



# **Cerebrospinal fluid (CSF)**

## Reference Books:

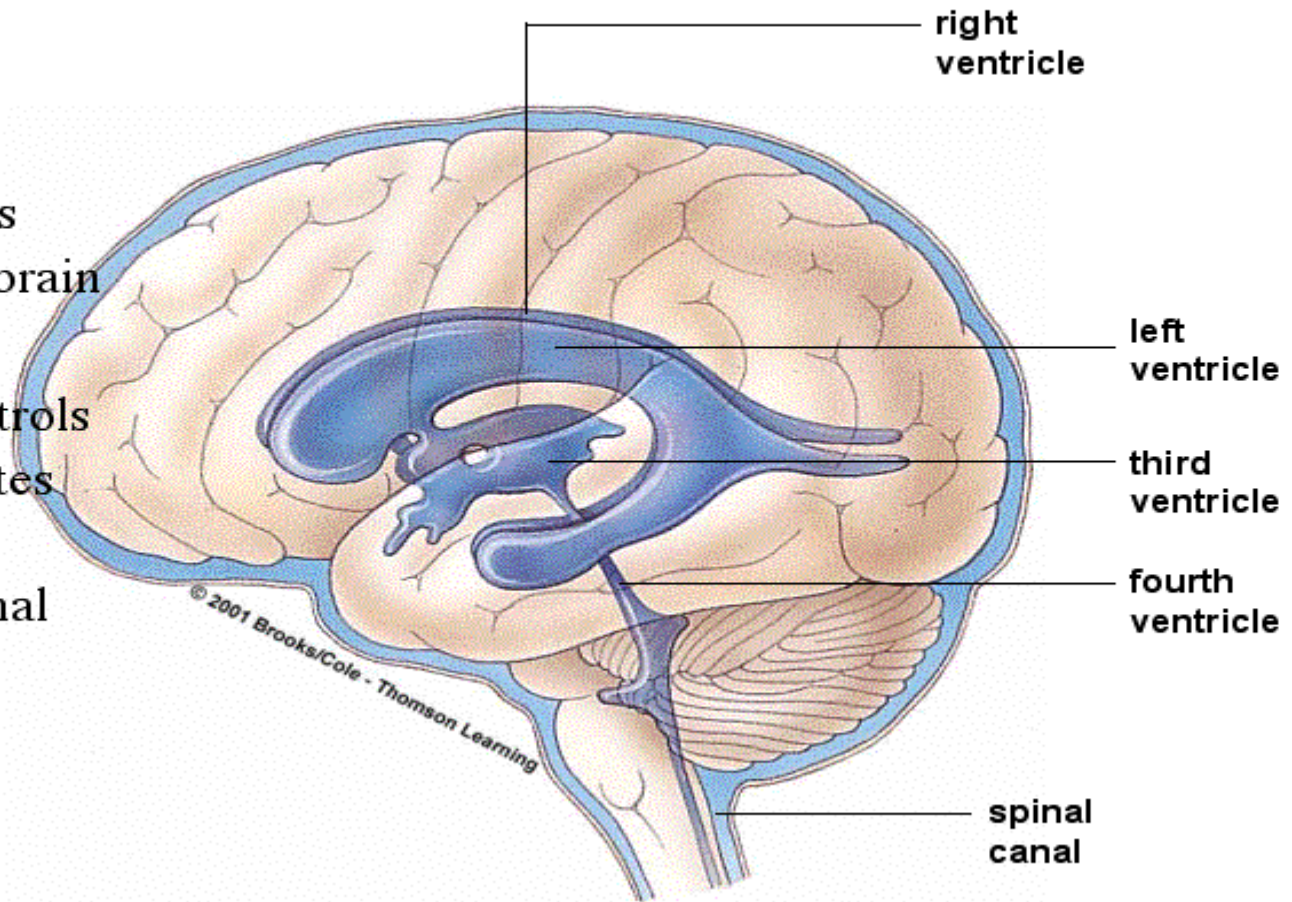
- **Urinalysis and body fluids** (Susan King Strasinger-Marjorie Schaub De Lorenzo) Fifth edition2

## Cerebrospinal fluid (CSF)

- Cerebrospinal fluid (CSF) is a major fluid of the body CSF provides a physiologic system to supply nutrients to the nervous tissue, remove metabolic wastes, and produce a mechanical barrier to cushion the brain and spinal cord against trauma.
- CSF is produced in the *choroid plexuses of the two lumbar ventricles and the third and fourth ventricles*.
- In adults, approximately 20 ml of fluid is produced every hour.
- The choroid plexuses are capillary networks that form the CSF from plasma by mechanisms of selective filtration under hydrostatic pressure and active transport secretion.

# Cerebrospinal Fluid

Surrounds the spinal cord  
Fills ventricles within the brain  
Blood-brain barrier controls which solutes enter the cerebrospinal fluid



- The chemical composition of the CSF does not resemble an ultrafiltrate of plasma. Capillary walls throughout the body are lined with endothelial cells that are loosely connected to allow passage of soluble nutrients and wastes between the plasma and tissues. In the choroid plexuses, the endothelial cells have very tight-fitting junctures that prevent the passage of many molecules. This tight-fitting structure of the endothelial cells in the choroid plexuses is termed the blood-brain barrier.

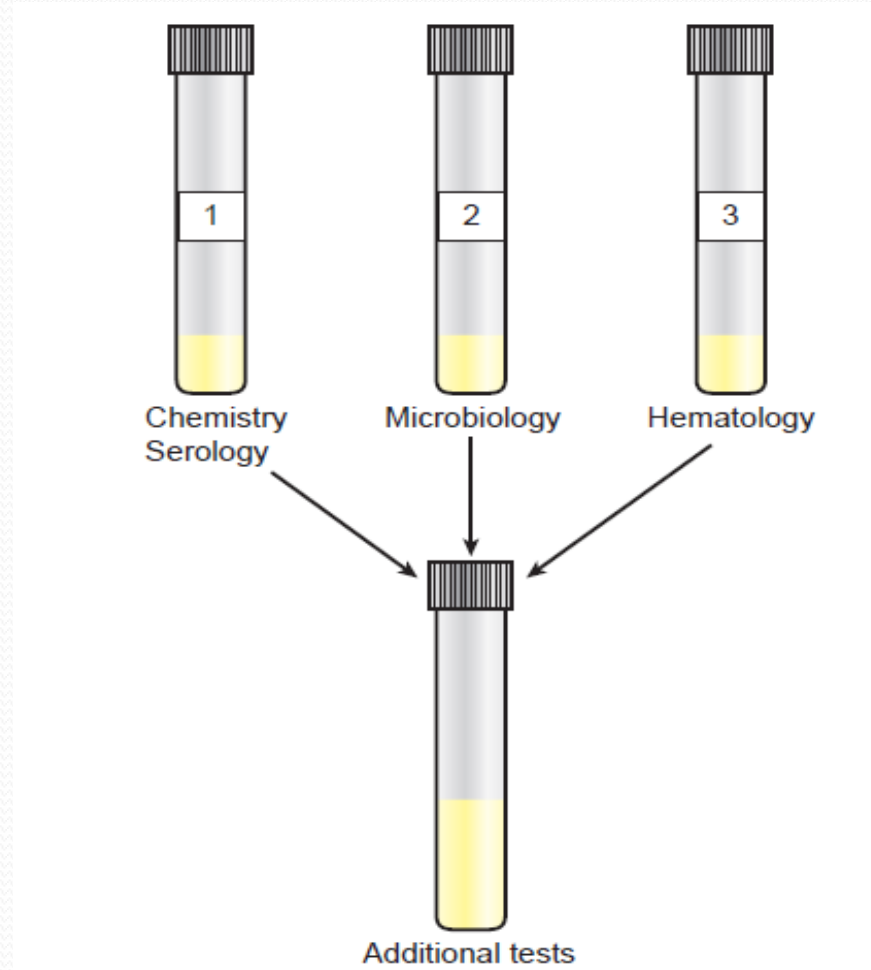
- Maintaining the integrity of the blood-brain barrier is essential to protect the brain from chemicals and other substances circulating in the blood that could harm the brain tissue. In contrast, the junctures also prevent the passage of helpful substances including antibodies and medications.

## **Specimen Collection and Handling**

- CSF is routinely collected by lumbar puncture between the third, fourth, or fifth lumbar vertebrae.

- Although this procedure is not complicated, it does require certain precautions, including measurement of the intracranial pressure and careful technique to prevent the introduction of infection or the damaging of neural tissue.
- The volume of CSF that can be removed is based on the volume available in the patient (adult vs. neonate) and the opening pressure of the CSF taken when the needle first enters the subarachnoid space. Elevated pressure requires fluid to be withdrawn slowly, with careful monitoring of the pressure, and may prevent collection of a large volume.

# Specimens are collected in three sterile tubes





- **Tube 1** is used for chemical and serologic tests because these tests are least affected by blood or bacteria introduced as a result of the tap procedure.
- **Tube 2** is usually designated for the microbiology laboratory.
- **Tube 3** is used for the cell count, because it is the least likely to contain cells introduced by the spinal tap procedure.
- **Tube 4** may be drawn for the microbiology laboratory to provide better exclusion of skin contamination or for additional serologic tests.

Radiographic contrast media

RBCs

Hemoglobin

Bilirubin

Carotene

Protein

Melanin

Protein

Clotting factors

Protein

Clotting factors

Production of IgG

Hemorrhage

Traumatic tap

Old hemorrhage

Lysed cells from tr

RBC degradation

Elevated serum bi

Increased serum l

Disorders affecting

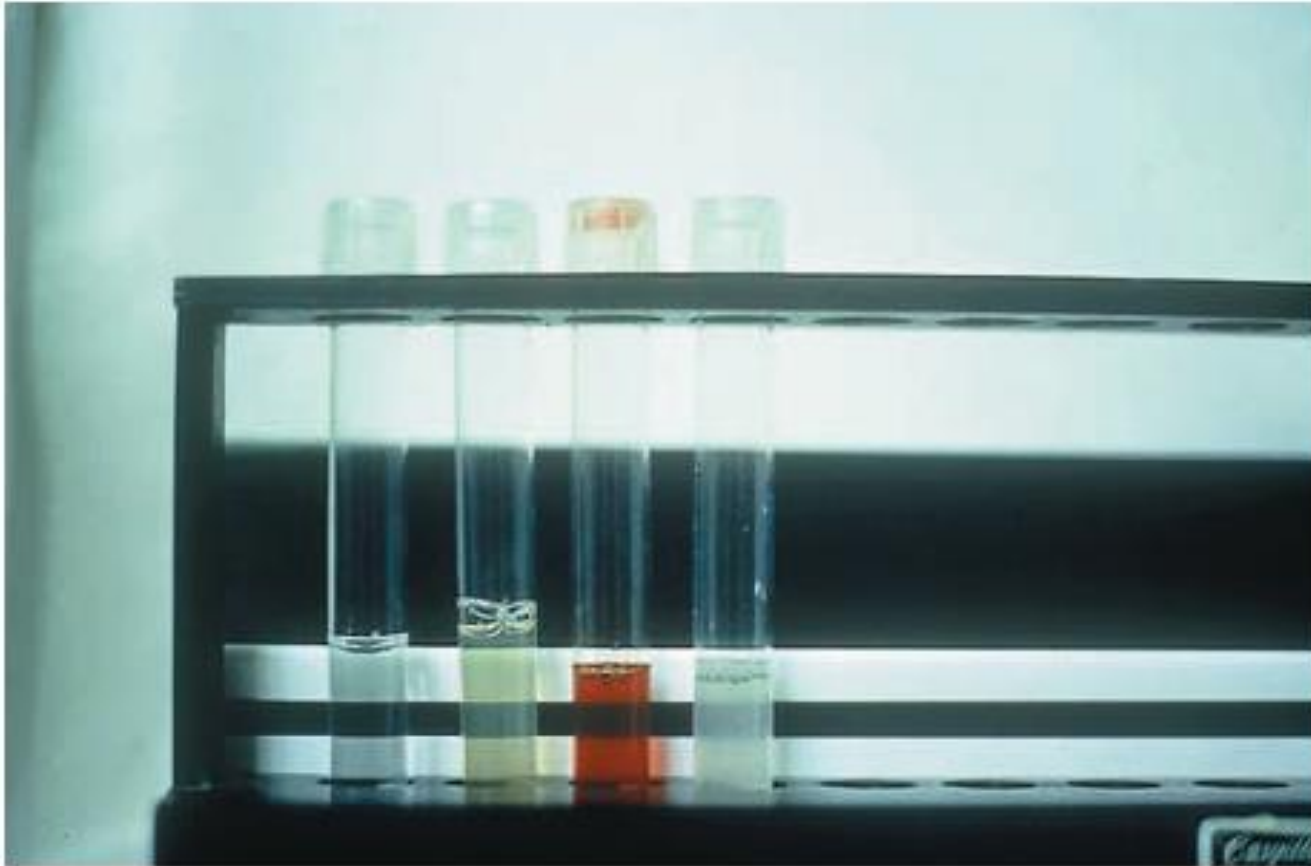
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**Tubes of CSF. Appearance left to right is normal, xanthochromic, hemolyzed, and cloudy**

## **Traumatic Collection (Tap)**

- Grossly bloody CSF can be an indication of intracranial hemorrhage, but it may also be due to the puncture of a blood vessel during the spinal tap procedure.

## **Uneven Distribution of Blood:**

- Blood from a cerebral hemorrhage will be evenly distributed throughout the three CSF specimen tubes.
- The heaviest concentration of blood in tube 1, with gradually diminishing amounts in tubes 2 and 3 in traumatic procedure.

- Streaks of blood seen in specimens acquired following a traumatic procedure.

## Clot Formation:

- Bloody CSF caused by intracranial hemorrhage does not contain enough fibrinogen to clot.
- Fluid collected from a traumatic tap may form clots owing to the introduction of plasma fibrinogen into the specimen.

## **Xanthochromic Supernatant**

RBCs must usually remain in the CSF for approximately 2 hours before noticeable hemolysis begins; therefore, a xanthochromic supernatant would be the result of blood that has been present longer than that introduced by the traumatic tap.

### **Cell Count:**

- The cell count that is routinely performed on CSF specimens is the leukocyte (WBC) count.
- The RBC count can be calculated by performing a total cell count and a WBC count and subtracting the WBC count from the total count

- Any cell count should be performed immediately, because WBCs (particularly granulocytes) and RBCs begin to lyse within 1 hour, with 40% of the leukocytes disintegrating after 2 hours.

### **Cytocentrifuge Recovery Chart**

Number of WBCs Counted in Chamber	Number of Cells Counted on Cytocentrifuge Slide
0	0–40
1–5	20–100
6–10	60–150
11–20	150–250
20	250

# Predominant Cells Seen in Cerebrospinal Fluid

Type of Cell	Major Clinical Significance	Microscopic Findings
Lymphocytes	Normal Viral, tubercular, and fungal meningitis Multiple sclerosis	All stages of development may be found
Neutrophils	Bacterial meningitis Early cases of viral, tubercular, and fungal meningitis Cerebral hemorrhage	Granules may be less prominent than in blood Cells disintegrate rapidly
Monocytes	Normal Viral, tubercular, and fungal meningitis Multiple sclerosis	Found mixed with lymphocytes
Macrophages	RBCs in spinal fluid Contrast media	May contain phagocytized RBCs appearing as empty vacuoles or ghost cells, hemosiderin granules and hemo-toidin crystals
Blast forms	Acute leukemia	Lymphoblasts, myeloblasts, or monoblasts
Lymphoma cells	Disseminated lymphomas	Resemble lymphocytes with cleft nuclei
Plasma cells	Multiple sclerosis Lymphocyte reactions	Traditional and classic forms seen
Ependymal, choroidal, and spindle-shaped cells	Diagnostic procedures	Seen in clusters with distinct nuclei and distinct cell walls
Malignant cells	Metastatic carcinomas Primary central nervous system carcinoma	Seen in clusters with fusing of cell borders and nuclei



## Chemistry Tests

### Cerebrospinal Protein

- Normal CSF contains a very small amount of protein. Normal values for total CSF protein are usually listed as 15 to 45 mg/dl.
- CSF contains protein fractions similar to those found in serum.
- Elevated total protein values are most frequently seen in pathologic conditions. Abnormally low values are present when fluid is leaking from the CNS.
- The causes of elevated CSF protein include damage to the blood-brain barrier, production of immunoglobulins within the CNS, decreased clearance of normal protein from the fluid, and degeneration of neural tissue.

## Cerebrospinal Fluid and Serum Protein Correlations

	Fluid (mg/dL)	Cerebrospinal (mg/dL)	Serum Ratio
Prealbumin	1.7	23.8	14
Albumin	15.5	3600	236
Ceruloplasmin	0.1	36.6	366
Transferrin	1.4	204	142
Immunoglobulin G	1.2	987	802
Immunoglobulin A	0.13	175	1346

Adapted from Fishman, RA: Cerebrospinal fluid in diseases of the nervous system, 2nd ed, WB Saunders, Philadelphia, 1992.

# Clinical Causes of Abnormal CSF Protein Values

## Elevated Results

- Meningitis
- Hemorrhage
- Primary CNS tumors
- Multiple sclerosis
- Guillain-Barré syndrome
- Neurosyphilis
- Polyneuritis
- Myxedema
- Cushing disease
- Connective tissue disease
- Polyneuritis
- Diabetes
- Uremia

## Decreased Results

- CSF leakage/trauma
- Recent puncture
- Rapid CSF production
- Water intoxication

## Cerebrospinal Fluid Glucose

- Glucose enters the CSF by selective transport across the blood brain barrier, which results in a normal value that is approximately 60% to 70% that of the plasma glucose. If the plasma glucose is 100 mg/dl, then a normal CSF glucose would be approximately 65 mg/dl.
- Elevated CSF glucose values are always a result of plasma elevations.
- The finding of a markedly decreased CSF glucose accompanied by an increased WBC count and a large percentage of neutrophils is indicative of bacterial meningitis.

- If the WBCs are lymphocytes instead of neutrophils, tubercular meningitis is suspected. Likewise, if a normal CSF glucose value is found with an increased number of lymphocytes, the diagnosis would favor viral meningitis.
- Decreased CSF glucose values are caused primarily by alterations in the mechanisms of glucose transport across the blood-brain barrier and by increased use of glucose by the brain cells.

## Cerebrospinal Fluid Lactate

- The determination of CSF lactate levels can be a valuable aid in the diagnosis and management of meningitis cases.
- In bacterial, tubercular, and fungal meningitis, the elevation of CSF lactate to levels greater than 25 mg/dl.
- Levels greater than 35 mg/dl are frequently seen with bacterial meningitis, whereas in viral meningitis, lactate levels remain lower than 25 mg/dl.
- CSF lactate levels remain elevated during initial treatment but fall rapidly when treatment is successful, thus offering a sensitive method for evaluating the effectiveness of antibiotic therapy.

- Destruction of tissue within the CNS owing to oxygen deprivation (hypoxia) causes the production of increased CSF lactic acid levels. Therefore, elevated CSF lactate is not limited to meningitis and can result from any condition that decreases the flow of oxygen to the tissues. CSF lactate levels are frequently used to monitor severe head injuries. RBCs contain high concentrations of lactate, and falsely elevated results may be obtained on xanthochromic or hemolyzed fluid.

## Cerebrospinal Fluid Glutamine

- Glutamine is produced from ammonia and  $\alpha$ -ketoglutarate by the brain cells. This process serves to remove the toxic metabolic waste product ammonia from the CNS.
- The normal concentration of glutamine in the CSF is 8 to 18 mg/dl.
- Elevated levels are found in association with liver disorders that result in increased blood and CSF ammonia.
- Increased synthesis of glutamine is caused by the excess ammonia that is present in the CNS; therefore, the determination of CSF glutamine provides an indirect test for the presence of excess ammonia in the CSF.



## Summary of Cerebrospinal Fluid Chemistry Tests

### Protein

1. Normal concentration is 15 to 45 mg/dL.
2. Elevated values are most frequently seen in patients with meningitis, hemorrhage, and multiple sclerosis.

### Glucose

1. Normal value is 60% to 70% of the plasma concentration.
2. Decreased levels are seen in patients with bacterial, tubercular, and fungal meningitis.

### Lactate

1. Levels  $>35$  mg/dL are seen in patients with bacterial meningitis.
2. Levels  $>25$  mg/dL are found in patients with tubercular and fungal meningitis.
3. Lower levels are seen in patients with viral meningitis.

### Glutamine

1. Normal concentration is 8 to 18 mg/dL.
2. Levels  $>35$  mg/dL are associated with some disturbance of consciousness.

# Major Laboratory Results for the Differential Diagnosis of Meningitis

Bacterial	Viral	Tubercular	Fungal
Elevated WBC count	Elevated WBC count	Elevated WBC count	Elevated WBC count
Neutrophils present	Lymphocytes present	Lymphocytes and monocytes present	Lymphocytes and monocytes present
Marked protein elevation	Moderate protein elevation	Moderate to marked protein elevation	Moderate to marked protein elevation
Markedly decreased glucose level	Normal glucose level	Decreased glucose level	Normal to decreased glucose level
Lactate level >35 mg/dL	Normal lactate level	Lactate level >25 mg/dL Pellicle formation	Lactate level >25 mg/dL Positive India ink with <i>Cryptococcus neoformans</i>
Positive Gram stain and bacterial antigen tests			Positive immunologic test for <i>C. neoformans</i>