BIOCHEMISTRY OF CSF

Color index:

- Important
- Extra explanation

"BE THE CHANGE THAT YOU WISH TO SEE IN THE WORLD"

Check this link before studying to know if there is any corrections in the teamwork

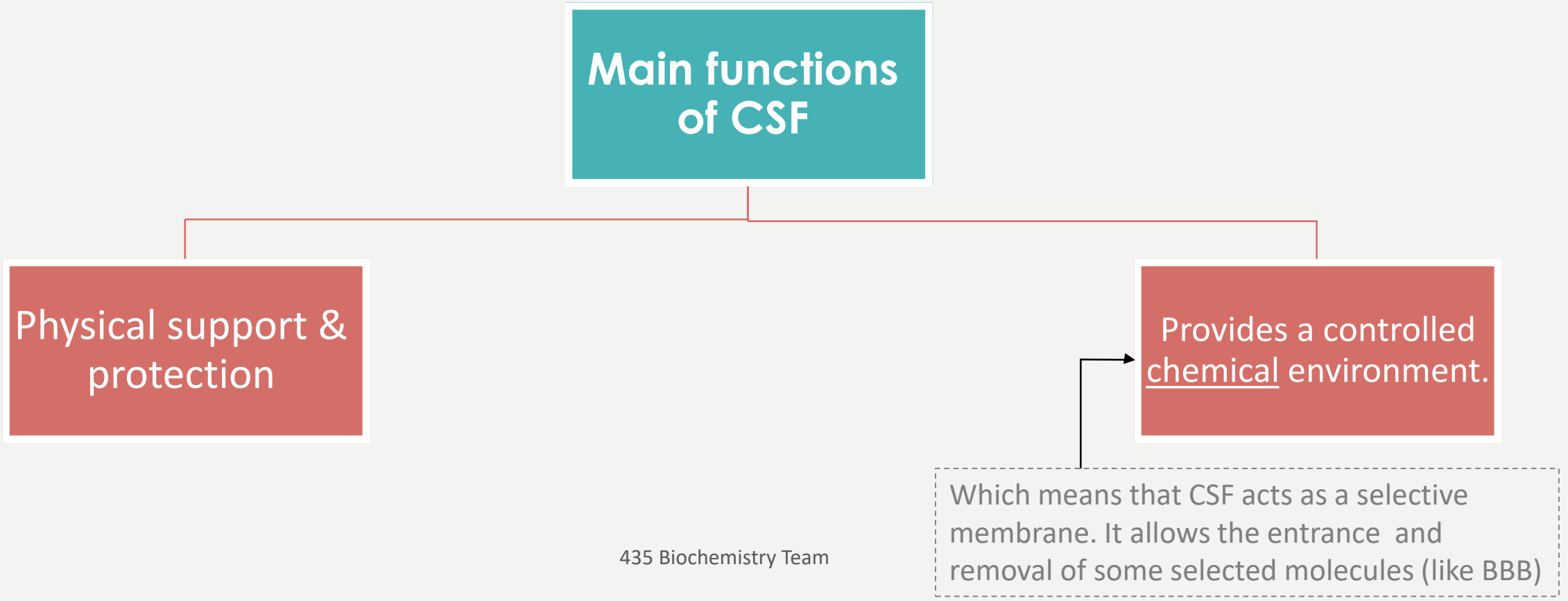
OBJECTIVES:

- 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 proteins.
- To study the composition of normal CSF and discuss the abnormal findings in pathological conditions.
- To define otorrhea and rhinorrhea.

CSF : DEFINITION & FUNCTION

What is CSF?

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



CSF: Formation & Circulation

Where is it formed?

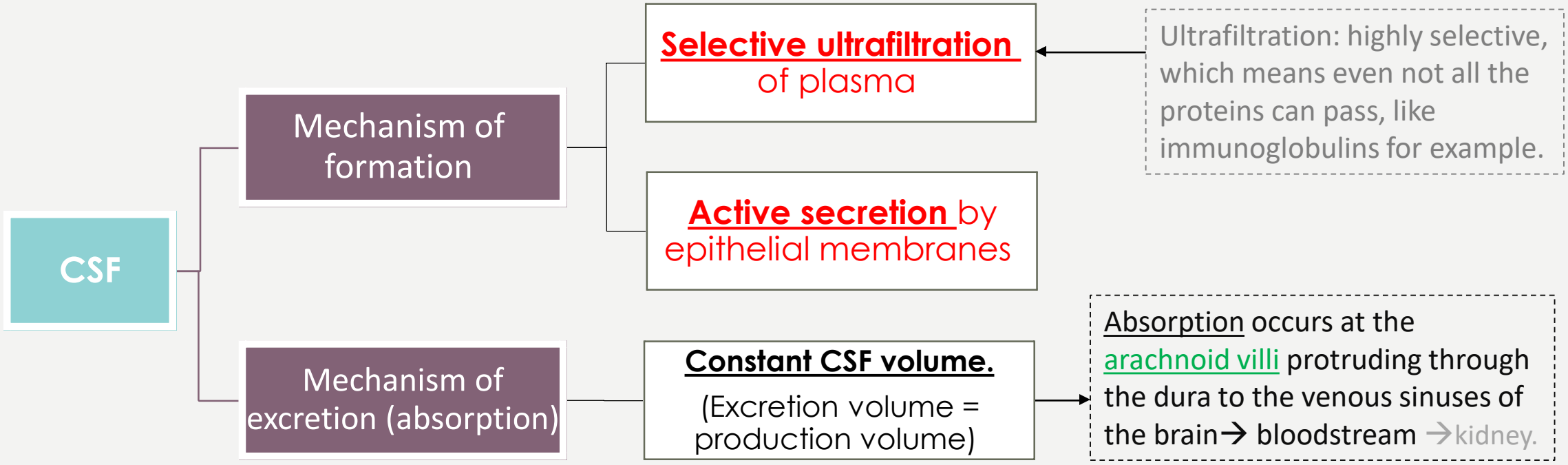
CSF is formed at the choroid plexuses & by the cells lining the ventricles.

- Normal blood brain barrier (BBB) is important for the normal chemistry results of CSF.

In other words: BBB maintains the chemistry results by allowing the nutrients to pass from the blood stream to CSF, and removing the wastes from CSF to the blood stream.

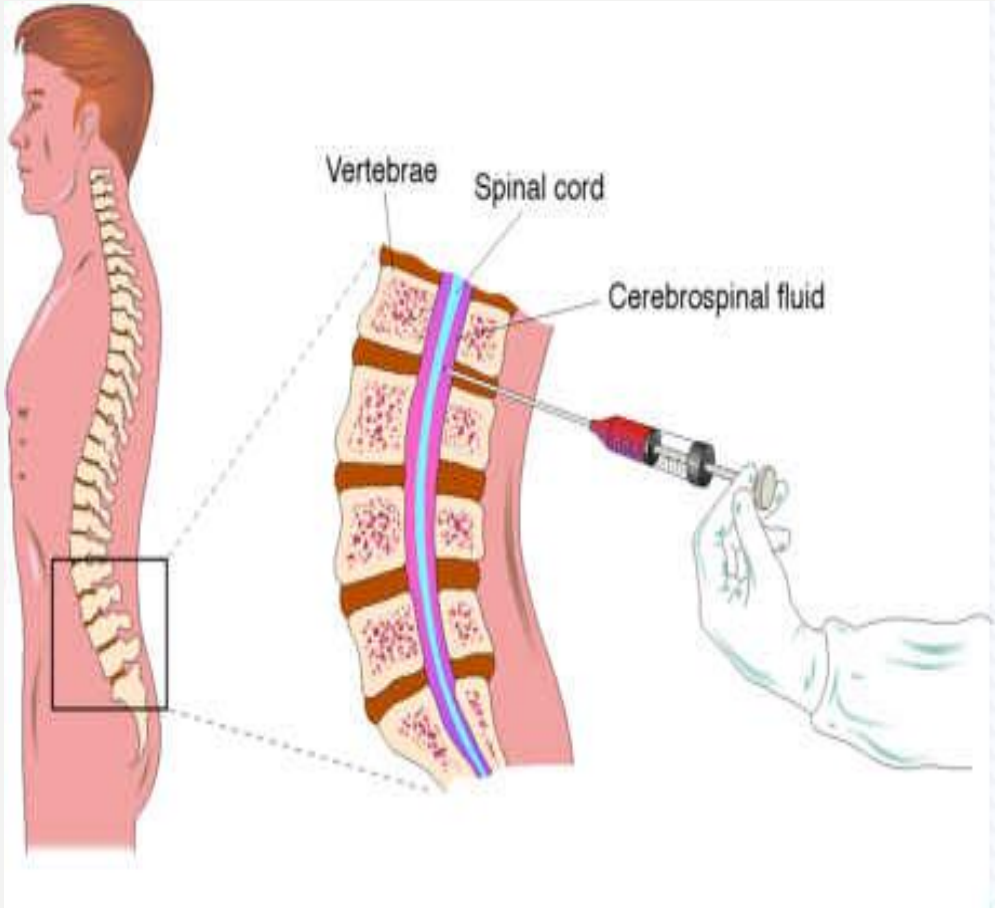
The rate of formation of CSF is :

500 ml/day.



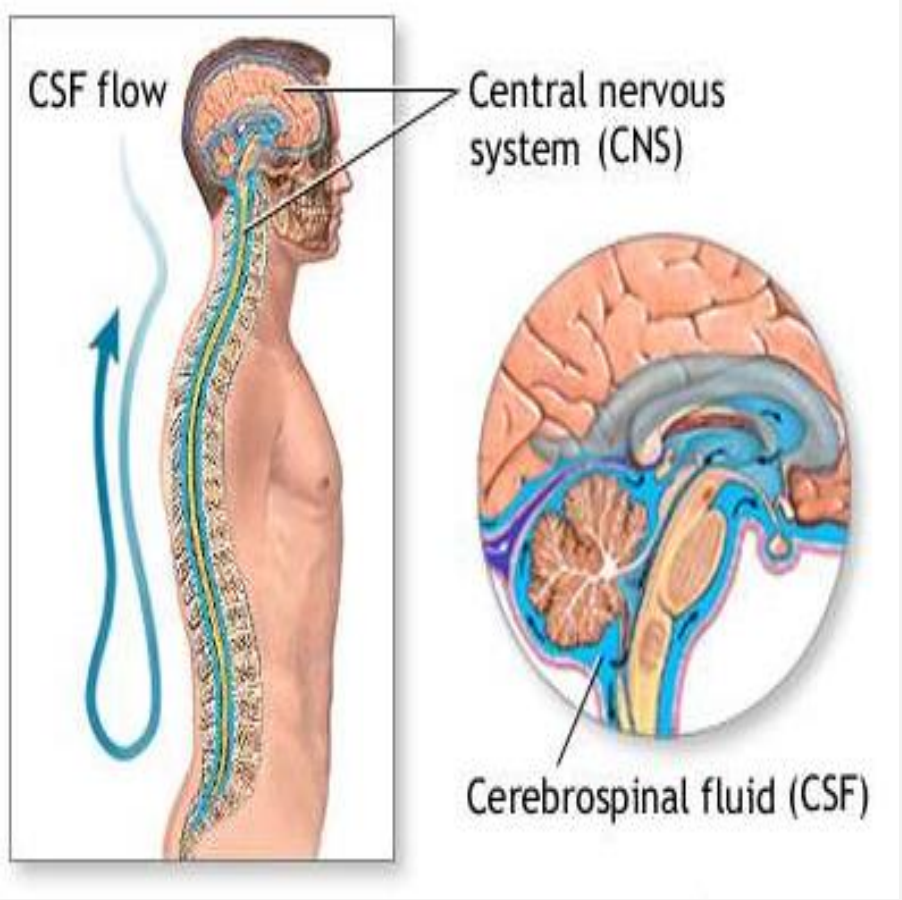
sampling & Circulation

Method of CSF Sampling



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

CSF Circulation



CSF Specimen Collection

By which method we obtain the specimen?

It's Obtained by lumbar puncture using aseptic technique (At the interspace **L3-4**, or lower. Why? To not damage the spinal cord which ends at L2).

CSF is separated into 3 aliquots: (means: 3 different tubes. Each tube got a different test) for chemistry, serology and microbiology.

The sample needs an Immediate analysis, why?

- Because It's a **precious sample**: so we have to Preserve any remaining sample.
- Because the technique we used may be not aseptic and there is a bacteria that may consume the sugar - for example - in the sample, so the sample won't be normal.
- They test CSF in both biochemistry and microbiology labs and if the results are not matched they have to repeat them.

Physical examination: normal CSF is: -similar to water

Colorless	Clear	Free of blood	Free of clots

CSF Specimen Collection

Indications for laboratory investigation of CSF

When do we have to an investigation of CSF? When we have one of these 4 conditions.

- **CNS infection**
  - -Ex: Meningitis
- **Demyelinating diseases**
- **CNS Malignancy**
- **Hemorrhage in CNS**
  - -Ex: due to Trauma

Contraindications for performing lumbar puncture (IMP.)

We don't perform lumbar puncture in these 3 conditions

Increased susceptibility to bleed, mostly due to hypocoagulability

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

Physical examination of CSF

If CSF was cloudy (turbid) (not clear), we then should perform microscopic examination to know the cause of this turbidity:
It's usually due to the presence of leucocytes, but sometimes it may be due to the presence of micro-organisms.

Blood & Hemoglobin pigments in CSF

It happens due to a damage to blood vessels occurs by mistake in taking a CSF sample (blood found in CSF).

(hemoglobin breakdown pigments) = RBCs lysis & metabolism previously occurred (at least 2 hours earlier)

Traumatic tap

Because there's a little amount of RBCs in CSF.

- bright red color
- RBCS in decreasing number as the fluid is sampled

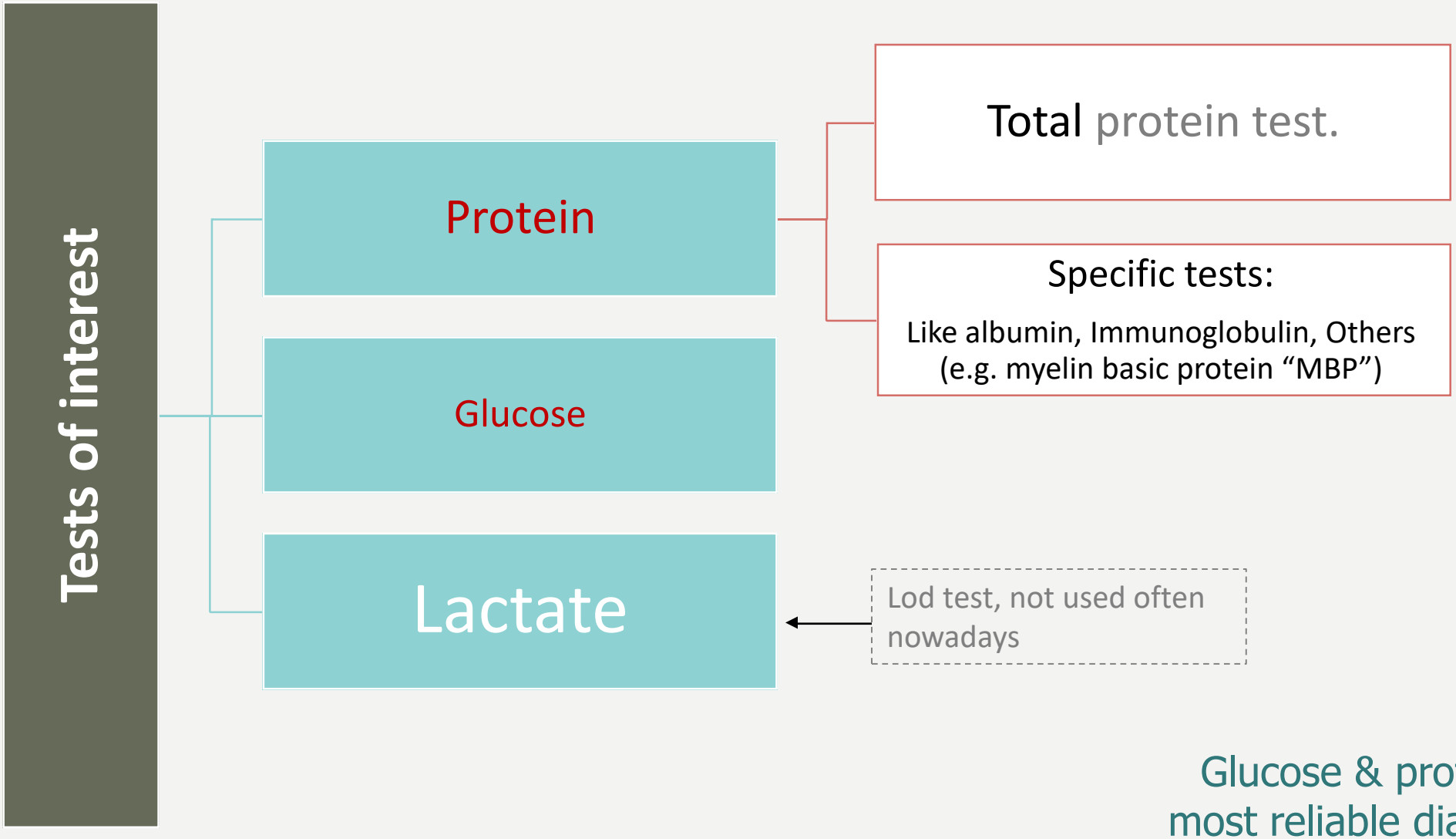
Subarachnoid hemorrhage (SAH)

"Xanthu" means yellow, this term means the CSF turned to yellow.

- Xanthochromia

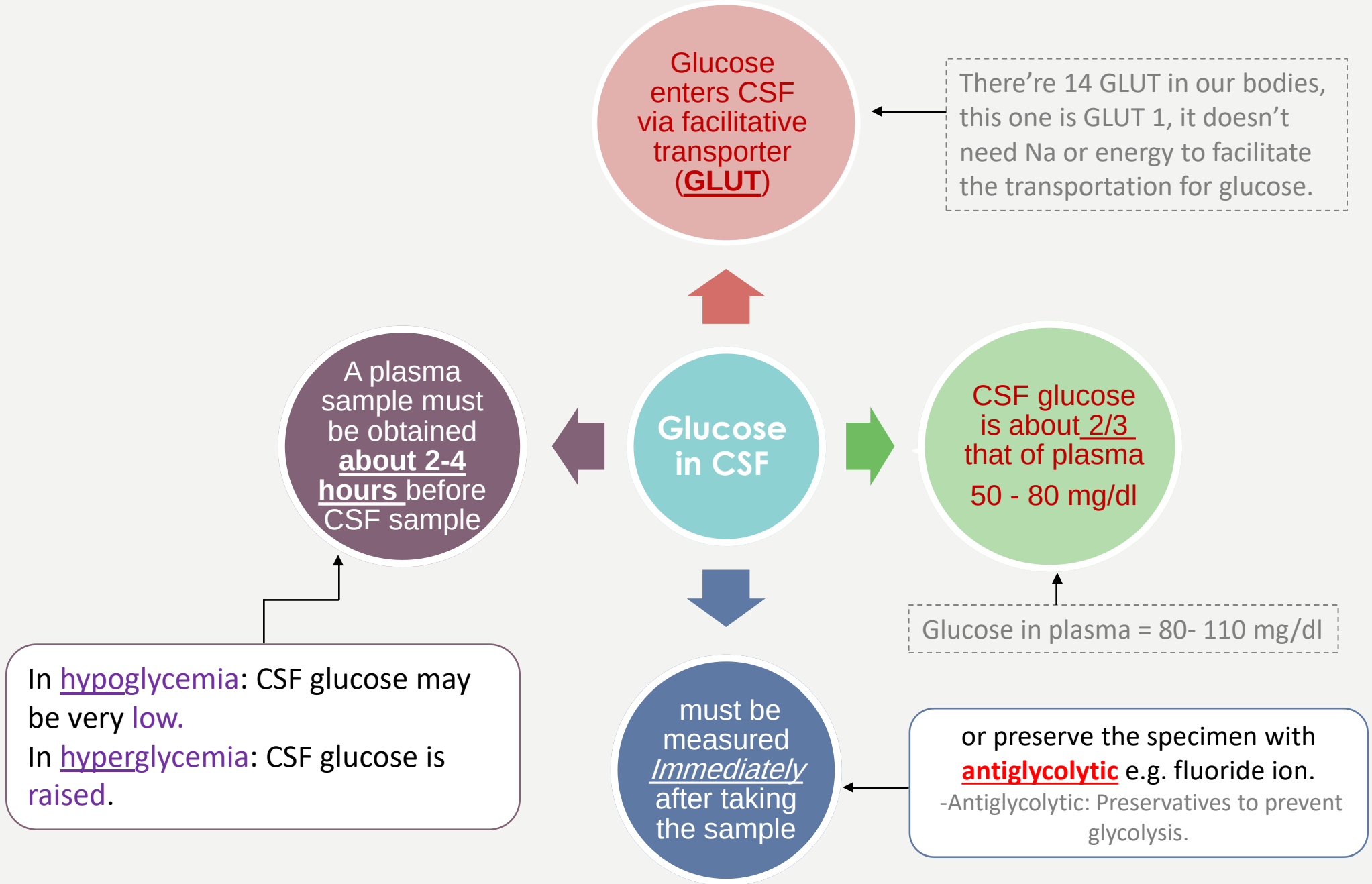
When would Xanthochromia indicate hemorrhage?
It will if we exclude:
1-Prior traumatic tap
2- Hyperbilirubinemia (bilirubin > 20 mg/dL)

Biochemical analysis of CSF



Glucose & protein are the most reliable diagnostically & accessible analytically

Glucose in CSF



Abnormal glucose in CSF

Abnormal Glucose in CSF

Elevated CSF glucose

- Not clinically informative.

- Provides only confirmation of hyperglycemia.

So basically, ↑ glucose in CSF means the patient has elevated glucose level in his blood (due to diabetes usually), but it doesn't mean that he has a problem in his CSF.

In viral meningitis, CSF glucose is usually normal or may be decreased due to hypoglycemia.

Decreased CSF glucose (hypoglycorrhachia)

1- Disorder in carrier-mediated transport.
e.g. TB meningitis, sarcoidosis.

2- Active metabolism of glucose by cells or organisms (like bacteria):
e.g. acute purulent, amebic, & fungal meningitis.
So: meningitis = ↓ glucose in CSF except **viral meningitis** (may be normal or ↓).

3- Increased metabolism by the CNS.
e.g. by CNS neoplasm.

Proteins In CSF

Normally : 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.

  (80% is albumen, 20% is immunoglobulin).

Abnormal CSF total proteins:

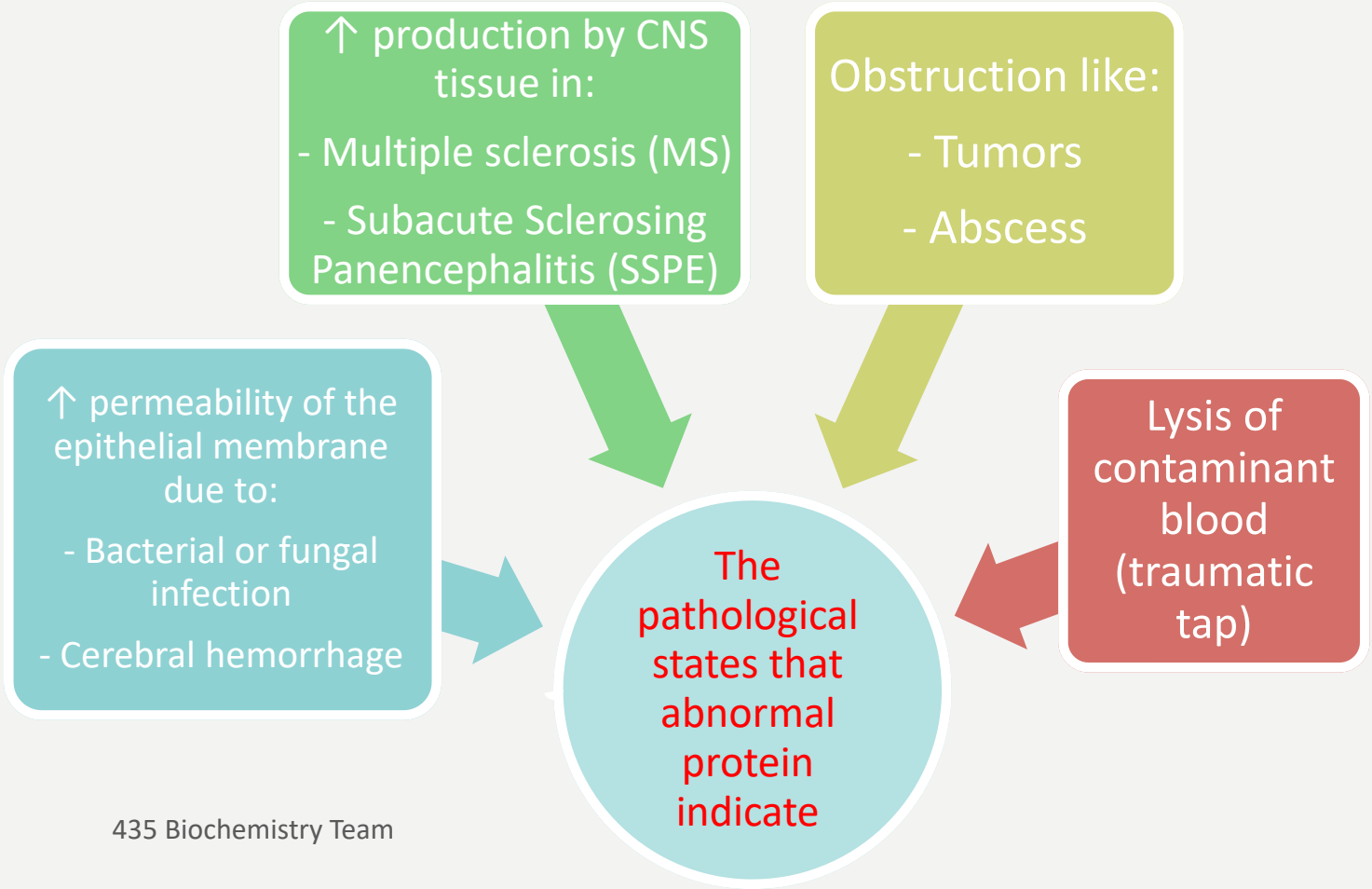
↑ CSF total protein:

1. Must be compared to the serum protein.

2. Useful nonspecific indicator of pathological states (just tells you that there is a problem).

It's nonspecific, so we need to use another method with it.

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



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, e.g. :

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

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

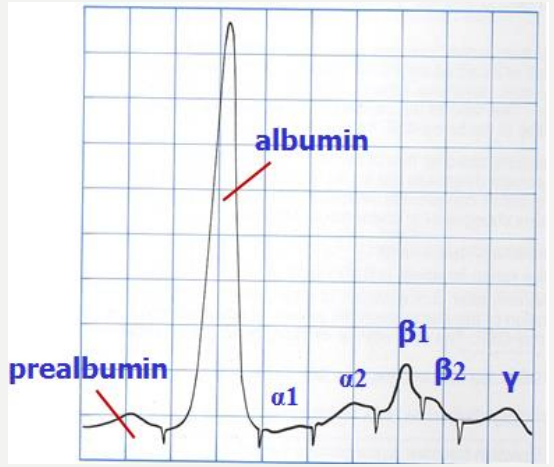
1. Perform electrophoretic separation.
2. If multiple banding (oligoclonal bands) of the γ-globulin is detected.

the following differential diagnosis is suspected:

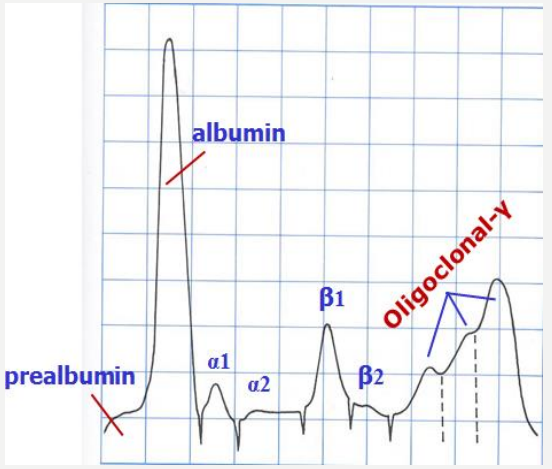
- MS
- SSPE
- inflammatory diseases

CSF Electrophoresis

Normal Pattern



Oligoclonal Banding



COMPOSITION OF CSF

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

Appearance	Clear ,Colorless
Lymphocytes	Less 5 mm3
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

No need to memorize them. References rates will be given in the exam.

Abnormal Findings Of CSF In Some Pathological Conditions (IMP.)

Parameter	Condition		
	Bacterial Meningitis (pyogenic)	Tuberculous Meningitis	Viral Meningitis
Appearance	Often turbid	Often fibrin web	Usually clear
Predominant cell	Polymorphs	Mononuclear	Mononuclear
Cell count/mm3	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 (↑ ↑)	less than 1 (normal)
Glucose (2.8-4.2 mmol/L)	(↓↓) <1/2	(↓↓) <1/2	normal or slightly decreased.
Chlorides (115 - 130 mmol/l)	↓↓	↓↓	or normal ↓

pathological condition related to CSF :

- **Otorrhea**: leakage of CSF from the ear.
- **Rhinorrhea**: leakage of CSF into the nose.

The doctors said this table is very important and we should memorize it !

MCQs

1-Where does the CSF form:

A. Subarachnoid space
B. Choroid plexuses
C. Dura mater
D. 4th ventricle

2-Which protein is mostly normally found in CSF:

A. Albumin
B. Hemoglobin
C. Glucose
D. Tau

3-Where does the albumin produced:

A. Kidney
B. Pancreas
C. Spleen
D. Liver

4-The appearance of CSF in bacterial meningitis is:

A. Turbid
B. Clear
C. Fibrin web
D. None of them

5-CSF sampling is contraindicated in which one of the following:

A. Vertigo
B. CSF infections
C. Increased intracranial pressure
D. Immunocompromised patients

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

MCQs

6-CSF (glucose) in a patient with viral meningitis is expected to be:

A. Very high
B. Normal
C. Very low
D. Depend on the case

7-In bacterial meningitis glucose CSF level shows:

A. High
B. Normal
C. Depend on the case
D. Low

8-Which one of the following components is present in higher levels in CSF than in the blood:

A. Chloride
B. Calcium
C. Zinc
D. Phosphate

9-The rate of formation of CSF is:

A. 400 ml /day
B. 500 ml /day
C. 450 ml /day
D. 300 ml /day

10-Otorrhea is a condition in which the CSF leaks from:

A. Nose
B. Eye
C. Ear
D. Mouth

6-B
7-D
8-A
9-B
10-C

SAQs

❖ **Q1: At which level the CSF specimen collection should be obtained ?**

A: At the interspace between L3 & L4 or lower, by lumbar puncture.

❖ **Q2: What are the sources of CSF proteins ?**

A: 80% from plasma by ultrafiltration & 20% from intrathecal synthesis.

❖ **Q3: Mention four indications for laboratory investigation of CSF.**

A: 1- CNS infection. 2- demyelinating diseases. 3- CNS malignancy. 4- hemorrhage in CNS.

❖ **Q4: Mention three contraindications for performing lumbar puncture.**

A: 1- Bleeding diathesis. 2- Increase intracranial pressure. 3- Infection at site of needle insertion.

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