The physiology of CSF is a complex topic, and treatment for hydrocephalus typically depends on its cause.

Cerebrospinal Fluid and Hydrocephalus: Physiology, Diagnosis, and Treatment

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Background: Cerebrospinal fluid (CSF) is found around and inside the brain and vertebral column. CSF plays a crucial role in the protection and homeostasis of neural tissue.

Methods: Key points on the physiology of CSF as well as the diagnostic and treatment options for hydrocephalus are discussed.

Results: Understanding the fundamentals of the production, absorption, dynamics, and pathophysiology of CSF is crucial for addressing hydrocephalus. Shunts and endoscopic third ventriculostomy have changed the therapeutic landscape of hydrocephalus.

Conclusions: The treatment of hydrocephalus in adults and children represents a large part of everyday practice for the neurologist, both in benign cases and cancer-related diagnoses.

Cerebrospinal Fluid Production

Approximately 70% of cerebrospinal fluid (CSF) is produced by the choroid plexus of the lateral ventricles and the tela choroidea of the third and fourth ventricles. There is also extrachoroidal secretion of CSF by the epithelium of the ependyma and by the capillaries via the blood–brain barrier. Choroid plexus can develop as early as the 41st day in the embryo.

In general, the volume of CSF in an adult is approximately 150 mL (125 mL in the subarachnoid space, 25 mL in the ventricles), whereas the total volume of CSF is 50 mL in newborns. The daily amount of CSF secreted is 500 mL, meaning that CSF is renewed 3 times every 24 hours.

Function

Spector et al. studied the multiple functions of CSF, noting that CSF serves as a cushion for the brain and provides buoyancy. The average adult brain alone weighs more than 1000 g, but this force is effectively 10 to 15 times less with CSF. Because molecules are circulated through the blood–brain and blood–CSF barriers, the neural tissue is nourished and toxic products of metabolism are carried away.

Absorption and Circulation

The CSF circulates from the lateral ventricles through the interventricular foramina to the third ventricle and then via the cerebral aqueduct into the fourth ventricle. From there, via the 2 lateral apertures and median aperture, it enters the subarachnoid space and is distributed into the cerebral hemispheres and around the spinal cord. The spinal cord has a thin...
central canal that also contains CSF and contributes to the distribution of CSF within the vertebral column.

The sites of CSF absorption are mainly the arachnoid villi in the superior sagittal sinus. The arachnoid villi are protrusions of the arachnoid layer into the sinus and are lined with epithelium. The villi are thought to function as valves.

Additional sites of CSF absorption include the spinal arachnoid villi close to the epidural spinal veins and the meningeal sheaths of the spinal and cranial nerves. Lymphatics located proximal to arteries and nerves are also part of the mechanism of CSF absorption.

**Composition**
The CSF is a clear, colorless liquid. In an average adult lying down, the opening pressure of CSF as measured via lumbar puncture is approximately 10 to 20 cm H$_2$O; in a sitting individual, this pressure ranges from 20 to 30 cm H$_2$O; in children and newborns, the range is lower.

In general, the CSF of an adult has fewer than 5 white blood cells, a plasma glucose level of 60% to 80%, and a protein level of 20 to 40 mg/100 mL, although significant differences can be observed depending on where the collection of CSF was obtained. The protein level will be higher if the collection is obtained via lumbar puncture than if obtained via a ventricular tap.

In clinical practice, it is useful to have a method for distinguishing between CSF and other fluids, especially in questionable cases of CSF leak. The ratio of β-2 transferrin protein in the fluid to the serum has been proven to deliver accurate results.

**Dynamics of Circulation**
A detailed description of the dynamics of CSF is beyond the scope of this paper. Marmarou et al. have pioneered research in this field. Briefly, 3 components are important for the dynamics of CSF, namely the (1) formation, (2) storage, and (3) absorption of CSF. In general, the formation of CSF is considered to be constant under normal circumstances. The storage of CSF is proportional to the compliance of the ventricles. The reabsorption is proportional to the pressure gradient between CSF and the sagittal sinus and inversely proportional to flow resistance. Volumetrically, the production of CSF is equal to the storage added to absorption. Based on the equation of Marmarou et al. for intracerebral pressure, an increase in the production of CSF or outflow resistance at the level of the arachnoid villi or at the dural sinus can lead to higher intracerebral pressure.

**Blood–Brain Barrier and Blood–Cerebrospinal Fluid Barrier**
The blood–CSF barrier consists of tight junctions at the epithelial cells of the choroid villi that project into the sinus. Similarly, the blood–brain barrier separates the brain tissue from the surrounding blood vessels. Both barriers selectively allow the passage of different molecules.

**Hydrocephalus**

**Classification**
Hydrocephalus is defined as the accumulation of an abnormal quantity of CSF in the ventricles. However, this description is oversimplified because hydrocephalus is multifactorial. In textbooks of neurosurgery, numerous classification schemes can be found. Generally, hydrocephalus falls into the obstructive or communicating group.

External hydrocephalus is considered to be a separate entity. The condition refers to abnormal collections of CSF over the hemispheres and is a form of communicating hydrocephalus. It can be caused by infection, trauma, or prior surgery.

Multiple pathologies cause obstruction at different levels. At the interventricular foramina, a colloid cyst or astrocytoma may cause obstruction. At the level of the third ventricle, craniopharyngioma or optical thalamic glioma may account for obstruction. Pineal cysts and solid tumors can also obstruct the cerebral aqueduct. Gliomas, plexus papillomas, ependymomas, and medulloblastomas are examples of possible disease entities for occlusion at the level of the fourth ventricle.

Some causes for nonobstructive (communicating) hydrocephalus include infections that cause adhesions (eg, meningitis), hemorrhage following stroke, intracerebral bleeding, the leptomeningeal spread of cancer, or sinus thrombosis.

In the fields of pediatrics and neonatology, it is important to mention the posthemorrhagic hydrocephalus of prematurity related to bleeding in the subependymal germinal matrix. This condition affects premature neonates and manifests in the first weeks of life. The germinal matrix is fragile, and fluctuations in cerebral blood flow can lead to subependymal bleeding with or without rupture to the ventricle. Blood in the ventricle can cause obstruction of the CSF pathways and subsequent posthemorrhagic hydrocephalus.

Chiari malformation — particularly type 2 — is associated with hydrocephalus, and these patients will require shunting.

Normal pressure hydrocephalus can be clinically diagnosed using the Hakim triad of urinary incontinence, memory loss, and gait unsteadiness. In such cases, CSF pressure is generally below 20 cm H$_2$O. This type of hydrocephalus can be common in older individuals, although it is not exclusive to this patient population. According to a Norwegian study, the prevalence rates in Norway ranged from 3.3 per 100,000
Pseudotumor cerebri syndrome (PTCS) is an entity that includes idiopathic intracranial hypertension and secondary PTCS (when a cause is discerned). The pathogenesis of PTCS is relatively unknown, although theories have been proposed and have included venous thrombosis, increased resistance to CSF outflow, altered vitamin A metabolism, and obesity, among others. Regardless of its pathogenesis, ventriculomegaly is not present in cases of PTCS, but intracerebral pressure as measured via lumbar puncture (opening pressure) will be higher than normal.

**Diagnosis**

The diagnosis of hydrocephalus is generally made using a combination of clinical signs, findings on radiological imaging, and, on some occasions, CSF pressure readings.

In children, a bulging frontal fontanelle indicates increased intracranial pressure. Ultrasonography or computed tomography will show ventriculomegaly and possibly help reveal the cause of hydrocephalus. In adults, standard imaging modalities include computed tomography and magnetic resonance imaging. In many cases, high-volume lumbar puncture is performed for diagnostic purposes. If the patient experiences significant clinical improvement, then shunting may be offered to them. More sophisticated imaging, such as CSF flow studies or radionuclide distribution over the hemispheres, can also be used to make the diagnosis. In rare cases, invasive monitoring via a ventricular catheter has been reported.

**Treatment**

The type of therapy indicated is directed by the cause of the hydrocephalus. For example, shunting may no longer be necessary if the cause of the hydrocephalus is eliminated. In cases of hemorrhage or tumors, surgical evacuation might be an appropriate option in combination with or without shunting.

In general, shunting is required to correct myelomeningocele in patients with type 2 Chiari malformation. In utero myelomeningocele repair is ideal so that brain herniation can be prevented, although this procedure is not yet the standard of care. Decompression of the foramen magnum and duraplasty are the therapeutic plan of choice for type 1 Chiari malformation. Shunting of recurrent hygromas in cases of external hydrocephalus or evacuation may also be appropriate options.

Endoscopic third ventriculostomy is indicated in cases of aqueduct stenosis when the fourth ventricular enlargement is absent. Nonetheless, endoscopic third ventriculostomy has been used for other cases of hydrocephalus but with variable outcomes.

In the field of pediatric neurosurgery, endoscopic third ventriculostomy has been used in cases of shunt failure, posthemorrhagic hydrocephalus, and Chiari malformations. It has also been combined with choroid plexus cauterization.

**Conclusions**

The physiology of cerebrospinal fluid is a complex topic still undergoing rigorous research. Circulatory abnormalities of cerebrospinal fluid are common and often require neurosurgical attention. In many cases, the course of hydrocephalus can be significantly changed with neurosurgical intervention (eg, posthemorrhagic hydrocephalus, normal pressure hydrocephalus), thus offering patients a normal life span; however, in those with cancer-related hydrocephalus, therapeutic options may be limited to palliative care. Endoscopic third ventriculostomy is an option for selected patients with pineal or posterior fossa tumors and may circumvent the need for a shunt.

**References**