

BODY FLUIDS: Cerebrospinal Fluid

Dr Rana Hasanato

Clinical Biochemistry Unit, Pathology Dept.

CSF Definition & Functions

CSF definition:

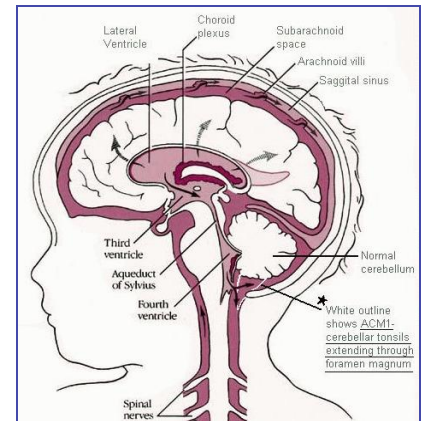
The liquid surrounding the brain and spinal cord
It flows in subarachnoid area (the space between the arachnoid & pia matter)

Main Functions:

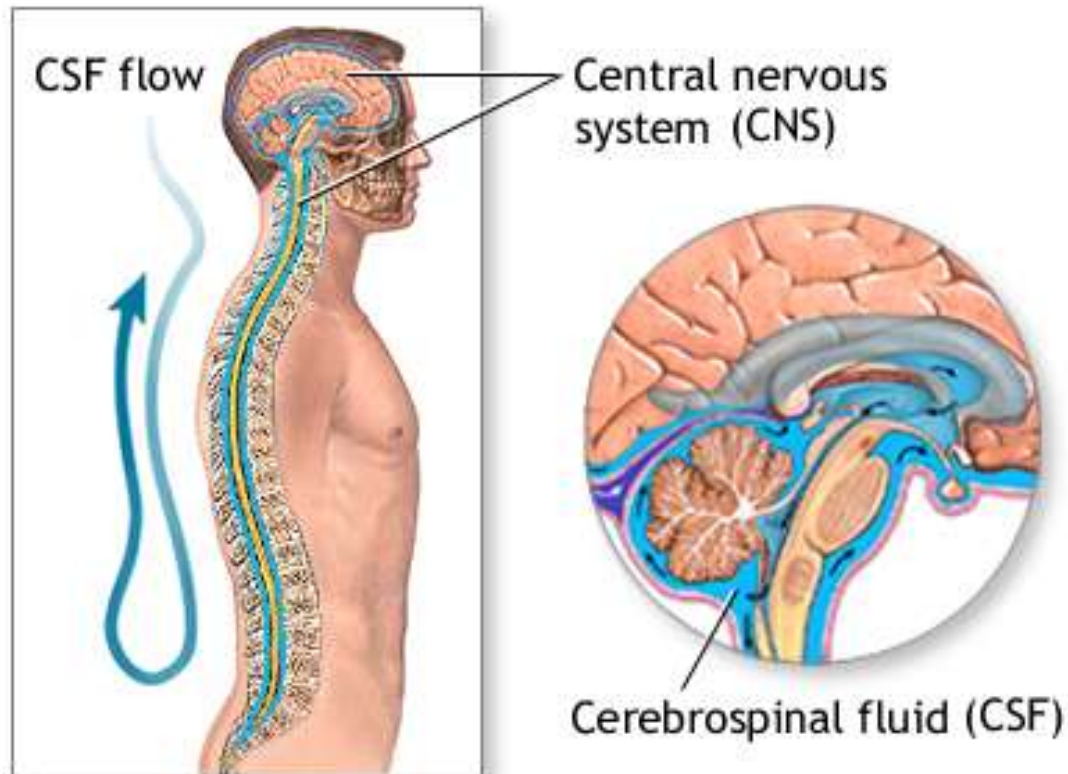
- Physical support & protection
- Provides a **controlled** chemical environment → nutrient supply & waste removal

CSF Formation & Circulation

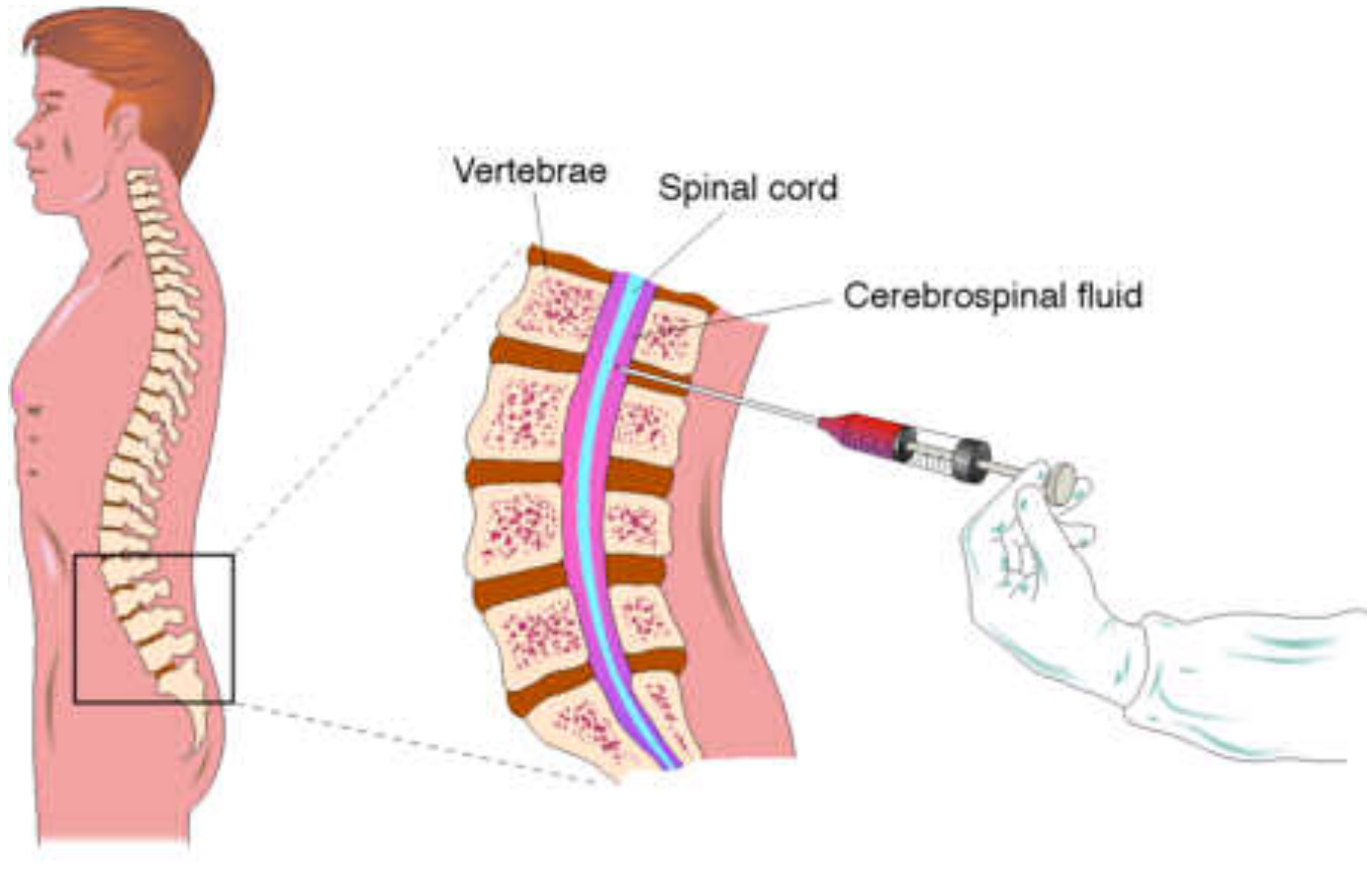
- CSF is formed at the choroid plexuses & by the cells lining the ventricles.
- Normal blood brain barrier is important for the normal chemistry results of CSF
- Rate of formation:
 - 500 ml/day
- Mechanism of formation:
 - Selective ultrafiltration of plasma
 - Active secretion by epithelial membranes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

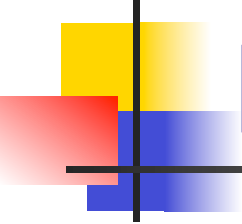


**Traumatic tap (damage to blood vessel during specimen collection)
→ blood in CSF**



CSF Specimen Collection

- Obtained by **lumbar puncture** (At the interspace L3-4, or lower)
- Using **aseptic** technique
- CSF is **separated** into 2 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:

1- 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:

2- 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

- Glc 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] :**
 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



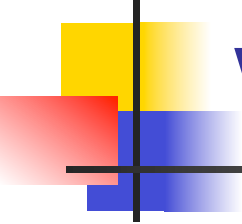
CSF Albumin

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



CSF Immunoglobulin

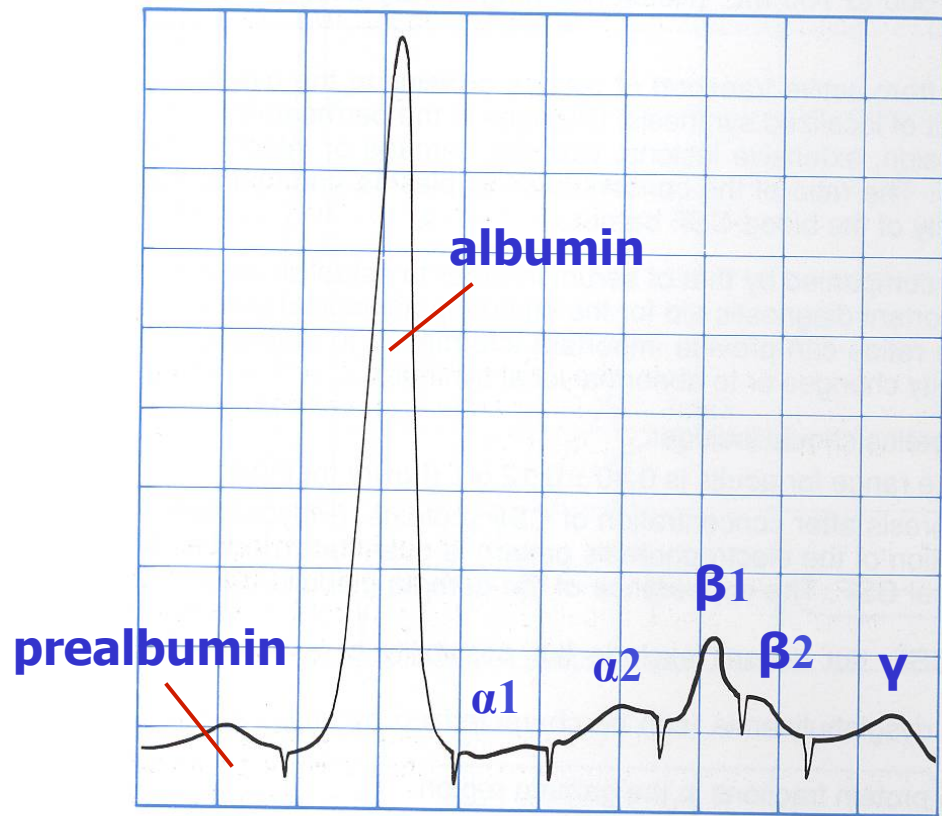
- CSF IgG can arise:
 - from *plasma cells* within CSF
 - from the *blood* through BBB
- ↑ [IgG] and normal [Alb] of CSF suggests local production of IgG, e.g.,
 - Multiple sclerosis (MS)
 - Subacute sclerosing panencephalitis (SSPE)



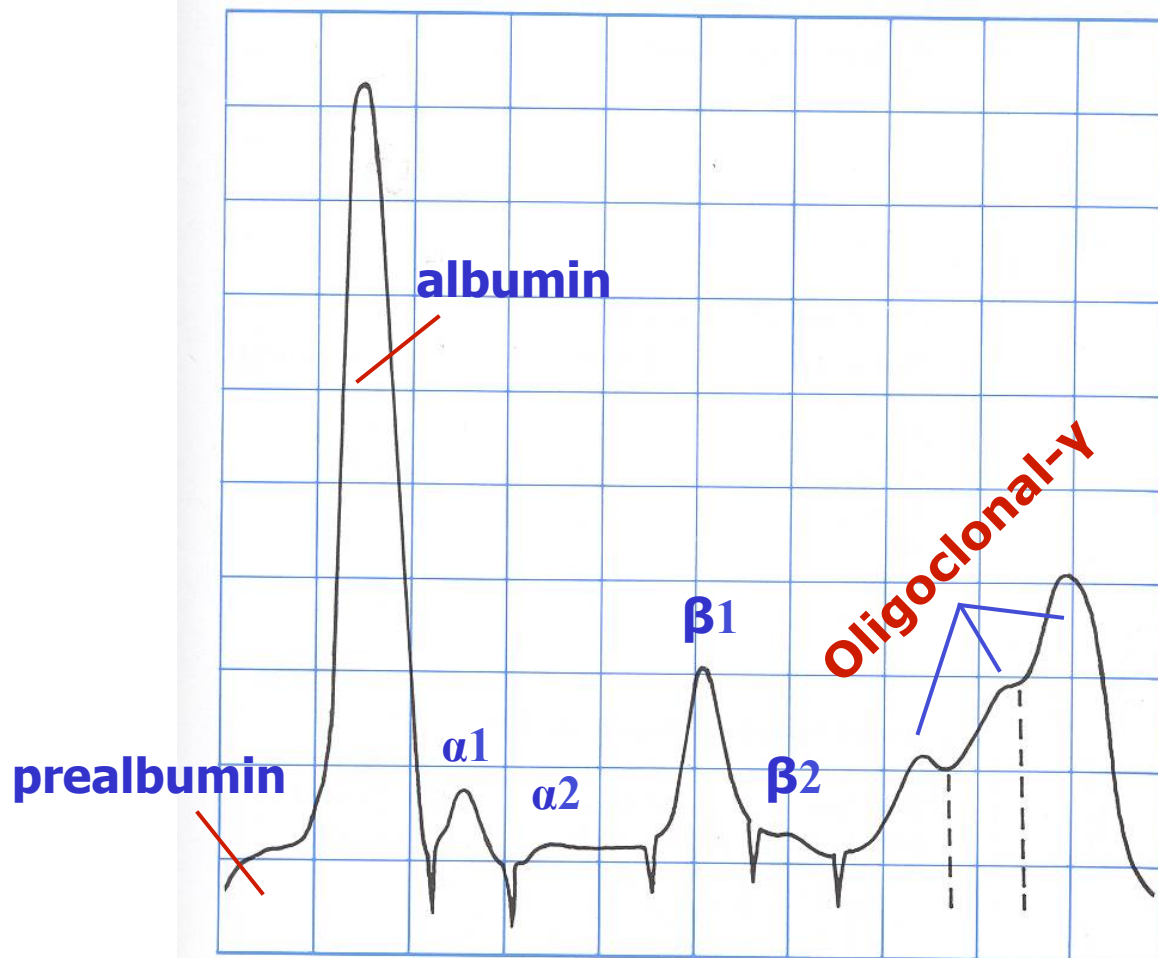
What to do if \uparrow CSF [protein] was detected?

- 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



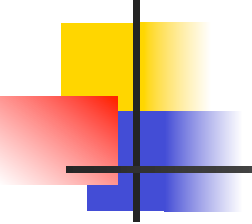
Other Chemical Components of CSF

- 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 |

Abnormal findings of CSF in some pathological conditions, 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 MESSAGE

- 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



THANK YOU
