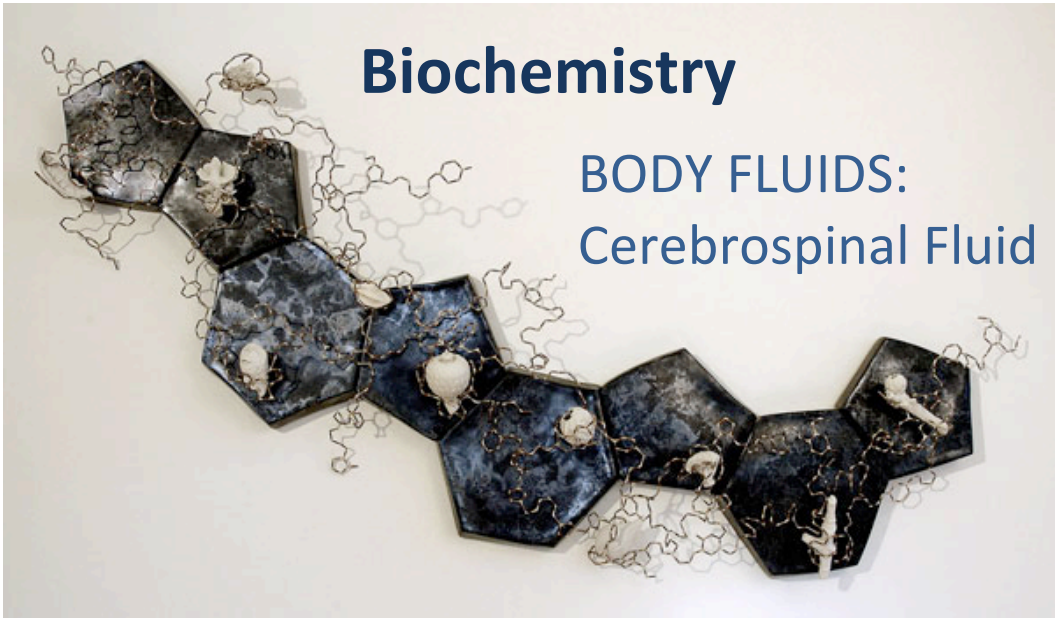


# Biochemistry

## BODY FLUIDS: Cerebrospinal Fluid



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**As the doctor said:**

Anything in the green is not important.

### CSF definition:

It is the liquid surrounding the brain and spinal cord.

It flows in subarachnoid area (the space between the arachnoid & pia matter).

### Functions:

- Physical support & protection.
- Provides a controlled chemical environment → nutrient supply & waste removal.
- Intra- & extracerebral transport: Neuroendocrine function.

### CSF Formation & Circulation:

nCSF is formed at the choroid plexuses & by the cells lining the ventricles.

nNormal blood brain barrier is important for the normal chemistry results of CSF.

### Rate of formation:

n 500 ml/day.

### Mechanism of formation:

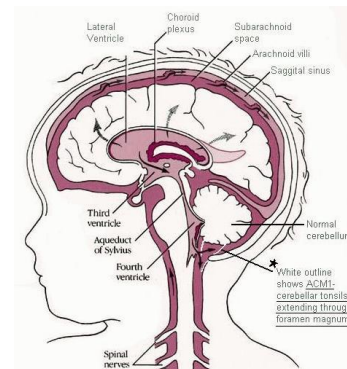
n Selective ultrafiltration of plasma.

n Active secretion by epithelial membranes.

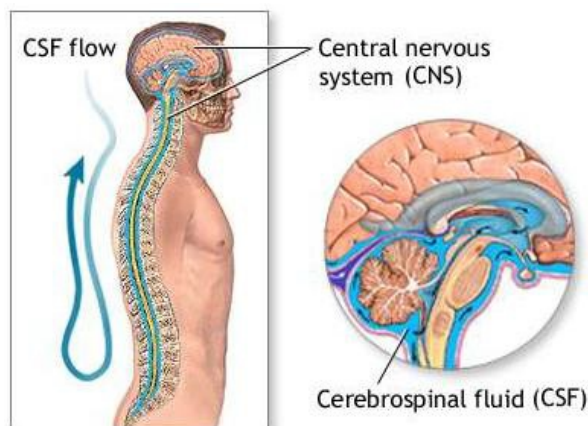
### Mechanism of excretion (absorption):

n Excretion volume = production volume → constant CSF volume.

n Absorption occurs at the arachnoid villi protruding through the dura to the venous sinuses of the brain → bloodstream.



### CSF Circulation:



## Method of CSF Sampling:

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

## CSF Specimen Collection:

nObtained by lumbar puncture  
(At the interspace L3-4, or lower).

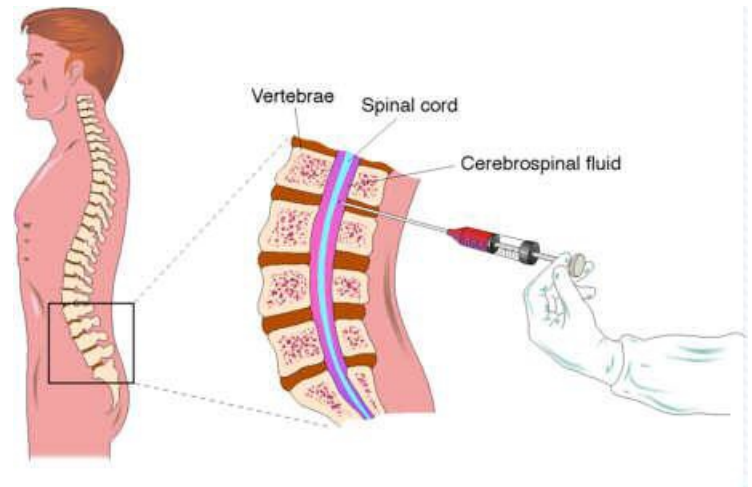
nUsing aseptic technique.

nCSF is separated into 3 aliquots:

- For chemistry & serology.
- For microbiology.
- For cell count.

nImmediate analysis.

nIt's a precious sample: Preserve any remaining sample.



## Contraindications for performing lumbar puncture:

- **Bleeding diathesis.**
- **Increased intracranial pressure.**
- **Infection at site of needle insertion.**

## Indications for laboratory investigation of CSF:

- CNS infection.
- Demyelinating diseases.
- CNS Malignancy.
- Hemorrhage in CNS.

CSF analysis is not used for diagnosis only for confirmation.

## Examination of CSF:

### 1- Physical examination:

nNormal CSF is:

- Colorless.
- Clear.
- Free of clots.
- Free of blood.

nIf CSF is cloudy (turbid) → perform microscopic examination:

- Is usually due to leucocytes. (cells)
- May be due to micro-organisms. (organisms)

## Blood & Hemoglobin pigments in CSF:

### Traumatic tap

nbright red color, (fresh).

nRBCS in decreasing number as the fluid is sampled.

Usually they are collecting the CSF in more than one tube, so we can compare the color in all the tubes.

### Subarachnoid hemorrhage (SAH)

→ Xanthochromia, (the color (hemoglobin breakdown pigments) = RBCs lysis & metabolism previously occurred (at least 2 hr. earlier).

We measure the xanthochromia by the spectrophotometer because we don't depend on what we see.

## When would Xanthochromia indicate hemorrhage?

nIf you exclude:

- Prior traumatic tap.
- Hyperbilirubinemia (bilirubin > 20 mg/dL).

## 2- Biochemical analysis of CSF

nTests of interest:

- Glucose
- Protein
- Total
- Specific:
  - Albumin
  - Immunoglobulin
  - Others (e.g. myelin basic protein; MBP)
- Lactate
- Glutamine (replaced by measuring plasma [ammonia])

The most reliable diagnostically & accessible analytically

not measured now, but when it measured and found high that's due to high anaerobic consumption of glucose due to genetic disease where the respiratory chain is not functioning well, so it even increase more than the blood.

Albumin only synthesized in the liver so to be in the CSF it should have crossed the BBB. But the globulins can be synthesized in the CSF.

# Glucose in CSF:

nGlucose enters CSF via facilitative transporter (GLUT).

nCSF [glucose] is ~ 2/3 that of plasma:

- 50 - 80 mg/dl

nA 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.

nMeasure CSF [Glucose]:

- Immediately. (because the glucose will be consumed by the cells so the result will be wrong).
- Or preserve the specimen with and antiglycolytic e.g. fluoride ion. (usually the tubs already has the fluoride).

## Abnormal CSF [Glucose]:

n↑ CSF [glucose]:

- Not clinically informative.
- Provides only confirmation of hyperglycemia.

n↓ CSF [glucose] (hypoglycorrachia):

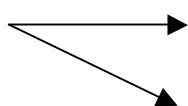
1. Disorder in carrier-mediated transport (GLUTs):  
e.g. TB meningitis, sarcoidosis.
2. Active metabolism of glucose by cells or organisms:  
e.g. acute purulent, amebic, & fungal meningitis.
3. Increased metabolism by the CNS:  
e.g. by CNS neoplasm.

nIn viral meningitis CSF [glucose] is usually normal.

### ■ 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 [total proteins]

↑ **CSF [total protein]:** (Dr.Reem said it's V.imp)

**\*\*\*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:
  - Bacterial or fungal infection
  - Cerebral hemorrhage
- ↑ production by CNS tissue in:
  - Multiple sclerosis (MS)
  - Subacute Sclerosing Panencephalitis (SSPE)
- Obstruction e.g. in: (Space occupying lesion causing a problem in CSF circulation)
  - Tumors
  - Abscess

## CSF Albumin

- Albumin is produced solely in the liver
- Its presence in CSF must occur through BBB
- The equation is not important

## CSF Immunoglobulin

- CSF IgG can arise:
  - from **plasma cells** within CSF
  - & from the **blood** through BBB
- ↑CSF [IgG] without concomitant ↑ in CSF [Alb] suggests local production of IgG:
  - multiple sclerosis (MS)
  - subacute sclerosing panencephalitis (SSPE)
  - The equation is not important

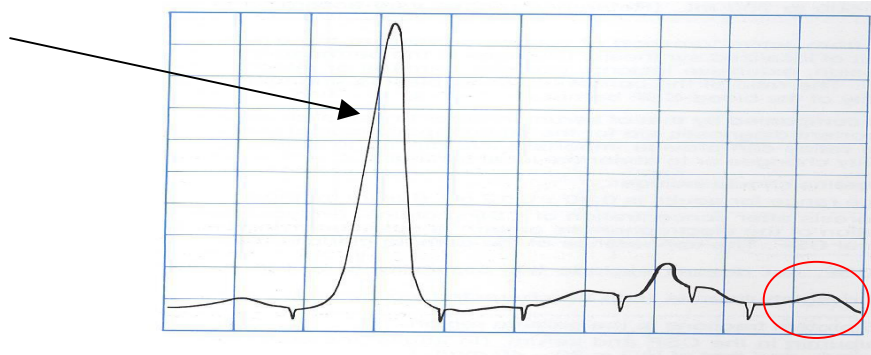
What to do if ↑ CSF [protein] was detected?

- Perform electrophoretic separation
- If multiple banding of the IgG band is detected (**oligoclonal bands**):
  - MS
  - SSPE
  - Inflammatory diseases

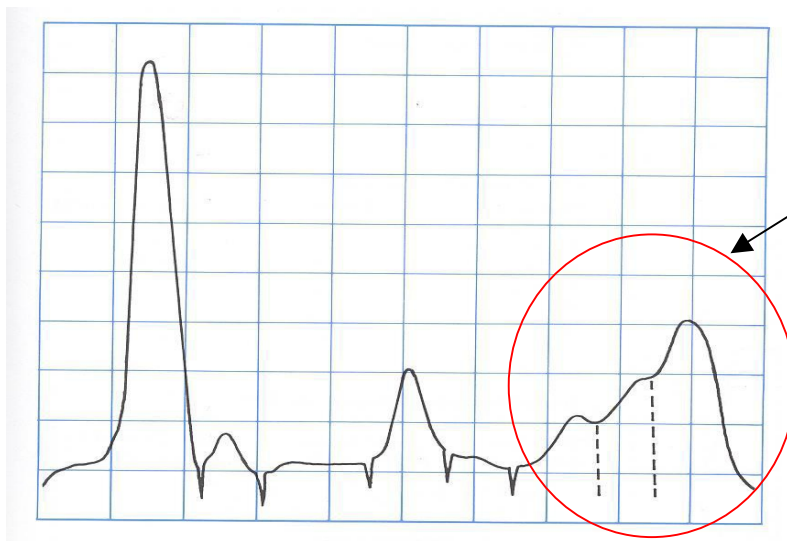
**Electrophoresis is the separation of proteins according to their electrical charge. Why? For diagnostic purposes, to know which protein is causing the problem**

## CSF Electrophoresis: Normal Pattern

Albumi



## CSF Electrophoresis: Oligoclonal Banding



Could be;

- MS
- SSPE
- Inflammatory disease

## Other Chemical Components of CSF

- CSF [Calcium], [Potassium] & [Phosphates] are lower than their levels in the blood
- CSF [Chloride] & [Magnesium] are higher than their levels in the blood
- Abnormal CSF [Chloride]
  - **marked** ↓↓ in acute bacterial meningitis
  - **slight** ↓ in viral meningitis & brain tumors

# Normal composition of CSF

(The doctor didn't say this was not important, but she ran through it very quickly and didn't explain much)

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

## Abnormal findings of CSF in some pathological conditions

(The doctor said the table is VERY IMPORTANT)

Parameter (reference range)	Condition		
	Bacterial Meningitis (pyogenic)	Tuberculous Meningitis	Viral Meningitis
Appearance	Often turbid	Often fibrin web	Usually clear
Predominant cell	Polymorphs	Mononuclear	Mononuclear
Cell count/mm <sup>3</sup>	90-1000+	10-1000	50-1000
Bacteria	In smear & culture	Often none in smear	None seen or cultured
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 ↓



## Otorrhea & Rhinorrhea

- **Otorrhea:** leakage of CSF from the ear
- **Rhinorrhea:** leakage of CSF into the nose
- **How to identify it as CSF?**
  - Measure  **$\beta$ -transferrin** (a protein unique to the CSF)

## TAKE HOME MESSAGE

- 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.

## Questions:

- Which one of these chemical components is lower in the blood than in the CSF???
  - a) Calcium
  - b) Potassium
  - c) Magnesium
  - d) Phosphates
- The appearance of CSF in Bacterial Meningitis is???
  - a) Turbid
  - b) Fibrin web
  - c) Clear
  - d) None of the above
- Xanthochromia indicates which of the following ?
  - a) a- subacute sclerosing panencephalitis (SSPE)
  - b) b- sarcoidosis
  - c) c- Subarachnoid hemorrhage
  - d) d-hyperglycemia

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Answers; C, A,C