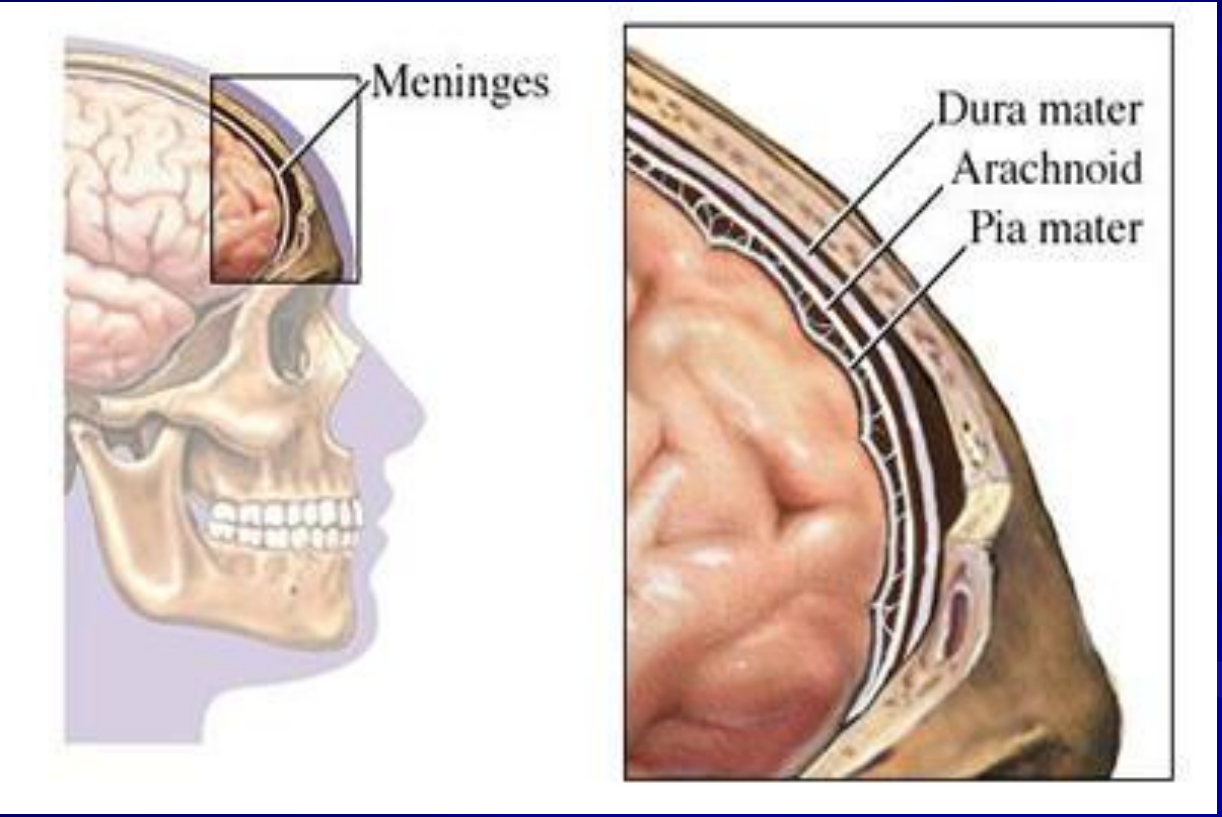
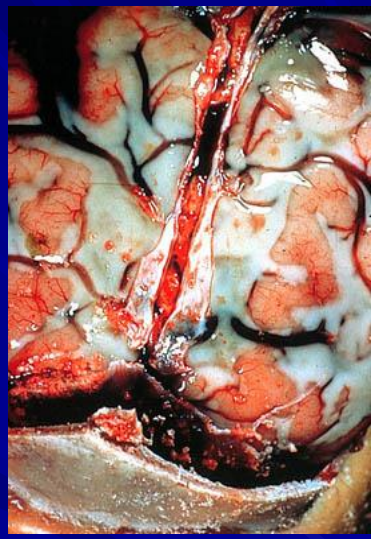
Acute Bacterial Meningitis

A medical emergency





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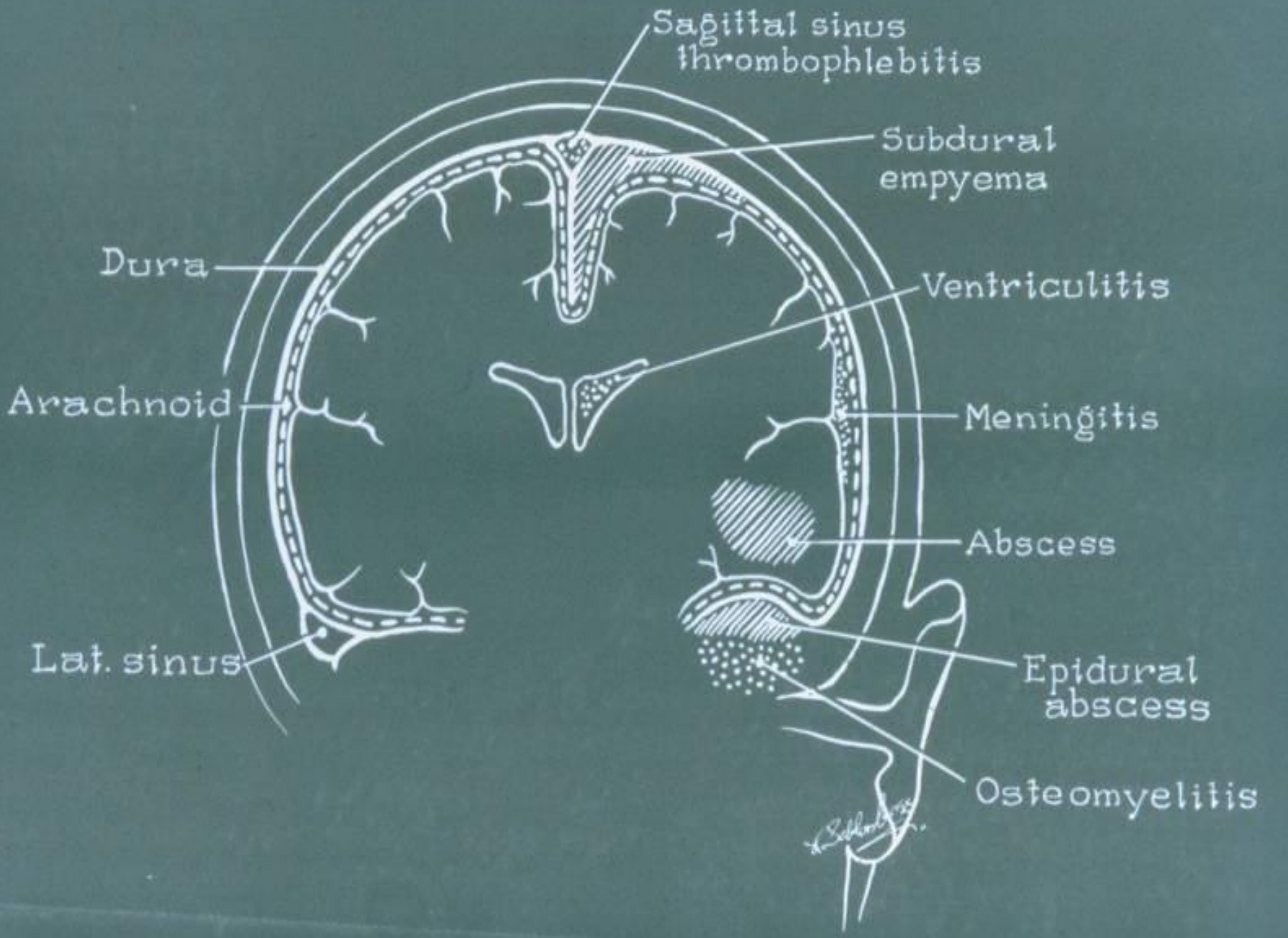
Bacterial Meningitis factors in improving mortality & Morbidity

1. The understanding of the pathophysiology of meningitis
2. The Recognition of Meningitis
3. The rapid determination of the most likely etiology
4. Prompt initiation of appropriate treatment
5. Preventive measures


Sagittal sinus thrombophlebitis
Subdural empyema
Dura
Ventriculitis
Arachnoid
Meningitis
Abscess
Lat. sinus
Epidural abscess
Osteomyelitis

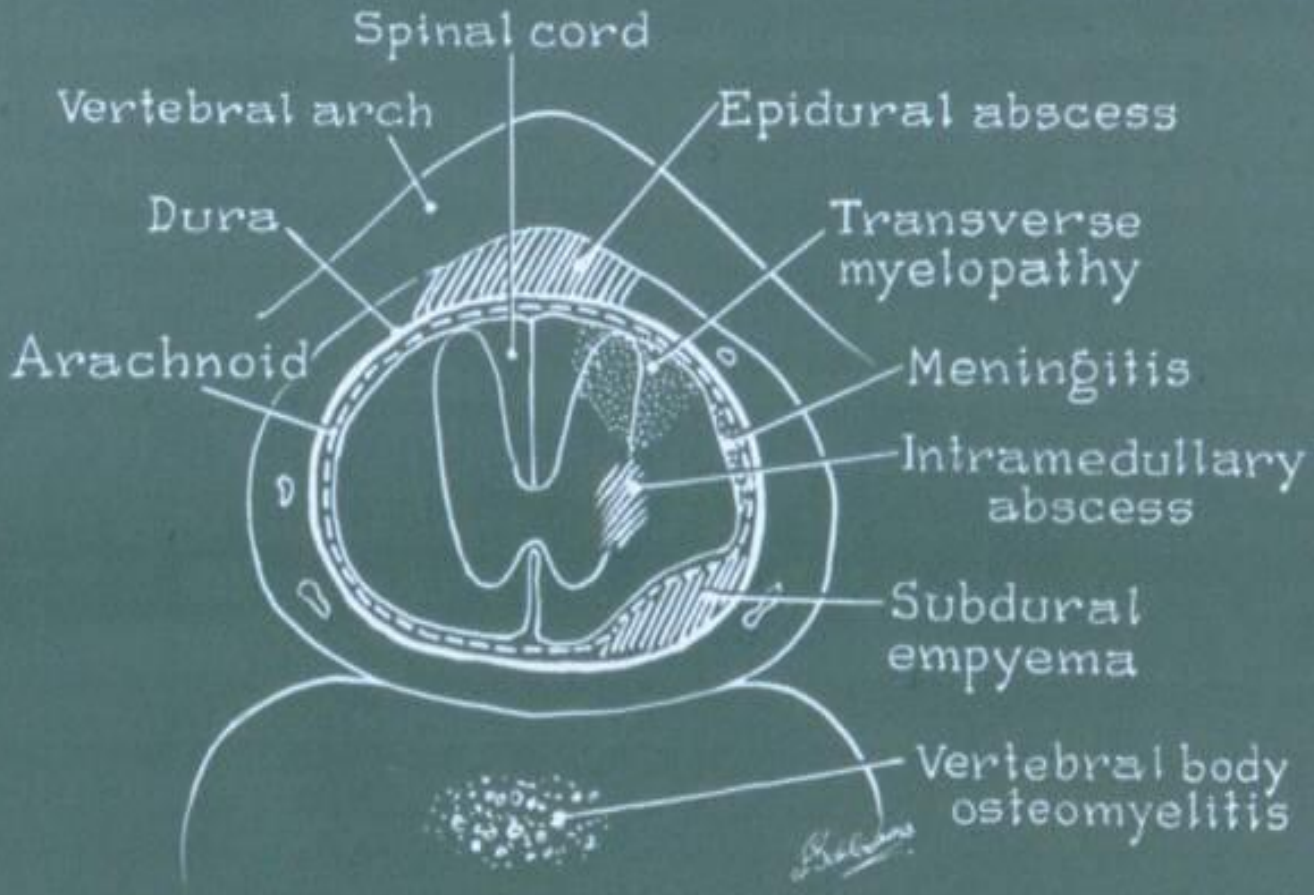
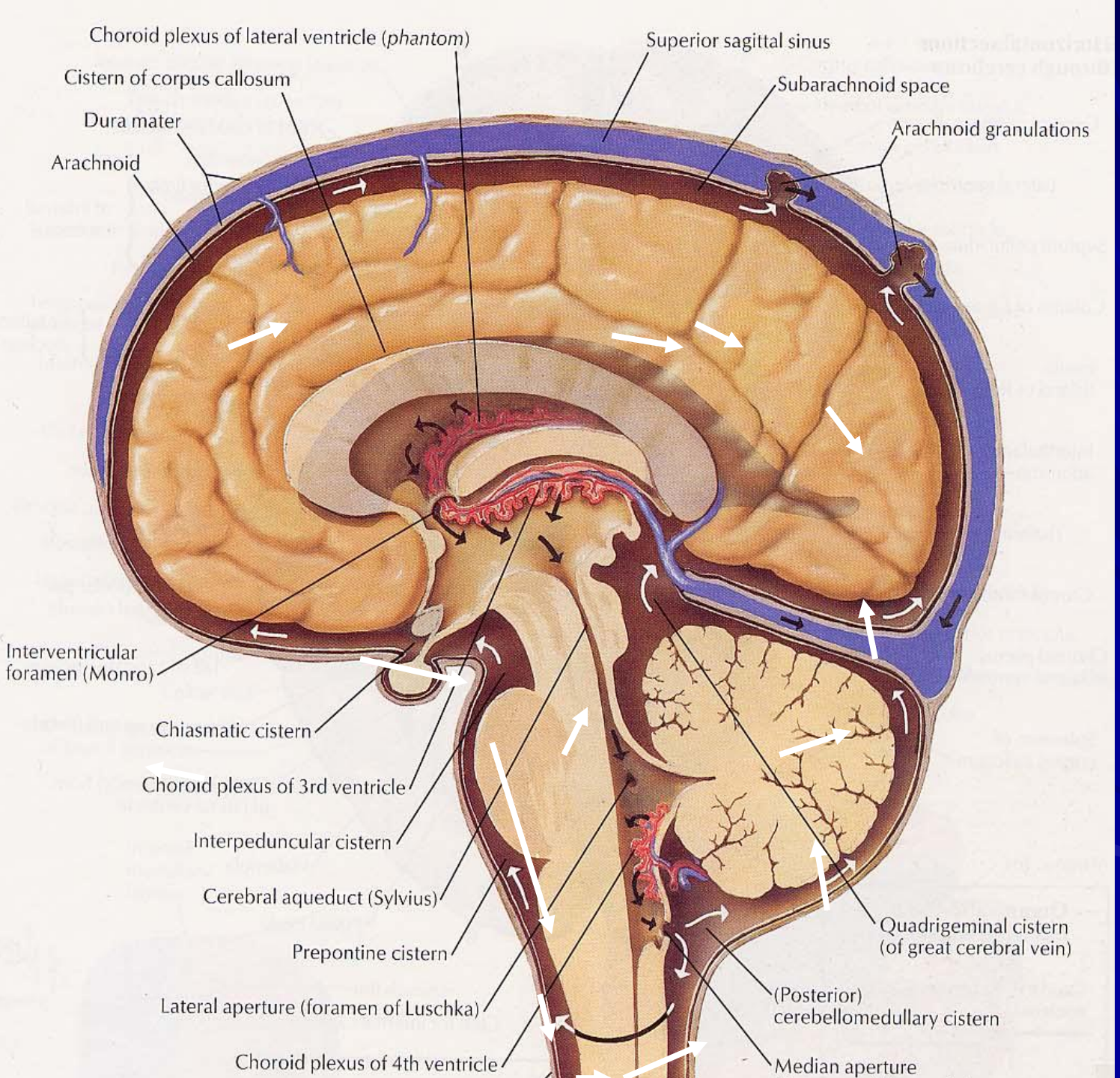


Figure 1. Relationships of the brain and spinal cord with their surrounding protective layers.

CSF flow


Choroid plexus of lateral ventricle (*phantom*)
Superior sagittal sinus
Cistern of corpus callosum
Subarachnoid space
Dura mater
Arachnoid granulations
Arachnoid
Interventricular foramen (Monro)
Chiasmatic cistern
Choroid plexus of 3rd ventricle
Interpeduncular cistern
Cerebral aqueduct (Sylvius)
Quadrigeminal cistern (of great cerebral vein)
Prepontine cistern
(Posterior) cerebellomedullary cistern
Lateral aperture (foramen of Luschka)
Choroid plexus of 4th ventricle
Median aperture

Causes of purulent meninfitis

	AGE	Organism
1	Neonate	*E. Coli* *Group B Strep.* *Listeria*
2	Infant, Toddlers, 6-12 yrs	*H. Influenza* *S. Pneumoniae* *N. Meningitidis*
3	Over 12 yrs	*S. Pneumoniae* *N. Meningitidis*
4	Over 60 yrs	*Unusual organism*

Causes of purulent meningitis

	Historical data	Organism
1	C5-C8	
2	properdin system	
3	asplenia	
4	AIDS or malignancy	
5	CSF leak	
6	dermal sinus & meningomyelocele	
7	shunt infections	

Pathophysiologic Basis for Clinical Course of Meningitis

1. Increased intracranial pressure
2. Vascular and parenchymatous changes
3. Subdural effusion
4. Inappropriate secretion of A.D.H
5. Glucose methabolism & O2 utilization
6. Nerve Inflammation

Clinical findings

Infants: Fever, hypothermia, bulging fontanel, lethargy, irritability, seizures, respiratory distress, poor feeding, vomiting.

Older children: Fever, headache, photophobia, meningismus, nausea/vomiting, confusion, lethargy, irritability.

Evaluation

Laboratory testing – Initial laboratory testing should include (STAT):

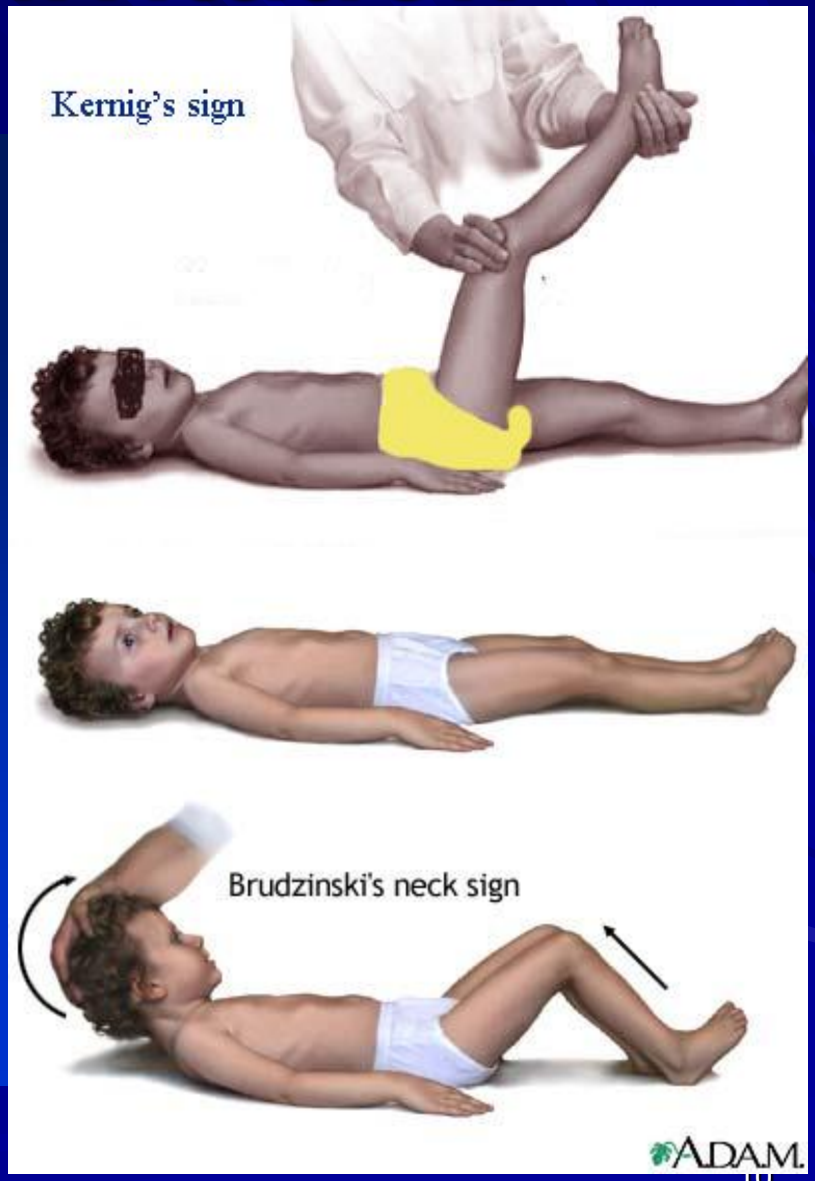
- Blood cultures (two sets).
- CBC with differential and platelet count.
- Serum electrolytes, BUN, creatinine, glucose.
- PT, INR, and PTT.

- VBG
- Ca, ph. Alb if seizure

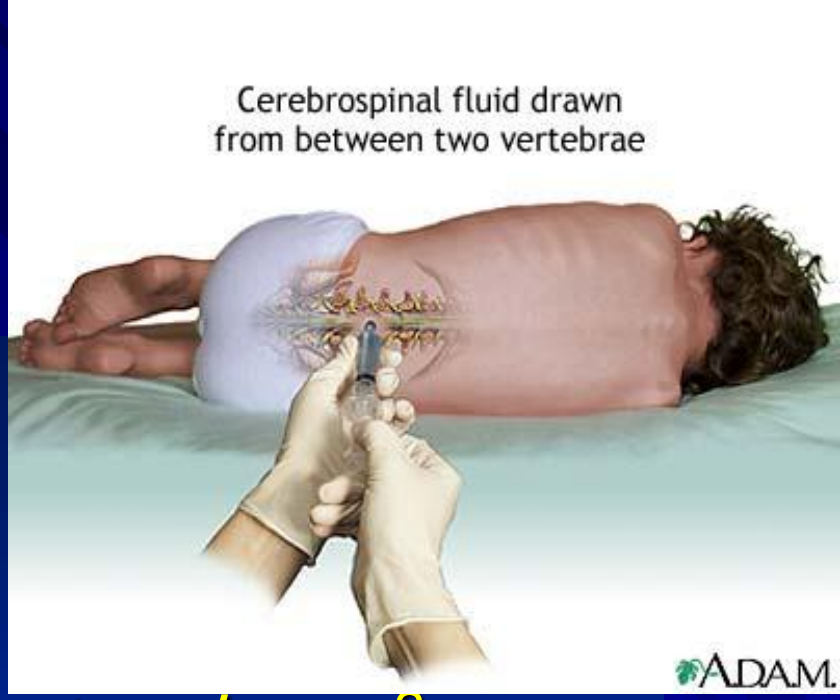
Lumbar puncture:

Meningeal irritation

- Nuchal rigidity
- Kernig sign
- Brudzinski sign



Examination of CSF



- Pressure: **50–80** mmH2O
- Color
- RBC
- WBC: **<5, ≥75% lymphocytes** / mm^3
- Protein: **20–45** mg/dl
- Glucose:, **>50 (or 75% serum glucose)**
- Stained smear of CSF
- CSF culture

Typical cerebrospinal fluid findings in central nervous system infections*

	Glucose (mg/dL)		Protein (mg/dL)		Total white blood cell count (cells/microL)		
	<10 ¶	10 to 40 Δ	100 to 500 ◊	50 to 300 §	>1000	100 to 1000	5 to 100
More common	Bacterial meningitis	Bacterial meningitis	Bacterial meningitis	Viral meningitis Nervous system Lyme disease (neuroborreliosis) Encephalitis Neurosyphilis TB meningitis ¥	Bacterial meningitis	Bacterial or viral meningitis TB meningitis	Early bacterial meningitis Viral meningitis Neurosyphilis TB meningitis
Less common	TB meningitis Fungal meningitis	Neurosyphilis Some viral infections			Some cases of mumps and LCMV	Encephalitis	Encephalitis

Lumbar puncture:

- LP should be performed in all children with suspected meningitis unless there is a specific contraindication to LP.

5

Contraindications to LP include: Cardiopulmonary compromise, clinical signs of increased intracranial pressure, papilledema, focal neurologic signs, and skin infection over the site for LP. If there is a contraindication to or inability to perform an LP, or if the LP is delayed by the need for cranial imaging, antimicrobial therapy should **not** be delayed. Blood cultures should be obtained and empiric antibiotics administered as soon as is possible.

- CSF should be sent for the following (STAT): Cell count and differential, glucose and protein concentration, Gram stain, and culture.

Neuroimaging (eg, head CT):

- In children who require neuroimaging before LP, **blood cultures should be obtained and empiric antibiotics administered before imaging.** LP should be performed as soon as possible after neuroimaging is completed, provided that the imaging has not revealed any contraindications.

6 Indications for neuroimaging before LP include: Severely depressed mental status (coma), papilledema, focal neurologic deficit (with the exception of cranial nerve VI or VII palsy), history of hydrocephalus and/or presence of a CSF shunt, recent history of CNS trauma or neurosurgery.

Management

Supportive care:

- Ensure adequate oxygenation, ventilation, and circulation.
- Obtain venous access and initiate cardiorespiratory monitoring while obtaining laboratory studies.
- Keep the head of bed elevated at 15 to 20 degrees.
- Treat hypoglycemia, acidosis, and coagulopathy, if present.

- Restrict IV fluid

Antimicrobial therapy – Antibiotic therapy should be initiated immediately following the LP if the clinical suspicion for meningitis is high:

- **Administer first dose of empiric antimicrobial therapy:**

Antimicrobial therapy – Antibiotic therapy should be initiated immediately following the LP if the clinical suspicion for meningitis is high:

- **Administer first dose of empiric antimicrobial therapy:**
  - **Vancomycin (15 mg/kg IV), plus**
  - **Ceftriaxone (50 mg/kg IV) or cefotaxime (100 mg/kg IV; where available).**
- Consider dexamethasone therapy* (0.15 mg/kg IV) in patients with certain risk factors (eg, unimmunized patients, young children [age ≥6 weeks to ≤5 years], children with sickle cell disease, asplenic patients) or if there is known or suspected *Haemophilus influenzae* infection (eg, based on Gram stain results).
- If dexamethasone is given, it should be administered before, or immediately after, the first dose of antimicrobial therapy.

Dexa: every six hours for two to four days

Antibiotic therapy in purulent meningitis

Haemophilus influenzae	Ampicillin Cefotaxime Ceftriaxone Chloramphenicol
Neisseria meningitidis	Penicillin G
Streptococcus pneumoniae[†]	Penicillin G Chloramphenicol Vancomycin Cefotaxime/ceftriaxone

Unknown (<1 mo of age)	Ampicillin plus cefotaxime plus vancomycin
Unknown (>1 mo of age)	Cefotaxime or ceftriaxone plus vancomycin

DURATION OF ANTIBIOTIC THERAPY

- *S. pneumoniae* meningitis
  - 10-14 days
- uncomplicated *N. meningitidis*
  - 5-7 days
- Uncomplicated *H. influenzae* type b meningitis
  - 7-10 days

DURATION OF ANTIBIOTIC THERAPY

- Gram-negative bacillary meningitis
  - 3 wk or for at least 2 wk after CSF sterilization
    - after 2-10 days of treatment .
- Change antibiotic according to susceptibility test

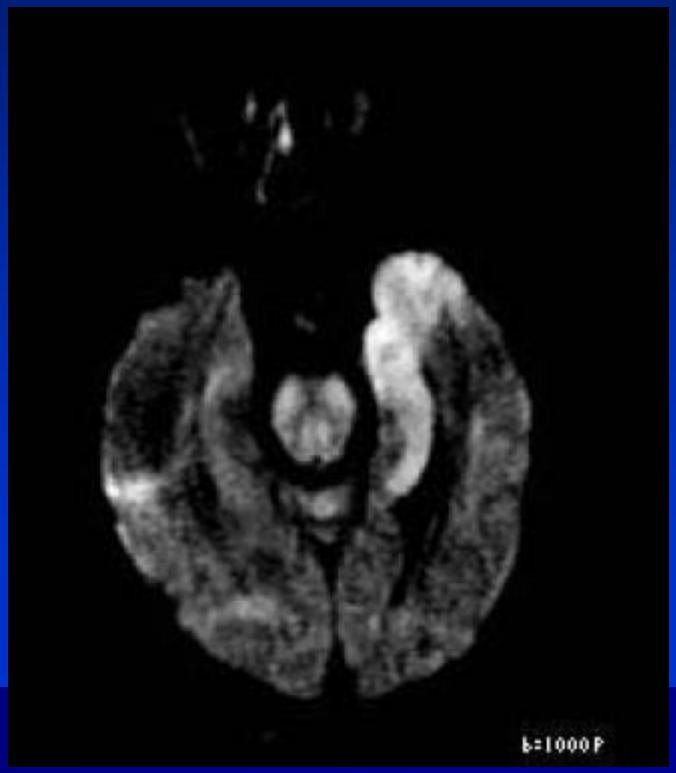
Encephalitis

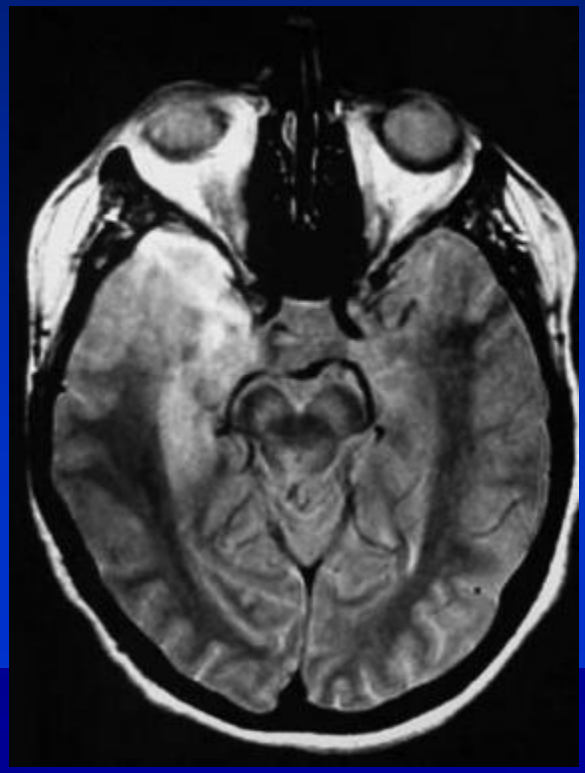
- the leading cause of **fatal, sporadic encephalitis** in children and adults
- Beyound neonatal period: **HSV-1**
- CSF analysis:
  - moderate **lymphocytosis**
  - a mildly elevated **protein** concentration
  - a normal or slightly decreased **glucose** concentration
  - Often a moderate number of **erythrocytes**.

PCR for DNA

Imaging
MRI & CT scan

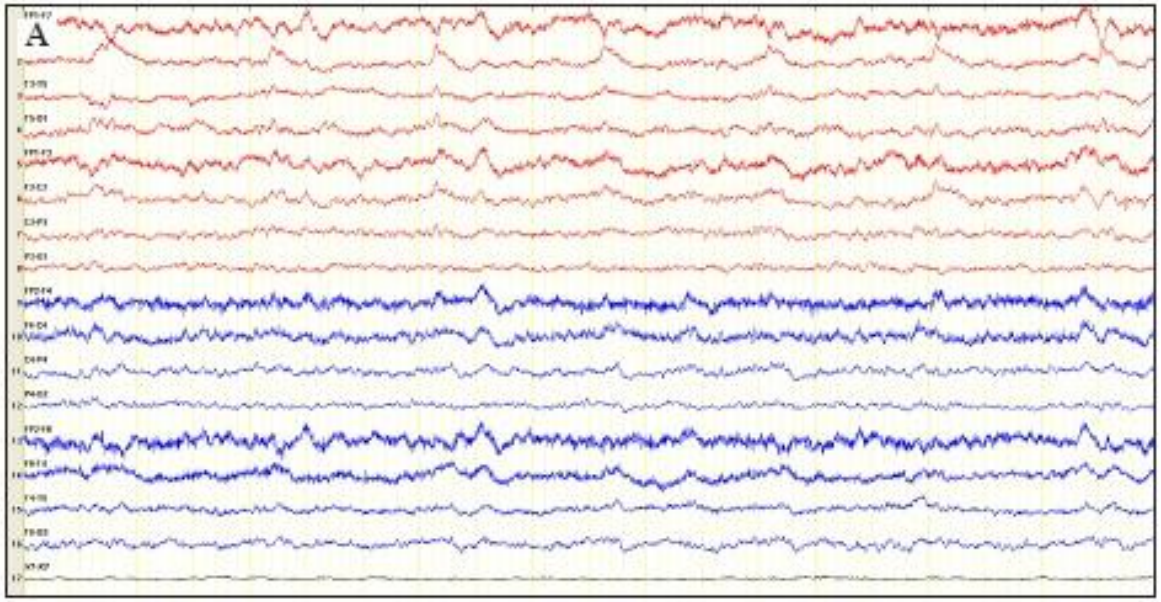
- Characteristic feature:
  - Focal CNS disease……. **Temporal lobe**

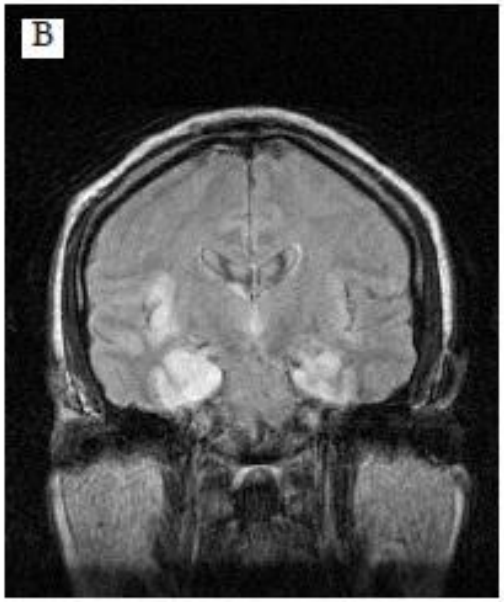




EEG

- Periodic lateralized epileptiform discharges (PLEDs)
- Low specificity (32%) but 84% sensitivity





Patient 3. Male, 51 years. A) EEG, longitudinal mountage: PLEDs occuring every 3 sec in the left temporal region. B) MRI-FLAIR, coronal image: hyperintense signal over medial temporal regions, parahippocampal cortex, hippocampus and insula, with right sided predominance.

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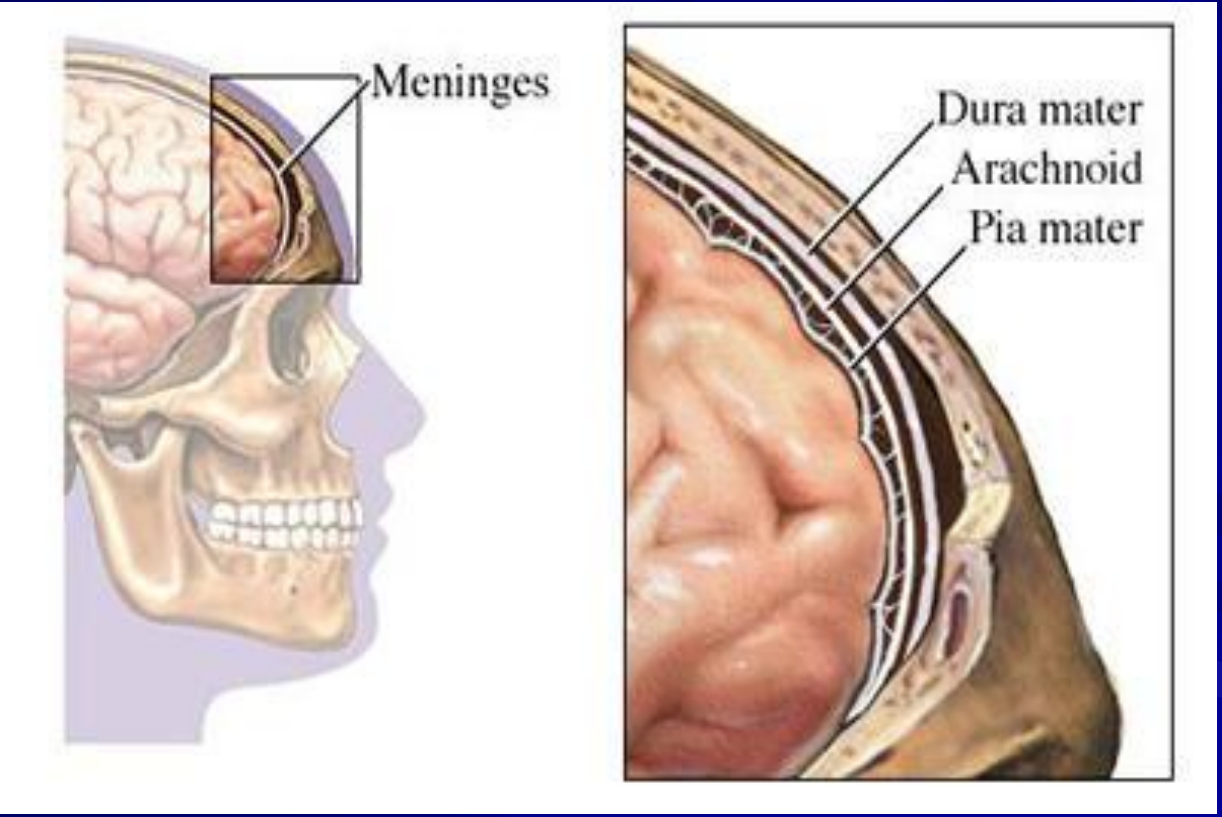

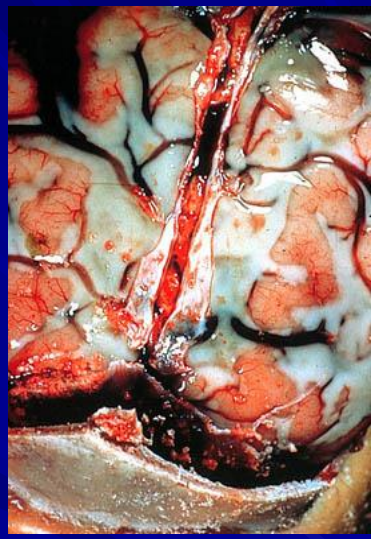

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Factors affecting susceptibility to meningitis

- Host factors
- Genetics
- Closed communities

Research Centers for Bacterial Meningitis-Iran

Etiology of Bacterial meningitis, Age 2 mo. – 15 yr. (23,Sep. 2004 - 22,Sep. 2006) IRAN

City	Hib	N. men.	S.pneu.	Others
Sari	2	3	1	3
Tabriz	7	3	13	4
Shiraz	10	2	9	5
Ahwaz	17	3	10	6
Sanandaj	1	0	2	5
Total	37	11	35	23

2 Sterp.g.B
Strep.g.A

Pseudomonas
G+cocci
Salmonella
Klebsiella

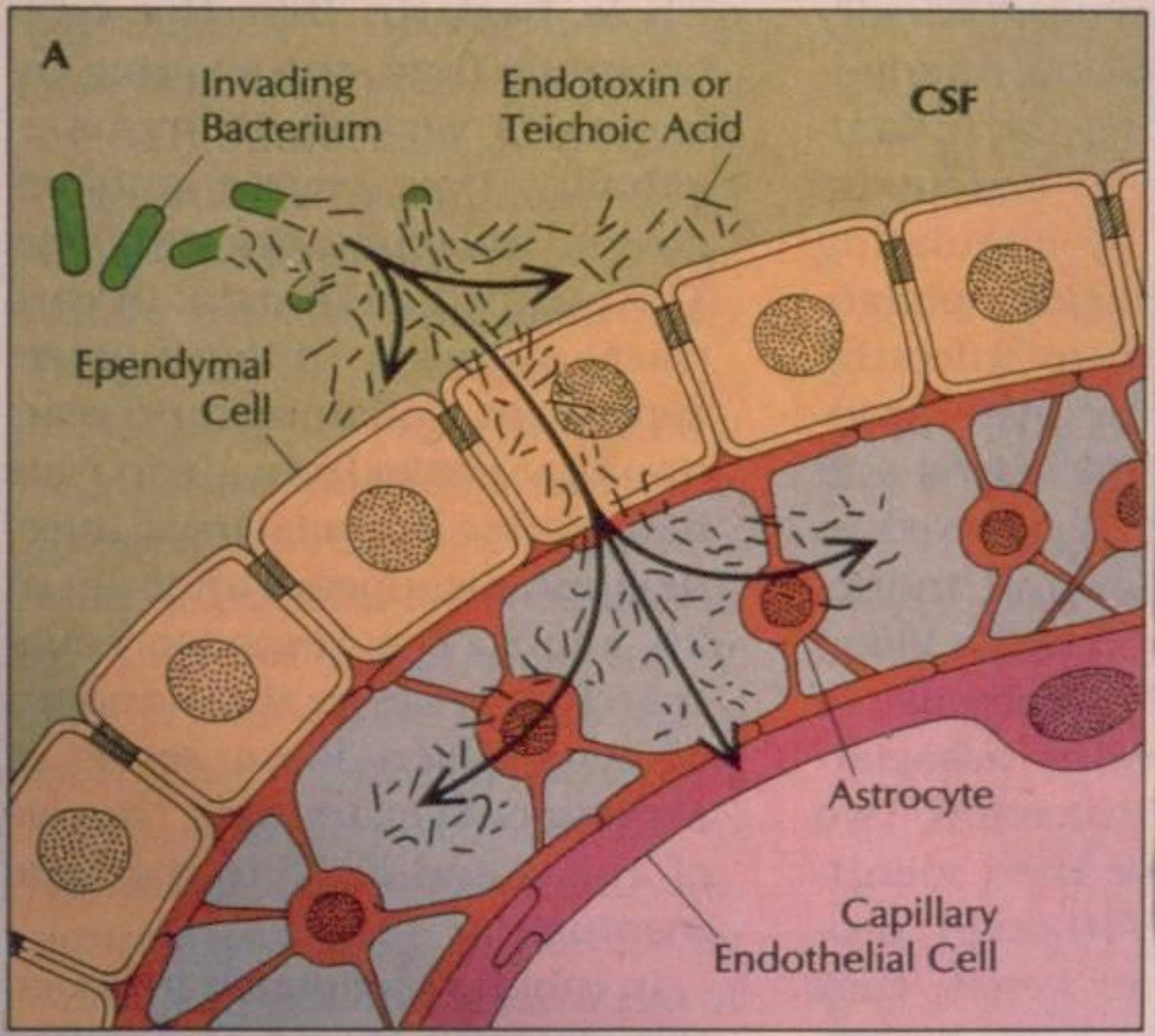
4 Gr+ Cocci
Strep.g.B

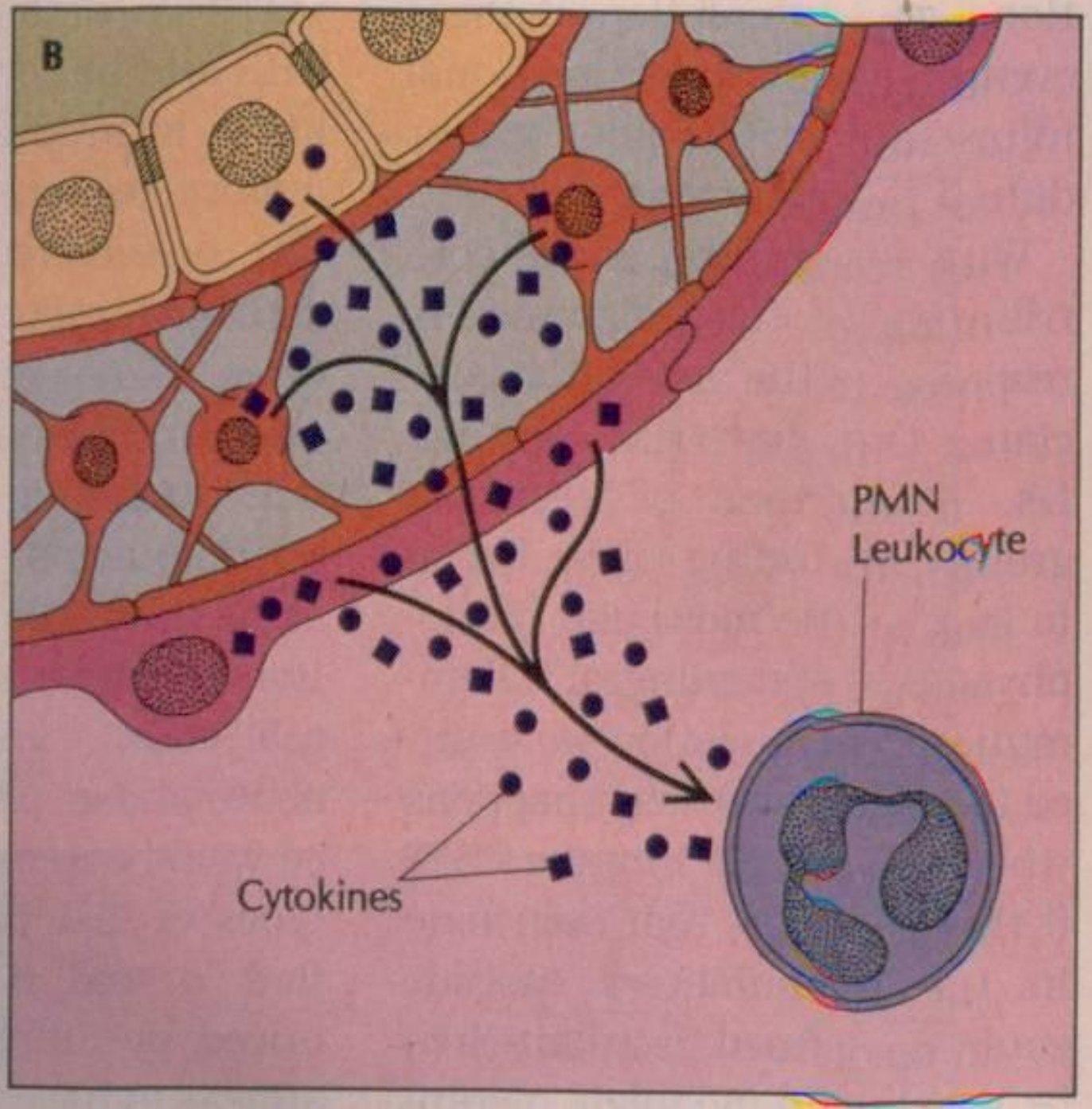
Salmonella
Gr+ bacilli
2 Gr+ Cocci
2 Strep.g.A

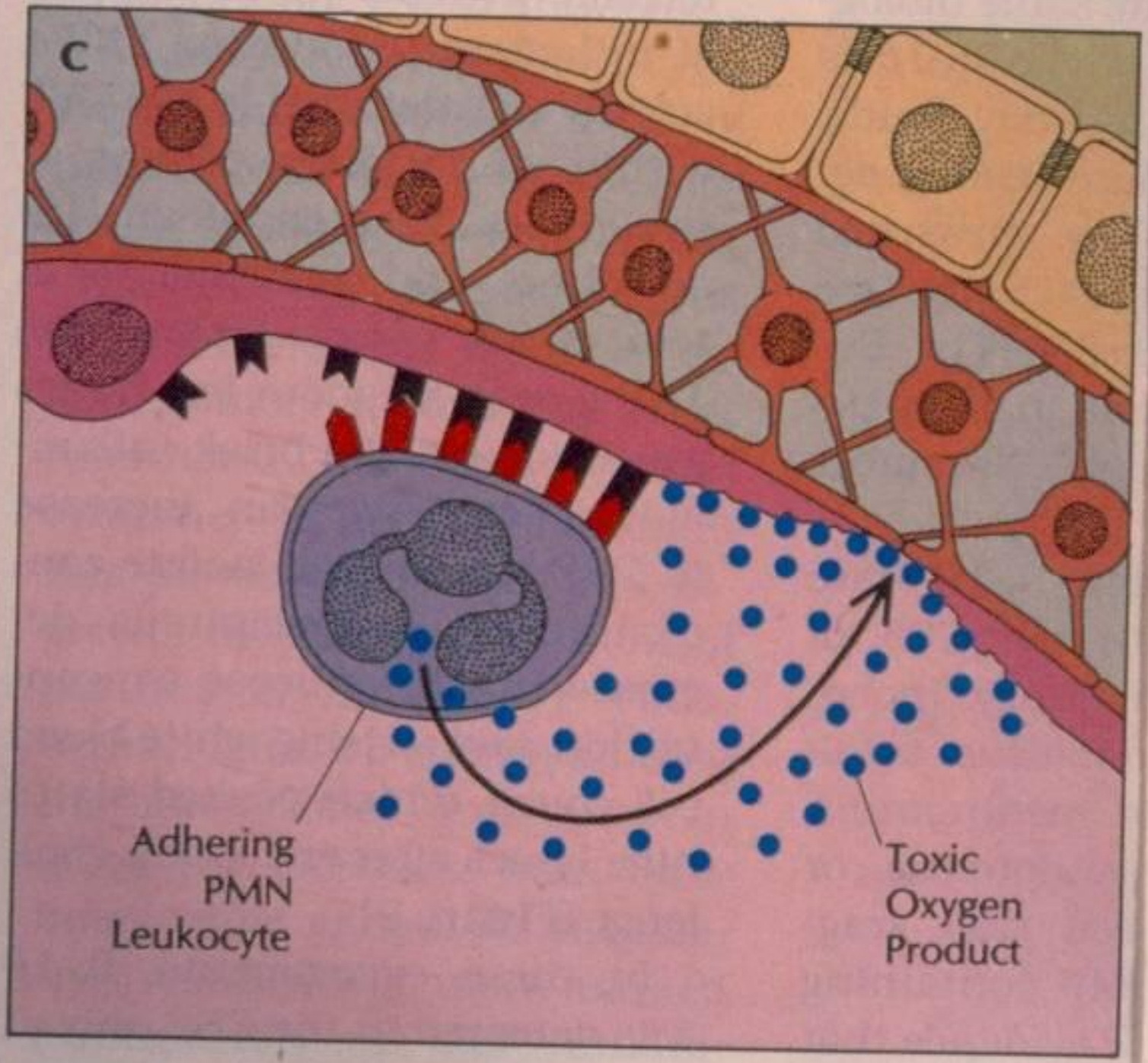
Staph D-
2G+ cocci
G- bacilli
B.anthracis

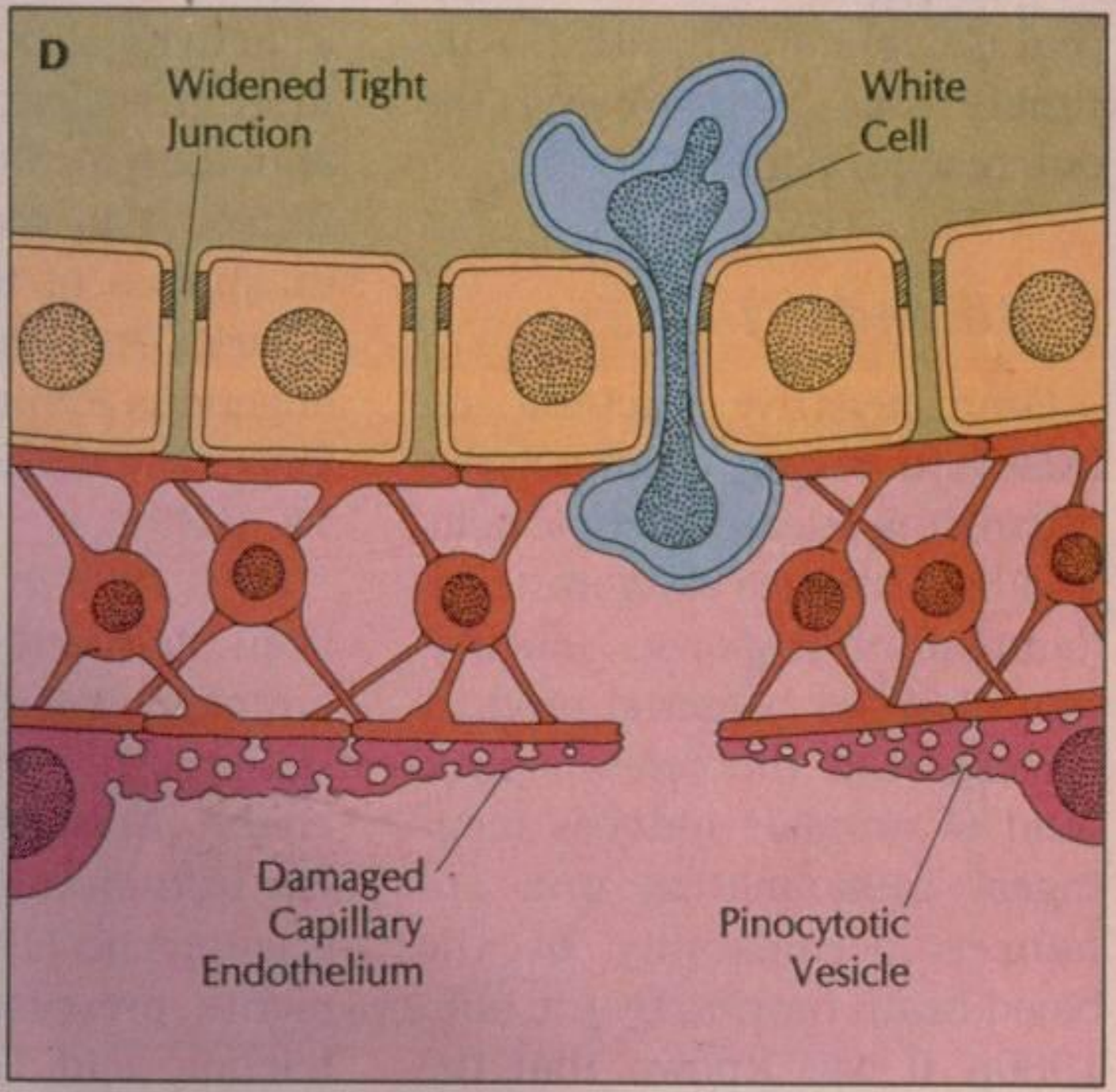
Progress steps of bacterial meningitis

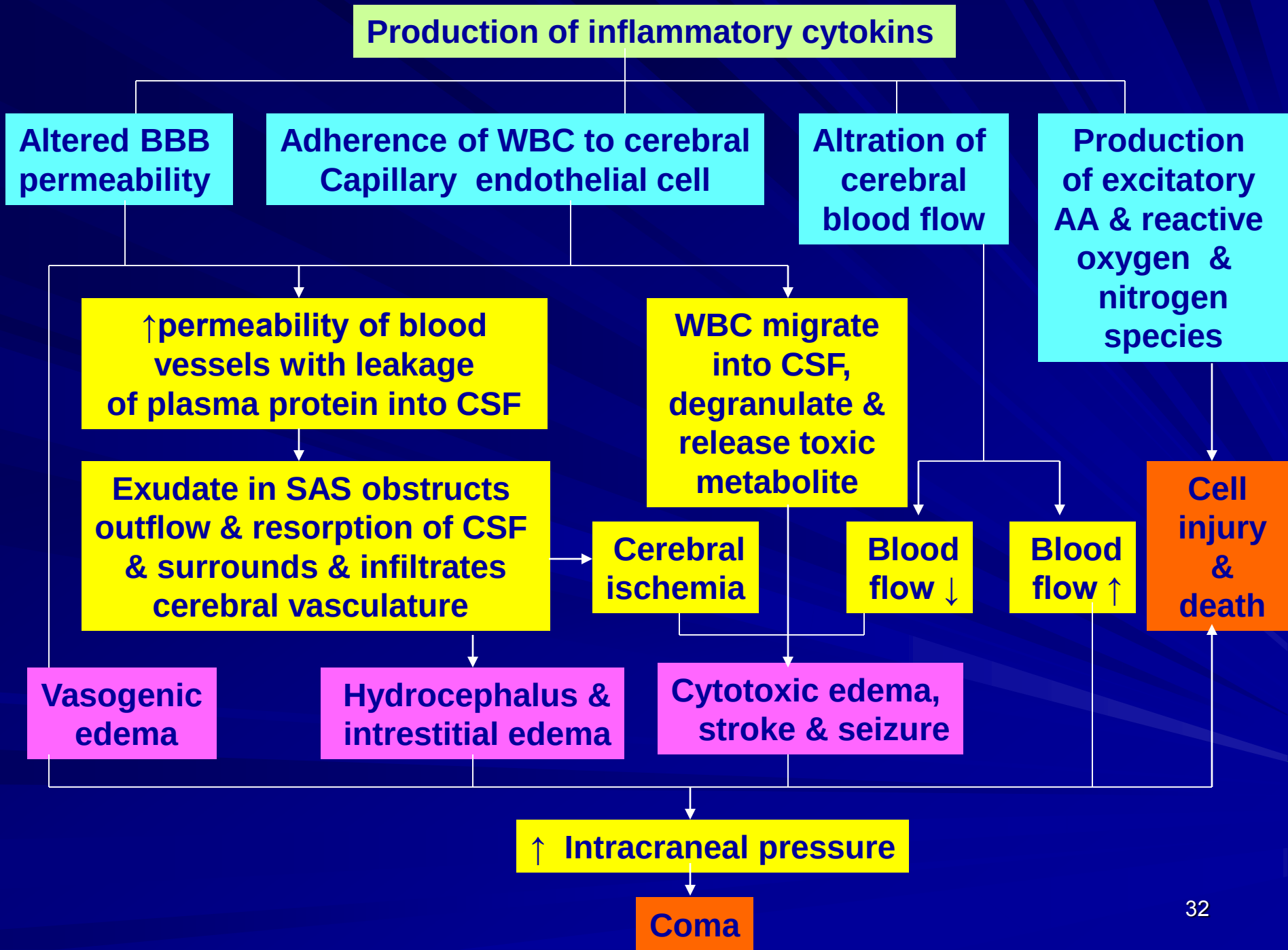
1. Infection of upper respiratory tract
2. Invasion of the blood from the respiratory focus
3. Seeding of the meninges by the B.B.B
4. Inflammation of the meninges and brain


A
Invading Bacterium
Endotoxin or Teichoic Acid
CSF
Ependymal Cell
Astrocyte
Capillary Endothelial Cell


B
PMN
Leukocyte
Cytokines


C
Adhering
PMN
Leukocyte
Toxic
Oxygen
Product


D
Widened Tight Junction
White Cell
Damaged Capillary Endothelium
Pinocytotic Vesicle


Production of inflammatory cytokins
Altered BBB permeability
Adherence of WBC to cerebral Capillary endothelial cell
Altration of cerebral blood flow
Production of excitatory AA & reactive oxygen & nitrogen species
↑permeability of blood vessels with leakage of plasma protein into CSF
WBC migrate into CSF, degranulate & release toxic metabolite
Exudate in SAS obstructs outflow & resorption of CSF & surrounds & infiltrates cerebral vasculature
Cerebral ischemia
Blood flow ↓
Blood flow ↑
Cell injury & death
Vasogenic edema
Hydrocephalus & intrestitial edema
Cytotoxic edema, stroke & seizure
↑ Intracraneal pressure
Coma

Mode of progression of meningitis

- Insidious pattern (1-3 days)
- Acute and fulminant (few hours)

Signs or conditions that can be associated with meningitis

1. Cutaneous manifestations
2. Seizures
3. Focal neurologic findings
4. Altered state of consciousness
5. Ataxia and hearing loss
6. Systemic condition

Signs or conditions that can be associated with meningitis

- Cutaneous manifestations

1. Petechea, purpura

2. Tache cerebrale
   - which is elicited by stroking the skin with a blunt object and observing a raised red streak within 30–60 sec.

Signs or conditions associated with meningitis

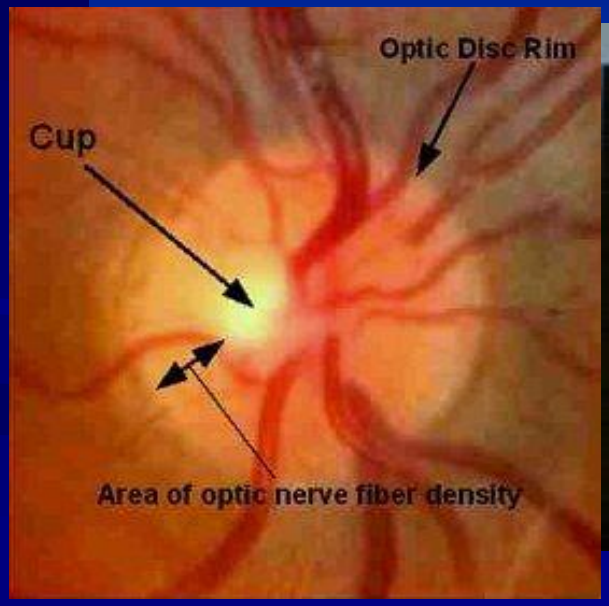
- **Seizures**
  - **1-2 days**
  - **Later**
    - **SIADH**
    - **Cerebritis**
    - **Subdural effusion**
    - **Vascular thrombosis**
    - **Abscess formation**

Signs or conditions associated with meningitis

- Focal neurologic findings
  - Hemiparesis, quadriparesis, facial palsy
  - Visual field defect
  - An unresponsive dilated pupil
  - Papilledema
    - Venous sinus thrombosis
    - Subdural collection
    - Brain abscess

Papilledema

- Note swelling of the disc, hemorrhages, and exudates, with preservation of the physiologic cup

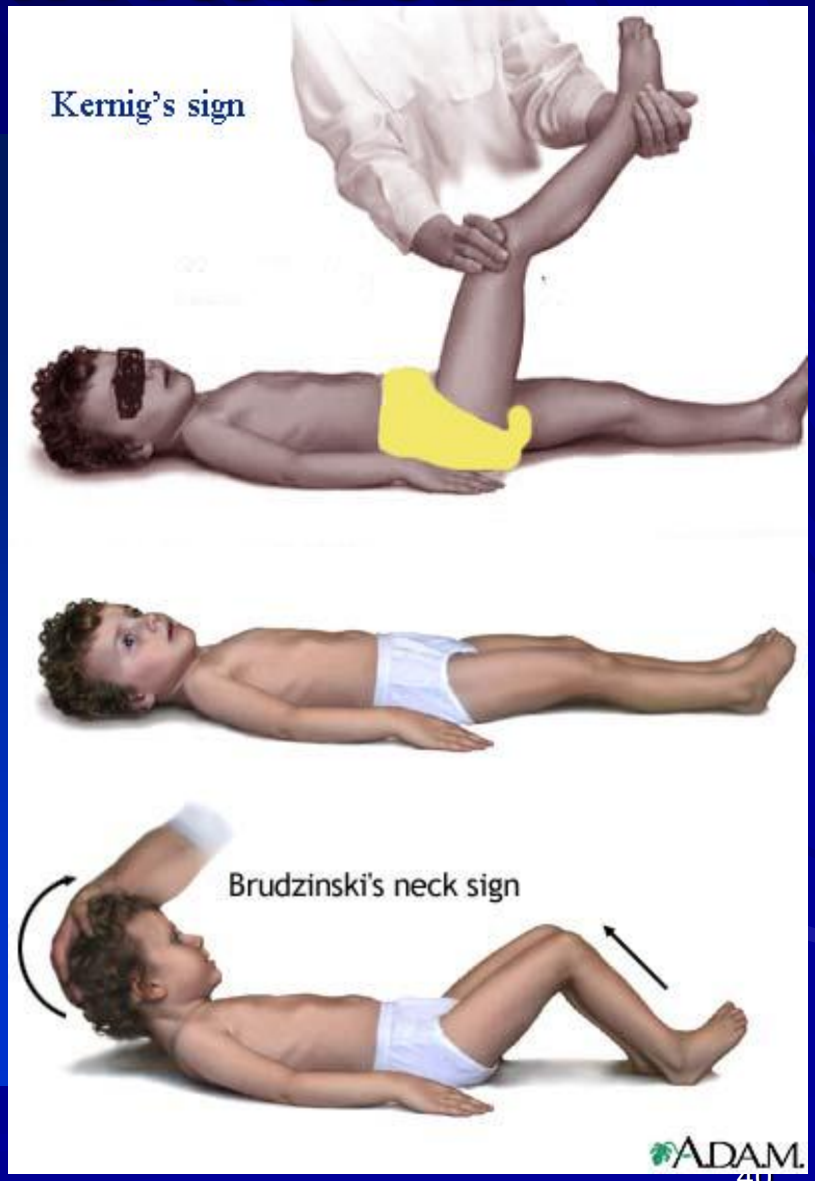


Meningeal irritation

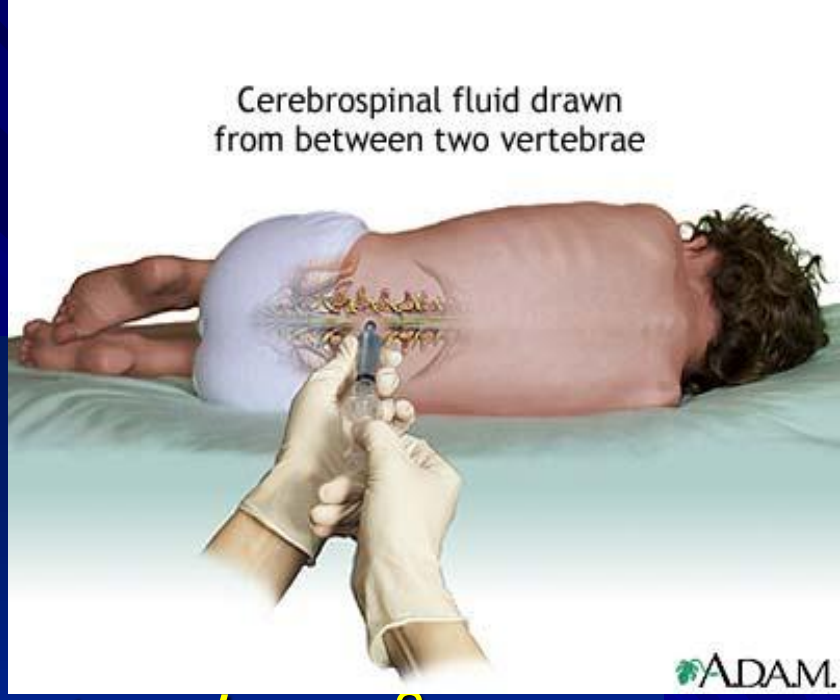
Nuchal rigidity

Meningeal irritation

- Nuchal rigidity
- Kernig sign
- Brudzinski sign



Examination of CSF



- Pressure: **50–80** mmH2O
- Color
- RBC
- WBC: **<5, ≥75% lymphocytes** / mm^3
- Protein: **20–45** mg/dl
- Glucose:, **>50 (or 75% serum glucose)**
- Stained smear of CSF
- CSF culture

The classic CSF abnormalities in bacterial meningitis

(1) PMN leukocytosis (>100 cells/ L in **90%**)

(2) decreased glucose concentration (<40 mg/dL) and/or CSF/serum glucose ratio of <0.4 in **~60%]**

(3) increased protein concentration (>45 mg/dL) in **90%**

(4) increased opening pressure (>180 mm H2O in **90%**).

- CSF bacterial cultures are positive in **>80%** of patients,
- CSF Gram's stain demonstrates organisms in **>60%**.

Rapid diagnostic test

- Countercurrent immun.
- Latex agglutination
- ELISA
- Polymerase chain reaction

Criteria for repeat lumbar puncture

- After negative result in an initial lumbar puncture
- After an positive result in initial lumbar puncture

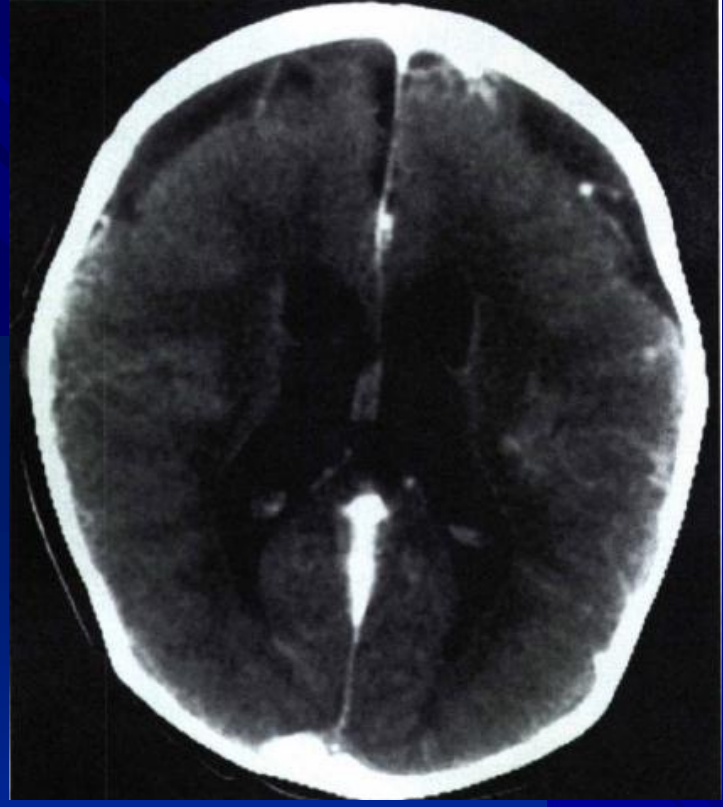
Reasons to withhold lumbar punctures

1. Important cardiovascular compromise
2. Signs of ↑ ICP
3. Infection in the area of obtaining CSF
4. History or signs of bleeding disorders such as hemophilia

Other tests helpful in diagnosis

- ENT consult
- Blood culture
- Urine culture
- Skin lesions
- Middle ear effusion

Neuroimaging



(1) focal neurological signs

(2) persistently positive CSF cultures despite appropriate antibiotic therapy

(3) persistent elevation of CSF PMN leukocytes (> 30% to 40%) after more than 10 days of therapy

(4) recurrent meningitis.

Treatment of Meningitis

- Selection of initial antibiotic therapy
- Duration of antibiotic

Antibiotic therapy in purulent meningitis

Haemophilus influenzae	Ampicillin Cefotaxime Ceftriaxone Chloramphenicol
Neisseria meningitidis	Penicillin G
Streptococcus pneumoniae[†]	Penicillin G Chloramphenicol Vancomycin Cefotaxime/ceftriaxone

Unknown (<1 mo of age)	Ampicillin plus cefotaxime plus vancomycin
Unknown (>1 mo of age)	Cefotaxime or ceftriaxone plus vancomycin

MIC of *S.pneumonia* against to penicillin

Patients	MIC µg/ml	
1	4	HR
2	2	HR
3	1	MR
4	0.5	MR
5	0.125	MR
6	0.06	S
7	8	HR
8	1	MR
9	0.5	MR
10	0.5	MR
11	1	MR

HR= High resistant, MR=Moderate resistant, S= Sensitive

DURATION OF ANTIBIOTIC THERAPY

- *S. pneumoniae* meningitis
  - 10-14 days
- uncomplicated *N. meningitidis*
  - 5-7 days
- Uncomplicated *H. influenzae* type b meningitis
  - 7-10 days

DURATION OF ANTIBIOTIC THERAPY

- Gram-negative bacillary meningitis
  - 3 wk or for at least 2 wk after CSF sterilization
    - after 2-10 days of treatment .
- Change antibiotic according to susceptibility test

CORTICOSTEROIDS

- a reduction in permanent auditory nerve damage if administered 15–20 min before the first dose of an antimicrobial agent
  - sensorineural hearing loss
  - Outcome in pneumococcal meningitis

Complications
acute CNS complications

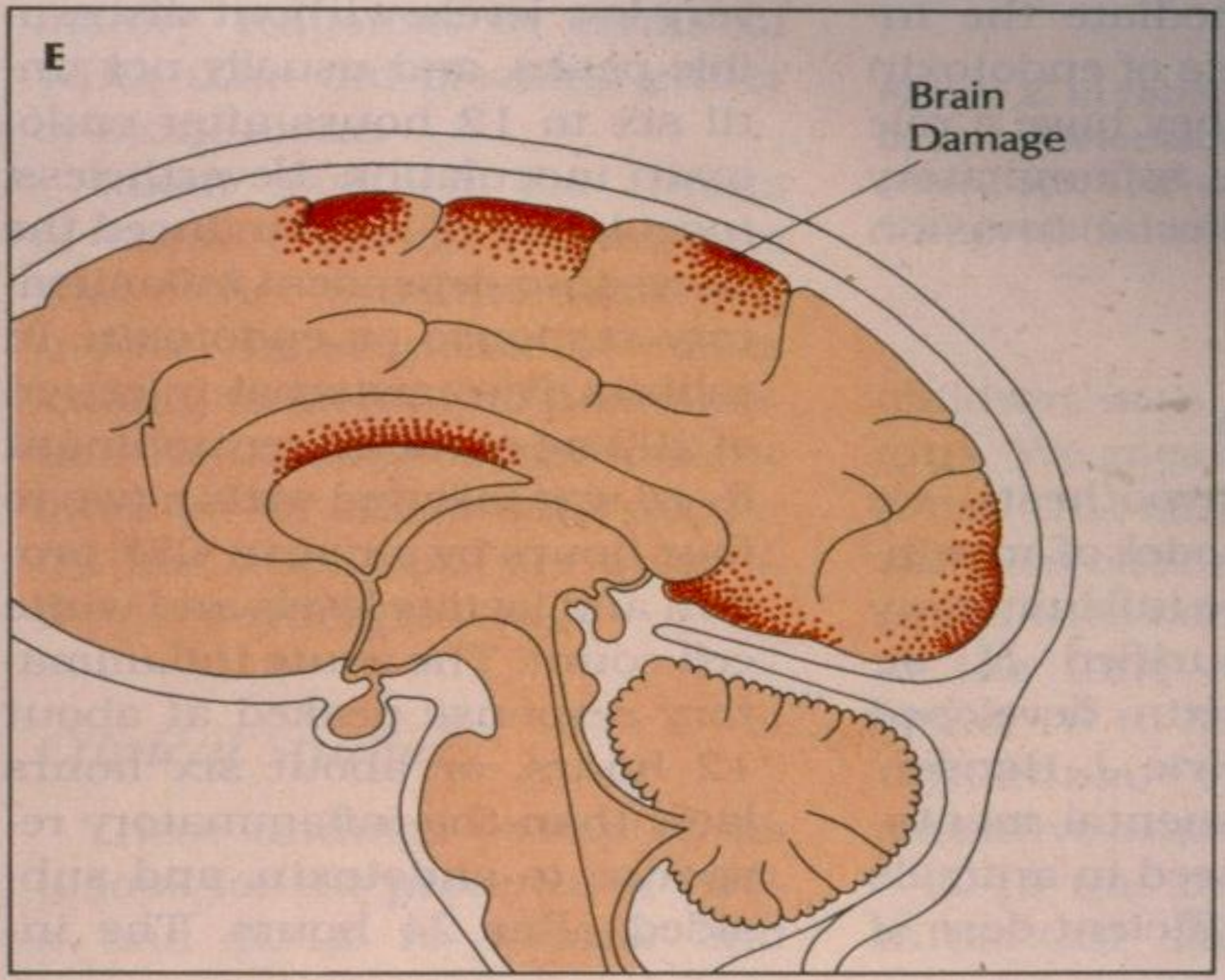
- Seizures
- increased ICP
- cranial nerve palsies
- Stroke
- cerebral or cerebellar herniation
- Thrombosis of the dural venous sinuses
- Subdural effusions

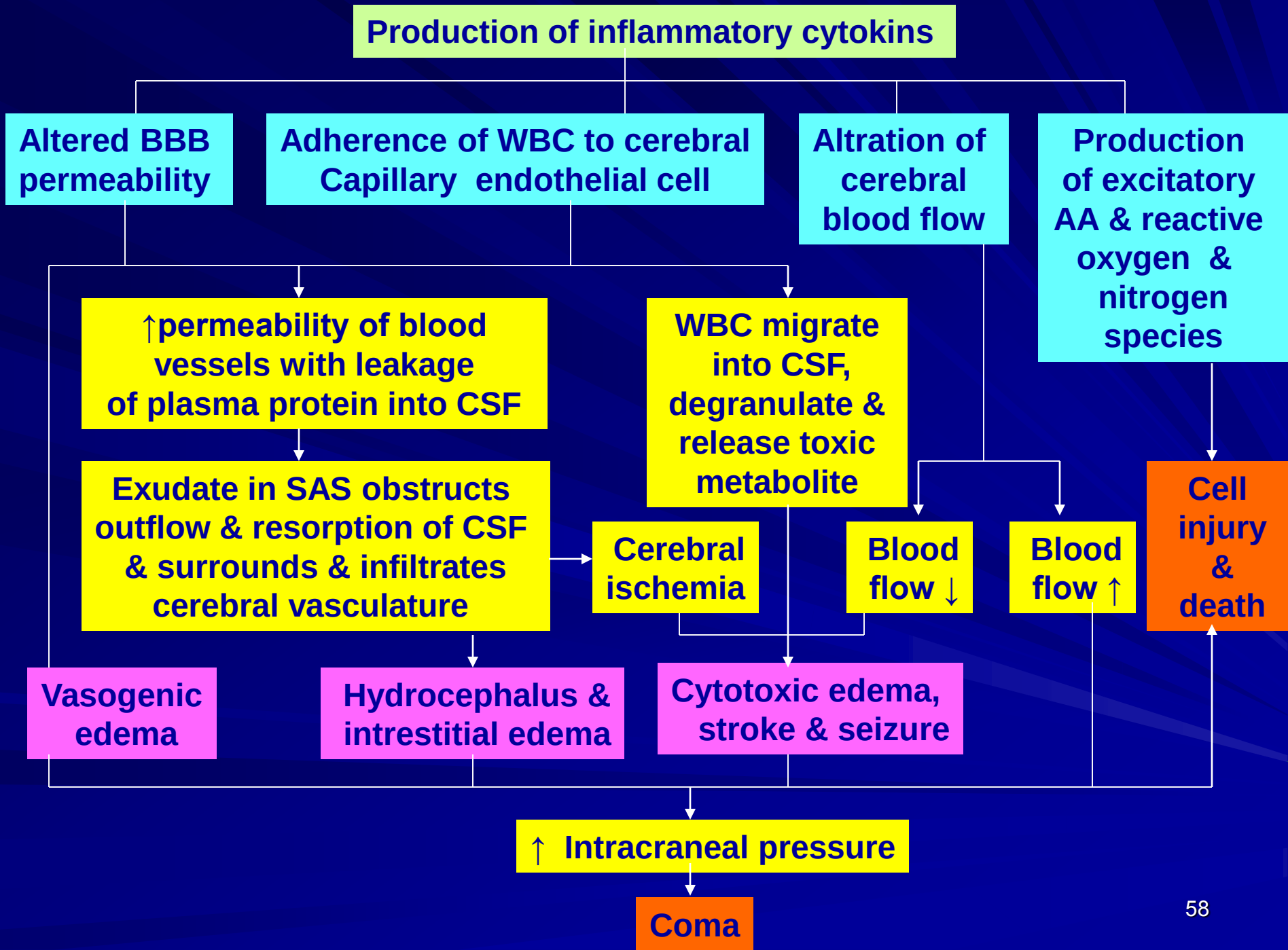
The most common neurologic sequelae

- hearing loss
- Mental retardation
- Recurrent Seizures
- delay in acquisition of language
- visual impairment
- behavioral problems

Prevention

- Post exposure chemoprophylaxis
  - HiB
  - Meningococcus
- Vaccination
  - Routine
  - High risk


E
Brain
Damage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Altered BBB permeability
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Production of excitatory AA & reactive oxygen & nitrogen species
↑permeability of blood vessels with leakage of plasma protein into CSF
WBC migrate into CSF, degranulate & release toxic metabolite
Exudate in SAS obstructs outflow & resorption of CSF & surrounds & infiltrates cerebral vasculature
Cerebral ischemia
Blood flow ↓
Blood flow ↑
Cell injury & death
Vasogenic edema
Hydrocephalus & intrestitial edema
Cytotoxic edema, stroke & seizure
↑ Intracraneal pressure
Coma