



BODY FLUIDS:
Cerebrospinal Fluid (CSF)



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 & Functions

CSF definition:

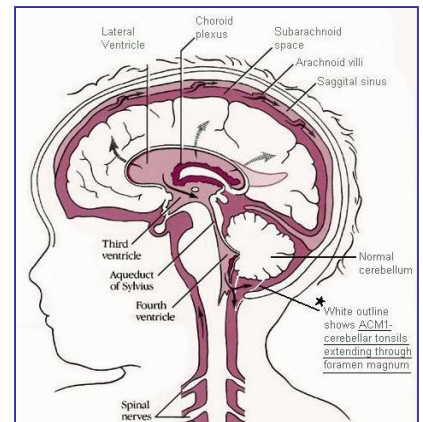
The liquid surrounding the brain and spinal cord. It flows in subarachnoid area (the space between the arachnoid & pia matter)

Main Functions:

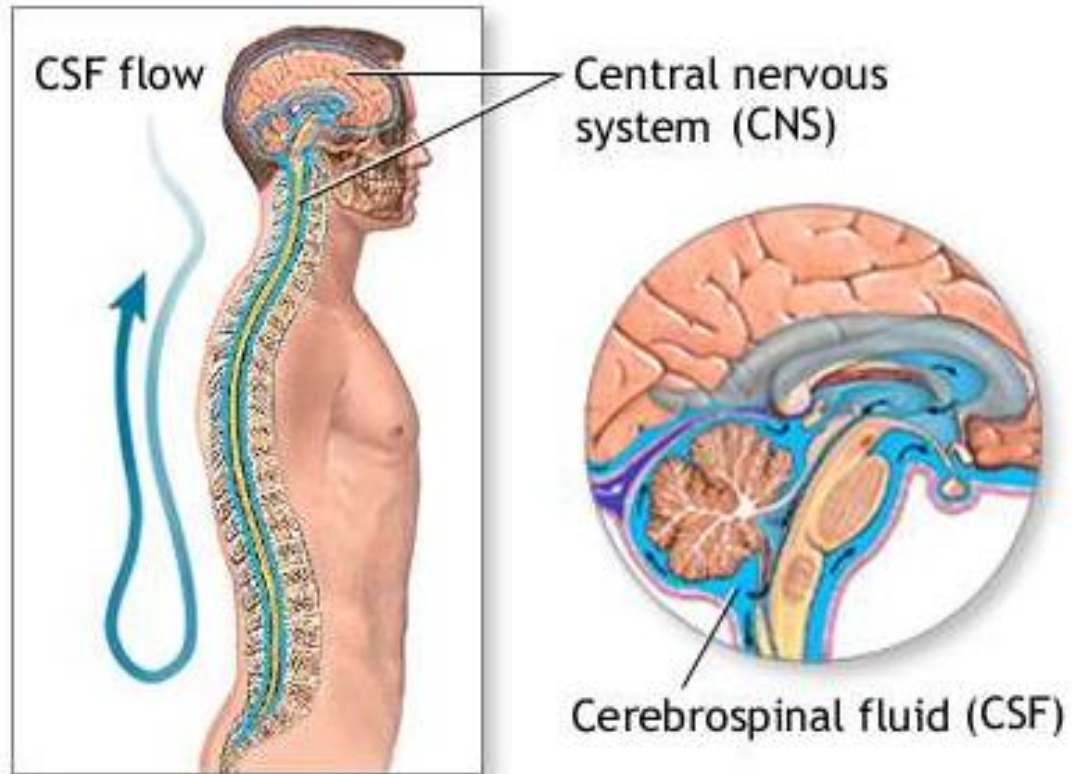
- Physical support & protection
- Provides a controlled chemical environment → nutrient supply & waste removal

CSF Formation & Circulation

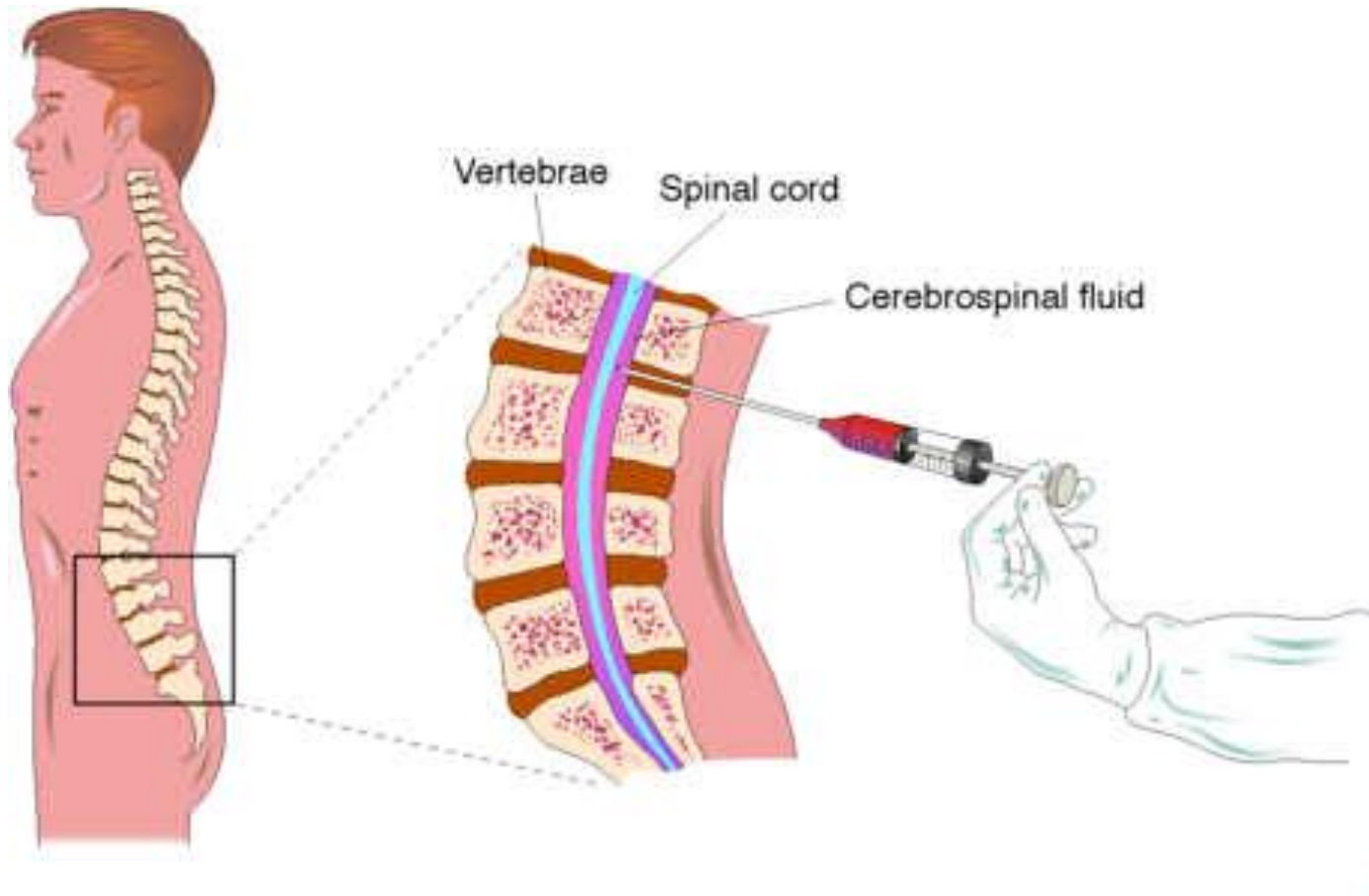
- CSF is formed at the choroid plexuses & by the cells lining the ventricles.
- Normal blood brain barrier is important for the normal chemistry results of CSF
- Rate of formation:
 - 500 ml/day
- Mechanism of formation:
 - Selective ultrafiltration of plasma
 - Active secretion by epithelial membranes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

- 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



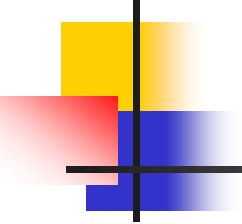
Contraindications for performing lumbar puncture

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



Indications for laboratory investigation of CSF

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



Examination of CSF

(Physical examination)

- **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

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?

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



Examination of CSF

(Biochemical analysis of CSF)

- **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]

- **↑ 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]

- **↑ 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

- 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

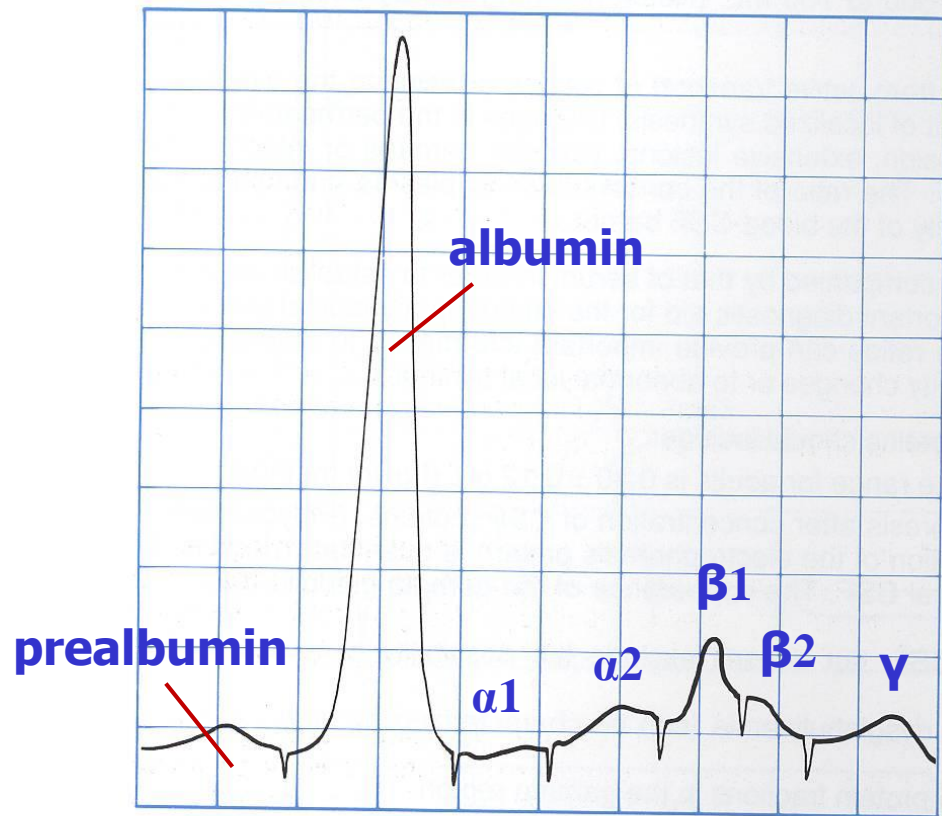
- **↑ [IgG] and normal [Alb] of CSF suggests local production of IgG, e.g.,**
 - Multiple sclerosis (MS)
 - Subacute sclerosing panencephalitis (SSPE)



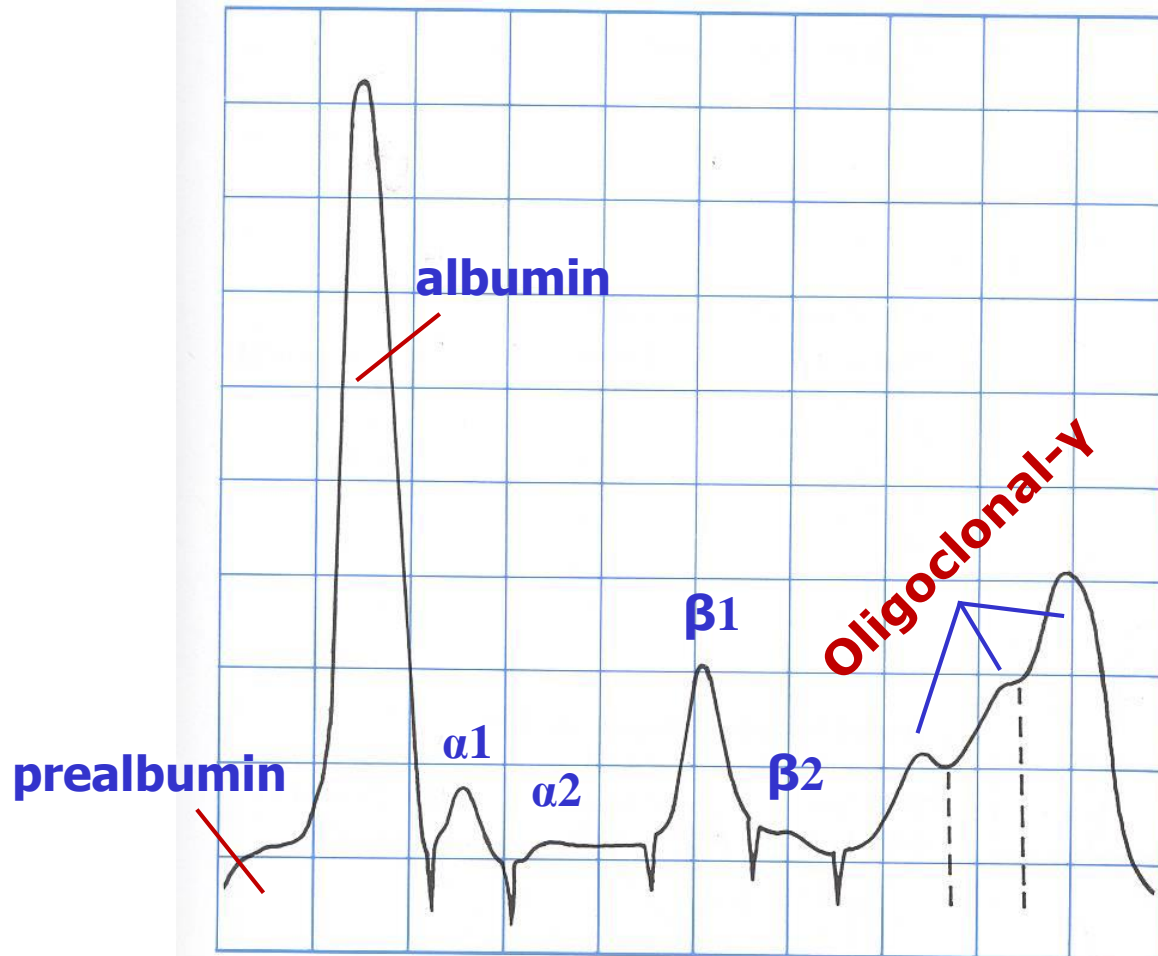
What to do if ↑ CSF [protein] was detected?

- Perform electrophoretic separation
- 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)*



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

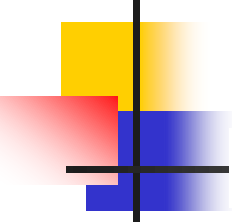
Normal composition of CSF

Appearance	Clear ,Colorless
Lymphocytes	<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

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	-ve smear or culture

Continued...



Parameter (reference range)	Condition		
	Bacterial Meningitis (pyogenic)	Tuberculous Meningitis	Viral Meningitis
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**



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



References

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