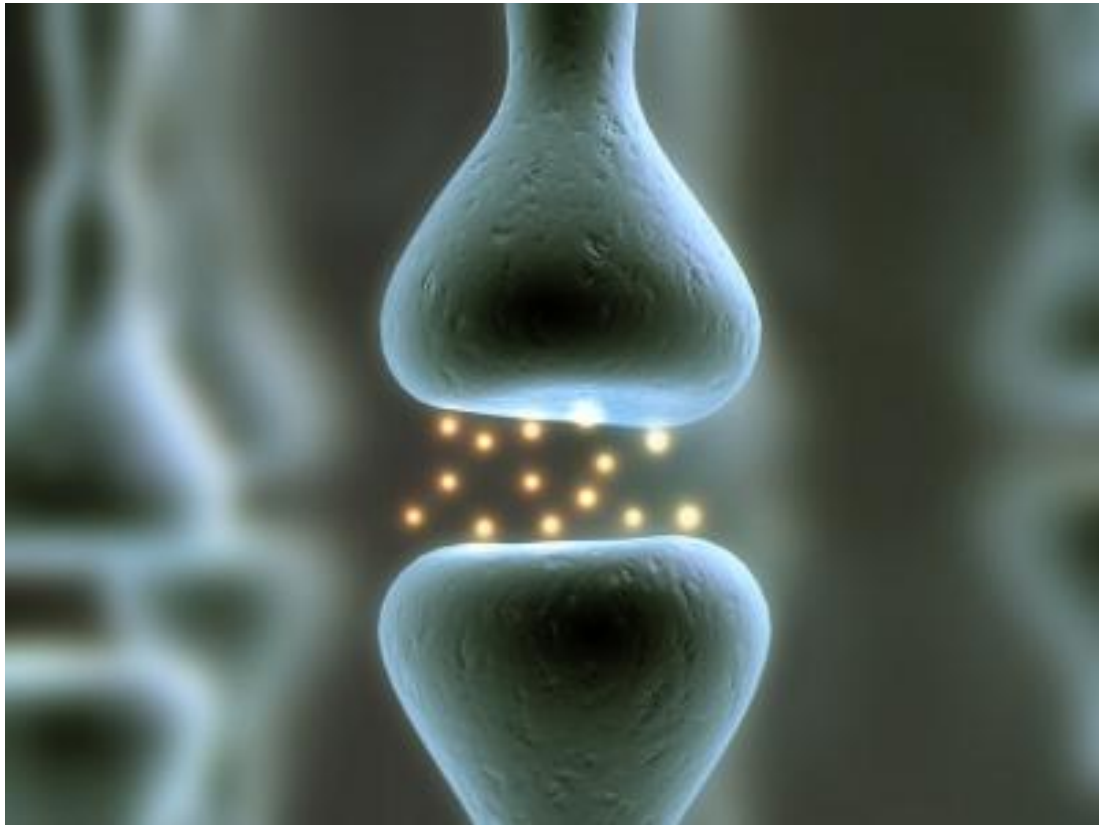


Biochemistry of the CNS



5th lecture:

Biochemical aspects of CSF

Done by:

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Introduction..

❑ CSF definition:

- The liquid surrounding the brain and spinal cord.
- It flows in subarachnoid area (the space between the Arachnoid & Pia-matter).

❑ Functions:

- Physical support & protection * **shock absorber**.
- Provides a **controlled chemical environment** → nutrient supply & waste removal.
 - ✓ What does controlled mean: (To supply nutrient's for the CNS, brain & spinal cord & excretion or disposal of the waste through the blood stream).
- Intra- & Extracerebral transport: Neuroendocrine function.

☆ 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.

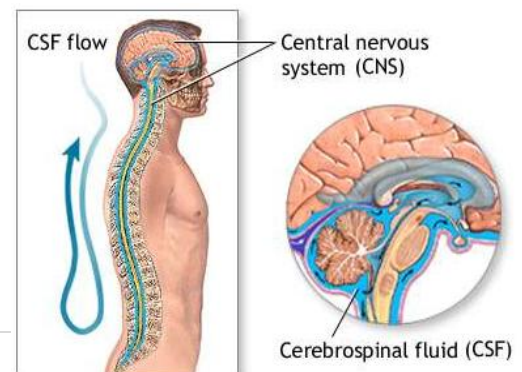
❑ Rate of formation: 500 ml/day. (daily + constant).

❑ Mechanism of formation:

1. Selective **ultra-filtration** of plasma = 80%, Ultra means more filtration by BBB.
2. **Active secretion** by epithelial membranes, found in the CNS itself =20%

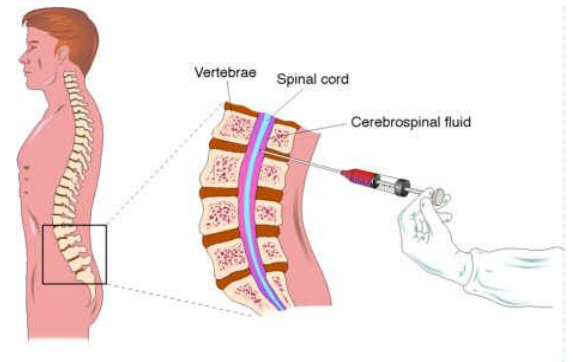
❑ Mechanism of excretion (absorption):

- 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.



Method of CSF Sampling: "Related to differential diagnosis"

- Traumatic tap or Iatrogenic (damage to blood vessel during specimen collection) → **Blood in CSF**. *the blood shouldn't be there. However, it doesn't affect our readings*



★ CSF Specimen Collection:

- Obtained by **lumbar puncture** (At the interspace L3-4, or lower).
- Using **Aseptic** technique: **So there will be No infection.**
- CSF is **separated** into 3 aliquots (means: sub tubes): **Molecular testing.**
 - For chemistry & serology.
 - For microbiology.
 - For cell count.
- **Immediate** analysis. (Analyze it quickly so we don't get false Hypoglycemia)
- It's a **precious** sample: Preserve any remaining sample.

Indications for laboratory investigation of CSF:

- 1) CNS **infection**.
- 2) **Demyelinating** diseases.
- 3) CNS **Malignancy**.
- 4) **Hemorrhage** in CNS.

Contraindications for performing lumbar puncture:

- 1) Bleeding diathesis (**bleeding tendency**).
- 2) Increased intracranial pressure.
- 3) Infection at site of needle insertion.

For your information

☆ Examination of CSF: 1- Physical examination

- ❑ **Normal CSF is:**
- 1) Colorless.
 - 2) Clear.
 - 3) Free of clots.
 - 4) Free of blood.

☆☆ ❑ **If CSF is cloudy (turbid) → perform microscopic examination:**

- 1) Is usually due to **Leucocytes**.
- 2) May be due to **Micro-organisms**.

☆ **Blood & Hemoglobin pigments in CSF:**

Traumatic tap

- → Bright red color.
- → RBCs in decreasing number as the fluid is sampled.

Subarachnoid hemorrhage (SAH)

- → **Xanthochromia:** (hemoglobin breakdown pigments) =
 - RBCs lysis
 - & Metabolism previously occurred (at least 2 hr earlier).

- ✓ Subarachnoid Hemorrhage:
It's originally from CSF, due to Disease.
- ✓ Xanthochromia: Means yellowing due to bilirubin breakdown which is a blood breakdown pigment.
- ✓ Traumatic: It's originally not from CSF, It's a Trauma done by human hand; the normal CSF is contaminated by skin blood vessels due to wrong tap.

When would Xanthochromia indicate hemorrhage?

❑ **If you exclude:**

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

☆ Examination of CSF: 2- Biochemical analysis of CSF:

- ❑ Tests of interest: **(Protein and glucose is the most important).**

1) **Glucose.**

2) **Protein:**

- Total.

- **Specific:**

1. **Albumin.**

2. **Immunoglobulin.**

3. Others (e.g. myelin basic protein; MBP).

3) **Lactate.**

4) **Glutamine** (replaced by measuring plasma [ammonia]).

**The most reliable
diagnostically & accessible
analytically**

☆ **Glucose in CSF:**

- ❑ Glucose enters CSF via facilitative **transporter (GLUT).**

- ❑ CSF [glucose]: **is (2/3 of the 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.

- ❑ Measure CSF [Glucose]:

- **Immediately.**

- Or preserve the specimen with and **Antiglycolytic** e.g. fluoride ion. ***We use Anti Glycoltic to prevent consumption of glucose***

☆ Abnormal CSF [Glucose]:

☐ ↑ CSF [glucose]:

- Not clinically informative
- Provides only confirmation of hyperglycemia

Just know if the glucose high or low without the mechanism.

☐ ↓CSF [glucose] (hypoglycorrhachia):

- Disorder in carrier-mediated transport:
e.g. TB meningitis, sarcoidosis.
- Active metabolism of glucose by cells or organisms: (consumption or eating the glucose)
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 or slightly less.

Protein in CSF:

☐ Proteins, **mostly albumin** (Because of its low molecular weight), are found in the CSF (0.15-0.45 g/L).

☐ Source of CSF proteins:

- 80% from plasma by ultra-filtration.
- 20% from intrathecal (within the brain) synthesis.

Just know that 80% from plasma, and 20% from CNS.

☆ Abnormal CSF [total proteins]:

☐ ↑ CSF [total protein]: *4 main causes*

- **Must be compared to the serum [protein].**
- Useful nonspecific indicator of pathological states:
 - ☐ **Lysis of contaminant blood** (lysis of the blood that got it due to 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: No need to memorize the equation:

$$\frac{\text{CSF Albumin (mg/dL)}}{\text{Serum Albumin (g/dL)}} = \text{CSF serum albumin index:}$$

If < 9 = **intact BBB**

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

CSF Immunoglobulin: No need to memorize the equation:

$$\frac{\text{CSF IgG/Serum IgG}}{\text{CSF serum Albumin index}} = \text{CSF IgG index:}$$

Normally: < 0.7

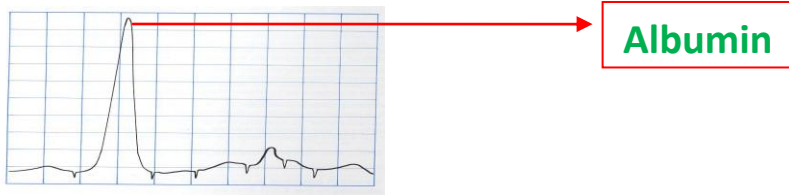
- ❑ CSF IgG can arise:
 1. From **plasma cells** within CSF
 2. From the **blood** through BBB.

- ❑ \uparrow CSF [IgG] without concomitant \uparrow in CSF [Alb] suggests local production of IgG : (If the IgG is High in the CSF and in the Blood Normal we will have):
 1. Multiple Sclerosis (MS).
 2. Subacute Sclerosing Panencephalitis (SPEE).

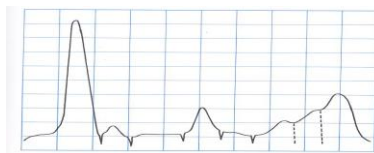
What to do if \uparrow CSF [protein] was detected?

- ❑ Perform electrophoretic separation.
- ❑ If multiple banding of the IgG band is detected (**oligoclonal bands**):
 - Multiple sclerosis “MS”.
 - Subacute Sclerosing Panencephalitis “SSPE”.
 - Inflammatory diseases.

CSF Electrophoresis: Normal Pattern: * For Your Information*



CSF Electrophoresis: Oligoclonal Banding:



★ 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 $\downarrow\downarrow$ in acute bacterial meningitis.
 - Slight \downarrow in viral meningitis & brain tumors.

Normal composition of CSF: *for your information*

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: *don't

memorize any numbers just know if it's high or low*

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 ³	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: (Extra)

❑ **Otorrhea:** Leakage of CSF from **the ear** (due to fracture of base of the skull).

❑ **Rhinorrhea:**

- Leakage of CSF into **the nose**.
- How to identify it as CSF?
- Measure **β -transferrin** (a protein unique to the CSF).

Q. Glucose is less in our Plasma or in our CSF??

Ans. In our CSF

Take home message + Summary:

- ✓ CSF is formed in the choroid plexuses.
- ✓ Usually CSF volume is constant because the Formation = the Excretion.
- ✓ Formation occurs by two sides:
 - 1) Ultra Filtration from plasma = 80%.
 - 2) Active secretion by Epithelial membrane = 20%.
- ✓ It's excreted by Absorption through blood stream.
- ✓ The CSF specimen needs to be Aseptic, Separated, immediate, precious.
- ✓ The physical appearance of CSF is colorless, clear and free of clots or blood.
- ✓ If the CSF is turbid it's due to Leucocytes and Micro-organisms.
- ✓ Blood traumatic tap originally not from the CSF, but the Subarachnoid Hemorrhage it's originally from the CSF.
- ✓ Most important in the Biochemical analysis is Protein & Glucose.
- ✓ For specific Proteins is Albumin & for the Immunoglobulin is IgG.
- ✓ Glucose: ↓ for Bacterial, T.B & for Viral is Normal.
- ✓ Protein: ↑ for Bacterial, Fungal & T.B.. & for Viral is Normal.
- ✓ If the Immunoglobulin IgG is High in the CSF and in the Blood Normal we will have:
 - *Multiple Sclerosis (MS).
 - *Subacute Sclerosing Panencephalitis (SPEE).
- ✓ CSF is essential for the physical protection of the CNS.
- ✓ The physical & chemical analysis of CSF is essential for diagnosis of certain diseases
- ✓ Abnormal CSF (Chloride):
 - *Marked ↓↓ in acute bacterial meningitis.
 - *Slight ↓ in viral meningitis & brain tumors.