

Cerebrospinal fluid

By
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CSF

- CSF is a colorless, clear liquid that fills the ventricles (cavities) of the brain and the spinal cord.
- Acts as lubricant and a mechanical barrier against shock
- About 100 – 150 ml in adults
- 10 – 60 ml in infants - children
- It is mainly 99% water
- It has low amounts of protein and lipids compared to blood

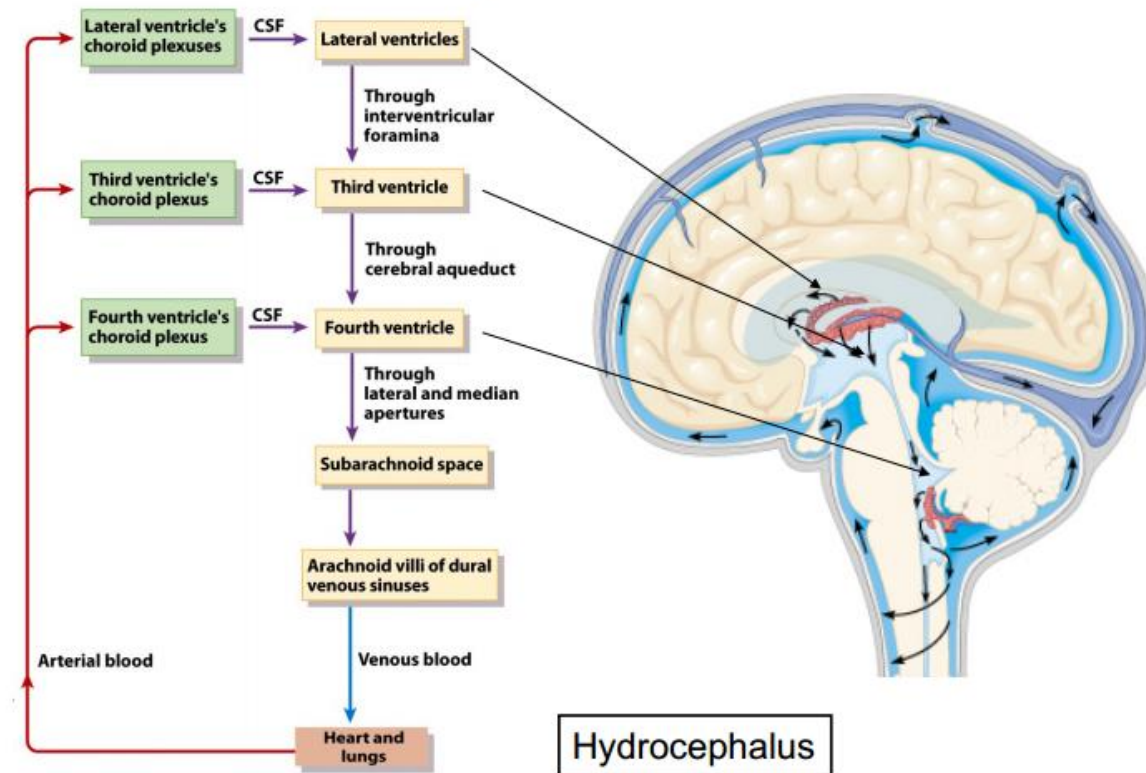
CSF

- **Formations**
- Basically CSF is a secretion product of ultra filtration of blood
- Its composition is the result of material exchange between blood and adjacent brain tissue
- Circulates through the foramen of Monro from the two lateral ventricles to the third ventricle.
- Some of the CSF travels down the central canal of the spinal cord.

CSF

- Circulation

Pathway of CSF flow



CSF

- **Functions**
- The central nervous system (CNS) : Brain and spinal cord are floating by the cerebrospinal fluid medium.
- This provides CNS with support and protection against rapid movements and trauma by acting as cushion
- CSF provides nutrition for both neuron and glial cells
- CSF functions as lymphatic system by providing medium for removing waste products of metabolism of CNS cells

CSF

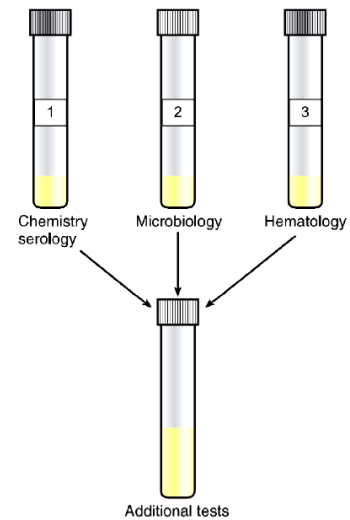
- **Functions**
- CSF plays role in maintaining the microenvironment like ionic concentration
- Might serve as transport system of biological active substances like co-factors, hormones, neurotransmitters and several metabolites
- As CSF and extracellular space of brain are in continuity, analysis of CSF provides information about the normal and pathological state of CNS function

CSF

- **Sample collection**
- Lumbar puncture or spinal tap is the most common procedure of collecting CSF
- Patient positioned on side with knees and chin tucking towards abdomen
- Occasionally can be done in sitting position bending forward
- Sterile conditions has to practiced throughout the procedure
- 10-20 ml can be collected as required

CSF

- **Sample collection**
- Sample must be collected under sterile conditions
- Proper labeling should be done before collecting
- Immediate examination is required
- Usually collected in 3 tubes
 - Chemical analysis
 - Microbiology
 - Cell count



CSF

- Purpose of CSF analysis
- To diagnose medical disorders that affect CNS
- Viral and bacterial infections
 - Meningitis and encephalitis
- Tumors or cancers of CNS
- Hemorrhage around brain and spine
- Multiple sclerosis
- Syphilis – a type of STD

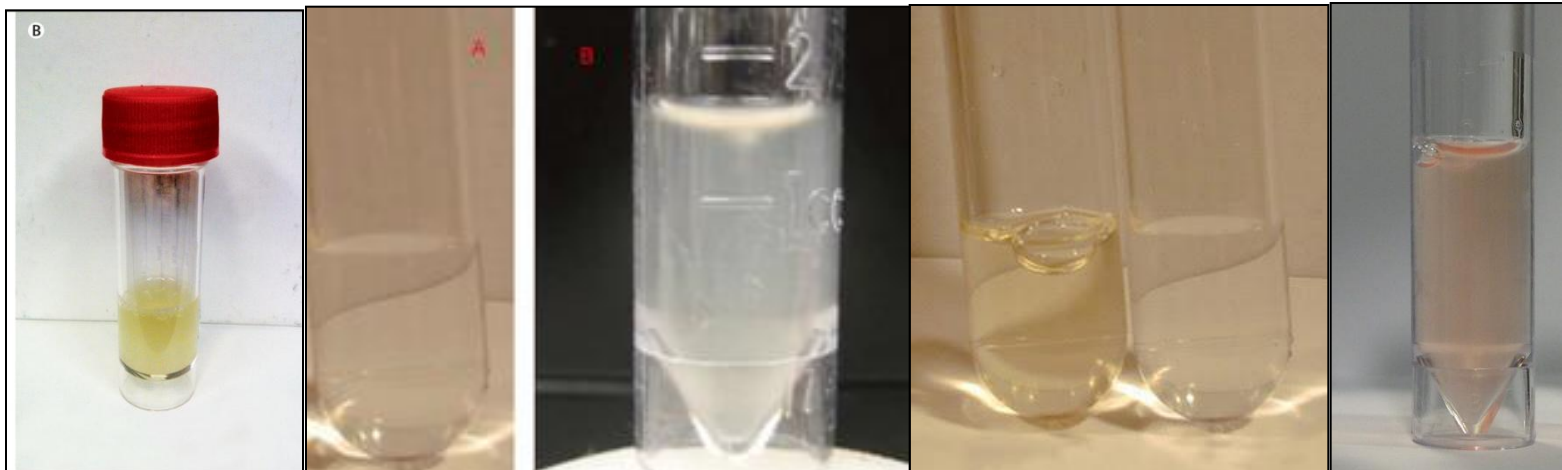
CSF

- Purpose of CSF analysis

Collect in Tube #1-4	Routine Test Request	Minimum Volume Required per Test		Additional Test Requests	Minimum Volume Required per Test	
		Adults/Children	Neonates		Adults/Children	Neonates
#1 Hematology ¹	Refer to Note 1	1.0 mL	0.5 mL			
#2 Microbiology	Aerobic C&S includes Gram Stain	1.0 mL	N/A	Cryptococcal Antigen	1.0 mL	0.5 mL
	Anaerobic² C&S Includes Aerobic Culture and Gram Stain	1.0 mL	0.2 mL	Fungal Culture³ , includes Cryptococcal Antigen and Calcofluor White Stain	3.0 mL	1.5 mL
				Acanthamoeba⁴ culture	10.0 mL	N/A
#3 Reference Microbiology* Esoteric Testing	Refer to minimum volumes required for specific test requests; also refer to: CLS Guide to Laboratory Services Alphabetical Test Directory			AFB⁵ Culture , includes special stains	3.0 mL	N/A
				Viral Culture⁶	0.5 mL	0.2 mL
				Viral PCR⁶	1.0 mL	0.5 mL
				West Nile Virus⁶ (WNV)	1.0 mL	N/A
				Creutzfeldt-Jacob Disease⁶ (CJD) (14-3-3 Protein)	3.0 mL	N/A
#4 Hematology and Chemistry	Cell Count/ Differential	1.0 mL	0.5 mL	Flow Cytometry	2.0 – 10.0 mL	1.0 mL
	Total Protein	0.2 mL	0.1 mL	Cytopathology⁷	2.0 mL	1.0 mL
	Glucose	0.2 mL	0.1 mL	Immunoglobulin Index	0.2 mL	N/A
				Oligoclonal Banding (Electrophoresis – serum sample also required)	3.0 mL	N/A
				Albumin	0.2 mL	0.1 mL
				Lactate	0.2 mL	N/A
				pH	0.5 mL	N/A
			Lactate dehydrogenase	0.2 mL	N/A	

CSF analysis

Physical examination	Color :
Appearance	<p>Normal CSF is colorless clear liquid. Looks almost similar to water (crystal clear)</p> <p>Cloudy or turbid, milky appearance indicate abnormal conditions like presence of RBC, microorganisms etc.....</p>
Specific gravity	1.006 – 1.008



CSF analysis

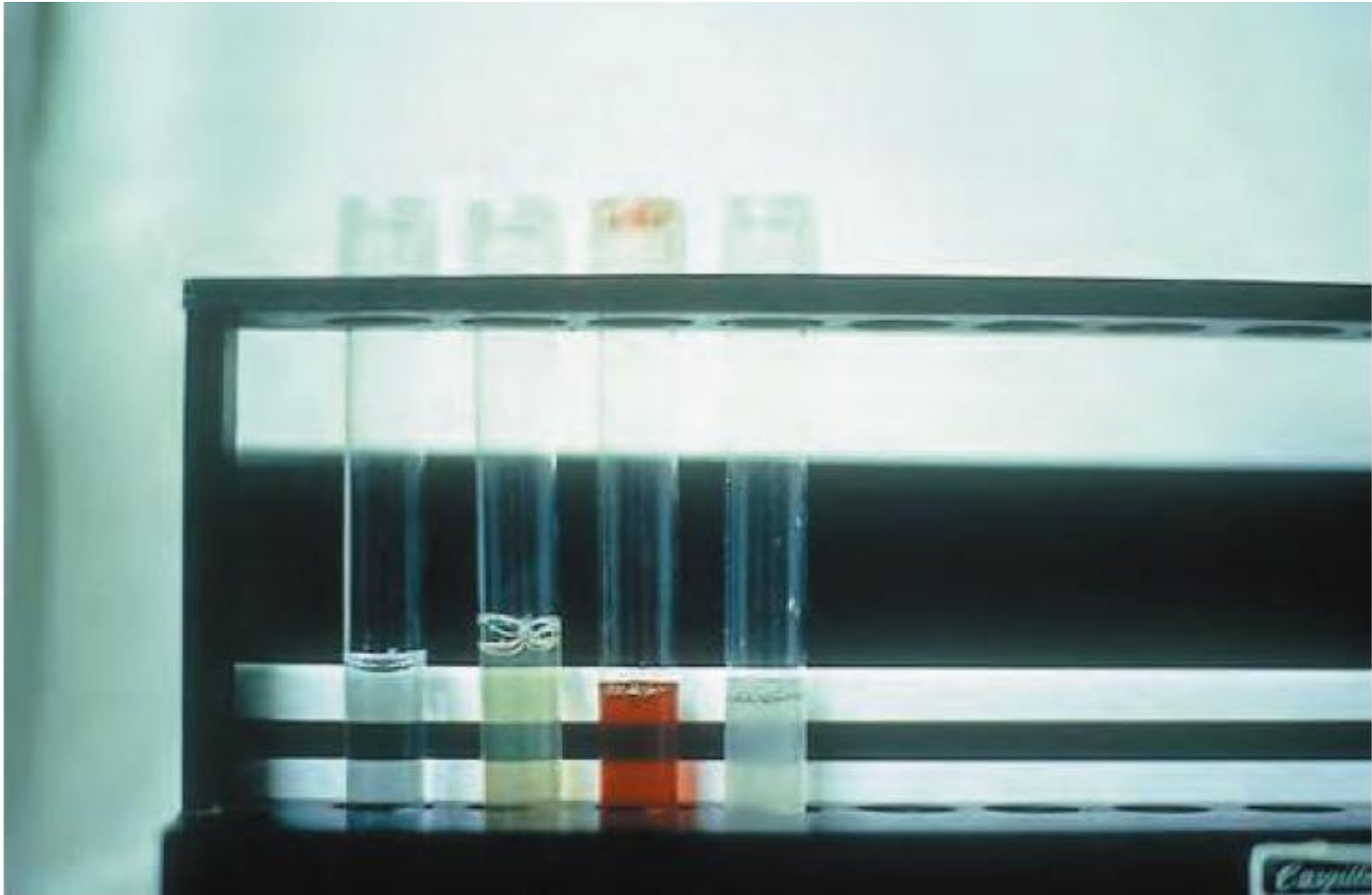


Figure 9-4 Tubes of CSF. Appearance left to right is normal, xanthochromic, hemolyzed, and cloudy.

CSF analysis

Physical examination	Color :
Appearance	Xanthochromic CSF <ul style="list-style-type: none">• Xanthochromia is a term used to indicate pink/orange/yellow CSF which may be caused by the following conditions• Oxyhemoglobin from lysed RBC present before spinal tap or traumatic spinal tap• Bilirubin from lysed RBC or direct bilirubin with normal blood-brain barrier or in immature infants• High protein levels because of traumatic tap• Contamination from disinfectants used• Carotinoids in CSF due to hypercarotenemia• Melamin in CSF because of meningeal melanosaarcoma

CSF analysis

Physical examination	Color :
Appearance	Bloody appearance <ul style="list-style-type: none">• Highly bloody CSF indicate hemorrhage• It can also be due to puncture of blood vessel during spinal tap• It can be differentiated by....• Uneven distribution of blood : traumatic tap shows more blood in last sample• traumatic tap often shows clear supernatant after brief centrifugation• Traumatic tap shows clot formation• Care should be taken while reporting• A recent hemorrhage would have the same properties as blood vessel damage

CSF analysis

Physical examination - summary

Table 9-1 Clinical Significance of CSF Appearance

Appearance	Cause	Major Significance
Crystal clear		Normal
Hazy, turbid, milky, cloudy	WBCs	Meningitis
	Microorganisms	Meningitis
	Protein	Disorders affecting blood-brain barrier Production of IgG within the CNS
Oily	Radiographic contrast media	
Bloody	RBCs	Hemorrhage Traumatic tap
		Xanthochromic
Xanthochromic	Hemoglobin	Old hemorrhage Lysed cells from traumatic tap
	Bilirubin	RBC degradation Elevated serum bilirubin level
	Carotene	Increased serum levels
	Protein	Disorders affecting blood-brain barrier
Clotted	Melanin	Meningeal melanosaarcoma
	Protein	Disorders affecting blood-brain barrier
	Clotting factors	Introduced by traumatic tap

CSF analysis

Chemical examination

pH

Normal CSF is alkaline in nature as plasma

Spontaneous clotting

- Occurs when there is an excess of fibrinogen in the specimen.
- This usually associated with high protein concentration
- Classically this is associated with tuberculous meningitis or tumors in CNS

CSF analysis

Chemical examination

- CSF is formed by filtration of plasma
- Same chemicals can be found in CSF as plasma
- However because of selective filtration process and the chemical composition is adjusted by the blood brain barrier, normal values of CSF chemicals are not the same as plasma values
- Abnormal values can be attributed to alterations in the permeability of blood-brain barrier or increased metabolism by neuronal cells in response to pathological condition
- Rarely chemical properties are checked

Lactate

- Measurement of lactate may be useful as part of investigation of inborn errors of metabolisms like
- Disorders of gluconeogenesis
 - Disorders of pyruvate dehydrogenase complex
 - Disorders of Krebs cycle and ETC
 - Also in children with neurological diseases

CSF analysis

Chemical examination

Proteins

Most frequently done test is protein determination. Normal CSF has very low amount.

- Normal CSF protein is less than 1% of plasma
- Usually 15 – 45 mg / dl

Elevated protein can be found in

- Froin's syndrome – complete spinal block)
- Cerebral tumors
- Meningitis
- In all diseases there is decreased clearance of normal protein, and degeneration of neural tissue.
- Increased local synthesis of Immunoglobulins
- Increased capillary permeability due to blood brain barrier damage

CSF analysis

Chemical examination

IgG – albumin index

The IgG-albumin index can be used to distinguish diseases affecting **permeability (meningitis, cerebral infarctions, tumors of the brain)** from diseases resulting in **increased immunoglobulin (usually IgG) synthesis** (multiple sclerosis) and some inflammatory diseases (idiopathic polyneuropathies). A normal range for this index has been proposed to be 0.34-0.58. In diseases associated with increased IgG production, the ratio is elevated, whereas in diseases affecting CSF permeability, the ratio is decreased because of increased CSF albumin concentration. Some disorders can affect both CSF IgG concentration and blood permeability.

CSF analysis

Chemical examination

Glucose

Glucose enters CSF by active transport across blood brain barrier. CSF glucose is little lower than that of Plasma and is usually 60-70% of plasma
Relative comparison has to be done with blood glucose

Low CSF glucose can be of considerable diagnostics value in determining the causative agents in meningitis

- An increased WBCs with large percentage of neutrophils indicate bacterial meningitis
- WBCs count and later percentage of T cells indicate tubercular meningitis

- Low glucose values can be associated with diseases of glucose transport, utilization of glucose by brain cells, bacteria and leukocytes

CSF analysis

Chemical examination summary

Chemical Substance	Reference Concentration Value, Normal CSF	Significance of Increased Concentration	Significance of Decreased Concentration
Protein	15 to 45 mg/dL	Meningitis Hemorrhage Multiple sclerosis	CSF leakage
Glucose	60% to 70% of plasma concentration	None	Bacterial, tubercular, and fungal meningitis
Lactate	10 to 24 mg/dL	>35 mg/dL: Bacterial meningitis	None
Glutamine	8 to 18 mg/dL	>35 mg/dL: Some disturbance of consciousness	None

CSF analysis

Microscopic examination

Stain & culture

Acid-fast for TB or Immunofluorescence staining for cryptococci

CSF can be cultured aerobically and anaerobically for acid-fast bacilli and fungi

Serological examination

For enterovirus.

Viruses are rarely isolated from CSF

Can be tested with antibody panels

VDRL and cryptococcal tests are often performed

CSF analysis

Table 9–6 Major Laboratory Results for 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	Lactate level >25 mg/dL
		Pellicle formation	Positive India ink with <i>Cryptococcus neoformans</i>
Positive Gram stain and bacterial antigen tests			Positive immunologic test for <i>C. neoformans</i>

Next class

Cystic fibrosis & sweat analysis	