



**BODY FLUIDS:**  
**Cerebrospinal Fluid (CSF)**



# Objectives

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- 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 & Functions

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## *CSF definition:*

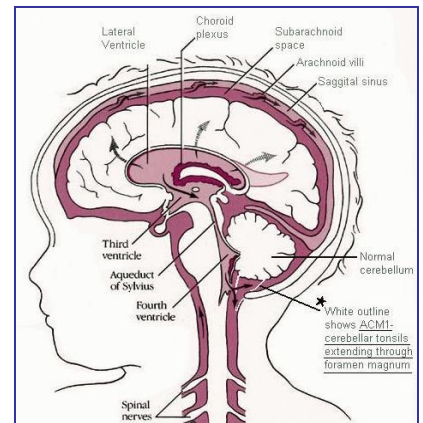
The liquid surrounding the brain and spinal cord. It flows in subarachnoid area (the space between the arachnoid & pia matter)

## *Main Functions:*

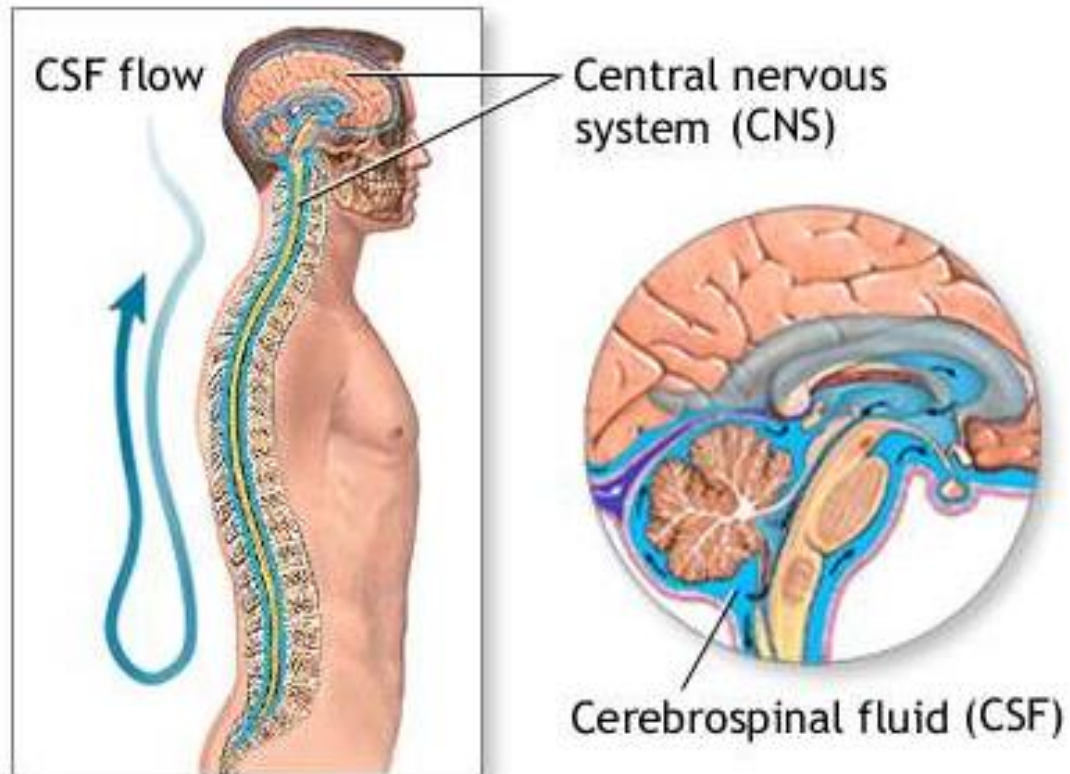
- Physical support & protection
- Provides a controlled chemical environment → nutrient supply & waste removal

# CSF Formation & Circulation

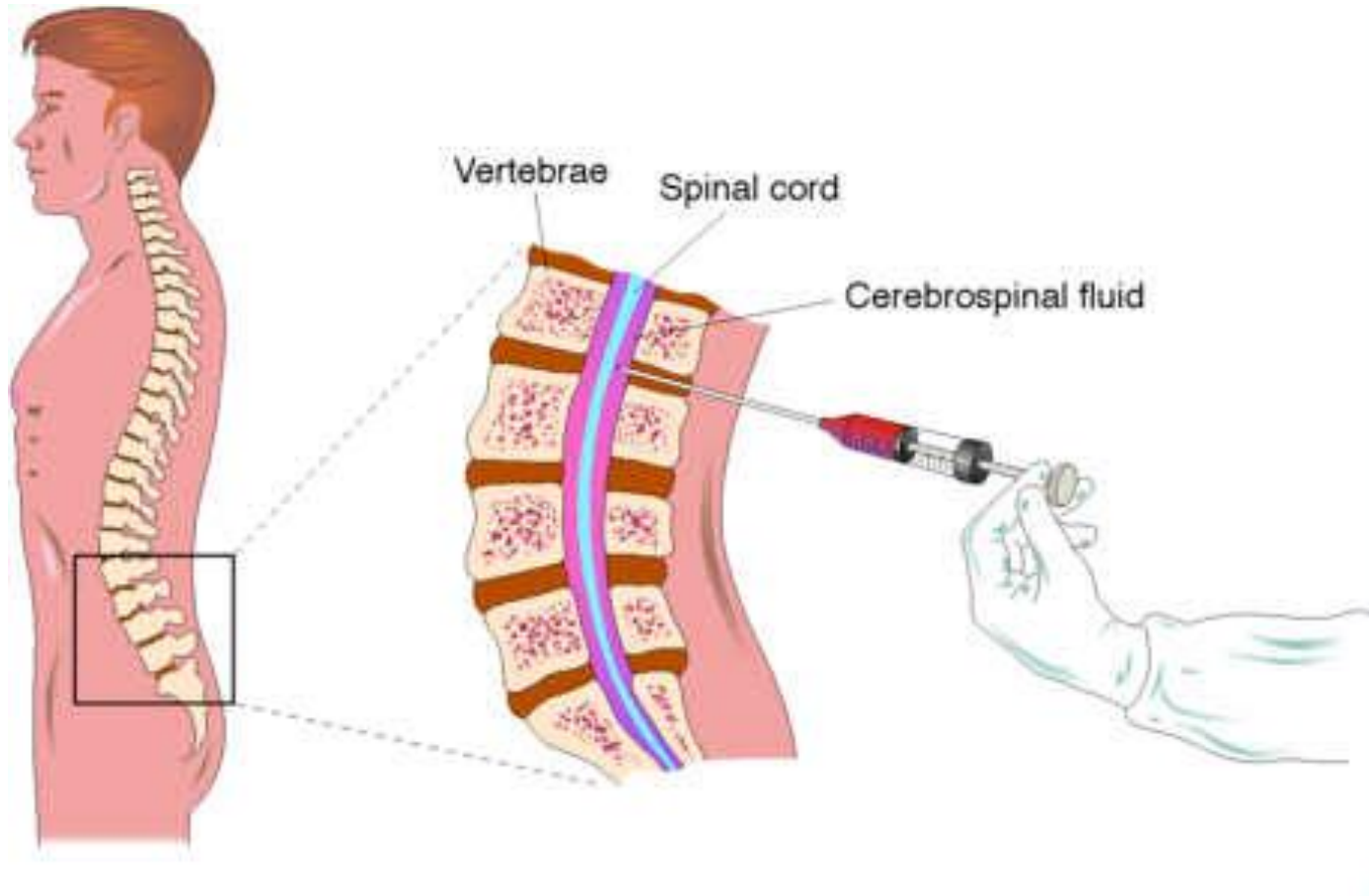
- CSF is formed at the choroid plexuses & by the cells lining the ventricles.
- Normal blood brain barrier is important for the normal chemistry results of CSF
- Rate of formation:
  - 500 ml/day
- Mechanism of formation:
  - Selective ultrafiltration of plasma
  - Active secretion by epithelial membranes
- 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



# CSF Circulation



# Method of CSF Sampling



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



# CSF Specimen Collection

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- Obtained by **lumbar puncture** (At the interspace L3-4, or lower)
- Using **aseptic** technique
- CSF is **separated** into 3 aliquots:
  - for chemistry & serology
  - for microbiology
- **Immediate** analysis
- It's a **precious** sample: Preserve any remaining sample



# Contraindications for performing lumbar puncture

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- 1) Bleeding diathesis
- 2) Increased intracranial pressure
- 3) Infection at site of needle insertion

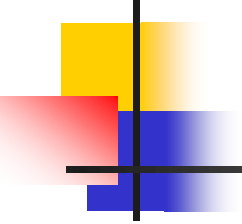




# Indications for laboratory investigation of CSF

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



# Examination of CSF

## *(Physical examination)*

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- **Normal CSF is:**
  - Colorless
  - Clear
  - Free of clots
  - Free of blood
- **If CSF is cloudy (turbid) → perform microscopic examination:**
  - is usually due to leucocytes
  - may be due to micro-organisms



# Blood & Hemoglobin pigments in CSF

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## 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)



# When would Xanthochromia indicate hemorrhage?

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- **If you exclude:**
  - 1) Prior traumatic tap
  - 2) Hyperbilirubinemia (*bilirubin* > 20 mg/dL)



# Examination of CSF

## *(Biochemical analysis of CSF)*

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- **Tests of interest:**

- ✓ ■ Glucose
- ✓ ■ Protein
  - Total
  - Specific:
    - Albumin
    - Immunoglobulin
    - Others (e.g. myelin basic protein; MBP)
- Lactate

**The most reliable  
diagnostically &  
accessible analytically**

# Glucose in CSF

- Glu enters CSF via facilitative transporter (**GLUT**)
- CSF [glucose] is  $\sim 2/3$  that of plasma
  - **50 - 80 mg/dl**
- A **plasma sample** must be obtained  $\sim 2-4$  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



# Abnormal CSF [Glucose]

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- **↑ CSF [glucose]:**
  - Not clinically informative
  - Provides only confirmation of hyperglycemia
- **↓ CSF [glucose] (*hypoglycorrachia*):**
  - 1) Disorder in carrier-mediated transport
    - 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
- In **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]

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- **↑ 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:
      - Bacterial or fungal infection
      - Cerebral hemorrhage
    - ↑ production by CNS tissue in:
      - Multiple sclerosis (MS)
      - Subacute Sclerosing Panencephalitis (SSPE)
    - Obstruction e.g. in:
      - Tumors
      - Abscess



# CSF Albumin

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



# CSF Immunoglobulin

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- **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)

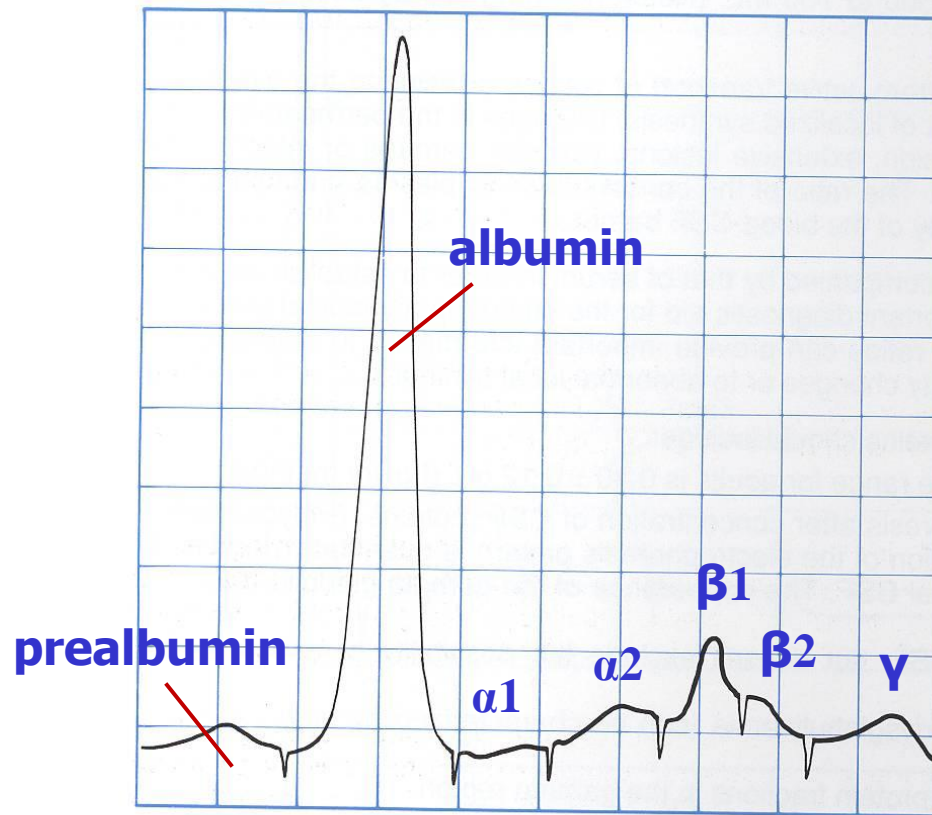


# What to do if ↑ CSF [protein] was detected?

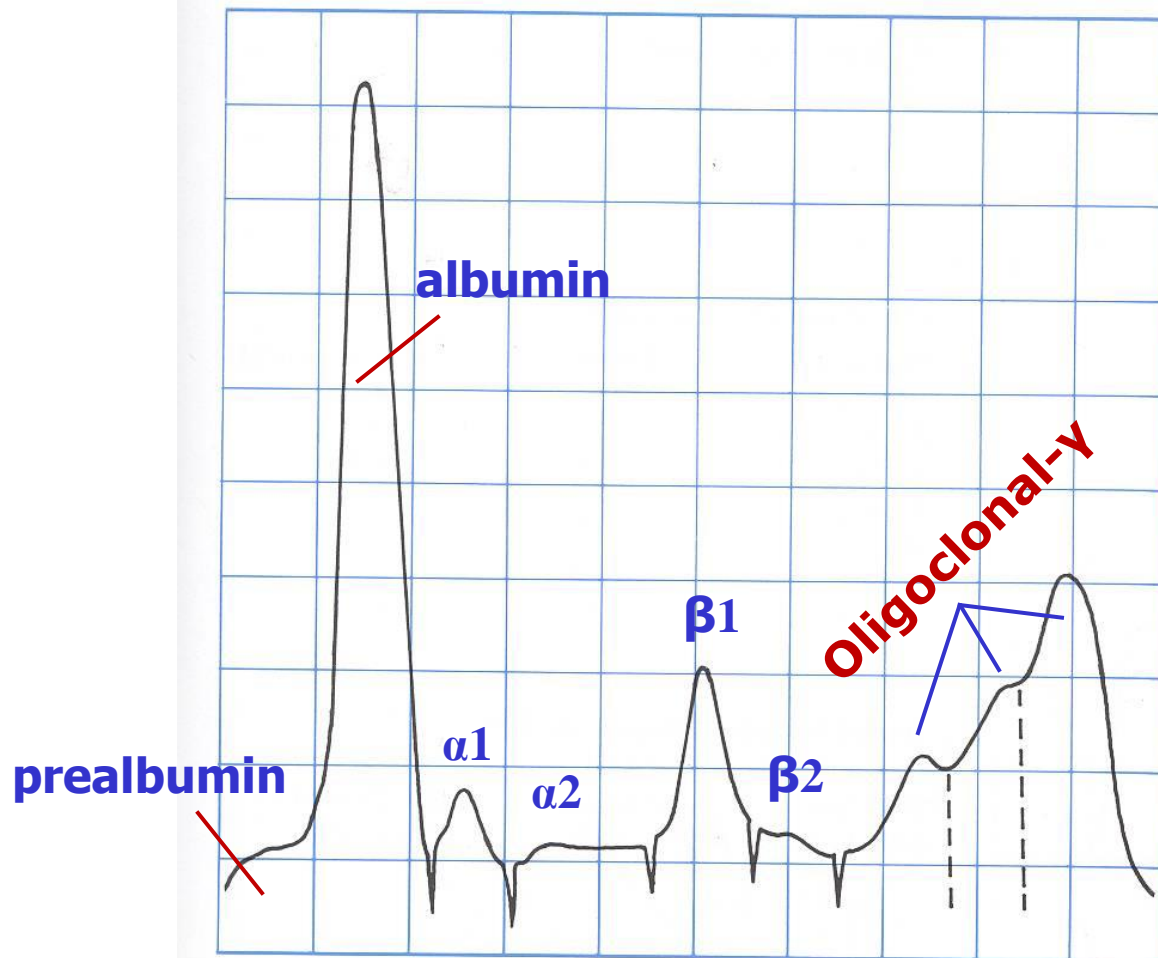
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- Perform electrophoretic separation
- If multiple banding (*oligoclonal bands*) of the  $\gamma$ -globulin is detected, the following differential diagnosis is suspected:
  - MS
  - SSPE
  - inflammatory diseases

# CSF Electrophoresis *(Normal Pattern)*



# 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 ↓↓ in acute bacterial meningitis
  - slight ↓ in viral meningitis & brain tumors

# Normal composition of CSF

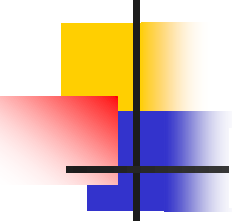
<b>Appearance</b>	<b>Clear ,Colorless</b>
<b>Lymphocytes</b>	<b>&lt;5/mm<sup>3</sup></b>
<b>Polymorphs</b>	<b>Nil</b>
<b>pH</b>	<b>7.4</b>
<b>Total Volume</b>	<b>100 - 150 ml</b>
<b>Daily Secretion</b>	<b>450 - 500 ml</b>
<b>Specific Gravity</b>	<b>1.006 - 1.007</b>
<b>Protein</b>	<b>0.15 – 0.45 g/L</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

Parameter	Condition		
	<b>Bacterial Meningitis (pyogenic)</b>	<b>Tuberculous Meningitis</b>	<b>Viral Meningitis</b>
Appearance	Often turbid	Often fibrin web	Usually clear
Predominant cell	Polymorphs	Mononuclear (lymphocytes)	Mononuclear (lymphocytes)
Cell count/mm <sup>3</sup>	90-1000+	10-1000	50-1000
Bacteria/virus	+ve smear & culture	Often none in smear	-ve smear or culture

# Continued...



<b>Parameter (reference range)</b>	<b>Condition</b>		
	<b>Bacterial Meningitis (pyogenic)</b>	<b>Tuberculous Meningitis</b>	<b>Viral Meningitis</b>
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

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



# Take home messages

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- 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



# References

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- Lecture notes, Clinical Biochemistry, Wiley BlackWell, 8<sup>th</sup> edition, 2010, chapter 19, page 274-277
- Clinical Chemistry, Principles, Procedures, Correlations, Lippincott Williams & Wilkins, 5<sup>th</sup> edition, 2005, chapter 27, page 560-563.