L6

Neuropsychiatry Block

Biochemistry of Cerebrospinal Fluid

Editing File

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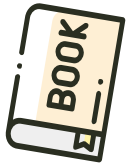
Objectives

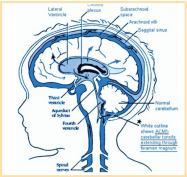


1. To define CSF and its functions, formation and circulation
2. To discuss the CSF sampling procedure (Lumbar puncture) and its indications and contraindications
3. To describe the physical and biochemical laboratory investigations of CSF and the electrophoretic pattern of CSF proteins
4. To study the composition of normal CSF and discuss the abnormal findings in pathological conditions
5. To define otorrhea and rhinorrhea

CerebroSpinal Fluid (CSF)

Definition

The liquid surrounding the brain and spinal cord It flows in subarachnoid area (the space between the arachnoid & pia mater)

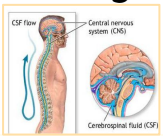


Main Functions

- Physical support & protection
- Provides a **controlled** chemical environment ⟶ nutrient supply & waste removal

Formation & Circulation

- CSF is formed at the **choroid plexuses & by the cells lining the ventricles.**
- Normal blood brain barrier is important removal for the normal chemistry results of CSF
- **Rate of formation: 500 ml/day**



CerebroSpinal Fluid (CSF)

Formation

- Selective ultrafiltration of plasma
- Active secretion by epithelial membranes
  Ab or waste products

Excretion (absorption)

- Excretion volume = production volume → constant CSF volume
- Absorption occurs at the **arachnoid villi** protruding through the dura to the venous sinuses of the brain bloodstream

Specimen & sampling of CSF

Male's dr: Possible SAQ
(How to collect CSF?)

CSF Specimen collection

Video

Obtained by lumbar puncture (At the interspace L3-4, or lower) Using **aseptic** technique CSF sterile technique

CSF is separated into 2 aliquots (two small sample tubes) :

I. for chemistry & serology

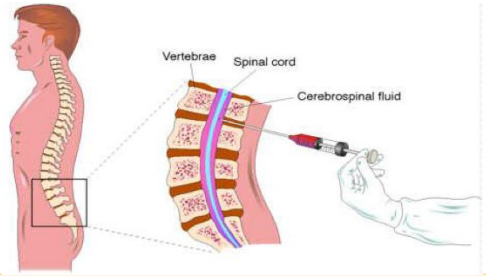
II. for microbiology

Immediate analysis because we don't want glycolysis to happen because once it happened, it may lead to wrong diagnosis.

It's a precious sample: Preserve any remaining sample.because it's not easy to obtain it like urine or blood samples , lumbar puncture sample needs skilled physician to take it

Method of CSF Sampling

Traumatic tap (damage to blood vessel during collection) **blood in CSF**



Specimen & sampling of CSF

Indications for laboratory investigation of CSF

- CNS infection
- Demyelinating disease
- CNS Malignancy
- Hemorrhage in CNS

Contraindications for performing lumbar puncture

Male's dr: Possible SAQ

Bleeding diathesis

It will Increase risk of bleeding in the puncture side

Increased intracranial pressure

Increased intracranial pressure (pressure in the skull) is a contraindication, due to risk of brain matter being compressed and pushed toward the spine.

Infection at site of needle insertion

If the patient have abscess in a region near the spinal cord you should avoid inserting the needle through it, because you'll take the infection and the bacteria inside the CSF which will cause meningitis.

Examination of CSF

	Physical examination	Biochemical analysis
Normal CSF	• **Colorless** • **Clear** • **Free of clots** • **Free of blood**	• **Glucose** • **Protein:** - Total - Specific: Albumin Immunoglobulin, others (e.g. myelin basic protein; MBP) • **Glucose & protein are the most reliable diagnostically & accessible analytically** • **Lactate**
Cloudy turbid—> perform microscopic examination	• is usually due to leukocytes • May be due to microorganisms Turbid CSF can either indicate bacterial or fungal infections	
Blood & (Hemoglobin Pigments in CSF)	**Traumatic tap** **- Bright red color** **- RBCS in decreasing number as the fluid is sampled** - 437: Not a haemorrhage, but rupture of a blood vessel during specimen collection → blood in the CSF (contaminated CSF) - CSF sample in the beginning RBCs are found (red) as a result of rupturing the blood vessel, then as the needle gets deeper it's not found (white) • **Subarachnoid hemorrhage (SAH)** - **Xanthochromia (hemoglobin breakdown pigments) = RBCs lysis & metabolism previously occurred** (at least 2hr earlier) - #team437: Real haemorrhage due to trauma or any other causes and xanthochromia - Blood in the CSF , rupture of RBCs (like a bruise) [heme degrades-biliverdin (green)-bilirubin(yellow)] **When would Xanthochromia indicate hemorrhage?** If you exclude: - Prior traumatic tap - Hyperbilirubinemia (bilirubin > 20 mg/dL) RBCs lysis—> releases hemoglobin which releases bilirubin	

Examination of CSF

Glucose and Protein in CSF

Glucose in CSF

- Glucose enters CSF via facilitative transporter (GLUT)
- **CSF (glucose) is ~ 2/3 that of plasma "50 - 80 mg/dl"** Possible MCQ
- A **plasma sample** must be obtained ~ 2-4 hr before CSF sample:
  In **hypoglycemia**: (CSF glucose) may be very low,
  In **hyperglycemia**: (CSF glucose) is raised Directly proportional to plasma glucose level
- Measure CSF (Glucose):
  - **immediately**
  - or preserve the specimen with an **antiglycolytic** e.g. fluoride ion Fluoride ion is a glycolysis suppressor, we need it to protect glucose in obtained CSF from breaking down, thus we don't give a wrong diagnosis.

Protein in CSF

- Proteins, mostly albumin are found in the CSF **(0.15-0.45 g/L)**
- Source of CSF proteins:
  - 80% from plasma by ultrafiltration
  - 20% from intrathecal synthesis

Protein in CSF

- Proteins, mostly albumin are found in the CSF (0.15-0.45 g/L)

Sources of CSF proteins

80% from plasma by ultrafiltration

20% from intrathecal synthesis
production of substances within the cerebrospinal fluid

CSF Albumin

- **Albumin is produced solely in the liver**
- **Its presence in CSF must occur through BBB**

Abnormal CSF Glucose & total proteins

↑ CSF (glucose)	• Not clinically informative • Provides only confirmation of hyperglycemia
↓CSF (glucose) (hypoglycorrhachia) Male's dr: Possible SAQ	• **Disorder in carrier-mediated transport** e.g. TB meningitis, sarcoidosis • **Active metabolism of glucose by cells or organisms:** e.g. acute purulent, amebic, & fungal meningitis • **Increased metabolism by the CNS** e.g. by CNS neoplasm
In viral meningitis	• CSF (glucose) is usually normal viruses don't use glucose thats why its not decreased in viral infections
Abnormal ↑ CSF (Total protein)	• **Must be compared to the serum (protein)** • Useful nonspecific indicator of pathological states: - **Lysis of contaminant blood (traumatic tap)** - **↑ permeability of the epithelial membrane due to:** 1- Bacterial or fungal infection 2- Cerebral hemorrhage - **↑ production by CNS tissue in:** 1- Multiple sclerosis (MS) 2- Subacute Sclerosing Panencephalitis (SSPE) - **Obstruction** e.g. in: 1-Tumors 2-Abscess

CSF Albumin and Immunoglobulin

CSF Albumin

- Albumin is produced solely in the liver
- Its presence in CSF must occur through BBB

CSF IgG can arise from:

- Plasma cells within CSF
- The blood through BBB

↑ IgG and normal (Alb) of CSF suggests local production of IgG, eg-

- Multiple Sclerosis (MS)
- Subacute Sclerosing Panencephalitis (SSPE)

What to do if ↑CSF protein was detected

- **Perform electrophoretic separation**

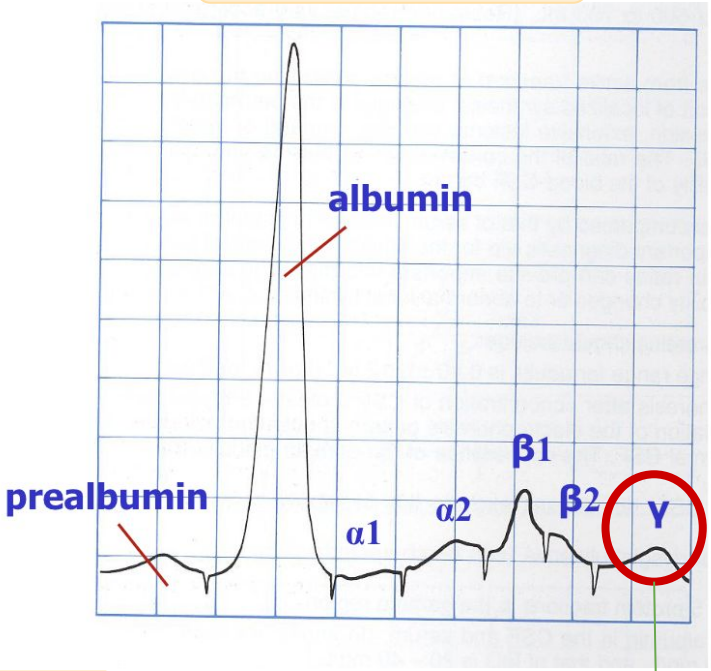
Important!
It might come as SAQ.

If multiple banding (**oligoclonal bands**) of the **γ-globulin** is detected, the following differential diagnosis is suspected:

- **Multiple Sclerosis**
- **Subacute Sclerosing Panencephalitis (SSPE)**
- **Inflammatory Diseases**

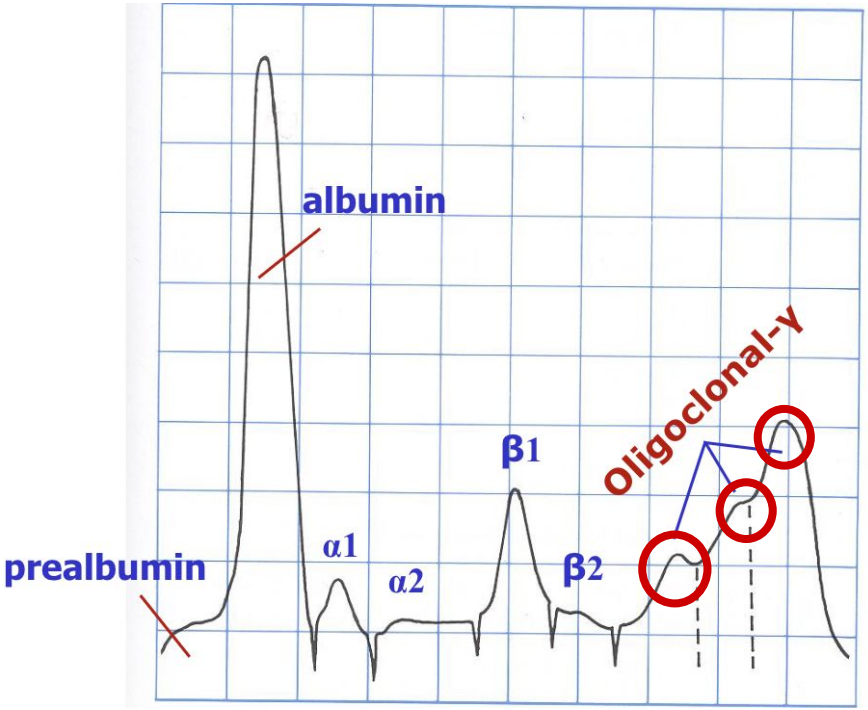
CSF Electrophoresis

Normal Pattern



Only 1 Band

Oligoclonal Banding



Male Dr.: “Oligo- usually refers to anything less than 5, in this case it’s oligoclonal bands because we see 3”

Other Chemical components of CSF

In comparison to plasma

Important!
It might come as MCQ.

Lower in CSF

- Calcium
- Potassium
- Phosphates

Higher in CSF

- Chloride
- Magnesium

Abnormal CSF [Chloride]

- Marked ↓↓ in acute bacterial meningitis
- Slight ↓ in viral meningitis & brain tumors

Otorrhea and Rhinorrhea

Otorrhea

- Leakage of CSF from the ear

Rhinorrhea

- Leakage of CSF from the nose

Normal Composition of CSF

Normal composition of CSF			Male's dr: know its comparison to plasma and know the range for glucose
Appearance	Clear ,Colorless	**Protein**	0.15 – 0.45 g/L
Lymphocytes	<5/mm^3	**Glucose**	50 - 80 mg/dL, (2.8-4.2 mmol/L), (>50% plasma level)
Polymorphs	Nil	**Chloride**	115 - 130 mmol /L
pH	7.4	**Calcium**	1.0 - 1.40 mmol/L
Total Volume	100 - 150 ml	**Phosphorus**	0.4 - 0.7 mmol/L
Daily Secretion	450 - 500 ml	**Magnesium**	1.2 - 1.5 mmol/L
Specific Gravity	1.006 - 1.007	**Potassium**	2.6 - 3.0 mmol/L

Abnormal Findings of CSF in some Pathological Conditions

Parameter (Reference Range)	Condition		
	Bacterial Meningitis (pyogenic)	**Tuberculous Meningitis**	**Viral Meningitis** Usually the findings of viral meningitis are normal
Appearance	Often turbid	Often fibrin web	Usually clear
Predominant cell	Polymorphs	Mononuclear (lymphocytes)	Mononuclear (lymphocytes)
Cell count/mm^3	90-1000+	10-1000	50-1000
Bacteria/virus	+ve smear & culture	Often none in smear	-ve smear or culture
Protein (0.15-0.45 g/L)	**>1.5 (↑ ↑)**	**1-5 (↑ ↑)**	**<1 (Normal)**
Glucose (2.8-4.2 mmol/L)	**<1/2 plasma (↓ ↓)**	**<1/2 plasma (↓ ↓)**	**>1/2 plasma (Normal or slightly ↓)**
Chlorides (115 - 130 mmol/L)	**↓ ↓**	**↓ ↓**	**Normal or ↓**

Take Home Messages

- CSF is formed in the choroid plexus
- It is essential for the physical protection of the CNS
- The physical & chemical analysis of CSF is essential for diagnosis of certain diseases

Summary!

MCQs

Q1: Mg and Cl are HIGHER in CSF than plasma							
A	True	**B**	False	**C**	Depends	**D**	idk
Q2: A patient has 35 mg/dl glucose in CSF, what's his condition?							
A	Normal	**B**	hypoglycorrhachia	**C**	DM	**D**	Viral meningitis
Q3: Hypoglycorrhachia happens in which of the following ?							
A	Viral meningitis	**B**	Kidney neoplasm	**C**	Sarcoidosis	**D**	Multiple sclerosis
Q4: A CSF sample was taken from a 64-years old female for her annual check up, the biochemistry lab noted the presence of oligoclonal band of of γ-globulin In electrophoresis, this can indicate which of the following?							
A	Bacterial meningitis	**B**	Fungal meningitis	**C**	Viral meningitis	**D**	SSPE
Q5: Which of the following is defined as hemoglobin breakdown pigments, which will lead to RBCs lysis and metabolism ?							
A	Xanthochromia	**B**	Traumatic tap	**C**	Purulent meningitis	**D**	Hyperbilirubinemia

1) A
2) B
3) C
4) D
5) A

SAQ

Q6: Patient presents with persistent headaches and neurological symptoms, CSF analysis has been deemed necessary. What's the procedure where CSF is collected and how is it done?

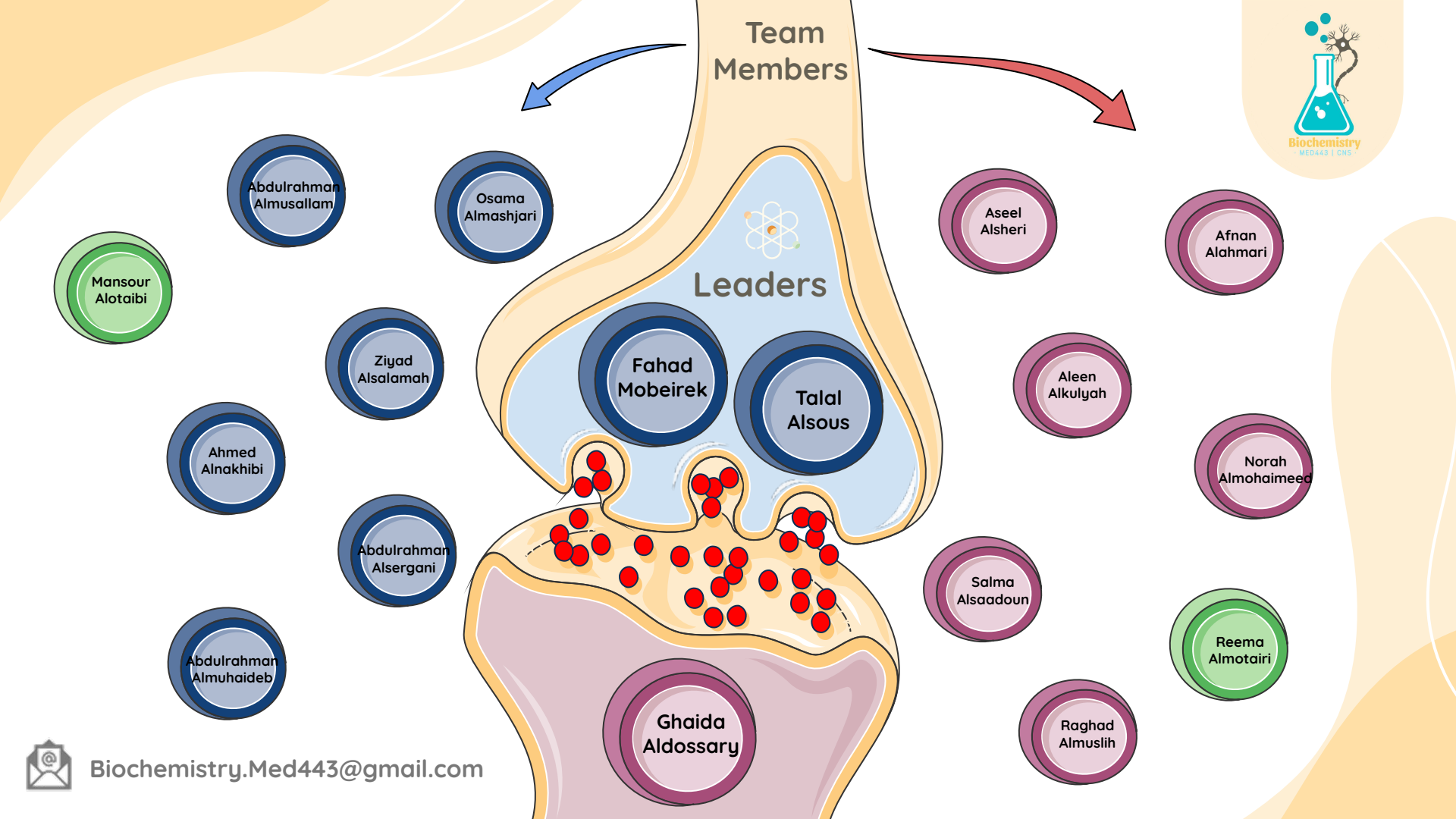
Answer: Obtained by lumbar puncture (At the interspace L3-4, or lower)

Q7: List the contraindications for performing Lumbar Puncture

Answer:
- Bleeding diathesis
- Increased intracranial pressure
- Infection at site of needle insertion

Q8: List 3 causes of hypoglycorrhachia

Answer:
- **Disorder in carrier-mediated transport**
  e.g. TB meningitis, sarcoidosis
- **Active metabolism of glucose by cells or organisms:**
  e.g. acute purulent, amebic, & fungal meningitis
- **Increased metabolism by the CNS**
  e.g. by CNS neoplasm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