CSF

Color Index:

- Main Topic
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- Important
- Extra info, Drs' notes
- Only in girls' slides
- Only in boys' slides

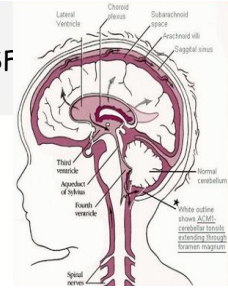
Editing File

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	CSF is the liquid surrounding the brain and spinal cord. It flows in the subarachnoid area
Main Functions	1- Physical support and protection 2- Provides a Controlled chemical environment → nutrient supply and waste removal
Formation	• 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 rate of formation is: **500 ml/day**



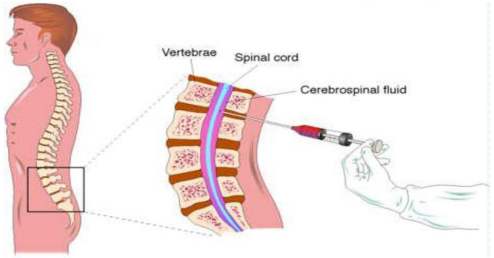
Mechanism of formation → Selective ultrafiltration of plasma → Active secretion by epithelial membranes

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→to the bloodstream

CSF specimen collection

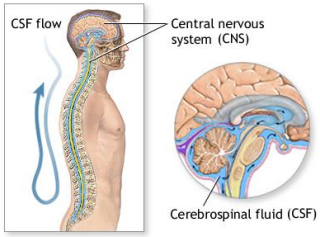
- CSF sample is obtained by lumbar puncture (At the interspace L3-4, or lower)
- Using an antiseptic technique, (to avoid and prevent the patient from getting an infection)
- CSF is separated into (3) aliquots:
  - ➢ For chemistry & serology
  - ➢ For microbiology
- Immediate analysis
- It's a precious[1] sample: preserve any remaining sample

Method of CSF Sampling



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

CSF Circulation



1. It's precious because it's dangerous and difficult to get, it requires skills and is preserved in case there is a need to do other tests.

Contraindications for performing Lumbar Puncture[1]

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

1. Dr note: Contraindications = infection outside CSF

Indications for laboratory investigation of CSF[2]

- Demyelinating diseases
- CNS Malignancy
- CNS infection
- Hemorrhage in CNS

2. Dr note: Indications = infection inside CSF

Examination of CSF

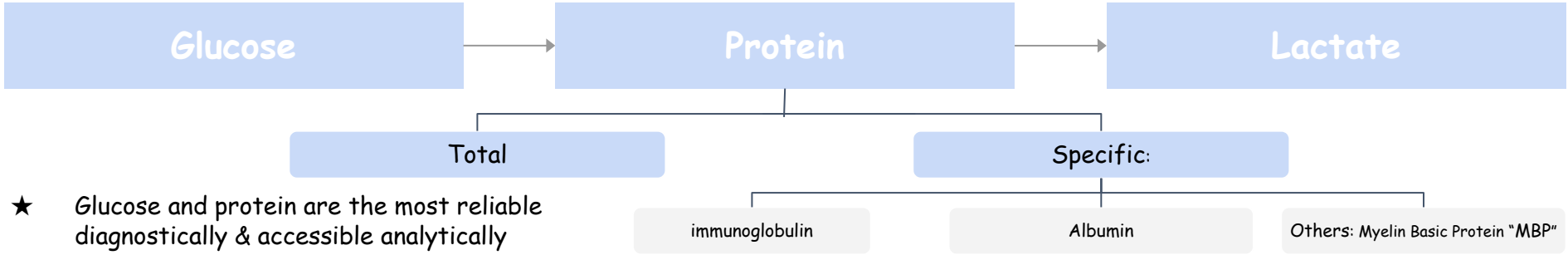
1- Physical examination:

If CSF is **cloudy (turbid)** → perform microscopic examination:

- Usually due to **leucocytes**
- May be due to **microorganisms**

2- Biochemical analysis:

Tests if interest



★ Glucose and protein are the most reliable diagnostically & accessible analytically

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 hours earlier)

When would Xanthochromia indicate hemorrhage?

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

Glucose in CSF

- Glucose enters CSF via facilitative transporter (GLUT) "GLUT type 1"
- CSF (glucose) is ~ 2/3 that of plasma "50 - 80 mg/dl"

"Divided it by 18 to get mmol/L"

E.g. 100 in blood, then 66 in CSF

A plasma sample must be obtained ~ 2-4 hr before CSF sample[1]

In hypoglycemia: (CSF glucose) may be very low

In hyperglycemia: (CSF glucose) is raised

Measure CSF (glucose)

Immediately

Or preserve the specimen with an antiglycolytic e.g. fluoride ion[2]

1. We take a blood sample first, then 2~4 hours later we take a CSF sample, why? To measure and compare the plasma glucose with CSF glucose level.

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

↑CSF [glucose]

Not clinically informative

Provides only confirmation of hyperglycemia

↓CSF [glucose] (hypoglycorrhachia)

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.

↑CSF [total protein]

Must be compared to the serum [protein]

Useful nonspecific indicator of pathological states:

1)Lysis of contaminant blood (traumatic tap).

2)↑permeability of the epithelial membrane due to:[1]

e.g. Bacterial or fungal infection, Cerebral hemorrhage.

3)↑production by CNS tissue in:[1]

e.g. Multiple sclerosis (MS), Subacute Sclerosing Panencephalitis (SSPE).

4) Obstruction in:

e.g. Tumors, Abscess

★★ In viral meningitis CSF [glucose] is usually normal

1. Dr note: ↑ permeability will ↑level of albumin, while ↑ production will ↑ IgG immunoglobulin.

CSF [protein]

CSF Albumin

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

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[1], inflammatory diseases

CSF Immunoglobulin

↑[IgG] and normal [Alb] of CSF suggests local production of IgG:

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

CSF IgG can arise:

- from plasma cells within CSF
- from the blood through BBB

Other Chemical Components of CSF

CSF [Ca] [K] [PO_4] < blood [Ca] [K] [PO_4]
CSF [Cl] [Mg] > blood [Cl] [Mg] [1]

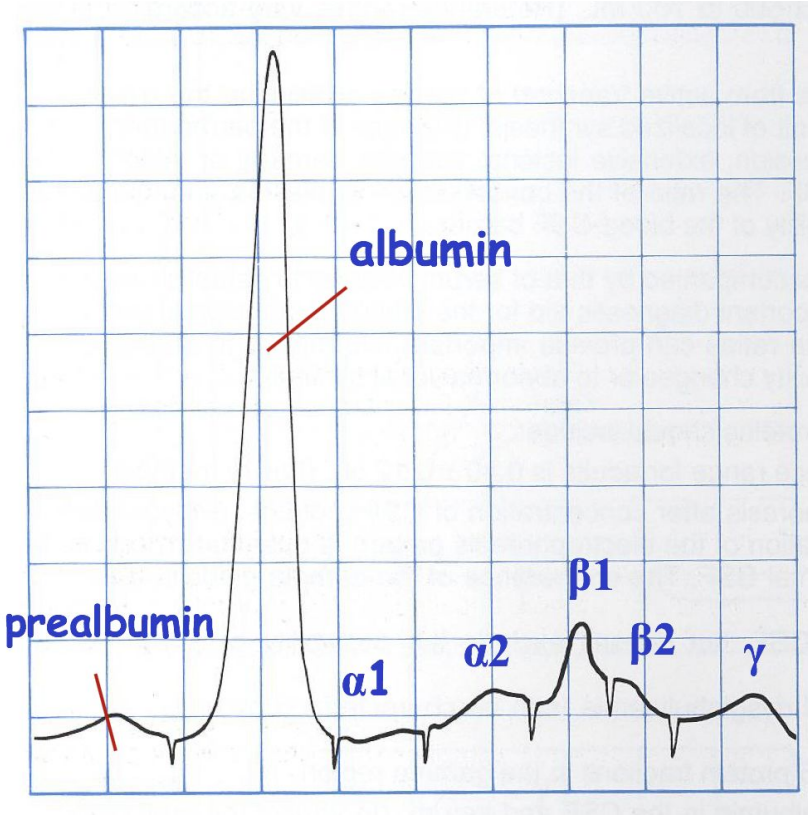
Abnormal CSF [Chloride]

marked ↓↓	In acute bacterial meningitis
In viral meningitis & brain tumors	slight ↓

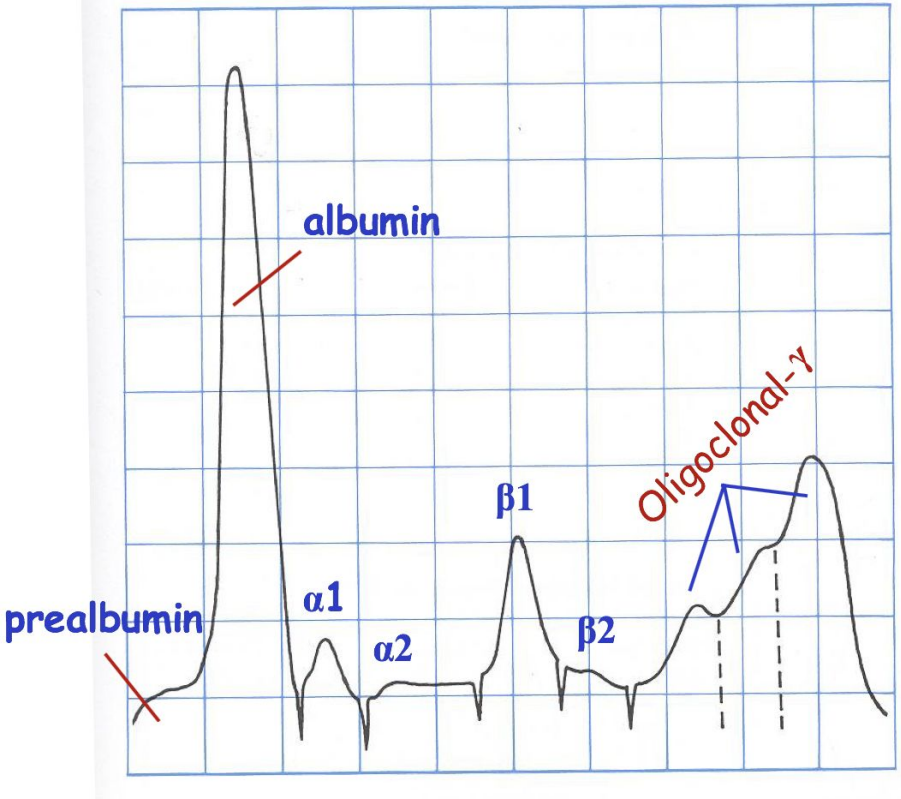
(1) CSF [Calcium], [Potassium] & [Phosphates] are lower than their levels in the blood. CSF [Chloride] & [Magnesium] are higher than their levels in the blood.

1. SSPE: Subacute sclerosing panencephalitis

CSF Electrophoresis (Normal Pattern)



CSF Electrophoresis (Oligoclonal Banding)



Normal composition of CSF[1]

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

1. Dr note: This table is more likely for the practical, but focus in these 4 in

Abnormal findings of CSF in some pathological conditions

Parameter	Condition		
	Viral Meningitis	Tuberculous Meningitis	Bacterial Meningitis (pyogenic)
Appearance	Usually clear	Often fibrin web	Often turbid
Predominant cell	Mononuclear (lymphocytes)	Mononuclear (lymphocytes)	Polymorphs
Cell count/mm^3	50-1000	10-1000	90-1000+
Bacteria/virus	-ve smear or culture	Often none in smear	+ve smear & culture
Protein (0.15-0.45 g/L)	<1 (Normal)	1-5 (↑ ↑)	>1.5 (↑ ↑)
Glucose (2.8-4.2 mmol/L)	>1/2 plasma (Normal or slightly ↓)	<1/2 plasma (↓ ↓)	<1/2 plasma (↓ ↓)
Chlorides (115 - 130 mmol/L)	Normal or ↓	↓ ↓	↓ ↓

leakage of CSF

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.

Summary

CSF

Function
1- Physical support & protection
2- Provides a controlled chemical environment

Formed by
Choroid plexuses & ventricle cells
And Obtained by lumbar puncture (At the interspace L3-4)

Indications for Laboratory Investigation
- CNS infection
- Demyelinating diseases (ex: MS)
- CNS Malignancy
- Hemorrhage

Contraindications for performing lumbar puncture
- Bleeding diathesis
- Increased intracranial pressure
- Infection at site of needle insertion

Analysis of CSF

- **Chemical**
  - **Glucose**
    CSF glucose is 2/3 of plasma
    - **Decreased**
      1-Disorder in carrier-mediated transport
      - TB meningitis
      - sarcoidosis

      2- Active metabolism of glucose by cells or organisms
      - acute purulent
      - amebic
      - fungal meningitis

      3-Increased metabolism by the CNS
      - CNS neoplasm
    - **Increased**
      Hyperglycemia
  - **Protein**
    Albumin & IgG
    - Increase CSF total protein

      1- Lysis of contaminant blood
      - Traumatic tap

      2- Increased permeability
      - Bacterial or fungal infection
      - Cerebral hemorrhage

      3- Increased production by CNS
      - Multiple sclerosis (MS)
      - Subacute Sclerosing Panencephalitis (SSPE)

      4- Obstruction
      - Tumors & abscess
    - If IgG is high and albumin in normal
      (oligoclonal bands of Y-globin)

      1-Multiple sclerosis (MS)
      2-Subacute Sclerosing Panencephalitis (SSPE)
- **Physical**
  Normally Clear & colorless

Quiz

MCQs :

Q1: Which one of the following is the main functions of CSF?

a) Physical support **b)** Waste removal
c) Nutrient supply **d)** All the them

Q2: All of the following are contradicted for performing lumbar puncture except

a) Demyelinating diseases **b)** Infection at the site of needle insertion
c) Increased intracranial pressure **d)** Bleeding diathesis

Q3: Protein is normal in?

a) Multiple sclerosis **b)** Tuberculous meningitis
c) Viral meningitis **d)** Bacterial meningitis

Q4: Leakage of CSF into the nose?

a) Sialorrhea **b)** Otorrhea **c)** Menorrhea d) Rhinorrhea

Q5: Which of the following is an example of increase CSF total protein Due to increased permeability of the epithelial membrane?

a) Tumor **b)** Cerebral hemorrhage
c) Multiple sclerosis **d)** Traumatic tap

Q6: Which substance is lower in CSF?

a) Calcium **b)** Chloride **c)** Magnesium **d)** Sodium

SAQs :

Q1: What are Normal composition of protein and glucose in CSF?

Q2: When would Xanthochromia indicate hemorrhage?

Q3: What do increased igG and normal albumin indicate?

Q4: Name 4 indications for laboratory investigation of CSF

★ MCQs Answer key:

1) D 2) A 3) C 4) D 5) B 6) A

★ SAQs Answer key:

1) Protein (0.15 – 0.45 g/L) & Glucose (50 – 80 mg/dL)

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

3) Multiple Sclerosis, SSPE

4) 1- CNS infection, 2- Demyelinating disease, 3- CNS Malignancy, 4- Hemorrhage inn CNS

Team members

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★ سيفتح الله باباً كنت تحسبه من شدة اليأس لم يُخلق بمفتاح

438 BIOCHEMISTRY TEAM

We hear you