



Important Doctors slides
Extra Information **Doctors notes**



Biochemistry

Cerebrospinal fluid

We can't direct the wind, but we can adjust the sails

[Editing file](#)

OBJECTIVES

By the end of this lecture, the students should be able to:

- To identify the CSF functions, formation and circulation.
- To recognize the method of CSF sampling, and the procedure for specimen collection, and processing
- To identify the indications and contraindications of lumbar puncture and laboratory investigation of CSF
- To recognize and explain the normal and abnormal findings of physical and biochemical examination of CSF (with special emphasis on the glucose, protein, electrolytes and cellular content of CSF)
- To interpret CSF electrophoresis pattern
- To define expressions describing abnormal locations of CSF as otorrhea and rhinorrhea

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- ✓ Key principles:
 - ✓ CSF overview Functions, circulation ... etc.
 - ✓ CSF investigations and specimen collection
 - ✓ Types and components of CSF examination
 - ✓ Electrophoresis
 - ✓ Abnormal pathological conditions effect

CSF Definition & Functions:

CSF definition :

The liquid surrounding the brain and spinal cord, that flows in subarachnoid space (the area between arachnoid & pia matter)

Main Functions:

Provides a controlled chemical environment → nutrient supply & waste removal

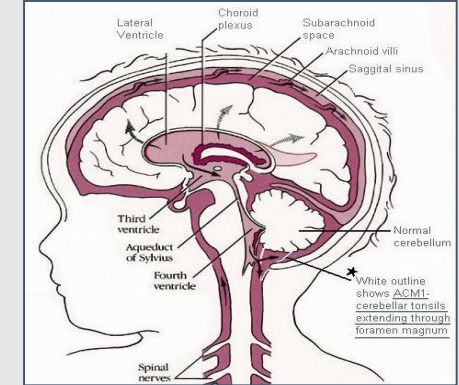
Physical support & protection

CSF also has a certain transportation functions

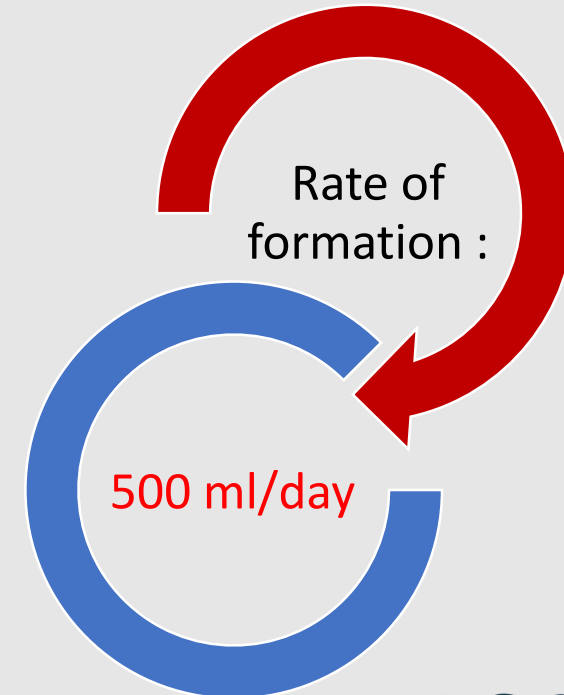


CSF Formation & Circulation:

- 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

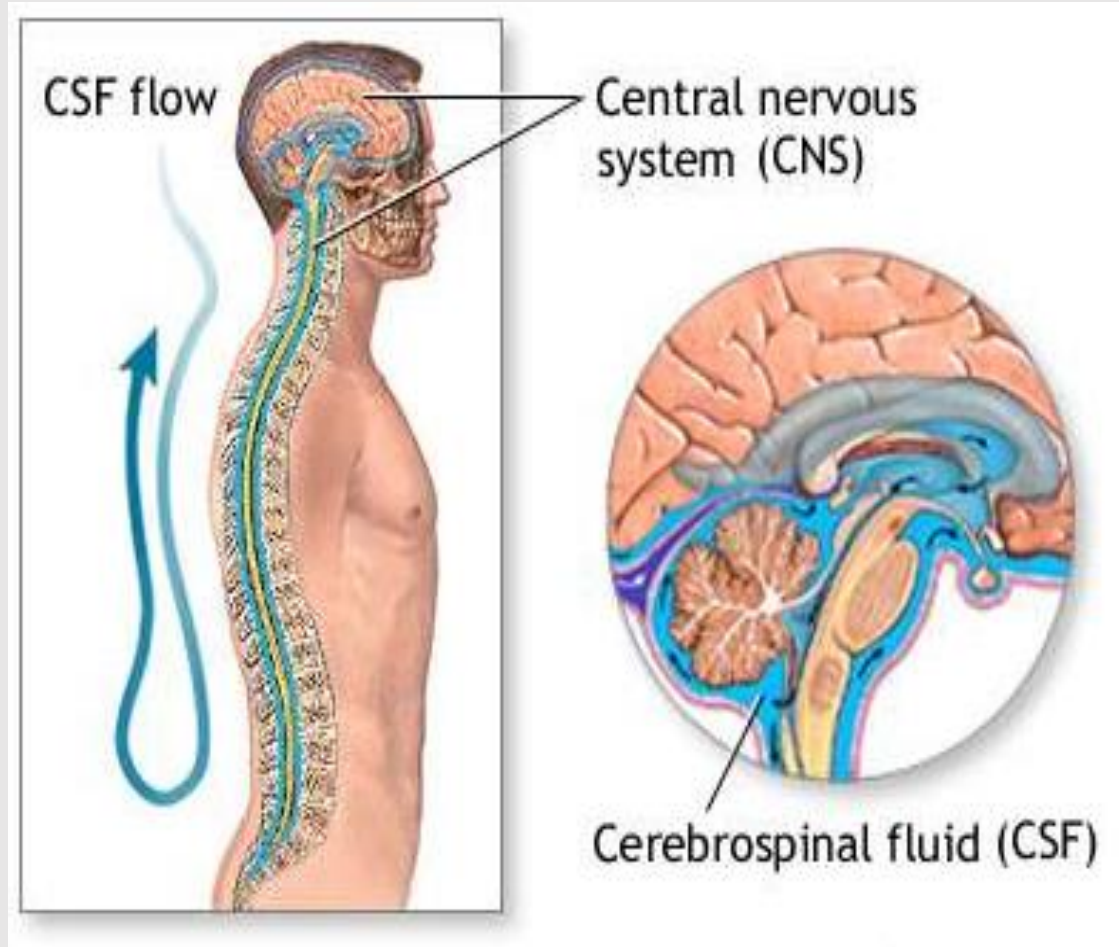


The rule of equilibrium is production = excretion, but in CSF our absorption is instead excretion



CSF Formation & Circulation:

CSF Circulation:



CSF Formation & Circulation:

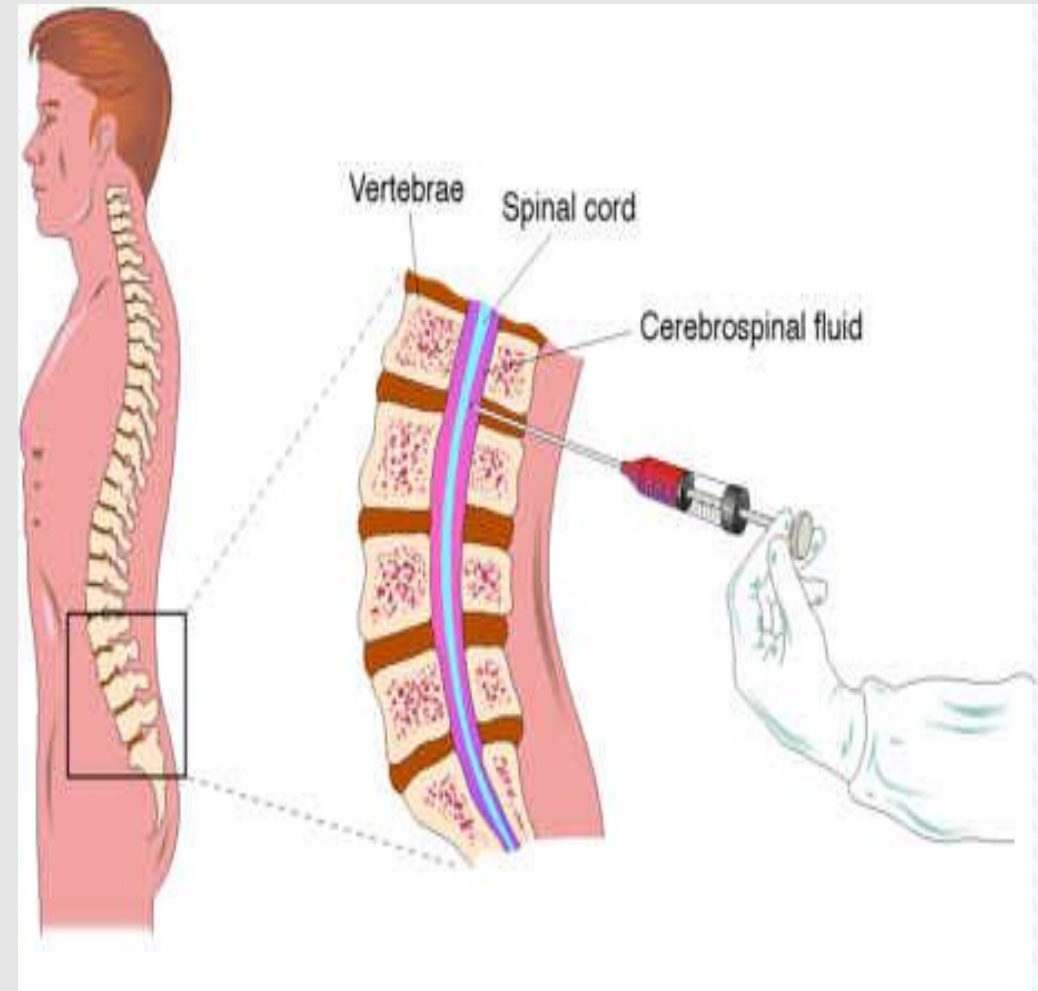
Method of CSF Sampling:

The person taking the CSF sample should be professional to prevent traumatic tap (rupturing the blood vessels), because CSF is considered as a precious sample since its difficult to obtain.

We always start with the non invasive procedures like taking blood and urine specimens, and then if we needed CSF we may take it.

To differentiate between traumatic tap and hemorrhage:

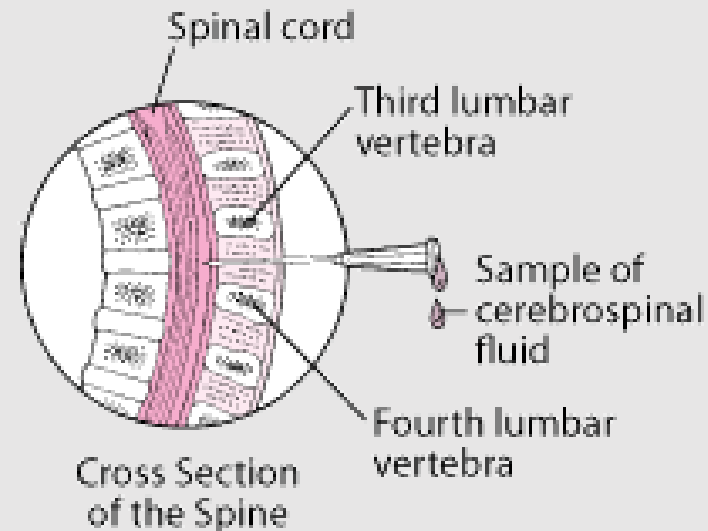
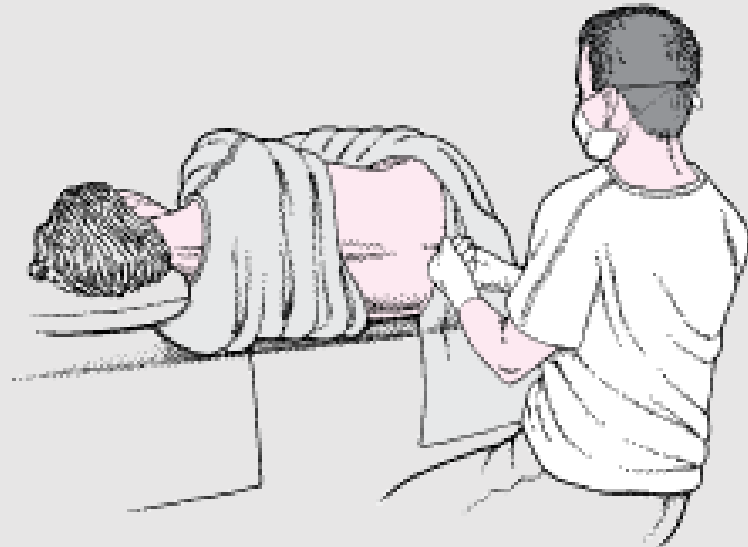
1\ the blood is bright. 2\ the more CSF we withdrawal the lighter the blood becomes because it's a new rupture made to the blood vessel from the needle.



Sample is taken by a needle from between the lumbar vertebrae "L3-L4"

CSF Specimen Collection:

- Obtained by **lumbar puncture** (At the interspace L3-4, or lower)
- Using aseptic technique
 - “ Because CSF has low defense against microbes ”
- CSF is **separated** into 2 aliquots:
 1. for chemistry & serology
 2. for microbiology “ and hematology ”
- **Immediate** analysis
- It's a **precious** sample: Preserve any remaining sample



Extra

CSF investigation

Indications for laboratory investigation of CSF:

CNS infection

Demyelinating diseases
e.g. MS

CNS Malignancy

Hemorrhage

Contraindications for performing lumbar puncture:

Bleeding diathesis

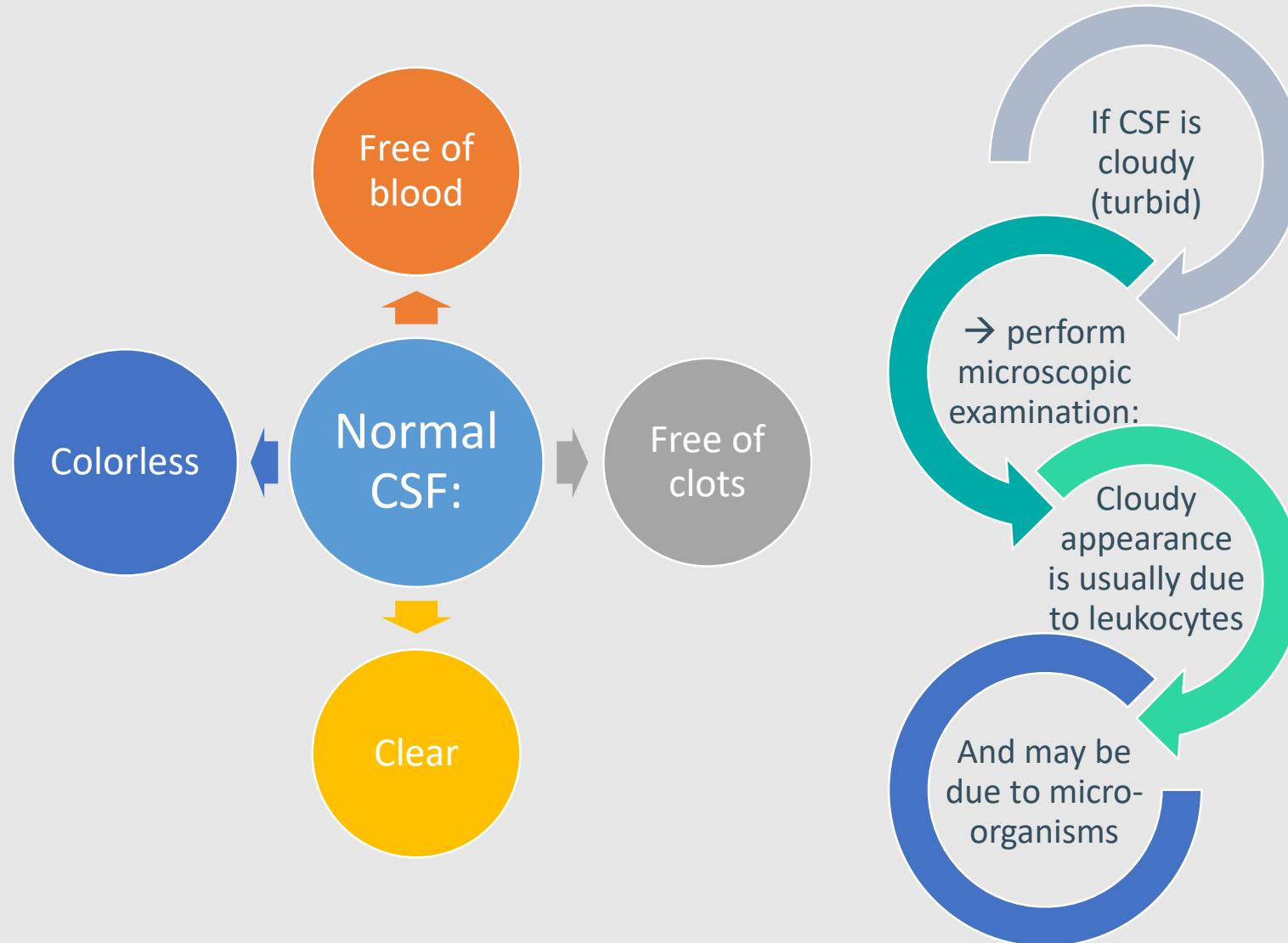
Increased intracranial pressure

Infection at site of needle insertion

If the patient has a skin infection at the normal obtaining sites of lumbar puncture what to do ?
If the condition is so serious and can not wait then an expert should perform the LP even at the levels of spinal cord " above L3 " and it has a specific technique ..
Otherwise they have to wait until the infection is treated "

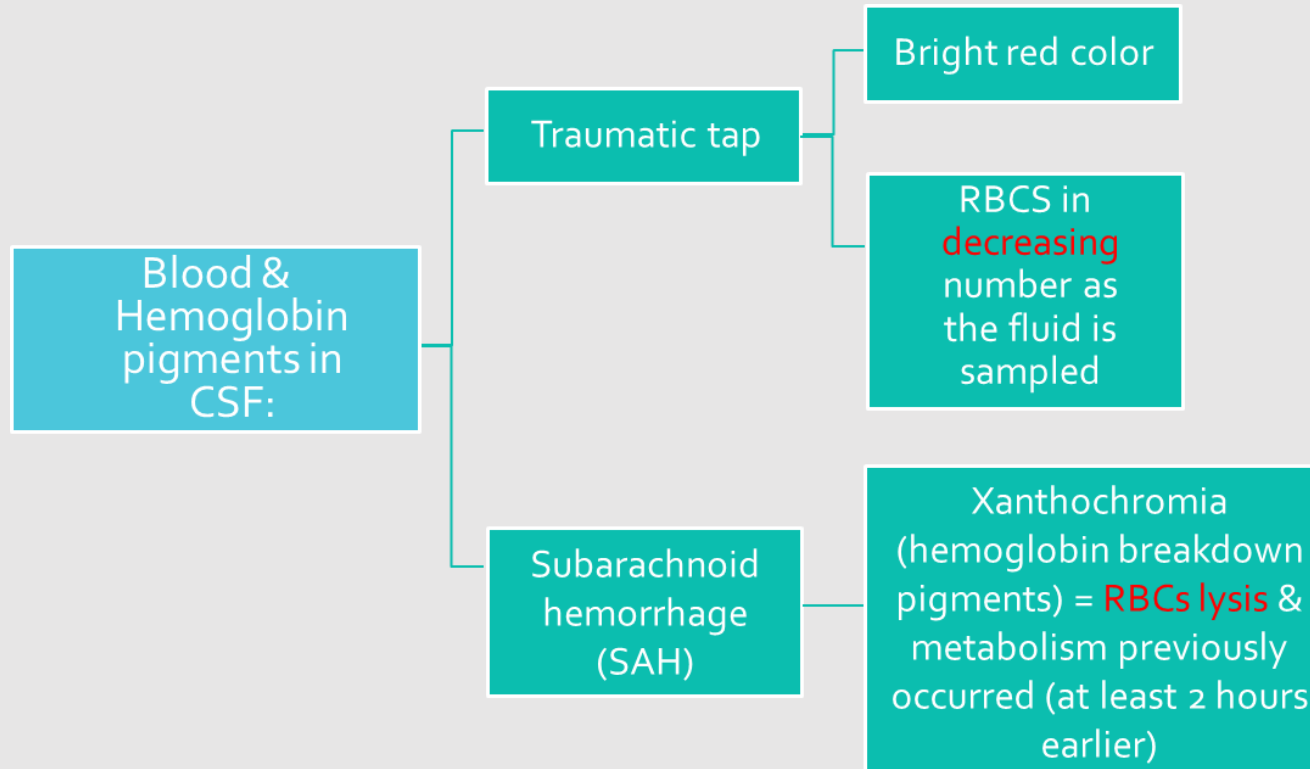
Examination of CSF

1- Physical examination



Blood & Hemoglobin pigments in CSF:

" IMPORTANT SLIDE "



It's important to differentiate between the traumatic and SAH in the blood.

When would Xanthochromia indicate hemorrhage?
If you exclude:

Prior traumatic tap

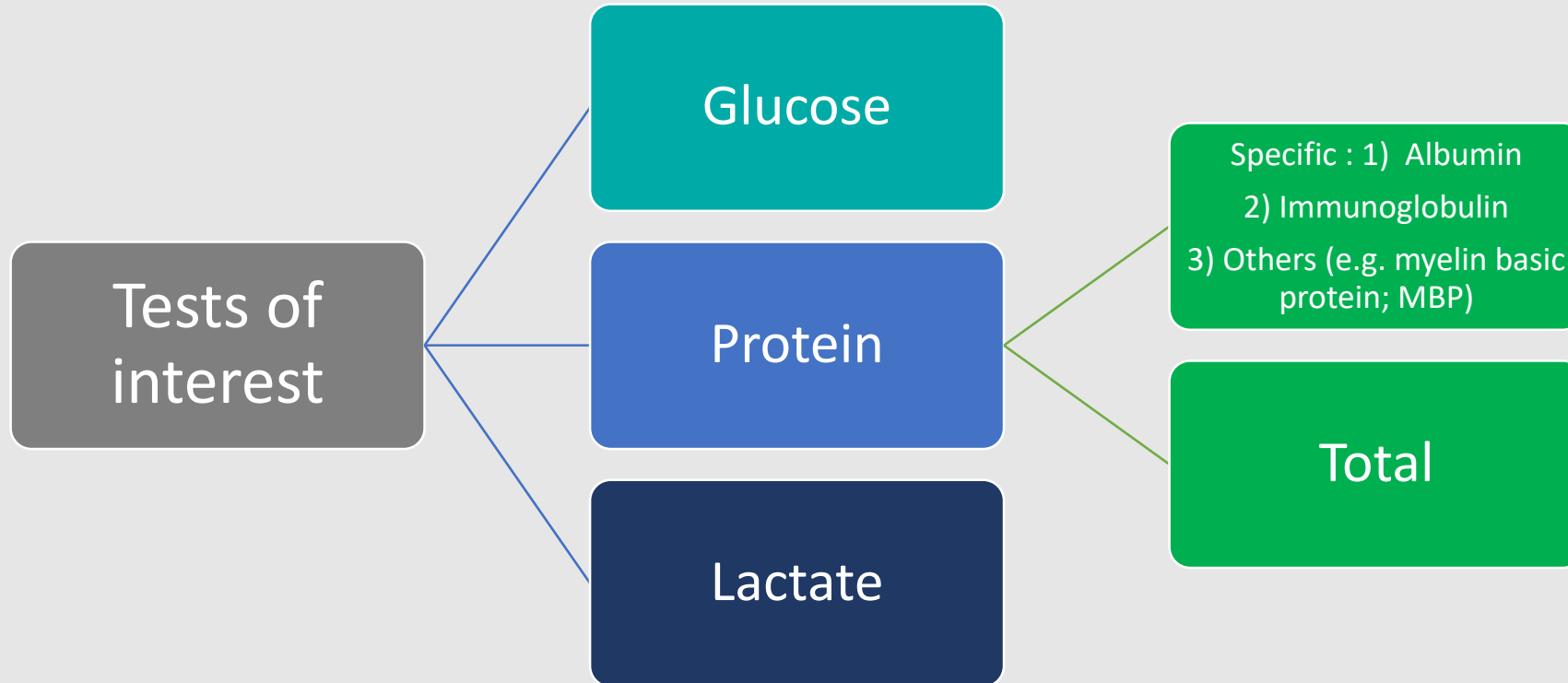
Hyperbilirubinemia (*bilirubin > 20 mg/dL*)

Xantho : لون تغير Chromia : لون
✓ Hemoglobin has heme (which has a ring that would break down giving us the changing color from red to green) -> like what happens in bruising.
✓ Also its not bright, and is color changing

A "traumatic tap" occurs if the needle inadvertently has entered an epidural vein during insertion. A yellowish tinge to the CSF fluid is called xanthochromia. Xanthochromia is usually caused by red blood cell degeneration in the CSF as would be seen in subarachnoid hemorrhage (SAH).

Examination of CSF

2- Biochemical analysis of CSF:



Lactate not tested any more

Glucose and specific protein tests are the most reliable diagnostically & accessible analytically

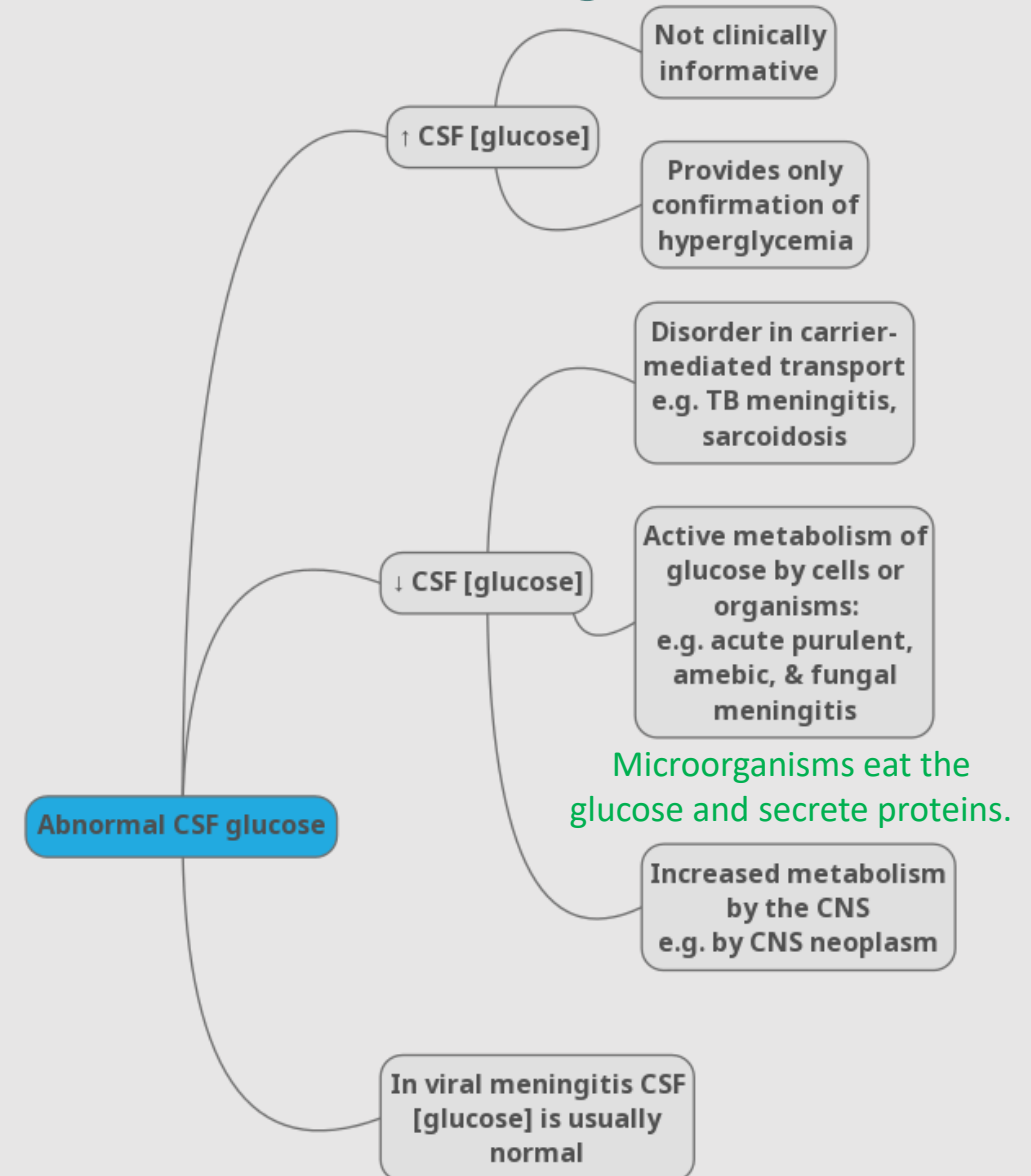
Specimens are sent to the microbiology lab to differentiate whether its bacterial\ viral meningitis and glucose\ protein are measured in the biochemistry lab. → the case will be half micro half biochemistry in the final

CSF Glucose

- ❖ Glucose enters CSF via facilitative transporter (**GLUT**) “Sodium independent”
- ❖ CSF [glucose] is ~ 2/3 that of plasma
 - ✓ **50 - 80 mg/dl**
- ❖ A plasma sample must be obtained ~ **2-4 hours** 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

Usually they call it a grey tap tube and it has fluoride that would inhibit glycolysis. --> this info is just for your information.
A question can be asked: CSF in glucose is more or less than plasma? It is 2/3 glucose of plasma because it enters CSF via facilitative transporter.

Abnormal CSF glucose “IMPORTANT”



CSF proteins

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

Source of CSF proteins:

- ✓ 80% from plasma by ultrafiltration
“Albumin which is small in size”
- ✓ 20% from intrathecal synthesis
“Immunoglobulin protein which is quite big”

CSF Albumin

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

If albumin is normal and IGP is high -> local synthesis
disease -> MS (demyelinating disease)

Abnormal CSF proteins

We must know how to compare for example if the patient has nephrotic syndrome then his protein levels ↓ .

Abnormal CSF proteins

↑ **CSF [total protein]**

Useful nonspecific indicator of pathological states:

First we exclude traumatic tap. It will have high protein

Must be compared to the serum [protein]

1. Lysis of contaminant blood (traumatic tap)

2. ↑ permeability of the epithelial membrane due to:

- A. Bacterial or fungal infection
- B. Cerebral hemorrhage

3. ↑ production by CNS tissue in:

Multiple sclerosis (MS)
Subacute Sclerosing Panencephalitis (SSPE)

4. Obstruction e.g. in:
Tumors & Abscesses

SSPE is less common, usually tests in lab are made for MS

CSF proteins

CSF Immunoglobulin

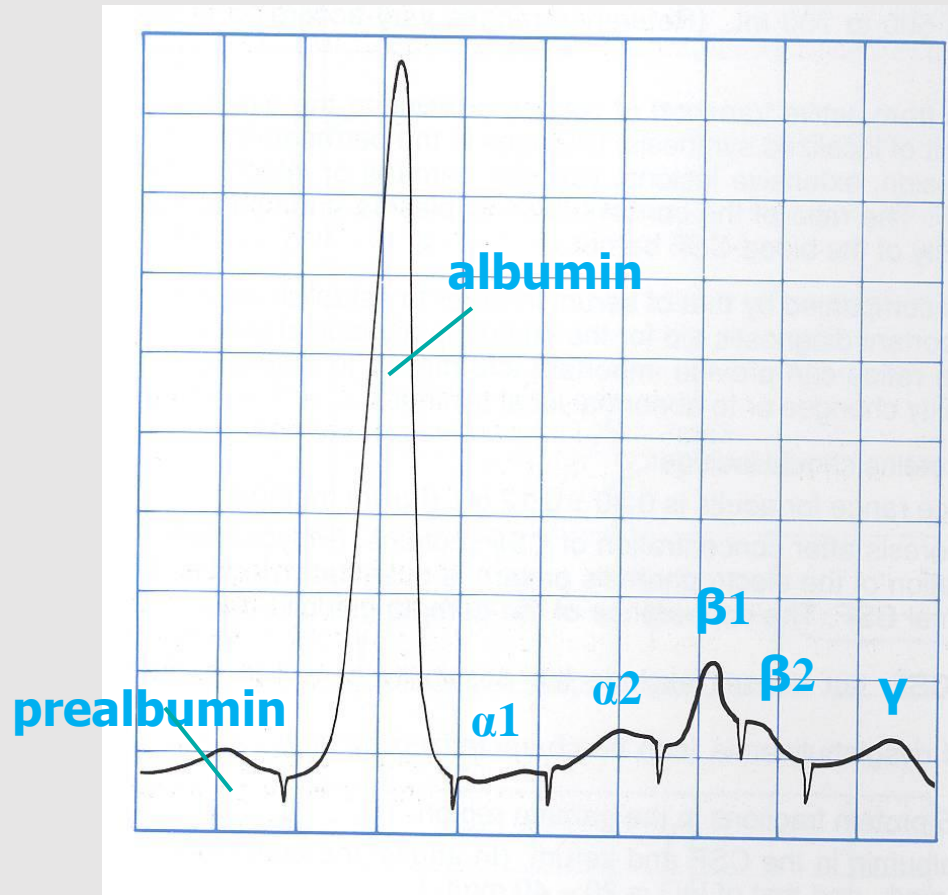
- Glucose enters CSF via facilitative transporter CSF IgG can arise:
 - a) from **plasma cells** within CSF
 - b) from the **blood** through BBB
- **↑ [IgG] and normal [Alb] of CSF** suggests local production of IgG, e.g.,
 - ✓ Multiple sclerosis (MS)
 - ✓ Subacute sclerosing panencephalitis (SSPE)

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

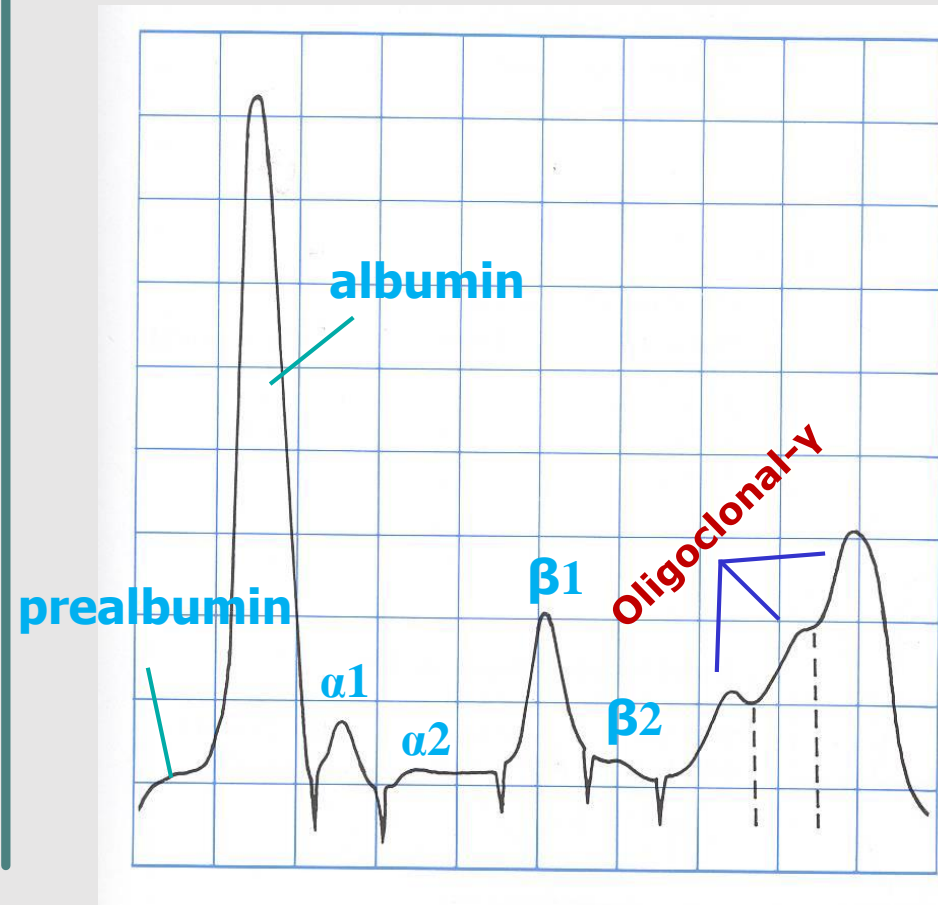
- 1) Perform electrophoretic separation
- 2) If multiple banding (**oligo-clonal bands**) of the γ -globulin is detected, the following differential diagnosis is suspected:
 - I. **MS**
 - II. SSPE
 - III. Inflammatory diseases

Normal pattern

Electrophoresis is a techniques used in labs to separate proteins or immunoglobulins in a specimen (urine – blood – CSF).



Oligo-clonal banding "MS or SSPE"



- ✓ Oligo clonal bands are for diagnosing MS
- ✓ Oligo clonal means multiple bands
- ✓ We don't have to know the bands or explain the electrophoresis. We just need to know that **oligo clonal gamma** means MS and in the normal is a **one big spike of monoclonal albumin band and small bands.**

Other Chemical Components of CSF

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

- 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 reduction in acute bacterial meningitis
slight reduction in viral meningitis & brain tumors

In TB meningitis chloride and glucose are LOW and protein HIGH.

- **Don't memorize numbers normal ranges are given in test!**

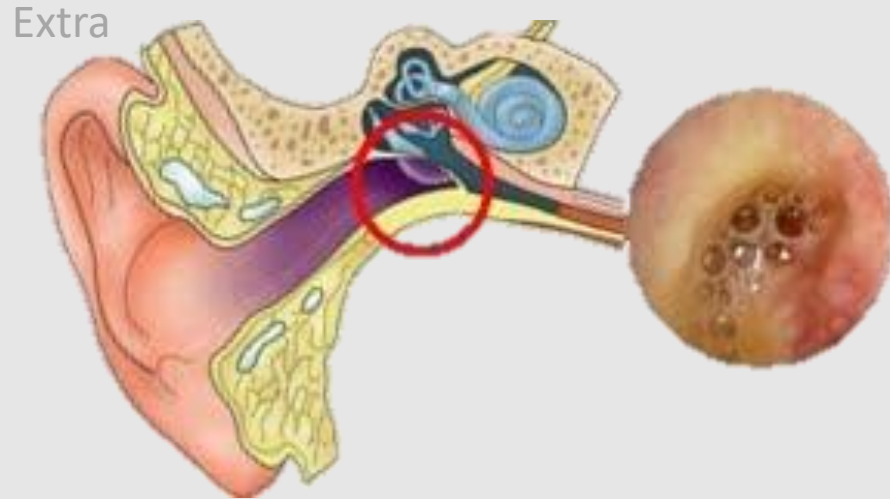
Abnormal findings of CSF in some pathological conditions

Parameter	Condition		
	Bacterial Meningitis (pyogenic)	Tuberculous Meningitis	Viral Meningitis
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	negative 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 ↓

Otorrhea & Rhinorrhea

Otorrhea : leakage of CSF from the **ear**

Rhinorrhea : leakage of CSF into the **nose**



In Otorrhea blood tests are outdated =>
MRI is done instead because its faster.

- **Otorrhea happens to people who had a trauma.**

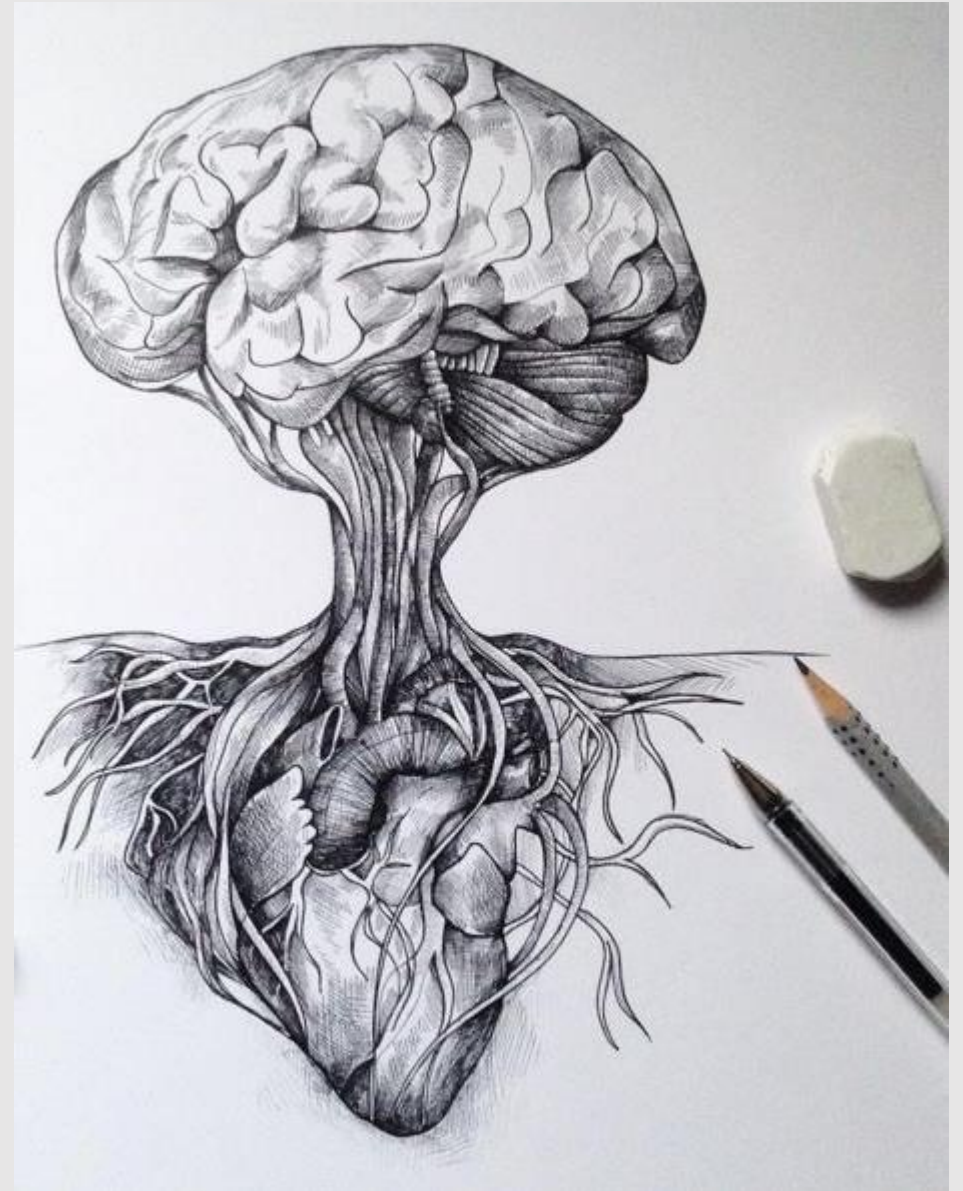
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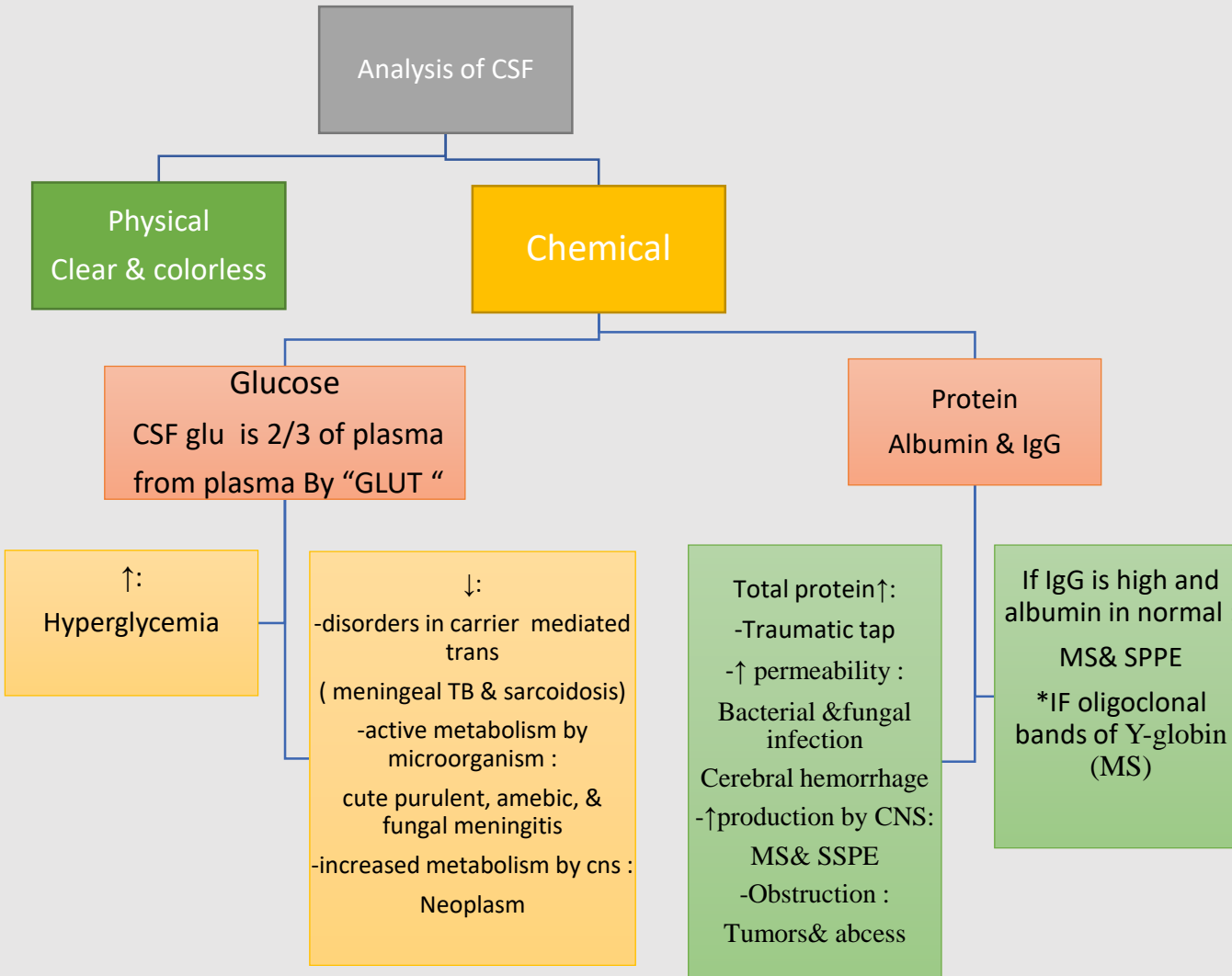
Take home messages

- ❖ 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

Good luck doctors



Summary



Function of the CSF (Normal blood brain barrier is important for the normal chemistry results of CSF)	<ol style="list-style-type: none"> 1-Physical support& protection 2-controlled chemical environment .
Formed by	Choroid plexuses & ventricle cells (500 ML/day)
Mechanism of formation	<ol style="list-style-type: none"> 1-Selective ultrafiltration of plasma 2-Active secretion by epithelial membranes
Excretion (absorption)	arachnoid villi → venous sinuses → blood stream Excretion volume = production volume
Collection of specimen by	Lumber puncture (L3-L4)
indications	<ol style="list-style-type: none"> 1- CNS infection 2-hemorrhage 3-CNS malignance 4-demyelination
Contraindications	<ol style="list-style-type: none"> 1-Bleeding diathesis 2. ↑ intracranial pressure 3. Infection at site of needle

Quiz

1) In which of the following situations the lumbar puncture is contraindicated ?

- a) CNS infection
- b) Multiple sclerosis
- c) Elevated intracranial pressure
- d) CNS hemorrhage

2) The appearance of CSF in bacterial meningitis is ?

- a) Turbid
- b) Fibrin web
- c) Clear
- d) None of the above

3) Xanthochromia indicates which of the following ?

- a) Subacute sclerosing panencephalitis (SSPE)
- b) Sarcoidosis
- c) Subarachnoid hemorrhage
- d) Hyperglycemia

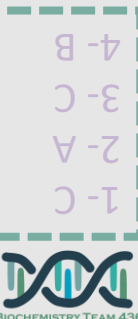
4) What is the situation of CSF glucose level if the patient has bacterial meningitis ?

- a) Elevated
- b) Decreased
- c) Depends on the type of the bacteria
- d) Normal

Q : When would Xanthochromia indicate hemorrhage ?

Q : What is the normal range of CSF proteins ?

[Suggestions and recommendations](#)





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OUR WORK**



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