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# History, Anatomy, Histology, and Embryology of the Ventricles and Physiology of the Cerebrospinal Fluid

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## Abstract

Cerebrospinal fluid is an essential, clear, and colorless liquid for the homeostasis of the brain and neuronal functioning. It circulates in the brain ventricles, the cranial and spinal subarachnoid spaces. The mean cerebrospinal fluid volume is 150 ml, with 125 ml in subarachnoid spaces and 25 ml in the ventricles. Cerebrospinal fluid is mainly secreted by the choroid plexuses. Cerebrospinal fluid secretion in adults ranges between 400 and 600 ml per day and it is renewed about four or five times a day. Cerebrospinal fluid is mainly reabsorbed from arachnoid granulations. Any disruption in this well-regulated system from overproduction to decreased absorption or obstruction could lead to hydrocephalus.

**Keywords:** arachnoid villi, cerebrospinal fluid pressure, choroid plexus, hydrocephalus, ventricular system

## 1. Introduction

Cerebrospinal fluid (CSF) is located in the brain ventricles, the cranial and spinal subarachnoid spaces [1, 2]. It acts as a cushion and plays a significant role in brain development, in the regulation of the interstitial fluid of the brain parenchyma and healthy neuronal functioning [1]. CSF is mainly produced from the choroid plexuses and mainly absorbed through arachnoid villi. The mean CSF volume is 150 ml, with 125 ml in subarachnoid spaces and 25 ml in the ventricles. In this chapter, historical understanding, anatomy, histology, embryology of ventricles, and physiology of CSF will be discussed.

## 2. Historical understanding of the ventricular system and cerebrospinal fluid

In ancient times, ventricles were thought to be the site of emotions, mind, judgment, and memory. Hippocrates (460–375 BC), described congenital hydrocephalus as ‘water’ around the brain [3]. Most likely, Aristotle (384–322 BC) was the first one who noticed the presence of brain cavities, especially the lateral ventricles [4]. A Greek physician, Herophilos of Chalcedon (335–280 BC) was the true discoverer

of the first human cadavers dissections [5]. He also described the choroid plexuses [6]. Erasistratus of Ceos (304–250 BC), a scholar of Herophilus, suggested the ventricular theory [7]. Rufus of Ephesus (110–180), master of Galen of Pergamum, elaborated the lateral, third, and fourth ventricles and the mesencephalic aqueduct [7]. Galen (130–200) also described the ventricular system detailly and mentioned *pneuma*, a breath that arises from the cosmos which circulates through the brain cavities, and serves as a mediator between body and soul [7, 8]. He also specified that obstruction of the ventricular system causes seizures. In *Anathomia* (1316), Mondino de Luzzi (1270–1326) preserved the tricameral theory for cerebral ventricles, which is mostly influenced by Galenic tradition [9]. Leonardo da Vinci (1452–1519) made the first ventriculography on the ox brain and extracted a three-dimensional template that showed the shape of the ventricular labyrinth [2, 10]. In 1859, a German anatomist and surgeon Benedict Stilling (1810–1879) describe the terminal ventricle as a cystic cavity lined by ependymal cells located in the *conus medullaris* for the first time [7]. Then, in 1875, Krause called it the fifth ventricle, named after him as Krause's ventricle [7].

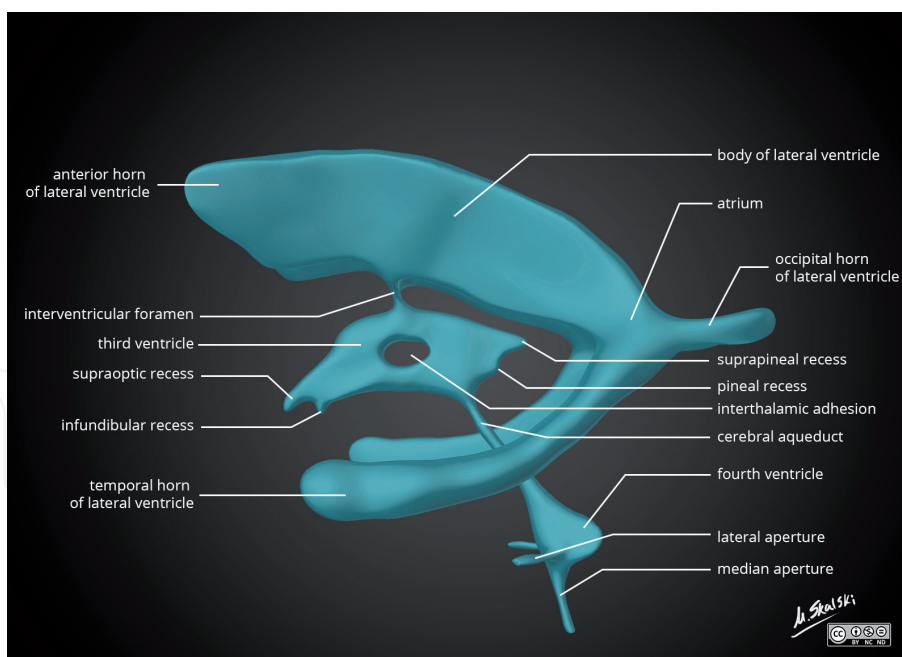
Cerebrospinal fluid is discovered by E. Swedenborg (1688–1772) [11]. In 1747, a Swiss physician A. von Haller (1708–1777), presented that in the brain the 'water' is secreted into the ventricles and absorbed in the veins. Hydrocephalus has resulted from excess secretion, which descends to the skull base and into the "spinal marrow" [12]. Domenico Felice Antonio Cotugno [13] was the one who first defined the connection between cerebral ventricles and subarachnoid space. A French physiologist, F.J. Magendie (1783–1855) also confirmed this finding [13]. An opening in the roof of the fourth ventricle, *foramen Magendie*, was discovered by Magendie, however, erroneously mentioned that CSF was secreted by the *pia mater* [14]. T. Willis (1621–1675), an English physician, described "a liquid" in the aqueduct of Sylvius that connects the ventricles, and continued that the consistency of the "liquid" is altered in "epidemic fever," i.e., meningitis [15]. In 1891, W.E. Wynter (1860–1945) by tapping the spinal subarachnoid space treated tuberculous meningitis [16]. H. Quincke (1842–1922), a German internist and surgeon popularized lumbar puncture and advocated its use for diagnostic and therapeutic reasons [17]. In 1912, a neurologist W. Mestrezat (1883–1928) described the chemical composition of the CSF accurately [18], and in 1914, a pioneer neurosurgeon H.W. Cushing (1869–1939), made it clear that the CSF is secreted by the choroid plexus [19].

### 3. Anatomy of the ventricular system

In the brain, there are 4 ventricles: 2 lateral ventricles, the third ventricle in the diencephalon, and the fourth ventricle in the hindbrain (**Figure 1**) [2]. It is continuous with the central canal of the spinal cord caudally.

#### 3.1 The lateral ventricles

The lateral ventricle is a C-shaped cavity with a capacity of 7–10 ml [2]. It encompasses the thalamus and diencephalon and is divided into five segments. The lateral ventricle has body (central portion), atrium (trigone), and 3 horns (cornua); anterior (frontal), posterior (occipital), and inferior (temporal) horns [21, 22]. The corpus callosum forms the roof of the lateral ventricle, and the posterior portion of the septum pellucidum lies medially. Septum pellucidum is a thin vertical sheet of nervous tissue covered with ependyma on both sides of the ventricles. The caudate nucleus, the lateral dorsal surface of the thalamus, the anterior part of the body of the fornix, the choroid plexus, and stria terminalis form the floor of the lateral ventricle.



**Figure 1.**  
 Illustration of ventricular system anatomy [20].

### 3.1.1 The body of lateral ventricle (central part)

The body of the lateral ventricle lies within the parietal lobe [2]. The anterior limit is the interventricular foramen and the posterior limit is the splenium of the corpus callosum. The inferior surface of the body of the corpus callosum forms the roof. Mostly septum pellucidum forms the medial wall and in the lower part of the medial wall, there is the body of the fornix. From medial to lateral; choroid fissure, choroid plexus that invaginate into the lateral ventricle through a slit space between the fornix and upper surface of the thalamus, the lateral part of the superior surface of the thalamus, thalamostriate vein, stria terminalis, and the body of the caudate nucleus forms the concave floor.

### 3.1.2 The horns of the lateral ventricle

#### 3.1.2.1 The anterior (frontal) horn

The frontal horn is located anterior to the interventricular foramen and moves anteriorly and slightly lateral and downward to lie in the frontal lobe [2]. It has an anterior and medial wall, a roof, and a floor. The posterior surface of the genu of the corpus callosum and the rostrum forms the anterior wall. The medial wall is formed by the septum pellucidum. The roof is formed by the inferior surface or anterior part of the body of the corpus callosum. By a majority, the floor is formed by the head of the caudate nucleus, while the upper surface of the rostrum of the corpus callosum forms a small portion on the medial side.

#### 3.1.2.2 The posterior (occipital) horn

Posterior horn turn inversely and medially to lie in the occipital lobe [2, 21, 22]. It is mostly asymmetrical. The tapetum (sheet of fibers of corpus callosum) forms the roof and lateral wall. The posteriorly sweeping optic radiation is separated with tapetum from the cavity of the posterior horn. The upper part of the medial wall is formed by the forceps major (fibers of the occipital lobe sweeping backward). The

calcar avis, the lower part of the medial wall corresponds to the in-folding of the anterior part of the calcarine sulcus. There is no choroid plexus at the anterior and posterior horn.

### 3.1.2.3 The inferior (temporal) horn

The inferior horn is located inside of the temporal lobe, and it is the longest and largest of the 3 horns [2]. It creates a trajectory around the posterior end of the thalamus, goes posterolaterally and anteriorly into the temporal lobe. The roof is covered laterally by the inferior surface of the tapetum of the corpus callosum and medially by the tail of the caudate nucleus and stria terminalis. The floor is formed medially by collateral eminence produced by the hippocampus and laterally by a collateral sulcus. The hippocampal fibers form the alveus which covers the ventricular surface and form the fimbria converges medially. On the most medial side on the floor, the choroid plexus passes through the choroid fissure rest. The choroid plexus passes from the lateral ventricle into the inferior horn. The amygdaloid complex is situated at the anterior end of the inferior horn [21, 22]. The atrium (collateral trigone) connects the body of the lateral ventricle with the occipital and temporal horns.

## 3.2 Foramen of monro

Interventricular foramen of Monro is the communication between lateral and third ventricles, and it is bordered by the fornix, caudate nucleus, septum pellucidum, corpus callosum, and thalamus. The size of the ventricles determined the size and shape of the foramen. If the ventricular size is big, each foramen is rounded-shaped. As the ventricular size decreases, the foramen takes a crescent shape. The medial posterior choroidal arteries, the septal veins, and the superior choroidal vein pass through this structure [23].

## 3.3 Third ventricle

The third ventricle is located in-between the 2 thalami and some portion of the hypothalamus. This narrow vertical cavity of the diencephalon communicates with the lateral ventricles in the anterosuperior aspect, while on its posteroinferior aspect through the cerebral aqueduct of Sylvius, it communicates with the fourth ventricle [2]. The third ventricular cavity is lined by ependyma and is traversed by massa intermedia (interthalamic adhesion) that connects the 2 thalami which are located posterior to the foramen of Monro. It has a roof, a floor, 2 lateral walls, anterior and posterior walls.

A sheet of ependyma forms the **roof** which connects the upper border of the lateral wall of the ventricle. A triangular fold of pia mater, tela choroidea, covers the roof and it gives rise to the choroid plexus of the third ventricle. The **floor** descends ventrally and is formed by the optic chiasma, mammillary body, tuber cinereum, infundibulum, posterior perforated substance, and tegmentum of the midbrain [2].

From the interventricular foramen to the cerebral aqueduct, a curved hypothalamic sulcus extends and forms the **lateral wall**. The lateral wall is divided into 2 parts by the sulcus. The medial surface of the anterior two-thirds of the thalamus forms the larger upper part. The hypothalamus forms the smaller lower part and it is continuous with the floor. The anterior columns of the fornix that divided laterally into the lateral walls, the anterior commissure, and the lamina terminalis form the **anterior wall**. The lamina terminalis is a thin sheet of gray matter that extends superiorly from the rostrum of the corpus callosum, inferiorly to the optic



chiasma. The cerebral aqueduct, the pineal gland, and the posterior commissure form the **posterior wall**.

The anterior recess (vulva of the ventricle), infundibular recess, optic recess, pineal recess, and supraspinal recess are the protrusions of the third ventricle into surrounding structures [24].

### 3.4 The aqueduct of sylvius

The Sylvian aqueduct measures 18 mm approximately and it is the narrowest part of the brain ventricular system. From the second fetal month, the luminal size of the aqueduct reduces due to the development of neighboring neural tissue [25]. The interventricular blockade mostly occurs here.

### 3.5 Fourth ventricle

The fourth ventricle is a wide, diamond-shaped cavity of the hindbrain [2]. It is located posterior to the pons and rostral part of the medulla, and anteroinferior to the cerebellum. On the sagittal section, it is seen as triangular, and on the horizontal section, it is seen as a rhomboidal shape. The floor of the fourth ventricle is also named the rhomboid fossa. It is continuous superiorly with the cerebral aqueduct and inferiorly with the central canal of the spinal cord. The fourth ventricle has 2 *lateral recesses*, a *medial dorsal recess*, and 2 *lateral dorsal recess*.

The fourth ventricle is bounded superolateral by the superior cerebellar peduncle and inferolateral by cuneate and gracile tubercles and inferior cerebellar peduncles.

Two superior cerebellar peduncles form the cephalic portion of the roof. Their medial margins overlap the ventricle on reaching the inferior colliculi. Superior medullary velum bridges the space between the superior cerebellar peduncle. Dorsally, it is covered by the lingula of the superior vermis of the cerebellum. The caudal portion of the roof is covered by the inferior medullary velum, which is formed by the tela choroidea of the fourth ventricle and the ventricular ependyma.

The lateral foramen of Luschka (located near the flocculus of the cerebellum) and the median foramen of Magendie (a large midline aperture, located in the roof of the ventricle at the lower part of inferior medullary velum) are the openings where the fourth ventricle communicates with the subarachnoid space. Mostly, the CSF passes through the median foramen into the cerebellomedullary cistern, i.e., cisterna magna. The cerebral aqueduct does not contain choroid plexus.

## 4. The histology and embryology and the ventricular system

Ependymocytes (ependyma), which are a special type of cells that are columnar or cuboidal epithelium derived from the neuroepithelium cover the ventricular system of the brain [2]. The choroid plexus lies just below the ependymal layer and is responsible for CSF production.

A layer of subependymal glial cells tighten with the astrocyte processes and form the blood-brain barrier. Circumventricular organs lack this barrier and have fenestrated capillaries with increased permeability. They have secretory and sensory functions. These are the area postrema, median eminence, pineal gland, organum vasculum of lamina terminalis, neurohypophysis, subcommissural organs, and subfornical organ [26]. The ciliary movement is oriented in the anteroposterior neuroaxis which is essential for the movement of CSF.

The ventricular system of the brain develops from the cavity of the neural tube [2]. Around the fourth week of gestation the neural tube is formed. Soon after, the spinal neurocele closes, and the neural cavity is separated from the amniotic cavity.

The choroid plexuses firstly appear in the 4th ventricle on the 41st day [27]. Different embryonic tissues give rise to cerebral and spinal meninges. At the third month of intrauterine life, the three meningeal layers differentiate [1]. The choroid plexus epithelium which is derived from the neural tube is continuous with the ependyma. The leptomeningeal axis is derived from the paraxial mesoderm. From the 26th week, cerebral veins dilate in the superior sagittal sinus at their anastomosis site. In the 35th week, the arachnoid villi are formed. The arachnoid stroma lined by endothelium protrudes into the lumen of the superior sagittal sinus via a defect in the dura mater. At the 39th week, real arachnoid granulations appear [28] and continue to develop around 18 months [29].

## **5. The blood supply and lymphatics of the ventricular system**

The choroid plexus of the lateral ventricle is supplied from the anterior and posterior choroidal arteries, which are the internal carotid artery and the posterior cerebral artery branches respectively [2]. The posterior choroidal arteries supply the choroid plexus of the third ventricle. The anterior and posterior inferior cerebellar arteries supply the choroid plexus of the fourth ventricle.

## **6. The physiology of the cerebrospinal fluid**

### **6.1 The cerebrospinal fluid secretion**

Normal CSF formation rate is about 0.35 ml/min for adults, and this ranges from 400 to 600 ml per day [1, 30, 31]. CSF is renewed about four times a day. CSF production is elevated nocturnally and this may be due to cerebral metabolism alterations during sleep [32]. CSF formation also alters in disease states [33]. The choroid plexuses of the lateral ventricles and the tela choroidea of the third and fourth ventricles are responsible for most of the CSF secretion (60–70%) [1, 30]. Other sources of CSF are interstitial fluid, ependyma, and capillaries.

An asymmetrically positioned ion transporters at the blood- and CSF-facing membranes mediates fluid secretion into the ventricles. The choroid plexus epithelium is like the kidney proximal tubule, and transfer copious volumes of fluid [34]. The net transfer of sodium ( $\text{Na}^+$ ) and chloride ( $\text{Cl}^-$ ) from blood to ventricles determine CSF production [35–37]. From plasma across the basolateral membrane,  $\text{Na}^+$  entry into choroid plexus epithelium is on a downhill gradient. Potassium ( $\text{K}^+$ ),  $\text{Cl}^-$ , and bicarbonate ( $\text{HCO}_3^-$ ) move downhill across the apical membrane into CSF at the other side of the choroid cell. These downhill ionic movements are set up by uphill active transport through the primary  $\text{Na}^+$  pump both basolaterally and apically. This process requires chemical energy as adenosine triphosphate [ATP]. Choroid cell  $\text{Na}^+$  concentration is kept relatively low by active  $\text{Na}^+$  pumping into CSF [38] so a basolateral inward driving force for  $\text{Na}^+$  transport from plasma into the epithelium was established [39].

For fluid formation the epithelial transport polarity is essential. From blood to CSF net fluid movement is enabled by the polar distribution of certain active transporters and passive channels. Streaming of ions and water were mediated by basolateral (interstitial) and apical (CSF) transporters and channels.

The direction of fluxes in CSF formation is mostly from interstitium to parenchyma to ventricles.  $K^+$  and  $Cl^-$  passive diffusion (apical efflux) were allowed by channels into nascent CSF [40]. CSF formation is mainly produced by net secretion of  $Na^+$ ,  $Cl^-$ , and  $HCO_3^-$ . Other ions, i.e.,  $K^+$ ,  $Mg^{2+}$ , and  $Ca^{2+}$  also have a role. Through the apical membrane water osmotically follows ion transport.

#### 6.1.1 Sodium secretion

In CSF formation, the pivotal initiating step is the primary active transport of  $Na^+$  from choroidal epithelium to ventricle [41].  $Na^+$ ,  $K^+$ -ATPase creates the electrochemical gradient, generates ATP, and empowers  $Na^+$  pumping [42]. While CSF is being produced, the apical  $Na^+$  efflux is balanced by permanent basolateral  $Na^+$  influx through the epithelial  $Na^+$  channel (ENaC) and  $Na^+$ -inward transport coupled with  $HCO_3^-$ , by the  $Na^+$ ,  $HCO_3^-$  cotransporter, NBCn2/NCBE in order to equilibrate choroid pH and epithelial volume [39, 43–45].

#### 6.1.2 Chloride secretion

Chloride, one of the primary anion in CSF secretion, is actively transported through the transcellular route in exchange for cellular  $HCO_3^-$  across the basolateral membrane [46]. Then for gathering above electrochemical equilibrium, plasma  $Cl^-$  goes into the epithelium [47]. In certain circumstances, intraepithelial  $Cl^-$  diffuses into CSF through the efflux arm of the  $Na^+$ - $K^+$ - $Cl^-$  cotransporter [48]. The downhill diffusion of  $Cl^-$  into CSF across apical  $Cl^-$  channels is the main pathway by which  $Cl^-$  accesses the ventricles to sustain fluid formation [40].

#### 6.1.3 Bicarbonate secretion

In the choroid plexus,  $HCO_3^-$  has two sources. First, in choroid plexus epithelial cells to form  $H^+$  and  $HCO_3^-$  ions carbonic anhydrase catalyzes the hydration of carbon dioxide ( $CO_2$ ) [49]. Acetazolamide inhibits CSF secretion at least 50% which indicates that carbonic anhydrase is involved in CSF secretion [50]. Additionally, via  $Na^+$ -coupled  $HCO_3^-$  transport,  $HCO_3^-$  is pulled from plasma into the epithelium [43]. When the  $HCO_3^-$  accumulates, by two mechanisms it is ready for release through the CSF facing membrane. Firstly, in the epithelium downhill through an anion channel  $HCO_3^-$  diffuses into CSF [51]. Secondly, at the apical membrane  $HCO_3^-$  is transferred through an electrogenic  $Na^+$ -coupled  $HCO_3^-$  cotransporter [45, 52]. CSF rich in  $HCO_3^-$  show increased movement of  $HCO_3^-$  into ventricles as CSF is produced [53].

#### 6.1.4 $K^+$ transport

$K^+$  enters into the cells in two ways: from the blood by the  $Na^+$ - $K^+$ - $2Cl^-$  cotransporter-1 (NKCC1) and from the interstitial fluid by the  $Na^+$ -pump [54]. On both sides the influx exceeds the net flux across the cells, and thus at each membrane, there are thought to be pathways for efflux of most of the  $K^+$  that enters through  $K^+$  channels.

#### 6.1.5 Water secretion

CSF has excretory, distributive, and buffering functions [31]. Water constitutes 99% of the CSF. After osmotically active  $Na^+$ ,  $Cl^-$ , and  $HCO_3^-$  ions are transport into CSF, water follows them into the ventricles via a transcellular route by diffusing



down its chemical potential gradient in the apical membrane through aquaporin 1 (AQP1) channels [55, 56]. AQP1 facilitates water transport from the interstitium to the CSF in the luminal and basolateral membrane [42]. Across the choroid plexus, transcellular water diffusion is a potential drug target to modulate CSF dynamics [55]. In regulating water molecule traffic through AQP1 channels agents structurally related to acetazolamide, furosemide, and bumetanide, and steroid hormones show promise [55, 57]. The composition of CSF and comparison with serum content were summarized in **Table 1**.

6.2 Regulation of cerebrospinal fluid regulation secretion and composition

The choroid plexuses receive adrenergic, peptidergic, cholinergic, and serotonergic autonomic innervation [1]. The cholinergic system increases CSF secretion while the sympathetic nervous system reduces CSF secretion. Circadian variations of CSF secretion may be regulated by the autonomic nervous system.

The targets of humoral regulation are enzymes and membrane transporters. The activity of carbonic anhydrase is regulated by the acid-base disorders, membrane carrier proteins (i.e., the NaK<sub>2</sub>Cl cotransporter), and aquaporins. Neuropeptide factors and monoamines also have a role. Atrial Natriuretic Peptide (ANP), Arginine Vasopressin (AVP) dopamine, serotonin, and melatonin receptors are present on the surface of the choroidal epithelium. ANP and AVP decrease CSF secretion [60], as ANP acts on AQP1.

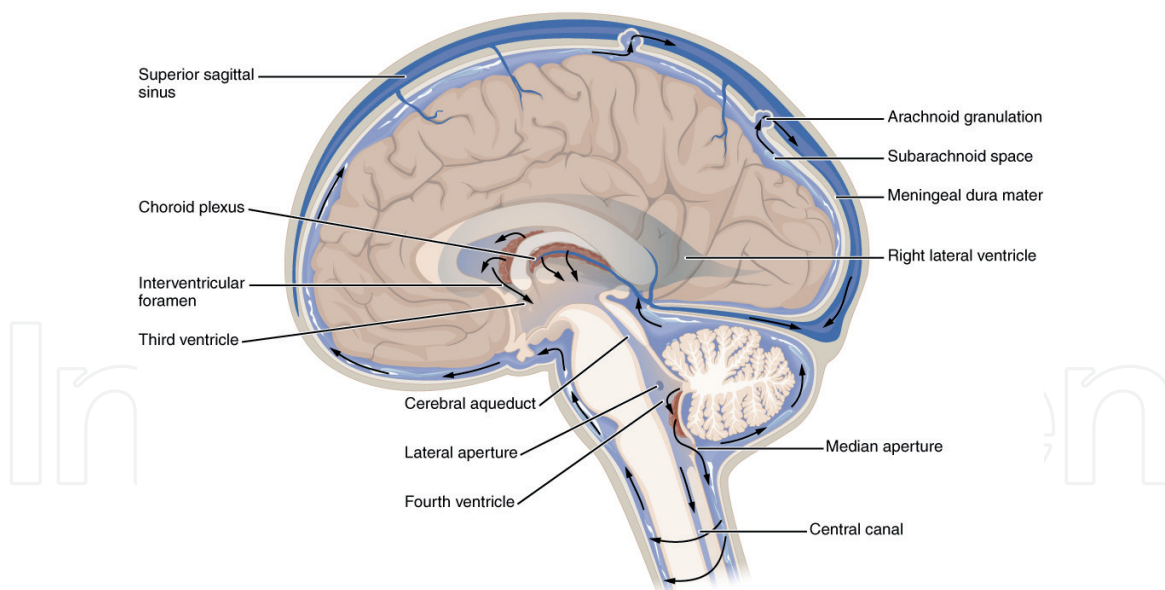
Carbonic anhydrase inhibitors and loop diuretics decrease CSF secretion and turnover via enzymatic mechanisms, which could change the neuronal milieu, making prone the elderly to age-related neurodegenerative disorders.

6.3 Cerebrospinal fluid circulation

There is a one-way rostrocaudal CSF flow in ventricular cavities and a multi-way CSF flow in subarachnoid spaces from the sites of secretion to the sites of absorption (**Figure 2**) [1]. CSF flow is mainly affected by the systolic pulse wave in choroidal arteries and rapid respiratory waves. In the lateral ventricles, through interventricular foramina, CSF enters the third ventricle, and through the cerebral aqueduct, it enters the fourth ventricle. Thereafter, through the foramen of Magendie CSF goes to the subarachnoid spaces. Rostrally CSF circulates to the

Substance	CSF	Serum
Water content (% wt)	99	93
Total protein (mg/dl)	35	7000
Glucose (mg/dl)	60	90
Osmolarity (mOsm/l)	295	295
Sodium (mmol/l)	138	140
Potassium (mmol/l)	2.8	4.0
Calcium (mmol/l)	2.1	4.8
Magnesium (mEq/l)	2.0–2.5	1.7
Chloride (mmol/l)	119	103
pH	7.33	7.41

**Table 1.**  
*The composition of cerebrospinal fluid and comparison with serum [58, 59].*



**Figure 2.**  
 Important structures for cerebrospinal fluid circulation [61].

villous sites of absorption and caudally it circulates to the spinal subarachnoid space in the cranial subarachnoid space. The spinal arachnoid villi partly absorb the CSF, and CSF circulates rostrally to the cranial subarachnoid space.

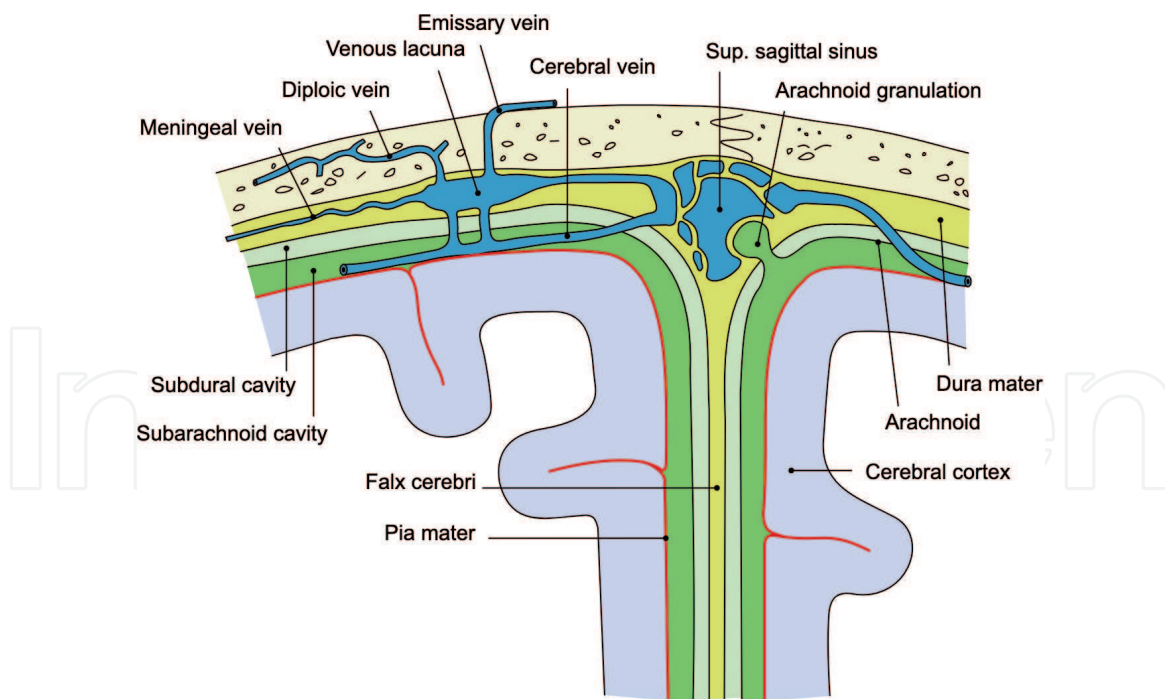
The subcommissural organ also has a role in CSF circulation. It is a differentiation of the ependyma at the rostral extremity of the cerebral aqueduct and synthesizes SCO-spondin [62]. This protein accumulates and forms Reissner fibers, which direct the CSF circulation via the cerebral aqueduct. Early during development in man, the subcommissural organ disappears. Certain forms of congenital hydrocephalus could be explained by an intrauterine abnormality of the subcommissural organ [63].

## 6.4 Cerebrospinal fluid absorption

CSF circulation was determined mainly by the arterial pulse from secretion site to absorption site [1]. The main site for CSF absorption into the venous outflow system are the cranial and spinal arachnoid villi. The cribriform plate, the cranial and spinal nerve sheaths, and the adventitia of cerebral arteries may also serve as alternative pathways for CSF drainage into the lymphatic system.

Arachnoid villi or granulations are endothelium-lined finger-like protrusions of the arachnoid outer layer via the dura mater in the venous sinus lumen (**Figure 3**) [65]. Villous absorption of CSF both in the brain or spine is a dynamic process that adapts the filtration rate to CSF pressure. The pressure gradient among the venous sinus and subarachnoid spaces is essential to assure CSF drainage is between 3 and 5 mmHg [66]. Especially during physical exertion, spinal arachnoid villi and the epidural venous plexus offer an alternative pathway for CSF absorption.

The cranial and spinal nerve sheaths and ependyma can also absorb CSF with respect to pressure gradients [1]. Via Virchow-Robin perivascular spaces, absorption through the interstitial compartment happens. On meningeal sheaths, CSF absorption surfaces have also been shown, especially the meningeal recesses of cranial and spinal nerve roots (i.e., the trigeminal and cochlear nerve). In its meningeal sheath, the optic nerve exerts a long extracranial course. With constructive interference in steady-state magnetic resonance imaging, a high-intensity ring around the optic nerve was observed in hydrocephalus. This finding indicates that when needed there is also a salvage pathway for reabsorption.



**Figure 3.**

*Diagrammatic representation of a section across the top of the skull, showing the membranes of the brain, and arachnoid granulation [64].*

When the cranial arachnoid villi capacities are exceeded, lymphatic absorption of CSF establishes an accessory pathway [1]. Particularly, this pathway is active in neonates. Arachnoid villi are completely functional after the age of 18 months. It becomes dysfunctional in the elderly due to fibrous changes of arachnoid granulations.

The cochlear aqueduct, which is located in the petrous part of the temporal bone, has a connection between the perilymphatic space of the cochlea and the subarachnoid space of the posterior cranial fossa. It is patent in 93% of cases [67]. This could clarify the effect of intracranial pressure changes on cochlear function (i.e., tinnitus after ventriculoperitoneal shunting and at high altitude).

## 6.5 Cerebrospinal fluid pressure

Ventricular cavity is a dynamic pressure system. CSF pressure is defined as the intracranial pressure (ICP) in the prone position. It is the outcome of a dynamic equilibrium between CSF secretion, resistance to flow, and absorption [1]. CSF pressure can be monitored invasively with a pressure transducer placed in the brain parenchyma or via an external ventricular/lumbar drain connected to CSF spaces. On Doppler ultrasound, to evaluate CSF pressure vascular flow can be traced as a non-invasive method. CSF pressure determines ICP with physiological values. In infancy, it ranges between 3 and 4 mmHg, and in adults, it ranges between 10 and 15 mmHg. Higher values indicate intracranial hypertension. Respiratory waves, jugular venous pressure, state of arousal, abdominal pressure, the subject's posture, and physical effort also modulate CSF flow dynamics and pressure.

The cranial content includes parenchymal, venous, and CSF compartments. CSF pressure is established by parenchymal and venous pressures. When fontanelles are open if ICP increases macrocephaly could be observed due to an increase in intracranial volume. When the fontanelles are closed, blood volume (particularly venous) reduction is seen as compensation.

Brain compliance is described as the volume needed to change ICP. It is the indication of the intracranial contents capacity to adapt to volume changes. Brain compliance is lower in men and changes with age. The volume needed to induce a

10-times increase in ICP is 8 ml in neonates, 20 ml in 2-year-old children, and 26 ml in adults. The brain volume must be considered when brain compliance is calculated (average of 335 ml in neonates and 1250 ml in young adults).

The regulation of CSF pressure occurs at the secretion, circulation, absorption phase of CSF. When intraventricular pressure is increased, the cerebral perfusion pressure (CPP) and the pressure gradient across the blood-CSF barrier decreases, and choroidal secretion is negatively affected. The concentrations of neuropeptides (ANP and AVP) in CSF and their receptor expression in the choroidal epithelium increase with CSF pressure increase and in the state of acute hydrocephalus [68, 69]. These neuropeptides cause a decreased choroidal secretion of CSF. They also induce dilatation of pial arteries to compensate for the reduction of CPP in acute hydrocephalus [70].

## 6.6 Cerebrospinal fluid homeostasis

CSF protects the neuraxis hydromechanically. CSF plays an important role in the regulation of cerebral interstitial fluid and the neuronal environment via arranging the circulation of active molecules, electrolyte balance, and elimination of catabolites. Via CSF, the products of choroid plexus secretion are transported to their action sites. The activity of certain brain regions is modulated by impregnation by this way. However, more rapid changes of activities happen via synaptic transmission [71].

## 7. Hydrocephalus

In hydrocephalus, an increased amount of fluid accumulates in the brain ventricular system [2]. Impairment in the CSF circulation at any point could lead to this disease. Mostly, abnormal enlargement of the cerebral ventricle and increased ICP are observed. The common symptoms include headache, irritability, blurred vision, vomiting, gait disturbance, and drowsiness. A rapid increase in head circumference is the main sign in infants.

Hydrocephalus can be classified as communicating or non-communicating type. Impaired absorption of CSF by the arachnoid granulations causes communicating hydrocephalus and this can be the result of any leptomeningeal processes (i.e., inflammation due to infectious or carcinomatous meningitis or hemorrhage as in acute subarachnoid hemorrhage).

Hydrocephalus can also be classified as congenital or acquired. Aqueductal stenosis is the most common cause of congenital hydrocephalus. This can be seen in the case of aqueductal atresia (genetical) or in the case of tumors of neighboring structures compressing the aqueduct or epididymitis (acquired). This results in the enlargement of both lateral and third ventricles with a normal fourth ventricle. The foramen of Magendie and Luschka could be obstructed in Chiari malformation. In this condition, the downward displacement of the cerebellum via the foramen magnum could result in internal hydrocephalus. In the case of inflammatory fibrosis of the meninges, the foramen could be obstructed and result in congenital hydrocephalus [25]. Trauma, infection, tumor, and hemorrhage could result in acquired hydrocephalus.

## 8. Surgical approaches

Here we will briefly mention the most preferred methods for hydrocephalus management.



In ventriculostomy, a hole in the ventricles is created for CSF drainage and/or ICP monitoring. External ventricular drain is placed in the ventricle. Kocher’s point is the commonest entry point on the skull which is 3–4 cm lateral to the midline and 11 cm posterior to the glabella. The frontal horn of the lateral ventricle is the target [72].

In ventricular shunting, CSF is diverted from ventricles to body compartments such as the peritoneal cavity (ventriculoperitoneal shunt), right atrium (ventriculoatrial shunt), pleural space (ventriculopleural shunt).

In order to drain the CSF directly into the basal cisterns, an incision could also be made on the floor of the third ventricle.

9. Conclusion

CSF is an essential liquid for brain homeostasis. It has a well-balanced ionic content and has a certain secretion and absorption rate. Choroid plexuses are the main secretion site, while arachnoid villi are the main absorption site. When there is disequilibrium in secretion, absorption or any obstruction in the ventricular system hydrocephalus could be seen. There are alternative treatment methods for this condition which depend on the etiology. In this chapter, we review the historical understanding of ventricular anatomy and CSF, main anatomical structures of the ventricular system, histology of embryology of the ventricular system, CSF physiology. We also briefly mentioned hydrocephalus and the main treatment alternatives.

Conflict of interest

The authors declare no conflict of interest.

Appendices and nomenclature

ANP	atrial natriuretic peptide
AQP1	aquaporin 1
AVP	arginine vasopressin
BC	before Christ
Cl <sup>-</sup>	chloride
CO <sub>2</sub>	carbondioxide
CPP	cerebral perfusion pressure
CSF	cerebrospinal fluid
ENaC	epithelial Na <sup>+</sup> channel
HCO <sub>3</sub> <sup>-</sup>	bicarbonate
ICP	intracranial pressure
Na <sup>+</sup>	sodium
NKCC1	Na-K-2Cl cotransporter-1
Wt	weight

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