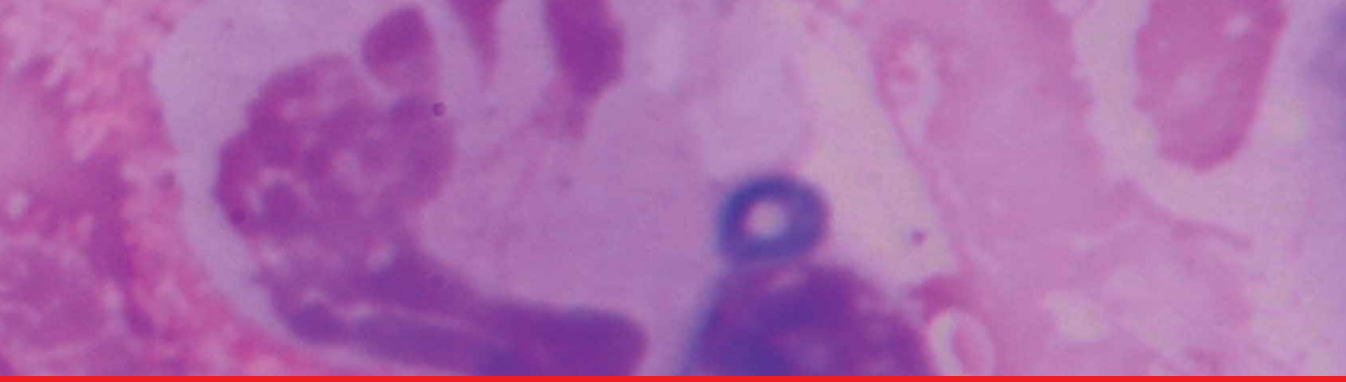

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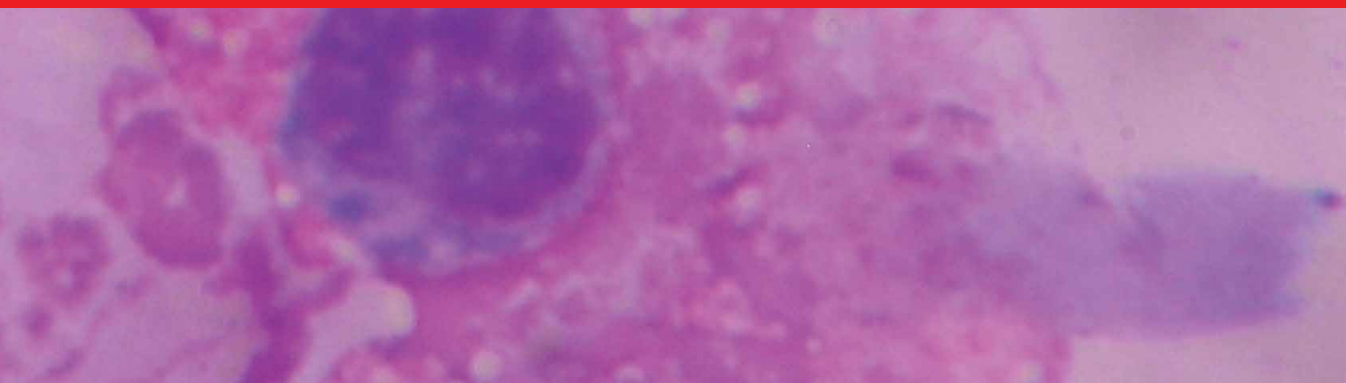

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Meet the editors

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Contents

Preface

Hydrocephalus is a common neurosurgical disease that is frequently secondary to other neurosurgical diseases, which contributes to its poor prognosis. Advancements in hydrocephalus research in recent years have provided a more comprehensive understanding of its pathogenesis. Previously, it was believed that hydrocephalus was caused by a flow disorder of cerebrospinal fluid circulation. Now, however, scholars have realized the limitations of this theory and pioneered the theory of brain tissue penetration, which has enriched the etiological research of hydrocephalus. In addition, advancements in neurosurgery technology have led to improved treatment methods such as ventriculoperitoneal shunt, endoscopic third ventriculostomy, neuroendoscopic ventriculostomy, choroid plexus coagulation, neuroendoscopic aqueductoplasty, and others. This book discusses the latest advances in hydrocephalus treatment, including recent research developments in ventriculoperitoneal shunt surgery and neuroendoscopic treatment. Furthermore, it examines rare types of hydrocephalus, including hydrocephalus associated with myelomeningocele, hydrocephalus in tuberculous meningitis, hydrocephalus in arachnoid hemorrhage, and pediatric hydrocephalus.

We would like to thank all the authors for their contributions. We would also like to acknowledge the encouragement, motivation, and assistance from the Beijing Municipal Administration of Hospitals Incubating Program (PX2020039), Beijing, China, and Tsinghua Precision Medicine Foundation (20219990008), Tsinghua University, Beijing, China. We are grateful to the Author Service Manager Ms. Tea Jurcic at IntechOpen for her dedication and hard work in ensuring the smooth publication of this book. Finally, we owe a debt of gratitude to Professor Zhongcheng Wang, academician of the Chinese Academy of Engineering and the founder and pioneer of Chinese neurosurgery, for without his tireless efforts over the decades, Chinese neurosurgery would not be what it is today.

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Section 1

Acquired Hydrocephalus

Chapter 1

Aneurysmal Subarachnoid Haemorrhage (aSAH) and Hydrocephalus: Fact and Figures

Nissar Shaikh, Arshad Chanda, Kazim Mohammed, Ahmed Balfaqih, Muhammad Mohsin Khan, Seema Nahid, Abdelrahman Balal, Muhammad Zubair, Rahman MA, Hossam Algallie, Gamal Al-Ameri, Abdulnasser Thabet and Ali Ayad

Abstract

Hydrocephalus (HCP) occurs due to the injurious effect of subarachnoid haemorrhage (SAH). It causes increased morbidity and mortality. It can be acute and frequently occurs within 48 hours and up to 7 days. Subacute hydrocephalus may occur up to 14 days and is chronic if remained or develops after 2 weeks of the subarachnoid haemorrhage. Acute hydrocephalus after aneurysmal subarachnoid (aSAH) bleeding is non-communicating or obstructive and occurs due to physical obstruction by a clot, the effect of blood in the subarachnoid space, and inflammation. Chronic hydrocephalus is due to fibrosis and adhesion, which hampers cerebrospinal fluid (CSF) absorption and increased secretion of CSF from gliosis. Various risk factors for developing hydrocephalus in aneurysmal subarachnoid haemorrhage patients range from female gender to high severity scores. Acute hydrocephalus frequently requires diversion drainage of CSF by external ventricular drain (EVD); it usually subsides within a week, and EVD is removed. Fewer patients will develop or continue to have hydrocephalus, requiring either short or longer shunting of the CSF namely by ventriculoperitoneal shunt or other modes of CSF drainage.

Keywords: aneurysmal subarachnoid haemorrhage, cerebrospinal fluid (CSF), hydrocephalus, communicating, non-communicating, external ventricular drain (EVD), ventriculoperitoneal (VP) shunt

1. Introduction

Subarachnoid haemorrhage (SAH) is blood in the space between the arachnoid membrane and pia matter around the brain (subarachnoid space). Hydrocephalus after aSAH (aneurysmal subarachnoid haemorrhage) is a frequent complication that

can be acute, subacute, or chronic, requiring a diversion procedure such as external ventricular drain (EVD) or ventriculoperitoneal shunt insertion.

Up to 85% of subarachnoid haemorrhage occurs due to the rupture of a cerebral aneurysm, and SAH (subarachnoid haemorrhage) accounts for 5% of strokes. The overall incidence of aneurysmal subarachnoid bleeding is decreasing trend. However, aSAH (aneurysmal subarachnoid haemorrhage) remains a devastating clinical emergency with increased morbidity and mortality. aSAH varies according to geographic variation, with Finland and Japan having higher cases of SAH [1].

2. Epidemiology

The incidence of hydrocephalus (HCP) after aSAH is reported from 6 to 67%, and this wide range is due to various backgrounds and clinical situations of reporting. More recently, the incidence of hydrocephalus has been reported to be around 20–30% of subarachnoid haemorrhage [2].

One of the tertiary cares centre from the Indian subcontinent reported that 18.6% of their aSAH had hydrocephalus. Posterior circulation aneurysms were found to cause more frequent hydrocephalus than anterior circulation aneurysms [3].

3. Classification and types of hydrocephalus in aSAH

Hydrocephalus (HCP) in aSAH is divided into acute, subacute and chronic. In most of these patients, HCP is acute and occurs within 3 days of the bleeding. Subacute HCP occurs within 4 to 14 days of bleeding, and hydrocephalus after 2 weeks of aSAH is called chronic HCP, and it occurs in up to 20% of aSAH patients.

Further to it, HCP can be communicating or non-communicating. In the initial days of aSAH, it is non-communicating due to blockage and obstruction to the free flow of CSF due to narrowing and obstruction of the cerebral aqueduct. However, when it becomes chronic, it becomes communicating due to fibrosis of subarachnoid granulation. In this type, the flow of CSF is obstructed or blocked after the cerebral ventricles and usually results from a thickened arachnoid layer. Details are described in the etiopathology section.

4. Risk factors

Various reports suggest that the following are the risk factors for the development of acute hydrocephalus (obstructive or non-communicating) following aSAH are mentioned as follows: [4]

1. Female gender
2. Higher grade of aSAH
3. Higher modified fissure grade
4. Location of aneurysm
5. Meningitis

6. Known hypertension

According to Chen S et al., following are risk factors for communicating, non-obstructive chronic hydrocephalus [5]

1. Poor neurological grades

2. Massive intraventricular haemorrhage

3. Rebleed

4. Increased CSF secretion

5. Impaired CSF absorption

6. Advanced age

HCP in aSAH with the increased risk for shunt requirements [6]:

1. Larger aneurysm

2. Posterior circulation ruptured aneurysm

3. Intraventricular haemorrhage

4. Higher Hunt and Hess, Modified Fisher grade, and low admission Glasgow comma score (GCS)

5. Rebleeding and more significant intraventricular haemorrhage

6. Elderly patients (age > 60 years)

Other factors, like economy, medical development and techniques for aneurysms obliteration also detect the requirement of temporary or permanent shunts [7].

5. Pathophysiology of HCP in aSAH

The hydrocephalus after aSAH is either obstructive (non-communicating) or non-obstructive (communicating) hydrocephalus. Acute hydrocephalus is usually obstructive as the blood in the subarachnoid space causes both physical obstruction and direct effect on neurons (**Figure 1**). Blood clots in the CSF circulation cause obstruction to the flow, and platelets stimulation TGF (transforming growth factor) initiate fibrosis in the subarachnoid space. Thrombin of the blood in CSF causes epithelial ciliary damage and obstruction of CSF flow, and the product of blood formation also contributes to the ciliary damage. The direct effect of the blood in subarachnoid space leads to direct injury to neurons and releases HMGB1 (High Mobility Group Protein B1), which stimulates toll-like receptors (TLRs) and RAGE (*Receptor* for Advanced Glycation End products), leading to an acute surge of pro-inflammatory mediators (IL1, IL6 and TNF-9), and this contributes to ciliary

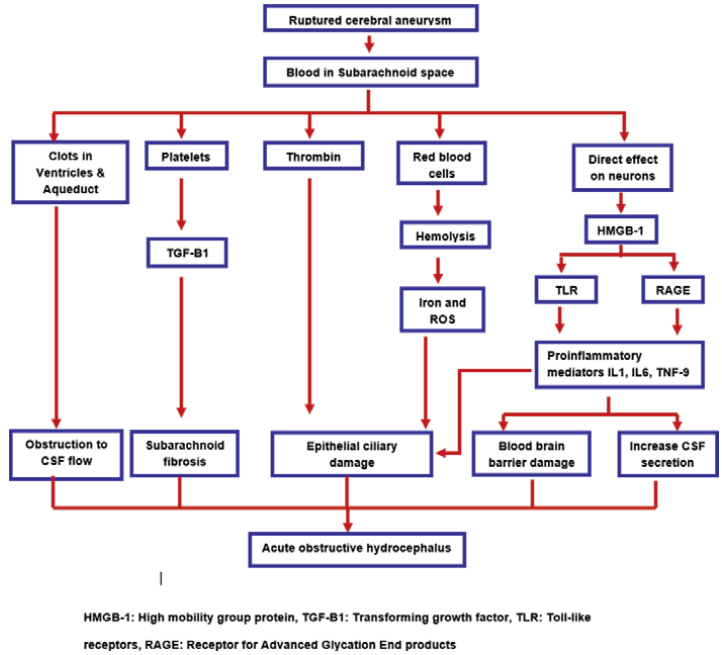

Figure 1.
Pathophysiology of acute hydrocephalus in aSAH.

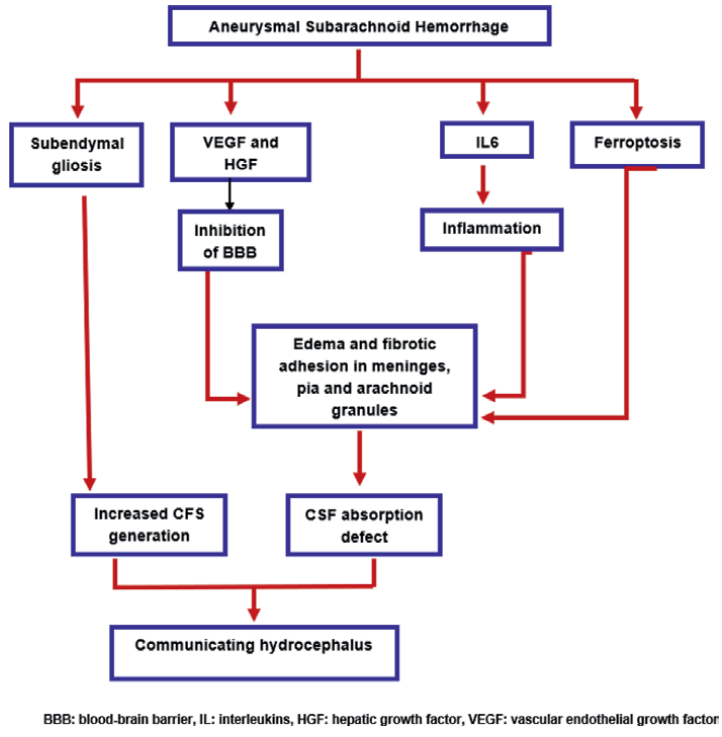

Figure 2.
Chronic hydrocephalus pathophysiology.

damage as well as subarachnoid fibrosis and ultimately contributes to the acute hydrocephalus formation (**Figure 1**) [8].

Chronic hydrocephalus after aneurysmal subarachnoid haemorrhage is either communicating or non-obstructive type. The pro-inflammatory biomarkers surge and presence of iron cause inhibition of the blood-brain barrier and pro-inflammatory changes, oedema and ferroptosis. The combined effect of these is the fibrotic changes and adhesions in the meningeal pia mater and arachnoid granules (**Figure 2**). Subependymal gliosis causes increased secretion of CSF, and all these combinations can cause communicating or non-obstructive hydrocephalus in aSAH patients (**Figure 2**) [8, 9].

6. Diagnosis

Acute hydrocephalus after aSAH has no specific clinical signs or symptoms. Often, patients show a sudden decrease in the level of consciousness or Glasgow comma score (GCS). Other typical manifestations are vomiting, papilloedema, increasing headache and dizziness. Imaging studies are essential to diagnose hydrocephalus after aneurysmal and non-aneurysmal subarachnoid haemorrhage. The imaging studies are ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI). CT is the preferred method for diagnosis as it is quick and widely available and has a short examination time. Current guidelines and protocols recommend the Evan's index (IE)

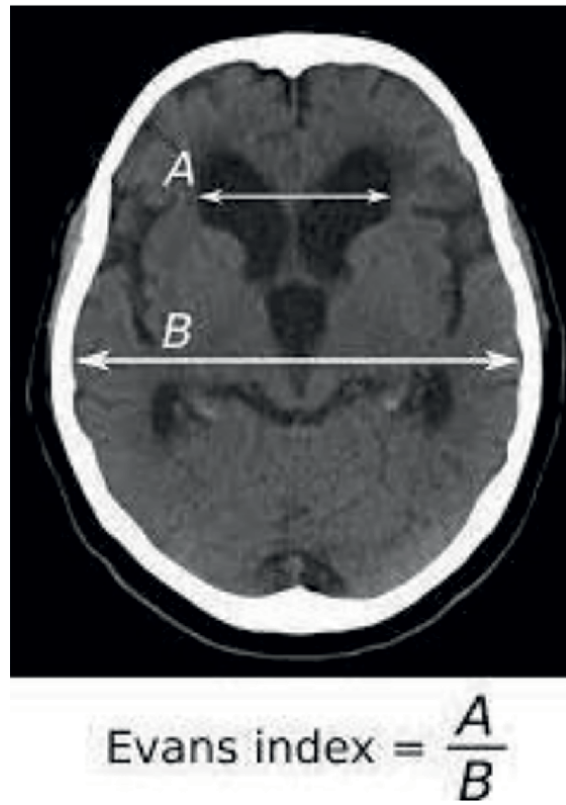

Figure 3.
Evan index.

as the gold standard for hydrocephalus. Evan's index can be used as a marker for ventricular enlargement or ventriculomegaly and ventricular volume. Evan's index gives a rough idea of ventricular dilatation, and one must be careful as it varies with location and slice angle. IE is defined or proposed by William Evan in 1942, as the ratio of the maximum width of the frontal horn of the lateral ventricle and the maximum internal diameter of the skull, as the same CT or MRI axial level (**Figure 3**). A normal Evans index is between 0.20 and 0.25, an index between 0.25 and 0.30 indicates possible or early ventriculomegaly, while a ratio of >0.30 indicates definite ventriculomegaly [10].

7. Management

Acute hydrocephalus is managed by the insertion of EVD (external ventricular drain). Bhattacharjee et al. described in their experience that 15% of their SAH patients required EVD insertion and only 9% required VP shunt [3].

EVD is required for a few days; as the CSF secretion and hemodynamics stabilise, it can be weaned and removed. The issue with EVD is that it can slowly remove blood and blood products and have a risk of blockage. The role of continuous drainage of CSF through EVD is to relieve the symptoms, clear the blood, reduce shunt occlusion and improve cerebral perfusion [3]. Olson et al. demonstrated that the intermittent opening of the EVD is safe and has lower malfunctioning [11].

There are two schools about removing the EVD. One school suggests removing EVD as early as possible and early, as it helps in opening the clogged CSF pathway, hence acquiring early normal flow of CSF, reducing the risk of ventriculitis and ultimately decreasing the length of intensive care stay. In contrast, the other group of physicians favours gradual weaning and removal of EVD. Here, the EVD is raised gradually keeping it open for a more extended period and over days followed by clamping and removal of the EVD [12].

Al-Tamimi et al., in LUMAS trial, which was a single-centre, controlled randomised trial, recruited around 200 patients with aneurysmal subarachnoid haemorrhage and concluded that lumbar drainage reduces the delayed cerebral ischemia but failed to improve the outcome [13].

In many retrospective studies, lumbar CSF drainage has shown to be a safe, feasible measure to remove blood from CSF. The reason to use lumbar CSF drainage in patients with aSAH is to promote CSF circulation from the ventricle and the subarachnoid space. It also removes the CSF blood from the spinal cistern and improves the CSF flow from the ventricles, thus not only decreasing the incidence of shunt-dependent hydrocephalus and reducing cerebral vasospasm [14]. But one must be careful about lumbar CSF drainage to avoid brain hernia due to excessive and frequent CSF drainage and needs strict aseptic precautions to prevent infection. Acute hydrocephalus is self-limiting, but fewer patients may require a permanent shunt and commonly ventriculoperitoneal shunt, but if the abdomen is infected or frozen then a ventriculopleural shunt cannot be performed. Approximately 1 to 45% of aSAH reported to require permanent shunt [15].

Chronic hydrocephalus and shunt requirements in aSAH had guarded prognosis and cognitive deficits with readmissions. Short- or long-term shunting has a risk of obstruction and infection, which can be life-threatening. Factors found to increase shunt requirements were increasing age, ruptured posterior circulation aneurysm, poor-grade aSAH, presence of IVH, higher modified Fisher grade, mode of treatment and female gender [11]. As for as lumbar drain in aSAH-induced hydrocephalus, we preferred intermittent lumbar drainage

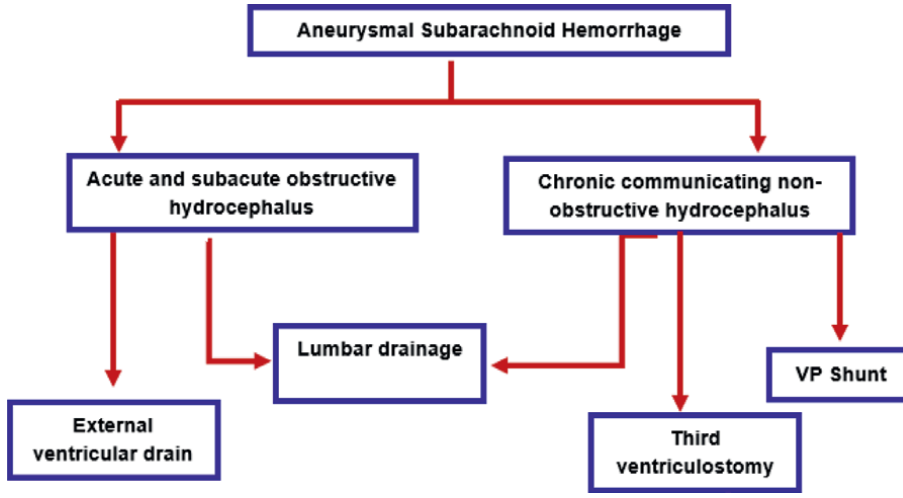

Figure 4.
Management of hydrocephalus after aSAH.

to the continuous one, as continuous drainage with lumbar catheter drain has higher risk for over drainage and leads to brain tonsillar herniation, hence unsafe.

Endoscopic third ventriculostomy (EVT) is a minimally invasive endoscopic procedure that helps to avoid VP shunt and has fewer chances of over-drainage complications and is a durable surgical option. Rarely it is infective; in general, the procedure is well tolerated. The known complications include infection and bleeding. This procedure was initially described in 1900 by *Dandy* with open and primitive endoscopy choroid plexectomy. William performed the first EVT in 1923 [16]. ETV is preferred for acute obstructive HCP, especially with mesencephalic aqueduct obstruction, as the fenestration made with ETV will clear the obstruction for CSF flow. Although Hailong et al [17] mentioned used of ETV in the communicating HCP due to other causes than aSAH, in aSAH communicating HCP main problem is oversecretion and at the same time impaired absorption; hence, ETV may not be useful. ETV also does not terminate or delay the fibrotic process of leptomeninges and subarachnoid granules, and there for not improving the CSF hemodynamics (**Figure 4**) [5].

8. Conclusion

Cerebral aneurysm rupture is a common cause of subarachnoid haemorrhage. One of the frequently occurring complications in these patients is hydrocephalus. Hydrocephalus can be acute, subacute or chronic. Acute hydrocephalus is either obstructive or non-communicating, while chronic hydrocephalus is communicating or non-obstructive. Acute hydrocephalus is commonly managed with the insertion of EVD, and fewer of these patients progress further into chronic hydrocephalus requiring shunt or long-term shunting of CSF.

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Chapter 2

Hydrocephalus Associated with Myelomeningocele

Bamidele Oludele Adebayo

Abstract

Hydrocephalus (HCP) is one of the most common associations of myelomeningocele, and it may be overt and present at birth or be latent and develop following the repair of myelomeningocele. In patients with myelomeningocele, aqueductal stenosis, fourth ventricular obstruction, subarachnoid obstruction at the tentorial hiatus, and the crowded posterior fossa, which are all related to Chiari II malformation, are the various causes of hydrocephalus. The clinical manifestations depend on the age at presentation, but most patients present with macrocephaly and craniofacial disproportion, increasing head size, bulging anterior fontanelle, calvaria sutural diastasis, distended scalp veins, poor feeding as well as signs of raised intracranial pressure such as vomiting, headache, and altered consciousness. Diagnosis is based on clinical features and supportive radiological investigations such as transcranial ultrasound, brain computerized tomographic scan, and brain magnetic resonance imaging. Prompt treatment is very important to obtain optimal clinical outcomes, and this may be by inserting a shunt or performing endoscopic third ventriculostomy with or without choroid plexus cauterization.

Keywords: hydrocephalus, myelomeningocele, ventriculoperitoneal shunt (VPS) insertion, pathogenesis of hydrocephalus, neonates and infants

1. Introduction

Hydrocephalus may be defined as abnormal accumulation of cerebrospinal fluid (CSF) within the ventricles of the brain, leading to ventricular expansion or enlargement and usually associated with raised intracranial pressure [1, 2]. Hydrocephalus (HCP) is one of the most common associations of myelomeningocele, and it may be overt and present at birth or be latent and develop following the repair of myelomeningocele. It complicates 35–91% of myelomeningocele [3, 4].

It has been reported that the rate of treated hydrocephalus in patients with myelomeningocele varies with the anatomic level of the lesion, 60.7% for sacral, 82.4% for lumbar, and 92.2% for thoracic [4].

Prenatal (fetal) myelomeningocele repair has been shown to significantly reduce the need for insertion of ventriculoperitoneal shunt at 1 year following fetal surgery (prenatal group: 40% vs. postnatal group: 82%) [5].

2. Pathogenesis of hydrocephalus in patients with myelomeningocele

Several obstructive and absorptive factors act together to cause hydrocephalus in patients with myelomeningocele.

The unified theory proposed by McLone and Knepper is the most popular postulation for the evolution of hydrocephalus in patients with myelomeningocele. It postulates that persistent CSF loss from the neural tube defect impairs brain and CSF pathways development, which results in the downward displacement of the brain stem and crowding of the posterior fossa that leads to hydrocephalus [6].

Type II Chiari malformation with an overcrowded posterior fossa causes obstruction of the fourth ventricular outlets and disturbance in the flow of cerebrospinal fluid at the craniocervical junction, and it is the major factor responsible for obstructive hydrocephalus in patients with myelomeningocele [7]. There may be associated stenosis or forking of the cerebral aqueduct, also causing obstruction to CSF flow. The crowded posterior fossa results in venous compression, which leads to increased venous pressure that impedes CSF absorption [7, 8]. Furthermore, there is a higher resistance to the flow of CSF across the tentorial hiatus and there may be associated underdevelopment of the arachnoid granulations, which results in impaired or inadequate CSF absorption [9].

These factors result in progressive ventriculomegaly and raised intracranial pressure if unchecked, which are responsible for the clinical and radiologic features of hydrocephalus seen in these patients.

3. Clinical features

This depends on the age at presentation and the time after the onset of symptoms or previous surgical intervention.

3.1 Neonates and infants

At birth, hydrocephalus is apparent in about 15% of neonates with myelomeningocele, with features such as macrocephaly with craniofacial disproportion, increasing head size, bulging anterior fontanelle, calvaria sutural diastasis, distended scalp veins, poor feeding, vomiting, sunsetting eyes, bradycardia, and recurrent apnea [1].

Patients who have had myelomeningocele repair may present with pseudomeningocele at the site of repair; CSF leak from the repair and lower brainstem compromise from the Chiari II malformation may cause stridor from vocal cord weakness, a weak high-pitched cry, swallowing difficulties, poor feeding, nasal regurgitation of feeds, weakness, and hypotonia [10].

Occipito-frontal circumference measurement is important because the patent fontanelles and calvarial sutures may mask overt signs of raised intracranial pressure due to increasing head size, though there may be significant pathology in the brain. When OFC crosses centiles or increases rapidly, surgical intervention is mostly indicated [11].

3.2 Post infancy

Beyond infancy, hydrocephalus typically presents with features of raised intracranial pressure such as headache, vomiting, and altered consciousness. They may also

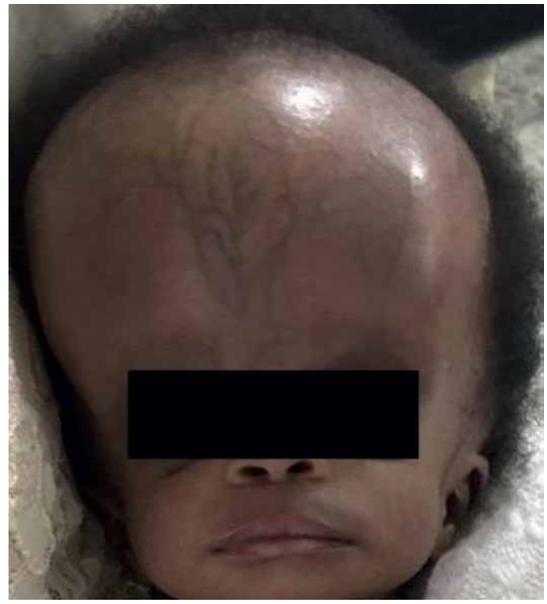

Figure 1.
Clinical picture of an infant with macrocephaly, bulging anterior Fontanelle, craniofacial disproportion, and distended scalp veins.

present with loss of developmental milestones, diplopia, unsteady gait, and impaired cognitive functions (**Figure 1**) [1].

4. Investigations

4.1 Trans Fontanelle ultrasound

Trans fontanelle ultrasound is useful in patients with open anterior fontanelle. It is easy to carry out, cheap, and widely available. It can assess ventricular size, evaluate other anatomic anomalies, and detect other pathologies such as intraventricular hemorrhage [11].

4.2 Brain magnetic resonance imaging (MRI)

It is a noninvasive, more accurate, and sensitive investigation modality; however, it is expensive and may not be readily available, particularly in low- and middle-income countries (**Figures 2** and **3**).

4.3 Brain computerized tomographic scan

It is a sensitive and widely available modality, but with exposure to radiation, there are concerns for the risk of tumors and adverse effects on cognition (**Figure 4**) [11].

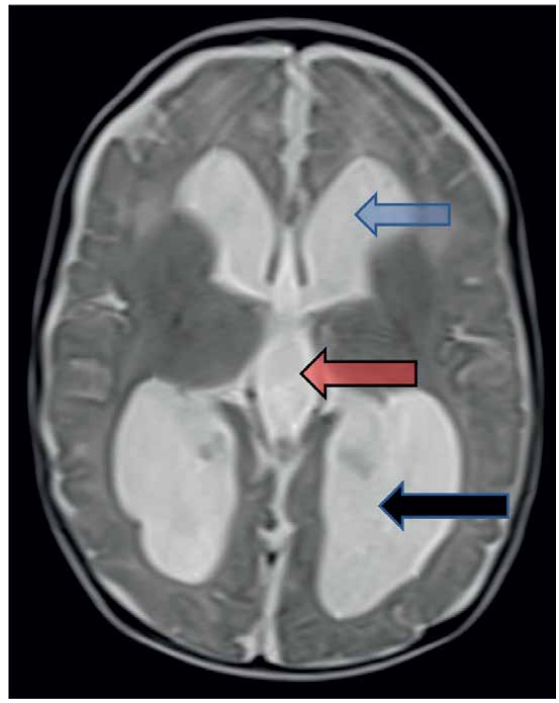

Figure 2.
Axial T2 weighted MRI, blue arrow shows enlarged frontal horn of lateral ventricle, red arrow shows enlarged third ventricle, and black arrow shows disproportionately large occipital horn of the lateral ventricle (colpocephaly).

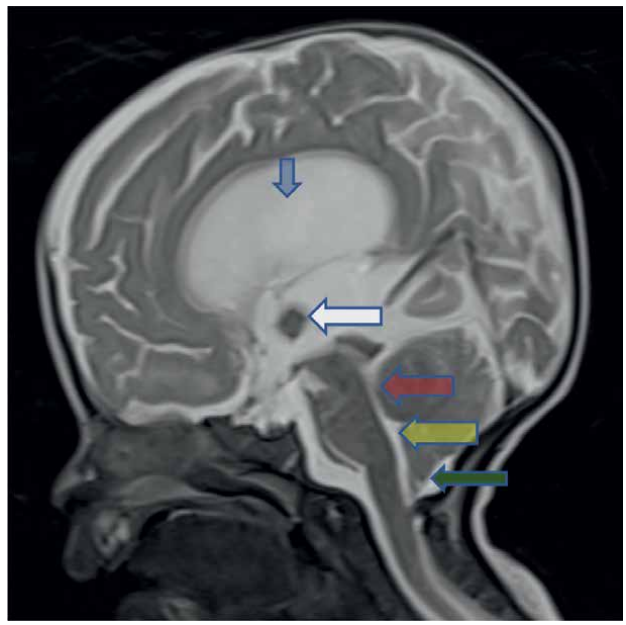

Figure 3.
Sagittal T2 weighted MRI of a patient with Chiari II malformation, blue arrow shows enlarged lateral ventricle, white arrow shows enlarged Massa intermedia, red arrow shows aqueductal stenosis, yellow arrow shows small 4th ventricle, and green arrow shows inferiorly displaced cerebellar tonsil.

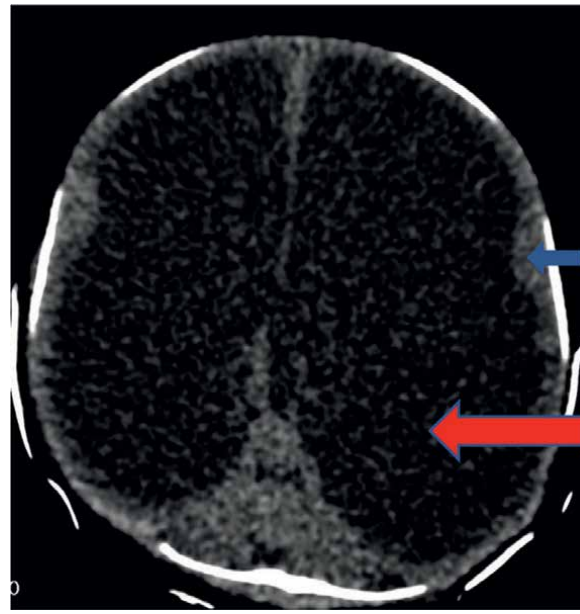

Figure 4.
Axial non-contrast CT showing marked thinning/flattening of the cerebral cortex (blue arrow) and severe ventriculomegaly (red arrow).

5. Diagnosis

Based on clinical findings and supportive radiologic investigations.

5.1 Prenatal diagnosis

5.1.1 Fetal ultrasound

High-resolution fetal ultrasound may be used to diagnose hydrocephalus prenatally. It is a noninvasive, sensitive, readily affordable, and available investigation, but it is observer dependent [11].

5.1.2 Magnetic resonance imaging

Fetal magnetic resonance imaging (MRI) is a more accurate and noninvasive, but expensive investigation which may not be readily available and is subject to motion artifacts. It is very useful when fetal ultrasound is not conclusive and also provides accurate anatomic details about other anomalies of the brain and spinal cord that may be present [11].

6. Treatment

6.1 Nonoperative management

Asymptomatic patients with static or slowly increasing head size may be managed with routine clinic visits, to measure head circumference, monitor ventricular size

with trans fontanelle ultrasound or MRI and assess for symptoms of hydrocephalus or associated Chiari II malformation [6].

6.2 Ventriculoperitoneal shunt (VPS) insertion

Shunts may be inserted simultaneously with the repair of myelomeningocele or after. There is no consensus on the timing of placement of shunts, but it has been reported that simultaneous repair of myelomeningocele and shunt insertion is not associated with increased risk of shunt complications [12, 13].

The shunt has three parts: a ventricular catheter, a unidirectional valve that controls CSF drainage, and a peritoneal catheter that drains CSF into the peritoneal cavity. The VP shunt drains CSF from the ventricles to the peritoneal cavity. However, if the peritoneal cavity is not a viable option, the shunt may be inserted into the pleural cavity or right atrium of the heart [6]. The ventricular catheter may be inserted in a right frontal, parietal, or occipital region [14]. A shunt passer is tunneled subcutaneously between the abdominal and scalp incisions, the peritoneal catheter is passed from the cranial incision to the abdominal incision and the shunt passer is withdrawn, leaving the catheter in the subcutaneous space. The ventricular and peritoneal catheters are connected with a connector and secured to the pericranium. Distal flow of CSF is confirmed from the peritoneal catheter, which is subsequently inserted into the peritoneal cavity under direct vision or laparoscopically.

Complications of VP shunt insertion may range from 1 to 40% and include shunt extrusion, breakage, over drainage, obstruction, infection, and migration. Shunt infection rates of 2–9% have been reported in developed countries and 8.6–50% in developing countries [15].

6.3 Endoscopic third ventriculostomy with choroid plexus cauterization (ETV + CPC)

ETV + CPC is becoming an increasingly popular first-line treatment for hydrocephalus associated with myelomeningocele with a success rate as high as 76%. It has been reported that ETV alone has a low success rate (35%) among patients with myelomeningocele when compared with ETC + CPC (76%) [16, 17].

ETV success score was developed for predicting the success rate of ETV, and it is based on the age of the patient, etiology of hydrocephalus, and whether the patient has had a VPS inserted previously or not. It was proven that age > 6 months, etiology such as aqueductal stenosis and tectal tumors, as well as no previous shunt insertion, were factors that increase the success rate of ETV. Myelomeningocele, previous shunt insertion, and age < 6 months were predictive of low success rates. Benjamin Warf modified the ETV success score by adding choroid plexus cauterization and termed it Cure Children's Hospital of Uganda (CCHU) ETV success score. He reported that choroid plexus cauterization significantly increased the success rates following ETV [18, 19].

The main attractions of this modality of treatment are the absence of a foreign body and its related complications, much lower risk of postoperative infection, and non-dependence on extracranial mechanical drainage system [11, 15].

ETV with CPC may be performed through a right frontal incision at the lateral corner of the anterior fontanelle, using a flexible or a rigid endoscope, which is maneuvered into the third ventricle. A ventriculocisternostomy is created in the floor of the third ventricle using a Bugby wire, to allow CSF flow into the prepontine and

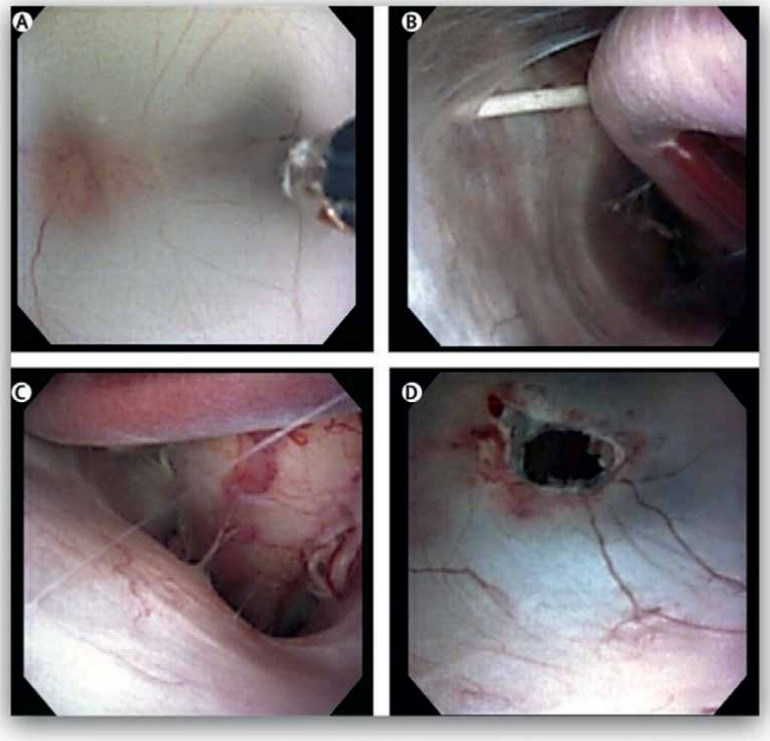

Figure 5.
(A) Endoscopic image of the floor of the 3rd ventricle with the tip of Bugby wire used to perforate the floor on right and the infundibular recess on left; left is anterior. (B) Basilar artery on right and VI cranial nerve on the left after passing endoscope through the third ventriculostomy into the prepontine cistern; clivus is anterior at left. (C) Distal intracisternal image of the right vertebral artery and junction of upper cervical spinal cord and lower medulla at the level of the foramen magnum; clivus is anterior at lower left. (D) Endoscopic image of endoscopic third ventriculostomy opening in floor of the third ventricle after withdrawing scope from prepontine cistern. (courtesy. Kahle KT, Kulkarni AV, Limbrick DD Jr., Warf BC. Hydrocephalus in children. Lancet. 2016 Feb 20;387(10020):788–99. Doi: 10.1016/S0140-6736(15)60694-8.)

peri mesencephalic cisterns. Choroid plexus cauterization is done with a flexible endoscope whenever it is indicated, and if the septum pellucidum is intact, a septostomy is done to gain access to the contralateral ventricle [20]. It has been theorized that CPC decreases the secretion of CSF, enough to help the poorly developed CSF absorption mechanism to cope with the new flow of CSF through the stoma [21].

Complications of ETV + CPC include meningitis, CSF leakage, infections, subdural hygroma, and intraoperative hemorrhage (**Figure 5**) [22].

6.4 Treatment failure

Shunt failure has been defined as the need for any additional hydrocephalus-related surgery following the initial implantation of a shunt [23].

ETV failure has been defined by various authors as persistence or deterioration of clinical signs and symptoms of raised ICP after ETV, reappearance of symptoms of intracranial hypertension, repeated CSF diversion procedure, and death within 30 days of surgery. Most failures of ETV + CPC occur within 6 months of the primary surgery [22, 24].

Treatment failure can be managed by a repeat ETV + CPC or shunt insertion [24].

7. Conclusion

Hydrocephalus is a common association or complication of myelomeningocele, which may be present at birth or develop after the repair of myelomeningocele. In utero repair reduces its incidence postnatally. Prompt treatment with VP shunt or ETC + CPC is essential to improve the outcome of care.

Conflict of interest

None.

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Chapter 3

Hydrocephalus in Tuberculous Meningitis

Olga Adriana Caliman-Sturdza and Andrei Cucu

Abstract

Hydrocephalus is a frequent complication of tuberculous meningitis. We present the incidence of hydrocephalus in patients diagnosed with tuberculosis of the nervous system, the therapeutic possibilities and the evolution of these patients. A consensus definition for tuberculous meningitis (TBM) stratified the cases as definite, probable and possible. In various studies, radiological investigations (CT, MRI) can be normal in the initial stages of the disease in approximately 30% of cases, but they do not exclude the possibility of a TBM. The most common radiological changes found in TBM are communicating hydrocephalus (up to 80% of cases), increased basal contrast (50%), cerebral tuberculomas (30%) and cerebral infarcts (10–40%). MRI has been shown to be more sensitive than a CT scan for diagnosed TBM. Communicating hydrocephalus is among the short-term complications of TBM (approximately 80% of cases), being more frequent than non-communicating ones. In these cases, the need to perform a ventriculo-peritoneal unit must be taken into account. Long-term complications are cognitive impairment, epilepsy, stroke, hydrocephalus, myelitis, damage to the hypothalamus or the pituitary gland manifested by obesity, growth disorders and diabetes insipidus. Sequels may occur frequently in TBM such as dementia, epilepsy, neurological deficits, behavioral disorders, blindness and deafness.

Keywords: hydrocephalus, meningitis, tuberculosis, short-term complications, long-term complications

1. Introduction

Tuberculous meningitis is an infection of the leptomeninge caused by *Mycobacterium tuberculosis* and represents one of the three forms of tuberculosis located in the central nervous system, along with tuberculoma and spinal arachnoiditis [1]. It is estimated that 2 billion of the planet's inhabitants are infected with *Mycobacterium tuberculosis*, and 10% of them develop various forms of active tuberculosis. Tuberculous meningitis (TBM) represents 1% of all forms of tuberculosis and 5% of forms of extrapulmonary tuberculosis (**Figure 1**) [2].

The etiological diagnosis of TBM continues to represent a real challenge for the clinician, despite the progress made in the diagnosis of *M. tuberculosis* infection. Modern diagnostic methods, based on molecular biology techniques and gamma

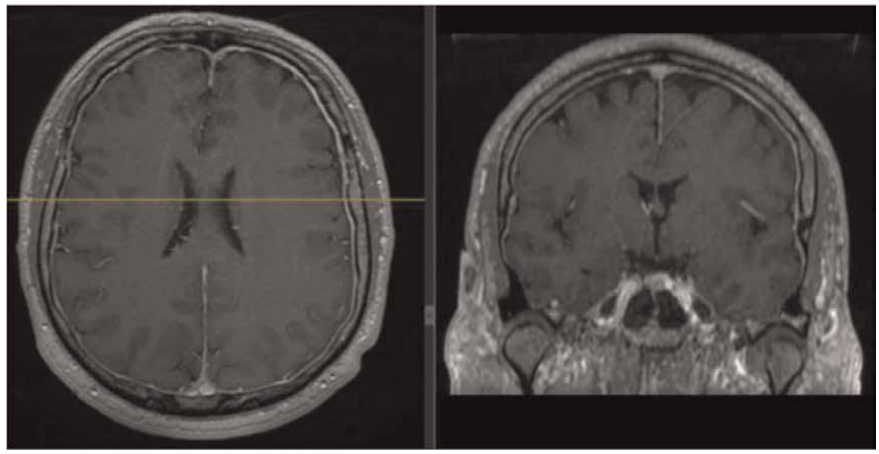

Figure 1.
Axial and coronal contrast-enhanced T1-weighted MRI showing tuberculous meningitis (leptomeningeal enhancement) (courtesy Dr. Bogdan Dobrovat).

interferon release tests, have substantially improved TBM prognosis, although the gold standard for diagnosis remains cerebrospinal fluid culture on special media.

TBM complicates 0.3% of untreated TB infections in children, is more common between 6 months and 4 years. The clinical progression of TBM can be rapid or gradual. Rapid progression is more common in infants and young children [3]. Occasionally, TBM occurs many years after infection.

People at increased risk of TBM are also patients with immunodeficiency caused by aging, malnutrition, HIV/AIDS infection and cancer, but also patients under treatment with biological therapies, such as tumor necrosis factor alpha (TNFα) antagonists [4].

TBM is the most severe form of extrapulmonary tuberculosis (TB), diagnosis remains difficult, and early recognition is crucial for a better prognosis. The mortality rate is high, and sequelae occur frequently in survivors [5]. The optimal treatment has not yet been well established. The increase in the number of TBM cases is also related to the increase in the number of HIV-seropositive patients.

TBM is associated with a multitude of complications such as optochiasmatic and spinal arachnoiditis, tuberculous mass lesion in the brain, periventricular infarcts or hydrocephalus [5, 6]. Among these, hydrocephalus represents a negative predictive factor [5]. Regarding hydrocephalus in patients with TBM, studies have shown that it is found in approximately 80% of children with TBM [3, 7].

Hydrocephalus is one of the most frequent complications of TBM, and its management represents a real challenge for the clinician [8].

2. Pathogenesis

Tuberculosis of the central nervous system in adults is almost always secondary to a latent tuberculosis focus or active pulmonary tuberculosis. In children, TBM is secondary to the primary complex, which disseminates hematogenously in the early stage of evolution, the maximum number of illnesses being recorded in the age group of 1–3 years.

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In adults, extraneural tuberculosis foci are represented by miliary, bone, urogenital or serous tuberculosis [9]. The main defensive mechanism of the host that intervenes at the beginning against Mycobacterium tuberculosis is the alternative pathway of complement activation, but once it reaches the CSF the bacteria has every chance to survive because the humoral defense is absent at this level. Two important mechanisms are involved in the immunopathogenesis of tuberculous meningitis: activation of the monocyte/macrophage system and T lymphocytes with the release of cytokines in the CSF; temporary and reversible depression of cellular immunity by decreasing the number of CD4 T lymphocytes, especially in severe forms, independent of immunodeficiency induced by other causes (including HIV infection) [10].

Tuberculous meningitis is a granulomatous meningitis whose main morphopathological aspects are meningeal inflammation with fibrinous exudate and small disseminated tubercles predominantly in the basal cisterns; inflammation of the choroid plexuses and the ventricular and ependymal epithelium (**Figure 2**); inflammation of the cerebral arteries, with the possibility of their secondary thrombosis and the appearance of cerebral microinfarcts. Infarction of small arteries causes symptoms similar to encephalitis; cerebral tuberculomas, with more frequent localization in the brain stem, thalamus and cerebral hemispheres; they behave as expansive intracerebral processes; cerebral edema, of variable degree and extent [9, 10].

In severe forms, severe disorders of CSF hydrodynamics occur, with the consequent appearance of hydrocephalus, both by blocking the aqueduct of Sylvius and the foramen of Lushka, and by decreasing CSF resorption at the level of Pachionii granulations [8, 9]. Due to the accumulation of a large amount of serofibrinous exudate at the base of the brain, compression of the cerebral arteries is also found at this level. The lesions of the choroid plexuses are morphologically identical to those observed in the meninges: fibrin deposits, specific perivascular follicles, obliteration, their fibrous organization leading to cloazonation. One of the consequences of choroid plexites is liquid hypersecretion, the direct consequence of specific exudation. This exudate, as well as the cloazonation, favors the occurrence of internal hydrocephalus, which

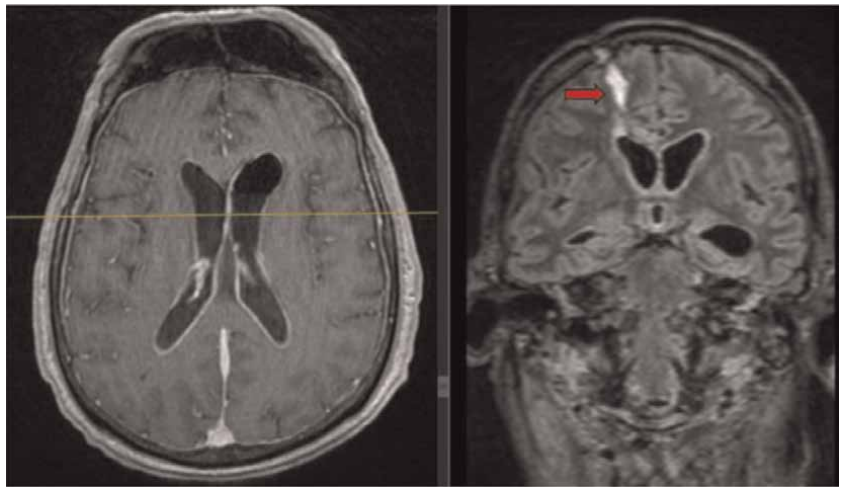

Figure 2.
Axial contrast-enhanced T1-weighted MRI showing tuberculous meningitis (first image). Coronal FLAIR MRI sequence showing postoperative images of an external ventricular drainage in case of tuberculous hydrocephalus. The red arrow marks the place where the external catheter was inserted into the lateral ventricle (the second image) (courtesy Dr. Bogdan Dobrovat).

mainly affects the frontal, temporal and occipital extensions of the ventricles. Arachnoid lesions are mainly located in the basal optochiasmatic region, being responsible for eventual blindness from TBM [9].

3. Clinical characteristics of tuberculous meningitis

Clinical forms of tuberculosis of the central nervous system are represented by

3.1 Intracranial tuberculosis

- Tuberculous meningitis
- Tuberculous meningitis with tuberculous miliary
- Tuberculous encephalopathy
- Tuberculous vasculopathy
- Cerebral tuberculosis
- Cerebral tuberculous abscess.

3.2 Tuberculosis of the spinal central nervous system

- Vertebral tuberculosis with paraplegia
- Tuberculous arachnoiditis
- Spinal meningitis.

Classically, the onset in TBM is insidious (for several weeks), but it can be fulminant in certain cases. A more rapid progression of the disease may occur in young infants in whom symptoms develop only a few days before the onset of acute hydrocephalus, cerebral infarction or seizures.

Clinical manifestations can be divided into three stages, and each stage lasts about 1 week.

3.3 Stage 1 (prodromal stage)

- Lasts 1–2 weeks, consists of non-specific symptoms.
- The child becomes apathetic or irritable, loses interest in playing, has fever, anorexia, vomiting, constipation and weight loss.
- May complain of headache and drowsiness.
- No focal neurological signs.
- Loss or stagnation of developmental stages may occur in children.

3.4 Stage 2—Starts more suddenly

- Signs of meningeal irritation with increased CSF pressure and neck stiffness
- Positive Kernig and Brudzinski signs
- Headache is a cardinal symptom in older children and adults with constant fever.
- Vomiting and constipation can become severe
- Cranial nerve palsies/focal neurological signs
- Lethargy
- Hydrocephalus/Vasculitis
- Some patients have manifestations of encephalitis:
- Disorientation
- Movement disorders
- Speech disorders.

3.5 Stage 3

- Coma sets in quickly
- Irregular high-grade fever and convulsions
- There may be hemiplegia or paraplegia
- Extreme stiffness of the neck, opisthotonus
- Decerebration posture, rigidity
- Deterioration of vital signs, especially the appearance of hypertension
- Death can occur if treatment is started late at this stage.

3.6 Diagnostic categories according to Ogawa (1987)

Confirmed TBM: presence of Koch bacillus in CSF (direct staining, culture) and/or at autopsy
Probable TBM: pleocytosis in CSF, culture negative for bacteria and fungi with one of the following:

- Positive tuberculin test
- Evidence of extra-CNS TB or history of pulmonary TB

- active or significant exposure to TB
- CSF glucose < 40 mg/dL
- CSF proteins > 60 mg/dL [11].

3.7 Diagnostic categories according to Thwaites et al. 2005

Confirmed TBM: Clinical meningitis, abnormal CSF parameters and acid-fast bacilli in CSF (microscopy) and/or positive culture for Mycobacterium tuberculosis.
Probable TBM: Clinical meningitis, abnormal CSF parameters and at least one of the following:

- Suspicion of active pulmonary tuberculosis (chest x-ray)
- BK found in any sample other than CSF.

Possible TBM: Clinical meningitis abnormal CSF parameters and at least 4 of the following:

- History of tuberculosis
- Predominance of lymphocytes in CSF
- Illness lasting > 5 days
- CSF glucose/blood glucose ratio < 0.5
- Alteration of the state of consciousness
- Xanthochromic CSF
- Focal neurological signs [12].

3.8 Classification of tuberculous meningitis

Stage I

- Lack of focal neurological deficit
- Coma score Glasgow 15

Stage II

- Coma Glasgow score 11–14 with focal neurological deficit

Stage III

- Coma Glasgow score 10 or less with or without focal neurological deficit [13].

4. Diagnosis of tuberculous meningitis

The diagnosis of tuberculous meningitis is often a real challenge for the clinician, based in some cases on the clinical aspects and the changes found in the CSF, without bacteriological confirmation. The insidious onset with persistent symptoms for more than 6 days, the presence of neurological manifestations represented by cranial nerve paralysis or peripheral paralysis and the presence of a moderate inflammatory reaction in the CSF are elements that are suggestive for the diagnosis of TBM.

In TBM, the following changes in the cerebrospinal fluid are characteristic:

- pleocytosis, the number of leukocytes is usually between 100 and 500 cells/μL, with a predominance of lymphocytes; at the onset of TBM the number of leukocytes may be lower and neutrophils predominate,
- elevated protein levels, usually between 100 and 500 mg/dL,
- low glucose, usually less than 45 mg/dL or CSF:plasma ratio <0.5 [13].

4.1 CSF examination

- CSF pressure is increased, the color is clear, opalescent or xanthochrome.
- Chloride may be low
- Ziehl–Nelson stained smears can reveal the presence of acid-fast bacilli; they are positive in up to 30% of cases
- CSF culture confirms the diagnosis. The culture is positive in 50–70% of cases, the positive results being related to its volume, it is preferable to collect 5–10 mL of CSF by lumbar puncture [14, 15].
- Antigen detection by polymerase chain reaction (PCR), GeneXpert in CSF and

other useful explorations for the diagnosis of TBM are as follows:

- Immunological tests—the Quantiferon TB Gold blood and CSF test
- Tuberculin intradermoreaction (IDR)—negative in up to 50% of cases
- Cultures of other body fluids can help confirm the diagnosis (pleural fluid, ascites fluid and pericardial fluid)
- Elevated VSH, normal number of leukocytes in the blood with a predominance of lymphocytes;
- The HIV test must be performed in all patients suspected of TBM.
- Gastric lavage in children or sputum examination in adults and older children can reveal tuberculosis bacilli.

- Lymph node biopsy in certain cases to confirm the diagnosis.
- Fundus examination may reveal choroidal tubercles, papillary edema or optic nerve atrophy.

A high index of clinical suspicion is where the patient is in contact with a confirmed case of tuberculosis.

Several studies reveal decreased CSF leukocyte counts and protein levels in HIV-positive patients. CSF examination may even be normal in 5% of HIV-positive patients with TBM [16].

The identification of Mycobacterium tuberculosis in CSF by direct smear or cultures remains the gold standard for confirming TBM, but CSF being a paucibacillary liquid, isolation is only possible in a small number of cases. Moreover, the growth time of the cultures being 3–6 weeks, the diagnosis and the initiation of the treatment can be delayed [14, 17]. For these reasons, the diagnosis of TBM is based in many cases only on the clinical manifestations with slow onset and the neurological signs, associated with the characteristic cytochemical changes in the CSF: moderate inflammatory reaction with a predominance of lymphocytes, low levels of glucose and increased proteins.

The differential diagnosis of TBM is sometimes difficult to make with other forms of meningitis with clear fluid, such as viral meningitis, fungal meningitis, carcinomatous meningitis, partially treated bacterial meningitis, brain abscesses, brucellosis, neurosyphilis and neurosarcoidosis [18]. Meningitis with Cryptococcus neoformans has the same clinical picture and changes in CSF as TBM, but with a delayed evolution (sometimes 2–6 months) and occurs more frequently in immunocompromised people, such as patients with HIV infection [19].

New diagnostic methods of TBM based on the CSF study have been developed to make it more efficient and faster. The BACTEC method allows reducing the time until obtaining a positive culture for M.tuberculosis to 1–3 weeks, and microscopic observed drug susceptibility (MODS) allows the microscopic highlighting of the unique growth characteristics of the Koch bacillus in 5–7 days, also allowing testing simultaneous resistance to antituberculosis medication [20]. Unfortunately, these modern methods are not widely available in all countries.

Nucleic acid amplification (NAA) tests represented by the chain polymerization reaction or M.tuberculosis DNA amplification in CSF ensure a faster diagnosis of TBM, the execution time being 24–48 hours. Being specific, more sensitive and faster than culture, PCR for mycobacteria in CSF constitutes a modern and very useful method in the diagnosis of TBM.

The detection of the IS6110 insertion sequence, used in the initial studies, had a sensitivity between 32–100% and a specificity of 38–100% [21]. Many initial studies conducted to establish the effectiveness of the PCR technique in the detection of M.tuberculosis in CSF used a single target gene, which can cause false negative results. Currently, the multiplex-PCR technique is used, which targets and simultaneously amplifies several genes, such as protein antigen B, MBP64 and IS6110. According to some studies, the sensitivity of this technique is 94.4%, and the specificity is 100% [22].

The Gene Xpert MTB/RIF method is an RT-PCR technique used for the simultaneous detection of M.tuberculosis and sensitivity to rifampicin. It is a quick diagnostic technique, the result being obtained in 2–3 hours. The Gene Xpert technique has a sensitivity of approximately 95% and a specificity of up to 99% for sputum

samples, but the sensitivity in CSF is much lower (approximately 80%) and the specificity is around 97.8%. This is due to the fact that CSF is paucibacillary and the possible presence of substances that inhibit amplification [23].

Molecular diagnostic tests cannot replace direct microscopic bacteriological examination and CSF culture for M.tuberculosis, but they are useful as complementary tests, especially when direct smears are negative. Currently, most experts conclude that commercial NAA tests can confirm TBM but cannot rule it out [22–24].

Another diagnostic method of TBM is the measurement of adenosine deaminase (ADA) activity in CSF. ADA is an element of cellular immunity, its activity being increased in diseases in which cellular immunity is involved, a fact also found in TBM. The sensitivity of ADA varies between 60–90% and the specificity between 80–90%, but the method has not yet been well standardized and is not routinely recommended in the diagnosis of TBM [24, 25]. The detection of M.tuberculosis specific antibodies or antigens in the CSF is a rapid method of diagnosing TBM. The direct detection of cells secreting specific antibodies by the ELISPOT method has a sensitivity of 84% and a specificity of 91.8%, the sensitivity being higher if the test is performed in the first 4 weeks after the onset of the disease [26].

In recent years, two blood tests for in vitro diagnosis of tuberculosis: Quantiferon TB. Gold (Cellestis, Australia) and T-SPOT.TB (Oxford, Immunotec, United Kingdom), based on the pathogenic specificity of ESAT-6 (Early Secretory Antigen Target) and CFP-10 (Culture Filtrate Protein -10) have been developed for clinical use. The cellular immune response is an important component of the immune response regarding M. tuberculosis, the induction of a protective response translating into the synthesis of TH1-type cytokines, especially gamma interferon (IFN-gamma). IFN-gamma detection is the basis of the principle of these two tests. The sensitivity (approximately 89%) and specificity (approximately 98%) are clearly improved compared to those of the PPD skin test [27]. The Quantiferon TB.Gold (QFT-G) test produced by the Cellestis company measures the amount of interferon gamma cytokine released by T lymphocytes after stimulation with ESAT-6 and CFP-10, through a sensitive ELISA technique. QFT-G is a rapid immunological test, with results obtained in 24–48 hours. With its help and in conjunction with clinical, epidemiological data and the CSF examination, it allows a rapid diagnosis, before obtaining a positive culture for M. tuberculosis. QFT-G can be performed from both blood and CSF, a positive result in CSF being a solid argument for the diagnosis of TBM [28].

5. Imaging exploration in TBM

Chest X-ray can be normal in 20–50% of cases; There is usually some evidence of pulmonary tuberculosis (hilar adenopathy, pneumonia or miliary tuberculosis). **Computed tomography (CT)** and **nuclear magnetic resonance (MRI)** of the brain are normal in the early stages of the disease, but as TBM progresses they may show increased basal contrast, communicating hydrocephalus, signs of cerebral edema, one or more clinically silent tuberculomas, most often in the cerebral cortex or thalamic regions [29, 30].

In various studies, MRI has been shown to be more sensitive than a CT scan, but cerebral CT is easier to perform in children, MRI requiring general anesthesia in small children. A CT scan may initially be normal in nearly 30% of cases, which does not

initially exclude the possibility of a TBM [31]. Common neuroimaging findings seen in TBM are outlined below:

Communicating hydrocephalus—80%; basal meningeal enhancement—75%; cerebral infarctions—8–44%; tuberculomas—8–31% [29, 30].

Thwaites performed computed tomography in 60 cases of tuberculous meningitis and found hydrocephalus in 87% of cases in children compared to 12% in adults [32]. In children, this complication appears after 6 weeks of infection. Vascular infarcts were found in 28% of cases, most of them being located in the territory of the middle cerebral artery. Severe prognosis is associated with basal and periventricular exudate [33].

The performance of the magnetic resonance images is due to the intravenous use of gadolinum. Hyperdensity in the basal cisterns is a good predictor for tuberculous meningitis [33, 34]. Both imaging methods give suggestive information on when neurosurgical intervention for hydrocephalus should be performed.

Imaging differences were also noted depending on the age group and the association or non-association of HIV infection.

In the statistics of Thwaites, the presence of basal exudate in 82% of cases and hydrocephalus in 77% of patients is reported in adults who underwent cerebral magnetic resonance [34]. During treatment, 74% of patients develop tuberculoma, most cases being asymptomatic. Children and adults with tuberculous meningitis and HIV infection have less hydrocephalus and basal exudate, and more frequent infarcts, increased convolutions, and multiple lesions compared with patients without HIV [35–37].

Patients with HIV infections more frequently develop cerebral atrophy [35, 36].

6. Classification of TBM

In 2010, a new consensus definition was proposed, the criteria for defining TBM being applicable regardless of patients' age or HIV status. According to these criteria, patients are stratified as definite, probable and possible tuberculous meningitis [38].

1. **Clinical Criteria** include

   - symptoms duration > 5 days (4 points)
   - symptoms suggestive of TB (> 1 of the following): weight loss/low weight gain; night sweats; cough> 2 weeks (2 points)
   - cranial nerve palsy (1 point)
   - altered consciousness (1 point)
   - focal neurologic deficit (excluding cranial nerve paralysis) (1 point);
   - a close contact with a person confirm with TB or positive tuberculin test or Quantiferon TB Gold/ElI-SPOT TB positive test (2 points).

   The maximum score of clinical criteria is 6.

2. **The criteria regarding the CSF examination** are represented by

   - clear CSF (1 point);
   - the number of cells between 10–500/μL (1 point);
   - lymphocytic predominance with lymphocytes > 50% (1 point);
   - protein concentration > 1 g/l (1 points).
   - absolute CSF glucose <2.2 mmol/L (1 points).

   The maximum score is 4 points.

3. **The radiological criteria are based on the existence of the most frequently encountered changes in MTB:**

   - hydrocephalus (1 point);
   - basal meningeal hyperdensity (2 points);
   - basal meningeal thickening (2 points);
   - tuberculomas (2 points);
   - cerebral infarcts (1 point)
   - pre-contrast basal hyperdensity (2 points).

   The maximum score for this section is 6 points.

4. **The presence of extraneuraxial TB increases the probability of the diagnosis of MTB and includes**

   - radiographically detectable pulmonary tuberculosis (2 points);
   - miliary TB (4 points);
   - CT or MRI suggestive for TB outside the central nervous system (2 points);
   - fast-identified bacilli or M. tuberculosis cultivated from another source (e.g., sputum, ganglia, gastric lavage, urine and blood cultures) (4 points)
   - PCR positive for M. tuberculosis from extraneural sources (4 points).
   - The maximum score from these criteria is 6 points.

Clinical entry criteria: Symptoms and signs of meningitis including one or more of the following: headache, irritability, vomiting, fever, neck stiff ness, convulsions, focal neurological deficits, altered consciousness or lethargy [38].

According to new consensus, TBM are classified as definite, probable and possible [38].

Definite tuberculous meningitis means the demonstration of the presence of M.tuberculosis in the CSF. The diagnosis of **probable TBM** requires a score of at least 12 points when imaging techniques are available or at least 10 points when radiological methods are not available, excluding alternative diagnoses.

The diagnosis of **possible TBM** requires a score of 6–11 points when imaging techniques are available or 6–9 points when they are not available, excluding alternative diagnoses.

The exclusion of differential diagnoses requires the performance of Gram stains, routine cultures, cryptococcal antigen, serology (e.g., Borrelia, syphilis) or histopathological examination of brain tissue/meninges (tumors and lymphoma).

7. Treatment of tuberculous meningitis

Various guidelines recommend an intensive first phase, with the use of four drugs: rifampicin, isoniazid, pyrazinamide (RHZ) + streptomycin (S) or ethambutol (E) or ethionamide [39–41]. There follows a continuation phase consisting in the administration of two drugs (RH), the total duration of treatment varying in different protocols between 9–12 months. For newly diagnosed TBM cases, intensive phase treatment will consist of 8 weeks of isoniazid, rifampicin, pyrazinamide and ethambutol. According to the recommendations of the Center for Disease Control and Prevention (CDC) and Infectious Diseases Society of America, the ideal duration of antituberculosis treatment should be between 9–12 months [39]. The British Infection Society recommends 12 months of treatment, and the WHO considers that 9–12 months of antituberculosis medication would be sufficient to reduce complications and sequelae [40, 41]. Clinical and biological monitoring should be performed at least once a month to observe any adverse reaction to the antituberculosis treatment. However, the optimal treatment of TBM has not yet been established in clinical trials. The same drug can have different pharmacokinetics in the blood and in the CSF.

7.1 Isoniazid

- Isoniazid is the first antituberculosis drug of choice among antituberculosis drugs, being bactericidal on growing bacteria and having good penetration into the CSF, where it achieves concentrations of 20% of the plasma titer.

- The dose is 5–10 mg/kg/day (maximum 300 mg) for adults and 15 mg/kg/day for newborns.

- Potential side effects are peripheral neuropathy due to pyridoxine deficiency, optic neuritis, hypersensitivity reactions manifested by skin rashes and fever.

- Isoniazid can also cause hepatoxicity, manifested by the increase of liver enzymes after 4–12 weeks of treatment and sclerotegumentary jaundice [42]. Antituberculosis treatment must be continued, combining hepatotrophic drugs, vitamins.

7.2 Rifampin

- It is bactericidal and it acts by inhibiting RNA polymerase.
- Penetrability in the CSF is lower than that of isoniazid and occurs slowly.
- The recommended dose 10–15 mg/kg/day (maximum 600 mg) and the duration of treatment minimum of 9 months.
- Potential side effects are hepatotoxicity, rash, flu-like syndrome and multiple drug interactions [42].

7.3 Pyrazinamide

- It is bactericidal in an acidic environment and easily penetrates the CSF.
- It is initially used as a third drug for 2–3 months
- The dose is 30–35 mg/kg/day (maximum 2 g)
- The main side effects are arthralgia, arthritis, hyperuricemia (gout).

7.4 Ethambutol

- Not recommended for children under 6 years of age.
- Dose 15–25 mg/kg (maximum 1 g) once a day.
- Side effects are optic neuritis and hypersensitivity reactions.

Due to the fact that the new generation of fluoroquinolones (FQs), e.g., levofloxacin, ofloxacin, and moxifloxacin, have potent activity against most strains of M. tuberculosis and have excellent CSF penetration and safety profiles, they could be used as part of therapy first line for TBM [43].

8. Pharmacokinetic activity and CSF penetration of anti-TB drugs

8.1 First-line drugs

- Rifampin bactericidal, 5–25%
- Isoniazid bactericidal, penetration into CSF 90–95%
- Pyrazinamide bactericidal, 95–100%
- Ethambutol bacteriostatic, 10–50%
- Streptomycin bacteriostatic, 20–25%

- Ciprofloxacin bactericidal, 15–35%
- Levofloxacin bactericidal, 60–80%
- Moxifloxacin bactericidal, 70–80%

8.2 2nd line drugs

- Ethionamide bactericidal 80–95%
- Bacteriostatic cycloserine 40–70%
- Amikacin bactericidal 10–25%
- Bactericidal streptomycin 10–20%
- Bacteriostatic capreomycin, penetration into CSF unknown
- Para-aminosalicylic acid bacteriostatic, unknown
- Bacteriostatic thioacetazone, unknown
- Linezolid bactericidal, 80–100%

8.3 New agents

- Bedaquiline (TMC207) bactericidal, unknown
- Delamanid (OPC-67683) bactericidal, unknown [39–45].

The treatment of tuberculous meningitis is a strictly supervised treatment (DOTS) for 12 months, intensive (2 months) + continuous phase (10 months). Why the treatment is so long, till routine DOTS regimen is 6 months? Because large doses are required to penetrate the blood–brain barrier and to prevent recidivism rates.

Children with TBM should be hospitalized, preferably for the first 2 months or until clinical stabilization. In intensive phase four drugs (RHZE/S) are recommended for 2 months and in continuation phase, isoniazid and rifampicin recommended for 10 months.

In recent years, resistance to antituberculosis drugs is increasing, and multidrug-resistant tuberculosis (MDR-TB) poses serious treatment problems. Clinical trials of examining the use of high-dose rifampicin and/or fluoroquinolones are likely to report in the near future [45].

HIV/AIDS infection significantly complicates the treatment of TBM by high prevalence of drug side effects, high risk of drug–drug interaction, reducing the absorption of antiviral drugs and risk of developing immune reconstitution syndrome (IRIS). In HIV seropositive patients, it is recommended to start the anti-tuberculosis treatment first and then, after 2–8 weeks, the antiviral one.

9. Adjuvant therapy with corticosteroids in TBM

Corticosteroids (dexamethasone, prednisone and methilprednisolon) are recommended for all children and adults with TB meningitis [46]. Patients with an average form of the disease will receive dexamethasone 0.3 mg/kg/day x 1 week, 0.2 mg/kg/day x 1 week after which oral treatment for 4 weeks. Patients with severe forms of TBM will receive for 4 weeks decreasing dexamethasone 0.4 mg/kg/day x 1 week, 0.3 mg/kg/day x 1 week, 0.2 mg/kg/day x 1 week, 0.1 mg/kg/day x 1 week, then oral treatment with the same preparation for another 4 weeks [47]. In HIV-positive patients, corticosteroid therapy is administered in the absence of life-threatening opportunistic infections. A study conducted in Vietnam in patients with TBM [46], randomized, double-blind, placebo-controlled trial (n=545), shows that dexamethasone is associated with a reduced risk of death or severe neurosequelae at 9 months, but does not prevent severe neurological disability [46]. It has been postulated that dexamethasone reduces the deleterious effects of the immune response and also reduces the incidence of hydrocephalus and brain infarction [32, 47].

10. Treatment of hydrocephalus in TBM

The most common classification system used in patients with TBM and hydrocephalus is Vellore grading system which was introduced for the first time in 1991 and later modified in 1998 [48, 49]. This system classifies TBM in four grades, grade I representing the patient with GCS 15 points, and grade IV representing the patient in a deep coma (**Table 1**).

There is no doubt that the treatment of TBM is represented by the prompt initiation of antituberculosis treatment (6). Regarding the treatment of hydrocephalus from TBM, we have two types of treatment: medical and surgical, the second being the most frequently used [7].

10.1 Medical treatment

Patients with communicating hydrocephalus are generally treated with medication. Studies have shown that the use of steroids reduces mortality in all patients with

Grading	Clinical characteristics
I	GCS 15 points Headache, vomiting, fever, neck stiffness without neurological deficit
II	GCS 15 points neurological deficit present
III	GCS 9–14 points neurological deficit may or not may be present
IV	GCS 3–8 points neurological deficit may or may not be present

GCS = Glasgow Coma Scale Score.

Table 1.
Modified Vellore grading for patients with tuberculosis meningitis and hydrocephalus [48, 49].

TBM; moreover, they reduce the incidence of neurological sequelae. Corticosteroid treatment reduces inflammation and vasogenic edema, improving the signs of intracranial hypertension [6, 46, 47]. Acetazolamides and diuretics can also be used, because they reduce CSF production and improve interstitial edema. In more severe cases, mannitol can be administered, especially to delay the surgical treatment of hydrocephalus [6].

10.2 Surgical treatment

The surgical treatment of hydrocephalus is reserved for patients who are refractory to drug treatment, or for patients in whom drug treatment no longer has any effect on hydrocephalus. The principle of surgical treatment of hydrocephalus is to divert the CSF flow. The main surgical options include bedside external ventricular shunt, ventriculoperitoneal shunt or endoscopic third ventriculostomy [7, 48].

A meta-analysis that included 19 studies and 1038 patients reported a good outcome in 58.3% of patients [49]. As expected, the best outcome was reported in patients with grade-I TBM, and the worst outcome was reported in patients with grade-IV TBM. Also, a frequently encountered complication is a malfunctioning shunt, which may require revision of the shunt [50]. The patients most exposed to this complication are those with very high CSF protein levels. Other complications included shunt displacement, shunt erosion or development of peritoneal cysts [51].

Endoscopic third ventriculostomy is an effective alternative method to ventriculoperitoneal shunt, this surgical method being particularly indicated in communicating hydrocephalus, such as Sylvius aqueduct stenosis occurred in TBM [51].

11. Evolution and complications

Among **short-term complications**, communicating hydrocephalus represents approximately 80% of cases of TBM, more common than non-communicative. Other frequent complications are paralysis of the cranial nerves (3,6, and 7). The VI nerve is the most frequently involved, its damage leading to relatively sudden ophthalmoplegia and diplopia. Blindness can occur due to compression of the optic nerve during the development of hydrocephalus, through optochiasmatic arachnoiditis or through optic nerve granuloma. The involvement of small and large vessels, with the development of vasculitis obliterans, can cause ischemic and hemorrhagic complications, which occur especially in the territory of the internal carotid artery, the middle cerebral artery and small perforating vessels. Ischemic vascular accidents occur in approximately 30% of TBM cases and can manifest in a variety of ways [52, 53].

Long-Term Complications are represented by cognitive disability, seizures, cerebrovascular accidents manifested by hemiparesis and aphasia, myelitis manifested by paraparesis and hydrocephalus complicated with increased intracranial pressure.

Affecting the hypothalamus in TBM can determine diabetes insipidus, obesity, adipose-genital syndrome, precocious puberty and delay in height growth [52].

The **sequelae** of TBM are represented by motor deficits, cognitive deficits, blindness, deafness, epilepsy, behavioral disorders, the decrease in school performance in children [52–54].

The appearance of hydrocephalus is clinically manifested by varying degrees of alteration of the state of consciousness in patients with tuberculous meningitis [5, 54]. Tuberculomas and brain abscesses can cause convulsions and motor deficits [54–56].

Hydrocephalus in infants with TBM can cause the following symptoms: vomiting, drowsiness, irritability, difficult feeding, convulsions, low muscle tone, "sunset" gaze, poor reactivity to external stimuli, lack of growth and development [49, 56].

The symptoms that make up the clinical picture of hydrocephalus in the case of a young child diagnosed with TBM are represented by headache, blurred vision or diplopia (double vision), increased cranial perimeter, drowsiness, loss of balance, poor coordination of movements, convulsions, decreased appetite and in certain situations, urinary incontinence (involuntary loss of urine) [49, 54, 56].

Behavioral and cognitive changes in children with hydrocephalus frequently include irritability, personality changes, delayed acquisition of age-specific skills (speech) or decreased school performance.

The treatment of hydrocephalus is etiological and involves performing a cerebral surgical intervention represented by

- Creation of a system of ventricular valves to ensure an optimal drainage of the cerebrospinal fluid, by diverting its circulation from the ventricles to the peritoneal level, with the help of flexible tubes equipped with valves;

- Endoscopic ventriculostomy of the third ventricle requires the creation of a continuity solution at the ventricular level to ensure a proper drainage of the cerebrospinal fluid [57, 58].

Drug treatment aims to reduce symptoms and involves the administration of diuretics and anticonvulsants to improve the patient's general condition. Medical therapy should be tried prior to any form of surgical intervention; manitol, furosemide, acetazolamide and dexamethasone should be used first. CSF pressure monitoring can be useful in cases where CSF (ventricular) drainage is considered in obstructive hydrocephalus, and the decision to perform the procedure must be based on the patient's level of consciousness and the degree of ventricular dilatation visualized on brain imaging (CT or MRI). If hydrocephalus is the cause of clinical deterioration, repeated lumbar punctures or external ventricular drainage has been recommended [49, 56, 57].

12. Prognosis of tuberculous meningitis

TBM prognosis depends on two factors: age of the patient and the stage of the disease at which the treatment began. Without treatment, the prognosis is fatal. In stage 1, a 100% cure rate is expected. Even with optimal therapy, mortality varies between 30–50%, and the incidence of neurological sequelae is 75–80%, especially in stage 3 [59]. In contrast, most patients diagnosed with stage 3 who survive have permanent disabilities: blindness, deafness, paraplegia, mental retardation and diabetes insipidus. Infants and young children have a poor prognosis compared to older children [60–62].

13. Conclusions

TBM is a severe form of extrapulmonary tuberculosis with a high mortality rate due to the delay in diagnosis and adequate treatment. In the absence of an early

diagnosis and treatment, tuberculous meningitis is characterized by high mortality (20–50%) and increased morbidity (20–30%). The diagnosis of TBM remains difficult as its presentation is non-specific and may mimic other causes of chronic meningoencephalitis. Cytological and biochemical analysis of the cerebrospinal fluid is the cornerstone for diagnosis, but there are often diagnostic difficulties in differentiating tuberculous meningitis from nontuberculous. Although the culture for mycobacteria from CSF remains the gold standard for the diagnosis of TBM, the diagnosis is often delayed due to the long time interval until cultures are obtained. Therefore, it is necessary to discover new rapid tests that optimize the diagnosis of TBM. The new molecular biology tests and those based on gamma interferon release have improved the prognosis through a faster diagnosis and promptly initiated anti-tuberculosis treatment. New studies on the pathogenesis of MTB would be necessary for a better understanding of the therapeutic mechanisms needed to improve the prognosis.

The optimal duration of antituberculosis treatment has not been established precisely, varying in different studies and recommendations. The discovery of new classes of drugs active on M.tuberculosis is imperative considering the growing number of patients diagnosed with multidrug-resistant TB (MDR-TB) or even extensively drug-resistant TB (XDR-TB). MTB in patients with HIV infection raises serious treatment problems due to drug interactions, the possibility of immune reconstruction syndrome and the more frequently unfavorable evolution, toward complications and death.

The role of corticosteroid treatment in MTB is controversial, the duration of treatment has not been clearly established, and their role in preventing complications and sequelae is not well defined.

More studies are needed to establish the role of surgical treatment, the optimal timing of surgery and the best method for the treatment of hydrocephalus.

Conflict of interest

The authors declare no conflict of interest.

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Section 2

Surgical Treatment of Hydrocephalus

Chapter 4

Ventriculostomy

Gobti Beltus Abongha, Ngeloh Meekness Afunui, Nkenganyi Aka Elvira, Kengo Nathan Ezie and Victor Meza Kyaruzi

Abstract

In neurosurgery, especially in pediatrics, the practice of ventriculostomy or placement of an external ventricular drainage (EVD) is a routine procedure. It consists of the implantation of a catheter in the ventricular system of the brain to temporarily divert cerebrospinal fluid or to measure the intracranial pressure. This method was created and improved during the past century, and it is now regarded as a standard procedure. Despite this standardization, EVD installation can still result in a variety of problems, the most serious of which is infection, which is associated with high rates of morbidity and mortality. The essential points of EVDs in the pediatric population are presented in the current chapter, with an emphasis on the indications for insertion, complications, and measures to prevent poor functional outcomes.

Keywords: CSF, external ventricular drain, intracranial pressure, hydrocephalus, ventriculostomy

1. Introduction

Ventriculostomy is a neurosurgical procedure where a drainage hole (or stoma) is made inside the cerebral ventricle. It is usually carried out on people who have hydrocephalus [1]. The ventricular system of the brain is reached by surgically entering the skull, dura mater, and brain gaining access to the lateral ventricle, usually from the non-dominant lobe (the right frontal lobe in most individuals [2, 3]. An external ventricular drain (EVD) is a typical term used to describe temporary catheter drainage. This is going to be the focus of this chapter.

By diverting the CSF often kept in the ventricular system, a ventriculostomy decompresses the spaces and makes it easier for ICP to return to normal [3]. Many clinical situations could urgently call for the implantation of an EVD. In this regard, the rate of EVD installation in the general population has gradually increased, notably in the industrialized world [4, 5].

CSF draining has been attempted numerous times in the past. Its initial technical description has undergone numerous modifications, and new applications for it have emerged as a result of technological advancement. Congenital hydrocephalus was originally treated with external ventricular drainage in the 18th century [6]. Claude-Nicholas Le Cat (1700–1768) described his technique for performing a ventricular

puncture using a trocar and catheter modified for the treatment of ascites. Early attempts, however, were unsuccessful [6]. Later, Robert Whytt (1714–1766) concurred with Benjamin Hill that ventricular drainage should never be done, not even as a last resort, believing it to hasten death [6]. Midway through the 19th century, advancements in the ventricular drainage method were seen, proving its usefulness. Three different developments each helped to achieve this: The use of the aseptic approach, understanding of the effects of excessive ventricular drainage, and determination of the best locations for catheter insertion [7].

Brain trauma, cerebral hemorrhage, and brain tumors are only a few neuropathological diseases that frequently cause issues and changes in CSF dynamics in the pediatric population [5]. EVD insertion has been proposed as the most significant and often lifesaving emergency therapy in neurosurgery in this context. These circumstances may demand an urgent treatment of secondary hydrocephalus or to ICP monitoring. Due of this, residents acquire it as one of their initial surgical skills while undergoing training.

While planning to insert an EVD, it's crucial to take into account both the patient's age and the nature of their illness because different indications and technical considerations may apply.

The management of EVD in the pediatric population is reviewed in this chapter. The discussion of indications and technical factors will follow a quick overview of some ventricular anatomy. Finally, the most significant EVD-related consequences are discussed, along with several evidence-based recommendations for preventing or treating those issues.

2. The ventricular system

The brain's ventricular system is a network of compartments filled with cerebrospinal fluid (CSF), which cushions the brain [8]. The purpose of the cerebral ventricles was unknown, despite the fact that their existence has been recognized since antiquity. In the past, researchers thought that the ventricles were where memory, logic, and emotion were stored.

The walls of the brain's ventricular system (ependyma) are lined by a special kind of cell called an ependymocyte. This cuboidal or columnar epithelium was developed from the neuroepithelium. A collection of permeable capillaries in a connective tissue matrix makes up the choroid plexus, which generates CSF and is situated right underneath the ependymal layer. A layer of subependymal glial cells lies beneath the ependyma. These cells and the astrocyte processes work together to generate the blood-brain barrier, which is tightly connected [8].

The ventricular system consists of four ventricles, with two of them located in each cerebral hemisphere, one in the diencephalon, and the other in the hindbrain. It is connected inferiorly to the spinal cord's central canal.

Each cerebral hemisphere contains a C-shaped hollow known as the lateral ventricle. Ependyma lines the inside, which is filled with CSF with a capacity of 7 ml to 10 ml. The septum pellucidum, a narrow vertical layer of nerve tissue that divides the two lateral ventricles, is surrounded by ependyma on both sides. The interventricular foramen of Monroe serves as its conduit to the third ventricle. The foramen becomes more rounded as the ventricular size grows. The superior choroidal vein, septal vein, and medial posterior choroidal arteries all travel via this foramen [8–10].

A median slit-like hollow known as the third ventricle sits between the two thalami and a portion of the hypothalamus. Through the cerebral aqueduct of

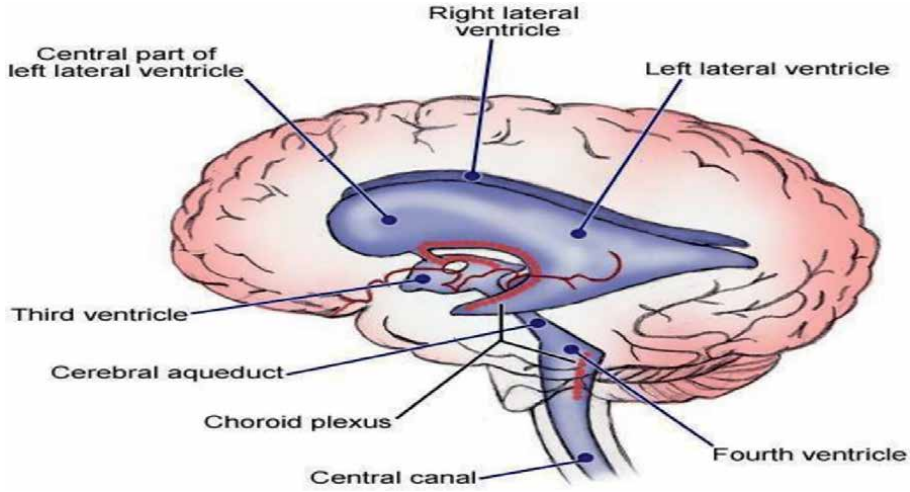

Figure 1.
The ventricular system of the human brain.

Sylvius, it communicates with the lateral ventricles on its anterosuperior aspect and the fourth ventricle on its posteroinferior aspect. Ependyma lines the third ventricle space, and a mass of gray matter known as the interthalamic adhesion or Massa intermedia, which is situated behind the foramen of Monroe and connects the two thalami, passes across it [8, 9].

The Sylvian aqueduct is the brain's ventricular system's thinnest section (as seen in **Figure 1**). It has a diameter of around 18 mm and is where interventricular blockage occurs most frequently. Due to the growth of the surrounding brain tissue, it has been found that the luminal thickness of the aqueduct lowers starting in the second foetal month [8, 9].

A large, tent-like cavity of the hindbrain filled with CSF is known as the fourth ventricle. The pons and cranial half of the medulla form its anterior border, and the cerebellum forms its posterior border. On a sagittal section, it appears triangular, and on a horizontal section, it appears rhomboidal. It connects to the cerebral aqueduct in the superior region and the spinal cord's central canal in the inferior region. The fourth ventricle interacts with the subarachnoid space by two lateral foramina of Lushka and one medial foramen of Magendie [9].

A solitary cavity, or hollow of the neural tube, is where the ventricular system originates. Around the fourth week of pregnancy, the neural tube begins to develop. The amniotic cavity and neural cavity are then segregated shortly after the spinal neurocele closes [8, 9].

Ventricles grow and expand to adult size in the early stages of development. After that, the brain tissue starts to grow in a different directions from the ventricles, from caudal to cephalic, and this difference in growth creates the adult ventricular shape. Any obstruction to the CSF's free passage through the ventricular system causes hydrocephalus [8, 9].

3. Indications and contraindications for ventriculostomy

3.1 Indications

Placement of an EVD is essential for many disorders in neurosurgery;

1. Acute symptomatic hydrocephalus: one of the most frequent indications for a ventriculostomy is for the management of acute symptomatic hydrocephalus. Hydrocephalus is a condition in which excess cerebrospinal fluid (CSF) builds up within the fluid-containing cavities or ventricles of the brain. Other causes of hydrocephalus such as normal pressure hydrocephalus and hydrocephalus ex vacuo which are usually chronic and non-symptomatic are usually not managed by this procedure. It is used in the management of congenital hydrocephalus and acquired hydrocephalus in children and adults usually following subarachnoid hemorrhage (SAH), strokes and meningitis [11]. This procedure is used as management for congenital hydrocephalus only when the baby is >6 weeks of age. For acquired hydrocephalus, it enables drainage of accumulated blood (in SAH), infected CSF (in meningitis) or peritoneal shunting of excess CSF [2, 11–13].

2. Intracranial pressure (ICP) monitoring: the ideal method for monitoring ICP is a ventriculostomy. It can be used to drain CSF or to estimate intracranial compliance and can be introduced by a twist drill craniostomy at the patient's bedside. The catheter can be attached to a filter-protected collection chamber for CSF drainage as well as a pressure transducer to assess intracranial pressure (ICP). To ensure that spontaneous CSF resorption is sufficient and ICP will not rise to unsafe levels, ICP is watched for at least 24 hours [12].

3. Adjunct management for malfunctioning or infected ventriculoperitoneal shunts (VPS): an effective treatment option for CSF shunt infection is endoscopic third ventriculostomy (ETV). It is possible to compare the ETV lifetime to that of reinserted VPSs. Use of ETV during infected CSF shunt removal can be considered a potent alternative or at the very least an adjunct to VPS reinsertion because the reinserted VPS has considerably better lifetime than a VPS reinserted without employing ETV, even in the event that ETV fails [14].

4. As a panacea for brain relaxation during intraoperative brain edema: ventriculostomy performed during intraoperative brain edema is associated with a high level of success in achieving brain relaxation. The use of this technique during pterional approaches for acute aneurysmal surgery in the tight, bulging brain to achieve relaxation and avoid secondary complications such as retraction contusions and resultant cerebral edema is also recommended [15].

5. Planning therapeutic interventions- thrombolytics, antibiotics, for managing vasospasms [2]: this indication is not considered a major indication as there are other conservative and noninvasive methods that can be used. A ventriculostomy in the case of managing vasospasms is considered an ICU intervention.

3.2 Contraindications

The contraindications for ventriculostomy include:

1. Concurrent use of anticoagulant drugs: ventriculostomy is contraindicated during concurrent use of anticoagulant drugs as these may predispose patient to excessive bleeding.

2. Bleeding disorders: ventriculostomy is usually associated with some initial bleeding during placement thus in patients with bleeding disorders this could lead to severe hemorrhage.

3. Scalp infection: scalp infections predispose patient to further complications as Ventriculostomy could cause translocation of infection.

4. Brain abscess: a common and often debated concern regarding CSF drainage with a ventriculostomy is that it can cause subfalcine herniation in the presence of a hemispheric mass or upward herniation of the cerebellum in the presence of an infratentorial lesion [13].

4. Ventriculostomy procedure

By diverting the CSF often kept in the ventricular system, a ventriculostomy decompresses the spaces and makes it easier for ICP to return to normal. In this treatment, the ventricle is reached by guiding a flexible silastic catheter through the brain parenchyma using a hard internal stylet [16] (**Figure 2**).

In about 10–40% of cases, there are recorded complications of ventriculostomy such as bleeding and unintentional insertion in brain tissue. In order to increase the precision and effectiveness of placement, technical advancements utilizing computed tomography (CT), ultrasound, endoscopy, and stereotactic neuronavigation have been made [2]. The incidence rate of these complications thus necessities a rigorous procedure for higher efficiency.

Equipment to include in the basic tool set include: Non-sterile gloves, soap, a brush, a towel, a razor, and a marker pen to prepare the components and mark the location where the monitor devices will be placed. A face mask, sterile gloves and

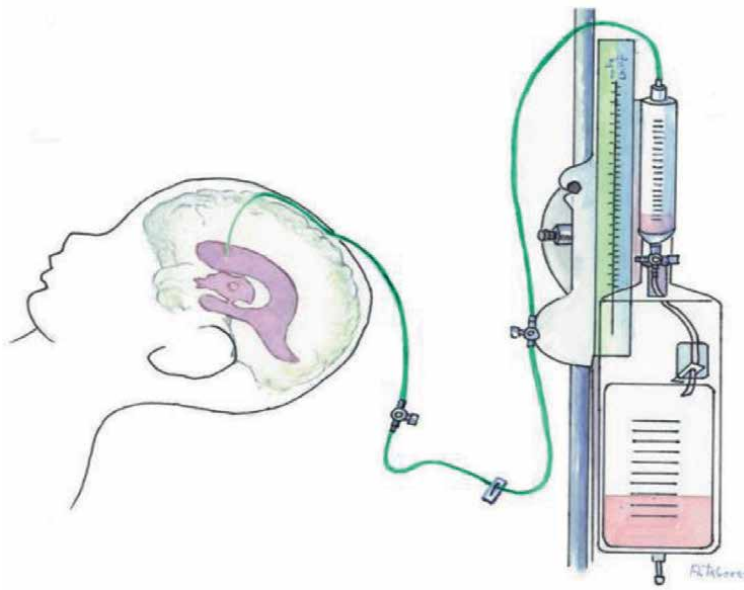

Figure 2.
Closed external ventricular device.

gown, antiseptic solution, drape, local anesthetic, 5-ml syringe, 15- or 11-number surgical blade, and ICP monitoring kit are required for the treatment itself. According to the techniques, a drill with a drill bit, a bolt, an ICP sensor, and a transducer, an aseptic dressing and suture material will be necessary.

A multidisciplinary medical team comprising of:

The brain surgeon (Neurosurgeon),

A competent assistant,

A nurse practitioner,

An anesthetist and.

A general assistance [17].

For the **procedure**, the patient is kept in the supine position with the head of the bed elevated at a 45-degree angle. It could be necessary to shave some hair with the

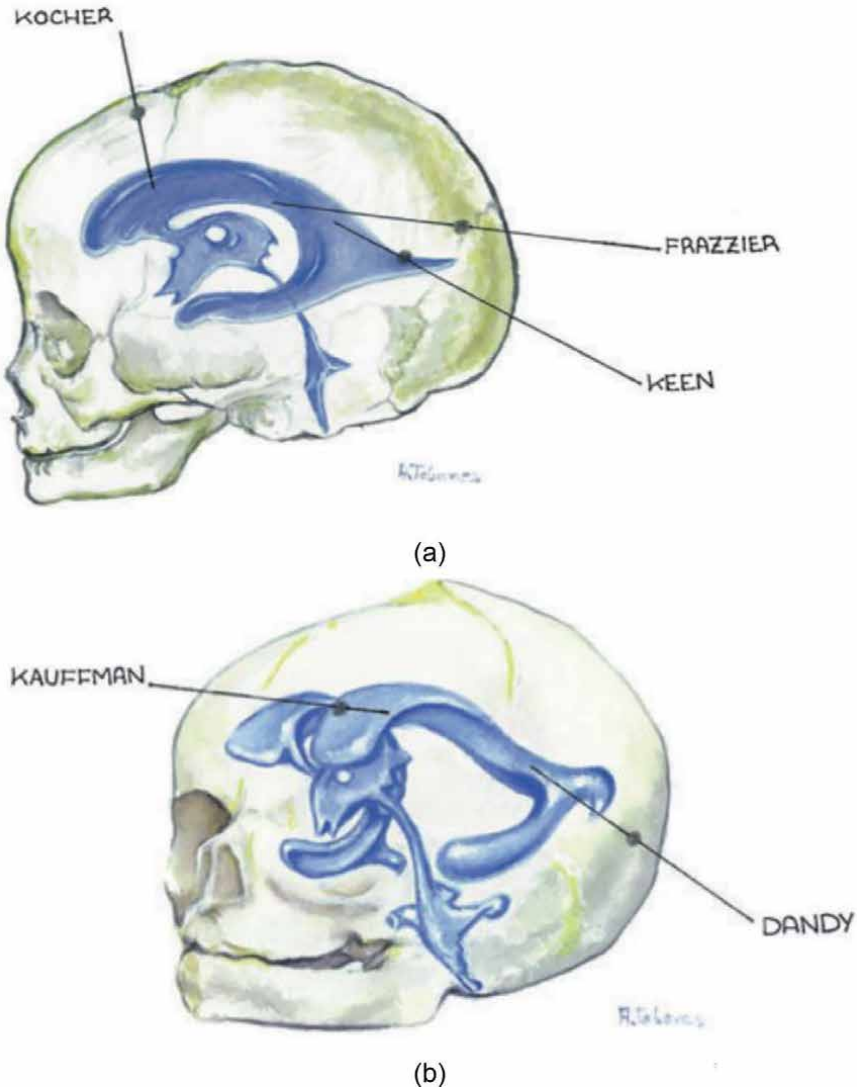

Figure 3.
(a and b) Main approaches and their trajectories for ventriculostomy.

aid of the razor and the area sterilized before the procedure. Given that it is not the dominant hemisphere for language function in >90% of patients, the right frontal cerebral hemisphere is the recommended site of entry. The reference point is that of Kocher which is located at 1–2 cm in front of the mid pupillary line's coronal suture, 11 cm behind the glabella, 3–4 cm to the side of the midline ipsilateral medial canthus, and a line going coronally from the ipsilateral tragus. The superior sagittal sinus and the motor strip of the frontal brain are avoided at this point. Other points include Keen's point which is 2.5–3 cm above the ear pinna and 2.5–3 cm posterior, Dandy's point: 2 cm laterally and 3 cm above the inion, Frazier's point: 4 cm laterally and 6 cm above the inion, Paine's point: the point of an isosceles triangle, whose two limbs each measure 2.5 cm and whose base is located along the Sylvian veins, and Tubbs' point: The trajectory points 45 degrees away from a horizontal line and 15–20 degrees medial to a vertical line, passing through the top of the orbit at a location just medial to the mid papillary point [2–4].

On the scalp, a 2 cm-tall incision is made that may be straight or horseshoe-shaped after local anesthetic has been given (**Figure 3**).

The twist drill is used to enter the skull along the path chosen for ventricular cannulation. The ventricular catheter is primed and advanced no further than 7 cm, aiming in the anteroposterior plane at a spot 1.5 cm anterior to the ipsilateral tragus, toward the ipsilateral Foramen of Monro, and in the coronal plane toward the medial canthus of the contralateral eye. After the catheter stylet has been removed, CSF flow may be seen, and it can then be transduced to determine the opening intracranial pressure. It is then connected to an external drainage system after being tunneled

Approach	Description
Keen	Entry point: 2.5–3 cm behind and 2.5–3 cm above the earpinna. For roughly 4–5 cm, the catheter is positioned perpendicular to the cortex with a small cephalic inclination.
Kocher	11 cm behind the glabella and 3–4 cm lateral to the midline or 1–2 cm anterior to the coronal suture at the middle pupillary line. When treating very young patients, it is recommended that the catheter be advanced no further than 6 cm. To guide catheter insertion, use the ipsilateral medial canthus in the coronal plane and the external acoustic meatus in the sagittal plane.
Dandy	3 cm above and 2 cm lateral to inion. The catheter is placed perpendicular to the cortex with a slight cephalic direction for about 4–5 cm
Frazier	3–4 cm lateral from the midline and 6–7 cm superior to the inion (depending on age and head size). For roughly 4 cm, the catheter is advanced perpendicular to the cortex, in the direction of the contralateral medial canthus.
Kauffman	3 cm from the midline and 4 cm above the nasion. The catheter is aimed for 6–7 cm at a point 3 cm above the external occipital protuberance.
Menovsky	Following an eyebrow incision, a catheter is angled 45 degrees toward the midline and 20 degrees away from an imaginary line parallel to the orbito-meatal line during a supraorbital craniotomy. About 5 cm of the cortex are passed through the catheter.
Hyun	The catheter is placed approximately 5 cm posterior along the anterior limb of Paine's triangle.
Park	It is 2 cm anterior to the posterior limb of Paine's triangle and 2.5 cm superior to the lateral orbital roof and 4.5 cm anterior to the Sylvian fissure. Inserting the catheter around 3.5 cm below the surface

Table 1.
Approaches for ventriculostomy and EVD insertion.

through the skin by a different incision away from the point of entry. Dissolvable stitches, which will gradually fall out over the following 7–14 days, will be used to sew the scalp back together [18] (**Table 1**).

5. Complications of ventriculostomy

It has been noted that with technological advancement and improvement of medica knowledge the management of hydrocephalus and ventricular pathologies has greatly improved. However, it is worth noting that despite these advancement in management we still have a lot of complications from ventriculostomy. These complications range from infection to death. Intraoperative, early (1 month), and late postoperative (>1 month) complications are all possible. Hemorrhage (cortical, ventricular, and cisternal vessels), neural injury (fornix, third cranial nerve, hypothalamus, and middle brain), subdural collections, pneumoventricle, hyponatremia, seizures, delayed awakening, bradycardia, hypothalamic dysfunction (diabetes insipidus, lack of thirst, amenorrhea), and hyperthermia are among the intraoperative and early complications. Reclosure of the stoma, weight increase, and premature puberty are examples of late problems.

The following paragraphs discuss these complications detailly;

1. Neurocognitive decline: to begin, most of these patients usually present with cognitive decline in the initial stages especially memory and executive function impairment [19]. They could be attributed to the fact that some neurocognitive complications attributed to surgery are often either underestimated or underdiagnosed [20]. Furthermore, lesions of important ventricular structures caused by surgical procedures are rarely assessed for and seldom described within reports in the literature, although such lesions potentially lead to incriminating neurocognitive morbidity. Other neurocognitive complications include severe personality changes as was recorded in a patient who underwent an endoscopic ventriculostomy for the treatment of slit ventricle syndrome; this was characterized by impulsiveness, physical hetero aggressiveness, binge eating, hypersomnia, and impairment of memory and frontal executive functions [21]. These symptoms referred to frontal lobe lesions and damage to the fornix and its connection to the hippocampus and mamillary bodies, which was confirmed by postoperative MRI. Also, an additional report of a woman undergoing surgery showing severe psychotic depression, occurring gradually within 3 weeks after surgery [22]. These clinical reports in essence go to highlight the cognitive damages which could be attributed to surgery or the disease in itself.

2. Pneumencephaly: often considered a minor or insignificant complication, this is described as air in the epidural, subdural or subarachnoid space within the brain parenchyma [23]. Pneumocephalus (pneumatocele or intracranial aerocele) can delay postoperative recovery and is often associated with headache, nausea, and vomiting (signs of increased intracranial pressure). Entrapment of air at the time of surgery can interfere with direct visualization of the anatomic landmarks that are essential to performing a third ventriculostomy safely. This can be minimized by carefully flushing all irrigation lines of air bubbles but not too fast nor rapid rate as this could lead to bradycardia [23]. Decompression of the ventricular system too rapidly can contribute to the formation of a subdural hematoma.

3. Infection (ventriculitis): ventriculitis is inflammation of the ependymal lining of the cerebral ventricles, usually secondary to infection. It has other names such as; ventricular empyema and pyogenic ventriculitis. It is an indolent but lethal infection and a source of persistent infection [24] Early diagnosis is essential for appropriate treatment. It is of particular concern in patients post ventriculostomy and has been associated with increased morbidity, mortality and financial costs [25]. This could be associated to either the asepsis intra op, introduction of foreign material, presence of stoma blockage or persistent leak which are often result in delayed wound healing.

6. Others

6.1 Blocked stoma

In cases of infective or post haemorrhagic pathologies there is often the presence of blood clot formation which favors the stoma closure. Also, in cases of rapid tumor progression or the presence of secondary membranes (liliquist) [26]; there is a high risk for the formations of plugs which block the stoma.

Situation	Action
Preoperative patient preparation	Wash the entire scalp with povidone-iodine or chlorhexidine the day before surgery
Operating room	1. Depending on the patient's features, surgery may be performed in the operating room (OR) or the pediatric critical care unit. 2. Reduce the necessary attendance in the OR 3. Sterile protocol: following proper hand hygiene procedures, surgeons and the assisting nurse should wear a cup and mask, sterile gowns, and gloves. 4. Taking a single dosage of preventative antibiotics 60 minutes before making an incision to protect the skin's flora 5. Before and after donning, wash your scalp with povidone-iodine or chlorhexidine. 6. If coated catheters are available and therapeutically necessary, use them. 7. Inserting the catheter as deeply as possible under the skin 8. Dress the wounds in sterile material. The dressing must always be dry.
Postoperative maintenance	1. When managing the system, handle it aseptically and try to avoid manipulating it. 2. During the drainage phase, do not administer preventive antibiotics 3. Avoid CSF sampling until an infection is clinically suspected 4. You should not routinely replace your clothes; just do so if they are jeopardized. 5. No routine EVD exchange if there is not an accompanying infection (option to periodic replacement in situations of meningitis or ventriculitis). Inspect the wounds if there is any possibility of a CSF leak.

Table 2.
Protocol for prevention of EVD-related infections.

6.2 Hypothalamic damage

This could be caused by ventriculostomy done away from the midline or thick wall perforation by blunt instrument. This could be manifested by endocrine disorders such as hypothyroidism, precocious puberty etc.

6.3 CSF leak

Which could be precipitated by persistent increased intracranial pressure or early suture removal. In infants with ventriculomegaly it has been noted that a thin cortical mental is associated with cerebrospinal fluid leakage. Moreover, this can delay wound healing, hence increasing risk for infection; and has been shown to be a sign of failure of the third ventriculostomy [27] (**Table 2**).

7. Clinical relevance of ventriculostomy

Subarachnoid hemorrhage (SAH) and Intracranial hemorrhage (ICH) are common complications which occur secondary to stroke and traumatic brain injury (TBI). These conundrums can cause massive intraventricular hemorrhage resulting into acute obstructive hydrocephalus and elevated intracranial pressure which may cause critical morbidity and mortality. Despite the management of ICP with medications such as sedatives and osmotic diuretics, always it is not effective to reduce the ICP thus necessitating the institution of external ventriculostomy also known as external ventricular drain (EVD). The existing body of evidence has revealed a significant difference of outcomes, the arm treated with conservative management had higher fatality rate compared to the arm subjected to the EVD management [28, 29].

Despite the feasibility of EVD placement it is not without flaws when misplaced, this can cause serious complications such as EVD associated hemorrhage and infections. Numerous factors contribute to increased risk of EVD associated hemorrhage including institutional and individual's practice pattern, timing of the CT scan, coagulation indices thresholds, platelet infusion practice for patient subjected to antiplatelet therapy or blood thinners, access site, drill bit size and thread distance, aggressive drilling, the use of irrigation saline. Removal of bone fragments prior to dura opening, sharp or blunt dura penetration, sharp or blunt pia opening, slow or fast access of frontal horn, removal of stylet at ventricular entry or upon advancement to the foramen of Monro and tightness of scalp closure [28–30].

The incidence of EVD related infections have been reported ranging from 0 to 22%, this has opened the mandatory use of prophylactic antibiotic regimen through the entire course of the EVD period. The contemporary use of antibiotic impregnated catheters has dramatically reduced the risk of ventriculostomy associated infections.

8. Conclusion

One of the most significant and often used techniques in pediatric neurosurgery is EVD implantation. Many pathological disorders, including those that pose a threat to life, are treated with it.

Since infection appears to be the most significant and well-researched issue with this procedure, EVD insertion and care protocols are required to prevent the difficulties that are connected with it.

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Conflict of interest

The authors declare no conflict of interest.

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Chapter 5

Neuroendoscopic Techniques in the Treatment of Hydrocephalus

Youtu Wu

Abstract

Neuroendoscopic techniques have been used to treat hydrocephalus for more than 100 years. With the personalized design of surgical approaches, increased knowledge of ventricular anatomy, and improved neuroendoscopic equipment, the last 20 years have witnessed tremendous advances in the development of neuroendoscopic technology, especially in the treatment of hydrocephalus. Except for obstructive hydrocephalus, the application of neuroendoscopic technology in the field of hydrocephalus is also expanding and has received good results, mainly in the fields of pediatric hydrocephalus and communicating hydrocephalus. Additionally, many scholars have achieved satisfactory results in the application of ventriculoscopy to complex hydrocephalus. Among neuroendoscopic techniques, the third ventricular floor fistula and cyst wall fistula methods are commonly used in the treatment of hydrocephalus and are highlighted in this chapter. Undoubtedly, neuroendoscopic technology has become one of the key treatment methods for hydrocephalus, with its high success rate, few complications, and accurate long-term efficacy.

Keywords: hydrocephalus, neuroendoscopic, endoscopic third ventriculostomy, fenestration, loculated hydrocephalus

1. Introduction

The modern endoscope was first introduced by German urologist Maximilian Carl-Friedrich Nitze (1848–1906); in 1879, he introduced the Nitze-Leiter cystoscope, which opened the door for neurosurgeons to adapt endoscopy to their procedures [1]. However, neuroendoscopic techniques for treating hydrocephalus date back to the early twentieth century when, in 1904, Lespinasse, a urologist in Chicago, used cystoscopic cauterization of the choroid plexus to treat two infants with hydrocephalus; one infant died postoperatively, and the other died 5 years after surgery, and the cases were reported publicly at a medical conference in 1910 [2, 3]. In 1922, the neurosurgeon Dandy used endoscopic techniques to treat two patients with hydrocephalus, during which he successfully cauterized and removed the choroid plexus; in an article published in the same year, he described in detail the anatomy of the lateral ventricle, interventricular foramen, transparent septum, and choroid plexus. On this basis, Dandy first proposed the concept of ventricular inspection using an endoscope and the term "ventriculostomy" [4].

The first doctor to complete an endoscopic third ventriculostomy (ETV) was William Jason Mixter [4, 5]; in 1923, he published an article on his successful use of cystoscopy to enter the third ventricle *via* the lateral ventricle foramen of Monro to perform ETV. Subsequently, ETV has been widely used to treat patients with obstructive hydrocephalus. In the same year, Dr. Temple Fay and Dr. Francis Grant developed a method to capture clear black-and-white images of the ventricles using a cystoscope. Their case report of a 10-month-old Italian boy illustrated an attempt to fenestrate the corpus callosum to treat hydrocephalus; however, they were unable to divide the corpus callosum due to a malfunction in the cystoscope they were using. Although the procedure did not go as planned, they concluded that it was safe to visualize the ventricle using an endoscope without causing ventricular hemorrhage or other complications as follows [5–7]:

1. Ventricular imaging and neuroendoscopy are possible in enlarged ventricles.

2. Neuroendoscopy is an intervention with diagnostic significance and can directly observe changes in the ventricles and locate the causes of hydrocephalic lesions.

3. If performed correctly, the patient's postoperative reaction will be mild.

Subsequently, this technique was widely used in the treatment of hydrocephalus. In 1934, Tracy J. Putnam reported on the technique of neuroendoscopic resection of the choroid plexus [8]. Additionally, he invented the electrocoagulation endoscope and designed a 7-mm ventriculoscope with a rod of optical glass, resulting in a wider optical aperture.

For some time, ETV, or endoscopic coagulation of the choroid plexus, was the mainstay of surgical treatment for hydrocephalus despite the associated high complication rate. In 1935, John Scarff (1898–1979) adapted an enhanced version of Putnam's ventriculoscope with an irrigation system to maintain intraventricular pressure, thereby preventing ventricular collapse [2, 9]. In 1947, H. F. McNickle made a significant contribution to the principle of ventriculostomy itself rather than the technique; he was unconvinced that the procedure should be limited to non-communicating hydrocephalus. Additionally, he argued that choroid plexectomy was not the optimal treatment for hydrocephalus since decreasing the production of cerebrospinal fluid (CSF) would not clear the obstruction itself [10].

At this time, neuroendoscopic technology was imperfect, the technology was limited, and patient disability and mortality rates were high. In view of these, the equipment was not popular in neurosurgery due to surgical discomfort, the risk of eye infection from the endoscope, burns from the heat of the lamp in the endoscope tip, and lower optical quality compared with that of a stereoscopic microscope.

From the 1950s to the 1970s, with the advent of magnetron pressure-regulating drainage tubes, the ventriculoperitoneal (VP) shunt was widely recognized by the medical community. After Putnam's initial success with a glass rod instead of lenses, Hopkins' patents, which used several glass rods to fill the former air spaces between the lenses, enabled the development of today's superb-quality rod-lens endoscopes. In 1959, Hopkins, a professor of physics at the University of Reading in the United Kingdom, made a modern optical fiber endoscope, and with the assistance of Karl Storz, they applied the column-lens system to the endoscope and combined it with optical fiber technology to greatly improve the illumination and resolution of the image [11]. In the subsequent 30 years, neuroendoscopic equipment continued to

improve, and coupled with the promotion of the concept of minimally invasive treatment, neuroendoscopic technology was widely used in the field of neurosurgery, and many new neuroendoscopic techniques were developed.

A breakthrough occurred in Paris with the development of the cold-light generator by Vulmiere and colleagues, which Guiot subsequently used as part of a "universal endoscope" [2, 12]. The first modern description of intraventricular endoscopic biopsy using a ventriculofiberscope was provided by Fukushima et al. in 1973 [13]. Around the same time, in England, Hugh Griffith recommended the endoscopic procedure as a first-line treatment for childhood hydrocephalus. He used Hopkins' rigid endoscope to perform ETV as well as choroid plexus coagulation (CPC) to treat hydrocephalus [14].

Advances in illumination and magnification and the refinement of endoscopic tools coupled with improved anatomical knowledge furthered the development of neuroendoscopy [15]. In 1980, Hoffman et al. reported a series of ETVs using stereotactic guidance, noting that the percutaneous stereotactic-guided approach yielded better results than with open craniotomy [16]. In 1991, Heilman and Cohen conducted endoscopic septostomy [17]; then, in 1993, K. Oka et al. performed both aqueductoplasty and ETV using flexible fiberscopes [18]. Finally, in 1996, Mohanty et al. reported the first foraminal plasty of the foramen of Monro [19].

From the 1960s to the 1990s, numerous articles were published that retrospectively described and summarized ventriculoscopic techniques. Scarff reviewed many cases of hydrocephalus in 1966 and 1970 [20, 21], comparing ventriculostomy, choroidectomy, and shunt surgery and highlighting the many advantages of neuroendoscopic techniques. In 1998, Duffer et al. comprehensively described the application of neuroendoscopic techniques on the treatment of hydrocephalus [22], including indications, the choice of surgical methods, complications, and prognosis. Since then, neuroendoscopic technology for the treatment of hydrocephalus has been widely accepted and popularized in academic circles, and neuroendoscopic technology and its theoretical basis have been progressively improved.

Another development came in 1996 and 2002. Endoscopy was respectively used in conjunction with ultrasound and stereotactic navigation to decrease vascular injury during the procedure, and in 2004, the first instance of a robot being used in ETV was reported [23].

At present, neuroendoscopic technology is widely used in neurosurgery, especially in the management of hydrocephalus, as it facilitates a wide range of possibilities for creating alternative CSF pathways (ETV), reducing CSF production, and restoring physiological CSF pathways. The advantages of endoscopy include minimal invasion, the avoidance of brain retraction, low blood loss, fast operation time, and reduced length of hospitalization. Neuroendoscopy provides a magnified view of the ventricular system from the inside and enhances the resolution of the surgical field. Additionally, it avoids the need to implant foreign bodies and reduces the demand for re-intervention, commonly observed in patients with shunts, with the potential to prevent shunt dependency.

2. Intraventricular anatomy

The importance of mastering intraventricular anatomy and landmarks is vital to ensuring successful surgery and limiting complications. The following is a brief description of the major anatomical features encountered in ETV.

Lateral ventricles: The lateral walls of the lateral ventricles abut the genu of the internal capsule at the level of the foramen of Monro. The choroid plexus is located at the bottom of the lateral ventricle from front to back and is situated at the anterior end of the interventricular foramen. The accurate identification of the choroid plexus helps to locate the interventricular foramen and enter the third ventricle. This marker is relatively constant, allowing accurate localization of the interventricular foramen by identifying the anterior segment of the choroid plexus, even in the presence of congenital encephalocele or ventricular deformation due to tumor compression. This may not be evident in enlarged ventricles, but finding the choroid plexus in the narrow ventricular cavity may be a quick and effective way to locate the interventricular foramen; particular attention should be given to locating the choroid plexus in the treatment of split-brain syndrome.

Fornix: The fornix is located at the front and top of the foramen of Monro, where it courses from the hippocampus to the mammillary bodies. Attention should be given to intraoperative protection, especially when entering the third ventricle through the interventricular foramen in ventricular endoscopy, in which it is very easy to damage the fornix.

Thalamus: The thalamus on both sides constitutes the lateral wall of the lateral ventricle. Within the third ventricle, the lateral walls comprise the anterior two-thirds of the thalamus and hypothalamus. The superior optic nucleus and the paraventricular arcuate nucleus of the hypothalamus are the structures most easily damaged in ETV, during which the supraoptic nucleus can secrete an antidiuretic hormone, and the paraventricular nucleus can secrete oxytocin. During surgery, care should be taken not to damage the thalamic structure to avoid corresponding postoperative complications.

The floor of the third ventricle: The floor of the third ventricle is the thinning and migratory part of the thalamus on both sides, and it overlies the interpeduncular fossa. The anterior floor is formed by the optic chiasm, optic recess, infundibulum, and infundibular recess. The floor posterior is the papillary body. Within this range, there is a relatively safe area for fenestration between the infundibular recess and the papillary body. When fenestration is performed anterior to this area, the fenestration is directly opposite the clivus, so it is relatively safe to choose a position at the midpoint of this area. Usually, in the middle area of the thinned floor, there is a bowed translucent blue area that provides a safe zone in which fenestration can be performed [24]. Fenestration along the anterior floor risks injury to the pituitary, while fenestration posteriorly risks injury to the mammillary bodies and brainstem.

Liliequist membrane: The Liliequist membrane is composed of arachnoid membrane and wraps the top of the basilar artery. It is a plate-like structure that separates the suprasellar cistern of the middle cranial fossa from the prepontine cistern of the posterior fossa. After fenestration, the Liliequist membrane wrapped around the basilar artery can be seen downward, and the prepontine cistern can be observed through the membrane. Opening the Liliequist membrane during ETV is critical to the open circulation of CSF between the third ventricular and the anterior pontine pool. Clear visibility of the clivus, basilar artery, and pontine is an important marker for successful ETV.

3. Endoscopic third ventriculostomy

3.1 Patient selection for endoscopic third ventriculostomy

In the last 10 years, high-resolution endoscopic images have further extended the usefulness of neuroendoscopy in the treatment of hydrocephalus. There are

indications for ventricular endoscopy for hydrocephalus. Obstructive hydrocephalus is widely considered suitable for treatment with neuroendoscopy. However, the use of neuroendoscopy in children with hydrocephalus, especially those under 2 years of age, is controversial. Satisfactory results in normal-pressure hydrocephalus and post-infection or traumatic communicating hydrocephalus have been achieved in recent years with neuroendoscopy [25–27].

Although ETV is widely used in the treatment of hydrocephalus, its success rate is below 100%, and about 25 to 40% of patients undergoing ETV require further ventricular-peritoneal shunting [25, 28, 29]. In a study by Iantosca, after analyzing the relationship between the etiology of hydrocephalus and the prognosis of ETV [30], patients with hydrocephalus were divided into three groups according to surgical success rates. The first group had a success rate of >75%, including hydrocephalus due to aqueduct sclerosis; hydrocephalus due to third-ventricle outflow obstruction, resulting from tumors, cysts, or infections; hydrocephalus due to lesions in the quadrigeminal corpus and pineal gland areas; and hydrocephalus due to ineffective shunting. The second group had a 50–75% success rate and included hydrocephalus due to occlusion of the fourth ventricular outlet, including tumors, cysts, inflammation and bleeding, and other causes; Dandy-Walker syndrome; and split-brain syndrome. The third group had a < 50% surgical success rate and included post-infection or hemorrhagic hydrocephalus and meningocele-induced hydrocephalus [without shunting].

A major point is the concept of the ETV success score (ETVSS) proposed by Kulkarni et al. [10, 31]. Based on this concept, neurosurgeons can now perform ETV surgery with confidence. The ETVSS is an estimate of the percentage probability of ETV success, ranging from 0 to 90%. There are three primary components: age, etiology, and history of shunt surgery. Although ETVSS does not determine the indication for surgery, it is an extremely practical rule that can predict surgical success rates based on only three factors.

3.2 Technical considerations of endoscopic third ventriculostomy

The desired trajectory for ETV allows for passage through the foramen of Monro and visualization of the midline floor of the third ventricle. A correct burr hole position is critical. The burr hole should be 3 cm away from the midline and anterior to the coronal suture. Planning the trajectory with frameless neuronavigation is helpful, and the burr hole is generally made on the side with the enlarged lateral ventricle and the foramen of Monro. Warm lactated Ringer's solution is connected to the irrigation port. The use of a pressure bag is not recommended because little pressure is required. Using low pressure to dilate the ventricles gently enables both better visualization and better navigation of the endoscope into the ventricles. The confluence of the thalamostriate vein, septal vein, and choroid plexus marks the foramen of Monro.

Generally, the surgeon navigates the endoscope through the foramen of Monro into the third ventricle. When navigating the endoscope through the foramen of Monro, care should be taken to avoid injury to the fornix. A large foramen of Monro enables safe endoscopic entry, so in cases with a small foramen of Monro, a flexible thin scope is recommended. When the endoscope is well positioned within the third ventricle, the anatomical landmarks along the floor of the third ventricle should be defined. The infundibular recess, the mammillary bodies, and the basilar artery are critical structures. In patients with a thinned, bowed translucent floor, often, the basilar artery may be observed. A thick massa intermedia and interhypothalamic adhesions increase the risk of hypothalamic injury, and sometimes, ETV has to be abandoned [28, 32].

The transparent site anterior to the basilar artery and between the mammillary bodies and the infundibular recess is the ideal site for fenestration. We prefer to use grasping forceps or scissors for fenestration *via* the floor of the third ventricle. As critical basilar artery and posterior cerebral artery branches may be at risk of thermal injury, monopolar diathermy should be used carefully. After the floor of the third ventricle has been fenestrated, a Fogarty balloon is centered and inflated to widen the opening. Cauterizing the stoma margins may prevent the opening from reclosing. Occasionally, mild bleeding may be observed from the tuber cinereum, which may be tamponaded with the inflated balloon. Additional bleeding generally resolves with copious irrigation.

Once the third-ventricle floor is perforated, CSF enters the cistern, producing a pulsatile beating of the third-ventricle floor. The absence of such movement indicates an increased chance of ETV failure. After careful inspection of the interpeduncular cistern, the Liliequist membrane must be removed to allow the egress of CSF from the third ventricle into the ambient or prepontine cistern. The naked basilar artery in association with good stomal pulsation indicates successful ETV.

3.3 Complications of endoscopic third ventriculostomy

The overall incidence of complications after hydrocephalus with ETV varies from 0 to 31.2%, but most scholars report rates ranging from 5 to 15% [33–39]. In a meta-analysis by Madsen and colleagues, overall perioperative mortality was 0.2 ± 0.1%, and the mean ETV failure rate was 34.7 ± 18.0% [40]. Bouras and Sgouros performed a systematic literature review of 34 studies reporting 2985 ETVs performed in 2884 patients. The early postoperative mortality rate was 0.21%, and the overall complication rate was 8.5%. The rate of intraoperative hemorrhage was 3.7%, and the rate of severe intraoperative hemorrhage was 0.6% [39].

Complications such as intraoperative hemorrhage, postoperative intracranial infection, and nervous system injury seriously affect both the surgical success rate and the prognosis of patients. Familiarity with common complications after ETV surgery, timely prevention, and correct treatment of these complications play an important role in improving the success rate of surgery.

The following are descriptions of common complications after ETV:

1. Intraoperative hemorrhage: Intraoperative hemorrhage is not uncommon as an ETV complication, and its incidence varies from 0 to 8.5% [41–44], although in most reports, it tends to be about 4% [39]. Intraoperative hemorrhage can occur at many stages of ostomy and may cause bleeding by damaging small vessels in the cerebral cortex and ependymal membrane during ventricular entry into the lateral ventricles. Such bleeding tends to be mild, easy to manage, mostly self-limiting, and small amounts of bleeding can be controlled by irrigation. Bleeding can also occur when the neuroendoscopy passes through the interventricular foramen into the third ventricle; this can be severe and often indicates damage to important veins, such as the transparent septum and thalamus. In such cases, hemostasis should be washed and electrocoagulation avoided as much as possible to prevent thrombosis during the electrocoagulation process and basal ganglia venous embolism. A small amount of bleeding from the floor of the three ventricles, which is not uncommon, may also occur during ETV, but it can be stopped with irrigation. The most severe bleeding during ETV is due to damage to the

basilar artery. According to statistics, its incidence is about 0.21% [39], although different scholars have reported it to be about <2% [42, 45].

Common injured blood vessels are located mainly in the interpeduncular cistern. The basilar artery, the P1 segment of the posterior cerebral artery, and the posterior choroidal artery pass through the anterior half of the cistern; the perforated branches of the basilar and posterior cerebral arteries run through the posterior half, both of which are located below the floor of the third ventricle. In the case of thinning of the dilated base of the three ventricles, the surgeon can observe these vascular structures through the floor of the third ventricle. At the same time, if the stoma is created strictly according to the safe zone in front of the midpoint of the third-ventricle floor, the chance of damaging these blood vessels is very small. However, in some pathological states, the shape, position, and thickness of the three ventricular floors may change, potentially damaging the above-mentioned important vascular structures. To avoid damage to the basilar artery, attention should be given to the position of the three-ventricle floor ostomy; this should be positioned at the infundibulum crypt and the midpoint of the papillary body, as here, the bottom of the three ventricles faces the saddleback, which avoids the basilar artery to the greatest extent. Additionally, the size of the fistula should be strictly controlled at 2.5–5 mm in children and 5–10 mm in adults [46]. If there is bleeding during surgery, CSF turbidity, anatomical structure variation, or other conditions that affect surgery, the surgical procedure should be abandoned promptly [44].

2. Bradycardia: Bradycardia is reported to be a common complication during surgery, but because it is often paroxysmal, it is also the most easily overlooked. El-Dawlatly et al. reported a 41% incidence of bradycardia in ETV [47]. The cause of its formation is not fully understood. Van Aken et al. believe that the increase in intracranial pressure during surgery is the main cause of arrhythmia, so the flow rate of ventricular flushing should be strictly controlled and measured [48]. It has also been suggested that intraoperative lavage, mechanical stimulation, or temperature changes that stimulate the preoptic area can lead to slowed heart rate and decreased blood pressure [41]. Additionally, it has been proposed that after the opening of the three-ventricle floor fistula, changes in pressure in the basal pool affect the pressure in the basilar artery, thereby interfering with the blood supply to the brainstem and eventually causing arrhythmias [49]. Mild arrhythmias are often transient, but severe arrhythmias can lead to surgical termination [50]. Gentle manipulation to avoid damage to thalamic structures, control intraventricular flushing velocity, and balance flush fluid intake should be the main preventions of such complications [41].

3. Neurological injury: The incidence of neurological injury varies from 0 to 18.7% [49, 51, 52]. Almost all such injuries are related to improper endoscopic access to the lateral ventricle or endoscopic access to the third ventricle *via* the interventricular foramen. In particular, the incidence in pediatric patients is higher than in adult patients, which may be related to anatomical differences between children and adults. For example, the interventricular foramen is narrow in children, the papillary body is not easy to identify, and a meningocele with congenital malformations increases the difficulty of surgery. For such patients, pre-surgery magnetic resonance imaging of the patient's head should be read carefully to

observe the morphology of the ventricles and correctly assess the difficulty and risk of surgery.

Hypothalamic injury is associated with its anatomical location. The hypothalamus is located on the lateral wall of the three ventricles, and endoscopic mechanical injury, thermal injury, and irrigation perfusion injury can easily cause hypothalamic dysfunction during ETV and should be avoided as much as possible during surgery. Hypothalamic injury can trigger endocrine dysfunction, of which diabetes insipidus is the most common symptom, reportedly occurring in approximately 0.5% of ETV cases [41, 53]. Most cases of diabetes insipidus tend to self-limit, and only three cases of long-term diabetes insipidus after ostomy have been reported [53, 54].

Papilloma and fornix damage predispose a patient to memory dysfunction because both the papilla body and fornix are associated with hippocampal structures. A very small number of patients have psychiatric symptoms after surgery, which may be related to corticostomy injury to the frontal lobe. It has also been suggested that psychiatric symptoms are associated with intraoperative ventricle flushing with cold saline, so it is recommended that the rinsing fluid is preheated before intraventricular lavage [41]. If the patient has postsurgical motor dysfunction, such as limb paralysis or oculomotor nerve palsy, it may injure the nucleus of the thalamic nerve, cranial nerve, and midbrain. When the diencephalon is damaged, hallucinations or Horner syndrome may occur. Cleft injury can cause visual field defects.

In general, the occurrence of postoperative neurological dysfunction is often related to the location of the corticostomy and the rough surgical methods of the intraoperative provider. Therefore, appropriately selecting the corticostomy's location to enable the neuroendoscopy to pass through the interventricular foramen smoothly; controlling the speed, flow, and perfusion fluid temperature of ventricular perfusion; and avoiding mechanical and thermal damage to important nerve structures of the ventricle wall have become important preventive measures to reduce postoperative neurological dysfunction.

4. Cerebrospinal fluid leakage: The leakage of CSF is a very common postoperative complication, with reported rates ranging from 0 to 5% and recent bulk meta-analyses suggesting an average incidence of 1.7% in all ETV patients [39]. This complication is particularly common in children, with CSF leakage occurring in 2–18% of cases [39, 41]. The mechanism of CSF leakage may result from a large amount of CSF entering the subarachnoid space in a short period after surgery; at this time, the absorption function of CSF is still in the adaptation period, and the secretion and absorption of CSF cannot reach an effective balance quickly, resulting in a potential fistula during surgery, an increase in intracranial pressure, and finally, CSF leakage. The reason for the higher incidence in infants and young children may be that the absorption function of pediatric arachnoid granules is not fully developed. When a large amount of CSF in the ventricle or cyst cavity enters the subarachnoid space, it cannot be absorbed by arachnoid particles; coupled with the weak healing ability of the pediatric scalp, the CSF gushes out along the ventricular endoscopic channel, resulting in CSF leakage [28].

In some cases, CSF leakage is an early manifestation of ETV failure. We believe that gentle handling during surgery to minimize damage to cerebral cortical channel and the use of artificial materials, such as gelatin sponges, to block the cerebral

cortical channel after the end of the stoma can reduce the incidence of CSF leakage to a certain extent. In most patients, postsurgical CSF leakage can be effectively treated by re-suturing the skin fistula; however, for some patients with CSF leakage, it is necessary to reduce intracranial pressure by lumbar puncture or ventricular drainage.

5. Intracranial hemorrhage: Almost all types of intracranial hemorrhage can occur after ETV, for example, acute and chronic subdural hematoma, subarachnoid hemorrhage, and intraventricular hemorrhage have all been reported. However, the overall incidence is less than 1% [49]. Intraventricular and subarachnoid hemorrhages are often triggered by intraoperative injury to the corresponding vessels [28]. Some researchers have concluded that the main cause of postoperative acute subdural hematoma is the reduction in brain volume caused by excessive drainage during surgery, which further damages the bridging vein [33, 44, 55]. A small amount of subarachnoid hemorrhage tends to be self-limiting, and intraventricular hematomas can be treated with ventricular drainage. However, the treatment of subdural hematomas is relatively complex and contradictory, and although the treatment principles are contrary to those of hydrocephalus, a relative increase in intracranial pressure is necessary.

6. Central nervous system infection: The latest statistics show that the incidence of central nervous system infection after ETV is 1.81%, including meningitis at 1.6% and ventriculitis at 0.21% [49]. However, varying overall rates of central nervous system infection have been reported, ranging from 1 to 6.1% [29, 33, 56]. Nevertheless, most scholars believe that neuroendoscopic treatment of hydrocephalus for central nervous system infection is closely related to a patient's previous history of shunt infection. There is also a view that the infection rate is age-dependent, and the postoperative infection rate in infants under 1 year of age can be as high as 11% [57]. This complication is one of the more serious complications of ETV. Fukuhara et al. identified central nervous system infection as an independent risk factor for ETV failure [28, 58, 59]. Despite the occurrence of infection, the prognosis is significantly better than that of patients with infection after shunt surgery, and in most cases, the infection can be controlled with targeted medical therapy [28, 29, 59].

7. Subdural effusion: The overall incidence of this complication has been reported as less than 2% [41, 55, 60, 61], but it can reach 5% in pediatric patients [62]. The sudden reduction in brain volume after ETV and the neuroendoscopic trajectory contribute to the subdural accumulation of CSF, which eventually leads to subdural effusion [55]. Preventing a large outflow of CSF during surgery, perfusing intraventricular irrigation fluid, and blocking the cerebral cortical sinus tract before the end of the ostomy have a certain preventive effect on the occurrence of subdural effusion. The treatment of subdural effusions is as complex as that of subdural hematomas, and large subdural effusions should be treated with external drainage and appropriate elevation of intracranial pressure [55, 63].

8. Late endoscopic third ventriculostomy failure: The rate of delayed failure is reported in the literature to range from 2 to 15% [35, 36, 56, 64]. Late failure resulting in rapid clinical deterioration is rare but has been described [25, 28]. Age appears to be a strong predictor of ETV success, with infants less than 6 months old having the highest risk of failure, in some cases up to a fivefold increase in

risk compared with that of older patients [28, 65, 66]. The mechanism of ETV failure may include the following factors: an inadequately sized stoma; impaired flow through the stoma; hemorrhagic obstruction facilitating closure or narrowing of the stoma; elevated CSF protein and fibrinogen; impaired CSF absorption by the arachnoid granulations, particularly in the context of infection; and tumor progression resulting in stomal blockage [28, 63].

3.4 Fenestration of loculated hydrocephalus

The use of the endoscope has been explored for other complicated forms of hydrocephalus. Septostomy can be performed endoscopically to treat isolated lateral ventricles. Recently, aqueductoplasty was reported in the treatment of trapped fourth-ventricle syndrome. Neuroendoscopic techniques have been extended to foraminoplasty of the foramens of Monro and Magendie as well as to endoscopic fourth ventriculostomy [67–69]. The fenestration of loculated hydrocephalus is another endoscopic technique widely used in the treatment of hydrocephalus [38, 70–72]. The presence of one or more non-communicating isolated compartments within the ventricular system that tend to enlarge despite a functioning shunt system is defined as loculated hydrocephalus [73]. Intraventricular septations or obstructions between the site of CSF production and the tip of the ventricular catheter can present a barrier to the flow of CSF and result in an accumulation of fluid in the excluded compartments [70]. Intraventricular septations develop secondarily from meningitis or ventriculitis, germinal matrix intraventricular hemorrhage, congenital brain anomalies, and postoperative gliosis [38, 70]. Patients with loculated hydrocephalus and intraventricular arachnoid bands or arachnoid cysts with extension into the ventricles are ideal candidates for intraventricular neuroendoscopy.

Historically, the management strategy for multiloculated hydrocephalus has been to place multiple catheters in isolated compartments. However, the use of multiple shunts has been associated with high morbidity and mortality owing to the cumulative risk of shunt infection and mechanical failure [38, 72]. Nowadays, the goal of surgery has evolved to create as wide and as many communications as possible among the isolated intraventricular compartments to achieve a simplified ideally unique ventricular environment. The fenestration procedure aims to create communication between the maximal possible number of isolated parts of the ventricular system by making openings in the septal walls to achieve CSF drainage using the minimal number of shunts; this, in turn, will lessen the frequency of shunt revisions [33, 71, 74, 75].

The first large research series on the endoscopic treatment of loculated hydrocephalus was published by Lewis et al. in 1995 [76]. Endoscopy reduced the annual rate of shunt revision from 3.04 to 0.25%. Subsequently, neuroendoscopy became popular [77]. Nowosławska et al. published the only study where the neuroendoscopic treatment of loculated hydrocephalus was compared with the conventional implantation of shunt systems (43 endoscopy/80 control group) [78]. They concluded that neuroendoscopic cases experienced a significantly higher clinical improvement, a better outcome (86 vs. 60% with a good outcome), fewer postoperative complications (23 vs. 66%), and fewer reoperations (average of 1.76 vs. 7.05 operation/patient, 3.95 vs. 1.02 revisions/year) compared with patients in a shunt control group.

In most cases, neuroendoscopy is considered the treatment of choice for loculated hydrocephalus, but if it fails, shunt placement is often required. Consequently, the second-best treatment is considered to be the implantation of a simplified shunt

system. Most neuroendoscopic procedures appear to achieve these goals in loculated hydrocephalus [38, 70, 79]. Following endoscopic fenestration, fewer shunt revisions per year are necessary [33, 73, 79]. In 2007, Spennato et al. reported a reduction from 2.07 to 0.35%, with a single shunt or no shunt present in 83.3% of cases [77]. In El-Grandour's study of uniloculated hydrocephalus including 31 children cases, the annual shunt revision rate fell from 2.7 to 0.25% [79]. Alice Noris's study seems to confirm these findings, with 75.6% of patients having no shunt or only one shunt implanted after neuroendoscopy [70]. Despite these encouraging findings, the rate of patients without shunts is low. In their study, the shunt-free rate was 28.9% [70], which is in line with data reported by other authors (26, 28, and 10% in Spennato's, Teo's, and Peraio's series, respectively) [33, 77, 80].

3.5 Technical considerations of the endoscope for loculated hydrocephalus

Neuronavigation is useful in maintaining orientation during surgery and avoiding damage to neural structures, even though the risk of a substantial shift in anatomical landmarks after fenestration of the isolated fluid compartments remains a major problem [64, 70, 71, 81]. The reported disadvantage of neuronavigation, namely the occurrence of an intraoperative brain shift that reduces the accuracy of the navigation for cerebral surgery, can be overcome during ventricular endoscopic neuronavigation; during this procedure, the most important consideration is the direction to follow. Gradual step-by-step opening of the isolated compartments to minimize CSF loss and continuous irrigation throughout the procedure are effective methods for minimizing the brain-shift effect during neuronavigation-aided ventricular endoscopy. These steps maintain the existing anatomy and dimensions of the cysts and the ventricular system as far as possible throughout the entire procedure [38, 81].

Surgical procedures are tailored according to the pathologic entity and the site of septations. In most cases, surgery can be performed through a coronal burr hole, including septostomy, cyst fenestration, and aqueduct stenosis. For fenestration, we prefer a rigid endoscope rather than a flexible one. The advantage of this system is that it enables a better view and better light. Compared with flexible endoscopes, the limited maneuverability of rigid instruments requires more careful placement of the burr hole and widening of the outer edge of the burr hole in selected cases [38].

Care should be taken during fenestration and resection to coagulate the cyst wall along its thickened portions before resection, as these portions of the wall may be vascular. Many instruments can be used to open cyst walls. The author used a thulium laser to fenestrate the septations. Because it is designed to operate in wet environments, and due to the very contained diffusion of energy from its tip (as low as <1 mm in depth), this instrument is much safer and more efficient than others, such as those used in monopolar cauterization. Fenestrations should be as wide as possible to reduce the risk of closure of the fenestration sites. Subsequent enlargement should be performed using grasping forceps and a balloon, with portions of the cyst wall removed using scissors and grasping forceps. If a ball valve exists at the basilar artery near the base of the clivus from an arachnoid cyst, complete resection of that aspect of the cyst may be required, unlike in fenestration, to prevent the symptoms from recurring.

3.6 Complications

The endoscopic treatment of loculated hydrocephalus has been associated with a reduced rate of perioperative morbidity due to its minimal invasiveness compared

with that of open surgery *via* craniotomy. The endoscopy complication rate ranges from 10 to 20% [70–72, 77, 82, 83]. Complications following the endoscopic approach are usually minor and are mostly treated conservatively. The most common complications include CSF infection, thalamic hematoma with transient akinetic mutism, minor intraoperative bleeding, bilateral subdural hematoma, and seizure.

4. Limitations of the endoscope in the treatment of hydrocephalus

While neurosurgeons increasingly advocate the use of the endoscope in the treatment of hydrocephalus, the development of instruments for endoscopic surgery has not followed the same pace. Neuroendoscopy can be improved by the use of even smaller optics with higher resolution than are currently used, providing more surgical space. The endoscope itself occupies space in an already limited surgical corridor. The ideal endoscope is thin and sturdy, does not generate heat, and provides high-resolution images. In addition, a self-irrigating feature could minimize the need to remove and reinsert the endoscope for cleaning.

In addition to the inadequacy of the instruments used, ETV surgery itself has certain limitations. The procedure is inferior to shunt placement in terms of acute infection, premature infants, and post-infective and post-hemorrhagic hydrocephalus. When ETV alone is ineffective, a CPC or VP shunt will be required. Moreover, multiloculated hydrocephalus is a complex and challenging condition, and endoscopic fenestration alone is not effective in controlling it. Therefore, endoscopic-assisted VP shunt insertions are useful for reducing shunt complications and should be considered a therapeutic option.

Conflict of interest

The author declares no conflict of interest.

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Chapter 6

Endoscopic Third Ventriculostomy in the Pediatric Patient

Juan Bosco Gonzalez

Abstract

Endoscopic third ventriculostomy (ETV) is one of the two surgical procedures for the treatment of hydrocephalus, its main indication being obstructive hydrocephalus. Its efficacy is related to the age of the patient and the etiology of the hydrocephalus; however, more studies appear where ETV has gained ground beyond obstructive hydrocephalus, and despite the fact that there is still a lack of evidence to issue a grade of recommendation. ETV has shown to be useful even in communicating hydrocephalus and in patients younger than 6 months. This chapter shows a summary of the most important points to take into account in this procedure. Likewise, the third endoscopic ventriculostomy gives us the opportunity to continue studying the intraventricular dynamics of the cerebrospinal fluid, the ventricular anatomy, the pathology around or within the ventricular system and other details that can open doors for us to understand the concept of hydrocephalus, improve its treatment and improve known surgical techniques.

Keywords: endoscopic third ventriculostomy, hydrocephalus, choroid plexus coagulation, VP shunt, ventricular anatomy

1. Introduction

It was the German urologist Maximilian Carl-Friedrich Nitze who introduced the modern endoscope (**Figure 1**) [1, 2]. Viktor Lespinasse was the first neuroendoscopist in 1910. He treated two children with hydrocephalus by using a urethroscope to access the lateral ventricles, [1–4]. In 1922, Dandy described ventriculoscopy [5, 6], as well as a technique for performing the third ventriculostomy as a treatment for hydrocephalus *via* frontal and subtemporal. In another hand, William Mixter was the first surgeon to combine diagnostic ventriculoscopy with ventriculostomy. In 1923, he used a urethroscope to perform an ETV to treat noncommunicating hydrocephalus in a 9-year-old girl [7, 8].

By 1932, Dandy was again attempting an endoscopic choroid plexectomy [2].

In 1934, Tracy Putnam, following the work of Dandy and Mixter, developed instruments for intracranial procedures for the ventriculoscope. In 1935, John Scarff made modifications to Putnam's ventriculoscope, adding an irrigation system [8, 9]. In 1947, H. F. McNickle reported two cases of communicating hydrocephalus that responded to ventriculostomy [10].

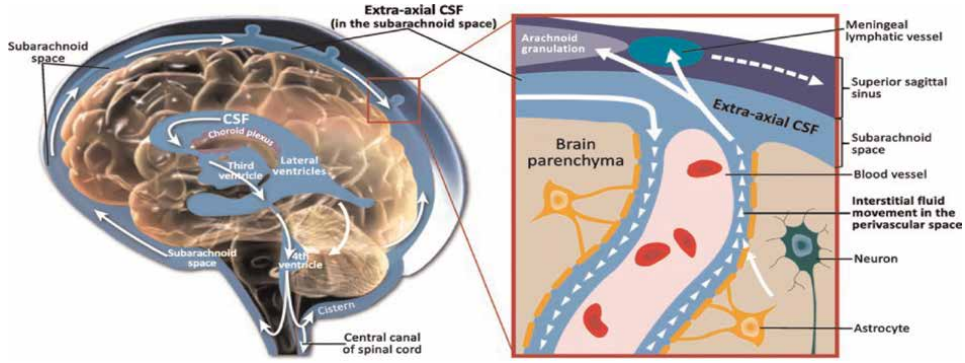


Figure 1.
CSF circulation.

Substance	CSF	Serum
Water content (%wt)	99	93
Protein (mg/dL)	35	7000
Glucose (mg/dL)	60	90
Osmolarity (mOsm/L	295	295
Sodium (mEq/L)	138	138
Potassium (mEq/L)	2.8	4.5
Calcium (mEq/L)	2.1	4.8
Magnesium (mEq/L)	2.0–2.5	1.7
Chloride (mEq/L)	119	102
pH	7.33	7.41

Table 1.
Comparison of serum and cerebrospinal fluid.

There were two reasons why neuroendoscopy had a recess at this time: one was Dandy's results, perhaps they were not the most encouraging with the first designs, and the second was in 1949 Frank Nulsen and Eugene Spitz introduced the concept of the shunt. In 1955, John Holter added a one-way valve to the device; Holter's invention was inspired by the death of his son, Casey, from the complications of myelomeningocele and hydrocephalus (**Table 1**) [2, 3].

2. Endoscopic anatomy

When performing a third endoscopic ventriculostomy, we must consider three spaces or cavities, in a descending direction:

1. **Cavity of lateral ventricles** (**Figures 2** and **3**) **in this space, we must identify:**

    a. Foramen of Monro.

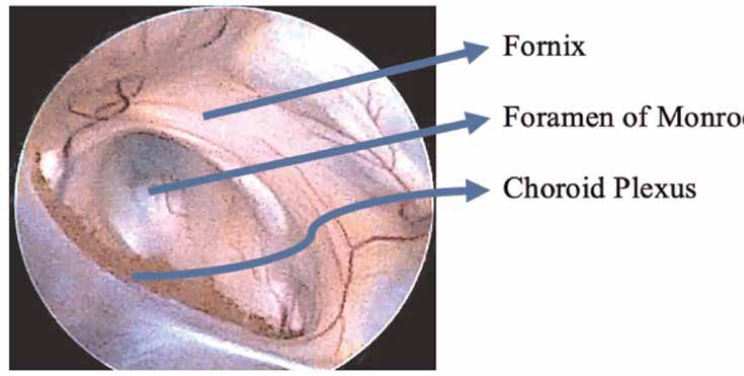


Figure 2.
Lateral ventricles, supraforaminal view.

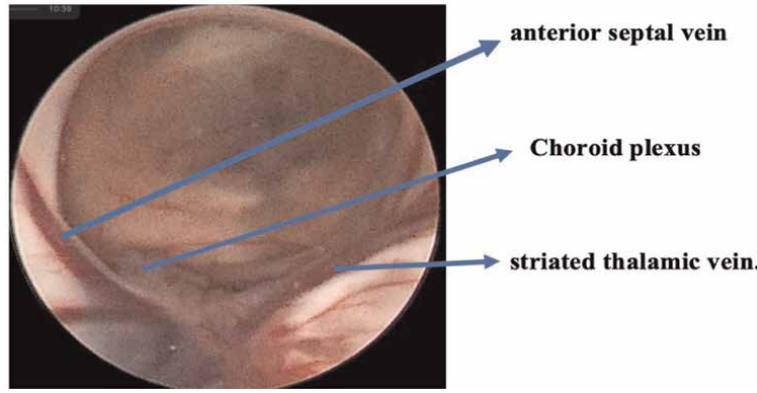


Figure 3.
View through Monroe's foramen.

b. Anterior septal vein.

c. Choroid plexus.

d. Striated thalamic vein.

e. Fornix.

In the ventricular cavity, it is advisable to initially identify the choroid plexus, which is the most reliable landmark for finding Monroe's foramen, since in some cases said foramen is not evident, due to some anatomical variant (**Table 2**).

2. **Cavity of the third ventricle in this space, we must identify:**

a. Mammillary bodies.

b. Premammillary membrane.

Anatomical site of the lesion	Clinical alteration
Fornix	Anterograde amnesia
Mammillary bodies	Episodic or recollective amnesia [11]
Infundibular recess	Primarily constitutes nerve fibers traveling from the hypothalamus to the pituitary gland. Rather than providing signaling to the gland, many of these fibers actually function as the source of the substances released by the posterior lobe of this gland [12]

Table 2.
Anatomical lesions and their clinical correlation.

c. Infundibular recess.

This space presents many anomalies or variants, as can be seen in the following figure, where a band was found that traversed the premammillary membrane transversely. The ostomy of the floor of the third ventricle is recommended to be performed at an intermediate point between the mammillary bodies and the infundibular recess, where in this case it is marked by this transverse band (**Figures 4–6**).

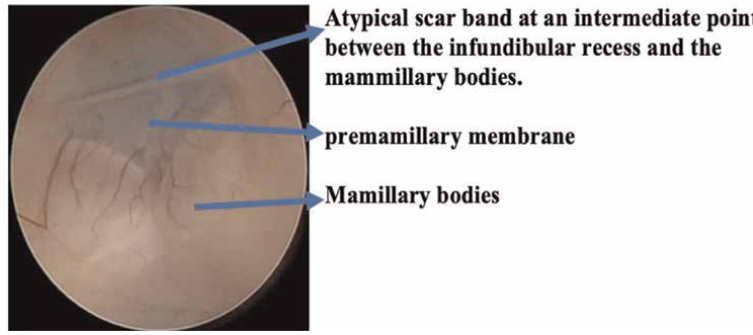


Figure 4.
Cavity and floor of the 3rd ventricle.

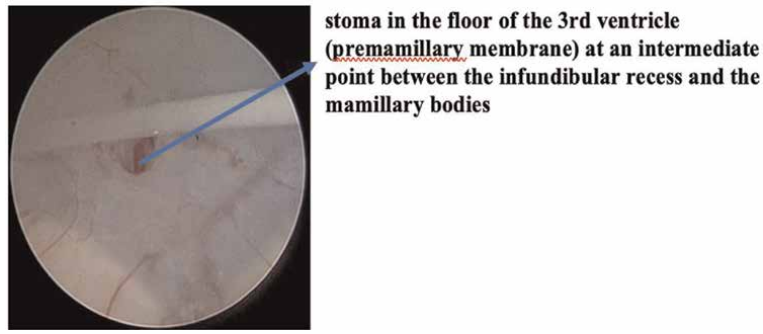


Figure 5.
3rd ventricle floor.

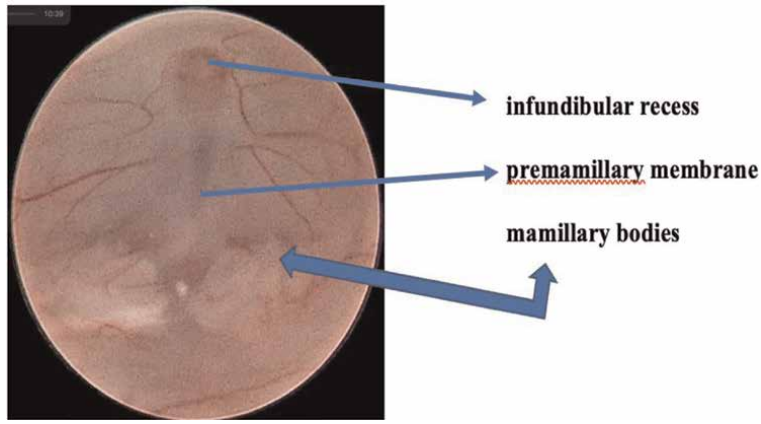


Figure 6.
Third ventricular floor.

3. **Cisternal space in this space, we must recognize:**

   a. Basilar artery and its terminal branches.

   b. Liliequist's membrane (sometimes trabeculated or some portion not present).

   c. Clivus (**Figures 7–10**).

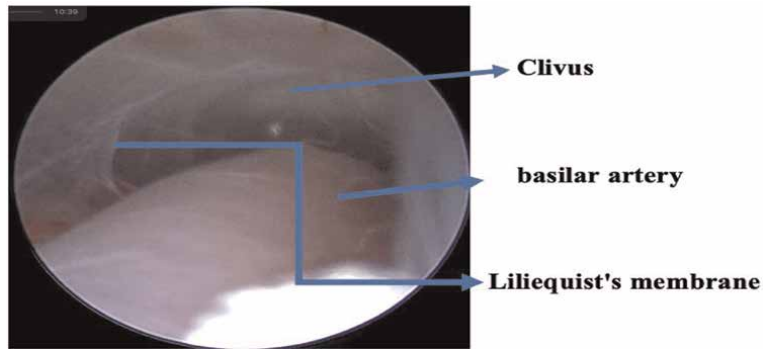


Figure 7.
Cisternal space (prepontine).

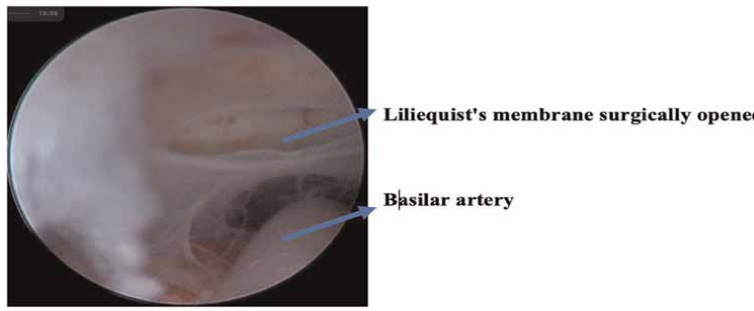


Figure 8.
Prepontine cisternal space.

Figure 9.
Prepontine space. Lilliequist's membrane (mesencephalic portion) open spontaneously, but present forming a tent in the cisternal space.

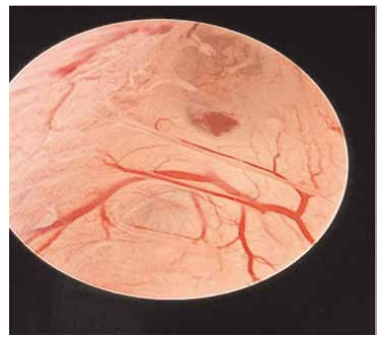


Figure 10.
Floor of the 3rd ventricle. Variant in a patient with hydrocephalus and myelomeningocele. Indistinguishable mammillary bodies, transparent premammillary membrane revealing the vascular anatomy: Basilar artery and its terminal branch.

Liliequist's membrane (mesencephalic portion) opens spontaneously but presents forming a tent in the cisternal space.

Liliequist's membrane.

Originally described by Key and Retzius in 1875, and after described by Liliequist in 1956 [13, 14] is an arachnoid membrane separating the chiasmatic cistern, interpeduncular cistern and prepontine cistern. It arises anteriorly from the diaphragma sellae and extends posteriorly separating into two sheets, The membrane of Liliequist is a partially trabecular, partially dense folded inner arachnoid membrane, and a very important anatomic landmark in the anatomy of the interpeduncular fossa and sellar and parasellar regions [15]. The membrane of Liliequist consists of two leaves: a superior diencephalic and an inferior mesencephalic one [16], these leaves are highly variable in their shape, distribution, and density, most commonly trabeculate (**Table 3**).

3. Anatomical injuries

With endoscopic access, there is a risk of injuring anatomical structures that are in the surgical corridor or adjacent structures that can be directly injured or by vascular lesions.

Score	Age	Etiology	Previous shunt
0	<1 month	Postinfectious	Previous shunt
10	1 month to <6 months		No previous shunt
20		Myelomeningocele, IVH, Nontectal brain tumor	
30	6 months to <1 year	Aqueductal stenosis, tecctal tumor, other	
40	<10 years		
50	> Or = 10 yrs		

Table 3.
ETVSS.

4. Indications

Obstructive hydrocephalus.

1. Aqueductal stenosis.
2. Posterior fossa tumors.
3. Sellar region tumors.
4. Multitabulated hydrocephalus.
5. Dandy-Walker malformation.
6. Galen vein malformation.
7. Chiari malformation.
8. Myelomeningocele.
9. Encephalocele.
10. Craniosynostosis.
11. Post-infectious hydrocephalus.
12. Shunt malfunction.
13. Posthemorrhagic.
14. Tumor etiology (supratentorial).
15. Cerebral or cerebellar infarcts.
16. Intraventricular tumors.

4.1 Communicating hydrocephalus

Even though this indication may be controversial, various studies have published its usefulness in normal pressure hydrocephalus. Sufficient evidence is lacking to establish a grade of recommendation [12, 17–19].

5. ETVSS

Kulkarni et al. created a scale considering the etiology of the hydrocephalus, the patient's age, and the presence of a previous shunt to calculate the success of the ETV with which the ETVSS was created [20].

This scale predicts the 6-month success rate of ETV for children with hydrocephalus, based on some characteristics Scores range from 0 (extremely poor chance of ETV success) to 90 (extremely high chance of ETV success), and it is calculated as the sum of the age score (max 50), etiology score (max 30), and previous shunt score (max 10).

The high-ETVSS group [21] is associated with a lower risk of failure right from the early postoperative phase. The moderate-ETVSS group [22–42] has a higher initial failure rate, but, after about 3 months, the risk of ETV failure becomes slightly lower than shunt failure. Finally, in the low-ETVSS group [43], the early risk of ETV failure is much higher than the risk of shunt failure, but the risk becomes lower than the risk of shunt failure at about 6 months following the procedure [20, 44, 45].

6. Preoperative imaging

1. The main requirement to be able to perform an ETV is ventricular dilatation, although in some cases depending on the clinical condition of the patient, etiology, and prognosis, among other factors, it is possible to perform an ETV with a moderate dilation guided by neuronavigation. If that ventricular dilation is evident at the time of diagnosis and, it is recommended:

2. Evaluate prepontine space in CT or MRI, there must be an evident space between the clivus and the protuberance, ideally greater than the diameter of the endoscope to be used (3.7–4.2 mm).

3. Evaluate the presence and shape of the mesencephalic and diencephalic portion of the liliequist membrane, using MRI.

4. Evaluate vascular anatomy through 3D sequence and multiplanar reformat images, these images can also help in the identification of liliequist's membrane.

5. Evaluate the distance of the frontal horn of the right lateral ventricle to the cerebral cortex.

6. Evaluate the cisterns with special emphasis on the prepontine cistern. In cases of cisternal neurocysticercosis, the vesicular ones are abundant at the base around the brain stem, which means that the TVE does not work.

7. Cine phase-contrast magnetic resonance imaging (CISS o FIESTA) can be utilized as a method of distinguishing between communicating and noncommunicating hydrocephalus and any abnormality in basal cisterns [46, 47].

7. Post surgical evaluation

Remember: Since the size of the ventricles, seen on CT or MRI after ETV, decreases more slowly than after shunt placement, in fact, ventriculomegaly after ETV can take weeks to reduce or persist [44].

G.Cinalli et al., established radiological criteria for the success of ETV: [45, 47–50].

1. Reduction in ventricular size ranging from 10 to 50% must be observed from the first week.

2. Periventricular lucency, if present before the operation, must disappear.

3. CSF flow artifact must be visible on sagittal median T2-weighted fast spin-echo MRI sequences and a flow void must be detectable on the stoma on 3D-CISS MRI.

4. The floor of the third ventricle, if bulging downward in the preoperative images must be straight on postoperative images.

5. Atrial diverticula and pseudocystic dilatation of the suprapineal recess, if present preoperatively, must disappear or decrease significantly.

6. Pericerebral sulci, if not visible before operation, must reappear or increase in size.

7.1 Remember

- The third ventricle is the quickest to decrease and remains stationary in size 3 months later.

- The downward deviation and flattening of the brainstem reverts within 1 year, whereas the width and height of the lateral ventricles continue to decrease steadily for 2 years [45, 51].

Mortality: 0.5–1.0% [44, 45, 52–54].

8. Complications

All complication rate of 8.5%, [43, 55–59].

1. Injury to the basilar artery **0.3%**.

2. Minor bleeding **16.5%.**

3. CSF leak **1.6%.**

4. Abandonment of the procedure **4.16%.**

5. Thalamic lesion **0.12%.**

6. Forniceal injury **0.04%.**

7. Hypothalamic lesion **0.04%.**

8. Postoperative fever **65.1–84.4%.**

9. Meningitis o ventriculitis **1.6–6.1%.**

10. Bradycardia at the time of fenestration **26.8–43%.**

11. Diabetes insipidus **0.64**%.

12. Gaze paralysis **0.60**%.

13. Endocrine and electrolyte disturbances **0.94%.** [22, 55–58, 60–63]

14. Other complications with very low frequencies: subdural, epidural, intracerebral, and intraventricular hematomas [57]. The author had a patient in the first 24 hours after performing the procedure, developed slit ventricles.

9. Avoiding complications

IR: infundibular recess.
MB: mammillary bodies.

1. Adequate surgical indication.

2. Carefully evaluate preoperative neuroimaging studies, assess prepontine space and look for anatomical alterations that may interfere with the passage of the endoscope, evaluate premammillary membrane density, vascular anatomy, and presence or absence of Liliequist's membrane [22].

3. Ventricular entry point: assess the trajectory and distance from the cerebral cortex to the ventricle. In some cases, such as intraventricular tumors with purely endoscopic access in which ETV is considered at the same time, it is advisable to modify the shape of the burr hole and **the trajectory** by modifying the entry point, (**Figure 11**), a burr hole can be used oval in case the endoscope inside the ventricular cavity has to be mobilized anteriorly or posteriorly [64].

4. In the event of intraventricular bleeding, apply constant irrigation, with increased pressure in the irrigation at the site of the hemorrhage and close one of the ports [23, 26], open the port intermittently to drain the amount of fluid

inserted and avoid increases in intracranial pressure, a lot of patience with the irrigation. In these cases, closely monitor changes in blood pressure and heart rate.

5. Move the tip of the fiber optic away, when inserting an instrument through the working port, and move the instrument closer to the target site only when you have visual control of the tip of said instrument. Remember that the visual range of the endoscope is less than 180° [56].

6. In the floor of the third ventricle, increasing the intensity of the light source, bring the optical fiber closer and visualize the position of the basilar artery, in most cases, it is possible to observe through the premammillary membrane, observe the blood vessels visible in this membrane as well as the distance from the mammillary bodies to the infundibular recess and make the stoma in the avascular area, (**Figure 12**), very gently irrigate and verify that there is no bleeding. When the ostomy was performed with a blunt object and without applying heat, expand the ostomy only when there is no bleeding. In case of bleeding at the ostomy site, insert the Fogarty balloon and apply pressure with it for 2 or 3 minutes.

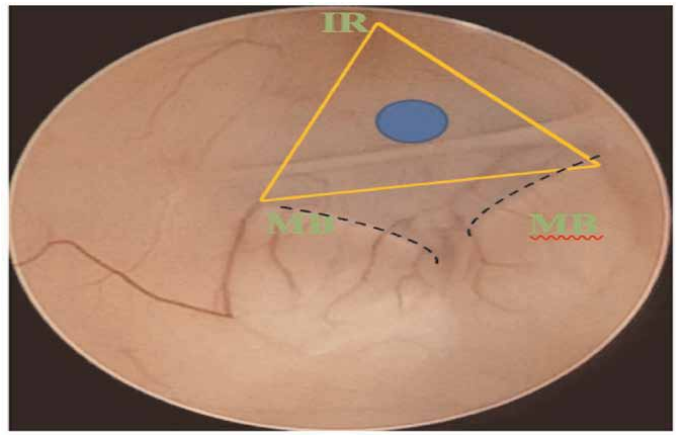


Figure 11.
IR: Infundibular recess; MB: Mammillary bodies.

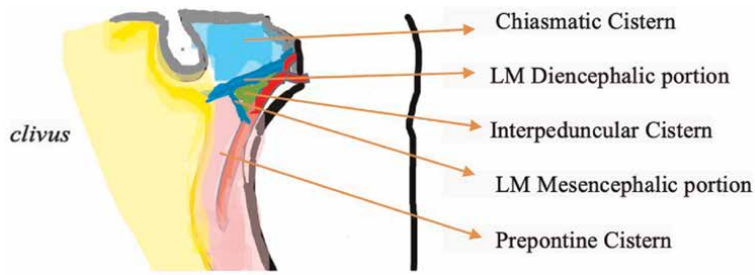


Figure 12.
Schematic representation of the Lilliequist membrane (LM) and its distribution, sagittal view.

7. Upon reaching the Liliquist (LM) membrane, evaluate its characteristics and increase the intensity of the light source when approaching to visualize the density of this membrane, remember that at this point the cranial nerve that can be injured is the third nerve. To avoid this, the diencephalic and mesencephalic portion of the LM must be carefully visualized and the opening performed delicately, patiently, and verify that a valvular effect occurs after opening it, the same that must be observed in the premammillary membrane already open (**Figure 13**).

8. Irrigate with Ringer's solution at a temperature of 36°C, making sure that the irrigation solution is not cold, which produces sudden and dangerous changes in heart rate, especially when irrigating the prepontine space.

9. Remember the vascular landmarks around Monroe's foramen and the 3D layout of the ventricular anatomy (**Figure 14**).

10. All efforts must be made to close the wound, layer-by-layer, using dura mater grafts, if necessary, perform the Valsalva maneuver by the anesthesiologist upon completion of the closure and verify that there is no leakage of CSF, it is convenient to place gelfoam and surgicel in the burr hole area. After placing the bone flap, close the epicranial fascia, if possible, subcutaneous tissue and skin (**Figure 14**).

10. Surgical technique

The Kocher point is the most common access site for ETV [31], it is located 2 cm lateral to the midline and 2 cm anterior to the coronal suture [33]. Other access points

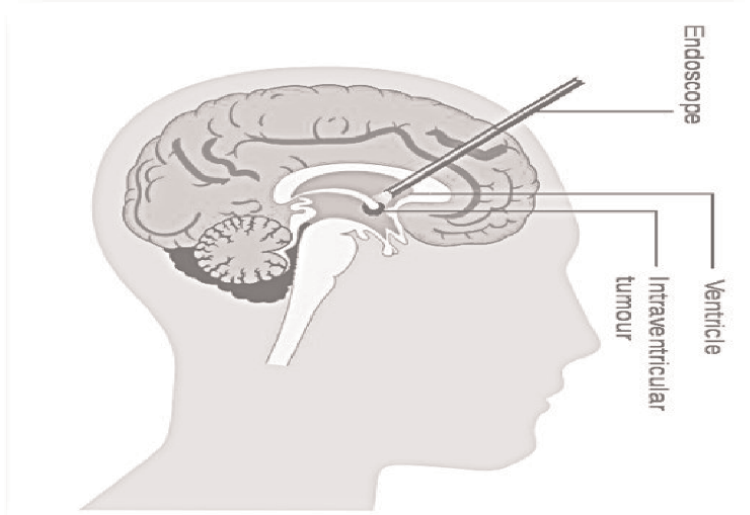


Figure 13.
Path through Kocher's point to access the floor of the 3rd ventricle in obstructive hydrocephalus.

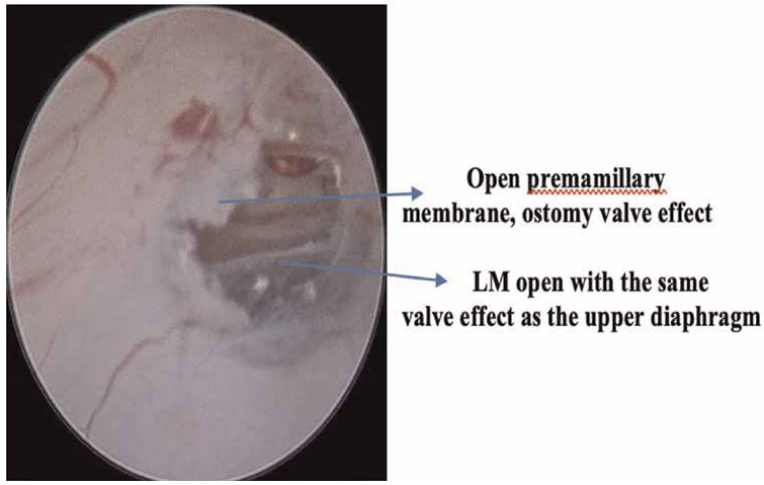


Figure 14.
Premamillary membrane and its relationship with the diencephalic portion of the membrane of Liliequist membrane (LM).

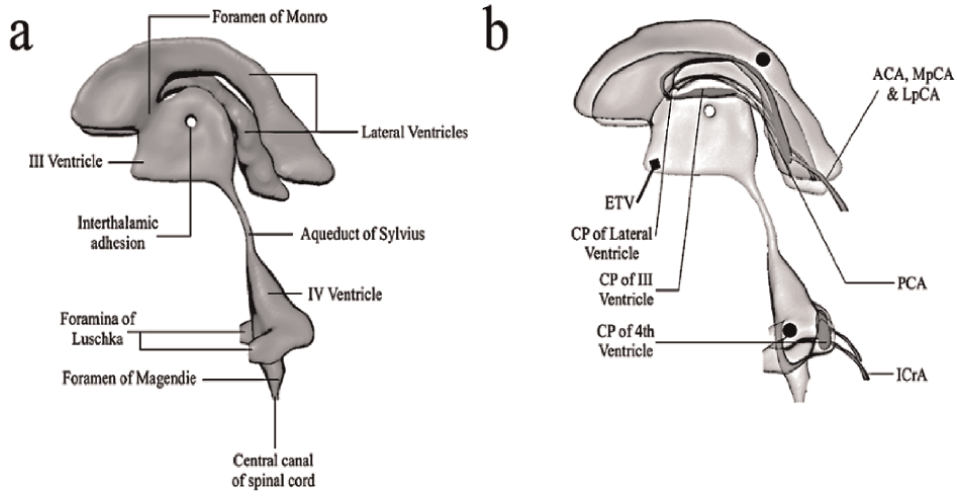


Figure 15.
Ventricular system and relationship with the endoscopic access points to the floor of the 3rd ventricle.

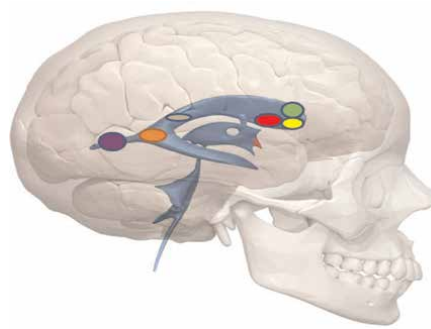
can be used, depending on the associated pathology [32]. In infants with a patent fontanelle, this corridor can be used by making the incision at the lateral end of the fontanelle rhombus (**Figure 15**) [33].

10.1 Other access points

1. Keen.
2. Frazier.
3. Dandy.
4. Kaufman.

5. Tubbs.

6. Kocher.



10.2 Before starting

1. Review the images.

2. Verify proper positioning of the head and neck.

3. Adjust the position of the monitors for an adequate vision.

4. Fluid for irrigation at 36°C (lactate ringer's).

5. Remember the distance from the cortex to the ventricle.

The insertion of the endoscope must be done gently, without exerting pressure on the endoscope, bearing in mind the distance measured in the neuroimaging, when reaching the ventricle and even though the brain parenchyma does not offer resistance to the insertion of the endoscope, a sensation can be felt. Change in resistance to the advancement of the endoscope.

Upon reaching Monroe's foramen, we must observe the landmarks of this point: choroid plexus, anterior septal and thalamus striate vein, and fornix. It is convenient at this point to observe all possible anatomical details of the third ventricle.

When descending to the third ventricle, the landmarks must be recognized: mammillary bodies, infundibular recess, and premammillary membrane. At this point, it is convenient to transilluminate the premammillary membrane to try to observe the anatomy of the basilar artery.

Perforation of the floor of the third ventricle must be done with a blunt object, it can be the coagulator (without activating heat), it has been mentioned that heat can generate an inflammatory response that leads to closure of the fenestration [31], or the clamp forceps, others have mentioned the use of laser as an option to perform fenestration [34]. The initial ostomy should be the size of the perforating object, it is also convenient to maintain irrigation at this time and observe if there is bleeding, gently remove the perforating object and if there is no bleeding, expand the ostomy with a Fogarty 3 or 4 catheter. If you do not have a Fogarty catheter, this amplification can be done with forceps, always gently and patiently, or with the coagulator moving on the edge of the ostomy from right to left from front to

back, very gently and making sure not to contact neural structures with the highest part of the endoscope.

The opening of the Liliequist's membrane (LM) is of vital importance for the success of the ETV, for which special attention should be paid to the prepontine space and to visualize as much as possible the characteristics of this membrane for its opening [31, 35, 37, 42], after this opening, the interpeduncular cistern and the prepontine cistern should be visualized, to inspect that there is no other arachnoid membrane that interferes with the passage of CSF.

11. TVE/VP shunt comparison

ETV was associated with a statistically significant lower risk of procedure-related infection compared to shunt [21]. It is generally accepted that true differences exist regarding complication rates among centers or among individual neurosurgeons, according to their personal experience [59, 65, 66].

Despite the fact that the calculation of the Costs to compare TVE vs. VP shunt may vary from country to country, ETV represents less economic costs if it is taken into account that no device is left, and the number of surgeries per patient may be less in the patient who receives TVE; however, there are not enough relative studies to establish a significant difference, since various studies that have been carried out were carried out in countries with different economic incomes and did not show statistical significance in terms of costs [67] others compared and the VP shunt, endoscopic third ventriculostomy (ETV) was proven to be better in terms of infection, length of hospital stay, cost-effectiveness, and complication rate [68].

Much more evidence and comparative studies are needed.

12. ETV & choroid plexus coagulation (CPC)

It may become an efficient treatment for obstructive HCP in infants [69]. However, the etiology of the hydrocephalus, the age of the patient, and the extent of coagulation of the choroid plexuses must be considered [70–72]. These factors can influence the results.

13. Conclusion

ETV is a safe, effective procedure, for many years included as one of the two surgical alternatives for hydrocephalus. In the pediatric patient with great value. In low-income countries, ETV represents an excellent alternative, where a wide variety of newer and more sophisticated shunting systems, self-regulating systems, or antibiotic-impregnated systems are not available. On the other hand, it has shown a lower frequency of complications and it is not necessary to leave any foreign body in the patient. Infections in shunt systems are common infections that require several days of stay, with high hospitalization and drug costs, and with functional complications derived from neuroinfection, especially in children under 1 year of age. ETV infections have been shown to be very rare and respond well to antibiotic treatment. For all these reasons, ETV should be considered the first treatment option for obstructive hydrocephalus in pediatric patients.

Thanks

To my father William.

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Chapter 7

CSF Bypass Surgery in Children with Hydrocephalus: Modern Possibilities, Prospects and Ways of Solving the Correction of Complications

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Abstract

The chapter discusses modern and promising approaches to the use of CSF shunting operations in children. CSF shunting operations remain the only effective method for correcting persistent CSF circulation disorders in CSF resorption disorders with the development of intracranial hypertension and hydrocephalus. The chapter is devoted to general ideas about CSF dynamics and biomechanical properties of the craniospinal system that affect CSF dynamics, and gives a pathogenetic assessment of CSF dynamics in the development of intracranial hypertension and hydrocephalus. Aspects of genetics and genomics of anomalies in hydrocephalus are touched upon. Pathological changes in the brain around old ventricular shunts are described. The authors consider the types of CSF shunting operations for hydrocephalus in children. Possible complications of CSF shunting operations are analyzed with the algorithm for their correction and management tactics for this group of patients.

Keywords: hydrocephalus, intracranial hypertension, craniospinal system, biomechanics, CSF dynamics, CSF bypass surgery, pathomorphology, genetic, complication

1. Introduction

Hydrocephalus has always been and remains one of the most complicated problems of pediatric neurosurgery. The progressive course of hydrocephalus leads to

severe neurological and mental disorders with a lag in intellectual and physical development, significantly affecting the incidence of disability and mortality of the child population.

The term "hydrocephalus" (from others-Greek ὕδωρ "water" + κεφαλή "head"), synonymous with "dropsy of the brain," is an excessive accumulation of cerebrospinal fluid (CSF) in the ventricles of the brain and/or external cerebrospinal spaces, accompanied by their expansion [1].

The problems of hydrocephalus pathogenesis, diagnosis, and treatment have always been relevant at all stages of neurology and neurosurgery development. Hydrocephalus affects an average of five children out of every thousand newborns. In neurosurgical patients, hydrocephalus syndrome is detected in every fourth patient. In one-third of children with hydrocephalus, the development of hydrocephalic hypertension syndrome is one of the causes of decompensation of the patient's condition [2–4].

Among central nervous system (CNS) injury cases of 25–80% lead to hydrocephalus as a complication at the late stages of the disease, while only 5–10% of cases develop in the acute period. In most patients with pathology of cerebral vessels (mainly ruptured cerebral aneurysms), persistent hydrocephalus, which needs correction, is observed in 5–7% of cases, and it is often found in strokes (up to 60%).

According to the data, the prevalence of congenital hydrocephalus ranges from 2.5 to 8.2 cases per 10,000 newborns, and in patients with malformations of the brain or spinal cord hydrocephalus is observed in up to 78% of cases. In patients with brain tumors, hydrocephalus occurs in 20–94%, with cerebrovascular pathology—in 6–67% of cases, with inflammatory diseases of the CNS—up to 5–60% of cases [5–7], with the indicators increasing every year. The mortality rate in hydrocephalus used to be more than 50% before the valvular fluid bypass operations were introduced. Since these operations became regular practice the mortality rate decreased to 2–5% [8].

State-of-the-art research considers hydrocephalus to be the result of persistent disorders of the CSF circulation.

2. Cerebrospinal fluid circulation and biomechanical properties of the craniospinal system (CSS)

2.1 Cerebrospinal fluid

CSF is normally a pure colorless liquid with a relative density of 1.007 and a pH of ≈7.33–7.35. Basically, it is produced by the vascular plexuses of the lateral, III and IV ventricles, passing through the holes of Monroe, the water supply of the brain, the holes of Mazhandi and Lyushka, and enters the subarachnoid space of the brain and spinal cord, from where it is absorbed into the venous system through a system of channels and pachyonic granulations [9, 10]. Two-thirds of the CSF volume is considered to be of choroidal origin. The other part of CSF is produced by the ependyma of the brain, its membranes, and brain tissue [11].

The rate of CSF production is 0.3–0.5 ml/min and it depends mainly on blood pressure, from the pressure in the choroidal artery, and from the activity of the membrane mechanisms involved in the formation of CSF—to be precise.

CSF absorption occurs through the membranes of the parasagittal zone (arachnoid granulations) of the brain. This is how the resorption of the main volume (2/3) of CSF is carried out. The other part of the CSF is absorbed through the membranes of the meningeal sheaths of spinal and cranial nerves, membranes, and parenchyma of the

brain. Under normal conditions, the rate of CSF resorption is balanced with its production [5, 10, 11].

2.2 Structural units of the cerebrospinal fluid circulation system

The ways of CSF circulation are fairly well described. The CSF circulates in a certain direction. Under normal conditions, CSF from the lateral ventricles through the holes of Monroe enters the III ventricle, then into the water supply of the brain and the IV ventricle. Further, through the holes of Luschka and Magendie, CSF enters the cisterns of the base of the brain (cerebellar-cerebral, covering the cistern of the bridge, chiasmal, and the cistern of the Sylvian furrow) and then onto the convexital surface into the subarachnoid space. Channels and cells of arachnoid shells are structural units of the liquor outflow pathway system. However, in pathological conditions, the arachnoid shell, being highly reactive, is able to rapidly proliferate arachnoid cells with the walls thickening, to accumulate water by collagen fibers, which finally disrupts normal circulation of the CSF.

Part of the CSF from the spanning cistern of the bridge enters the cisterns of the cerebellar worm. A smaller volume part of the CSF enters the cerebrospinal subarachnoid space (**Figure 1**).

The volume of the cranial part of the CSF is about 68% of the total volume of the craniospinal cavity, and the spinal part is 32%, respectively. Approximately 1/3 of the CSF volume is located in the ventricles of the brain, 1/3—in the subarachnoid cerebral and 1/3 of the volume—in the spinal subarachnoid spaces [4, 5, 10–12].

2.3 Physiological support of CSF circulation

CSF outflow is provided by the presence of a pressure gradient (15–30 mm of water) between the ventricles of the brain and the subarachnoid space [9].

CSF absorption is achieved due to the difference in pressure in the brain sinuses and CSF pressure. The rate of CSF resorption is directly proportional to the amount of CSF pressure and inversely proportional to the venous pressure in the upper

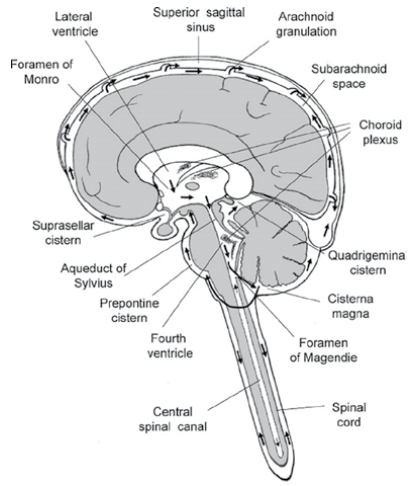

Figure 1.
Scheme of structural units and pathways of cerebrospinal fluid circulation [5].

longitudinal sinus [5, 9]. The intracranial pressure remains relatively stable, and with an increase in intracranial pressure up to 300 mm of water column CSF resorption becomes inhibited. The pressure in the upper sagittal sinus is about 12 mm Hg. With the CSF and intrasinus pressures being equalized (below 5 mm Hg), CSF resorption is disrupted. With an increase in intracranial pressure greater than 7 mm of water column, a linear increase in the rate of CSF resorption is observed [13, 14].

Resorption resistance is a characteristic reflecting the state of the CSF pathways and CSF outflow pathways into the venous system. Due to the fact that the resorption rate is linearly dependent on the pressure gradient, a change in the resorption resistance of the CSF is of practical importance [9, 11].

Pulse fluctuations have a significant effect on the CSF circulation, the volume of blood in the cranial cavity, and the waves propagate in the caudal direction.

Respiratory wave fluctuations in liquor pressure caused by the formation of respiratory pressure waves in the pleural and abdominal cavities are transmitted to the veins in the cavities of the skull and spine. Respiratory waves of venous pressure cause the flow of CSF from the cranial to the spinal cavity. Respiratory waves of arterial pressure and pressure in the inferior vena cava normally do not affect the fluctuation of intracranial pressure.

The liquor pressure equal to 112–130 mm of water column (about 9–10 mm Hg) is theoretically a "normal" pressure [5, 10, 11]. Normally, at constant pressure in the craniospinal cavity, the amount of liquor produced is equal to the volume of the absorbed.

The reasons for the excessive accumulation of CSF can be:

- acceleration of production,
- deceleration of suction,
- violation of transport through the liquor-diverting ways.

Excessive accumulation of CSF leads to a violation of the dynamic equilibrium of "production-resorption" and to the expansion of the cerebrospinal cavities and the decrease in the volume of the medulla [11, 15, 16].

2.4 Volumetric components of CSS

The "Monro-Kellie" theory describes the volumetric relationships within the CSF, or craniospinal cavity. The up-to-date version of the theory asserts that three volumetric components capable of changing their quantitative values are determined in the relatively rigid cavities of the skull and spine [5]:

1. Brain tissue with membranes.
2. Vascular bed with circulating blood.
3. Liquor system with CSF constantly formed and absorbed in it

The craniospinal cavity is represented by a closed space, limited by the meninges, in which the brain and spinal cord are enclosed. Some elasticity of the formations of the cranial cavities was also noticed due to the malleability of the tissues of the atlanto-

occipital membrane, the multitude of holes at the base of the skull, as well as the possibility of divergence of sutures in children with intracranial hypertension (ICH). Spinal tissues have significantly greater elasticity due to the extensibility of the intervertebral ligaments and the possibility of protrusion of the dura mater at the exit points of the spinal nerves. With the development of the pathological process at the compensation stage, an increase in one of these volumes is accompanied by a change in the other.

CSS has the properties of elastic materials of malleability (elasticity), viscosity (fluidity) and can be expressed mathematically [5, 10, 11, 17].

The malleability of brain tissue is characterized by the ability to deform under mechanical action. Malleability is closely related to the extensibility of interstitial spaces. The viscoelastic characteristics of the CSS vary depending on the inner pressure.

The biomechanical properties of CSF consist of the malleability of the bones of the cranial vault, the connective tissue membranes of the spine, the state of CSF circulation, changes in blood volume, and the degree of accumulation of water by the brain tissue. The malleability of the entire CSF is an algebraic sum of these indicators for the cranial and spinal cavities [5, 9, 11].

Blood volume and blood pressure level play an important role in changing the elasticity of the CSF. An increase in blood pressure leads to an increase in the volume of the brain due to an increase in the volume of blood in its vessels, an increase in the volume of water filtration, and an increase in the volume of the brain tissue itself, which occurs with a sharp increase in systolic blood pressure, when compensatory constriction of the arteries does not have enough time to develop in response to the increase in blood flow. Unlike arterial pressure, an increase in the venous pressure of the brain immediately leads to the directly proportional increase in intracranial pressure [11].

2.5 Quantitative indicators of liquor circulation and viscoelastic properties of CSF

Liquor circulation has a significant effect on the mechanical properties of CSF. The change of individual links of the liquor circulation is aimed at maintaining the constancy of the value of the resulting characteristic—the liquor pressure. Disruption of the compensatory capabilities of the CSS is manifested in the development of cerebrospinal hypertension.

Quantitative indicators of CSF circulation and viscoelastic properties of CSF are studied by the method of artificial change of CSF volume and registration of pressure changes in the craniospinal cavity [10, 15, 18].

Two reciprocal curves are used for quantitative characterization: "pressure–volume" P/V, characterized by an "exponential" dependence, or "volume–pressure" V/P (inverse P/V dependence). Both curves display the viscoelastic properties of the CSS and have three characteristic sections (**Figure 2**, **A**, **B**).

The fragment of the curve (a-b) has a flat section, as well as a section of a sharp increase in pressure (c-d) and an intermediate period (b-c). These sections of the curve correspond to the state of the system's backup capabilities. In other words, the elasticity of the system increases exponentially with the development of ICH.

There are three phases in ICH the system goes through: compensation, sub-, and decompensation. In the phase of compensated ICH (site a–b), there is a moderate increase in intracranial pressure, a slight increase in the elasticity gradient, a decrease in malleability, a normal value of resorption resistance, and the rate of CSF production.

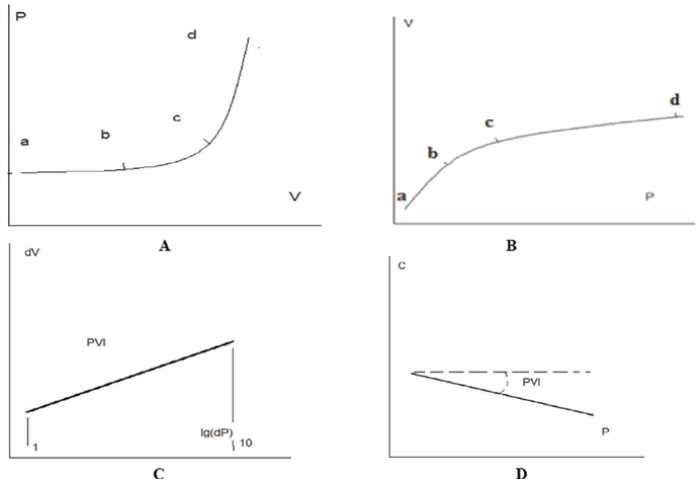

Figure 2.
Viscoelastic properties of SCC. A—P/V-dependence graph; B—V/P-dependence graph; C—logarithmic indicator of P/V dependence (pressure-volume index, PVI); D—CSS compliance. P—liquor pressure, V—liquor volume, C—compliance CSS.

In the subcompensation phase (b–c), there is an increase in intracranial pressure and an increase in resorption resistance. The decompensation phase (c–d) is characterized by the exhaustion of reserve mechanisms, increasing intracranial pressure, decreased CSF production, increased resorption resistance, and elasticity [5, 10, 11].

Marmarou A. and co-authors (1975) proposed a characteristic of the elastic properties of the system—the "pressure-volume" index (Eq. (1)).

$$PVI = \frac{dV}{\lg\left(\frac{P_p}{P_0}\right)}(\text{ml}) \tag{1}$$

where:
PVI—index "pressure-volume",
dV—volume change of the CSS,
Pp—increased liquor pressure after bolus administration,
Ro—initial liquor pressure before the bolus.

They processed the obtained data of the pressure-volume relationship using the logarithmic method and obtained a linear relationship [5] (**Figure 2**, **C**).

A linear equation for determining the compliance of the CSS was also proposed (**Figure 2**, **D**).

$$C = 0,4343 \cdot \frac{PVI}{P}\ (\text{ml/mm of water}) \tag{2}$$

where:
C—compliance (compliance),
P—the liquor pressure at a given time.

The angle of inclination of the curve is an individual constant characteristic of each individual CSS and reflects its compliance, individual ability to maintain constant

parameters during the development of any volumetric process (Eq. (2)). The pressure-volume index is a constant characteristic of the system in the compensation stage. Compliance is a dynamic characteristic of the system; it inversely depends on intracranial pressure [5, 11].

Pliability, elasticity of the CSS are individual characteristics. As the compensation mechanisms of the system are depleted in conditions of growing ICH, the elasticity of the CSF increases. According to various authors, normal PVI values are considered to be more than 25 ml. PVI indicators in children range from 8.2 to 30.1 ml [9, 10].

Thus, the viscoelastic properties of the craniospinal cavity are due to:

- its anatomical dimensions,
- the state of stretchable formations,
- biomechanical properties of the actual brain tissue,
- the state of the liquor circulation system,
- the state of the venous outflow of blood from the cranial cavity,
- changes in arterial blood filling.

3. Pathomorphology of hydrocephalus

Occlusive hydrocephalus is the most common among all types of hydrocephalus. It develops in early childhood and is associated with malformations of the CNS, the consequences of birth trauma, or intrauterine infection, accompanied by occlusion of the Lyushka holes and Majandi spikes.

In the first months of life the child's head circumference increases rapidly (sometimes up to 2 cm per week), reaching 50–100 cm by the age of 12 months. At the same time, the bones of the skull become thinner, the cranial sutures diverge, the bone structures of the Turkish saddle atrophy, and the pituitary gland is usually somewhat reduced in size and compressed (flattened). The ventricles of the brain are expanded to one degree or another, the brain cloak gradually atrophies, and its thickness can decrease to 5 mm. The brain in this case is a bubble filled with CSF. A child suffering from severe hydrocephalus is practically deprived of both coordinating systems—nervous and endocrine ones. Such patients can suddenly die from pain or emotional stress, mild acute respiratory viral diseases, etc. Without treatment they die, as a rule, at the age of two years.

4. Genetics and genomics of anomalies in hydrocephalus

Abnormalities of CNS are multifactorial. Both genetic and external factors may be critical, and they may be presented in the combination with synergy effect.

As of today, several groups of genes, associated with CNS abnormalities, are described. Methods of system genomics proved very useful for understanding

neuropathology development [19]. Our analysis was based on OMIM database actual at 17.01.23.

The most catastrophic scenario is neural tube defect up to hydroanencephaly. Combination of genetic and environmental factors is well described in Ref. [20]. Group of genes, associated with susceptibility to neural tube defects (182940), is presented in **Table 1**.

VANGL1 and VANGL2 are very similar with 73.1% primary amino acid sequences identity. Clinical cases are described both in family and sporadic forms [21]. All the forms in this group are autosomal dominant.

Errors in the folic acid cycle may cause neural tube defects. Group of folate-sensitive neural tube defects (NTDFS) (601634) is presented in **Table 2**.

Variants in MTHFR, MTR, MTRR, and MTHFD1 may lead to change in folic acid and cysteine concentration. Moreover, they may change individual need in folic acid and cobalamin. Clinical aspects are well described in [22].

Three autosomal recessive forms of congenital hydrocephalus are described (**Table 3**).

Additionally, 3 clinical variants (307000) with X-linked recessive inheritance are associated with L1CAM gene. Typical mechanism observed in this case is congenital stenosis of the aqueduct of Sylvius [23].

Megalencephaly-polymicrogyria-polydactyly-hydrocephalus syndrome (MPPH) is caused by heterozygous mutation in 3 genes. This fact illustrates genetic heterogeneity of clinically similar states [24] (**Table 4**).

Location	Phenotype	Phenotype MIM number	Inheritance	Gene/ Locus	Gene/Locus MIM number
1p13.1	{Neural tube defects, susceptibility to}	182,940	AD	*VANGL1*	610,132
1q23.2	Neural tube defects	182,940	AD	*VANGL2*	600,533
6q27	{Neural tube defects, susceptibility to}	182,940	AD	*TBXT*	601,397
17q12	{Spina bifida, susceptibility to}	182,940	AD	*CCL2*	158,105
19q13.33	{Neural tube defects, susceptibility to}	182,940	AD	*FUZ*	610,622

Table 1.
Susceptibility to neural tube defects.

Location	Phenotype	Phenotype MIM number	Inheritance	Gene/ Locus	Gene/Locus MIM number
1p36.22	{Neural tube defects, susceptibility to}	601,634	AR	*MTHFR*	607,093
1q43	{Neural tube defects, folate-sensitive, Susceptibility to}	601,634	AR	*MTR*	156,570
5p15.31	{Neural tube defects, folate-sensitive, susceptibility to}	601,634	AR	*MTRR*	602,568
14q23.3	{Neural tube defects, folate-sensitive, susceptibility to}	601,634	AR	*MTHFD1*	172,460

Table 2.
Folate-sensitive neural tube defects.

Location	Phenotype	Inheritance	Phenotype MIM number	Gene/ Locus	Gene/Locus MIM number
14q32.11-q32.12	Hydrocephalus, congenital, 1	AR	236,600	*CCDC88C*	611,204
9p23	Hydrocephalus, congenital, 2, with or without brain or eye anomalies	AR	615,219	*MPDZ*	603,785
17p13.3	Hydrocephalus, congenital, 3, with brain anomalies	AR	617,967	*WDR81*	614,218
Xq28	Hydrocephalus due to aqueductal stenosis	XLR	307,000	*L1CAM*	308,840
Xq28	Hydrocephalus with Hirschsprung disease	XLR	307,000	*L1CAM*	308,840
Xq28	Hydrocephalus with congenital idiopathic intestinal pseudoobstruction	XLR	307,000	*L1CAM*	308,840

Table 3.
Congenital hydrocephalus.

Location	Phenotype	Inheritance	Phenotype MIM number	Gene/ Locus	Gene/Locus MIM number
19p13.11	Megalencephaly-polymicrogyria-polydactyly-hydrocephalus syndrome 1	AD	603,387	*PIK3R2*	603,157
1q43-q44	Megalencephaly-polymicrogyria-polydactyly-hydrocephalus syndrome 2	AD	615,937	*AKT3*	611,223
12p13.32	Megalencephaly-polymicrogyria-polydactyly-hydrocephalus syndrome 3	AD	615,938	*CCND2*	123,833

Table 4.
Megalencephaly-polymicrogyria-polydactyly-hydrocephalus syndrome.

Several forms of genetic hydrocephalus in combination with other clinical features are described, usually as clinical cases. Generally, mutations in different genes may cause similar phenotypes, and mutations in one gene may lead to different clinical variants. Many pathways may be discussed, but the two are evident: errors in folic acid exchange and genetic-related stenosis of the aqueduct of Sylvius.

5. Assessment of intracranial hypertension and hydrocephalus syndrome

5.1 CSF infusion test or infusion-load test (ILT)

ILT with the calculation of resorption resistance of the CSF was one of the fundamental methods in choosing of surgical treatment of patients with hydrocephalus [9].

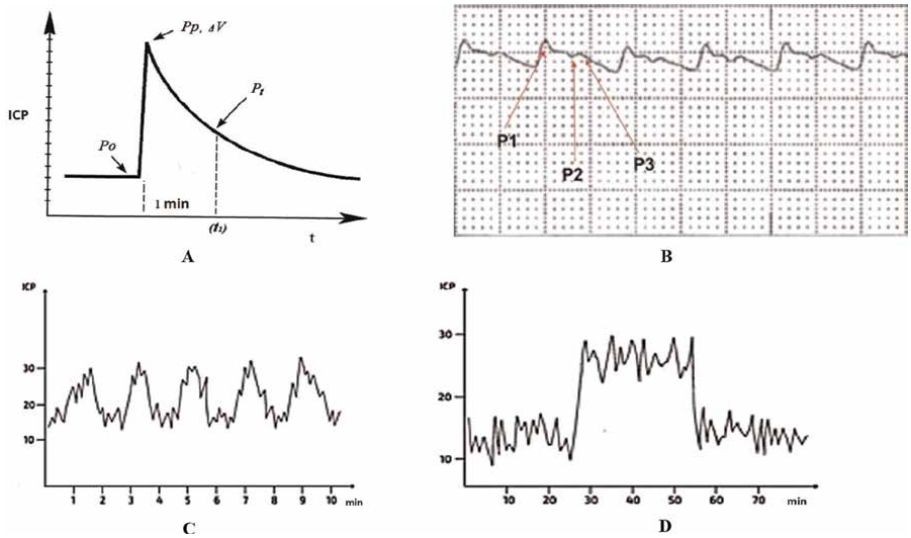

Figure 3.
A—Bolus INT circuit with recorded parameters: Po—initial liquor pressure; Pp—maximum pressure after bolus injection. Pt—liquor pressure after bolus injection after 1 minute in the relaxation phase; ΔV—volume of injected fluid. B is the type of pulse wave of ICP with a compensated state of intracranial compliance. P1—Systolic peak, P2—Vascular peak, P3—Diastolic peak. C—pathological Lundberg waves of type B caused by an increase in ICP without depletion of intracranial compliance. D—pathological Lundberg waves of type A caused by increased ICP with depletion of intracranial compliance.

During ILT, the bolus infusion technique of A. Marmarou is used. To do this, a ventricular catheter is inserted into the cavity of the lateral ventricle. The distal part of the ventricular catheter is connected to the ILT system. Within 2 minutes the background intracranial pressure, background spectral components of wave oscillations are recorded. Next, a saline solution is injected with a bolus volume of 2 ml at a rate of 1 ml/sec with an interval between boluses of 1 min [4, 10, 15, 17] (**Figure 3**, **A**).

From the ratio of the injected volume, the magnitude of the maximum increase in pressure and pressure after 1 minute during the relaxation period, according to A. Marmarou's formula, both the production rate (A) and the resorption resistance index (R) (a value proportional to the inverse value of its absorption) are calculated using an infusion-liquor test, which is based on excretion and administering a certain volume of CSF by boluses or once and measurement of the time during which the cerebrospinal pressure is restored as a result of CSF production or suction [15, 25].

The calculation is carried out according to the formulas:

1. CSF production rate (A) (Eqs. (3) and (4)):

$$\frac{\Delta V_1 \cdot \lg\left(\frac{P_1}{P_m}\right)}{t_1 \cdot \lg\left(\frac{P_0}{P_m}\right)} \tag{3}$$

2. CSF resorption resistance (R) (Eq. (4)):

$$\Delta V_2 \cdot \lg\left[\frac{P_2 \cdot (P_p - P_0)}{P_p \cdot (P_2 - P_0)}\right] \tag{4}$$

- V1 is the volume of the withdrawn liquid, P0 is the initial liquor pressure, Pm is the pressure immediately after the evacuation of the bolus, P1 is the pressure after a certain time t1,

- V2 is the volume of the injected liquid, Pp is the maximum pressure after injection, and P2 is the pressure on the curve of the reduction of the liquor pressure after injection after a certain period of time t2.

The evaluation of ILT results consists in the determination of intracranial pressure, fluctuations of CSF (amplitude-frequency changes), as well as registration of resorption resistance of CSF, followed by obtaining one of the variants of pressure-volume curves (P/V): normotensive, hypertensive, and atrophic [15].

5.2 Monitoring biomechanical properties of CSS in case of ICH

Currently, discrete values of intracranial pressure are of low practical importance, since they do not display indicators of intracranial compliance (ICC). To assess the severity of the pathological process in patients with increased ICP of various etiologies, including hydrocephalus and congenital malformations of the skull bones, an assessment of the pulse curve recorded when measuring ICP is used. These changes are typical of ICC changes of any etiology and characterize the amplitude of pulse oscillations, the morphology of pulse curve peaks, and the formation of plateau waves with a significant decrease in compliance. The classical view of the pulse curve is shown in **Figure 3**, **B**.

One cardiac cycle forms three peaks due to the increase in intracranial volume in the systole and its decrease in the diastole.

Accordingly, the P1 (systolic) peak turns out the most pronounced one on the normal ICP curve. Immediately upon reaching the pulse wave of the microcirculatory bed of the brain, a P2 peak should appear as the reaction of the arterial bed muscular layer to compensate systolic pressure and normalize the curve, and reduce the amplitude of pulse oscillations. At the moment of diastole, a dicrotic P3 peak is formed, which characterizes a decrease in intracranial blood volume and relaxation of the vascular bed. The morphology of the pulse curve depends on the initial state of the ICC and the volume of increase in the intracranial contents, which manifests clearly and underlies the infusion-load testing.

Formulas were used for discrete assessment of biomechanical properties and liquor circulation [15]:

$$PVI_d = \frac{dV_b}{\lg \frac{(meanICP_p)}{(meanICP_o)}} \tag{5}$$

where PVId is the discrete value of the PVI index; meapISRo is the average liquor pressure before bolus administration; mean ICPp is the average liquor pressure after bolus administration; dVb is injected (with a plus sign)/output volume (with a minus sign) of the bolus, ml.

$$C_d = \frac{0,4343 \cdot PVI_d}{meanICP_o} \tag{6}$$

where *Cd* is a discrete assessment of craniospinal compliance.

$$I_d = \frac{PVI_d \lg\left[\frac{(meanICP_p)}{(meanICP_t)}\right]}{dT} \tag{7}$$

where Id is a discrete estimate of the rate of resorption/production of CSF; dT is the time interval in minutes from the moment of bolus injection/withdrawal to the current meanICPt average pressure.

$$R_d = \frac{dT \cdot meanICP_o}{PVI_d \lg\left[\frac{meanICP_t(meanICP_p - meanICP_o)}{(meanICP_t - meanICP_o)meanICP_p}\right]} \tag{8}$$

where Rd. is a discrete estimate of the resorption resistance of the CSF.

In addition to changes in the pulse curve, the classic signs of an increase in ICP and a decrease in ICC are the appearance of pathological plateau waves (Lundbergwaves) on the ICP monitoring chart. There are three types of waves—A, B, C—while only type B and C waves are indicative of this or that change in compliance. Type C waves are associated with respiratory and cardiac cycles, manifested by an increase in ICP of a small amplitude. Their duration does not exceed the specified cycles. Type B waves are manifested by an increase in ICP to 30–50 mmHg and a duration of 1–5 minutes (**Figure 3**, **C**). Most often, the appearance of these waves is considered to provoke ICC without its obvious depletion. The appearance of type A waves—prolonged, up to 40 minutes, persistent increases in ICP up to 50 mmHg and above—is associated with the depletion of ICC (**Figure 3**, **D**).

The universality of these parameters resulting from compliance changes of any etiology seems to be significant. The identification of the ICP increase plateau is a significant diagnostic criterion for "latent" ICH, which is most often encountered in the long course of the pathological process. HCG in hydrocephalus can serve as an example of such condition, developing in patients with congenital malformations of the skull bones, or in patients with subcompensated forms of hydrocephalus in the neonatal period, when classical clinical signs of ICH are extremely rare.

5.3 Imaging methods, indices of the ventricular system of the brain

Modern imaging methods make it possible to identify hydrocephalus, establish the cause of the development of this process, conduct dynamic observation, and evaluate the effectiveness of the performed liquor bypass surgery. Currently, magnetic spiral computed tomography (MSCT) is considered to be the optimal method of radiation diagnosis of hydrocephalus, the use of which allows you to quickly measure the size and count the indices of the ventricular system of the brain, which is especially important in childhood when planning surgical treatment [26, 27].

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When interpreting the conducted radiation examination, the symmetry, degree of expansion, configuration, and contours of the ventricular system are taken into account.

The index of the anterior horns of the lateral ventricles is calculated in relation to the maximum distance between the most distant external parts of the anterior horns and the maximum bitemporal diameter of the skull multiplied by 100. Normally, the value of this index ranges from 25.4 (under the age of 5 years) to 29.4–31.0 (aged 71 to 80 years) (**Figure 4**, **A**).

The index of the central sections of the lateral ventricles is calculated with respect to the smallest distance between their outer walls in the recess area and the maximum bitemporal diameter of the skull on the same slice multiplied by 100. Normally, the value of this index ranges from 18.2 to 26.0 (**Figure 4**, **B**).

The index of the III ventricle is estimated in relation to its maximum width in the posterior third at the level of the pineal gland to the largest transverse diameter of the skull on the same section, multiplied by 100. Normally, the value of this index increases with age, reaching 3.0 at the age of 5 years and 4.8—from 71 to 80 years (**Figure 4**, **C**).

The index of the IV ventricle is calculated in relation to its largest width to the maximum internal diameter of the posterior fossa of the skull on the same slice. Normal indicators of this index are 11.9–14.0 (**Figure 4**, **D**).

Intraventricular hypertension is characterized by the appearance of periventricular edema, there are four stages of these changes:

Stage 1—blurring of the contours of the upper-outer corners of the anterior horns or a clearly limited border of reduced density of the same localization;

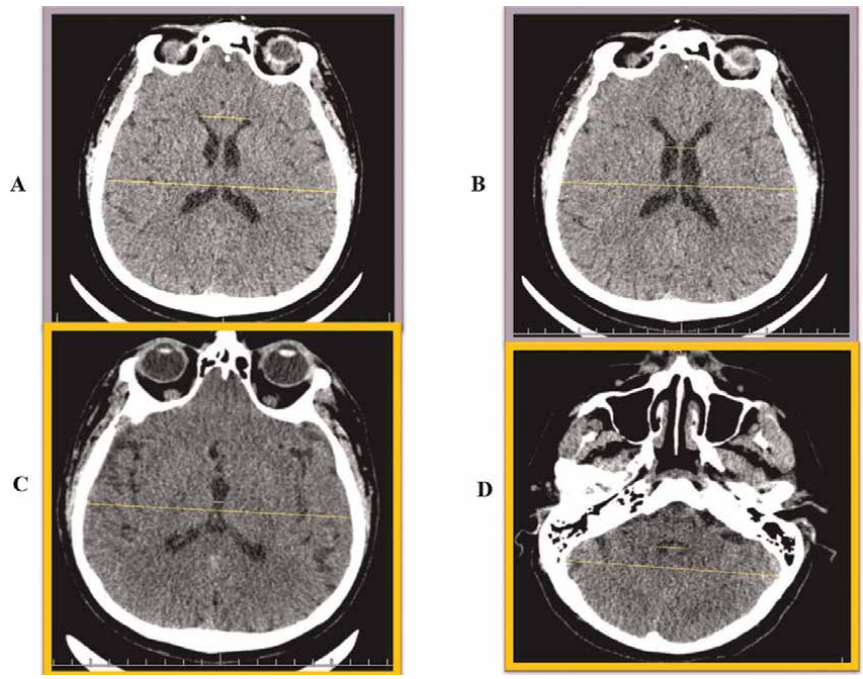

Figure 4.
MSCT of the brain. Measurement for calculating the index of the anterior horns of the lateral ventricles (A), measurements for calculating the index of the central divisions of the lateral ventricles (B). Measurement for calculating the index of the III ventricle (C), measurements for calculating the index of the IV ventricle (D).

Stage 2—reduction of density in the anterior and posterior horns;

Stage 3—edema along the perimeter of the lateral ventricles;

Stage 4—scalloped contours of the lateral ventricles and thinning of the brain substance.

Conducting magnetic resonance imaging (MRI) or MSCT with ventriculometry, in combination with a CSF examination, allows to timely diagnose hydrocephalus, to determine the severity and evaluate the results of the treatment.

6. Liquor shunting operations (LSO)

To correct persistent disorders of CSF circulation when it is impossible to use etiotropic treatment of decompensated hydrocephalus, LSO are used. The CSF shunting system is known to be an artificial analogue designed to compensate for disorders of CSF circulation, while its adequate functioning is determined by individual biomechanical parameters of the CSS.

Clinical and neuroimaging criteria, as well as their relationship with quantitative indicators of cerebrovascular circulation and cerebrovascular conjugation, determine the effectiveness of surgical treatment of hydrocephalus in children. Their importance while planning neurosurgical intervention is often underestimated. Solving these important tasks involves studying the disease aspects and taking into account how individual characteristics of the patient manifest—to develop a pathogenetically sound diagnostic system and personalize the hydrocephalus surgical treatment tactics.

In this regard, it is relevant to objectively evaluate these indicators and develop a system of minimally invasive monitoring of the viscoelastic properties of the CSS within the preoperative planning structure and to assess the effectiveness of hydrocephalus surgical treatment, taking into account changes in fluid dynamics.

Liquor anastomosis can be performed using shunts of various systems. The proximal part of the shunt is located in the cavity of the lateral ventricle, then the catheter passes through the brain substance, the soft and hard meninges, and bone and is connected to the pump. The pump is fixed to the bones of the skull and located directly under the skin. The pump valve regulates the pressure of the CSF at a predetermined level and allows it to pass in one direction only—from the cranial cavity to the extracerebral cavities. The distal part of the shunt is attached to the pump; it passes under the skin in the soft tissues of the neck and then, depending on the type of bypass surgery, plunges into the right atrium, transverse sinus, abdominal, pleural cavities, etc. (**Figure 5**).

Treatment of children with hydrocephalus involves various LSO. The removal of the CSF is carried out using implantable valve systems into the peritoneal cavity, with the inexpediency of classical methods, extracranial removal of CSF into the bloodstream (right atrium, jugular vein, sinuses of the dura mater, etc.) is used [28].

Indications for the CSF shunting operations with permanently implanted valve systems are persistent violations of CSF resorption, limiting the ability to normalize CSF circulation within the CSF system;

When choosing the parameters of the throughput of the CSF shunting system, they proceed from the results of measuring the biomechanical properties of the CSS and CSF circulation during surgery.

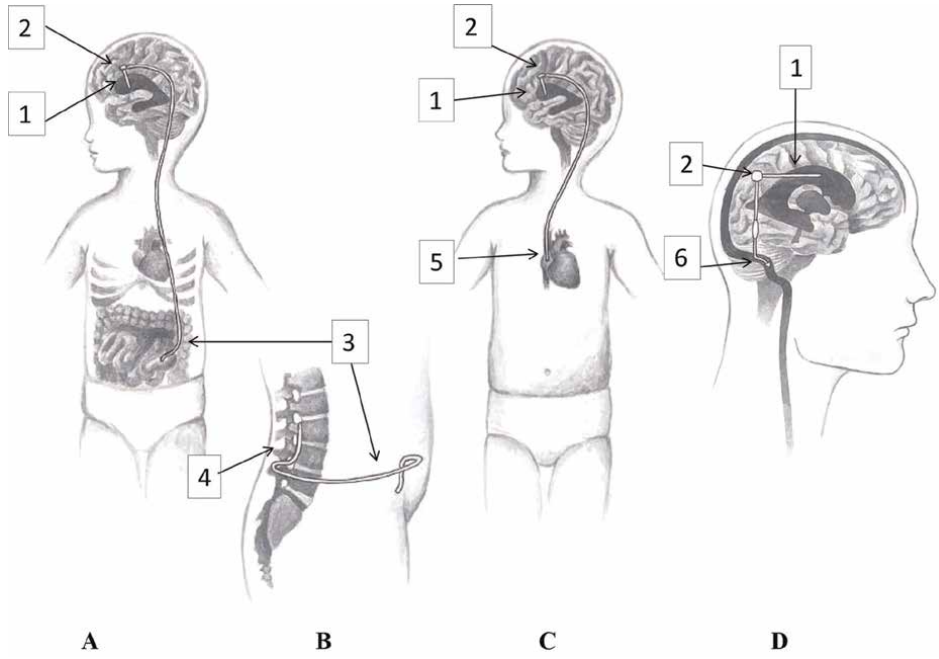

Figure 5.
Types of CSF bypass surgery. A—Scheme of ventriculoperitoneostomy. B—Scheme of lumboperitoneostomy. C—Scheme of ventriculoatriostomy. D—Scheme of ventriculosynustransverzostomy. 1—Ventricular catheter; 2—Bypass system valve; 3—Peritoneal catheter; 4—Lumbar catheter; 5—Atrial catheter; 6—Sinus catheter.

Types of LSO:

- **Ventriculoperitoneostomy** (**Figure 5**, **A**). During this operation, an anastomosis is formed between the ventricle of the brain and the abdominal cavity [10, 29].

- **Lumboperitoneostomy** (**Figure 5**, **B**). During this operation, an anastomosis is created between the CSF-containing space of the spinal canal and the abdominal cavity (mainly with the communicating form of decompensated hydrocephalus). Puncture lumboperitoneostomy is relatively low-traumatic; therefore, as of today, this operation is considered to be preferable in communicating hydrocephalus treatment [10, 15].

- **Ventriculoatriostomy** (**Figure 5**, **C**). During ventriculoatriostomy, an excessive amount of CSF from the ventricular system is removed into the right atrium cavity [10].

- **Ventriculosinustransverzostomy** (**Figure 5**, **D**). Unlike ventriculoperitoneostomy and ventriculoatriostomy, a distal catheter is implanted into one of the transverse sinuses. For ventriculosinustransverzostomy, a low or very low pressure drainage system is used. Bilateral ventriculosinustransverzostomy is not performed [12].

7. Pathomorphological changes of the brain around long-standing ventricular shunts

The puncture canal is a model of minor surgical brain damage and its outcome. Prolonged presence of an inert foreign body (shunt) determines the features of changes in the surrounding brain tissue [30].

As shown by a postmortem examination of brain tissue around shunts installed in occlusive hydrocephalus with various pathologies, a structured gliomesodermal capsule is formed more than 20 days ago (**Figure 6**).

As a result of completed reparative processes after puncture damage, along with a capsule mainly formed by mast astrocytes with connective tissue elements, a zone of perifocal changes in brain matter is detected, manifested by damage to myelin fibers and microcystic transformation (**Figure 7**).

Despite minimal brain damage during puncture, the outcome of reparative processes around the canal is the formation of a functionally "mute" zone, which is recorded during MRI examination in the form of a hyperintensive signal on T2 VI, IR IP, extending from the wall of the puncture canal up to 3 cm. The observed severity of perifocal changes around the shunt may cause neurological manifestations.

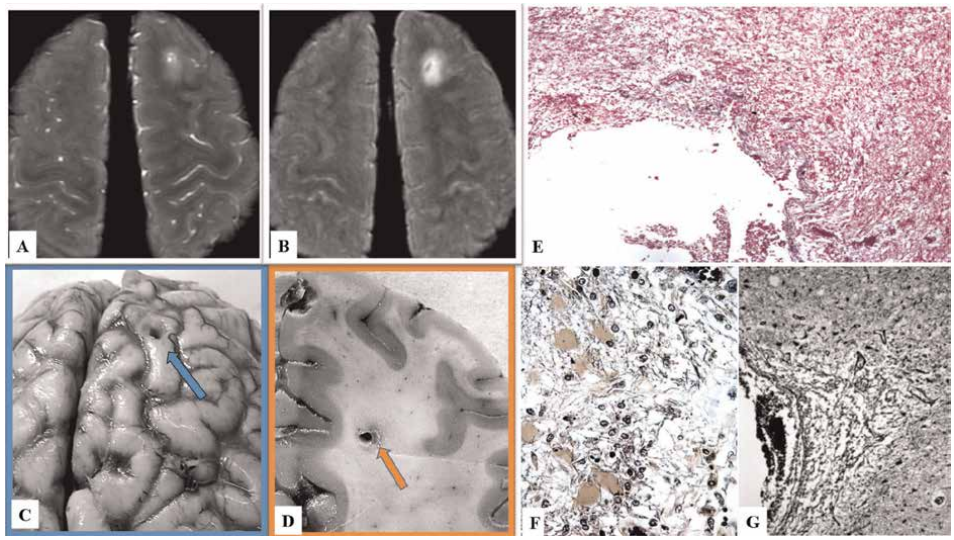

Figure 6.
Puncture canal in the right frontal lobe after installing a ventriculoperitoneal shunt through the anterior horn of the right lateral ventricle. The limitation period is 30 days. A—MRI T2-VI, axial plane. The three-layer structure of the puncture canal zone is differentiated; B—MRI IP-IR, axial plane. Puncture canal in the form of an oval hypointensive focus surrounded by a zone of perifocal changes; C—anatomical preparation, a type of puncture canal from the convexital surface; D is an anatomical preparation, a horizontal section at the level of the corresponding MR image. Perifocal changes recorded on MRI are not visualized; E—along the edge of the puncture canal is a gliomesodermal capsule with the presence of coarse collagen fibers of connective tissue. X 50. Mallory coloring; F—loose granulation tissue with an abundance of thin-walled vessels and reticulin fibers. X100. Impregnation with silver; G—cell gliosis of fibrous and obese astrocytes, around fragments of myelin fibers. X400. Coloring by Shpilmeyer.

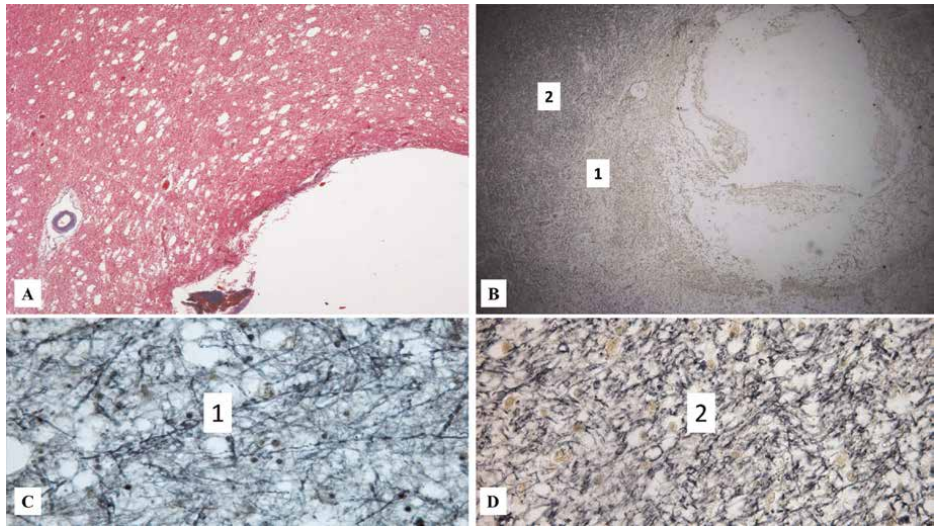

Figure 7.
Perifocal changes of the brain around the puncture canal. A—microcystic transformation of brain matter. X 50 H&E; B—demyelination of white matter around the channel. X 50, Shpilmeyer painting; C—single thinned myelin fibers with bulbous thickenings in the demyelination zone. X 200, Shpilmeyer coloring; D—fragmentation and formation of ring-shaped structures of damaged myelin fibers. .X 200, Shpilmeyer coloring.

8. Complications of LSO and their correction

The purpose of CSF shunting operations using valve drainage systems is to remove "excess" CSF outside the CSF system, eliminate ICH, and reduce the severity of deformation and expansion of CSF cavities [31].

In some cases, the goal is not achieved, and, with a liquor-shunting system implanted certain pathological manifestations occur. They are mainly associated with the peculiarities of the CSF shunting system functioning, namely with its permanent or transient dysfunction, and are combined into a single group of complications associated with inadequate operation of the shunting system [13, 31–33].

Pathological conditions, which are based on inadequate intensity of CSF outflow, are divided into two large groups: hyperdrainage and hypodrainage complications.

8.1 Hypodrainage conditions

In cases when the CSF outflow through the shunting system is insufficient to balance the CSF circulation and eliminate craniocerebral disproportion, manifestations of decompensated hydrocephalus persist even after CSF shunting operations [33].

This complication manifests in headaches, lethargy, drowsiness, hypophasia, hypodynamia, convergence disorders, paresis of looking up, suppression of photoreactions, suppression of abdominal reflexes, less often paroxysmal manifestations, the occurrence or preservation of pathological stop signs, and oral reflexes are observed. Ophthalmological studies reveal the persistence or reappearance of stagnant phenomena on the fundus, deterioration of vision, the field of vision narrowing.

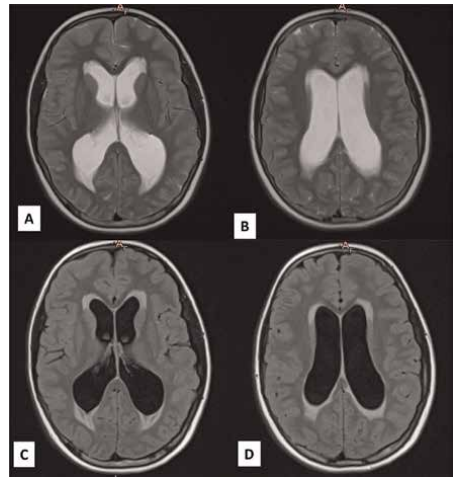

Figure 8.
MRI scan, axial projection of the brain 2 months after CSF bypass surgery. Progressive hydrocephalus. Shunt dysfunction. Ventriculomegaly with periventricular edema, absence of subarachnoid spaces. T2WI (A, B), Flair IP (C, D).

More often, a hypodrainage condition is detected during implantation of a drainage system of high or very high (≥ 120 mm of water) pressure, after previously performed ventriculoperitoneostomy or lumboperitoneostomy in patients with previous operations in the abdominal cavity or in the presence of pathology of the abdominal organs. Usually (in 3/4 of patients) hypodrainage is manifestated during the first week (month) after surgery, and the progressive course is slow.

CT, MRI studies reveal ventriculomegaly, narrowing of subarachnoid slits, preservation of periventricular edema (**Figure 8**).

The pathogenesis of hypodrainage conditions is far from being understood uniformly. Incorrectly chosen valve parameters of implantable systems can result in the valve pressure being higher than required. As a result, excessive CSF pressure persists. High peripheral resistance resulting from high intra-abdominal pressure, or high central venous pressure in those areas where liquor shunting systems are implanted, is considered to be another reason. There is still another mechanism leading to a hypodrainage state, which is a change in the "pressure-velocity" parameters of implantable systems under *in vivo* conditions due to obliteration of catheters and changes in the patency of the valve system [25, 33–35].

To diagnose a hypodrainage complication, one should state clinical and introscopic manifestations: the persistence of decompensated hydrocephalus, as well as ventriculomegaly, obliteration of subarachnoid spaces, periventricular edema according to CT, and MRI [33].

8.2 Hyperdrainage complications

With inadequately selected parameters of the shunting system, patients with hydrocephalus may develop specific conditions in the postoperative period, which include, inter alia, hyperdrainage complications. These conditions are based on excessively intense CSF outflow through the CSF shunting system, leading to low CSF pressure, accompanied by deformation of the CSF cavities of the brain, skull, and various clinical manifestations [33].

The frequency of this complication is noted in a wide range: from 5 to 55% [31, 35] and is more often observed in children under 6 months. Hyperdrainage leads to the development of such manifestations of craniocerebral disproportion as intracranial hypotension, slit-like lateral ventricle syndrome, subdural accumulation of CSF, isolated IV ventricle syndrome, and other cranial deformities [35].

Rapid removal of CSF by shunt leads to a rapid decrease in the volume of the ventricular system and deformation of the cerebral cloak, as a result of the resulting pressure gradient, and additional fluid accumulations (CSF or blood) form around the brain. In some cases, acute intracranial hypotension can lead to dislocation of the brain stem and the development of vital disorders [15, 34].

The most common manifestation of this pathological condition is characterized in modern literature as "slit ventricular syndrome."

8.2.1 The syndrome of slit ventricles of the brain

The term "slit ventricular syndrome" is widely used to describe the condition of chronic or transient headaches suffered by patients with hydrocephalus after CSF bypass operations accompanied by narrow (slit) ventricles (**Figure 9**).

There are several main pathophysiological mechanisms that cause slit ventricular syndrome: transient shunt dysfunction, intracranial hypotension, and against this background, a paroxysmal increase in ICP in the presence of a functioning shunt. At the same time, it is very important to distinguish situations when the ventricles are smaller than usual, or even almost invisible, but the clinical picture is asymptomatic and hence surgical correction is not required. Only when, in the presence of slit ventricles detected by CT/MRI examination, patients begin to suffer from an intense headache that interferes with normal life, and the diagnosis of "slit ventricular syndrome" is valid, requiring observation and treatment [36, 37].

Rekate H. suggests limiting the use of the term "slit ventricular syndrome" to cases characterized by a triad of signs: intermittent headache lasting 10–30 minutes, smaller than the normal size of the brain ventricles according to neuroimaging, slow filling of the pump reservoir after its mechanical pressure [37].

Headaches, hypodynamia, and general cerebral symptoms in these patients may be caused by both transient ICH and hypotension, and the relative significance of these mechanisms in each case seems difficult to determine.

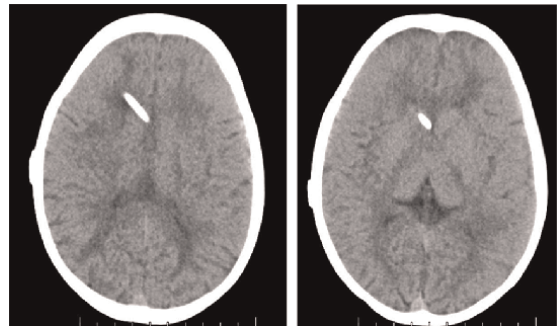

Figure 9.
CT scan, axial projection of the brain 20 years after ventriculoperitoneostomy. Congenital communicating hydrocephalus. Lateral ventricles are not traced, narrow subarachnoid slits, thickened skull bones with an enhanced pattern of finger depressions.

To accurately verify the diagnosis of slit ventricular syndrome, a comprehensive examination is required, including monitoring of intracranial pressure, which will help to exclude other causes of cephalgia, for example, cases of "childhood migraine", that is, not requiring surgical manipulations [37].

The frequency of this condition ranges from 0.9–37%, depending on the analyzed group of patients [36].

There are several pathogenetic mechanisms described in the literature and characteristic of the formation of this syndrome, underlying clinical manifestations: a sharp fluctuation of liquor pressure, deformation of liquor-containing cavities, changes in cerebrovascular conjugation, deformation of vascular collectors and redistribution of blood flow, changes in the viscoelastic properties of CSF, changes in the parameters of the regulatory mechanism implementation.

At the initial stage of the development of the slit ventricular syndrome, there is an inadequately intense CSF outflow through the shunting system, a hypotensive state, which actually leads to an excessive reduction in the size of the ventricular system. Further on, periventricular fibrosis, transient occlusion of the ventricular catheter, a decrease in the malleability of the brain, violations of venous outflow, increased intracranial pressure, etc. become the leading factors.

Neuroimaging methods are crucial in the diagnosis of slit ventricular syndrome, establishing the fact of microventriculia [37] (**Figure 10**).

Hyperdrainage syndrome requires replacement of the CSF bypass system with higher valve opening pressure values, implantation of an anti-siphon system. With narrow but asymmetric lateral ventricles, additional drainage of the opposite lateral ventricle, endoscopic perforation of the transparent septum is also proposed.

In case of confirmed dysfunction of the CSF system, it is revised with the replacement of occluded parts of the system. It is recommended to combine the revision of the liquor bypass system with the installation of an anti-siphon system, as well as during the primary implantation of the liquor bypass system, and this component should be used, which, in their opinion, prevents the development of slit ventricular syndrome [38].

In case of already formed craniostenosis with hyperdrainage in the background, when minimally invasive interventions are ineffective, when transient cephalgia persists while the shunt is functioning, and decompressive craniotomy or correction of

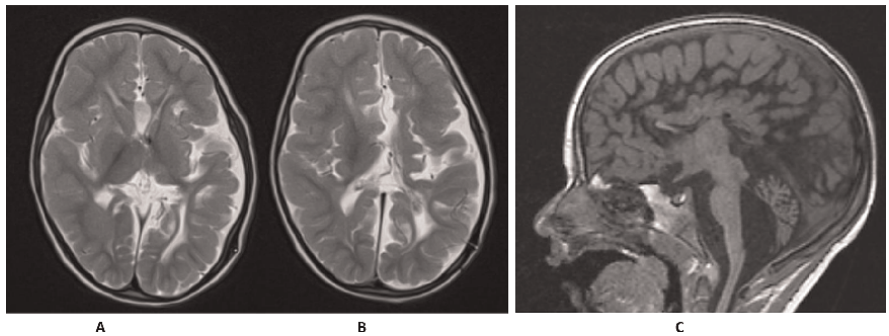

Figure 10.
MRI scan of the brain 9 months after CSF bypass surgery by a low pressure valve. Posthemorrhagic hydrocephalus. Expansion of the cavity of the IV ventricle against the background of slit-like lateral and III ventricles. A, B—T2WI, axial projection; C—T1WI, sagittal projection.

craniosynostosis is recommended. According to the authors, an increase in the volume of the cranial box, in this category of children, in most cases leads to a persistent positive effect and significantly reduces the frequency of repeated revisions of the CSF system [39].

Treatment of slit ventricular syndrome should be aimed at correcting the main mechanisms of this condition development, namely, the cessation of excessive CSF outflow through the CSF bypass system, correction of craniosynostosis, microcrania, and deformation of venous collectors through craniofacial or cranial reconstructive operations [33].

8.2.2 Isolated IV ventricle syndrome

One of the specific complications of cerebrospinal bypass surgery, in particular, as a manifestation of hyperdrainage, is the "sequesterization" of various parts of the ventricular system as a result of occlusion of interventricular openings (Monroe), Monroe openings in combination with brain plumbing, brain plumbing in combination with IV ventricular openings—isolated IV ventricular syndrome.

As a result of the closure of the plumbing of the brain and the openings of the IV ventricle (Lyushka and Majendi), its isolation from the CSF system occurs. With CSF continually produced, there is a gradual expansion of the cavity of the IV ventricle and compression of adjacent structures (brain stem, cerebellum), accompanied by appropriate clinical manifestations.

This variant is rare and this pathological condition in most cases is considered as a consequence of a hyper-drainage condition. The manifestation of the isolated IV ventricle syndrome consists in cerebellar disorders and signs of stem dysfunction. More often, patients complain of impaired coordination, double vision, headache, vomiting. The progression of the pathological process often leads to an increase in bulbar symptoms, impaired consciousness, and up to coma as a result of stem structure compression [14].

The introscopic picture in isolated IV ventricle syndrome has a specific character: A significantly expanded spherical IV ventricle is visualized, squeezing the stem structures anteriorly, the cerebellum posteriorly, the bottom of the rhomboid fossa being flattened, and dislocated anteriorly. With a pronounced and prolonged nature of the pathological process, there is a caudal displacement of the amygdala of the cerebellum and rostral dislocation in the tentorial tenderloin. Other manifestations of the hyperdrainage state of the supratentorial ventricles of the brain are also typical: dilation of subarachnoid spaces, narrow or slit-shaped lateral ventricles, subdural hydromes, or hematomas of the cerebral hemispheres [40].

Isolation of the IV ventricular cavity from the CSF system is clarified by contrast examination methods (CT-ventriculography). The pathogenesis of the formation of an isolated IV ventricle can be presented in several variants (**Figure 11**).

Correction of functional occlusion of the brain's plumbing is achieved by restoring adequate control over hydrocephalus (correction of hyperdrainage state). On the other hand, a positive result in the treatment of functional occlusion of the aqueduct and thereby regression of the isolated IV ventricle syndrome can be achieved after its temporary drainage by regular punctures or implantation of the Omaya reservoir (an undesirable option) [40].

Elimination of the pressure gradient between the supra- and subtentorial spaces makes it possible to restore the participation of the IV ventricle in the CSF circulation in the functional form of this syndrome.

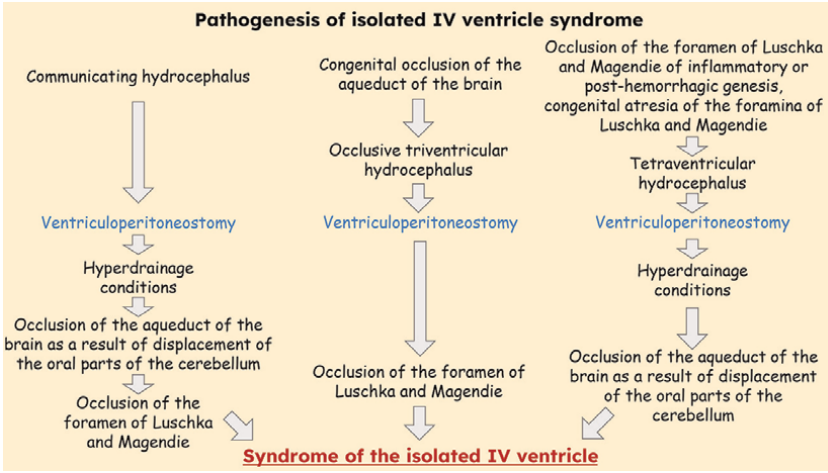

Figure 11.
Ways of formation of an isolated IV ventricle in patients with hydrocephalus after CSF bypass surgery.

In case of occlusion of the brain plumbing caused by morphological changes, surgical treatment is indicated. A number of authors practice open interventions with an isolated IV ventricle, performing microsurgical excision of adhesions, membranes causing the closure of the lumen of the brain plumbing, and ventricular openings, thus eliminating the "isolation" of the IV ventricular cavity and restoring liquor circulation by forming ventriculocysternostomy. At the same time, Dollo C. et al. recommend in some cases to complete the operation with "internal" shunting: implantation of a catheter from the cavity of the IV ventricle into the subarachnoid spinal space. The advantage of this method, according to the authors, is the prevention of re-overgrowth of the formed holes, the absence of a valve, and the position of the catheter along the rhomboid fossa bottom, which excludes damage to the latter [41].

IV ventricular bypass surgery has long been the most common method of surgical correction of the syndrome. It is worth noting that the course of the ventricular catheter should be as parallel as possible to the bottom of the rhomboid fossa, and its fixation should be reliable in order to avoid its migration into the cavity of the IV ventricle and traumatizing its bottom. When implanting a ventricular catheter, it is necessary to avoid damage to the transverse, sigmoid, and occipital sinuses [33].

A ventricular catheter is implanted through the hemispheres or, more rarely, the cerebellar worm [35] (**Figure 12**, A, B). The disadvantage of this method, according to some authors, is the impossibility of installing a ventricular catheter strictly parallel to the rhomboid fossa bottom, which does not exclude damage to the latter during surgery or when moving the brain stem against the background of ventricular drainage. With a decrease in the drainage cavity in volume, the risk of the ventricular catheter exit openings being obturated increases, which is also characteristic of this access [14].

The technique of shunting the IV ventricle through the frontal transventricular access can be described as follows: With the help of endoscopic assistance, a proximal catheter is passed through the lateral, III ventricles and installed into the cavity of the IV ventricle through the occluded water supply of the brain [42].

With this operation, simultaneous drainage of the lateral ventricles is possible with the formation of additional holes on the corresponding segments of the proximal

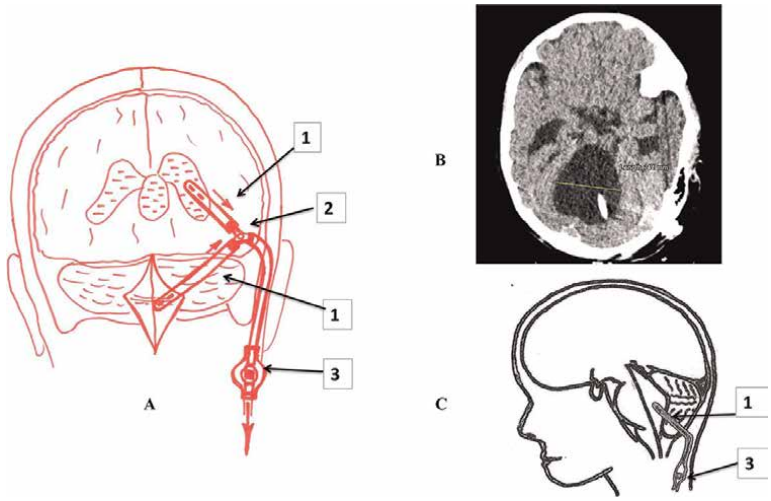

Figure 12.
Isolated IV ventricle syndrome. A—Ventricular ventricular IV ventricular peritoneostomy scheme; B—CT scan, axial projection of the brain after CSF bypass surgery with IV ventricular cavity catheterization; C—IV ventricular catheterization scheme. 1—Ventricular catheter; 2—Y-shaped connector; 3—Valve.

catheter, which will allow, if necessary, to avoid implantation of additional CSF bypass systems [14].

Unfortunately, this method is not feasible in the case of narrow or slit-shaped lateral ventricles, which is often characteristic of isolated IV ventricle syndrome.

The most adequate and pathophysiologically justified method, namely, peritoneostomy through the Y-shaped system, should still be considered, in which the IV and lateral ventricles are drained by a single valve system after being preliminarily connected (ventricular-ventricular IV ventricle). The technique of the operation has already been developed. The lateral and IV ventricles are catheterized, after which the extracerebral ends of both catheters are connected by a Y-shaped system, and the third arm of the connector is connected to the valve. Next, the distal catheter is implanted in the peritoneal cavity in the usual way. This is how uniform drainage of these isolated cerebrospinal cavities is carried out (**Figure 12**, C).

After implantation, the proximal catheter is included in the general cerebrospinal bypass system through a Y-shaped connector, or separate CSF bypass systems is implanted. At the same time, according to a number of authors, preference should be given to the first option, since this allows balancing the pressure above and below the tentorium [13, 32].

At the present stage, endoscopic methods of treatment of isolated IV ventricle syndrome are most popular: aqueductoplasty with or without stenting, perforation of the bottom of the III ventricle, and restoration of patency of the holes of Lyushka and Majendi [15]. However, due to the high risk of perioperative complications (bleeding, damage to vital structures), these manipulations are recommended to be carried out only in highly qualified medical institutions.

8.3 General complications of LSO

All CSF shunting operations create artificial homeostasis, which is characterized by depressurization of the CSS, constant removal of CSF into the extracranial cavities,

prolonged implantation into the CSF system and other body cavities of a foreign body (drainage system), and fixation of intracranial pressure at a predetermined level. Under these conditions, objective prerequisites are created for the development of complications both during surgery and in the postoperative period [43, 44].

8.3.1 Complication of punctures

Puncturing of the ventricles of the brain when the proximal shunt is inserted into them can be complicated by hemorrhages into the brain tissue along the puncture channel, subdural, and intraventricular hematomas [44, 45]. In some cases, when the shunt is standing for a long time, a gliomesodermal scar forms in the surrounding brain matter. According to various authors, from 5 to 48% of liquor bypass operations are complicated by the development of epilepsy [45]. Such a large spread of data is probably explained by different ways of performing operations by different authors. For example, the risk of epilepsy development increases significantly when a shunt is performed through the frontal or temporal lobes—the zones where epileptogenic foci are most often formed. Patients who have had at least a single convulsive attack in their anamnesis or who showed high convulsive readiness during EEG examination require special attention when performing LSO.

8.3.2 Inflammatory complications

Depressurization of the cranial cavity and prolonged implantation into the ventricular shunt system creates conditions for inflammatory complications [15, 46, 47]. In 3–17% of cases, there are limited or diffuse ventriculitis, meningitis, and encephalitis of varying severity [15, 46, 47]. In these cases, it is possible to spread the infection through the shunt and the occurrence of limited or diffuse peritonitis in this regard (with ventriculoperitoneostomy). With ventriculoatriostomy, the infectious agent gets directly into the blood, which sometimes leads to the development of sepsis [15, 41]. The greatest number of inflammatory complications develops in patients operated by underqualified neurosurgeons, as well as in emaciated patients and in the absence of drug prevention [44].

8.3.3 Thromboembolic complications

The imposition of ventriculovenous anastomoses is accompanied with the introduction of a foreign body directly into the bloodstream, which can lead to thrombosis in the lumen of the sinuses, veins, or right atrium [15, 44]. Blood clots cause either vascular occlusion or serve as a source of thromboembolism of the vessels of the small circle. The death of patients in this case may occur due to reflex cardiac arrest with thromboembolism of the main vessels. Closure of the lumen of the intrapulmonary vessels can lead to the development of lung infarcts and infarct-pneumonia. Our data include a case of jugular vein thrombosis and a case a pulmonary embolism of the branches of the pulmonary artery.

8.3.4 Perineal cyst

This complication occurs when the CSF is excreted into the abdominal cavity. In the abdominal cavity, a yellowish liquid rich in protein accumulates locally around the

peritoneal end of the catheter, around which a connective tissue capsule is formed as a result of the adhesive process, without any lining [15, 43, 48].

8.3.5 Tumor metastasis by shunt

Before cerebrospinal bypass surgery became a regular practice, extracranial metastasis of intracranial and especially glial tumors, even with a pronounced degree of anaplasia, used to be extremely rare, which, apparently, is associated with the protective function of the blood-brain barrier [49]. The artificial CSF pathway greatly facilitates the metastasis of the tumor beyond the skull, bypassing the blood-brain barrier. Depending on the type of bypass surgery, metastatic tumors may occur in the abdominal cavity (peritoneal location of the catheter) or in the lungs (with ventriculoatriostomy) [50]. We observed metastasis of a malignant glial tumor (medulloblastoma) [44]. The primary node was located in the cerebellum, and there were multiple cerebrospinal metastases to the brain and spinal cord. Tumor tissue growths similar to the primary node were also found around the distal part of the catheter located in the retroperitoneal tissue.

8.3.6 Violations of water-electrolyte metabolism

The development of water-electrolyte metabolism disorders is most likely during ventriculoatriostomy, since with this type of bypass a significant and incalculable amount of CSF is removed directly into the bloodstream for a short period of time. The protein content in the liquor is 0.3 g / l, and in the blood plasma 65–85 g/l; thus, almost protein-free liquid is poured directly into the blood, which can lead to the development of hemodilution. In case this risk is ignored, the signs of hemodilution—a decrease in the number of red blood cells, hemoglobin content, protein, can be regarded as post-hemorrhagic anemia, which in turn leads to improper treatment—transfusion of a large amount of fluid [32]. In one of our observations, the child is 10 months old. During the operation, 500 ml of protein-free solutions were poured during the anesthetic aid. Immediately after the operation, a picture of stagnation in the small circle of blood circulation developed (tachypnea, diffuse wet wheezing in both lungs, tachycardia, an increase in central venous pressure), anemia, microcirculation disorders (marbled color, increased turgor, and moisture of the skin), and stem symptoms. The patient's condition was regarded as dyscirculatory (hemic) hypoxia as a result of blood loss during surgery. Blood and blood-substituting fluids (250 ml of blood and 900 ml of other solutions) were transfused, but the patient's condition continued to deteriorate, and central respiratory and hemodynamic disorders joined, resulting in death of the patient 18 hours after the operation. The cause of death of the patient in such cases is pronounced hyperhydration and hemodilution [44].

8.4 Causes of death after CSF bypass surgery

The death of patients after LSO most often occurs due to the progression of the underlying disease. For example, the recurrence of the tumor can cause death of cancer patients. In some cases, the complications listed above (subdural and intraventricular hematomas of large volume, brain collapse, or pronounced disorders of water-electrolyte metabolism) can be the cause of death [44]. In some cases, the death of patients (usually infants) with severe occlusive hydrocephalus occurs in the coming hours after surgery. At the autopsy, no serious complications of LSO are detected. It can

be assumed that the death of patients who were in a subcompensated state with coordinating systems of homeostasis damaged before the operation occurs due to central respiratory disorders and the activity of the cardiovascular system [32]. These disorders are probably associated with decompensation of brain stem structures. In patients with severe hydrocephalus, there is a prolonged dislocation of the trunk, to which the patient adapts. During surgery, part of the CSF is usually released into the external environment during ventriculopuncture, especially in patients with very high CSF pressure. Then, the CSF enters the extracranial cavities through the pump, due to which the CSF and intracranial pressure decrease and the brain stem is being redislocated; the pressure of the CSF on the trunk from the IV ventricle also decreases. This can probably explain increased blood filling of the brain stem present in such patients, up to the occurrence of small perivascular diapedetic hemorrhages, detected by microscopic examination. It can be assumed that in such severe patients, even minor additional damage to the trunk is sufficient for decompensation of its function and death of the patient.

9. Prospects for the use of LSO

The prospective research should be aimed at studying subtle mechanisms of CSF resorption in order to identify the possibilities of its prosthetics in case of impaired CSF circulation and hydrocephalus development. It is necessary to determine the role of lymphatic vessels and the glymphatic system in the outflow of CSF, as well as to assess the importance of vascular plexuses as the only sources of CSF production, which is questionable.

Informative criteria determining the perspective of the method of treatment of children with hydrocephalus are histobiological and anatomical-topographic features of the root cause of the disease, the presence and level of ventricular-subarachnoid dissociation, the severity of deformation of the cerebrospinal cavities, resistance to resorption of CSF, morphometric features of intracranial fluid-containing cavities, the pressure-volume index of the ratio of the CSS, and brain compliance.

In our opinion, it is promising to study the tissue characteristics of the periventricular white matter of the brain in communicating and occlusive hydrocephalus by diffusion MRI, with a quantitative assessment of the measured diffusion coefficient (ICD) and fractional anisotropy (FA) [37]. The choice of rational tactics for the treatment of children with hydrocephalus, first of all, implies taking into account and personifying these specific features of the disease manifestation (**Figure 13**).

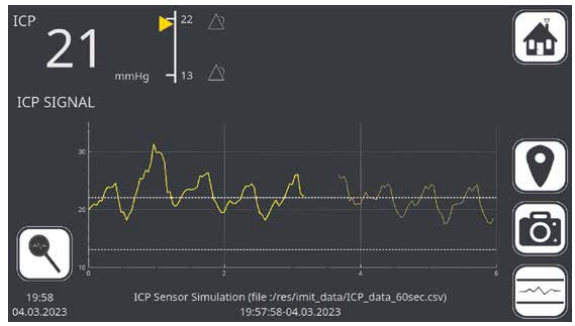

Figure 13.
High-tech instrument for analyzing intracranial pressure data.

Conducting CSF shunting operations with the selection of shunting systems require more accurate automated support, as well as digital processing and monitoring of intracranial pressure data. Modern software capabilities can allow for pressure monitoring, compliance calculation, graphical representation of pressure changes over time, external data export, etc. [51].

Improving software methods will reduce the risk of unsatisfactory results of hydrocephalus treatment by optimizing the selection of valve throughput parameters.

Thus, in the absence of currently alternative methods of surgical treatment of aresorptive hydrocephalus, it is necessary to further improve fluid shunting systems valves so that to make them capable of adapting to changing parameters of fluid circulation, including the principle of feedback.

10. Conclusions

It should be recognized that currently, the only effective and nonalternative method of treating aresorptive hydrocephalus is liquor bypass surgery. Performing LSO remains a priority mode of correcting hydrocephalus when etiotropic correction of the disease turns out to be impossible. To identify the individual features of the pathogenesis and severity of hydrocephalus, not only impaired CSF circulation, deformation of the cerebrospinal cavities and brain, but also a change in the biomechanical properties of the CSS, and evaluation of craniocerebral disproportion are significant. These mechanisms are mutually burdening each other, and their priority is variable and may change during the course of the disease, the treatment of hydrocephalus including.

The existing methods of diagnosing hydrocephalus in children based on quantitative indicators of biomechanical properties of CSF, parameters of CSF circulation, and craniocerebral ratio are sufficiently developed and informative. Strong relationship established between pulse fluctuations of intracranial pressure, brain compliance, "pressure-volume" ratio of CSF, and CSF circulation is of

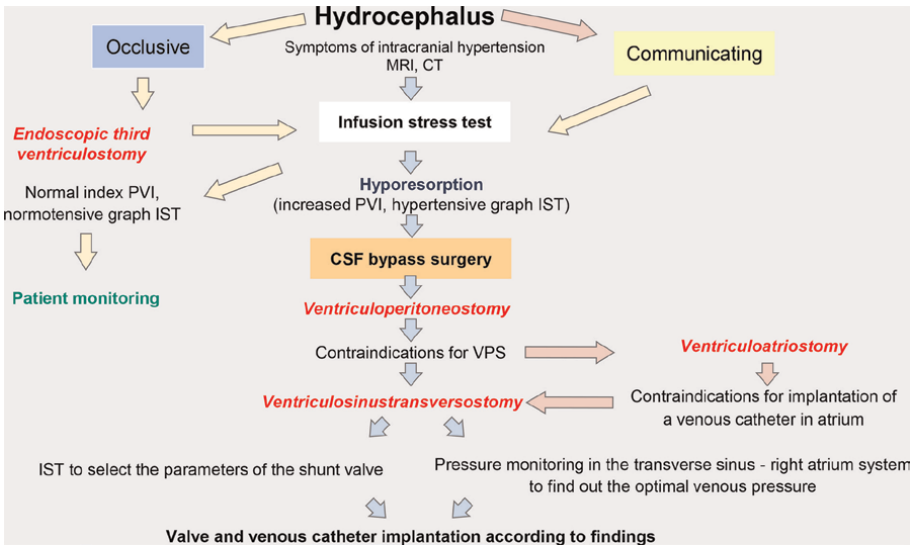

Figure 14.
Tactics for the treatment of hydrocephalus.

diagnostic significance. Evaluation of pulse fluctuations of intracranial volume allows minimally invasive personalized quantification of the parameters of CSF circulation and biomechanical properties of the CSS and craniocerebral ratio (**Figure 14**).

When choosing a treatment method, preference is given to pathogenetic interventions. The leading diagnostic method for hydrocephalus is a quantitative assessment of hydrocephalus, parameters of CSF circulation, and biomechanical properties of CSF (PVI, compliance, cerebrospinal pressure curve).

Evaluation of CSF circulation parameters and the CSS compliance requires modern hardware. In this regard, new evaluation methods are currently being developed and the existing ones are being improved to make the study accurate, minimally invasive, and informative.

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Conflict of interest

The authors declare no conflict of interest.

Appendices and nomenclature

CNS	central nervous system
CSF	cerebrospinal fluid
CSS	craniospinal system
ETV	endoscopic third ventriculostomy
ICH	intracranial hypertension
LS	liquor shunting operations
NTDFS	folate-sensitive neural tube defects
MPPH	Megalencephaly-polymicrogyria-polydactyly-hydrocephalus syndrome
ICC	intracranial compliance
IST	infusion stress test
MRI	magnetic resonance imaging
MSCT	magnetic spiral computed tomography
PVI	pressure volume index
VSTS	ventriculosinustransversostomy

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Section 3

Complications in Surgical Treatment of Hydrocephalus

Chapter 8

Abdominal Complications in Patients with a Ventriculoperitoneal Shunt

Yamila Marquez Basilotta, Romina Argañaraz and Beatriz Mantese

Abstract

Hydrocephalus is a complex disease. The placement of a ventriculoperitoneal shunt is a treatment that has been in use since the 1960s. Although in recent years, the development of the endoscopic technique has gained importance in the treatment of hydrocephalus, the use of valves continues to be used. Valves can be associated with different complications. In this chapter, we develop the abdominal complications associated with these devices. Both in patients with abdominal pseudocysts and with intestinal infections or ascites, they should be studied with brain tomography, x-rays of the valvular system, and ultrasound. The first step of treatment in these patients is to define if the valve works correctly or not. The second topic to take into account is the presence of infection associated with the catheter, which is detected by taking a sample of cerebrospinal fluid. The treatment of these valve-associated complications in many cases requires an approach involving multiple specialists, general practitioners, infectious diseases specialists, and general surgeons, among others. In patients with ventriculoperitoneal shunt-related abdominal complications, surgical treatment depends on symptom severity and the possible associated infection at the time of diagnosis.

Keywords: ventriculoperitoneal shunt, pseudocyst, bowel complications, ascites, abdominal complications

1. Introduction

Hydrocephalus is a complex disease, common in childhood, that can cause permanent damage to the development of cognitive functions. Hydrocephalus results from an imbalance between cerebrospinal fluid (CSF) production and absorption. Within the physio pathogenesis, they are classically classified into communicating and noncommunicating hydrocephalus.

Noncommunicating or obstructive hydrocephalus is due to the presence of a lesion within the ventricular system that causes its obstruction with the consequent accumulation of cerebrospinal fluid, for example, stenosis of the sylvian aqueduct or tumors.

The ventriculoperitoneal valve placement technique was developed in the 1960s. The ventriculoperitoneal valve is made up of three parts, a tubing that is placed

intracranially, the valve reservoir, and the distal catheter that is inserted into the peritoneum. Despite the passing of the years, this treatment is currently used effectively in patients with communicating hydrocephalus [1–3].

Although in recent years, the endoscopic technique has been developed for patients with obstructive hydrocephalus. Placement of a ventriculoperitoneal catheter continues to be used.

The placement of ventriculoperitoneal valves is a surgery that is not free of complications. The most frequent VPS-related complications are infection and shunt malfunction. Shunt infection can be caused by various microorganisms. The causes of the malfunction of the shunt may be due to obstruction of the proximal catheter with choroid plexus (more frequent). The distal catheter can be cut with growth in pediatric patients. Occlusion of the valvular reservoir can also occur in patients with a large amount of protein in the cerebrospinal fluid, among others.

There are other less frequent complications than infection and valve obstruction that involve the gastrointestinal tract. Within this group of pathologies are the abdominal pseudocyst (APC), ascites, or complications related to the intestine. Knowledge of possible abdominal diseases in patients with ventriculoperitoneal shunt is important for proper management in these cases [1, 4–7]. In this chapter, we propose management guidelines for patients with VPS-associated abdominal complications, such as APC, bowel-related complications, and ascites based on our experience at a tertiary-care hospital [8].

2. Patients with a VPS-related abdominal pseudocyst

Abdominal pseudocysts receive that name because they are not true cysts. They are produced by adhesion between the intestinal loops with the consequent accumulation of fluid [9–12]. These pseudocysts lack their own wall or capsule. One of the possible theories to explain the physio pathogenesis is that the same material of the valvular catheter produces an inflammatory reaction of the intestinal loops, thus generating this fluid-filled cavity and preventing the catheter from functioning correctly. Another theory is that there is an infection with some germ that generates adhesion between the intestinal loops (**Tables 1** and **2**).

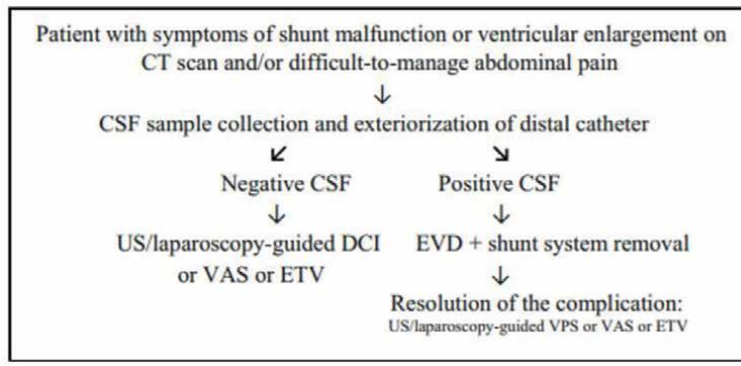

Table 1.
Management of patients with abdominal Pseudocyst, which cannot wait for the culture results, CFS cerebrospinal fluid, DCI distal catheter insertion, EVD external ventricular drainage, ETV endoscopic third ventriculostomy, US ultrasonography, VAS ventriculoatrial shunt, VPS ventriculoperitoneal shunt. Importantly, Conservative management is not advocated in any clinical scenario.

Oligosymptomatic patients without shunt malfunction CSF sample collection	
Negative CSF	Positive CSF
↓	↓
US/ laparoscopy-guided DCI or VAS or ETV	EVD + shunt system removal
	↓
	Resolution of the complication: US/laparoscopy-guided VPS or VAS or ETV

Table 2.
Management of patients with an abdominal pseudocyst and mild symptoms. CFS cerebrospinal fluid, DCI distal catheter insertion, ETV endoscopic third ventriculostomy, US ultrasonography, VAS ventriculoatrial shunt, VPS ventriculoperitoneal shunt. Importantly, Conservative management is not advocated in any clinical scenario.

This pathology should be suspected in patients who have had a ventriculoperitoneal valve placed and who present with fever, abdominal pain, and symptoms of intracranial hypertension. Since the correct functioning of the shunt may be affected by the presence of the abdominal pseudocyst [13–19], it is mandatory to perform complementary imaging studies to evaluate the shunt system.

A brain tomography should be performed to assess the size of the ventricles and some indirect signs of intracranial hypertension such as decreased subarachnoid spaces or the presence of periventricular transependymal edema. Radiographs of the system allow evaluation of the indemnity of the valvular system. It is recommended to perform a skull, thorax, and abdomen plate to evaluate the complete path.

The presence of a pseudocyst should be suspected when two abdominal radiographs show the tip of the catheter in the same position.

Abdominal ultrasonography is a useful and noninvasive method to confirm the presence of the pseudocyst by imaging. Although it is an operator-dependent method, which means that it requires the skills of the person who performs it, the tip of the distal catheter can be seen in contact with a hypoechogenic cavity.

In these patients, it should be initially suspected that APC may be associated with a shunt infection by a low-virulence or slow-growing organism [2]. As described in the literature, in recent years, about 41% of patients with abdominal valves and pseudocysts had an infection at the time of diagnosis [20, 21]. Due to this, we recommend ruling out the presence of a nervous system infection before deciding on surgical treatment. In a patient with VPS and an APC, a brain CT scan, radiographs,

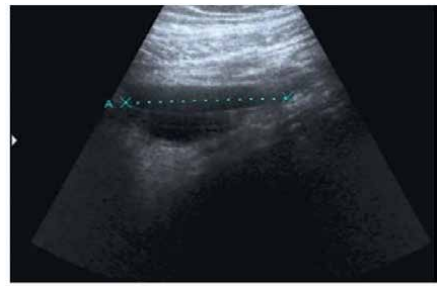

Figure 1.
Abdominal ultrasonography shows an anechoic fluid collection measuring 5 x 2 x 2 cm in the left iliac fossa, the region where the patient reported pain, around the tip of the distal catheter.

and abdominal ultrasound should be ordered to determine if the APC is causing the ventriculoperitoneal shunt to malfunction [7, 22].

In case of shunt malfunction, suspicion of APC is based on clinical manifestations (headache, fever, abdominal discomfort, etc.), lack of mobility of the distal tip of the catheter on routine x-rays, and is confirmed with abdominal ultrasound (US) (**Figure 1**). The latter study is safe and rapid and should be performed immediately as symptoms of shunt malfunction are already present [1, 4, 6, 7, 20, 23].

APC does not always cause the full spectrum of symptoms of intracranial hypertension syndrome [21]. It is recommended to collect CSF for culture, to rule out infection. The sample could be taken by lumbar puncture (LP), but sampling from the shunt is recommended because LP is not always possible, for example in patients with spinal dysraphism. Furthermore, in obstructive hydrocephalus, the lumbar cistern may not be in communication with the ventricular space [24, 25]. Some of the organisms responsible for this type of complication are slow growing. Therefore, it is recommended that the minimum reading time of the culture fluid be approximately one week (five to seven days).

It must also be taken into account that some microorganisms produce biofilm. Therefore, its recovery in cultures will be greater in prostheses, in this case, the ventriculoperitoneal valve.

After evaluating the CT scan, the severity of the symptoms of intracranial hypertension, and the degree of abdominal pain, we can classify patients as oligosymptomatic or asymptomatic. The treatment will be different according to the presence or not of severe symptoms.

In patients with an abdominal pseudocyst and symptoms of intracranial hypertension and/or ventricular enlargement on computed tomography or abdominal pain that is difficult to manage clinically with medication, it is recommended to remove the distal peritoneal catheter. The externalization of the distal catheter, that is to say, the removal of the system from the abdomen and its connection to a collecting system abroad should be carried out while awaiting the results of the culture [7]. To define the site where the outsourcing will take place, the patient's anatomy must be considered.

We found the thoracic site the easiest and safest to outsource the shunt since it is easy to palpate in this region. If this is not the case, x-rays can be used to locate it in the operating room. However other sites may be considered. It is recommended to attempt to evacuate the APC by aspiration through the proximal end of the severed distal catheter before removing it from the abdominal cavity. It is important to consider that some catheters have a non-return mechanism at the tip that prevents aspiration of the cyst. Some authors consider the possibility of performing an abdominal tomography and aspiration puncture of the pseudocyst. We do not consider it necessary, since it is not a true cyst, only the withdrawal of the catheter allows the absorption of the liquid.

If a microorganism is isolated from the CSF culture collected from the reservoir, it is an infection associated with the ventriculoperitoneal valve. In this case, the system should be removed and an external ventricular drain (EVD) placed. Long-term treatment consists of reinsertion of the shunt. Ultrasound- or laparoscopy-guided repositioning into the peritoneum may be considered. Placement of a ventriculoatrial shunt (VAS) may also be considered [5]. The decision should be made after an evaluation together with the general surgeon. If the ventricular anatomy is favorable and the endoscopic third ventriculostomy (ETV) success score is high, then ETV can be considered [26].

In patients with an abdominal pseudocyst without shunt malfunction or with mild symptoms of intracranial hypertension and/or mild abdominal pain, the result of the CSF sample can be awaited without externalizing the shunt system. CSF reading is recommended for approximately one week (five to seven days) to rule out low-virulence and slow-growing pathogens. If no germs are present, a new distal catheter can be inserted at another location in the abdomen. Ultrasound or laparoscopy can be used as a guide. Reinsertion into the abdomen can also be avoided by diverting it to the cardiac atrium. In candidate patients, endoscopic treatment of hydrocephalus should be considered; ETV is another option.

In the case of a central nervous system infection, the shunt system should be removed and an EVD placed temporarily until the infection resolves. Once the infection is resolved, a new shunt system should be placed taking into account the same aspects as in patients with negative cultures.

The two main theories about the pathophysiology of APCs are that it originates from an infection and the other that APC is caused by an allergic reaction. Therefore, shunt infection should always be ruled out. In case the patient has mild symptoms or no symptoms and can wait for the final result of the CSF culture, it is recommended to change the distal catheter with a new one in another location or to perform an endoscopy.

There is no high-grade evidence to support the exteriorization of a system in oligosymptomatic patients without infection in the nervous system. We propose not to carry out the exteriorization in a systematic way, since surgery and/or superinfection of the valve can be avoided when exteriorizing it.

3. Patients with VPS-related bowel complications

Within this group, we consider patients with appendicitis, intestinal perforation, intestinal adhesions, intestinal volvulus, fistulas, plastron, anal extrusion of the peritoneal catheter, bladder perforation, abdominal wall perforation, and migration of the distal end of the catheter to the scrotal sac.

In this group of patients, it is also important to evaluate the functioning of the ventriculoperitoneal shunt valve with brain tomography and system radiographs. Because infections, intestinal rupture, among others. Can generate a malfunction of the shunt.

In patients with intestinal complications, the characteristics of the intestinal process and whether it is in contact with the distal catheter in the peritoneum should be assessed initially with abdominal ultrasound [27–32]. The multidisciplinary evaluation of the patient is mandatory by a medical clinic, infectology, and general surgeons, because many of these pathologies are surgically resolved by the general surgery service. In case of an infectious process such as appendicitis, in contact with the catheter distal to the valve or perforation, exteriorization of the shunt at the thoracic level is recommended. The distal catheter is considered contaminated and must, therefore, be removed from the abdominal cavity [33]. A CSF sample for culture should be taken from all patients and culture results should be awaited before placing a new shunt.

In patients in whom the CSF culture is positive, it is most likely an ascending infection caused by germs of abdominal origin. As it is an infection in the nervous system, the entire shunt system must be removed and an EVD placed until the infectious process is resolved [7]. After completing the appropriate antibiotic treatment for the infection, a new catheter should be placed. Preferably in the atrium of the heart to avoid a new approach to the abdomen, abdominal surgeries and infectious processes predispose to the formation of intestinal adhesions and/or a peritoneum with less

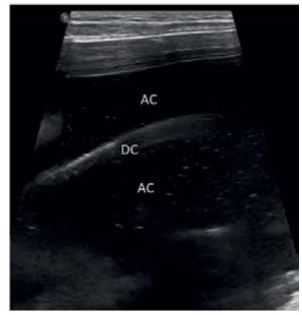

Figure 2.
Abdominal ultrasonography shows the distal catheter and abundant peritoneal fluid (ascites). DC distal catheter, AC ascites.

absorptive capacity. If the ventricular anatomy is favorable and the VTE success score is high, endoscopic surgery can be performed for treatment of hydrocephalus.

4. VPS-related ascites

Ascites are the abnormal accumulation of intraperitoneal fluid. Fluid accumulation occurs as a consequence of a nonabsorptive peritoneum. In addition to the clinical suspicion on physical examination, a globose abdomen, with an ascitic wave on palpation. Abdominal ultrasound is an imaging diagnostic method that, although it is operator dependent, is useful in diagnosing ascites (**Figure 2**). It is important to study the possible malfunction of the valve, so a brain tomography and x-rays of the system should also be requested [34–36].

In the case of the presence of ascites, CSF sampling is also recommended to rule out infection associated with the system. If the culture result is positive, removal of the shunt and placement of an EVD is recommended along with administration of antibiotics until resolution [37, 38].

If the patient has symptoms of intracranial hypertension, ventricular enlargement on CT scan, or dyspnea (respiratory distress) secondary to ascites, the shunt should be exteriorized while awaiting culture results. If cultures are negative, the site of choice for a new distal catheter is the atrium of the heart as reinsertion into the peritoneal cavity is not recommended [6, 35, 36] Although spontaneous resolution of ascites without the need for shunt intervention has been published, we recommend reinsertion of the catheter in a space other than the peritoneum [37]. If the patient is a candidate for endoscopic treatment of hydrocephalus, ETV could be considered.

Each patient must be managed individually based on their clinical context and the abdominal pathology associated with the shunt. The decision to remove the ventriculoperitoneal valve should be taken into account that CSF cell count, glucose, and protein may not be reliable indicators of infection and therefore do not justify immediate removal of the shunt [25].

5. Conclusion

DPVs have been used for the treatment of hydrocephalus for more than 60 years. Abdominal conditions in patients with shunts can make therapeutic decision-making

difficult. The analysis of each case taking into account the presence of symptoms of intracranial hypertension and/or infection is important since in many cases a multidisciplinary team is required for treatment.

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Chapter 9

Infections in Intracranial Pressure Management: Impact of New Technologies on Infection Rates

Roger Bayston

Abstract

It is now recognised that infections in CSF shunts and external ventricular drains (EVDs) are biofilm infections, and the scientific basis of these infections is better understood. Infection rates in shunts have now fallen but remain unacceptably high. There is an increase in infections due to multi-drug-resistant bacteria in EVDs. Reliance on antimicrobial prophylaxis has potential lifethreatening consequences and safer more effective measures are available. These consist of well-founded "bundles" or surgical protocols that have been shown to reduce infection by application of well known but not universally applied principles. New developments in antimicrobial technology have now been shown to be clinically effective and have reduced healthcare costs. The reduction in antibiotic use has led to fewer adverse effects. Problems with multidrug resistance in EVD infections remain and technology to address these has been developed but is not yet clinically available.

Keywords: CSF shunt, external ventricular drainage, antimicrobial prophylaxis, antimicrobial catheters, intracranial pressure management

1. Introduction

Intracranial pressure needs to be controlled in cases of hydrocephalus, or after cranial trauma, or cerebral oedema due to, for example, tumour. In hydrocephalus, the most common treatment involves placement of a shunt to drain cerebrospinal fluid (CSF) from the cerebral ventricles to a body cavity such as the peritoneum (ventriculoperitoneal, VP, shunt) or the right cardiac atrium (ventriculaoatrial, VA shunt). Sometimes other sites are used, such as the pleural space. Where there is free communication with the spinal theca and the ventricular system, a lumbar-peritoneal (LP) shunt can be used. Shunts are totally internal and are intended to be in place permanently, though they often require revision due to obstruction. In cases where the need for control of intracranial pressure is temporary, such as following cranial trauma or haemorrhage, or as part of the management of a shunt infection, an external ventricular drain (EVD) is used. This drains CSF from the cerebral ventricles, exiting through a burr hole to an external collecting system. It might be in place for a few days or a few weeks depending on the patient's condition. The collecting bag is changed when approximately 75% full. Another temporary means of controlling CSF pressure is insertion of a reservoir,

typically Ommaya or Rickham. As these are "blind" with no drainage tube, it is necessary to aspirate CSF percutaneously, typically daily. Reservoirs are also commonly used as access ports for administration of drugs to the ventricular system.

2. Infections in CSF drainage devices

All surgical procedures carry a risk of infection, and the presence of a biomaterial significantly increases the risk [1, 2]. The insertion of silicone CSF drainage devices is no exception to this, and infection poses a real clinical problem. Hydrocephalus shunts are at risk of infection almost exclusively at the time of insertion or revision, and not thereafter. The main pathogen is coagulase negative staphylococci (CoNS) derived mainly from the patient's skin [3, 4], and entering the operative field during the procedure. Other bacteria are also involved, including *Cutibacterium acnes* [5, 6], also a skin commensal, and less often gram negative bacteria such as *Escherichia coli*. Infection rates have fallen in recent years, but still remain high in infants less than 6 months old [3, 7], and less so in adults [8]. The microbiology and pathology have been elucidated in previous publications [9, 10]. As EVD is by its nature an external device which also connects with other tissues and the central nervous system, it is perhaps not surprising that the infection rate is higher than in shunts. While many large institutions report rates of 8–10% [11], some recent studies have reported rates in excess of 20% [12]. Again the most common EVD pathogen is CoNS, but there is a higher proportion of gram negative bacteria, and particularly multi-drug-resistant strains including *Acinetobacter baumannii* [13]. The sources of EVD pathogens are the patient's skin and mucous membranes, staff managing the EVD, and the hospital environment. Ventricular access reservoirs are at risk at the time of insertion, but mainly during use, as with EVD. Infection rates are 5–8%, with ventriculitis/meningitis accounting for most cases but cellulitis around the reservoir occurs in 20% of cases. Most pathogens are derived from the skin, and include CoNS (56%) and *C acnes* (24%) [14, 15].

Infected shunts and EVDs should be removed a soon as possible and systemic antibiotics given, often for several weeks, but relapses are common [16]. In the case of infected reservoirs, successful treatment has been achieved with systemic and intra-reservoir antibiotics without device removal [17, 18].

3. Non-technological prevention measures

In view of the morbidity, costs and difficulty in successful treatment of infected shunts and EVDs, prevention is a major goal. Great success has been achieved by institution of care "bundles," packages of procedures included in written protocols to which all personnel contribute and with which there is general consensus [19–21]. Infection rates usually fall, and spikes of infection can usually be attributed to a protocol violation [20]. The disadvantage of this approach is that infection rates tend to rise again due to habituation, or if the protocol lead moves on. More specific measures include reducing the duration of EVD use where possible, and tunneling the ventricular catheter a few centimetres away from the burr hole (or in some cases down to the abdominal wall [22].) Another innovation is the placement of a port in the subclavian region and the ventricular catheter tunnelled to connect with it [23]. The use of prophylactic antibiotics is controversial. They are used almost universally in shunt placement, but the evidence for their effectiveness is weak. In EVD, two regimens are used. One consists of a single

dose of antibiotic given just before EVD insertion, and the IDSA Guidelines recommend this [24]. However, in some institutions the systemic antibiotics are continued throughout the duration of EVD use. While there is some evidence that the long regimen can reduce EVD infection, it is clearly associated with higher healthcare costs [25] and with severe, often lifethreatening infection with *Clostridioides difficile* [26, 27].

4. New technology for infection prevention

4.1 Types of technology and modes of action

The technologies aimed at reducing infection in neurosurgical devices must satisfy basic criteria: biocompatibility in tissues of the central nervous system and elsewhere; activity against at least the most common pathogens involved; sufficient duration of activity to cover the period of risk; and ability to be sterilized without significant loss of activity or adverse mechanical changes. These criteria are difficult to achieve.

4.2 Laboratory testing of antimicrobial technologies

All materials and devices for use in neurosurgery must undergo testing for mechanical properties (to ensure their robustness and suitability for use, including in the case of catheters, measurement of the force needed to disconnect (pull-off), tensile strength and other properties. They also undergo tests for toxicology of component materials, biocompatibility using international standard tests [28, 29], and certification of sterility and shelflife. Any modification of the materials or device has potential to affect all of these and antimicrobial processes such as coatings will require significant further testing. The processing might affect the mechanical properties and this might affect the likelihood of disconnection during use. Biocompatibility of the antimicrobials or the coating material will need to be determined, and this must include the possible chemical effects of sterilization which can give rise to toxic degradation products. Any claim for reduction in infection, at this stage usually expressed as reduction in bacterial attachment, or killing of test bacterial in vitro, will need to be determined, and animal implantation and challenge is often undertaken. However, while all potential neurosurgical implants must pass these tests, the current standards are not sufficiently meshed to the intended use. An example is testing for antimicrobial activity by immersing the processed material in a liquid culture of bacteria and measuring reduction in viability. This rarely has any relevance to the intended use of the material or device, and merely "ticks the box" for regulatory purposes. Another example is implantation subcutaneously into the flank of a rodent of material intended for use as a catheter, again bearing no relevance to intended use or anatomical site, yet giving information for regulatory purposes. For the purposes of this paper, test methods for antimicrobial activity will be discussed.

4.3 Laboratory testing for antimicrobial activity of processed neurosurgical devices

4.3.1 Surface modification

Modification of catheter surfaces can take the form of biomaterial modification, coating with a secondary material, or application of an antimicrobial coating.

Application of a material intended to reduce or inhibit bacterial attachment, by changing the hydrophobicity or charge of the surface, can be tested by a variety of means including those of surface physics and microbiology. For the latter, simple immersion into a suspension of bacteria followed by counting of attached bacteria might give interesting data, but unless a conditioning film consisting of extracellular matrix proteins similar to that occurring in vivo is applied to the modified surface, the data will be potentially misleading. Such a conditioning film is deposited rapidly on all biomaterials after implantation, and the modified surface is easily obliterated. The conditioning film is the surface that potential device pathogens usually attach to and this must not be omitted. This is also true of antimicrobial coatings, intended to kill bacteria that attach to the material. Test results that do not include a conditioning film are unreliable. A polyvinylpyrrolidone (PVP)—coated shunt catheter was tested without a conditioning film after soaking in antimicrobial [30]. Here they found that the PVP coating reduced bacterial attachment irrespective of any antimicrobial soaking. They also carried out an in vivo study by inserting a coated, inoculated catheter intraventricularly in a rat model. After removal of the catheters 7 days later, they found that both coated and uncoated catheters were colonised. They concluded that, even if attached bacterial numbers were reduced, full colonisation would eventually occur unless bacterial attachment was totally prevented. The PVP-coated catheter was tested with a serum conditioning film after it had been rehydrated in a solution of rifampicin [31], and the deposited serum proteins significantly reduced the antimicrobial activity. The same coated catheter was tested by Bayston et al. [32] who also applied a plasma conditioning film. They also found that the conditioning film further reduced bacterial numbers attached to the catheter even in the absence of antimicrobial. However, they also found that, contrary to claims, the lumen surface of the catheters was uncoated and became fully colonised by bacteria. This is important as most shunt and EVD catheters are, at least initially, colonised on the lumen surface. A rather concerning observation was also made in an animal implantation study [33] that even dead bacteria were able to induce abscess formation around the PVP-coated catheter, suggesting that the PVP coating might modify the local cellular immune response. A heparin-coated catheter was investigated by Nomura et al. [34] with the intention of producing a hydrophilic silicone surface. They soaked their coated catheters in CSF and found that the conditioning film consisting of CSF proteins also reduced bacterial adhesion. CSF protein is mainly albumen, and this has been shown to reduce bacterial attachment to shunt catheter material [35]. Plasma also contains fibrinogen and fibronectin, and these are known to favour bacterial attachment [36, 37], so the choice of conditioning film for in vitro testing is important.

4.3.2 Antimicrobial coatings

Shunt or EVD catheters can be coated with antimicrobial substances, and the most common is some form of silver. In 1997 Guggenbichler et al. developed a new technique for mixing nanoparticulate silver with polyurethane, the water porosity of which was claimed to ensure release of antimicrobial silver ions for long periods [38]. This was not strictly a coating as the silver was dispersed throughout the polymer, but it was not an impregnation technique. Several publications followed, with variable results in laboratory studies [39, 40]. An explanation of why silver-processed catheters might not be effective has been offered by Schierholz et al. [41] More complex silver-processed catheters have shown reduction in bacterial attachment and biofilm formation in the laboratory [42, 43].

4.3.3 Antimicrobial impregnation

A technique for post-manufacture impregnation of silicone materials with antimicrobials has been developed [44]. This process allows even dispersion of molecules of certain antimicrobials throughout the silicone material, and ensures that they are able to migrate freely even in the absence of water. Molecules of antimicrobials removed from the surface by fluid flow are replenished by those migrating from the catheter material. In turn, this gives a long duration of activity. Laboratory testing on shunt and EVD catheters processed by this method have shown that bacterial colonisation and biofilm development can be prevented even with high-number bacterial challenges in flow conditions [44, 45]. The test catheters were perfused for up to 4 weeks with repeated weekly challenges, and were shown to be free of colonisation at the end of this period. Further studies have shown that the antimicrobial material does not prevent bacterial attachment, but that attached bacteria are all killed within 48 hr. (the tK100 test) [45]. The antimicrobials were chosen partly for their known spectrum of activity against common shunt pathogens (mainly staphylococci) and because of their compatibility with the impregnation process and to give the required post-impregnation performance. The two antimicrobials chosen were rifampicin and clindamycin hydrochloride (Bactiseal, Codman, Integra Life Sciences), and the processed catheters have no activity against gram negative bacteria.

Using the same impregnation process, a shunt catheter containing rifampicin alone has been investigated. A very high concentration of rifampicin was used, resulting in visible crystal formation on the catheter surface, and change in mechanical properties, tensile strength reducing by 27% and elasticity by 45% [46]. However, the catheter showed antistaphylococcal activity in vitro for more than 60 days, and protected shunts from bacterial colonisation in a rabbit model [47]. In a later study in two patients with existing shunt infections the rifampicin- impregnated shunt catheters replaced the infected shunts, and the two patients remained free of infection thereafter [48]. However, the shunt catheter was never commercialised, possibly because of the deleterious effect on mechanical properties, and possibly because of the well-known risk of resistance when rifampicin is used alone in any context. Using the same impregnation method, an experimental catheter containing rifampicin, mupirocin and fusidic acid was tested in vitro against *S epidermidis* and gave protective activity for at least 20 days [49]. A catheter containing rifampicin and trimethoprim was tested in vitro against *S aureus* and gave strong killing effect over the short period tested [50]. The same group used the same process to test a catheter impregnated with rifampicin and sparfloxacin against *S epidermidis* and showed prolonged drug release and protection against colonisation for 1 year, after static soaking [51]. A process for coating polyurethane catheters with rifampicin and minocycline was investigated in vitro [52]. The process was then revised to make it suitable for silicone. Though the nature of the process was very different from the impregnation process above [44], an antimicrobial EVD catheter using this process containing rifampicin and minocycline has been described (Ventriclear, Cook Inc) [53]. A legitimate concern has been voiced that antimicrobial devices might lead to increased bacterial resistance. A long-known but not widely recognised principle for avoidance of resistance is the use of two or more antimicrobials, each of which is active against a different bacterial target site, such as RNA polymerase (rifampicin) and DNA gyrase (sparfloxacin) or protein synthesis (clindamycin). This principle was introduced by Ehrlich [54] and has been extended by Zhao and Drlica [55] as the Dual Drug Principle. Experimental studies show clearly that exposure of bacteria

to a single antimicrobial usually results in resistant mutants arising whereas when exposed to dual or triple drugs, this does not happen. Some authors have emphasised this important principle when designing antimicrobial materials [44, 49, 51].

5. Interference of released antimicrobials with diagnostic tests

Concern has been raised that release of antimicrobials into the lumen of the catheter might interfere with diagnosis of ventriculitis by inhibiting or killing any bacteria before they can be grown on culture. This concern was reinforced by a study by Stevens et al. [56] who suggested, on the basis of in vitro studies, that it might be justified. However, the methods used did not simulate events encountered in practice, and the issue was revisited [57]. In this study, both the commercially available antimicrobially impregnated catheters (Bactiseal and Ventriclear) were included, and the methods were designed to mimic their use in an EVD system, with bacterial challenge and CSF sampling modelled on clinical events and procedures. The study found that, in samples taken on Day 1 of "EVD" bacterial viability was significantly reduced by the antimicrobial release, which occurred as a burst effect only in the first 24 hr. After this, no reduction was seen. It is unlikely that CSF sampling would be required as early as the first 24 hr. of EVD, and the conclusion was that no clinically relevant interference with diagnosis was found.

6. Activity of impregnated EVD catheters against multi-drug-resistant pathogens

Though the Ventriclear EVD catheter contains minocycline, neither this nor Bactiseal catheters are likely to have any useful effect against gram negative EVD pathogens. These include not only *E coli* and *Klebsiella pneumoniae*, but multi-drug-resistant (MDR) strains of these as well as intrinsically MDR bacteria such as *A baumannii*. A catheter with activity against these pathogens is badly needed. The catheter containing trimethoprim developed by Kohnen et al. [50] might have some activity against *E coli* and *K pneumoniae* (unless MDR) but these were not tested. A later development by the same authors, containing sparfloxacin, would probably show better anti-gram negative activity, but again they did not test this [51]. An EVD catheter impregnated with rifampicin, trimethoprim and triclosan, using the impregnation method previously described [44] has been tested in vitro [58]. The antimicrobials were again chosen to provide broad spectrum of activity against EVD pathogens, to reduce the risk of resistance developing (Dual Drug Principle) and for compatibility with the impregnation technology. The impregnated catheters were installed in a modular longterm flow apparatus and perfused constantly with nutrient medium. Both plain and impregnated catheters were challenged weekly with suspensions of test bacteria (10^5cfu/mL) and monitored for colonisation. Plain catheters all colonised within 24-48 hr., but none of the impregnated catheters colonised. The 17 test bacteria consisted of clinical isolates of *E coli* (including ESBL and NDM-1 producers), *Enterobacter cloacae*, *Klebsiella pneumoniae*, methicillin-resistant *Staphylococcus aureus* (MRSA) and *S epidermidis* (MRSE), and *A baumannii*. Also included was a series of 5 isolates of *S epidermidis* from Bactiseal shunt infections due to intrinsic resistance to either rifampicin or clindamycin, or both. Catheter segments were inserted stereotactically into the frontal lobes of rats

and the brains examined after either 1 week or 4 weeks for signs of neurotoxicity. Behavioural changes and weight gain in the rats was also monitored. All rats gained weight normally and did not show any behavioural anomalies. Neurohistochemical examination showed significant glial response in both control and impregnated segments after 1 week, considered to be due to surgical trauma, and this had subsided by week 4. The findings suggest that this EVD catheter might address the remaining problem of antimicrobial activity against MDR EVD pathogens including *A baumannii*. The catheter has not yet been commercialised. The same impregnation method was used to produce an EVD catheter containing rifampicin, clindamycin and trimethoprim [59]. The catheters were tested by the Serial Plate Transfer test (SPTT) [44, 60], which is useful as a screening test but does not dispense with the need for more rigorous clinically predictive tests. As expected, the catheter showed prolonged activity against *S epidermidis*, but not MRSA, in the SPTT. Animal inoculation was carried out by subcutaneous implantation to test for biocompatibility, but no implantation into the central nervous system was done.

7. Clinical studies

7.1 Surface-modified neurosurgical materials and devices

A silicone shunt catheter made from expanded polytetrafluoroethylene (e-PTFE) has been evaluated but failed due to its porosity allowing tissue ingrowth [61].

PVP-coated catheters have been commercialised (Bioglide, Medtronic, USA). They need to be handled carefully when dry to prevent cracking of the coating, and must be soaked and rehydrated for use. This gives the opportunity for the surgeon to add antibiotics such as vancomycin or bacitracin to the soak saline, with the intention that it will add antimicrobial activity to the hydrophilic anti-attachment surface. Kaufmann et al. [62] carried out a clinical trial of commercially available PVP-coated shunts pre-soaked in bacitracin and found no effect on infection rates ($p > 0.24$). According to the authors, the concentration of bacitracin was not expected to be sufficient to affect infection risk, and reliance was mainly on the hydrogel, but is has been common practice to soak shunt and EVD catheters in antibiotic solution. However, in vitro studies have not shown an advantage of antibiotic soaking of PVP catheters [30, 31] and this was the case even when high concentrations of various antibiotics were tested [32]. An increase in shunt infection when PVP catheters were used was observed in another study by Kestle et al. [63] though no details were given on antibiotic soaking. In this study, a clearly higher infection risk was seen with PVP catheters (OR 1.91, CI 1.19–3.05, $p = 0.007$). While the lack of PVP coating in the catheter lumen might have been a factor in failure to prevent infection, the higher risk of infection in PVP-coated catheters compared to plain catheters remains unexplained.

7.2 Antimicrobial coatings

Silver-processed shunt and EVD catheters have been the subject of several clinical studies. An insignificant reduction (2.7% vs. 4.7%) was reported by Fichtner et al. [64] from a retrospective cohort study, while Lackner et al. [65] reported a statistically significant reduction in EVD infections (25–0%) in a mixed retrospective/prospective cohort study with small numbers. A retrospective study comparing three

different types of polyurethane catheters, one of which was silver-processed, found a significant difference in infection rates between two non-silver catheters, both from different manufacturers, for unexplained reasons, but there was no significant difference in infection rates between the two polyurethane catheters (one containing silver) each from the same manufacturer [66]. This study would seem to indicate a difference in infection risk between two types of polyurethane catheter rather than any effect of silver, contrary to the claim in the title. A meta-analysis [67] found no significant overall reduction in EVD infection rate when silver-processed catheters were used, but they commented that their effect may be selective: a significantly lower rate of infection due to gram positive, but not gram negative, bacteria was found in the silver catheter groups. However, despite this, a large randomised controlled clinical trial of silver-processed EVD found a reduction in infection rate from 21.4 to 12.3% (13). The very high rate of infection in the plain catheter arm is unusual in UK, and the rate of 12.3% is still much higher than the 9.3% in most UK and Irish centres [68], though the authors state that they chose high-risk patients for their trial. A multicentre survey of EVD infections in UK and Ireland [68] found a higher infection rate (13.7%) in silver -processed catheters than in plain catheters (7.4%) but this did not reach statistical significance. Another randomised controlled trial of silver-processed catheters in CSF shunting failed to find any difference between plain and silver-processed arms [69] and this is consistent with studies of such catheters in other fields [70–72]. It is important to note that the precise nature of the silver -processing differs between studies, and this might affect the results.

7.3 Antimicrobial impregnation

The first technology for impregnation of silicone catheters with antimicrobials was published in 1989 [44]. This technology, resulting in a CSF shunt containing relatively small concentrations of rifampicin and clindamycin, was the subject of numerous clinical studies. The first was a prospective randomised study of 110 patients [73]. The infection rates were 6% in the impregnated group and 17% in the plain control group. Importantly all the infections were due to staphylococci in the control group, and there were no staphylococcal infections in the impregnated group. Of the three infected patients in the "impregnated" group, all had gram negative infections and one was also infected with HIV. In another study with historical controls, there were seven infections (15%) in the plain catheter group, and one (3%) in the "impregnated" group [74]. This was a child who scratched open the abdominal wound in the postoperative period, and contaminated the shunt with *S aureus*. In another study, again with historical controls, there were three shunt infections (1.2%) in the antimicrobial catheter group and 36 (6.5%) in the preceding plain catheter group ($p = 0.0015$) [75]. Of the three infections in the "impregnated" group, two were due to *S epidermidis*, both susceptible to rifampicin and clindamycin, and in one case the clinical course was complicated by EVD, reservoir placement and shunt revision for intraventricular haemorrage before the infection occurred. The third case was due to *Haemophilus influenzae* 8 months postoperatively. *H influenzae* was, at the time, a common cause of childhood community—acquired meningitis. The antimicrobial activity of the shunt would probably have declined by that time and in any case would not have been very effective against this bacterium. A retrospective study in children, again with historical controls, showed a statistically non-significant reduction in shunt infection (7 vs. 4 infections, $p = 0.534$). Two of the 4 infections in the antimicrobial catheter group were due to gram negative bacilli and only one was

due to *S epidermidis*. In the control group, four infections were due to *S epidermidis*. The authors concluded on this basis that there was no evidence of efficacy of antimicrobial shunt catheters [76]. A multicentre study in children, again with historical controls, had considerable problems with differences in results between centres, but concluded that antimicrobial shunt catheters might significantly reduce infection rates in paediatrics, but that a randomised controlled trial was needed [77]. An observational study [78] found no significant difference in shunt infection rates between antimicrobial and plain catheters. However, there were additional postoperative risk factors, such as further neurosurgical intervention, and the diagnostic criteria included late ulceration over the shunt in three of the five infections in the antimicrobial catheter group, leading to non-surgical shunt infection which, as the authors say, the antimicrobial shunt could not be expected to prevent. A systematic review found a significant reduction in shunt infection rate for antimicrobial catheters (RR 0.42, 95% CI 0.32–0.55) [79]. A retrospective review of VP shunts in high-risk children, defined as premature when shunted, post-meningitic, post shunt infection, or having undergone EVD, found a statistically significant reduction in infection in all these groups [80]. The reduction from 20 to 5.5% in the high-risk neonate group was also found by Hayhurst et al. [81] Parker also recorded the lack of adverse effects in this vulnerable group [81]. Their finding of a reduction in the group where EVD had been used was interesting, as others had suggested that this might have increased the risk of failure of the antimicrobial catheters. All of these studies used the rifampicin + clindamycin impregnated shunt. None of them was a randomised controlled trial and in many cases such a study was called for in the conclusions. There is a formal registry of CSF shunting in UK, based in Cambridge, and a report issued in 2009 on almost 2000 matched impregnated / plain cases showed a reduction from 4.7 to 3%, which just reached statistical significance ($p = 0.048$) [82]. However, there were limitations such as reporting bias, and use of an intention—to—treat analysis as well as very different rates and criteria from contributing institutions. Eventually, a formal multicentre randomised controlled trial, the BASICS study, was carried out, comparing plain shunts with silver-processed and antimicrobial impregnated ones in 1594 patients [69]. After a median follow-up of 22 months (IQR 10–24), the infection rates were 6% in both plain and silver-processed groups, and 2% in the antimicrobial impregnated group ($p = 0.0038$). This finding confirmed most of the previous retrospective or historically-controlled studies. Even before this definitive study, there had been a steady increase in uptake of antimicrobial-impregnated shunts in UK, so that since their introduction in 2001 they were used in approximately 70% of shunt surgeries in 2014 [83]. This seems to have been matched by a steady decline in shunt infection rates over this period.

7.4 Cost-effectiveness studies

The BASICS study raised the issue of healthcare cost savings based on reduction of treatment costs for infection. This had been addressed by Sciubba et al. who speculated that shorter hospital stay (30 vs. 17 days) and reduced adverse events due to treatment of shunt infection might lead to significant cost savings [84]. A German study found a cost saving of $17,300 in children and $13,000 in adults in those receiving antimicrobial -impregnated shunts compared to plain shunts [85]. An American study found that the hospital cost per 100 patients shunted was $151,582 and $593,715 for antimicrobial and plain shunts respectively, due to reduction in costs of treatment of infection [86]. In a meta-analysis and cost study, it was found

that, assuming 200 shunt operations per year, annual costs savings would range from $90,000 to $1.3 M in American centres [87]. The use of shunt catheters impregnated with rifampicin and clindamycin appears to reduce the incidence of shunt infection and by so doing, reduce healthcare costs very significantly. The benefit for patients and their relatives is also therefore obvious, with less morbidity, fewer shunt revisions for infection, and less time spent in hospital.

7.5 Impregnated EVD catheters

Two antimicrobial-impregnated EVD catheters have been commercialised and approved for human clinical use. A catheter impregnated with two antimicrobials, rifampicin and minocycline, has been the subject of a prospective randomised controlled trial [53]. They found a significant reduction in ventriculitis (from 36.7 to 17.9%) from plain EVD catheters to impregnated catheters respectively ($p = 0.00095$). EVD pathogens were mainly *S epidermidis* in the plain catheter group, with gram negative bacteria found in both groups. A study from USA considered the question of whether clinical trial results for this catheter translated into real-life clinical practice. In 113 consecutive patients who received the rifampicin-minocycline impregnated EVD, only one confirmed case of ventriculitis was seen, and this was due to *Enterobacter aerogenes*, against which the catheter offered no protection [88]. The same impregnated catheter was compared with the rifampicin-clindamycin impregnated catheter for EVD in another study but there were no infections in either group [89]. An interesting study comparing rifampicin—clindamycin and rifampicin- minocycline impregnated EVD catheter with plain controls in a sequence of five periods found an infection rate in Period 1 (plain catheters) of 6.7%, Period 2 (plain catheters with procedural changes) 8.2%, Period 3 (rifampicin-clindamycin catheters) 1%, and Period 4 (return to plain catheters) 7.6%, and Period 5 (rifampicin -minocycline catheters) 0.9% [90]. This showed clearly the advantage of both of the commercially available impregnated EVD catheters.

7.6 Does the use of antimicrobial devices increase the risk of resistant infections?

Concern has been expressed that antimicrobial shunt and EVD catheters might give rise to increased antimicrobial resistance. This has been investigated in vitro [91]. A central venous catheter impregnated in the same way and with the same antimicrobials as the rifampicin-minocycline EVD was serially exposed to bacteria in vitro for 21 days without any resistance, again due to the Dual Drug Principle. These in vitro findings confirmed an earlier study by Munson et al. [92] A clinical study of the rifampicin-clindamycin shunt showed that the overall infection rate fell and there was no increase in gram negative bacteria following its use [93]. However, in a systematic review of rifampicin-minocycline and rifampicin-clindamycin impregnated shunts and EVDs it was claimed that the use of these devices ran the risk of increase in more virulent and drug-resistant infections [79]. The evidence for this, cited by the authors, was a large study of over 2000 paediatric shunt placements using either plain catheters or the rifampicin-clindamycin shunts [94]. The authors found a statistically significant reduction in infection in the antimicrobial shunt group ($p < 0.005$). They also noted a change in the proportions of shunt pathogens. The proportions of *S aureus* infection in each group were approximately the same, whereas the proportions of *S epidermidis* infections fell from 52 to 16% in the

antimicrobial shunt group. Moreover, the proportions of shunt infections due to gram negative bacilli were identical. The authors stated that no unusually resistant bacteria were isolated in either group. The only significant change was the rate of *C acnes* infection: 2.2% in the control group and 16% in the antimicrobial shunt group. This was a sequential study with a historical control group, and the authors considered that the apparent proportional increase in *C acnes* infections was due to the introduction during the period that the antimicrobial shunt was used of extended culture times, which are essential for isolation of this organism. The statement by Konstantelias et al. [79] is therefore based on a misunderstanding of the source data cited. Increased rifampicin resistance was claimed to be due to the use of rifampicin-clindamycin impregnated shunts [95]. This study concerned the consecutive use of these shunts in all cases for 52 months, during which there were only 4 shunt infections (3.2%), all due to rifampicin—resistant *S epidermidis*. The authors felt that this had revealed a threat of selection of rifampicin resistance due to the use of these shunts. However, 4 shunt infections in 4.3 years equates to a shunt infection rate of 0.92%. Also, it is recognised that a very small proportion of *S epidermidis* strains are resistant to rifampicin, and an encounter with such a resistant strain by a patient with a rifampicin—impregnated shunt would be as likely to result in a shunt infection as if a plain catheter were used. There was no evidence in this study that the use of rifampicin-impregnated shunts had caused the rifampicin resistance.

Bacterial resistance due to drug exposure can arise in other ways than genetic mutation. One important example is the consequence of antibiotic exposure in "normal flora" sites such as the skin, intestine or mucous membranes. Here the maintenance of the balance of many different bacteria and fungi is important. The commensal bacteria at these sites are largely beneficial, but if the balance is disturbed so that one organism is allowed to predominate, then a disease state can result. A common example of this is the overgrowth of *Candida albicans*, a commensal yeast, that is a cause of thrush after a course of antibiotics. In the context of EVD management, prophylactic antibiotics are used either as one dose at insertion, or continued systemic administration throughout the use of EVD. These two regimens have been considered in terms of their potential to reduce EVD infection. A study of antibiotic prophylaxis for 24 hr. compared to an extended regimen for the duration of EVD found no significant difference in EVD infection but there was a statistically significant fall in the number of cases of *Clostridioides difficile* infection in patients with EVD [96]. *C difficil*e can cause life-threatening colitis that may require colectomy. The bacterium is a normal commensal of the colon in small numbers, but if the ecological balance of the colonic microbiome is disturbed by antibiotics, *C difficile* numbers rise and the toxin produced causes necrosis of the colonic epithelium and severe inflammation. Another study has confirmed this, with statistically significant falls in both *C difficile* infection and antibiotic use [26]. A similar result has been reported in the context of intracranial pressure monitoring, where there was difference in infection (0.7 vs. 1.4 per patient, ($p = 0.05$) and particularly in the number of multidrug resistant bacteria isolated per patient (0.03 vs. 0.33. $p < 0.01$) indicating no advantage in extended prophylaxis but a significant increase in infections due to resistant bacteria. This pattern was also seen in the ventilator-associated pneumonia (VAP) and septicaemia cases [97]. Prolonged antibiotic use has also been identified as a key factor in the increase in *A baumannii* infections in ventilated trauma patients [98]. Others have now questioned the use of extended duration antibiotic prophylaxis for EVD, on the grounds of both lack of benefit and risk of drug resistant infections and *C difficile* disease.

7.7 Antimicrobial devices and antibiotic prophylaxis

The role of antimicrobial EVD catheters in reducing the need for prophylactic antibiotics has also received attention. One sequential study compared ventriculitis rates between a group receiving a rifampicin+clindamycin EVD and single dose antibiotic prophylaxis with a second group that had extended antibiotics with plain EVD catheters. There was a non-statistically significant reduction in ventriculitis in the antimicrobial catheter group, indicating that the extended duration antibiotic regimen did not add any benefit over antimicrobial EVD catheters. However, an important finding was that there were 3 cases of serious *C difficile* disease in the group without antimicrobial catheters, one patient requiring a colectomy [27]. The authors concluded that the antimicrobial catheters were as effective in preventing EVD infections as extended antibiotic prophylaxis, but safer. Another sequential study with 545 EVD placements, all using the rifampicin+clindamycin catheter, showed that there was a statistically non-significant fall in ventriculitis rates after switch from extended antibiotic prophylaxis to single dose, but a statistically significant fall in nosocomial infections such as VAP. The authors concluded that there was no need for an extended prophylaxis regimen if antimicrobial EVD catheters were used [99].

8. Surgical bundles with antimicrobial devices

Despite the very positive findings showing the effectiveness of antimicrobial catheters in prevention of infection in both shunts and EVDs, it would be wrong to assume that other aspects of surgical procedures can be relaxed. The best approach would be to ensure that a robust surgical bundle was instituted along with adoption of an antimicrobial catheter. This was clearly illustrated by a study in which, after a preliminary period to establish a baseline, a completely new surgical bundle was introduced, that included rigorous aseptic technique and intensive staff training, and an antimicrobial EVD catheter [100]. The infection rate fell sequentially each quarter, from baseline of 9.2 to 2.6%, then to 0% over 4 years. In such a study, it is impossible to say whether the antimicrobial catheter alone, or the bundle alone, was responsible but it is likely that a combination of the two brought about the dramatic and sustained fall in infection rates.

9. Recommendations in international guidelines

The Infectious Diseases Society of America (IDSA) have issued guidelines for clinicians on reducing infections in patients with neurosurgical devices [24]. They say that "Use of antimicrobial-impregnated CSF shunts and CSF drains is recommended (strong recommendation, moderate confidence rating)." Similarly the Neurocritical Care Society published their guidelines for insertion and management of EVDs [101] and stated "We recommend using antimicrobial-impregnated catheters as part of a comprehensive management protocol to reduce the rate of VRI (strong recommendation; moderate-quality evidence)" These recommendations, and the quality-of-evidence assessments, were made before the latest RCT results were published in 2019 [69].

10. Reservoirs and intracranial pressure monitors

Infection in ventricular access reservoirs is rare, but when it occurs it can result in ventriculitis [15]. However, direct ventricular access is available for administration of antimicrobials. There is no current antimicrobial materials approach to reservoir infections. Techniques for measurement and monitoring of intracranial pressure vary and again, those not dependent on EVD have a low infection rate [102, 103].

11. Conclusions

There has been a dramatic fall in the rate of infections associated with CSF shunts and EVDs over the past two decades. This has been due to a much greater understanding amongst clinicians of the underlying science and the causes of the infections, and has led to well-thought-out non-technological approaches such as care bundles. However, these need to be more widely adopted. Their effect has been enhanced by improvements in anti-infective technology that has centred on development of coated and impregnated devices, and certainly the latter have been shown to be highly effective in reducing further the infection rates as well as healthcare costs. An additional benefit to this approach has been the reduction in antibiotic use, leading to less drug resistance and adverse effects. The use of antimicrobial shunts and EVDs has now been recommended as the standard of care in neurosurgery. Problems remain, especially in EVD where increase in infections due to highly drug-resistant bacteria is seen, and these are not currently preventable by the impregnation technology. New formulations that have been shown to have activity against even the most drug-resistant EVD pathogens have been thoroughly evaluated in the laboratory, but as yet they have not been commercial adopted.

Conflict of interest

The author is the inventor of the "Bactiseal" antimicrobial catheter, but he has not and does not receive any royalties or other payment. He receives speaker fees from Codman Inc., but not for personal gain and these are paid to his University.

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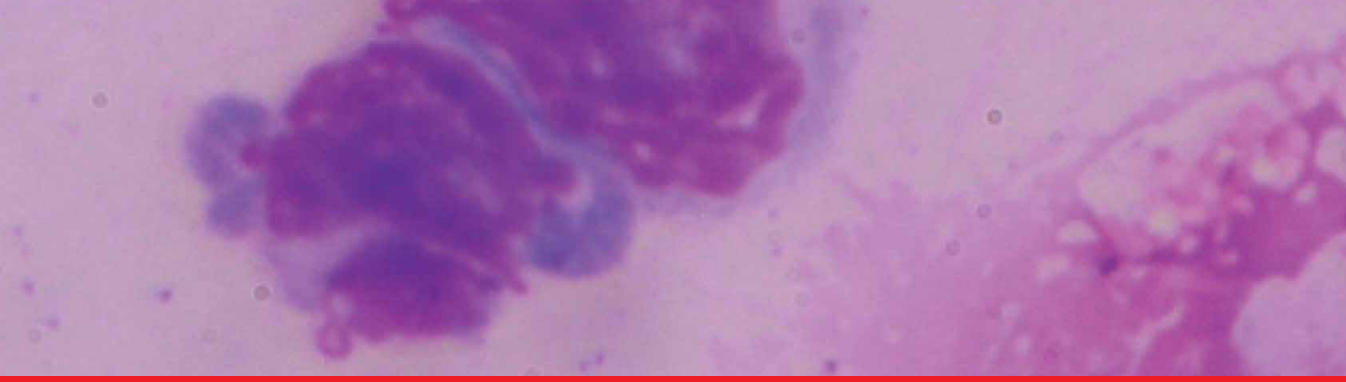

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This book represents the collective expertise and dedication of numerous scholars and professionals from around the globe who share a keen interest in hydrocephalus. As a specialized text, it delves into the most advanced concepts and technological developments in the diagnosis and treatment of hydrocephalus. This book offers an extensive introduction to the history of hydrocephalus treatment, the current state of therapeutic approaches, diverse treatment methods, common complications associated with hydrocephalus, and the diagnosis and treatment of several rare forms of the condition. While the book consolidates traditional viewpoints, it places even greater emphasis on presenting the most recent diagnostic and treatment concepts in hydrocephalus. The innovative inductive summaries of certain rare or unique types of hydrocephalus are particularly noteworthy. This comprehensive approach allows readers to gain a more profound and well-rounded understanding of the evolution and future trajectory of hydrocephalus. Catering to a diverse audience, this book is not only appropriate for junior neurosurgeons seeking a foundational understanding of hydrocephalus but also serves to satisfy the more in-depth inquiries of experienced senior neurosurgeons exploring the subject matter.

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