



**Kharkiv National Medical University  
Department of Infectious Diseases**

# **MENINGEAL SYNDROME IN CLINIC OF INFECTIOUS DISEASES**

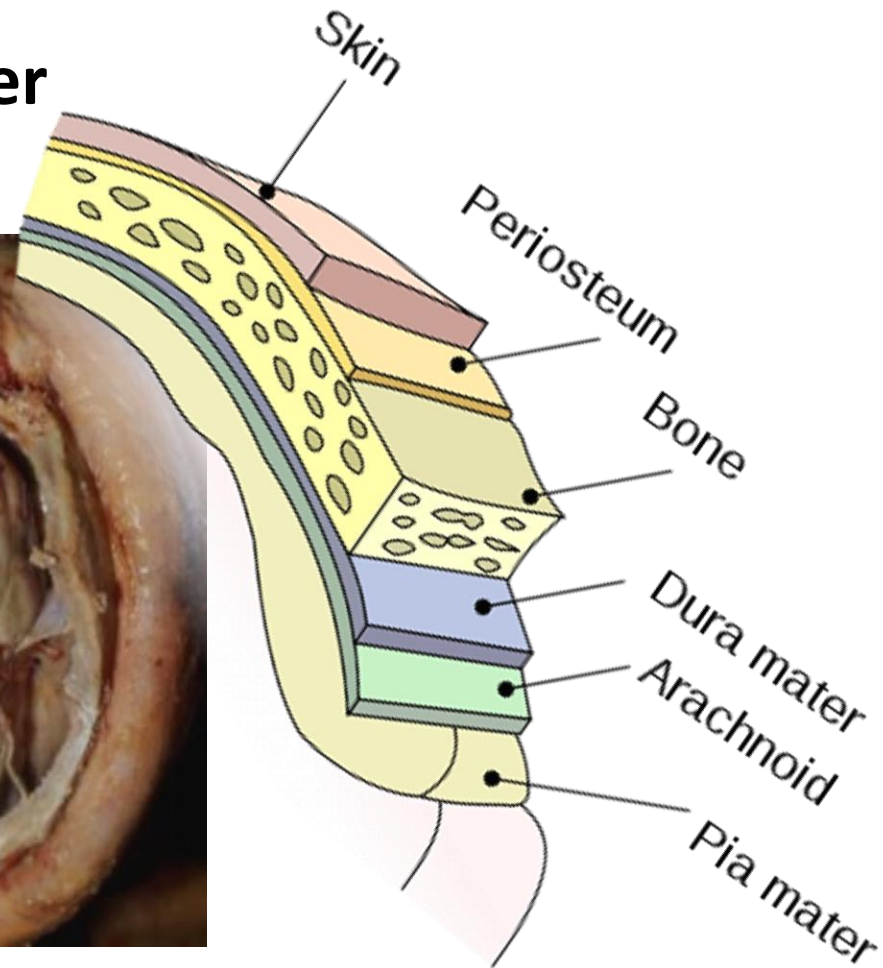
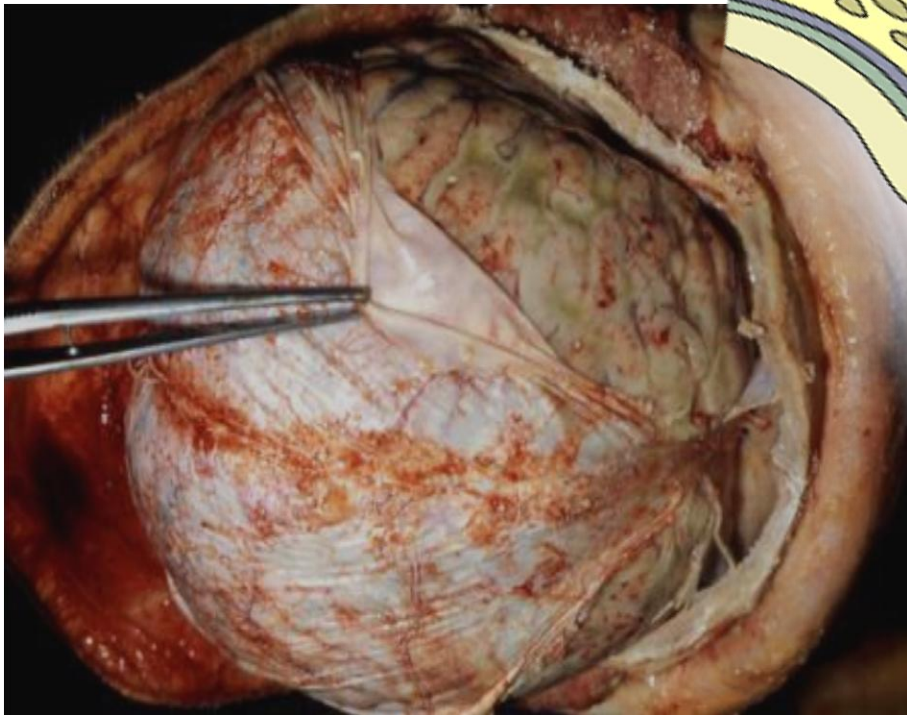
**D.Sc., Ass. Prof. Bondarenko A.V.**

The brain and spinal cord are covered by connective tissue layers collectively called the meninges which form the blood-brain barrier:

1 – the **pia mater**

2 – the **arachnoid mater**

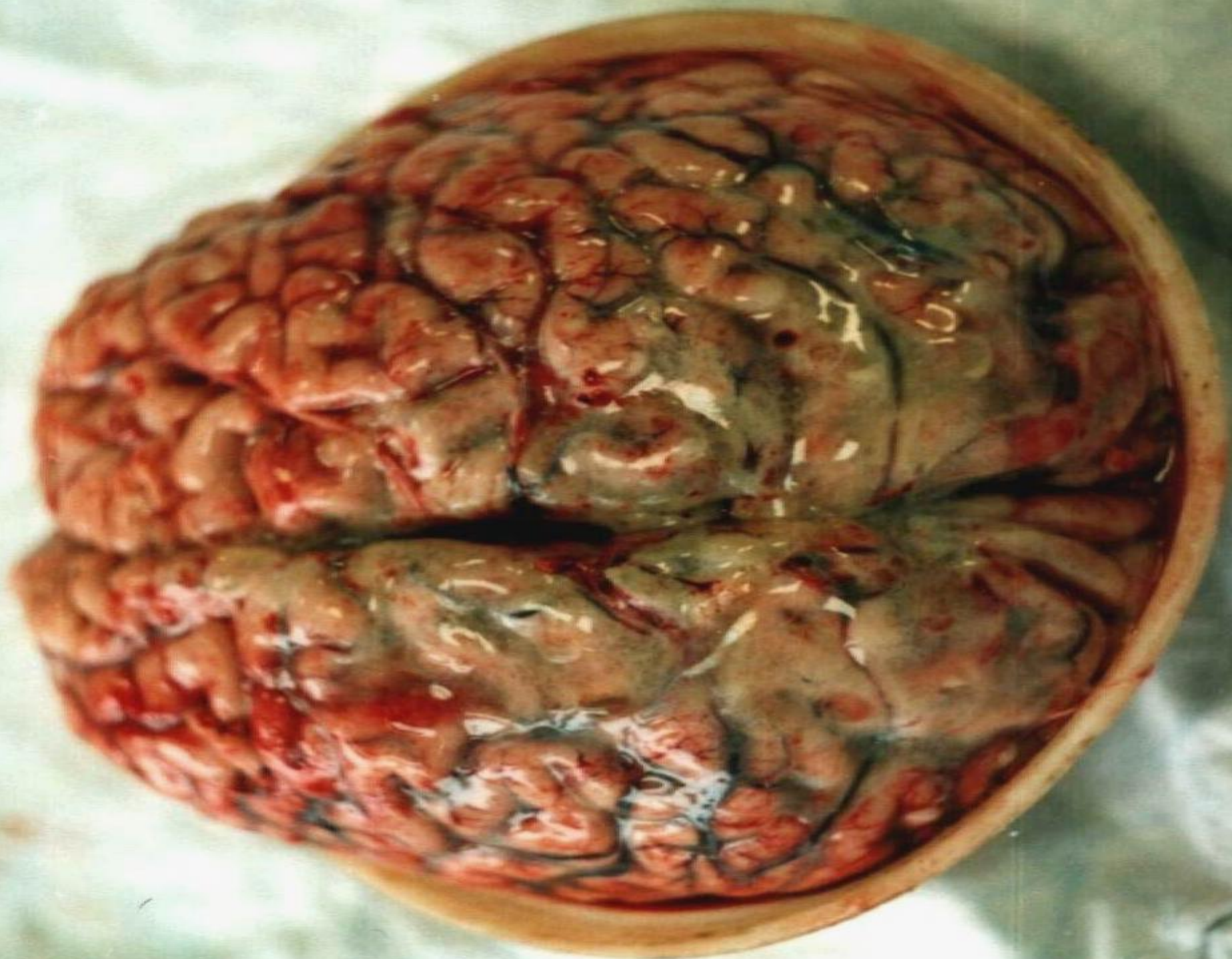
3 – the **dura mater**



- **MENINGITIS** – inflammation of meninges (inflammatory response is generally confined to arachnoid, subarachnoid space and pia mater – i.e. LEPTOMENINGITIS)
- **Leptomeningitis** - inflammation of the pia mater and arachnoid.
- **Arachnoiditis** - inflammation of the arachnoid membrane.
- **Pachymeningitis** - inflammation of the dura mater.
- **Encephalitis** - inflammation of the brain parenchyma (diffuse and/or focal).
- **Myelitis** - inflammation of the spinal cord parenchyma.

# Meningitis

- Cellular infiltration of the meninges.
- **Presence of meningeal syndrome:**
  - General symptoms of intoxication.
  - Signs of meningeal irritation.
  - Changes in mental status (apathy, somnolence, delirium).
  - “CSF syndrome” – increased cell and protein.
- **Brain parenchyma is intact**, except edema and radicular/cranial nerve lesions.
  - Focal neurological signs are absent.



# Meningism (pseudomeningitis)

- syndrome of headache and signs of meningeal irritation in patients (child or young adult) with acute febrile illness (usually of viral nature) in whom CSF is under increased pressure but normal in other respects.
- condition is brief in duration.
- pressure reduction by removal of CSF results in disappearance of symptoms.

# Etiology

- **Infection**
- **Inflammatory disorders:**
  - Serum sickness
  - Periarthritis nodosa
  - Systemic lupus erythematosus
  - Behçet's disease
  - Vogt-Koyanagi-Harada syndrome
  - Sarcoidosis
- **Malignant:**
  - Carcinomatous meningitis
  - Lymphomatous meningitis
- **Physical injury (air, blood, etc.) :**
  - Trauma to head or spine
  - Brain surgery
- **Chemical injury:**
  - Leakage into CSF of contents from epidermoid tumor, craniopharyngioma, cholesteatoma
  - Nonsteroidal anti-inflammatory drugs
  - Trimethoprim
  - Isoniazid
  - Intravenous immunoglobulin
  - Azathioprine
  - Muromonab-CD3

# Bacterial pathogens

- *Streptococcus pneumoniae*
- *Neisseria meningitidis*
- *Haemophilus influenzae* type B
- *Staphylococcus aureus*
- *Streptococcus agalactiae*
- Enterobacteriaceae
  - *Klebsiella* spp.
  - *Enterobacter* spp.
  - *Escherichia* spp.
  - *Serratia* spp.
  - *Proteus* spp.
- *Pseudomonas* spp.
- *Listeria monocytogenes*
- *Bacillus* spp.
- *Bacteroides* spp.
- *Clostridium* spp.
- *Fusobacterium* spp.
- *Mycobacterium tuberculosis*
- *Mycoplasma pneumoniae*
- *Leptospira* spp.
- *Anaplasma phagocytophilum*
- *Ehrlichia* spp.
- *Rickettsia rickettsii*
- *Borrelia burgdorferi*
- *Treponema pallidum*

# BACTERIAL PURULENT MENINGITIS

1. *Str. pneumoniae* (30-50%) (esp. in association with pneumonia, otitis media, skull base fracture with CSF leak); > 50% patients are > 50 years of age.
2. *N. meningitidis* (10-35%) (only major cause of epidemics in overcrowded conditions – military barracks, etc); most patients are adolescents and young adults.
3. *S. aureus* and coagulase-negative staphylococci (5-15%) – predominant organisms in CSF shunts or subcutaneous Ommaya reservoirs.
4. Gr- bacilli (1-10%) – most common in elderly (hospital-acquired infections).

## BACTERIAL PURULENT MENINGITIS

5. *Listeria monocytogenes* (5%) – most common in immunosuppressed patients.
6. Streptococci (5%)
7. *Haemophilus influenzae* type b (0,5-3%)
8. Anaerobic bacteria (< 1%) – suggest intraventricular rupture of brain abscess.
9. Polymicrobial meningitis (< 1%) – simultaneous recovery of two or more bacterial species.

# BACTERIAL SEROUS MENINGITIS

1. partially treated
2. parameningeal infection (brain abscess, subdural empyema, epidural abscess, septic thrombosis of intracranial venous sinuses; osteomyelitis of spine or skull)
3. *Mycobacterium tuberculosis*
4. *Listeria monocytogenes*
5. *Mycoplasma pneumoniae*
6. *Anaplasma phagocytophilum*
7. *Ehrlichia* spp.
8. *Rickettsia rickettsii*
9. *Leptospira* spp.
10. *Borrelia burgdorferi*
11. *Treponema pallidum*

# Viral pathogens

- Enteroviruses (up to 92%)
  - Echoviruses
  - Coxsackieviruses
  - Poliovirus
- Bunyaviruses
  - California encephalitis virus
- Flaviviruses
  - Japanese B encephalitis virus
  - Colorado tick fever virus
  - St. Louis encephalitis virus
  - West Nile virus
- Alphaviruses
  - Eastern equine encephalitis virus
  - Western equine encephalitis virus
  - Venezuelan equine encephalitis virus
- Herpes viruses
  - Herpes simplex viruses
  - Varicella-zoster virus
  - Epstein-Barr virus
  - Cytomegalovirus
  - HHV 6, 7, 8
- Paramyxoviruses
  - Mumps virus
  - Measles virus
- Arenaviruses
  - Lymphocytic choriomeningitis virus
- Retroviruses
  - Human T lymphotropic virus
  - HIV
- Influenza virus types A and B
- Adenoviruses

# Fungal and Protozoal

- *Candida albicans*
- *Cryptococcus neoformans*
- *Coccidioides immitis*
- *Histoplasma capsulatum*
- *Blastomyces dermatitidis*
- *Paracoccidioides brasiliensis*
- *Cladosporium trichoides*
- *Aspergillus fumigatus*
- *Toxoplasma Gondii*
- *Naegleria fowleri*
- *Acanthamoeba* spp.
- *Taenia solium*  
cysticercosis

# Epidemiology

## BACTERIAL MENINGITIS

- Annual incidence in the develop countries is approximately 5-10 per 100,000 people.
- 30,000 infants and children develop bacterial meningitis in USA each year (90% in children during the first 5 years of life).
- Incidence increases in late winter and early spring.
- Men are affected more than women.
- Meningococcal meningitis is endemic in parts of Africa.

## VIRAL MENINGITIS

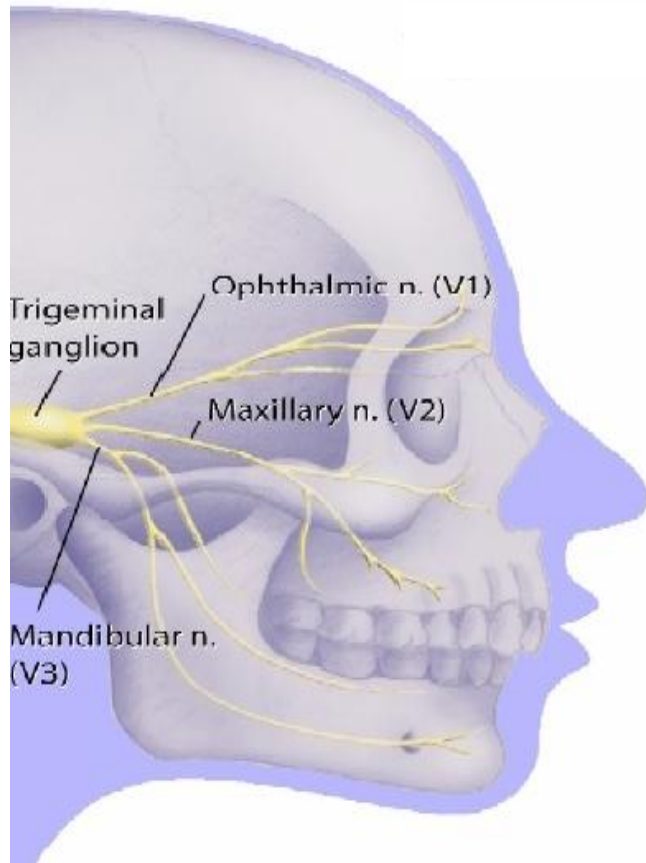
- actual incidence is unknown (most cases are unreported)  $\approx$  11-27 per 100,000 people.
- prominent increase in summer (seasonal predominance of enteroviruses and arboviruses).

# Epidemiology

## **Routes of bacterial infection:**

- Hematogenous spread to CNS.
- Direct extension from nearby focus (mastoiditis, sinusitis).
- Direct invasion (dermoid sinus tract, head trauma, meningomyelocele).

# Pathogenesis



## Routes of viral infection:

- Hematogenous spread to CNS.
- Retrograde transmission along neuronal axon.
- Direct invasion of the subarachnoid space after infection from olfactory submucosa.

# Pathogenesis

## PREDISPOSING HOST FACTORS

- 1) MECHANICAL DISTURBANCES (neurosurgical procedures, basilar skull fractures).
- 2) CONGENITAL DEFECTS (dermoid sinus tracts, meningomyeloceles).
- 3) IMMUNOLOGIC DEFICIENCIES:
  - a) cell-mediated immunity (lymphoma, organ transplant recipients, corticosteroid therapy, AIDS) → intracellular bacteria (esp. *M. tuberculosis*, *L. monocytogenes*).
  - b) humoral immunity (splenectomy, chronic lymphocytic leukemia, multiple myeloma, Hodgkin's disease after radiotherapy or chemotherapy) → encapsulated bacteria (*S. pneumoniae*, *H. influenzae* type b, *N. meningitidis*).
  - c) neutropenia → *P. aeruginosa*, Enterobacteriaceae.

# Pathogenesis

- Nasopharyngeal colonization and mucosae invasion.
- Evasion of the complement pathway.
- Bacterial cross the BBB to CSF.
- Host defense mechanism within the CSF are often ineffective (Ig and complement activity are virtually absent; opsonic activity is often undetectable, phagocytosis is inefficient).
- Bacterial proliferation stimulate a convergence of leucocyte into the CSF.

# Pathogenesis

- release of toxic factors from bacteria → activation of neutrophils → release of TNF- $\alpha$ , IL-1, 8, platelet activating factor:
  - cytotoxic cerebral edema.
  - increase in BBB permeability → vasogenic edema.
- 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.
- hydrocephalus causes transependymal movement of fluid from ventricular system into brain parenchyma (interstitial edema).

# Pathogenesis

- cerebral edema causes ICP $\uparrow$ .
- meningeal and superficial cortical vessels are engorged and stand out prominently.
- since subarachnoid space is continuous over brain, spinal cord, and optic nerves, infection in this space extends throughout cerebrospinal axis unless there is obstruction of subarachnoid space.
- ventriculitis is nearly uniformly present.
- brain parenchyma (cerebritis  $\rightarrow$  abscess), dura (pachymeningitis), subdural and epidural spaces may be secondarily involved.
- when patient recovers, phagocytes completely clear subarachnoid space; if low-grade infection persists, adhesions and leptomeningeal fibrosis develops.

# Classification

- **ACUTE MENINGITIS** – symptoms evolving over 1-24 hours after onset (most cases are bacterial).
- **SUBACUTE MENINGITIS** – symptoms evolving over 1-7 days (includes virtually all cases of viral meningitis, along with some of fungal etiologies).
- **CHRONIC MENINGITIS** – symptoms evolving over more than 1 week (causes are fungi, tuberculosis, syphilis, malignancy, systemic collagenoses, sarcoidosis, some viruses).
- **RECURRENT MENINGITIS** – bouts of acute meningitis with complete resolution between episodes.

# Classification

RECURRENT BACTERIAL MENINGITIS signals host defect in:

- Immunologic defenses
- Local anatomy - usually after trauma.

RECURRENT NON-BACTERIAL MENINGITIS:

- herpes simplex viruses
- chemical meningitis
- primary inflammatory conditions
- drug hypersensitivity (with repeated administration).

# Clinical Manifestation

- **toxic syndrome** (hyperpyrexia, vomiting without nausea, headache, seizures, muscle and back pain)
- **meningeal syndrome**
  - hyperesthesia, photophobia, irritability
  - suppression of skin reflexes
  - tenderness in sites of trigeminal nerve endings
  - stiff neck, positive Kernig's and Brudzinski's signs
- **lethargy and obtundation** progress to stupor or even coma

# Clinical Manifestation

## ACUTE MENINGITIS

Patients rapidly deteriorate:

- course is most dramatic in pyogenic meningitis;
  - course is much less acute in viral meningitis - patients may be in great discomfort but are not critically ill.
1. Patient looks **unusually ill with altered consciousness** (up to coma with shock); in viral meningitis – only mild lethargy or drowsiness.
  2. **Fever**
    - temperature is higher in bacterial than viral CNS infection.
    - temperature may be below normal (tuberculosis).
  3. **Diffuse headache** due to displacement & traction of blood vessels traversing through meninges.
    - typically frontal or retroorbital with pain on moving eyes in viral meningitis.

# Clinical Manifestation

## ACUTE MENINGITIS

4. Vomiting, photophobia, irritability
5. Meningeal irritation signs – nuchal rigidity, Kernig's sign, Brudzinski's sign.
  - meningeal signs are milder in viral meningitis.
  - meningeal signs may be falsely absent in:
    - a) elderly, infants
    - b) debilitated, immunosuppressed
    - c) receiving anti-inflammatory drugs or antibiotics.
6. Seizures (30-40% bacterial meningitis cases, typically during 1st week of illness; focal signs are not typical for uncomplicated viral meningitis).

Etiology:

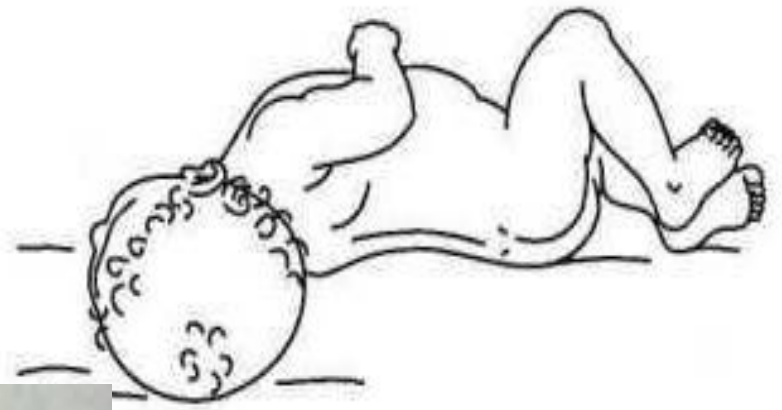
  - a) fever
  - b) focal ischemia, cortical venous thrombosis with hemorrhage
  - c) hyponatremia
  - d) subdural effusion / empyema (mass effect)
  - e) antimicrobial agents (e.g. imipenem, penicillin).

# Clinical Manifestation

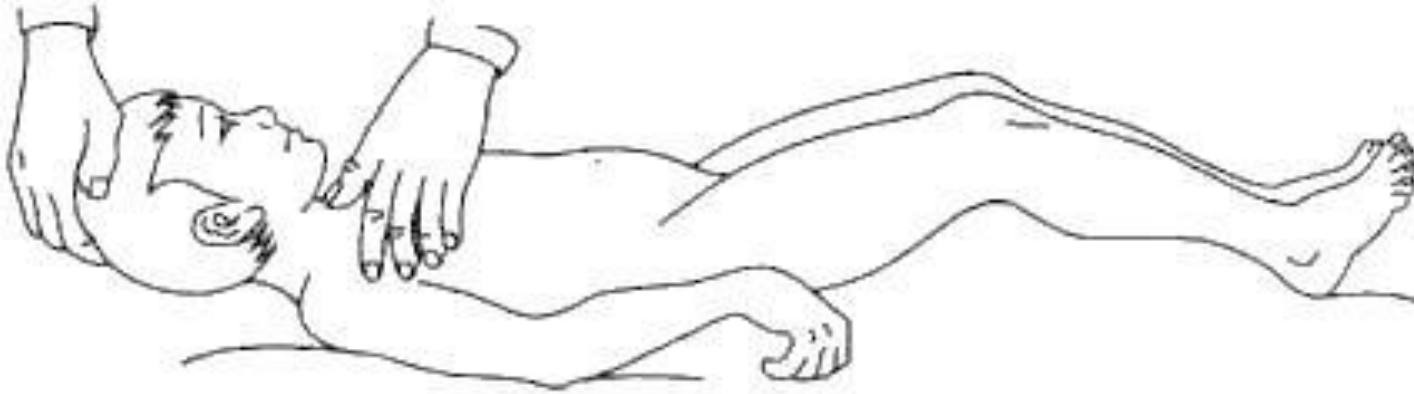
## **SUBACUTE / CHRONIC MENINGITIS**

- manifestations are similar to acute meningitis but evolve more slowly:
  - 1) Low-grade fever
  - 2) Chronic headaches
  - 3) Neck stiffness
  - 4) Subtle personality / mental status change (may be the only sign in elderly!)
  - 5) Cranial neuropathies, radiculopathies, hydrocephalus.
- may be fatal if not successfully treated.

# Meningeal pose



## Nuchal rigidity and positive upper Brudzinsky's sign



## Positive Kernig's and lower Brudzinsky's sign



# Meningism

- The brain membranes irritation with appearing positives meningeal signs without inflammatory data in CSF

## Clinical manifestation

- fever,
- headache,
- vomiting,
- irritability,
- stiff neck.
- upper Brudzinski sign positive.
- Kernig and lower Brudzinski signs are negative

# Clinical Manifestation

**Syndrome of consciousness disturbances includes**

- excitement with euphoric,
- excitement with negativism,
- somnolence,
- stupor,
- sopor,
- coma (I, II degree).

# Glasgow Coma Scale

Activity	Best Response	Score
Eye opening	Spontaneous	4
	To verbal stimuli	3
	To pain	2
	None	1
Verbal	Oriented	5
	Confused	4
	Inappropriate words	3
	Nonspecific sounds	2
	None	1
Motor	Follows commands	6
	Localizes pain	5
	Withdraws in response to pain	4
	Flexion in response to pain	3
	Extension in response to pain	2
	None	1

- Favorable prognosis for recovering  
13-15 points
- Doubtful prognosis  
9-12 points
- Unfavorable prognosis  
less 8 points

# Complications

## **BACTERIAL MENINGITIS**

1. Seizures
2. DIC, shock
3. Subdural effusions - usually in infants as self-limited process (as inflammatory process subsides, subdural fluid is reabsorbed);
4. Brain abscess, subdural empyema
5. Cerebral thrombophlebitis
6. Stroke:
  - a) vasospasm caused by subarachnoid infection
  - b) loss of cerebral autoregulation + hypotension
  - c) inflammatory infiltration of arterial wall (vasculitis).
7. Cranial nerve palsies (esp. sensorineural hearing loss; oculomotor paresis)
8. Consequences of ICP $\uparrow$  (incl. brain herniation)
9. Chronic adhesive arachnoiditis, hydrocephalus

# Complications

## **VIRAL MENINGITIS**

- Various complication related to the systemic effect  
- orchitis, parotitis, pancreatitis
- Usually all of these complication resolve without sequelae.

# Diagnosis

## Plan of examination

- Ophthalmoscopy (papilledema)
- Lumbar puncture and examination of CSF
- Blood cultures
- Cultures of the nose and throat
- CT scan or MRI

# Diagnosis

- **Lumbar Puncture Contraindication**
  - Present of infection in the skin, soft tissue at the puncture site.
  - Likelihood of brain herniation.
- **Indication for contrast-enhanced CT scan or MRI before LP in suspected bacterial meningitis**
  - Immunocompromised state
  - History of Stroke, Mass lesion, Focal infection, Head trauma
  - Seizure within last 7 days
  - Abnormal level of consciousness
  - Inability to answer question or follow command appropriately
  - Abnormal visual fields or paresis of gaze
  - Focal weakness or neurologic deficit
  - Abnormal speech
  - Papilledema

# Diagnosis

- nevertheless contraindications, two blood samples are drawn for culturing → empirical antimicrobial therapy is started.
- if ICP↑ is present – administer IV bolus of MANNITOL 1 g/kg (ideally 20 min before LP), use
- small (but minimum 22G) needle, obtain minimum required sample; in addition, patient can be intubated and hyperventilated.



# Diagnosis

## Antimicrobial therapy:

- **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.

# Diagnosis

## CSF Analysis

- **Opening pressure** - 50-180 mmH<sub>2</sub>O.
  - elevated in bacterial, TB, fungal.
  - moderately elevated (bacterial meningitis > viral meningitis).
  - falsely elevated in tense, obese, marked muscle contraction.

# Diagnosis

## Collection of Fluid

- At least 3 specimens (1.0-1.5 cc/spec)
- Immediated analysis of:
  - turbidity,
  - xanthochromia,
  - glucose,
  - protein,
  - cell count & diff.,
  - Gram's stain,
  - bacterial culture,
  - india ink,
  - acid-fast bacillus (AFB),
  - Venereal Disease Research Laboratory test (VDRL).

# Diagnosis

## Turbidity

- Completely clear, colorless.
- cloudy & straw-colored (bacterial meningitis)
- clear-cloudy & colorless (viral meningitis).
- leukocytosis is the most common cause of CSF turbidity ( $> 200 \text{ cell/mm}^3$ )

# Diagnosis

## Cell count and diff.

- $< 5$  WBC /mm<sup>3</sup>;  $< 1$  PMN /mm<sup>3</sup>;  $< 1$  Eosinophil /mm<sup>3</sup>
- Normal cell count&diff. do not absolutely exclude bacterial meningitis.
- Initial CSF analysis → lymphocytosis in 6-13% of bacterial meningitis.
- Viral meningitis and encephalitis (also in tbc, fungal, Lyme, syphilitic, toxoplasma, or chronic meningitis) → usually less than 500 cell/mm<sup>3</sup> (nearly 100% mononuclear).

# Diagnosis

## Cell count and diff.

- Early (< 48 hr.) in viral meningitis → PMN pleocytosis in 20-75% (especially in enterovirus, mumps and arbovirus infections).
- A repeat lumbar puncture in 8-12 hours frequently shows a change from neutrophil to lymphocyte predominance, with the remainder taking place in 24-48 hours.

# Diagnosis

## Traumatic LP

- Presence of a clot
- Decrease RBC count from tube 1 to 3
- CSF from traumatic LP  $\rightarrow$  1 WBC / 700 RBC
- CSF WBC (predicted) = CSF WBCs (detected) –  
[WBC in Blood  $\times$  RBC in CSF / RBC in Blood]

# Diagnosis

## Xanthochromia

- Lysis of RBC and release of breakdown pigments, oxyhemoglobin, bilirubin and methemoglobin into the CSF.
- Begin within 2 hr. → persist up to 30 days.
- Traumatic tap → ↑ CSF protein 150mg/dl or more
- Subarachnoid hemorrhage.

# Diagnosis

## Glucose

- 50-80 mg/dl
- CSF glucose/serum glucose = 0.6/1
- Abnormal CSF to serum glucose ratio
  - < 0.5 in normoglycemic or 0.3 in hyperglycemic
  - impaired glucose transport mechanism
  - increase CNS glucose use (pyogenic meningitis)
- Bacterial or fungal meningitis → “hypoglycorrachia”
- Mild decrease CSF glucose level → parameningeal process.
- Enterovirus, mumps, herpes simplex and lymphocytic choriomeningitis virus may have a mildly decreased glucose initially.
- Low glucose levels and a lymphocytic pleocytosis should suggest the presence of cryptococcal, listerial, or tuberculous meningitis.

# Diagnostic

## Protein

- 15-45 mg/dl
- Traumatic LP (corrected 1 mg/dl of protein/1000 RBC)
- Elevated CSF protein
  - usually higher than 150 mg/dl
    - Meningitis
    - CNS vasculitis
    - Subarachnoid haemorrhage
    - Viral encephalitis
    - Syphilis
    - Demyelination syndrome
    - Neoplasm
  - >1000 mg/dl -> suggest fungal disease
  - viral meningitis < 100 mg/dl.

# Diagnostic

	Normal CSF	Meningism	Viral meningitis	Bacterial meningitis
Colour	colourless	colourless	colourless	milk, greenish
Transparency	transparent	transparent	transparent	turbid
Cells count (in 1 ml)	1-10	1-10	20-1000	1000-15000
lymphocytes	80-85 %	80-85 %	80-100 %	0-60 %
neutrophils	3-5 %	3-5 %	0-20 %	40-100 %
Protein,g/l	0,16-0,24	0,16-0,45	0,33-1,0	0,66-16,0
Pandy reaction	“-”	“-”	“+”, “++”	“+++”, “++++”
cerebrospinal pressure	130-180	200-250	200-300	200-300

# Diagnosis

## Gram's stain

- Diminished 20-30% in prior treatment with ATB

*Staphylococcus*

G+cocci: single, double, tetrad, cluster

*Streptococcus pneumoniae*

G+cocci: paired diplococci

*Listeria monocytogenes*

G+rods: single or chain

*Haemophilus influenzae*

G-coccobacilli; pleomorphic

*Neisseria meningitidis*

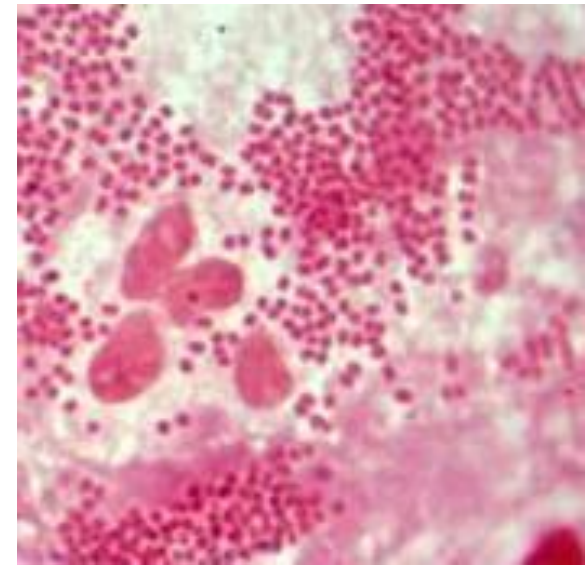
G-cocci: paired diplococci; kidney or coffee bean

*Enterobacteriaceae*

G-rods

*Pseudomonas aeruginosa*

G-rods

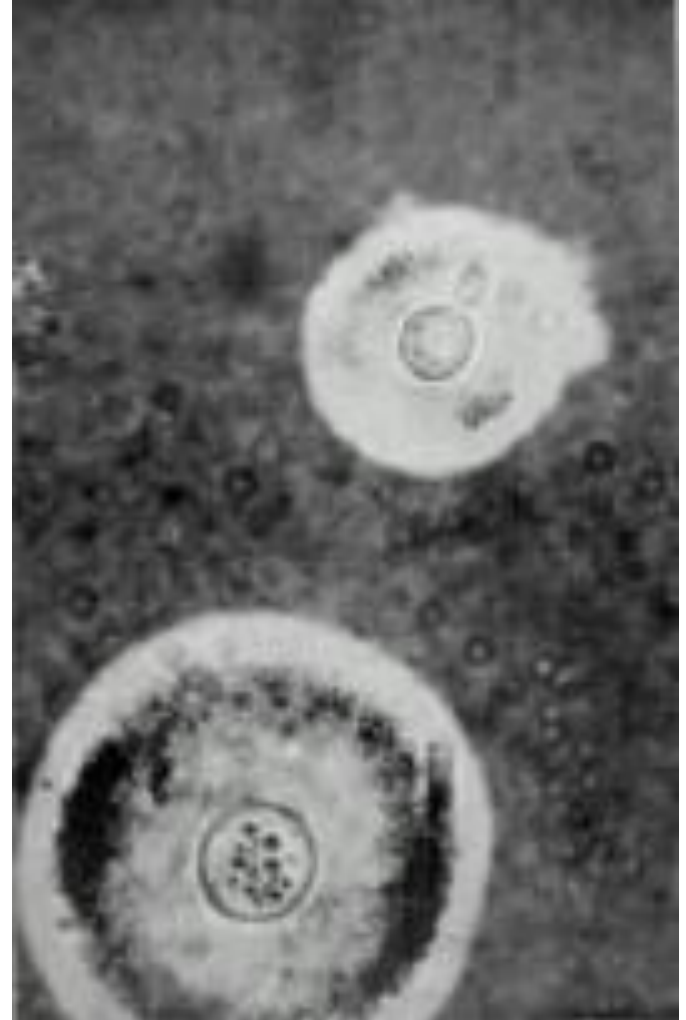


# Diagnosis

## India Ink Preparation

- Cryptococcal disease –  
1/3 of cases
- More definitive  
diagnostic test is  
cryptococcal antigen  
detection.

**Ziehl-Neelsen acid-fast  
stain (*Mycobacterium  
tuberculosis*).**



# Diagnosis

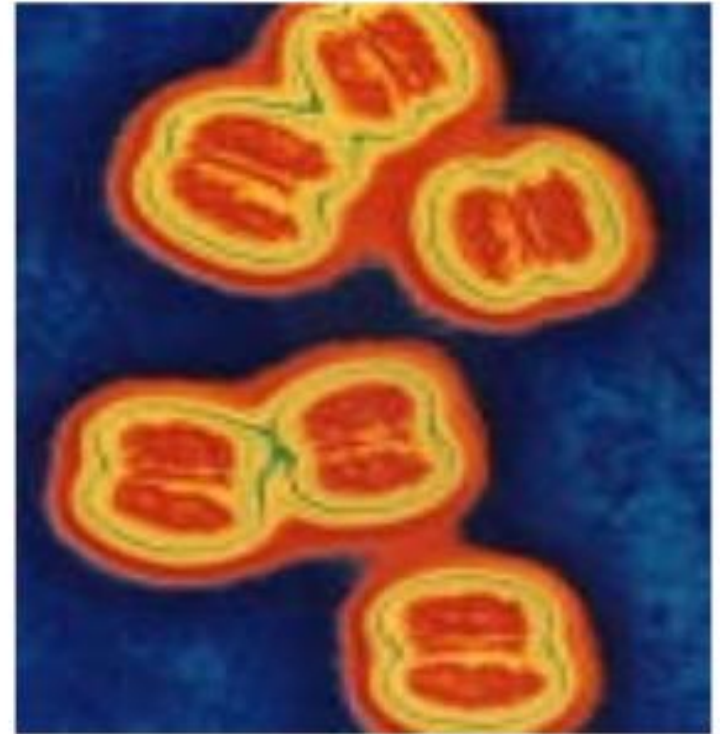
- **CSF/serum antigen/antibody detection** (for viruses, syphilis, Lyme disease)
  - Counterimmunoelectrophoresis (CIE)
  - Latex particle agglutination
  - Coagglutination
  - Immunofluorescence
- Unfortunately, antibodies appear in CSF too late to aid in any therapeutic decisions (used only for retrospective diagnosis).
- Useful in receiving ATB before CSF sampling
- Result - vary
- Presence only an antigen, not viable organism
- **Serum antibody** titers  $\uparrow \rightarrow$  fourfold rise in paired sera (for viruses).

# Diagnosis

## Bacteriologic culture

- *N. meningitidis* 37-55%
- *H. influenzae* 50%

Isolation of the organism  
from CSF or blood.



# Diagnosis

- PCR → resumed for less clear presentation, pretreat with ATB, care in which concern exists for TB, cryptococcal, treatable viral CNS infection.
- Sensitivities of detection in CSF by PCR for
  - *M. tuberculosis* 80-85% (specificity 97-100%)
  - *N. meningitidis* 88%,
  - *H. influenzae* 100%,
  - *S. pneumoniae* 92% (nearly 100% specificity)

# Diagnosis

## Organism detection in other fluids:

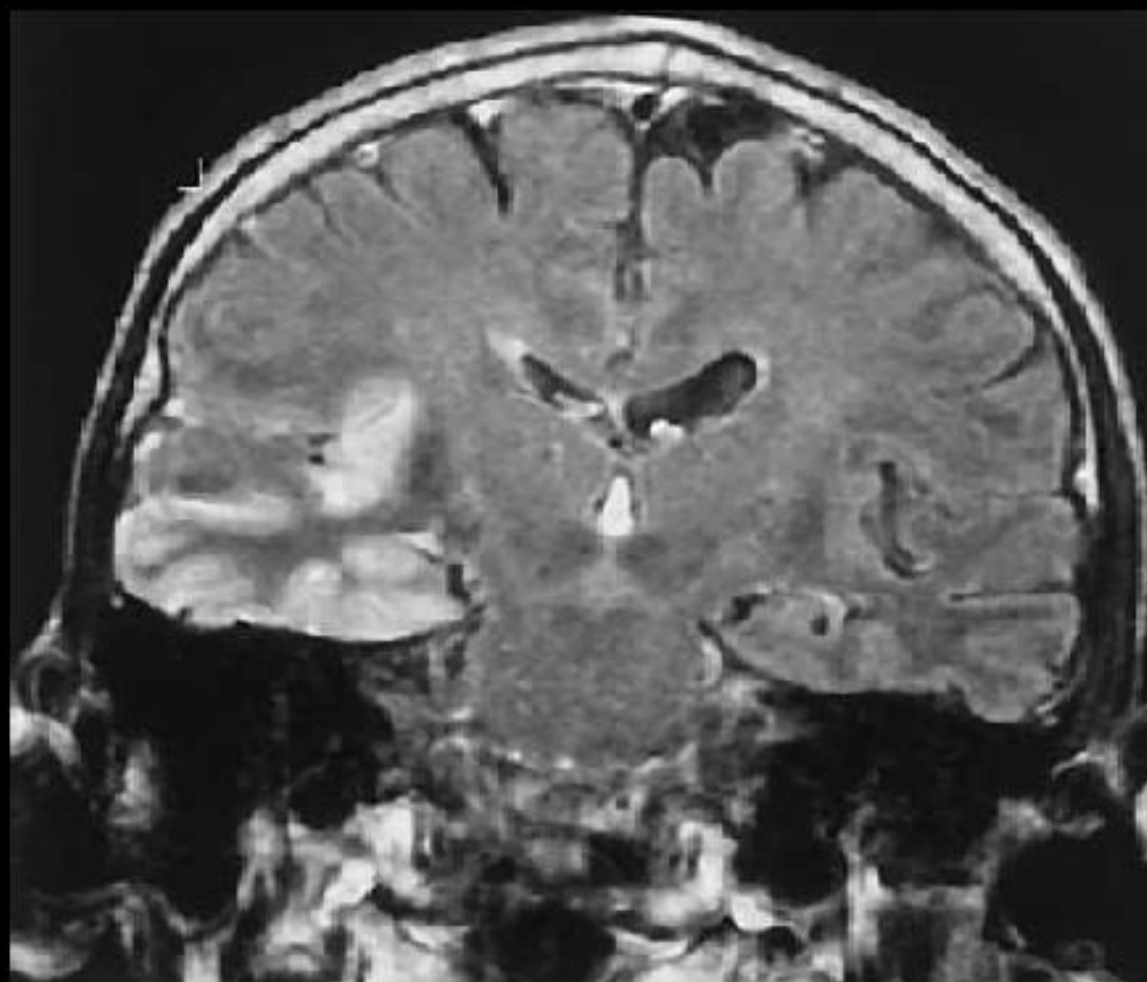
- **Blood culture** (positive in 80-90% patients with bacterial meningitis). Identify causative organism more often when the meningitis is caused by pneumococcus than meningococcus.
- **Stool specimen** may be better source of viral isolate (enteroviruses), but is not diagnostic of meningitis.
- **Virus isolation** from saliva, throat washing (mumps).
- Meningococci may be found in skin lesions, nasopharyngeal secretions.
  - In general, cultures of body surfaces and orifices are not helpful in identifying causative pathogen!

# Diagnosis

## Neuroimaging Technique

- Possibility of an intracranial abscess, intracranial hemorrhage, mass lesion
- CT scan should not unnecessarily delay LP or ATB
- Hypodensity CT scan in the temporal lobes -> HSV encephalitis

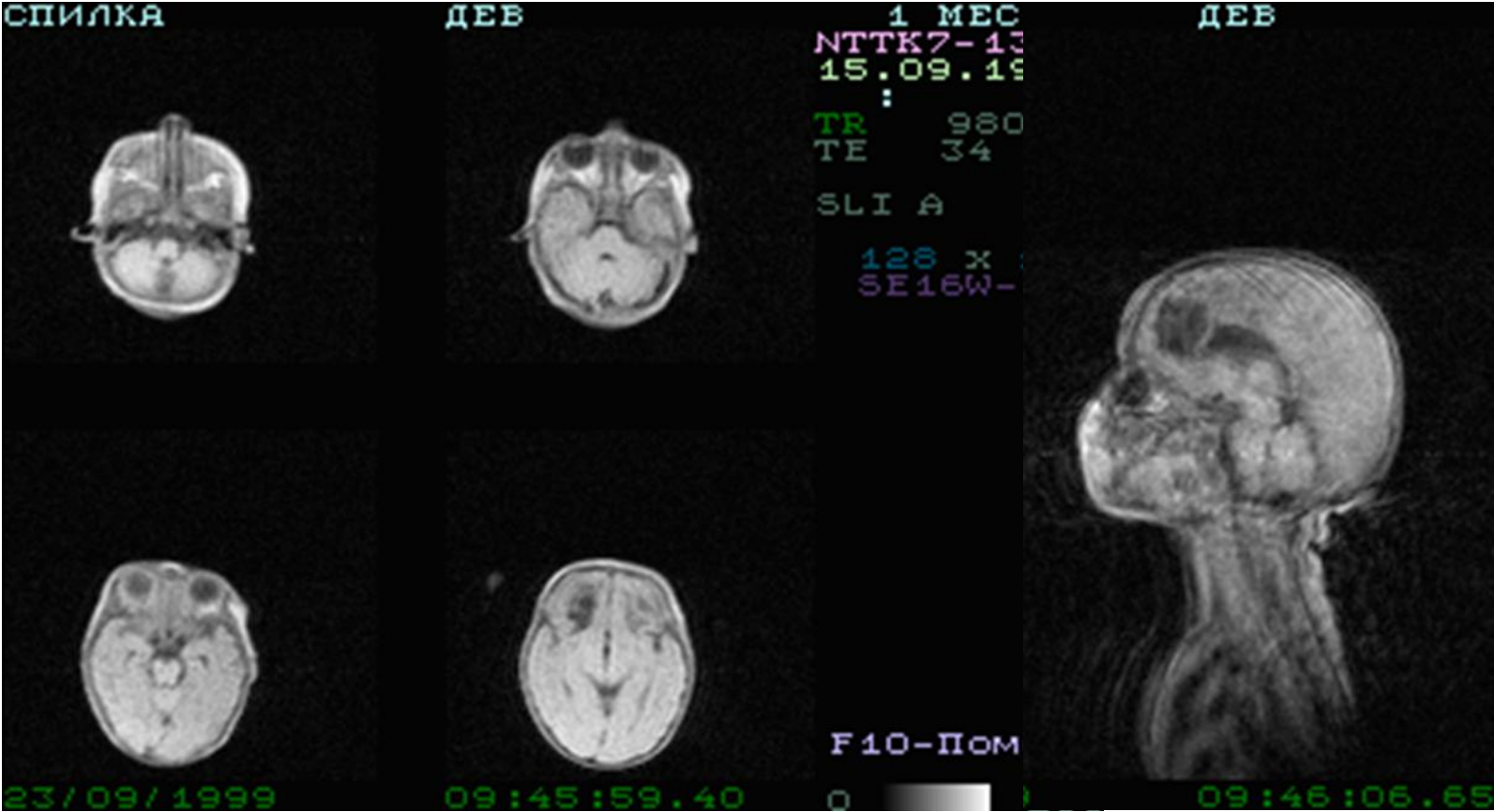
# MRI in HSV



# TB or Crypto meningeal involvement



# Computer tomography - intracranial hemorrhage



# Diagnosis

## **Additional Investigation**

- WBC count is markedly elevated in bacterial meningitis (mildly in viral meningitis).
- CBC may show leukopenia in elderly, immunosuppressed person.

# Diagnosis

## Additional Investigation

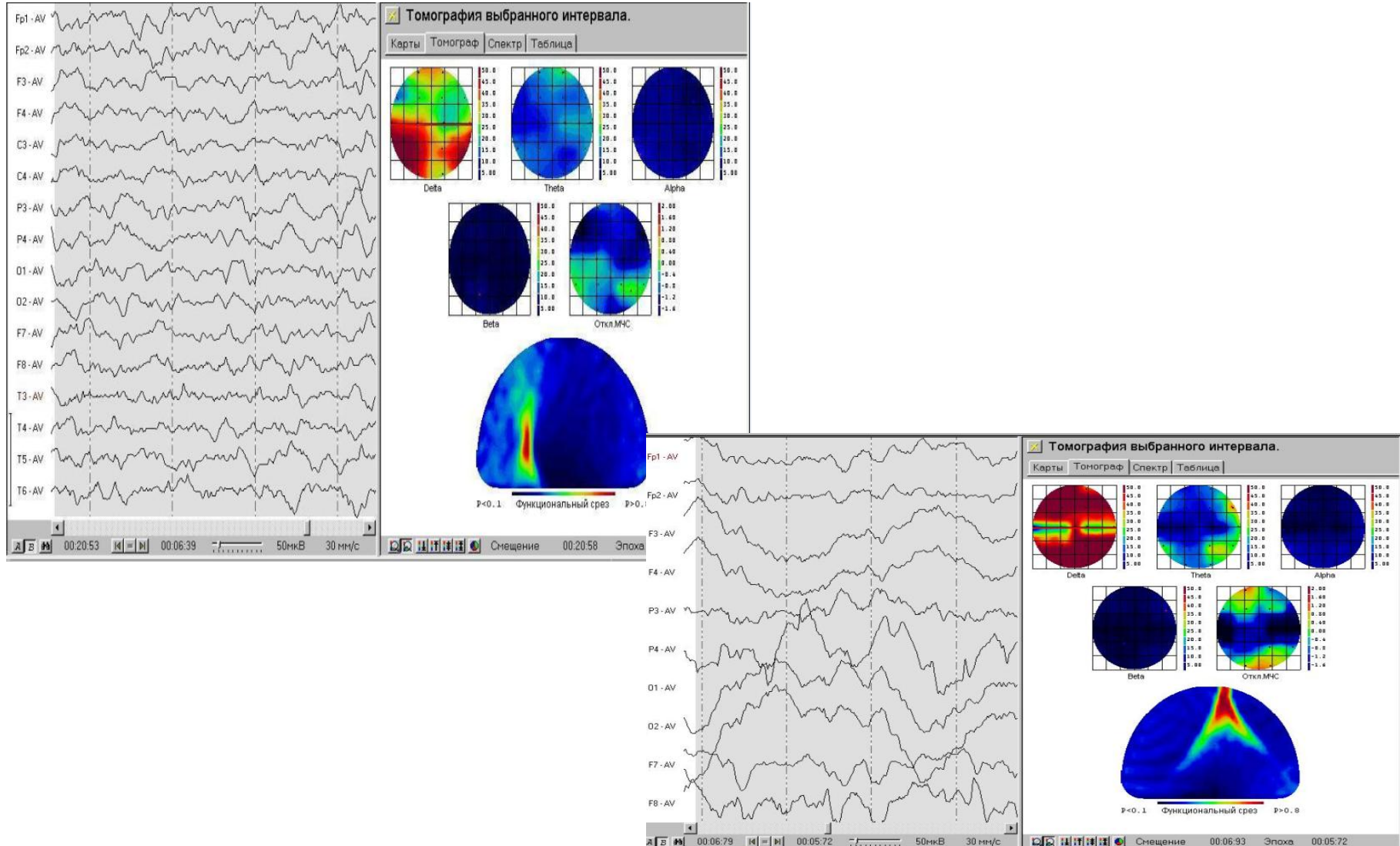
- 50% of patients with pneumococcal meningitis -> evidence of pneumonia on an initial **chest x-ray**.

# Diagnosis

## Additional Investigation

- **EEG** is usually normal or slightly slow.
- Focal or lateralized EEG abn. → associated with HSV encephalitis (strong evidence).

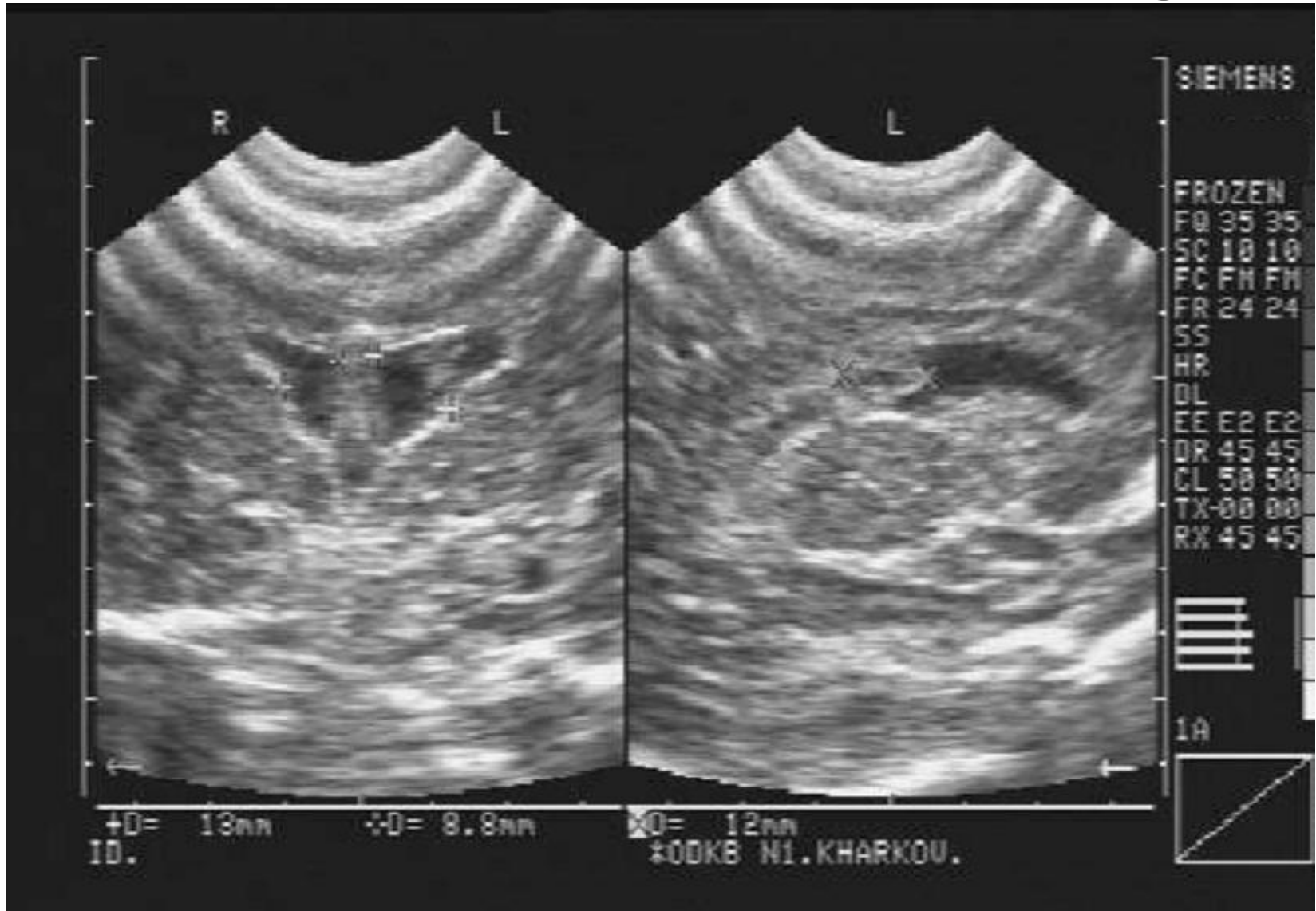
# Electroencephalography



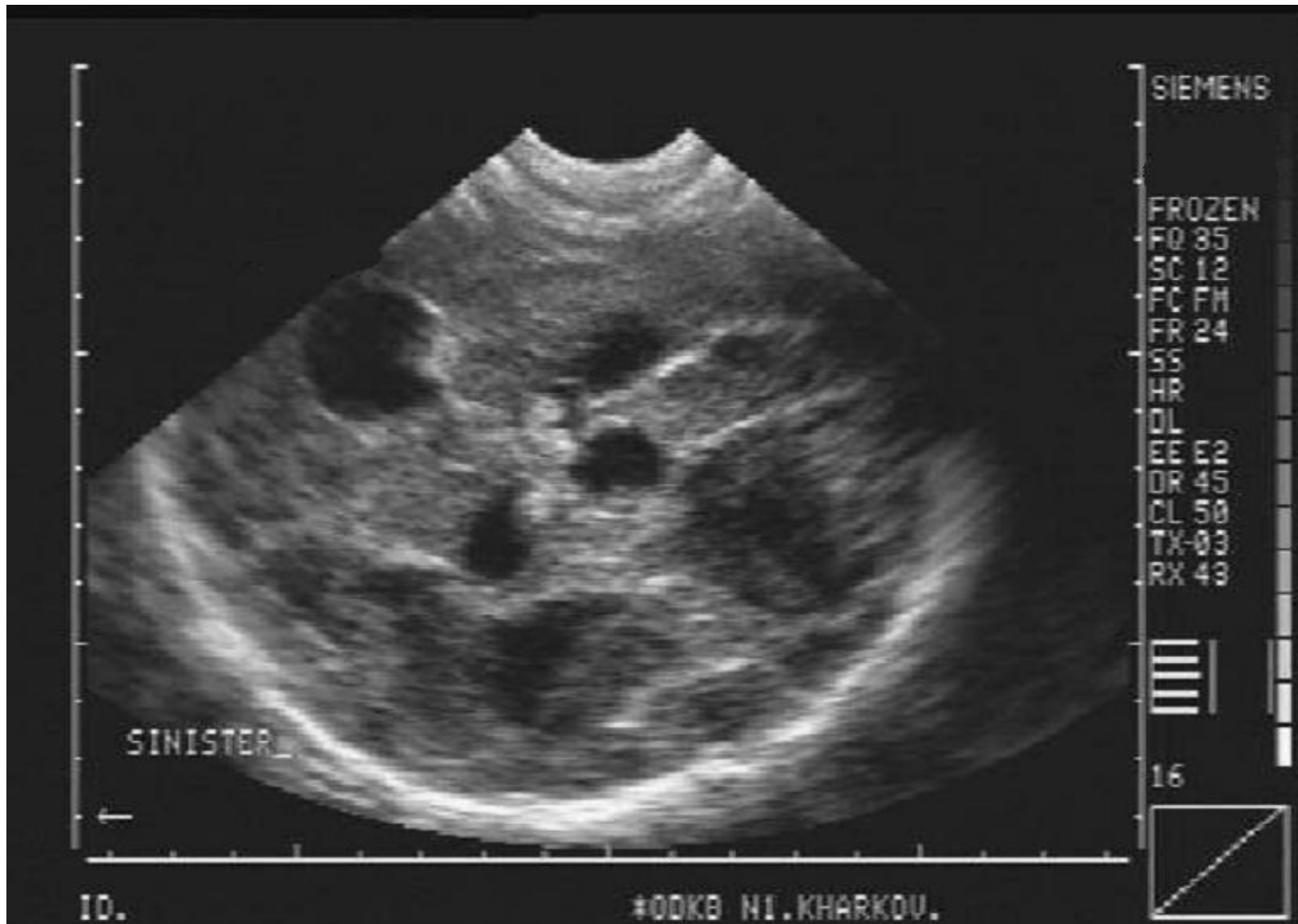
# Ultrasound investigation “Light- brain” – is a sign of meningitis



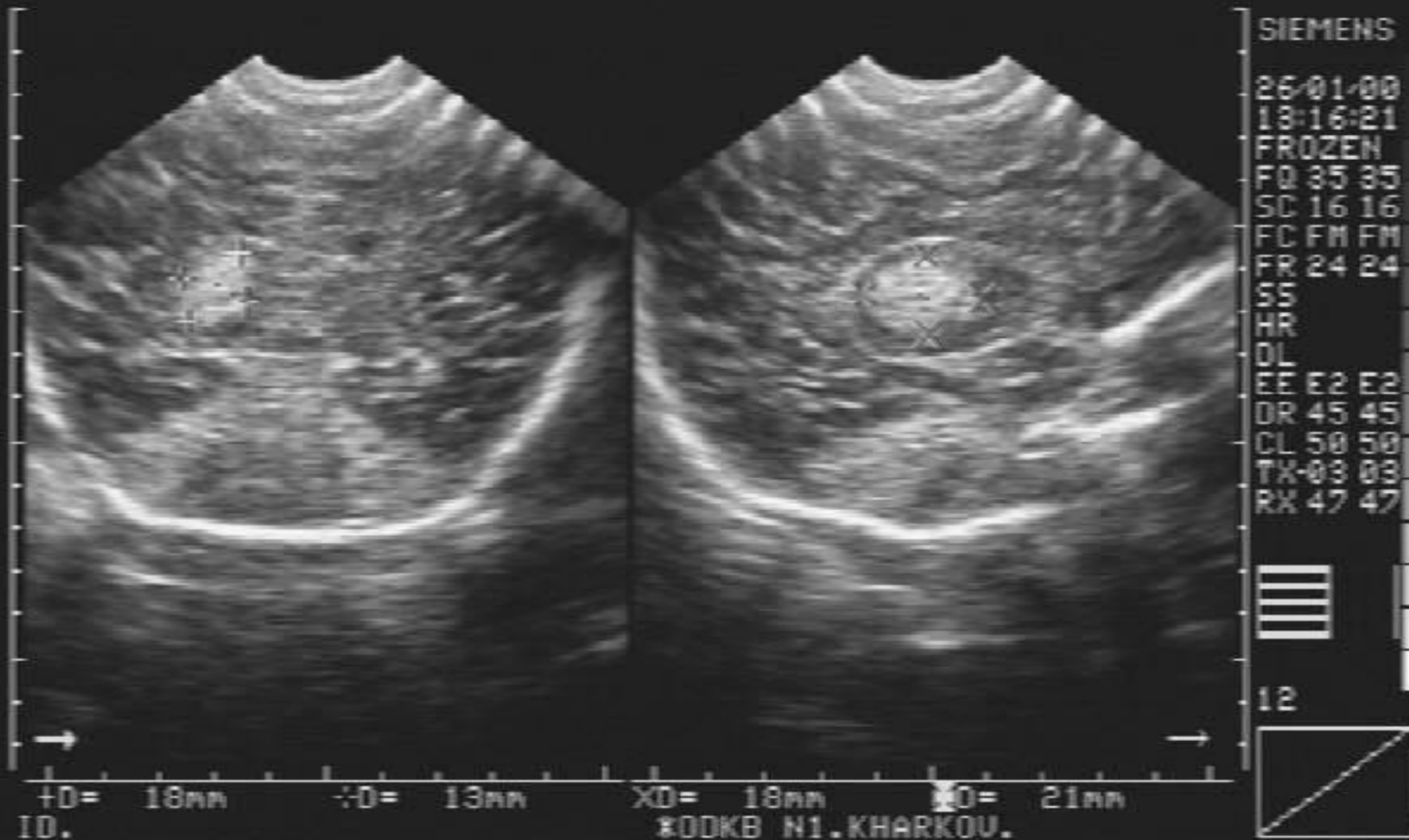
# Intracranial left-side hemorrhage



# Focus of brain necrosis



# Focus of brain ischemia



# Diagnosis

- Etiologic diagnosis in chronic meningitis may require **MENINGEAL BIOPSY** (→ histology, electron microscopy, PCR, cultures).
- Target regions that enhance with contrast on MRI or CT.
- With current microsurgical techniques, most areas of basal meninges can be accessed via limited craniotomy.
- Most common conditions identified – sarcoid (31%), metastatic adenocarcinoma (25%).

# Treatment

Patients prefer quiet, darkened room.

ANALGESICS - to relieve headache (often reduced by initial diagnostic lumbar puncture).

ANTIPYRETICS - to reduce fever.

Indications for hospitalization:

1. severe cases
2. deficient humoral immunity (trial of IVIG)
3. herpes meningitis (intravenous ACYCLOVIR)
4. potential nonviral causes.

FIELD STABILIZATION, TRANSPORT.

# Treatment

## ANTIMICROBIAL THERAPY

- Must be bactericidal in CSF – i.e. maximum tolerated doses!
- Intravenously (intrathecal / intraventricular therapy is not effective).
- Crucial step is to initiate antimicrobial therapy immediately!

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

# Treatment

## EMPIRIC THERAPY IN ADULTS

(*S. pneumoniae*, *N. meningitidis*).

All patients must be isolated for first 24 h of therapy.

Combination:

1. VANCOMYCIN

2. CEFTRIAXONE or CEFOTAXIME (CEFTAZIDIME in neurosurgical patient / immunocompromised patient – *P. aeruginosa* may be etiological agent).

3. add AMPICILLIN for older adult / immunocompromised adult (Gr- aerobic bacilli; *L.monocytogenes* – resistant to cephalosporins).

# Treatment

## **THERAPY ACCORDING TO GRAM STAIN:**

- Gr+ organisms → VANCOMYCIN + CEFTRIAXONE or CEFOTAXIME.
- if organisms are pleomorphic (*Listeria* sp.) → add AMPICILLIN.
- Gr- bacilli → TICARCILLIN or CEFTAZIDIME + AMIKACIN or GENTAMICIN.

# Treatment

IF CAUSATIVE ORGANISM HAS BEEN IDENTIFIED:

*N. meningitidis*: PENICILLIN G or AMPICILLIN or CEFOTAXIME or  
CHLORAMPHENICOL + (at end of therapy to eradicate  
nasopharyngeal carriage) oral RIFAMPIN for 2 d.

*S. pneumoniae*: VANCOMYCIN + CEFTRIAXONE or CEFOTAXIME

*Enteric Gr- bacilli*: CEFTRIAXONE or CEFOTAXIME + AMIKACIN or  
GENTAMICIN

*P. aeruginosa*: CEFTAZIDIME or CIPROFLOXACIN or TICARCILLIN ±  
GENTAMICIN

*L. monocytogenes*: AMPICILLIN or TMP-SMX

*H. influenzae* type b: CEFTRIAXONE or CEFOTAXIME or  
CHLORAMPHENICOL (with AMPICILLIN)

*S. aureus* (methicillin-sensitive): OXACILLIN

*S. aureus* (methicillin-resistant): VANCOMYCIN

*S. epidermidis*: VANCOMYCIN ± RIFAMPIN

# Treatment

- PRIMARY FOCUS OF INFECTION should be eradicated (by surgery if necessary; e.g. persistent CSF fistulas must be closed by suturing of dura - otherwise meningitis will almost certainly recur).
- unless dramatic response to therapy occurs, CSF should be re-examined 24-48 hours after initiation of treatment (to assess effectiveness of medication – CSF sterility + conversion to lymphocytic predominance).
- drug dosages should not be reduced when clinical improvement occurs (drug penetration decreases as meninges become less inflamed).
- duration of therapy (should be individualized and based on clinical response): *H. influenzae*, *S. pneumoniae* – 10-14 days; *N. meningitidis* – 7 days; Gr- aerobic bacilli - 3 weeks.

# Treatment

## DEXAMETHASONE

- prevents neurological complications by decreasing meningeal inflammation (due to released bacterial components by bactericidal antibiotics).
- for adults and children  $\geq 2$  months of age.
- dose - 0.15 mg/kg q6h IV.
- use H2 antagonist to avoid GI bleeding.
- use higher doses of VANCOMYCIN (15 mg/kg q6h) or intrathecal VANCOMYCIN.
- course - first 4 days of antimicrobial therapy (first dose of DEXAMETHASONE should be administered 20 min before first antimicrobial dose).
- if no bacteria grows in culture or is otherwise identified after 24-48 h, corticosteroids should be stopped, and antibiotic coverage reassessed (corticosteroids for 1 day should not be detrimental even if cause is virus, fungus, or TB).

# Treatment

## Viral meningitis

- Acyclovir 10 mg/kg 3 times per day during 7-10 days;
- In case of encephalitis – 15-30 mg/kg 3 times per day during 10-14 days, after that 200-400 mg 5 times (per os) during 14 days
- Ganciclovir, foscarnet-> effective in HHV infection.

# Treatment

## **Fungal meningitis**

- Amphotericin B
- Fluconazole
- Miconazole
- Flucytosine

# Prognosis

- Many deaths occur during first 48 hours of hospitalization.
- 50-90% in untreated cases.
- Fatality rate for **pneumococcal meningitis** ~ 20-25%.
- Higher fatality rate -> serious underlying, concomitant disease, advance age
- Prognosis -> related to degree of neuro impairment on presentation 20-30% of pneumococcal meningitis -> residual neuro deficit.
- 40% fatality rate for **Listeria meningitis**.
- ATB -> ↓ mortality from **meningococcal meningitis** < 20%
- Mortality rate in community-acquired **G-ve meningitis** < 20% in administration of 3rd gen cephalosporin.

# Prognosis

## VIRAL MENINGITIS

- prognosis for adults – full recovery is excellent (rarely - persisting headache, mild mental impairment, incoordination, generalized asthenia for weeks to months).
- **HSV encephalitis** -> 60-70% mortality (before use acyclovir) -> 30% (Acyclovir). Common sequelae -> seizure, motor deficit, change in mentation.
- **TB meningitis**. Death in adult age 10-50%. Focal ischemic stroke -> result from cerebral vasculitis. 25% of pt. -> required neurosurgical procedure (Ventriculoperitoneal shunt or drainage).
- **Fungal meningitis**. Abscess, papilledema, neuro deficit, seizure, bone invasion, direct invasion of the optic n. -> ocular abn. 40% in cryptococcal meningitis.

Sporadic Herpes Simplex Encephalitis  
Fulminant hemorrhagic and necrotizing  
meningoencephalitis



# Chemoprophylaxis

- Incidence of transmission of meningococcus is ~ 5%
- Household contact – Rifampin adult 600 mg child > 1 mo 10mg/kg child < 1 mo 5mg/kg oral q 12 hr. for a total of 4 doses.
- Health care worker -> do not required prophylaxis.

# Chemoprophylaxis

- Directed contact (mouth to mouth, ET tube, nasotrachial suction) – Ciprofloxacin 500 mg oral or Ceftriaxone 250 mg im. (<15 yr. 125 mg im.)
- No indication for chemoprophylaxis in pneumococcal meningitis.

# Immunoprophylaxis

- Vaccination is also available to confer immune protection against
  - JE virus
  - *H. influenzae* type B (use in pediatrics).

**"Only the prepared mind  
can help the impaired host."**

**Dr. Libero Ajello**