Cerebrospinal fluid

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Cerebrospinal fluid (**CSF**) is a clear colorless bodily fluid produced in the choroid plexus of the brain. It acts as a cushion or buffer for the cortex, providing a basic mechanical and immunological protection to the brain inside the skull and serves a vital function in cerebral autoregulation of cerebral blood flow.

The CSF occupies the subarachnoid space (the space between the arachnoid mater and the pia mater) and the ventricular system around and inside the brain and spinal cord. It constitutes the content of the ventricles, cisterns, and sulci of the brain, as well as the central canal of the spinal cord.

Vials containing human cerebrospinal fluid.

Contents

Functions

CSF serves four primary purposes:

1. **Buoyancy:** The actual mass of the human brain is about 1400 grams; however, the net weight of the brain suspended in the CSF is equivalent to a mass of 25 grams.[1] The brain therefore exists in neutral buoyancy, which allows the brain to maintain its density without being impaired by its own weight, which would cut off blood supply and kill neurons in the lower sections without CSF.[2]
2. **Protection:** CSF protects the brain tissue from injury when jolted or hit. In certain situations such as auto accidents or sports injuries, the CSF cannot protect the brain from forced contact with the skull case, causing hemorrhaging, brain damage, and sometimes death.[2]
3. **Chemical stability:** CSF flows throughout the inner ventricular system in the brain and is absorbed back into the bloodstream, rinsing the metabolic waste from the central nervous system through the blood–brain barrier. This allows for homeostatic regulation of the distribution of neuroendocrine factors, to which slight changes can cause problems or damage to the nervous system. For example, high glycine concentration disrupts temperature and blood pressure control, and high CSF pH causes dizziness and syncope.[2] To use Davson's term, the CSF has a "sink

action" by which the various substances formed in the nervous tissue during its metabolic activity diffuse rapidly into the CSF and are thus removed into the bloodstream as CSF is absorbed.[3]

4. **Prevention of brain ischemia:** The prevention of brain ischemia is made by decreasing the amount of CSF in the limited space inside the skull. This decreases total intracranial pressure and facilitates blood perfusion.

History

Various comments by ancient physicians have been read as referring to CSF. Hippocrates discussed "water" surrounding the brain when describing congenital hydrocephalus, and Galen referred to "excremental liquid" in the ventricles of the brain, which he believed was purged into the nose. But for some 16 intervening centuries of ongoing anatomical study, CSF remains unmentioned in the literature. This is perhaps because of the prevailing autopsy technique, which involved cutting off the head, thereby removing evidence of the CSF before the brain was examined. The modern rediscovery of CSF is now credited to Emanuel Swedenborg. In a manuscript written between 1741 and 1744, unpublished in his lifetime, Swedenborg referred to CSF as "spirituous lymph" secreted from the roof of the fourth ventricle down to the medulla oblongata and spinal cord. This manuscript was eventually published in translation in 1887.[4]

Albrecht von Haller, a Swiss physician and physiologist made note in his 1747 book on physiology that the "water" in the brain was secreted into the ventricles and absorbed in the veins, and when secreted in excess, could lead to hydrocephalus.[4]

Francois Magendie studied the properties of CSF by vivisection. He discovered the foramen Magendie, the opening in the roof of the fourth ventricle, but mistakenly believed that CSF was secreted by the pia mater.[4]

Thomas Willis (noted as the discoverer of the circle of Willis) made note of the fact that the consistency of the CSF is altered in meningitis.[4]

In 1891, W. Essex Wynter began treating tubercular meningitis by tapping the subarachnoid space, and Heinrich Quincke began to popularize lumbar puncture, which he advocated for both diagnostic and therapeutic purposes.[4] In 19th and early 20th century literature, particularly German medical literature, *liquor cerebrospinalis* was a term used to refer to CSF.

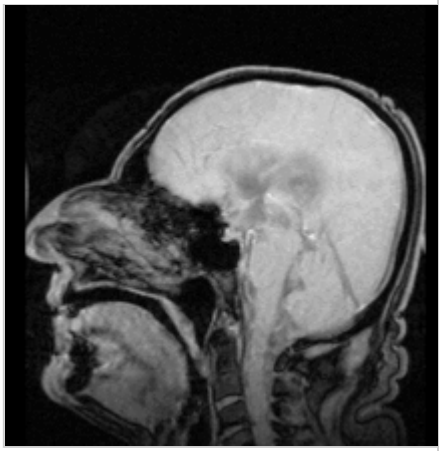
In 1912, William Mestrezat gave the first accurate description of the chemical composition of the CSF. In 1914, Harvey W. Cushing published conclusive evidence that the CSF is secreted by the choroid plexus.[4]

Circulation

CSF is produced in the brain by modified ependymal cells in the choroid plexus (approx. 50-70%) and the remainder is formed around blood vessels and along ventricular walls. It circulates from the lateral ventricles to the foramina of Monro (Interventricular foramina), third ventricle, aqueduct of Sylvius (Cerebral aqueduct), fourth ventricle, foramen of Magendie (Median aperture) and foramina of Luschka (Lateral apertures), subarachnoid space over brain and spinal cord. It should be noted that the CSF moves in a pulsatile manner throughout the CSF system with nearly zero net flow. CSF is reabsorbed into venous sinus

blood via arachnoid granulations.

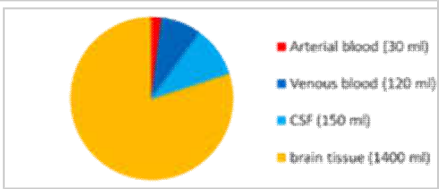
It had been thought that CSF returns to the vascular system by entering the dural venous sinuses via the arachnoid granulations (or villi). However, some[5] have suggested that CSF flow along the cranial nerves and spinal nerve roots allow it into the lymphatic channels; this flow may play a substantial role in CSF reabsorbtion, in particular in the neonate, in which arachnoid granulations are sparsely distributed. The flow of CSF to the nasal submucosal lymphatic channels through the cribriform plate seems to be especially important.[6]



MRI showing pulsation of CSF

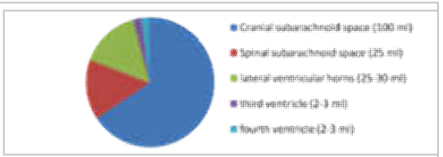
Amount and constitution

The CSF contains approximately 0.3% plasma proteins, or approximately 15 to 40 mg/dL, depending on sampling site,[7] and it is produced at a rate of 500 ml/day. Since the subarachnoid space around the brain and spinal cord can contain only 135 to 150 ml, large amounts are drained primarily into the blood through arachnoid granulations in the superior sagittal sinus. Thus the CSF turns over about 3.7 times a day. This continuous flow into the venous system dilutes the concentration of larger, lipid-insoluble molecules penetrating the brain and CSF.[8]



Intracranial volumetric distribution of cerebrospinal fluid, blood, and brain parenchyma

CSF pressure, as measured by lumbar puncture (LP), is 10-18 cmH_2O (8-15 mmHg or 1.1-2 kPa) with the patient lying on the side and 20-30cmH_2O (16-24 mmHg or 2.1-3.2 kPa) with the patient sitting up.[9] In newborns, CSF pressure ranges from 8 to 10 cmH_2O (4.4–7.3 mmHg or 0.78–0.98 kPa). Most variations are due to coughing or internal compression of jugular veins in the neck. When lying down, the cerebrospinal fluid as estimated by lumbar puncture is similar to the intracranial pressure.



Volumetric distribution of cerebrospinal fluid

There are quantitative differences in the distributions of a number of proteins in the CSF. In general, globular proteins and albumin are in lower concentration in ventricular CSF compared to lumbar or cisternal fluid.[10] The *IgG index* of cerebrospinal fluid is a measure of the immunoglobulin G content, and is elevated in multiple sclerosis. It is defined as $IgG\ index = (IgG_{CSF} / IgG_{serum}) / (albumin_{CSF} / albumin_{serum})$.[11] A cutoff value has been suggested to be 0.73, with a higher value indicating presence of multiple sclerosis.[11]

Reference ranges

Reference ranges for ions and metals in CSF

Substance	Lower limit	Upper limit	Unit	Corresponds to % of that in plasma
Osmolality	280[12]	300[12]	mmol/L	
Sodium	135[12]	150[12]	mmol/L	

Potassium	2.6[12]	3.0[12]	mmol/L
Chloride	115[12]	130[12]	mmol/L >100%[12]
Calcium	1.00[12]	1.40[12]	mmol/L ~50%[12]
Magnesium	1.2[12]	1.5[12]	mmol/L >100%[12]
Iron	0.2[12]	0.4[12]	µmol/L

Reference ranges for other molecules in CSF

Substance	Lower limit	Upper limit	Unit	Corresponds to % of that in plasma
Glucose	50[13]	80[13]	mg/dL	~60%[12]
	2.2,[14] 2.8 [12]	3.9,[14] 4.4 [12]	mmol/L	
Protein	15[12][13]	40,[7] 45[12] [13]	mg/dL	~1%[12]
Albumin	7.8[15]	40[15]	mg/dL	0[16] - 0.7%[16] - corresponding to an *albumin (CSF/serum) quotient* of 0 to $7x10^{-3}$
Lactate	1.1[12]	2.4[12]	mmol/L	
Creatinine	50[12]	110[12]	µmol/L	
Phosphorus	0.4[12]	0.6[12]	µmol/L	
Urea	3.0[12]	6.5[12]	mmol/L	
Carbon dioxide	20[12]	25[12]	mmol/L	

Reference ranges for other CSF constituents

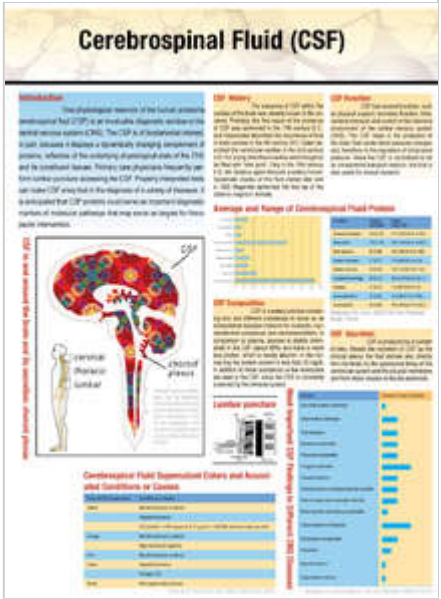
Substance	Lower limit	Upper limit	Unit	Corresponds to % of that in blood plasma
RBCs	n/a[13]	0[13] / negative	cells/µL or cells/mm^3	
WBCs	0[13]	3[13]	cells/µL cells/mm^3	
pH	7.28[12]	7.32[12]	(-log M)	
PCO_2	44[12]	50[12]	mmHg	
	5.9[17]	6.7[17]	kPa	
PO_2	40[12]	44[12]	mmHg	
	5.3[17]	5.9[17]	kPa	

Pathology and laboratory diagnosis

When CSF pressure is elevated, cerebral blood flow may be constricted. When disorders of CSF flow occur, they may therefore affect not only CSF movement but also craniospinal compliance and the intracranial blood flow, with subsequent neuronal and glial vulnerabilities. The venous system is also important in this equation. Infants and patients shunted as small children may have particularly unexpected relationships between pressure and ventricular size, possibly due in part to venous pressure dynamics. This may have significant treatment implications, but the underlying pathophysiology needs to be further explored.

CSF connections with the lymphatic system have been demonstrated in several mammalian systems.

Preliminary data suggest that these CSF-lymph connections form around the time that the CSF secretory capacity of the choroid plexus is developing (in utero). There may be some relationship between CSF disorders, including hydrocephalus and impaired CSF lymphatic transport.



Cerebrospinal fluid (CSF) at glance.

CSF can be tested for the diagnosis of a variety of neurological diseases.[18] It is usually obtained by a procedure called lumbar puncture. Removal of CSF during lumbar puncture can cause a severe headache after the fluid is removed, because the brain hangs on the vessels and nerve roots, and traction on them stimulates pain fibers. This pain can be relieved by intrathecal injection of sterile isotonic saline. Lumbar puncture is performed in an attempt to count the cells in the fluid and to detect the levels of protein and glucose. These parameters alone may be extremely beneficial in the diagnosis of subarachnoid hemorrhage and central nervous system infections (such as meningitis). Moreover, a CSF culture examination may yield the microorganism that has caused the infection. By using more sophisticated methods, such as the detection of the oligoclonal bands, an ongoing inflammatory condition (for example, multiple sclerosis) can be recognized. A beta-2 transferrin assay is highly specific and sensitive for the detection for, e.g., CSF leakage.

Cause	Appearance	Polymorphonuclear Leukocytes	Lymphocytes	Protein	Glucose
Pyogenic bacterial meningitis	Yellowish, turbid	Markedly increased	Slightly increased or Normal	Markedly increased	Decreased
Viral meningitis	Clear fluid	Slightly increased or Normal	Markedly increased	Slightly increased or Normal	Normal
Tuberculous meningitis	Yellowish and viscous	Slightly increased or Normal	Markedly increased	Increased	Decreased
Fungal meningitis	Yellowish and viscous	Slightly increased or Normal	Markedly increased	Slightly increased or Normal	Normal or decreased

Lumbar puncture

Lumbar puncture can also be performed to measure the intracranial pressure, which might be increased in certain types of hydrocephalus. However a lumbar puncture should never be performed if increased intracranial pressure is suspected because it can lead to brain herniation and ultimately death.

Baricity

This fluid has an importance in anesthesiology. Baricity refers to the density of a substance compared to

the density of human cerebrospinal fluid. Baricity is used in anesthesia to determine the manner in which a particular drug will spread in the intrathecal space.

Alzheimer's disease

A 2010 study showed analysis of CSF for three protein biomarkers can indicate the presence of Alzheimer's disease. The three biomarkers are CSF amyloid beta 1-42, total CSF tau protein and P-Tau_{181P}. In the study, the biomarker test showed good sensitivity, identifying 90% of persons with Alzheimer's disease, but poor specificity, as 36% of control subjects were positive for the biomarkers. The researchers suggested the low specificity may be explained by developing but not yet symptomatic disease in controls.[19][20]

See also

- Ventricular system
- Meningitis
- CSF rhinorrhea
- Lumbar puncture
- Hydrocephalus
- Craniosacral therapy
- Neuroglobin
- Pandy's test

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External links

- Circulation of Cerebrospinal Fluid (CSF) - Interactive Tool
- Cerebrospinal fluid

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