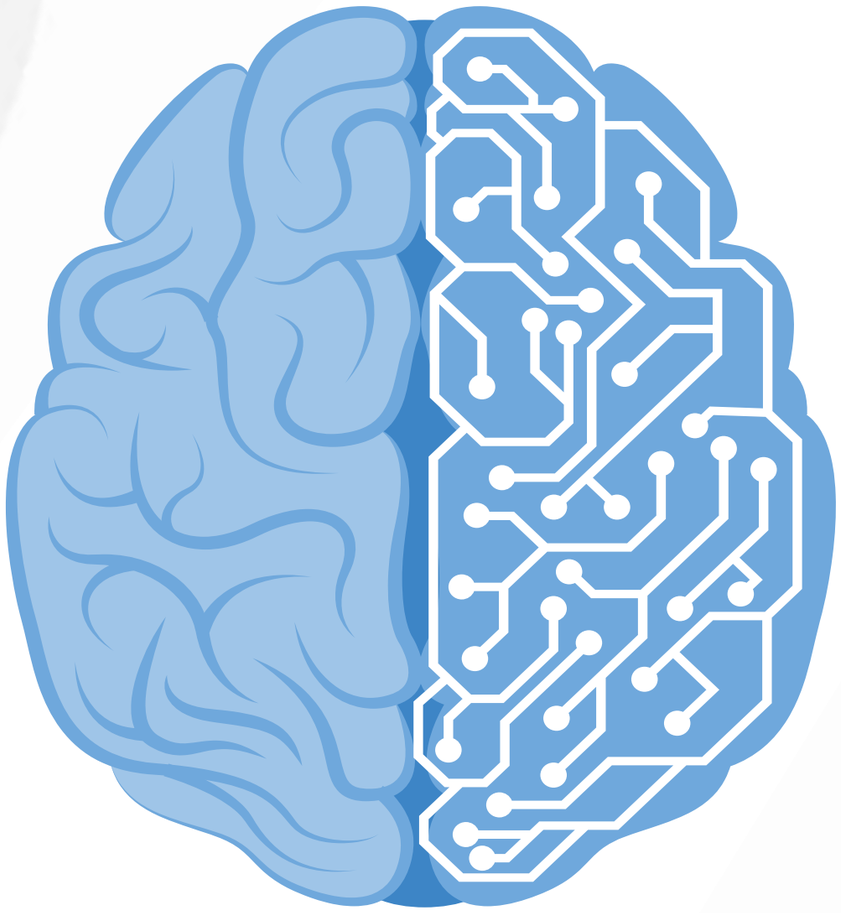
Revised & Approved

Abdullah Alsubaihi
Rania Almutiri

BIOCHEMISTRY TEAM
439

MED439
KING SAUD UNIVERSITY



Body Fluids: Cerebrospinal Fluid

Editing File

Color Index

- Main Text
- Important
- Extra
- Dr.'s Notes
- Girls slides
- Boys slides

Objectives

Click on the objective to go to the related slide

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

Level 6 (congrats! you reached the last level)
Hello my name is Domenico Felice Cotugno, Find me in this lecture!
Then click me for more info about what I discovered.

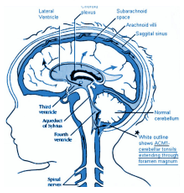
Click the number between the [ ] to see the related notes.

Objectives: 1& 2

CerebroSpinal Fluid (CSF)

CSF definition

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



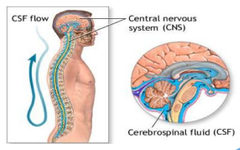
Main Functions

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

CSF Formation & Circulation

CSF is formed at the **choroid plexuses** & by the **cells lining the ventricles**.
-Normal blood brain barrier is important for the normal chemistry results of CSF

Rate of formation: 500 ml/day



Mechanism of Formation & Excretion

Formation

- Selective **ultrafiltration** of plasma
- **Active secretion** by epithelial membranes

Rate of formation must equal the rate of absorption

Excretion

- 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

CSF Specimen Collection (5:47 minutes)

Obtained by lumbar puncture (At the interspace **L3-4**, or lower) Using aseptic technique [1]

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

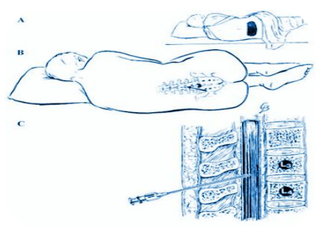
I. for chemistry & serology
II. for microbiology

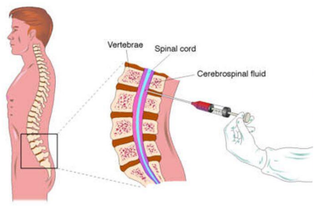
Immediate analysis [2]

It's a precious sample: Preserve any remaining [3] [4] sample

Method of CSF Sampling

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





Click the number between the [ ] to see the related notes.

Objective: 2 & 3

Indications for laboratory investigation of CSF

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

Contraindications for performing lumbar puncture

Bleeding diathesis

means a tendency to bleed or bruise easily. The word “diathesis” comes from the ancient Greek word for “state” or “condition.” Most bleeding disorders occur when blood doesn't clot properly. Symptoms of bleeding diathesis can range from mild to severe.

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 examination
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 [5]	
Blood **You have to differentiate between traumatic tap and xanthochromia**	• **Traumatic tap** [6] - Bright red color - RBCS in decreasing number as the fluid is sampled - #team437: 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 2 hr earlier)** [7] - #team437: Real haemorrhage due to trauma or any other causes - 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) [8]	

Click the number between the [ ] to see the related notes.

Objective: 4

Glucose and Protein in CSF

Glucose in CSF

Glucose enters CSF via facilitative transporter (GLUT) [9]

★ **Important**

CSF (glucose) is ~ **2/3 that of plasma** "50 - 80 mg/dl"

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. [10]

Measure CSF (Glucose):

- immediately
- or preserve the specimen with and antiglycolytic e.g. fluoride ion [11]

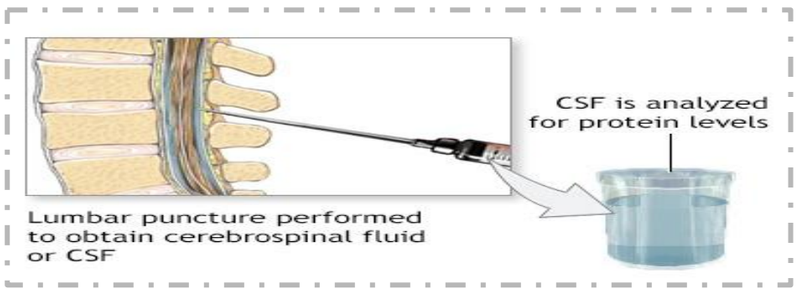
Protein in CSF

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



Abnormal CSF Glucose & total proteins

↑ CSF **(glucose)**	• Not clinically informative • Provides only confirmation of hyperglycemia
↓CSF (glucose) (hypoglycorrhachia)	• **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** [12]
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

Click the number between the [ ] to see the related notes.

Objective: 4 & 5

Protein in CSF

CSF Albumin [13]

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

CSF albumin test can be useful in distinguishing among causes of Meningitis. It is more likely to be elevated in bacterial meningitis than in viral meningitis.

CSF immunoglobulin

CSF IgG can arise:

- from plasma cells within CSF
- from the **blood** through BBB

↑ (IgG) and normal (Alb) of CSF suggests local production of IgG:

- **Multiple sclerosis (MS)**
- **Subacute sclerosing panencephalitis (SSPE)**

What to do if ↑ CSF (protein) was detected?

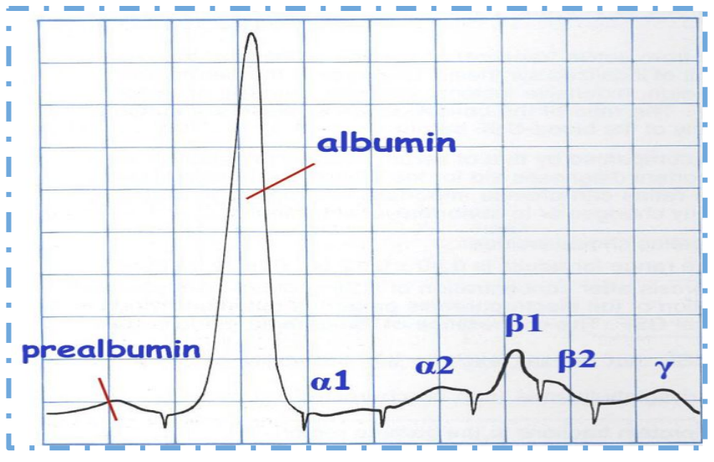
- Perform **electrophoretic** separation

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

- **MS**
- **SSPE**
- **Inflammatory diseases**

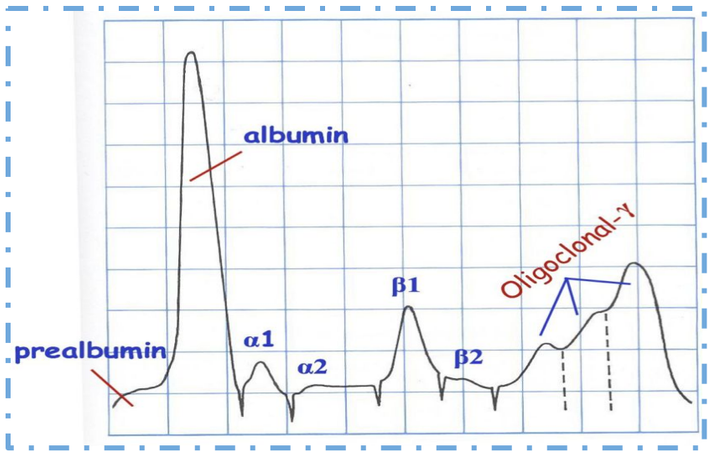
CSF Electrophoresis

Normal pattern [14]



Oligoclonal Banding

You just need to know if we have oligoclonal bands then it indicates MS



Other Chemical Components of CSF

In OSPE cases we only give you the chloride level and it will usually be normal/slightly low, which means it indicates Viral meningitis or brain tumors

1 CSF **(Calcium)**, **(Potassium)** & **(Phosphate)** are **lower** than their levels in the blood

2 Normally CSF **(Chloride)** & **(Magnesium)** are **higher** than their levels in the blood

3 **Abnormal CSF (Chloride):**

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

Leakage of CSF

Otorrhea

- leakage of CSF from the **ear**

In order for there to be drainage from the middle ear into the ear canal, there must be a connection present. This connection can result from a **perforation in the ear drum**, or if an ear tube was previously placed.

Rhinorrhea

- leakage of CSF into the **nose**

Cerebrospinal fluid (CSF) rhinorrhea is a condition where the protective fluid that surrounds the brain finds its way into the nose and sinuses, often appearing as a very watery runny nose. Most cases of CSF rhinorrhea occur **after major accidents** where the bones of the face and skull experience significant trauma.

Click the number between the [ ] to see the related notes.

Objective: 5

Female's doctor: No need to memorize it, we'll give you the normal range in OSPE cases

Normal composition of CSF

Appearance	Clear ,Colorless
Lymphocytes	<5/mm^3
Polymorphs	Nil
pH	7.4
Total Volume	100 - 150 ml
Daily Secretion	450 - 500 ml
Specific Gravity	1.006 - 1.007
Protein	0.15 – 0.45 g/L
Glucose	50 - 80 mg/dL, (2.8-4.2 mmol/L), (>50% plasma level)
Chloride	115 - 130 mmol /L
Calcium	1.0 - 1.40 mmol/L
Phosphorus	0.4 - 0.7 mmol/L
Magnesium	1.2 - 1.5 mmol/L
Potassium	2.6 - 3.0 mmol/L

Abnormal findings of CSF in some pathological conditions (4:34 minutes)

Parameters	Condition Check out our amazing microbiology team for more info about the first 4 findings		
	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 [15]	-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 ↓**

Doctors' Notes

Click the note to go back to the related slide

[1] Aseptic means a sterile technique

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

[3] we need to preserve CSF samples because its an invasive procedure and it's hard to collect another sample from the patient

[4] We call it precious sample because it's not easy to obtain it like urine or blood samples , lumbar puncture sample needs skilled physician to take it

[5] Turbid CSF can either indicate bacterial or fungal infections

[6] In traumatic tap there is a **bright blood** present in CSF due to rupture of vessels while taking the sample. After a while this bright blood will disappear and CSF become clear also In traumatic tap RBCs are not lysid that's why the blood is bright red, and the RBCs number should decrease as you collect the sample because the bleeding should stop.

[7] In xanthochromia the patient is already had hemorrhage in CSF, that blood is dark and pigmented.

[8] Because bilirubin can cross BBB and reaches to the CSF and gives some pigmentations, so it should be excluded if we diagnose for xanthochromia. Hyperbilirubinemia can indicate RBCs destruction because when hemoglobin is broken down it gives bilirubin.

[9] CSF glucose is lower than plasma glucose, that is why it requires active glucose transporter. We have 14 types of GLUT, GLUT1 transports glucose to the brain while GLUT3 transports glucose to neurons

[10] If the CSF glucose is high, it doesn't mean that the patient has diabetes. So diabetes is not diagnosed by CSF.

[11] Sodium fluoride is used to prevent glucose destruction because it inhibits an enzyme called enolase which plays a role in glycolysis,so the process of preserve the specimen with antiglycolytic is also called green tube, 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.

[12] virused don't use glucose thats why its not decreased in viral infections

[13] there are 2 proteins that are synthesized in the liver only, one for long term which is albumin and the other for short term which is prothrombin

[14] in CSF electrophoresis normally there is one band (spike) in the γ (gamma) region, if there is 3 bands (spikes) that's not normal

[15] In TB you can't stain the sample because TB has special stains and wont appear on regular stains, you also can't culture because it takes so much time for the culture to grow the bacteria

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.**

Congratulations ! You just finished all of the biochemistry lectures in CNS
Click on the picture to get your rewarding card

Summary

CSF	
Function	1- Physical support & protection 2- Provides a controlled chemical environment
Formed by	Choroid plexuses & ventricle cells And Obtained by lumbar puncture (At the interspace L3-4)
Indications for Laboratory Investigation	• CNS infection • Demyelinating diseases (ex: MS) • CNS Malignancy • Hemorrhage
Contraindications for performing lumbar puncture	• Bleeding diathesis • Increased intracranial pressure • Infection at site of needle insertion

Chemical Analysis of CSF		
Glucose **CSF glucose is 2/3 of plasma**	**Increased**	• Hyperglycemia
	Decreased	1-**Disorder in carrier-mediated transport** • TB meningitis • sarcoidosis 2- **Active metabolism of glucose by cells or organisms** • acute purulent • amebic • fungal meningitis 3-**Increased metabolism by the CNS** • CNS neoplasm
Protein **Albumin & IgG**	**Increase CSF total protein**	1- **Lysis of contaminant blood** • Traumatic tap 2- **Increased permeability** • Bacterial or fungal infection • Cerebral hemorrhage 3- **Increased production by CNS** • Multiple sclerosis (MS) • Subacute Sclerosing Panencephalitis (SSPE) 4- **Obstruction** • Tumors & abscess
	If IgG is high and albumin in normal	**oligoclonal bands of Y-globin** 1-Multiple sclerosis (MS) 2-Subacute Sclerosing Panencephalitis (SSPE)

MCQs

1-CSF Formation rate is ?
A- 250 ml/day
B- 200 ml/day
C- 500 ml/day
D- 440 ml/day

2-The functions of the CSF include all of the following except:
A-Removal of metabolic wastes
B- Producing an ultrafiltrate of plasma
C- Supplying nutrients to the CNS
D- Protection of the brain and spinal cord

3-Elevated CSF protein values can be caused by all of the following except:
A-Meningitis
B-Multiple sclerosis
C-Fluid leakage
D-CNS malignancy

4- Glucose level is usually normal in:
A- TB meningitis
B- Fungal meningitis
C- Viral meningitis
D- Sarcoidosis

5- Which substance has higher level in CSF?
A- Chloride
B- Calcium
C- Phosphates
D- Potassium

6- If CSF chloride is markedly decreased it suggests:
A- brain tumors
B- viral meningitis
C- bacterial meningitis
D- A&B

Answers key

1- C 2- B 3- C 4- C 5- A 6- C

SAQs

1- what are the finding in traumatic tap and xanthochromia? Told you important

- **Traumatic tap:**
  Bright red color
  RBCS in decreasing number as the fluid is sampled
- **xanthochromia**:
  RBCs lysis
  metabolism previously occurred (at least 2 hr earlier)

2- Is the glucose level in CSF higher or lower compared to plasma? and mention why?

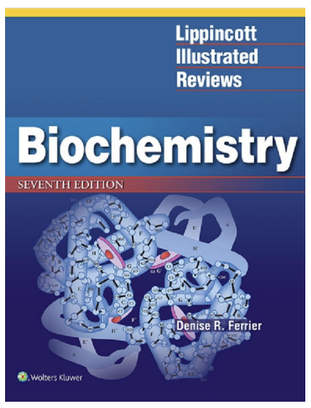
- CSF glucose level is lower than plasma, (it's **~ 2/3 the quantity of plasma**).
- Because Glucose enters CSF via facilitative transporter (GLUT).

3-What do increased IgG and normal albumin indicate?

- Multiple sclerosis (MS)
- Subacute sclerosing panencephalitis (SSPE)

Resources

Click on the book to download the resource



Leaders

Rand AlRefaei

Mohammed Alkathiri

Reviser

Rania AlMutairi

NoteTakers

Alaa AlSulmi

Fahad AlAjmi

Members

- Albandari Alanazi
- Norah AlKathiri
- Ibrahim Alabdulkarim
- Abdulaziz Alrabiah
- Farah AlSayed
- Ghadah AlSwailem
- Abdulmohsen Alqadeeb
- Renad AlHumaidi
- Yasmeen AlQarni
- Ghaida AlMarshood
- Mohammed alsunaidi
- Hamad Almousa
- Walid alzaid

Special thanks to Fahad AlAjmi for designing our team's logo.