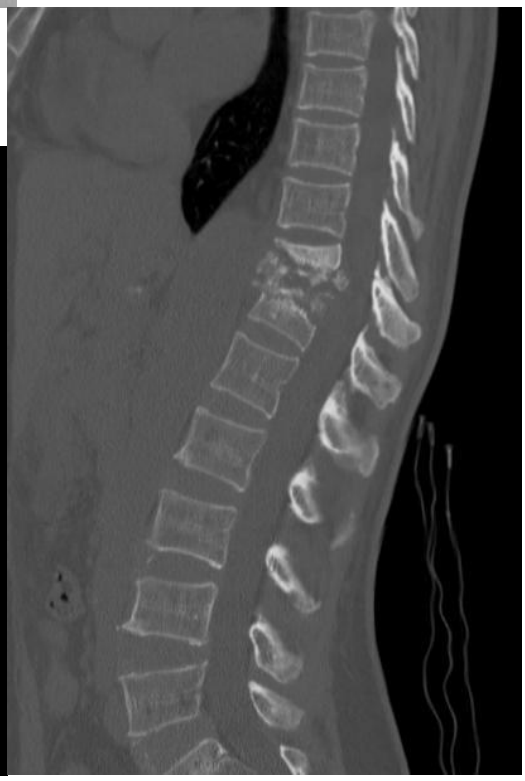
– tendency to involve *multiple segments* (through subligamentous paraspinal spread).
– highly aerobic bacteria - discs are spared until later in course – "skip" lesions

Radiographic changes:

1. Reactive sclerosis on a progressive lytic process
2. Enlarged psoas shadow = abscess formation
   In contrast to pyogenic disease, calcification is common in tuberculous lesions!
3. Collapse with anterior wedging (gibbus) → neuro deficits
4. Thin and smooth enhancement of abscess wall (vs. pyogenic spondylitis - thick and irregular enhancement of abscess wall)







PARASITES

NEUROCYSTICERCOSIS (NCC)

- intracranial encystment of larva of *Taenia solium*

- endemic in South and Central America + Madagascar.

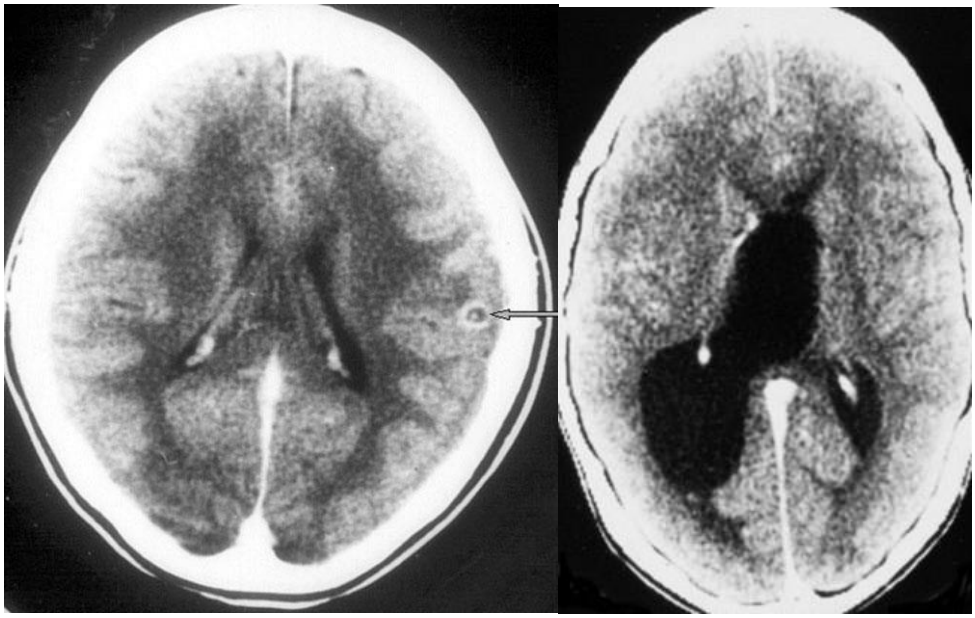
Life cycle of *Taenia solium* (pork tapeworm):
egg in human feces
↓
INTERMEDIATE HOST (pigs, humans): **egg** in mouth → **….** → **larvae** in tissues = **cysticercosis**
↓
DEFINITIVE HOST (only humans - nervous system is not affected): **larvae** in mouth → **adult tapeworm** in small bowel → **egg** in feces

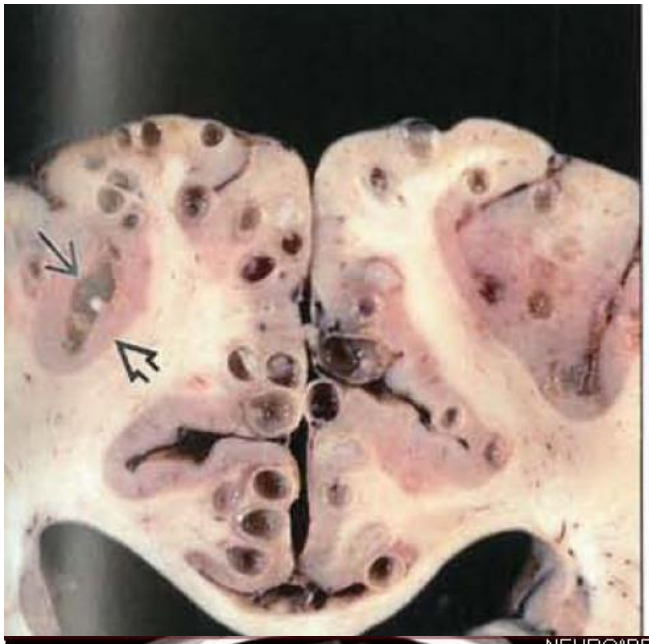
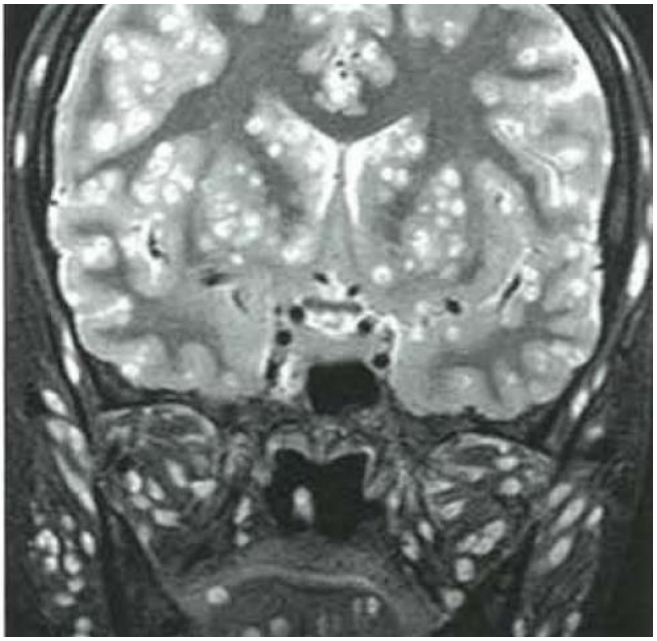
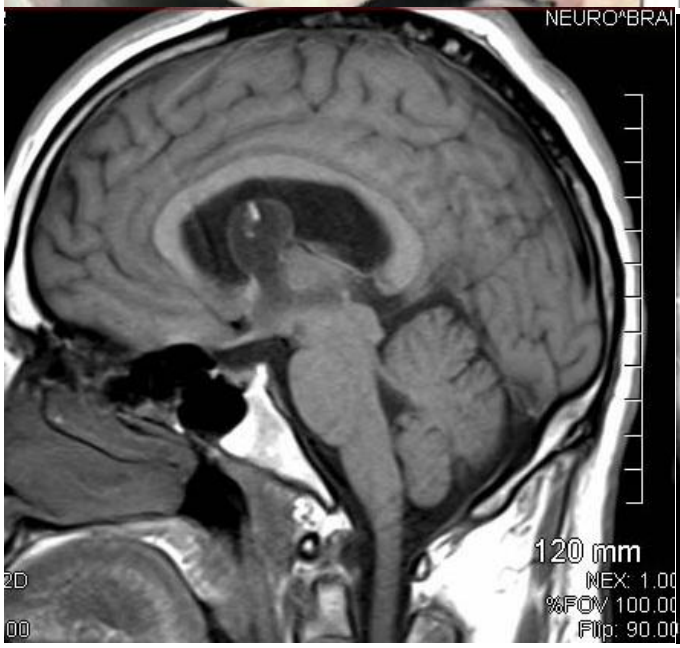
Little inflammatory response (edema) occurs as long as larva is alive!
Larva dies in brain 2-6 years after ingestion of eggs: release of antigens from dying parasite → vigorous inflammatory tissue reaction.
Eventually, calcified nodule.

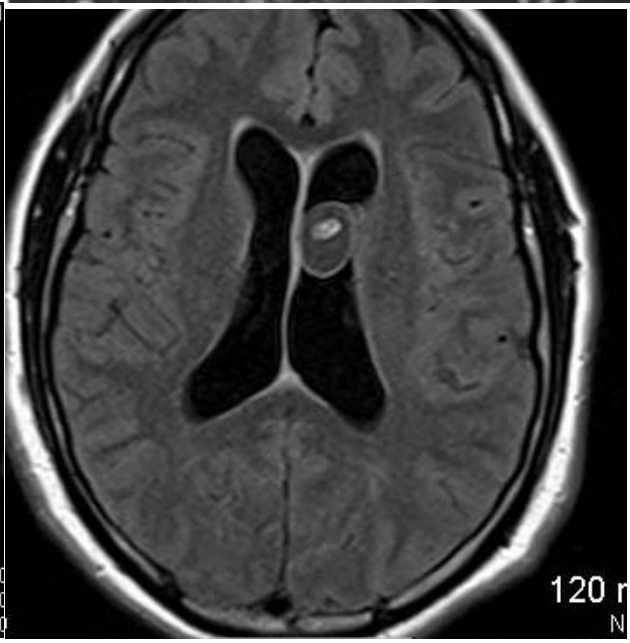
Location of cysts:

1. **Parenchymal** → seizures, other focal deficits; cysticercotic encephalitis produced by immunologic reaction → dementia, behavioral abnormalities.
2. **Meningeal**: chronic basal meningitis; obstructive hydrocephalus); *extremely high mortality*
3. **Ventricular**: obstructive hydrocephalus with intermittent intracranial hypertension (**BRUN syndrome**).
4. **Spinal cord**: radiculopathy or myelopathy.

CT, MRI
non-enhancing edema → ***homogeneous enhancing lesions*** → SYMPTOMATIC STAGE: low density ***nonenhancing*** cyst(s) with ***eccentric punctate high density*** (***scolex*** = tapeworm head) → ***ring enhancing*** cysts with inflammatory ***edema*** → ***complete resolution*** or oval ***calcifications*** without edema.





- test of choice is serum **serology**
- **eosinophilia**.
- **biopsy** - sometimes needed for diagnosis (no diagnostic test identifies all cases of cysticercosis).

TREATMENT

Inactive infection does not require treatment!

- anthelmintic ***not indicated*** when no longer enhancing and no edema.
- if cyst is calcified or ring-enhancing, treatment with anthelmintics is probably not necessary.

Antihelmintic drugs

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

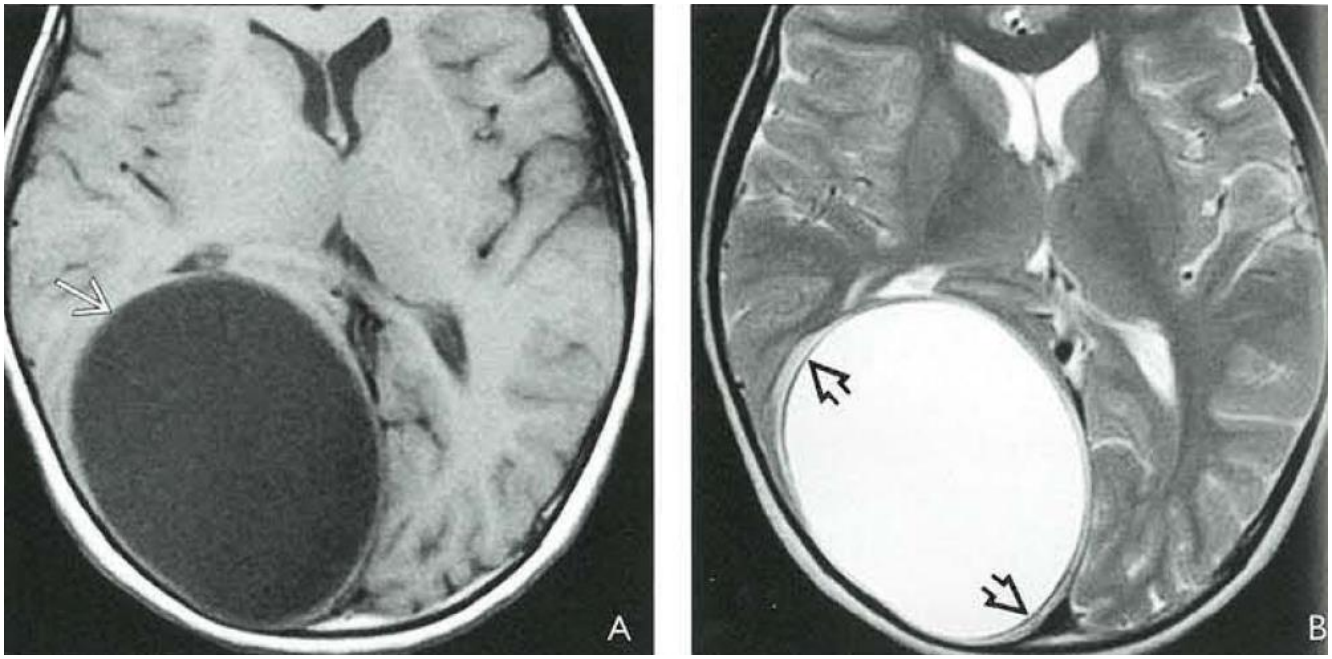
- **steroids** - for all patients concomitantly with anthelmintic (to reduce edema), start 2-3 d before antihelmintics.
- ALBENDAZOLE – cysticidal agent of choice

Surgery – symptomatic cases:

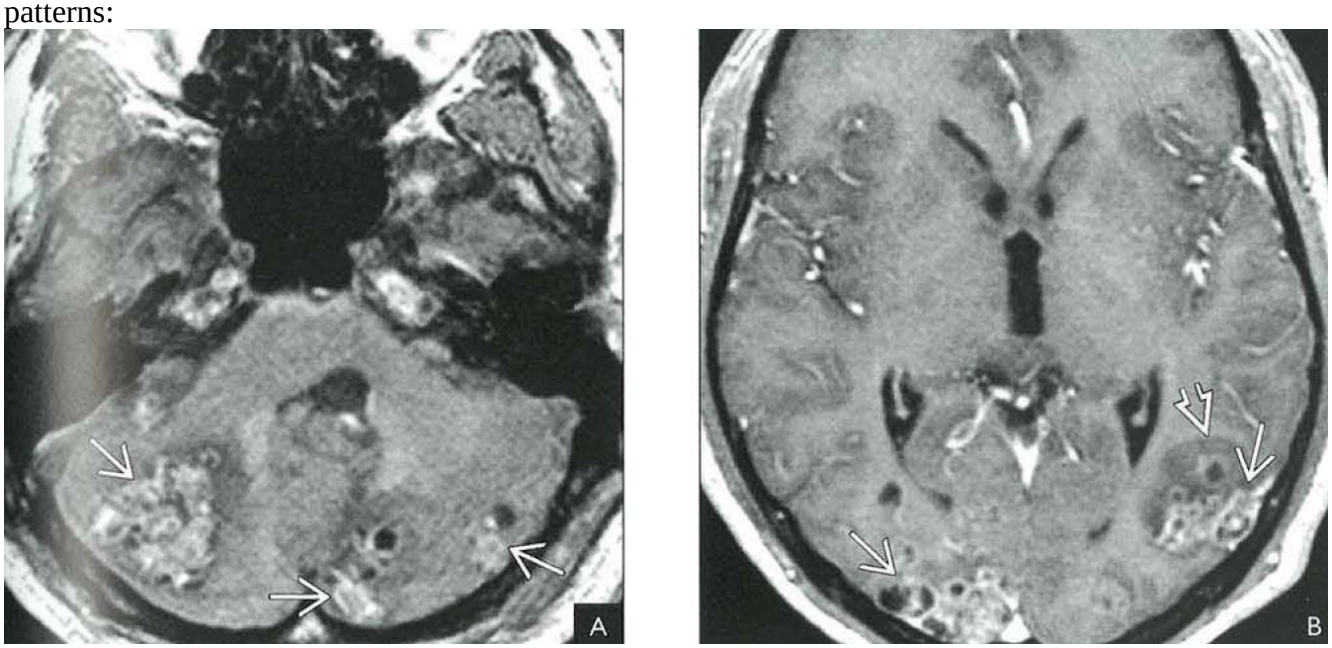
- unclear diagnosis → stereotactic **biopsy**.
- hydrocephalus → **CSF diversion**, **endoscopic resection**.
- giant cysts (> 50 mm) when intracranial hypertension persists despite steroids → **resection**.
- uncontrollable seizures → **resection**.
- spinal / orbital cysts → **resection** (inflammation associated with medical treatment may cause worsening of symptoms or loss of vision)

ECHINOCOCCOSIS

Hydatid cyst (HC) – single large thin-walled cyst; no calcification, no edema, no enhancement, fluid isodense / isointense to CSF



Alveolar echinococcosis – multiple irregular cysts that enhance in ring-like / nodular / cauliflower patterns:



AMEBIC MENINGOENCEPHALITIS, ABSCESS

N. FOWLERI

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

BALAMUTHIA MANDRILLARIS

- ameba is present in soil
- causes encephalitis in both immunocompetent and immunocompromised