

Hydrocephalus

CHAPTER 186

Hydrocephalus in Children: Approach to the Patient

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For years, the management of hydrocephalus has been the most common problem facing neurosurgeons who treat children. In most pediatric neurosurgery practices, hydrocephalus is responsible for 40% to 50% of the surgical interventions and clinic visits.

Recently, however, some evidence suggests that the incidence of pediatric hydrocephalus is decreasing. The number of first shunt insertions for children younger than 17 years decreased substantially in Canada between 1991 and 2000.¹ The decrease may be partially related to a decline in the number of children with spina bifida. Case control studies of the effects of folic acid have shown a significant reduction in the incidence of neural tube defects, which have a high association with hydrocephalus.² Furthermore, after a significant increase in the incidence of intraventricular hemorrhage between the 1970s and 1980s, there has been a marked decrease as experience with managing very preterm infants has grown. This too likely contributes to a decreased incidence of hydrocephalus in children.³ Societal decisions about how to treat very premature infants or those with significant malformations diagnosed *in utero*⁴ may also influence the incidence of hydrocephalus in live births.

Despite these trends, the burden of this illness remains large. Using the Healthcare Cost Utilization Project Kids' Inpatient Database, a cross-sectional survey was performed in 1997, 2000, and 2003. Each year there were almost 40,000 admissions, approximately 400,000 hospital days, and between \$1.4 billion and \$2 billion in hospital charges for pediatric hydrocephalus. This accounted for 3.1% of all pediatric hospital charges. In addition, the children identified in this cross-sectional study had an increasing frequency of comorbidities.⁵ Clearly, pediatric hydrocephalus represents a huge burden of illness for children and is part of the daily lives of neurosurgeons in general and those treating children in particular. As a further testament to the frequency of hydrocephalus, the Hydrocephalus Clinical Research Network, a newly formed cooperative clinical trial group consisting of four pediatric neurosurgical centers, accumulated almost 1000 shunt procedures in the first 8 months of data acquisition.

PRESENTATION

The clinical manifestations of pediatric hydrocephalus are those of raised intracranial pressure, which vary with age. An infant with open sutures usually presents with a gradually increasing head circumference. The importance of head measurement cannot be overemphasized. Standard head circumference charts

should be part of the medical record of every child, especially those in whom hydrocephalus is considered a possibility. Specific charts are available for premature infants as well as for children with achondroplasia. The most important finding is a head size crossing percentiles. Some children have larger heads than others, and an isolated finding of a large head in a well baby is usually not too concerning; however, serial measurements that indicate a head circumference crossing percentile curves should be investigated. Unusual irritability or excessive vomiting with no other explanation may be attributed to hydrocephalus, as may eye movement abnormalities, especially downward deviation of the eyes ("sunsetting"), or sixth nerve paresis.

As a child gets older and the sutures fuse, the presentation differs. The head size can still cross percentiles, but it does so very slowly, so changes in percentile growth become less helpful as a sign of hydrocephalus. In these children, the presentation usually includes headache and eventually nausea and vomiting. The dementia, ataxia, and incontinence seen in adult normal-pressure hydrocephalus are not part of the pediatric presentation. Papilledema may occur in long-standing cases if the onset is after suture closure. A child whose hydrocephalus begins while the sutures are open but presents later usually does not have papilledema but does have a very large head. Presentation beyond the first few years of life usually indicates hydrocephalus secondary to an acquired disorder, such as tumor, head injury, or meningitis.

The decision to treat a child with ventriculomegaly can be very difficult. Once a shunt has been implanted, it is very difficult to determine whether it can be removed. The use of adjunctive measures, such as intracranial pressure monitoring,⁶ magnetic resonance spectroscopy,⁷ and the magnetic resonance measurement of cerebral blood flow,⁸ has been reported in difficult cases, but the decision to treat is usually based on observation over time. Progressively increasing head size, enlarging ventricles, or progressive symptoms are the most common measures and form the most solid basis for making the decision to treat.

DISEASE-SPECIFIC CONSIDERATIONS

Congenital Hydrocephalus

The majority of children with hydrocephalus present at or soon after birth. Many of them have aqueduct stenosis, Dandy-Walker malformation, holoprosencephaly, or other more generalized

malformations of brain development. Aqueduct stenosis in males may be X-linked.⁹ In these children, the hydrocephalus is usually quite severe, and they have the clinical finding of adducted thumbs (Fig. 186-1). There may be other affected males in the family or maternal history of spontaneous abortion.

Dandy-Walker malformation is a less common but important cause of infantile hydrocephalus. It is an abnormality of cerebellar development resulting in an extremely large fourth ventricle, elevation of the tentorium, and, in some cases, supratentorial hydrocephalus. The large fourth ventricle usually does not require treatment, but progressive enlargement of the supratentorial ventricles should be evaluated in the same manner as other forms of hydrocephalus.

Hydrocephalus Associated with Myelomeningocele

A newborn with myelomeningocele undergoes closure of the spinal defect and then observation for the development of hydrocephalus. In the past, 80% of children were thought to require ventriculoperitoneal shunt placement, but reduced rates of shunt placement have recently been reported.¹⁰ The most common manifestations of hydrocephalus in these children are increasing head circumference, splitting sutures, and full fontanelle, but some children may develop a large pseudomeningocele at the myelomeningocele repair site or a cerebrospinal fluid leak. These manifestations are often thought to be related to hydrocephalus and require the placement of a shunt. The importance of hydrocephalus in this population is emphasized by a multicenter trial funded by the National Institutes of Health that aims to randomize 200 fetuses to in utero or postnatal myelomeningocele closure. Based on suggestive preliminary data,¹¹ the trial is testing the hypothesis that in utero closure can reduce the need for shunt placement by reducing the incidence of Chiari II malformation, the major cause of progressive hydrocephalus in this patient population.



FIGURE 186-1 Adducted thumb in a newborn with X-linked aqueduct stenosis. (From Gluf W, Kestle J. "Cortical thumb sign" in X-linked hydrocephalus. *Pediatr Neurosurg*. 2002;37:107-108.)

Arachnoid Cyst

Midline and posterior fossa arachnoid cysts in newborns commonly cause obstructive hydrocephalus. These may occur in the suprasellar area (Fig. 186-2), quadrigeminal cistern (Fig. 186-3), or cerebellopontine angle. Endoscopic fenestration of the cyst rather than treating the ventricular system may relieve obstruction and reestablish normal flow.

Posthemorrhagic Hydrocephalus

Intraventricular hemorrhage in premature newborns is common and is related to the degree of prematurity and the birth weight.¹² The probability of developing posthemorrhagic hydrocephalus depends on the grade of intraventricular hemorrhage. An overall 40% incidence of ventriculomegaly has been reported,¹³ but the incidence can be as high as 70% in patients with grade IV intraventricular hemorrhage.¹⁴ In managing these children, it should be recognized that a significant rate of arrest or resolution of this type of hydrocephalus has been reported.¹⁵ In these tiny infants, ventriculoperitoneal shunt insertion can be difficult and has a high rate of complications. A number of options for delaying shunt insertion have been used, including serial lumbar punctures or treatment with furosemide (Lasix) and acetazolamide (Diamox).

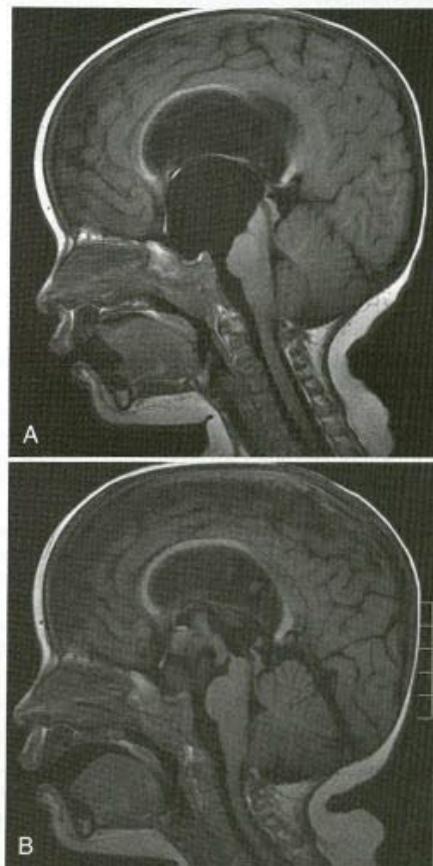


FIGURE 186-2 Magnetic resonance images of a 16-month-old girl with a progressively enlarging head from obstructive hydrocephalus secondary to suprasellar arachnoid cyst before (A) and 6 months after (B) endoscopic cyst fenestration into the third ventricle and preponine cistern.

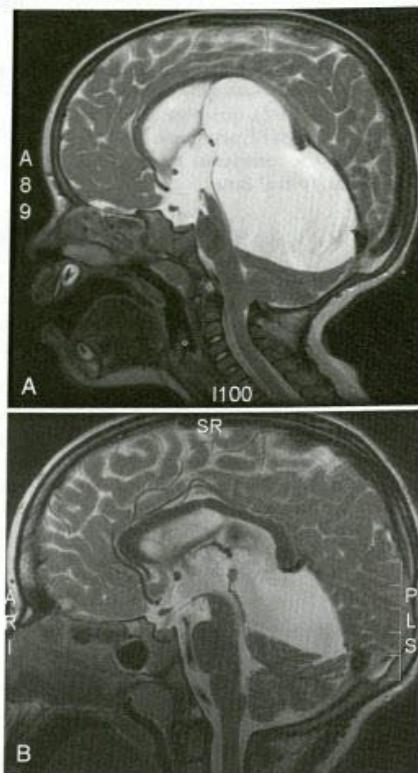


FIGURE 186-3 Magnetic resonance images of a quadrigeminal cistern arachnoid cyst with obstructive hydrocephalus in an 18-month-old girl with progressive head enlargement before (**A**) and 5 years after (**B**) endoscopic fenestration into the lateral ventricle.

None of these measures has been shown to reduce the incidence of long-term hydrocephalus in randomized trials.^{16,17} Temporizing with either a subgaleal shunt or a ventricular reservoir until the child reaches a weight of 1500 to 2000 g is a common practice. The proportion of children who receive such a temporizing measure and go on to permanent ventriculoperitoneal shunting is approximately 70% to 90%.¹⁸ An aggressive approach to reduce hydrocephalus after premature intraventricular hemorrhage was recently attempted using drainage, irrigation, and fibrinolytic therapy. Although a promising pilot study showed a reduced requirement for shunt surgery,¹⁹ a prospective randomized trial was stopped early because of an increased rebleed rate in the treatment group.²⁰ Despite that, the 2-year follow-up showed a reduction in death or severe disability.²¹

Hydrocephalus Associated with Brain Tumors

The tendency for children's brain tumors to occur in the posterior fossa and midline leads to a high incidence of associated hydrocephalus. Management with preoperative shunt placement is no longer common practice, and most surgeons opt to remove the tumor and monitor for the development of hydrocephalus. Recently, third ventriculostomy performed before tumor removal was reported to reduce the risk of hydrocephalus significantly.²² The criticism of this approach is that some of these third ventriculostomies may be unnecessary because a proportion of children will not develop progressive hydrocephalus after tumor

TABLE 186-1 Canadian Preoperative Prediction Rule for Hydrocephalus in Children with Posterior Fossa Neoplasms

| PREDICTOR | SCORE |
|--|-----------|
| Age <2 yr | 3 |
| Papilledema | 1 |
| Moderate to severe hydrocephalus | 2 |
| Cerebral metastases | 3 |
| Preoperatively estimated tumor diagnosis | |
| Medulloblastoma | 1 |
| Ependymoma | 1 |
| Dorsally exophytic brainstem glioma | 1 |
| Total possible score | 10 |

From Riva-Cambrin J, Lamberti-Pasculli M, Armstrong D, et al. The validation of a preoperative prediction score for chronic hydrocephalus in pediatric patients with posterior fossa tumors. *J Neurosurg*. 2005;102:A798.

removal. A validated patient score for predicting the development of hydrocephalus in these children before tumor resection has been reported (Table 186-1).²³ Based on age, papilledema, severity of hydrocephalus, metastatic disease, and estimated preoperative tumor type, the chance of developing hydrocephalus can now be predicted before resection of the tumor (Table 186-2). Evaluating these factors allows a more informed discussion with patients and families and possibly the selective use of endoscopic third ventriculostomy before tumor surgery. External ventricular drain insertion at the time of tumor removal is common for tumors within the fourth ventricle but may be avoided in cerebellar hemispheric tumors. Following surgery for tumors in the lateral ventricle that are associated with hydrocephalus, the surgical tract may lead to postoperative decompression of the hydrocephalus into the subdural space. When this collection persists as a subdural hygroma, it may require treatment with a subdural shunt.

TABLE 186-2 Predicted Probability of Hydrocephalus Based on Canadian Preoperative Prediction Rule for Hydrocephalus Score

| PATIENT SCORE | HYDROCEPHALUS AT 6 MONTHS |
|---------------|---------------------------|
| 0 | 0.071 |
| 1 | 0.118 |
| 2 | 0.191 |
| 3 | 0.293 |
| 4 | 0.422 |
| 5 | 0.562 |
| 6 | 0.693 |
| 7 | 0.799 |
| 8 | 0.875 |
| 9 | 0.925 |
| 10 | 0.956 |

From Riva-Cambrin J, Lamberti-Pasculli M, Armstrong D, et al. The validation of a preoperative prediction score for chronic hydrocephalus in pediatric patients with posterior fossa tumors. *J Neurosurg*. 2005;102:A798.

Posttraumatic Hydrocephalus

Compared with other types of hydrocephalus, posttraumatic hydrocephalus is less common in children. Affected children usually have fairly severe head injuries, and they present with a plateau or regression in their recovery. This is often identified by the rehabilitation team. The patients' scans show ventriculomegaly, and the differential diagnosis includes hydrocephalus and ventricular enlargement *ex vacuo* from atrophy secondary to extensive brain injury. The use of decompressive craniectomy to treat raised intracranial pressure after head injury has been associated with a significant incidence of hydrocephalus requiring shunt placement.²⁴

APPROACH TO THE PATIENT

Patients Presenting in Utero

Ventriculomegaly can be readily diagnosed in utero, and fetal magnetic resonance imaging (MRI) allows the visualization of associated brain anomalies.^{25,26} The neurosurgeon may be asked to meet with the parents before delivery, which provides an opportunity to discuss the usual course of events after the baby is born, the indications for shunt insertion, the procedure, and potential complications. Parents naturally want to know the prognosis for their child, but unfortunately, this can be difficult to provide. In a study of patients referred to neurosurgery based on fetal ultrasound examinations, 25 of 44 patients with prenatal hydrocephalus had other anomalies, but only 3 of them were diagnosed before birth.²⁶ Fetal MRI and ultrasonography were found to be equivalent in term of detecting fetal anomalies, with MRI usually confirming the earlier ultrasound findings.²⁷

Patients Presenting in Infancy

Several conditions that occur in children have excess extra-axial fluid in common. These have been labeled external hydrocephalus, communicating hydrocephalus, benign extracerebral fluid collections, benign extra-axial fluid of infancy, and subdural effusion. Many of these terms were based on computed tomography findings, so it was difficult to tell whether the fluid was in the subdural or subarachnoid space, but this has been clarified using MRI.^{27,28} If the excess fluid is in the subarachnoid space, cortical veins can be seen stretching across the fluid signal. If the excess fluid is in the subdural space, the veins are compressed against the brain. In addition, on MRI, the subarachnoid space can be seen extending into sulci, and the subdural space can be seen as a distinct, separate layer.

Patients with excess fluid in the subarachnoid space who present as infants (commonly referred to as benign extra-axial fluid of infancy) usually have a larger than average head and normal development, except perhaps for a slight motor delay because of the large head. They do not exhibit signs of raised intracranial pressure, and as time progresses, the additional fluid usually resolves on imaging, and their future development is normal. The presence of excess fluid in the subdural space may be confused with bloody fluid occurring after trauma; to complicate matters further, it has been proposed that preexisting external hydrocephalus (with excess subarachnoid fluid) might predispose children to bleeding into the subdural space.²⁹ This discussion often arises in the assessment of chronic subdural hematoma in infancy and whether there is a possibility of child abuse.

Older Children

Beyond infancy, both the cause of hydrocephalus and its potential management change. Congenital causes are less common in these

patients, and acquired disorders are more frequent. It is in this group of children that third ventriculostomy is a more appropriate treatment option. A recent multicenter review of the Canadian experience with third ventriculostomy found that age at the time of surgery is the most important factor predicting success.³⁰ In that study, 368 children averaging 6.5 years of age underwent third ventriculostomy. The 1- and 5-year success rates were 65% and 52%, respectively, and age was identified as the primary determinant of outcome. In patients initially treated when they were younger than 1 month, the 5-year success rate was 28%; the success rate progressively improved to 68% in patients older than 10 years.

Children with Suspected Shunt Malfunction

The likelihood of shunt failure is 40% in the first year after shunt implantation.^{31,32} Shunt failure can have a wide variety of presentations, but the most common mirrors a typical hydrocephalic presentation, with raised intracranial pressure, increasing head circumference, irritability, full fontanelle in a baby, and headache, nausea, and vomiting in older children. In addition, there may be fluid tracking along the shunt or fever, redness, or wound drainage in the setting of shunt infection. In evaluating a patient with possible shunt malfunction, it is helpful to remember that an individual child's pattern of shunt failure is often similar from one occasion to another. This pattern is usually well known by the family, and their opinion about whether this represents shunt malfunction can be extremely helpful and should be sought. In the setting of multiple, recurrent shunt "malfunctions," undiagnosed shunt infection should be considered, and cerebrospinal fluid should be sent for culture, even in the absence of fever or other signs of infection.

Children with spina bifida who present with a urinary tract infection may have clinical manifestations that are very similar to shunt malfunction. They may have headache, nausea, and vomiting but no obvious change in the ventricular system. An examination of the urine may reveal a urinary tract infection, and its treatment often resolves the symptoms, thus avoiding unnecessary shunt explorations.

Children with Shunts and Chronic Headaches

A small proportion of children with hydrocephalus have recurrent headaches but lack imaging evidence of shunt malfunction. Shunt failure can certainly occur without obvious ventricular enlargement on imaging, but the physician should not jump to this conclusion, which can lead to operating on the shunt unnecessarily. Children with shunts also have all the usual reasons for headache, and tension headache and migraine should be considered in the differential diagnosis. A small number of patients do have true slit ventricle syndrome, and their management can be quite complex. Although the syndrome is not common, it results in a large number of visits and, in some cases, procedures. It may be difficult to determine whether these children have a shunt malfunction or raised intracranial pressure based on clinical assessment and imaging. In such situations, intracranial pressure monitoring may be helpful. This is preferably done without any intervention on the shunt, via a separate fiberoptic pressure monitor. Detailed discussions of the management of slit ventricle syndrome are beyond the scope of this chapter, but excellent reviews are available in the literature.³³⁻³⁵

Children with Shunts and Fever

The significance of fever in a child with a ventriculoperitoneal shunt depends on the timing of presentation. The vast majority of shunt infections occur within the first 3 to 6 months after an intervention (surgery or shunt tap).³² Beyond that time, shunt

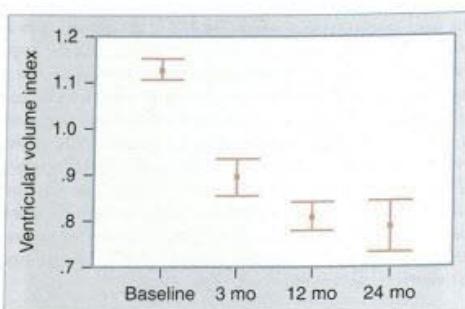


FIGURE 186-4 Graph showing ventricle size after initial ventriculoperitoneal shunt insertion in patients who did not require shunt revision. (From Kestle JRW. Clinical trials in hydrocephalus: what have we learned? In: Malucci C, Sgouros S, Abbott IR, eds. CSF Disorders throughout Life: Diagnosis, Management, and Controversies. New York: Informa Healthcare; 2009.)

infection is rare unless abdominal complications have developed. Bowel perforation or abdominal pseudocysts can present years after any shunt intervention. In the absence of obvious abdominal pathology, the yield of a shunt tap more than 6 months after a procedure is very low and probably not worth the risk of introducing a new infection. Even within the first 6 months after an intervention, other sources of fever should be sought first, with a complete clinical examination and simpler cultures such as urine, sputum, and throat swabs, depending on the physical findings. If these test results are negative and the fever is persistent, a shunt tap is a reasonable option.

Long-Term Monitoring

Children with shunted hydrocephalus frequently undergo regular evaluations by a neurosurgeon on an annual or biannual basis. An initial follow-up appointment after shunt surgery usually occurs within 2 or 3 months. Ventricular size may decrease over the course of the first year (Fig. 186-4), so a scan obtained at a 1-year follow-up appointment is a good basis for future comparison. Because of the high failure rate in the first year, an earlier scan at 2 or 3 months postoperatively may be worthwhile. If the child has an open fontanelle, follow-up by ultrasonography may be useful until the fontanelle closes.

Computed tomography as a method of diagnosis and follow-up has received recent attention because of concerns about radiation exposure in children.³⁶ The use of MRI in the monitoring of shunted patients has been proposed.³⁷ This has not been universally accepted, however, because of the demands on scanner time and the increasing use of adjustable shunt valves; these valves are susceptible to change in a magnetic field and may require readjustment after the scan. Evaluation of the valves often involves plain radiographs with radiation exposure, negating the radiation-avoiding benefits of MRI.

An argument for regular long-term imaging was based on an analysis of unexpected deaths in children with shunts.³⁸ In that study, the death rate of children with shunts fell once regular imaging was instituted, and this was attributed to the identification of asymptomatic shunt failure.

Children with Hydrocephalus Growing into Adulthood

One of the biggest challenges facing many pediatric subspecialties is the increasing population of young adults who have grown up with congenital or pediatric disorders. Their transition from pediatric to adult health care settings has raised some unique challenges. The management of pediatric hydrocephalus is significantly different from that of adult-onset hydrocephalus, and many neurosurgeons who treat adults are neither experienced nor interested in pediatric hydrocephalus. Several models for providing appropriate care for these young adults are being explored, but further work is urgently required to meet their needs.

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Infantile Posthemorrhagic Hydrocephalus

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Intraventricular hemorrhage (IVH) is a leading cause of infantile hydrocephalus. The management of hydrocephalus in these infants is critical because the initial neonatal treatment can have lifelong implications for both shunt survival and the child's neurological outcome. An understanding of the unique challenges in caring for these infants is essential to their proper management. IVH and subsequent posthemorrhagic hydrocephalus (PHH) arise from different pathophysiologic mechanisms, pose different clinical and management issues, and suggest different prognoses in preterm versus term infants. Thus, they are discussed separately.

INTRAVENTRICULAR HEMORRHAGE IN PRETERM INFANTS

Epidemiology

The incidence of preterm birth continues to rise in the United States, with 12.7% of infants born before 37 weeks' estimated gestational age (EGA), representing an almost 20% increase over the past 15 years.¹ Preterm infants are stratified by birth weight or EGA, or both. For classification purposes, the EGA of preterm infants is not rounded up. For example, an infant born at 26½ weeks is classified as a 26-week EGA infant.² The survival of all preterm cohorts has risen dramatically over the past few decades owing to improvements in perinatal medicine, but many of these infants remain at risk for neurodevelopmental deficits. According to the 2007 report from the Institute of Medicine's Committee on Understanding Preterm Birth, preterm infants account for 64% to 75% of infant mortality, 42% to 47% of children with cerebral palsy, 27% of children with cognitive deficits, 37% of children with visual impairments, and 23% of those with hearing impairments.³ Neurodevelopmental outcomes are discussed in more detail later.

The prevalence of IVH varies, depending on the availability and quality of neonatal intensive care, and only a small subset of patients requires neurosurgical intervention. The incidence of IVH increases inversely with decreasing birth weight or EGA.⁴ In a study of infants born in the mid-1990s weighing less than 1500 g, 22% had IVH, and one fourth of those infants had progressive ventricular dilation.⁵ Among survivors with progressive ventricular dilation, one third required surgical intervention.⁵ Although infants born more recently continue to suffer IVH, fewer require surgical intervention. A recent collaborative study from the National Institutes of Health (NIH) Neonatal Research Network following more than 6000 preterm infants born at less than 1000 g between 1993 and 2002 showed that one third suffered IVH, and one third of those with IVH developed progressive ventricular dilation.⁶ Ten percent of those with IVH (3% of the total weighing <1000 g) required shunt insertion for symptomatic PHH, a decrease from 15% in older studies.⁶ IVH is graded on Papile's scale from I to IV (Table 187-1).⁷ Although only 1% of infants with grade I or II IVH in this recent NIH study required shunt insertion, 18% of infants with grade III and

29% with grade IV IVH required a shunt.⁶ As perinatal care continues to improve, the proportion of preterm neonates who require shunt insertion will likely continue to decline.

Because less than 10% of infants with IVH develop PHH and require a shunt, strong collaboration between the neurosurgical team and the neonatology team is required to obtain neurosurgical consultation in a timely manner and to avoid unnecessary non-surgical consults. Intravenous access in cranial veins should be avoided in any preterm infants who might develop hydrocephalus.

Pathophysiology of Germinal Matrix Hemorrhage and Posthemorrhagic Infarction

The germinal matrix is a transient structure in the subependyma of the ventricular walls that generates neural cell progenitors for the overlying cortex, primarily from 8 to 28 weeks' EGA. The germinal matrix typically completes involution by 32 weeks' EGA. The proliferative germinal matrix is a metabolically active area with friable, immature vessels prone to hemorrhage.⁸ Hemorrhage can be limited to within the germinal matrix (grade I), but about 80% of germinal matrix hemorrhages rupture through the ventricular wall into the ventricle (grade II, III, or IV; see Table 187-1). Grade IV is also called *periventricular hemorrhagic infarction*.⁹ Venous infarction is believed to result from the germinal matrix hemorrhage rather than direct expansion of the hemorrhage into the parenchyma.

Multiple factors contribute to the germinal matrix's propensity to hemorrhage, and the pathophysiology is incompletely understood. Because of their immaturity, preterm infants have impaired cerebral autoregulation. Systemic fluctuations in blood volume, flow, and pressure that commonly occur in preterm infants are thus transferred to the friable germinal matrix without the buffer of cerebral autoregulation. In addition, the germinal matrix has lower levels of fibronectin and other extracellular matrix components than do other areas of the late-gestation brain, and this likely contributes to the propensity to hemorrhage.¹⁰ An experimental study suggests that prenatal betamethasone treatment may enhance fibronectin levels and thus decrease the risk of hemorrhage. This correlates with the decreased risk of IVH observed clinically with prenatal betamethasone treatment.¹¹ Although neonatologists have worked aggressively with obstetricians to minimize stress to preterm infants during the peripartum, the risk for IVH most likely reflects a combination of genetic and environmental factors. After IVH occurs, the absorption of cerebrospinal fluid (CSF) is impaired, likely caused by a combination of decreased absorption across the arachnoid villi into veins and from ependyma into parenchyma.⁸

IVH can occur in association with periventricular leukomalacia (PVL), injury to the developing white matter. PVL can occur as both deep cystic white matter lesions and diffuse noncystic loss of oligodendrocytes with associated astrocyte gliosis.¹² Cystic PVL is visible on cranial ultrasonography (US), and most attention has focused on the white matter injury. Observations during the past decade from magnetic resonance imaging (MRI) and

TABLE 187-1 Papile's Classification of Preterm Intraventricular Hemorrhage on Ultrasonography

| GRADE | DESCRIPTION |
|-------|--|
| I | Isolated germinal matrix hemorrhage |
| II | Intraventricular hemorrhage without ventricular dilation |
| III | Intraventricular hemorrhage with ventricular dilation |
| IV | Intraparenchymal plus intraventricular hemorrhage |

autopsy studies have shown that injury to the developing central nervous system affects both white and gray matter.¹³ The combined injury has been designated *encephalopathy of prematurity*, which more accurately reflects the widespread nature of the injury not only to the cerebral gray and white matter but also to the diencephalon, brainstem, and cerebellum.¹⁴ PVL is about 10-fold more common than IVH among infants weighing less than 1500 g at birth. At least half of these infants have imaging signs of PVL, but only 5% have IVH.¹⁴

Clinical Presentation and Diagnostic Evaluation

Most IVH occurs within the first 72 hours of life, when most preterm newborns are quite unstable (Fig. 187-1). IVH is readily diagnosed by bedside cranial US. Transport to obtain computed tomography (CT) or MRI can cause additional stress and potential injury in these very fragile patients. CT scans also involve radiation, and repeated exposure of the preterm brain to radiation should be minimized if possible. In general, CT scans should be reserved for the evaluation of diffuse, life-threatening cerebral hemorrhages when MRI is not feasible. US provides a reliable means of identifying ventricular dilation and IVH. If possible, all preterm newborns weighing less than 1500 g should have a cranial ultrasound examination within the first 48 hours of life, and then weekly or biweekly as needed. PVL can also be assessed by US. Although the interreader reliability for grades III and IV IVH is excellent, the reliability for grades I and II IVH and for PVL is less.¹⁵ These limitations of cranial US rarely present a problem for neurosurgical management (Fig. 187-2).

Most preterm infants develop symptomatic hydrocephalus over several days, with a gradual shift in their clinical course. Infants with IVH should be observed closely with daily measurement of the occipitofrontal circumference. An increase of 0.5 to 1 cm/day for 2 to 3 consecutive days often suggests symptomatic hydrocephalus. The anterior fontanelle in very small infants is often quite large; usually the shift from a soft, slightly bulging fontanelle to a tense, full one can be appreciated. Widening of the space between the bone edges along the sagittal and coronal sutures (splayed sutures) is often a reliable finding on daily examination to assess the development of symptomatic hydrocephalus. Preterm infants with symptomatic hydrocephalus can have episodes of spontaneous apnea or bradycardia. Other symptoms and signs of increased intracranial pressure include refractory seizures, lethargy, and impaired upward gaze ("sunset" phenomenon). In addition to the daily clinical examination, serial ultrasound studies every few days are useful to assess for additional hemorrhage or the development of ventricular dilation. Rarely, preterm infants experience acute clinical deterioration due to a rapid onset of increased intracranial pressure. In these patients, more extensive and severe intracerebral hemorrhage may have occurred, often in association with other systemic problems such as sepsis and coagulopathy. Urgent interventions may be needed to sustain these infants, but the heroic nature and poor

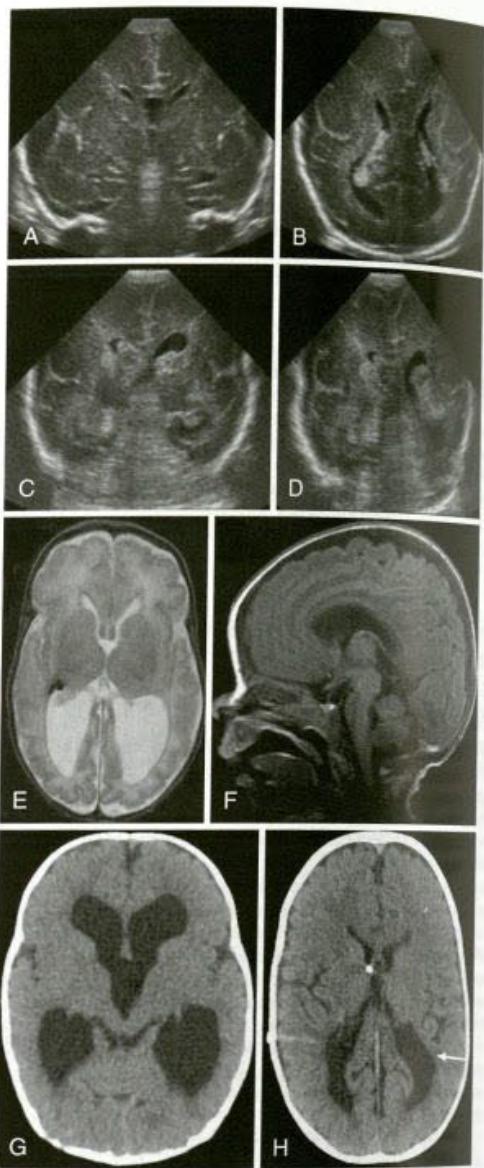


FIGURE 187-1 Typical imaging findings in posthemorrhagic hydrocephalus from germinal matrix hemorrhage after preterm birth at 27 weeks' gestation. Cranial ultrasonography (US) in the coronal (**A**) and axial (**B**) planes at 12 hours of life shows minimal abnormalities. Repeat US 2 days later reveals bilateral grade IV intraventricular hemorrhage (**C** and **D**), also termed periventricular hemorrhagic infarction. The patient did not develop signs of symptomatic hydrocephalus as a neonate. At term equivalent, magnetic resonance imaging shows a paucity of white matter, suggesting the diffuse form of periventricular leukomalacia (**E**). Also note the small cerebellum, a typical finding among former preterm infants (**F**). At 8 months of age he developed symptomatic hydrocephalus, with an enlarging head circumference and dilated ventricles observed on CT (**G**). Several months later, a baseline CT scan shows well-decompressed ventricles, but the paucity of white matter remains (**H**, arrow).

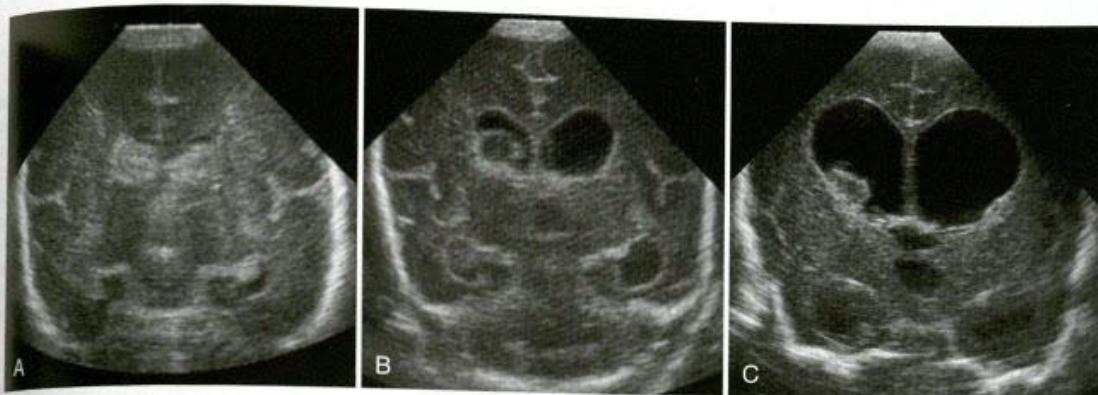


FIGURE 187-2 Progressive ventricular dilation on cranial ultrasonography (US) in the neonatal period. Initial US of this infant born at 27 weeks' gestation shows bilateral grade II intraventricular hemorrhage (IVH) (**A**). Although distinguishing between the lower grades of IVH on cranial US may be difficult for the average observer, the progressive ventricular dilation, with retraction of the germinal matrix clot, at 2 weeks (**B**) and 3 weeks (**C**) is readily apparent. After **B**, serial lumbar punctures were initiated for an enlarging head circumference with splayed sutures, but they failed to control the hydrocephalus. After **C**, a ventriculosubgaleal shunt was inserted.

long-term outcome of these interventions should be discussed with the parents.

Hydrocephalus *ex vacuo* refers to ventricular dilation without increased intracranial pressure. In the mid-1990s, 24% of surviving infants with IVH had ventricular dilation without progression.¹ Hydrocephalus *ex vacuo* reflects encephalomalacia, or a lack of adequate parenchymal brain growth; the implications for developmental outcomes are discussed later. Infants can have transient symptomatic hydrocephalus that spontaneously resolves. Distinguishing hydrocephalus *ex vacuo* from symptomatic hydrocephalus can be challenging. With continued observation, the type of hydrocephalus typically declares itself.

Treatment

Preterm infants are challenging patients. Their relatively poor nutrition, immature immune system, and other comorbidities make them less than ideal surgical candidates. For example, many preterm infants have anemia of prematurity treated with erythropoietin, red blood cell, and platelet transfusions. Even with scrupulous attention to minimizing blood loss during surgery, a preterm neonate may require a transfusion after a surgical procedure. Because grades III and IV IVH tend to occur in the smallest and sickest infants, they are more likely to have other confounding illnesses. Interventions for symptomatic hydrocephalus are offered in a stepwise progression to identify patients in whom permanent CSF diversion is not required. This process allows surgery to be avoided in all but the few who definitely need it. It also shows the family that every reasonable nonsurgical measure has been tried. This is important because neither CSF shunts nor endoscopic third ventriculostomy offers highly effective lifelong treatment without complications.

Nonsurgical Treatment

A commonly used treatment paradigm begins with serial lumbar punctures. In many cases, serial lumbar punctures can be used as a temporizing measure until the infant is older and more medically stable and thus a better surgical candidate. Ideally, lumbar punctures should be initiated as soon as progressive ventricular dilation is observed.¹⁶ This may reduce the need for a permanent shunt. The fourth ventricle is sometimes difficult to visualize by cranial US, and the tentative diagnosis of aqueductal stenosis may

be suggested by the radiologic interpretation. As long as there is no large posterior fossa hemorrhage, most preterm infants can safely undergo lumbar puncture. Fortunately, progressive ventricular dilation after IVH spontaneously resolves in a significant proportion of infants. Infants with transient hydrocephalus should be followed for the late development of symptomatic hydrocephalus. The chance of surgical intervention becoming necessary continues to decline for these infants over time. If serial lumbar punctures are inadequate and the patient is a relatively stable candidate for surgery, a temporary CSF diversion device is used to delay the need for definitive surgical treatment as long as possible. A meta-analysis of repeated lumbar or ventricular punctures failed to show that CSF removal improved outcomes compared with no intervention.¹⁷ This study, however, included ventricular taps, which have a higher rate of complications and poorer outcomes; it also included patients without progressive ventricular dilation. Serial CSF removal would not be expected to improve the outcome for children with hydrocephalus *ex vacuo*.

As observed in many areas of medicine in which definitive surgical treatment is not ideal, many nonsurgical interventions have been attempted to minimize the need for neurosurgical intervention. Unfortunately, these interventions have not been effective. Currently, medical therapy is not recommended for preterm infants with symptomatic hydrocephalus. Diuretic therapy, including acetazolamide and furosemide, is not effective in this population and may increase the risk of nephrocalcinosis and other complications.¹⁸ Likewise, intraventricular streptokinase is not effective in this population.¹⁹

Temporary Surgical Interventions

Some infants do not obtain adequate relief of symptomatic hydrocephalus with serial lumbar punctures, as defined by stabilization of the head circumference on a reasonable growth curve and stabilization or reduction of ventricular dilation on cranial US. In these cases, temporary shunts are used to treat symptomatic hydrocephalus and allow the infant to grow and recover from other complications of prematurity before undergoing definitive surgical therapy. Preterm infants have immature immune systems, fragile skin, and impaired wound healing. In addition, infants weighing less than 1500 g often have insufficient peritoneal absorptive capacity to handle the CSF volume.

Also, in the subset of infants with transient symptomatic hydrocephalus that persists only for several weeks, temporary shunts avoid permanent shunt placement. Clinical judgment is crucial to balance the timing and risk of surgical intervention against the potential detriment of temporarily and inadequately treated hydrocephalus. For example, preterm infants with a history of bacterial infection of the blood or CSF are at higher risk of significantly poorer neurological outcomes than comparable infants without infection.²⁰ The need to weigh the potential detriment of delaying surgery for several days to allow infection to be eradicated against the risks associated with symptomatic hydrocephalus is not uncommon for pediatric neurosurgeons and neonatologists.

Ideally, the neurosurgical team begins interacting with the infant's family when it is clear that serial lumbar punctures are failing. Because surgical intervention for this population is associated with a relatively high rate of complications, including potential shunt revisions and infections, the family needs to understand that all nonsurgical means were exhausted. Infants with symptomatic hydrocephalus have poorer neurodevelopmental outcomes than those without hydrocephalus.²¹ Therefore, the family needs to be advised that treatment of hydrocephalus is necessary to optimize brain development, but it does not mitigate the neurological deficits associated with preterm IVH.

Temporary ventricular CSF diversion can be achieved with either a ventricular access device^{22,23} or a ventriculosubgaleal CSF shunt.^{24,25} A ventricular access device consists of a reservoir that caps a ventricular catheter, and the reservoir is accessed via a needle through the scalp every 12 to 48 hours to withdraw enough CSF to maintain a stable head circumference. Ventriculosubgaleal shunts are also composed of a ventricular catheter and reservoir, with a 4- to 8-cm piece of shunt tubing exiting the reservoir and ending in a subgaleal pocket. CSF collects in the subgaleal scalp pocket and is slowly reabsorbed. When the subgaleal shunt is functioning, the CSF forms a large, sometimes tense pocket in the scalp, but the fontanelle is soft and flat, and the cranial sutures are not splayed.

Both temporary shunt methods are widely used, and some institutions may have slightly better results with one method than the other. With both procedures, meticulous technique is essential to minimize complications. No randomized multicenter trial comparing the two methods has been performed. Temporary shunts can be used for several months if necessary. Both methods can provide adequate temporary relief from symptomatic hydrocephalus, and both are prone to infection, wound dehiscence, and catheter occlusion.^{22,26} Some have proposed that subgaleal shunts provide more consistent ventricular decompression compared with the fluctuation in ventricular size that occurs with daily aspiration from a ventricular access device, but the daily fluctuation has not proved harmful. Specially trained nonphysician health care providers can safely and reliably perform shunt taps.

Direct ventricular taps with a needle through the fontanelle should generally be avoided as a routine treatment modality. Ventricular taps are reserved for life-threatening emergencies because they are associated with a markedly increased risk of infection and loculated hydrocephalus in childhood. Similarly, external ventricular drains have a much higher risk of complications in preterm infants than in older neurosurgical patients.²⁷ They have a higher risk of infection than temporary internalized shunt devices and have the same risk of catheter occlusion from debris in the CSF. A randomized trial comparing standard treatment with aspiration through a ventricular access device and a more aggressive protocol consisting of drainage, irrigation, and fibrinolytic therapy showed no difference in the number of patients who died or required permanent shunts, and those receiving more aggressive therapy were much more likely to have a secondary IVH.²⁸

Permanent Cerebrospinal Fluid Diversion Procedures

Permanent ventriculoperitoneal shunts are required in only a small minority of preterm infants who suffer IVH. As mentioned earlier, the family needs to understand that although shunts and other surgical procedures are lifesaving, they are not without risks and complications. These children are prone to cerebral palsy, epilepsy, cognitive delay, and behavioral abnormalities regardless of whether the CSF diversion is effective. Insertion of the permanent shunt is frequently delayed through the use of a temporary shunt as long as feasible. This likely decreases the risk of shunt infection.²⁹ Permanent shunt insertion at an older age in the neonatal period also likely decreases the need for shunt revisions throughout childhood. Among 79 preterm infants with grade III or IV IVH born before 32 weeks' EGA, weighing less than 1500 g, and followed for a mean of 10 years, the shunt revision rate for those with permanent shunts inserted at 3 to 5 months of age (uncorrected) was about half (55%) the shunt revision rate for infants with permanent shunts inserted before 3 months (Robinson and colleagues, unpublished results). Some have advocated that low-pressure valves be inserted initially in preterm infants. However, in a retrospective study of children with infantile hydrocephalus of all causes, medium- and high-pressure valves inserted during infancy were associated with a lower shunt revision rate during childhood.³⁰ Many former preterm infants develop slit ventricle syndrome during childhood, which can be associated with more shunt revisions. The high-pressure valve may deter slit ventricle formation in some but not all patients.

Shunt Technique

Recent studies to minimize shunt complications have shown that consistent techniques and protocols are effective in reducing some risks, particularly infection. Despite our best efforts, however, infections and other complications are still likely in this vulnerable population with inadequately developed immune systems. Shunt insertion in small infants also requires meticulous attention to positioning, aseptic technique, and wound closure. Local anesthetic (0.1% lidocaine with epinephrine 1:1 million, up to 4 mL/kg body weight) infiltration of the incisions minimizes blood loss and the need to coagulate the fragile scalp. Both frontal and occipital approaches can be used, with equal rates of long-term success. Unless there is concern for infection, we typically place the permanent shunt through the same opening used for the temporary shunt. Care is taken during opening of the incision to preserve the galea to facilitate optimal wound closure and to avoid cutting through the dura near the fontanelle. We typically make a bur hole adjacent to an open cranial suture. To make a bur hole, the pericranium is coagulated, and the bone is removed with curets and Kerrison rongeurs. Hemostasis in the bone can often be achieved with coagulation. After the dura and pia are coagulated and incised, the ventricular catheter is inserted using standard landmarks, and CSF is collected for protein, glucose, cell count, and culture. For permanent shunts, the catheter should be as long as safely possible (e.g., 5 cm for frontal) to minimize the chance the child will outgrow it as the cerebral cortex expands. Many infants have relatively thin cerebral cortices, and care is taken to avoid overdrainage that may precipitate a subdural collection. Low-profile shunt hardware is ideal, and care should be taken to minimize suture knots that may protrude through the thin skin. In some patients it may be necessary to approximate the shunt reservoir to the pericranium while the wound heals. The choice of shunt components depends on the surgeon's preference, and no components have proved more effective or less problematic than others.

For a ventricular access device, the only components are the reservoir and ventricular catheter, and the wound is closed after they are inserted and secured. For a ventriculosubgaleal shunt, the subgaleal pocket is created from near the catheter insertion site to the contralateral hemisphere, extending as far as possible and at least 8 cm in diameter. A 4- to 8-cm length of tubing is attached to the outflow side of the reservoir. Ideally, after the subgaleal shunt is inserted, the outflow tubing is temporarily occluded while most of the closing sutures are placed, to minimize overdrainage and collapse of the ventricles. The pocket fills with CSF after the wound is closed and remains full. The tubing in the subgaleal pocket is massaged a few times a day during the first few days to prevent early closure of the pocket.

A substantial number of patients who require a permanent shunt may also require a gastrostomy tube; inserting the distal shunt away from the left upper quadrant of the abdomen may minimize shunt difficulties caused by the gastrostomy tube later in childhood. When passing the shunt tubing from the abdomen to the cranium, care should be taken to avoid the nipple and any central lines in the upper chest and to avoid penetrating the skin in the neck. Once the plastic sheath has penetrated the subgaleal space at the skull base, it can often continue to be passed over the cranium in the subgaleal space without the metal stylet to minimize pressure on the skull and the need for passing incisions. A full length of distal shunt tubing can be placed to minimize the need to lengthen the tubing in the future.

Endoscopic Third Ventriculostomy

Endoscopic third ventriculostomy is a very effective treatment for noncommunicating hydrocephalus in children older than 2 years. Its use in young infants and in communicating hydrocephalus remains controversial, however. Several studies have shown that endoscopic third ventriculostomy is not effective in more than half of infants with nonobstructive hydrocephalus.³¹ In a few circumstances, despite the relatively low chance of success, it may still be the best option available.

Complications

Infection

In preterm infants, seeding of the shunt hardware from bacterial and fungal systemic infections is common, and the shunt may be contaminated when it is inserted or any time it is manipulated. CSF glucose levels are typically lower at baseline in preterm infants, and hypoglycemia, especially when mild, does not necessarily imply infection. Similarly, the CSF protein concentration may be higher than normal due to IVH. Markedly elevated white blood cells compared with red blood cells in the CSF suggests that infection is likely, but a moderate level of white blood cells may be present as a reaction to the resolving IVH. Elevated CSF white blood cell and protein levels may persist for weeks to months after the IVH. Ideally, CSF should be sent for culture every time any CSF is obtained. Unlike in older children, shunt infection can often be treated initially with antibiotics without removal of the hardware.²² After the infection has cleared, the temporary shunt can be replaced with a permanent shunt. As part of their immature immune systems, some infants produce insufficient immunoglobulins and benefit from immunoglobulin G infusions. Despite good surgical technique, reservoirs can migrate through the thin scalp, and any exposed shunt components are presumed to be infected. The scalp erosion tends to progress quickly, and the hardware typically must be removed. In some patients ventricular drainage at the time of shunt removal can provide temporary relief for several days before a new temporary shunt is inserted. This allows the CSF infection to be

treated before inserting new hardware; rarely, the temporary shunt may not require replacement.

Malfunction in Temporary Shunts

Ventricular access devices fail if no fluid can be aspirated from the reservoir. For subgaleal shunts, a deflated pocket is worrisome for shunt malfunction. Lack of a scalp CSF collection with a full fontanelle, splayed sutures, and increased ventricular dilation on cranial US suggest a malfunctioning shunt, whereas lack of a scalp CSF collection with no other signs of symptomatic hydrocephalus suggests that the hydrocephalus may have resolved spontaneously. The reservoir can be tapped if the subgaleal shunt fails to drain CSF into the scalp pocket or if infection is suspected.

Other Complications

Rarely, epidural, subdural, or intraparenchymal hematomas are observed on postoperative cranial US. The hematomas arise from a combination of factors, including friable vessels and a relatively soft, deformable cerebral cortex. In the vast majority of patients these hematomas resolve spontaneously without any intervention.

Neurological Outcome and Comorbidities

Preterm infants with IVH who require a shunt are more likely to have neurological deficits than those with IVH without PHH, suggesting that the need for a shunt is an independent risk factor for poor outcome.⁶ A small subset of preterm infants with PHH does not demonstrate significant neurological deficits at follow-up, and it is difficult to predict outcomes for children when they are infants. The likelihood of neurological deficits should be explained to the parents and caregivers to help them understand that the goal of a shunt is to optimize neurodevelopment. Shunt insertion and revision do not cause the neurological deficits associated with prematurity, but PHH and the need for a shunt clearly represent a more extensive central nervous system injury during development. For example, about two thirds (59% to 66%) of former preterm infants with grade IV IVH surviving at 2 years have motor deficits, and almost half (44% to 50%) have cognitive delay.³²⁻³⁴ A study from the Netherlands showed that 80% of children with grade IV IVH and a shunt had cerebral palsy.²¹ Children with shunts can be expected to have more deficits in all realms. Among 79 children who were born at less than 32 weeks' EGA, weighed less than 1500 g, required shunt insertion for PHH, and were followed for an average of 10 years, only 29% performed at the expected grade level, ambulated without an assistive device, and were free of seizures (Robinson and colleagues, unpublished results).

An inherent part of using standardized techniques to assess outcomes in young children is that studies of preterm infants tend to focus on severe, well-defined deficits present at about 2 years of age. Although this allows an accurate comparison of various interventions, the more subtle deficits that can significantly impact a child's achievement are not well documented. For example, 26% of former preterm (<1500 g) infants have symptoms strongly suggestive of autism spectrum disorders,³⁵ yet these disorders are not routinely assessed in outcome studies. A recent study compared the intellectual function of children aged 6 to 16 years with shunted PHH who performed within 1 year of expected grade level and that of normal controls; the investigators found that the full-scale, verbal, and performance IQ in children with shunts averaged a full standard deviation below that of controls.³⁶ This study likely overestimates the performance of former preterm children with shunts, because only half the patients in the study were born preterm, and those not performing near expected grade level were excluded.

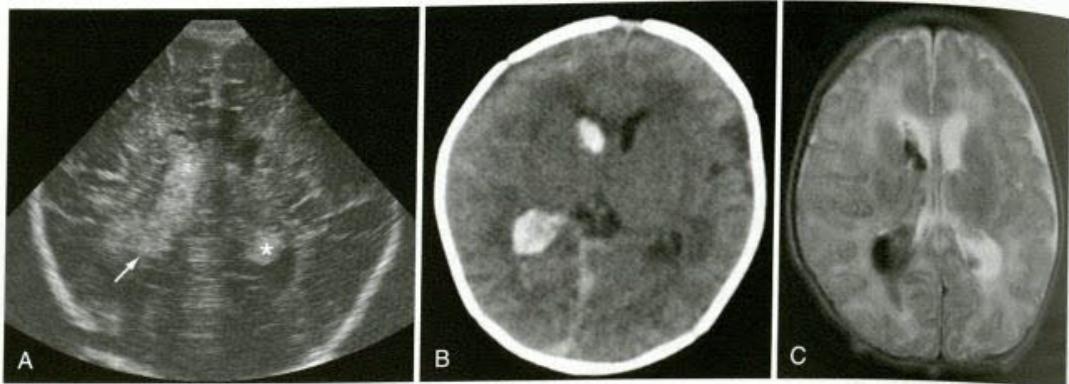


FIGURE 187-3 Grade IV intraventricular hemorrhage (IVH) in a term infant illustrated with multiple imaging modalities. Ultrasonography was performed when the newborn demonstrated lethargy and recurrent seizures on day 2 of life (**A**). Note the echodensity of the right grade IV IVH (arrow) and the normal left choroid plexus (asterisk). CT was performed the same day (**B**). Magnetic resonance imaging was performed 2 days later (**C**). Symptomatic hydrocephalus developed at 5 months of age, and the patient underwent insertion of a ventriculoperitoneal shunt.

INTRAVENTRICULAR HEMORRHAGE IN TERM INFANTS

Epidemiology

IVH in term infants is rare. Among the more than 2675 full-term infants admitted to a neonatal intensive care unit from 2003 to 2005, approximately 15% had peri- or intraventricular hemorrhage.³⁷ At another institution, 66 full-term infants with any type of intracranial hemorrhage were identified during a 12-year period, and only 30% had IVH.³⁸ In contrast to the minority of preterm infants who have low-grade IVH, 71.7% of term infants had a grade I lesion on cranial US, and 27.7% had grade II. Only two infants had grade III IVH, and one had grade IV.³⁷

Pathophysiology

Similar to preterm infants, IVH appears to arise from both genetic and environmental factors in term infants. Male gender, poor Apgar score, respiratory distress syndrome, and hyperbilirubinemia increase the risk of IVH.³⁷ Similarly, another study showed that forceps were used during delivery in 45% of infants with IVH, Apgar scores were less than 9 in 90% at 1 minute and in 60% at 5 minutes, and intubation after birth was required in 35%.³⁸ Term infants are more likely to develop IVH from venous infarction due to hypercoagulopathy or from hemorrhage of the choroid plexus. In many cases a cause cannot be identified. An increased frequency of the *PLA2* (platelet glycoprotein IIb/IIIa Leu33Pro polymorphism) allele was found in term infants with IVH compared with controls.³⁹ The exact mechanism is likely to be poorly understood in most patients.

Clinical Presentation

Term infants with IVH typically present with lethargy or seizures. A subset of infants presents with distress at birth, and the remainder often present within the first week. Some infants have already been discharged home from the newborn nursery and return through the emergency department. Magnetic resonance angiography or venography can sometimes visualize underlying abnormalities and suggest a diagnosis, but MRI rarely affects

urgent surgical decisions (Fig. 187-3). These infants often have seizures that are difficult to control, and the timing of the MRI needs to be coordinated with the need for electroencephalographic monitoring. Most term infants with IVH benefit from a coagulation evaluation, but typically this cannot be completed conclusively until the infant is about 1 year old. Many infants have no or transient ventricular dilation in the period immediately after the hemorrhage. A significant proportion may eventually develop symptomatic hydrocephalus and require a shunt, usually during the first year of life.

Treatment

Term infants can undergo ventriculoperitoneal shunt insertion similar to other full-term neonates and infants. Endoscopic third ventriculostomy has not been reported frequently in this population.

Neurological Outcome and Comorbidities

Very few outcome studies have been published. Overall, children who were term infants have much better outcomes than those who were preterm infants. Epilepsy is not uncommon. Cognitive and behavioral abnormalities are not unusual, but they are typically not as severe as those observed in former preterm infants.

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Cerebrospinal Fluid Physiology

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Under normal physiologic conditions, most of the cerebrospinal fluid (CSF) is secreted by the choroid plexus and flows through the ventricular system to emerge from the fourth ventricle. The CSF then traverses the subarachnoid space (SAS) and drains from the central nervous system (CNS) through unidirectional open channels as a result of a hydrostatic pressure difference. This chapter examines the clinical and experimental evidence for these conclusions. First reviewed is the CSF physiology of the developing fetus because this sets the stage for what is to follow.

CEREBROSPINAL FLUID PHYSIOLOGY OF THE DEVELOPING FETUS

Cerebrospinal Fluid Pathways

Development of the ventricular system begins with closure of the neural groove to form a neural tube. Fluid is present within the neural tube even before the choroid plexus anlage appears. This fluid serves as structural support for the neural tube, as well as a pathway for diffusion of metabolites before the formation of blood vessels. In the small thin-walled fetal brain, fluid movement is characterized by a lack of communication between the ventricles and the meningeal fluid spaces. Ciliary action inside the ventricles produces directional streaming, whereas fluid mixing aids in diffusing substances from the outer surface of the brain via the extracellular spaces (ECSs) through the wall of the neural tube into the ventricular cavity and vice versa.

The mechanism of ventricular formation appears to be well conserved in vertebrates, with ventricular shape being determined by adjacent cellular proliferation. The initial ventricular fluid is not dependent on the presence of blood vessels. The CSF within the ventricles contains hormones, proteoglycans, and ions and its composition varying with time and from site to site within the ventricles, depending on adjacent parenchymal development.¹ Ventricular enlargement is present in early development but steadily decreases to its size at term by approximately 30 weeks' gestation.^{2,3}

The mesenchyme surrounding the brain thins out in a definitive, organized pattern to form the pia-arachnoid membrane, the dura, and the SAS. The residual mesenchyme forms the trabecular meshwork of the arachnoid. Ultrasonography has largely been supplanted by magnetic resonance imaging (MRI) for study of the ventricular system and SAS in the fetus.⁴ The width of the SAS in early development is fairly large until 32 to 34 weeks' gestation, when it declines to its size at term. The volume of the SAS is related to CSF formation, CSF absorption, and fetal CNS development. An enlarged SAS can indicate chromosomal abnormalities, infection, and CNS underdevelopment. Enlargement of the cisterna magna (CM) can be seen with trisomy 18 and 21, Dandy-Walker malformation, cerebellar hypoplasia, and posterior fossa cysts.⁵ A large CM by itself can be an isolated finding and compatible with normal development. A small CM can also be seen in patients with Chiari malformations.

The SAS and its configuration are virtually complete at birth.⁴ The SAS develops independently of choroid plexus CSF secre-

tion and does not require the presence of CSF circulation. There is no movement of fluid out of the ventricular system during early development of the SAS.⁵ The outlets to the fourth ventricle are covered with a membrane, even after the choroid plexus begins to secrete CSF. This membrane does not appear to impair outflow of CSF from the ventricles because drainage occurs via intracellular pores in the membrane.⁶ The membrane subsequently becomes progressively attenuated, and larger and larger holes develop until it is no longer present.

Resistance to outflow from the ventricles increases as gestation progresses, but it does not change to any degree after birth.⁷ Resistance to CSF drainage in turn is the end product of differentiation of the cells that make up the pathways. Glycoconjugates appear to influence development of the matrix of the drainage pathways and to determine the degree of resistance.⁸ Presumably, impaired function or absence of normal glycoconjugates could lead to increased resistance, which if significant, would result in hydrocephalus.

Choroid Plexus

The choroid plexus of the third and fourth ventricles arises from invaginations in the roof plate, whereas the choroid plexus of the lateral ventricles arises from the choroidal fissure of the developing telencephalon. The choroid plexus consists of an epithelium covering a stromal core. The stromal core, or *tela choroidea*, is derived from mesenchyme, whereas the epithelium arises from neural tube spongioblasts lining the ventricles. The epithelium is initially pseudostratified but is subsequently transformed into a single layer of cuboidal cells. During development, the choroid plexus forms lobules, which in turn become fronds covered with microvilli. This process markedly increases the surface area of the choroid plexus while reducing the proportional volume that the choroid plexus occupies within the ventricular system. The microvilli become progressively more convoluted, which may relate to secretory activity. In humans, as in animals, the fourth ventricular choroid plexus is the first to develop. However, the greatest choroid plexus bulk resides within the lateral ventricles and is attached to the medial ventricular walls, where it is supplied by branches of the anterior and posterior choroidal arteries. The remaining choroid plexus hangs from the roof of the third and fourth ventricles and is supplied by branches of the medial posterior choroidal artery and the anterior inferior and posterior inferior cerebellar arteries, respectively. The choroidal veins drain mainly into the internal cerebral vein, a part of the deep venous or galenic system.

Various genetic factors that result in malformation or abnormal function of the choroid plexus have been described in animal models but not thus far in humans.⁹ Tight junctions between the epithelial cells of the choroid plexus become operative early in development and limit the free passage of proteins (Fig. 188-1). Synthesis or transport of proteins (or both) into and out of the CSF by the choroid plexus appears to influence neurogenesis.^{10,11} When developed, the choroid plexus, in addition to secreting CSF, also performs regulatory functions such as transporting various substances out of the CSF, neutralizing substances that

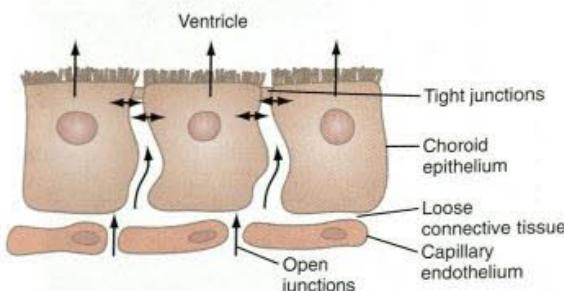


FIGURE 188-1 Diagrammatic representation of the choroid plexus. The capillary endothelium is of the attenuated fenestrated type, which allows an ultrafiltrate of plasma to reach the basal side of the epithelial cells. Tight junctions at the apical or ventricular side of the epithelial cells restrict molecular movement and constitute the blood-CSF interface.

could be harmful to the CNS, and helping maintain the homeostasis needed for normal CNS function.

The locations of the lateral, third, and fourth ventricular choroid plexus may also play a unique role in CNS development inasmuch as trophic substances can be added or removed from CSF at specific sites. The CSF in the lateral ventricles is in continuity with the germinal matrix, the main site for cortical cell proliferation and subsequent migration, whereas the CSF in association with the choroid plexus of the fourth ventricle may more likely influence structures in the basal cisterns.¹²

Development of the Cerebrospinal Fluid–Blood–Brain Barriers

The earliest CSF is most likely an ultrafiltrate of plasma. With development of the CSF–blood–brain barriers, CSF becomes a secretion. The concept that these barriers are less developed in the fetus and infant is based on observations that blood-borne dyes stain the immature brain more extensively, that the concentration of protein in CSF is higher in the newborn, and that metabolites and various solutes enter more readily and reach higher concentrations in the fetal brain than in the adult brain.¹³

However, many problems exist in trying to determine the permeability of the CSF–blood–brain barriers in an immature brain because there are many different and continual changes occurring during gestation. The very early embryonic brain has no blood vessels, so exchanges with blood in vessels external to the CNS must occur indirectly. The main route of transfer appears to be from blood into CSF and then into the parenchyma, and it seems likely that the choroid plexus and early CSF have important roles in nutritional supply to the developing brain.¹⁴

After vascularization begins, the initial low density of blood vessels increases steadily with gestation. The number of blood vessels and cerebral blood flow increase in relation to metabolic needs. The ECS appears to be larger at certain stages, so there is less restriction to free diffusion. In addition, an increase in ventricular volume takes place. This increases the volume distribution, which in turn decreases CSF/plasma concentration ratios for small, passively diffusing molecules and may not reflect changes in permeability.¹⁵ The volume of the brain is initially small relative to its surface area, and the amount of CSF is proportionally higher. The kinetics of CSF circulation is different in the fetus such that removal of dyes and other

markers of permeability, such as inulin, is not the same as in the adult CNS.

Finally, the concentration of various substances in the CNS depends on many different active transport mechanisms, which mature independently. It has been shown that the developing choroid plexus distinguishes between different types of albumin. All these factors produce alterations that make it difficult to assess any changes in the passive permeability characteristics of the CSF–blood–brain barriers.¹⁷ Despite these complexities, experimental models have been designed and are able to answer some of the questions regarding the development of barriers particular to the CNS.

The CNS barriers are indeed more permeable in the fetus, but this greater permeability does not relate to the tightness of the junctions at either the brain capillary endothelium¹⁹ or the choroid plexus epithelium.^{19,20} Indeed, the intracellular junctions at these locations are well formed very early in fetal development and do not differ significantly from those in adults. The degree of permeability relates instead to the size of the intracellular channels, and it is a decrease in the size and perhaps the number of these “pores” that tightens the barrier.^{11,21}

For the barrier to tighten, however, it is necessary for astrocytes to be present. It has been shown that capillaries of CNS origin grown outside the CNS lose their normal barrier properties whereas non-CNS capillaries grown in the CNS acquire the appropriate characteristics.^{22,23} Additional evidence to support the contention of the inductive influence of astrocytes is the loss of normal capillary barrier function in the mature brain at the site of tumors.

For the brain to have its protected environment, there must be a barrier with the equivalent of tight junctions at the arachnoidal membrane comparable to those present in the capillary endothelium and the choroid plexus epithelium. The timing of completion of the arachnoidal barrier in the fetus is unknown, but it may coincide with the development of tight junctions in the blood vessels and choroid plexus (Fig. 188-2).

The protein content of the CSF of fetuses, premature infants, and infants has been studied extensively.²⁴ Total protein levels reach a peak concentration at 20 weeks’ gestation and then fall steadily. For full-term infants younger than 2 months, it is normal to find a protein level of up to 100 mg/mL. Premature infants have an even higher protein level. The concentration of protein in CSF varies with conceptual age but not with birth weight or with postnatal life span, thus indicating that maturation of the barrier, as reflected by a decline in protein, is not influenced by the timing of birth. The protein level represents a steady state at the time of sampling and is dependent on multiple factors, including the CSF secretion rate, volume of distribution, CSF circulation, and absorption rates of macromolecules. The CSF acts as a sink to clear macromolecules. Consequently, the protein level is not dependent solely on the degree of barrier permeability at the time of sampling. The proteins do not appear to emanate from the brain side of the barrier because they have an electrophoretic pattern similar to that of plasma.¹¹

Although cited as an indication of barrier immaturity in the neonatal CNS, focal deposition of bilirubin in the basal ganglia (i.e., kernicterus) does not reflect increased permeability to this substance. The conjugated form of bilirubin is not lipid soluble and does not cross the neonatal CNS to any significant degree. However, the unconjugated lipid-soluble form of bilirubin easily crosses into the CNS, as is also true in adults. That the unconjugated lipid-soluble form does not usually enter the brain is due to the fact that it is bound to plasma proteins. It is only when the binding capacity of the plasma proteins is exceeded that the free, lipid-soluble bilirubin enters the CNS. Overloading of the binding capacity of plasma proteins may result from reduced numbers of available binding sites on the plasma proteins

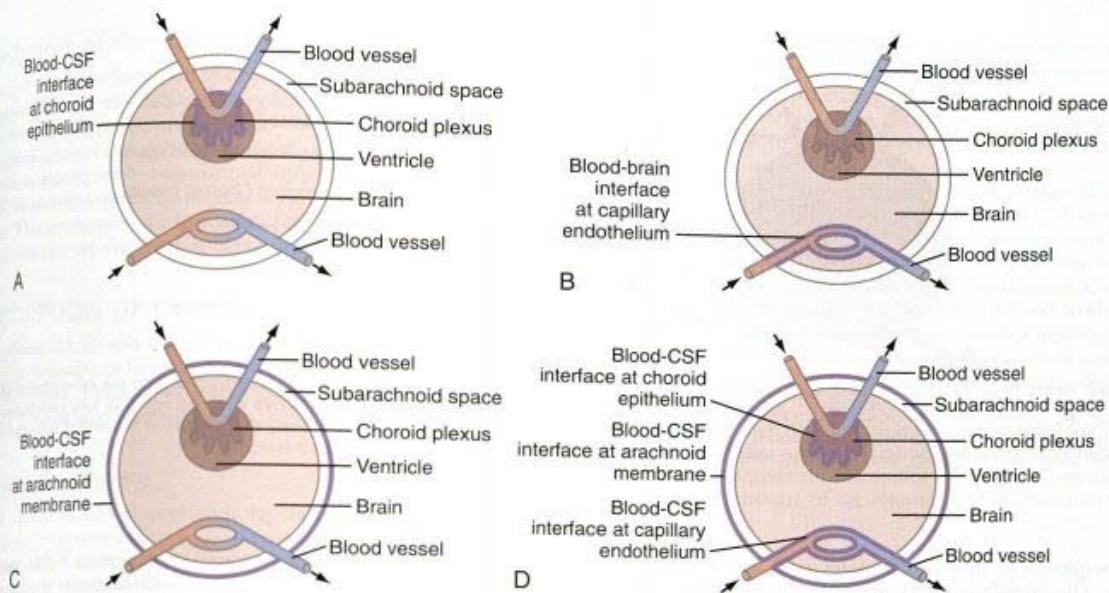


FIGURE 188-2 Diagrammatic representations of the central nervous system. **A**, Blood-CSF interface at the choroidal epithelium. **B**, Blood-brain interface at the capillary endothelium. **C**, Blood-CSF interface at the arachnoid membrane. **D**, It is the three interfaces depicted in **A**, **B**, and **C** that provide the specialized environment of the central nervous system.

secondary to competition from drugs or lower blood pH. Why bilirubin should selectively affect some regions more than others and why the developing brain is more sensitive to this substance are not known.

Formation and Absorption of Cerebrospinal Fluid

Formation of CSF is dependent on a number of transporters and enzymes, the most important of which appear to be carbonic anhydrase, sodium-potassium adenosine triphosphatase (Na^+/K^+ -ATPase), and aquaporin-1. Low levels of carbonic anhydrase and Na^+/K^+ -ATPase are present early in fetal development, but whether these enzymes are functional when they first appear is not known.^{21,25} Their presence coupled with aquaporin-1 water channels and concomitant enlargement of the ventricles does, however, lend support to at least some degree of CSF formation fairly early in fetal development.¹⁴

The relationship of CSF formation to brain maturation has been studied in several animal species but not in humans.²⁶ The data indicate that CSF production increases at a rate greater than can be accounted for by the corresponding increase in choroid plexus weight or brain weight. Thus, the increased production of CSF may reflect maturation of the enzyme systems involved. Oversecretion of CSF does occur in the presence of a choroid plexus papilloma. In utero, hydrocephalus secondary to the presence of a choroid plexus papilloma has been demonstrated as well.²⁷

No studies exist regarding CSF absorption in fetal animals or humans. Arachnoid villi, visible only microscopically, and arachnoid granulations, visible with the unaided eye, have long been thought to be the site of CSF absorption and are not found in the fetus. These structures begin to be present at birth and increase in size and number with age, with villi becoming arachnoid granulations. If they are not present, how is CSF absorbed? Although no fetal studies have been performed, neonatal animal

studies confirm CSF absorption via the extracranial lymphatics, with drainage into the venous sinuses through the arachnoidal structures being secondary.²⁸

Hydrocephalus

Normal dilation of the ventricular system is needed for the cells of the germinal matrix to multiply and migrate to form the normal cortical architecture. Various factors are found to be altered with hydrocephalus, but it is difficult to determine cause and effect.^{29,30} One study has shown that CSF taken from hydrocephalic animals in and of itself can inhibit neurogenesis but does not alter cell migration from the germinal matrix.³¹ Experimental models of hydrocephalus are discussed in Chapter 189.

Currently, the only genetic defect directly linked to fetal hydrocephalus is the X-linked L1-NCAM mutation; however, the CNS is severely altered as well.^{32,33} The ventricular dilation seen with extensive structural CNS abnormalities may have other different underlying genetic causations.

Simpson and colleagues attempted to delineate the dynamics of fetal intracranial pressure in utero at the time of therapeutic abortion.³⁴ Although their studies suffered from having only seven patients with diverse CNS malformations, they could not correlate the type of CNS lesions with the intracranial pressure found in fetuses with an excessive amount of CSF. In hydrocephalic fetuses, an attempt has been made to correlate ventricular size with velocity waveforms of pulsed Doppler recordings of cerebral blood flow, but no correlation has been found.^{35,36}

In utero imaging studies now make it possible to detect developmental abnormalities, mass lesions, and evidence of infection and hemorrhage, any of which can result in hydrocephalus. The antenatal diagnosis of hydrocephalus may influence the timing of delivery, the mode of delivery, and the possibility of terminating the pregnancy. In a situation that is fairly analogous to in utero hydrocephalus, a retrospective analysis was undertaken to assess the efficacy of aggressive surgical management of progressive

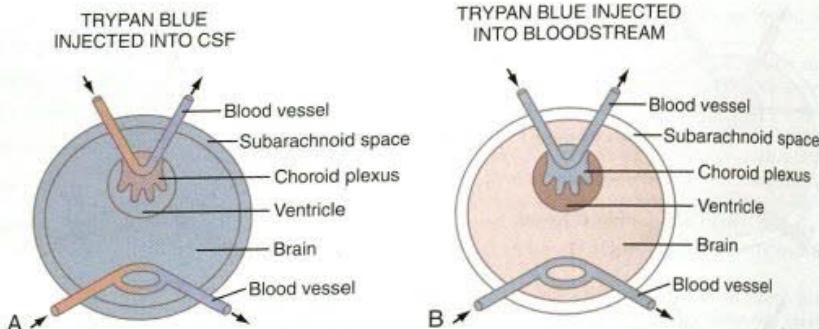


FIGURE 188-3 Diagrammatic representation of Goldman's experiments in which trypan blue was injected either into the bloodstream (A) or into CSF (B). The fact that dye injected into the bloodstream did not enter CSF or the brain whereas dye injected into CSF fully penetrated the brain gave rise to the first concept of a blood-brain barrier. In view of the extensive metabolic activity that occurs at the endothelial cell level between blood and the brain, this region is better described as an interface rather than simply as a barrier.

hydrocephalus in preterm neonates with intracranial hemorrhage. The overwhelming factor in determining the outcome of this patient group was the extent of intracranial hemorrhage and parenchymal damage. The degree of hydrocephalus and aggressive treatment of it were not significant.³⁷ There is no evidence that early control of hydrocephalus significantly improves neurological function because functional outcome is determined by the underlying insult to the CNS rather than the hydrocephalus.

BLOOD-BRAIN BARRIER

In 1885, Ehrlich demonstrated that many dyes injected into the systemic circulation of laboratory animals stain virtually all the organs in the body except the brain and spinal cord.³⁸ Ehrlich's disciple Goldman continued these experiments and showed that intravenously administered trypan blue fails to stain the CNS and CSF,^{39,40} although the choroid plexuses and meninges were stained. In his second paper, he demonstrated that interventricularly injected trypan blue rapidly stains brain parenchyma. Thus, it was concluded that there is a barrier between blood and the brain and that this barrier could be circumvented by direct injection of dye into CSF (Fig. 188-3).

Electron microscopic cytochemical studies from the late 1960s duplicated Goldman's first and second experiments.^{41,42} Horseradish peroxidase (HRP) injected intravenously was found in the lumen of brain microvessels, but no further movement of the label beyond the endothelial membrane was observed. When HRP was injected interventricularly, it readily infused across the ependyma and along the basement membranes of capillaries, but it did not enter blood via the endothelial membrane. These experiments established the anatomic concept of the blood-brain barrier and suggested that the endothelial membrane restricts free exchange of substances between blood and the brain because of the presence of tight junctions in the cerebral capillary endothelium.

During the past several decades, accumulating information has challenged the anatomic concept of an impermeable blood-brain barrier by showing that what is true for some vital dyes and HRP does not hold for many other biologically important molecules^{43,44} or for cells of the immune system. In addition, several classes of metabolic substrates, regulatory peptides, transport plasma proteins, steroid hormones, ions, and various groups of centrally active pharmacotherapeutics are able to use specialized shuttle services at the blood-brain barrier. In fact, the concept of a blood-brain barrier should be replaced with that of a blood-brain interface because the endothelial layer in reality regulates

homeostasis of the neural milieu by numerous highly specific transport, enzymatic, receptor, and cell-mediated mechanisms rather than simply impeding exchange of solutes between blood and the brain.

FORMATION OF CEREBROSPINAL FLUID

Formation Sites

It is generally agreed that most CSF is formed within the ventricular system. Possible sites of origin include the choroid plexus, the ependyma, and the parenchyma. A method has not been developed to separate the function of the ependyma from the remainder of the parenchyma, so the role of the ependyma in bulk CSF formation is not known, although from a morphologic standpoint its contribution is most likely to be insignificant. However, the choroidal epithelium has histologic features characteristic of epithelia specialized for transcellular transport of solutes and solvents.^{45,46} The discussion that follows is limited solely to the bulk secretion of CSF.

Results from isolated choroid plexus preparations would indicate that 80% or more of CSF production is derived from this source alone.^{26,47,48} However, perfusion of a portion of the ventricular system devoid of choroid plexus has demonstrated that 30% to 60% of CSF is produced from nonchoroidal sources,^{49,50} which may explain the failure of choroid plexectomy in the clinical setting to control progressive hydrocephalus.⁵¹ It may be added that this operative procedure removes the choroid plexus only from the lateral ventricles and not from the third and fourth ventricles. The contributions of the remaining intact choroid plexus to the formation of CSF is not clear, and whether it can compensate for the portion of the choroid plexus removed is not known.

The various lines of evidence showing the ECS to be approximately 15% of the brain's volume has been summarized by Welch.²⁶ The established presence of substantial ECS, the lack of ependymal resistance to free exchange between fluid in the ECS and CSF, and the similar composition of ECS fluid and CSF have a direct bearing on the possibility that the parenchyma may be the main source of nonchoroidal CSF formation.^{26,41,51,52} In summary, it appears that normally roughly 80% of CSF secretion is derived from the choroid plexus, with the remaining portion probably originating from the parenchyma. The obvious candidate for the parenchymal source is the capillary endothelium because its high content of mitochondria could provide the metabolic energy required for such a function.⁵³

Mechanism of Cerebrospinal Fluid Formation

The first step in the formation of CSF is passage of an ultrafiltrate of plasma through choroidal capillary endothelium without tight junctions by hydrostatic pressure into the surrounding connective tissue stroma beneath the epithelium of the villus. The ultrafiltrate is subsequently transformed into a secretion (namely, CSF) by an active metabolic process within the choroidal epithelium. This mechanism, the formation rate, and alterations in the formation rate are discussed in detail in Chapter 33.

ABSORPTION OF CEREBROSPINAL FLUID

Absorption of CSF and its constituents depends on bulk flow in addition to passive or facilitated diffusion and active transport of specific solutes. This section deals exclusively with bulk flow, the forces involved, and where it occurs.

Absorptive Forces

The rate of CSF absorption is dependent on pressure and is relatively linear over a fairly wide physiologic range has been well established.⁵⁸⁻⁵⁹ Resistance to flow appears to diminish at higher than normal physiologic pressures^{60,61} and may relate to the opening of channels not available at lower pressures.

Weed proposed an incremental colloid osmotic force, in addition to a hydrostatic force, that would by necessity require the presence of a semipermeable membrane between CSF and the site of absorption.⁶² Subsequent physiologic studies have shown that a colloid osmotic force does not exist; instead, Weed's previous observations are explained by particulate matter or an increase in viscosity occluding the absorptive sites, thereby slowing bulk flow.^{50,51,64} Studies have shown that the presence of pinocytotic vesicles in the arachnoid endothelial cells lining the venous sinuses is influenced by pressure.^{65,66} However, the process may not be metabolically dependent in that the absorption process is reported to be unaltered by death of the animal.^{67,68} Thus, the only proven force responsible for bulk CSF absorption is that of a hydrostatic gradient.

Absorption via the Arachnoid Villus

The arachnoid villus would seem to be ideally situated to drain CSF from the SAS into the major dural sinuses inasmuch as it consists of a cell cluster that projects from the SAS into the lacrime laterales adjacent to these venous structures. Electron microscopic studies have shown that the villi are covered by a layer of endothelium with tight junctions that are continuous with the undersurface of the venous sinuses.^{69,70} These villi, also called "arachnoid granulations" or "pachionian bodies," are grossly visible and are functionally similar to those that are not.⁷¹ Key and Retzius⁷² and Weed⁷³ firmly established that these structures drain CSF. Welch and Friedman, using a flux chamber containing a section of monkey superior sagittal sinus with arachnoid villi, found unidirectional flow from the SAS to the venous sinuses when a critical opening pressure was exceeded.⁶⁴

A point of controversy regarding the structure of the arachnoid villus is the existence of open channels connecting the arachnoid side with the venous side, for the presence or absence of such channels would mean a basic physiologic difference in the manner in which CSF and its constituents drain. The open villus model would be solely pressure responsive and would allow passive escape of macromolecules, whereas a villus covered with a continuous endothelial membrane with tight junctions would add the factors of osmosis and filtration, and macromolecules would require an active transport process to cross the barrier. Earlier anatomic studies were fairly evenly divided between these two possibilities; more recent ones, however, support the open-

channel pathway. The discrepancy in findings may relate in part or entirely to the manner in which the villus is prepared for histologic study: a zero pressure gradient between the arachnoid and the venous side of the villus during fixation would allow its collapse, and as a result the open channels would not be apparent.⁷⁴

Another possible mechanism that could bridge the gap between the open- versus closed-channel theory of CSF drainage was proposed by Tripathi.⁷⁵ He reported the presence of a dynamic transendothelial vacuolization process that temporarily creates an open channel across the villus endothelium through which CSF and its constituents can flow from the SAS to blood.⁷⁶ The effect of pressure on this mechanism was not investigated.

Attempts have been made to determine the size of passageways in the arachnoid villus⁷⁷ and also to see whether they are responsive to pressure, which they were not.⁷⁸ The size of the passageways in the arachnoid villus is only pertinent if this site is virtually the exclusive location for bulk egress of CSF into the bloodstream. If a significant fraction of CSF and its constituents drains elsewhere, the size of the channels in the arachnoid villus is less relevant.

Absorption into the Lymphatic System

The fact that CSF might drain at sites other than the arachnoid villus, under normal or abnormal physiologic conditions, has been given increasing consideration.

Weed's work firmly established that the arachnoid villus is a major site for bulk CSF outflow.⁷¹ It is rarely mentioned, however, that Weed acknowledged drainage of his injected solutions into the mucosa of the paranasal sinuses, nasal mucosa, cranial nerve root sheaths, and cervical lymph nodes; he thought that these routes were accessory. The idea that a proportion of CSF could and did drain via the lymphatics was gradually relegated to obscurity, and for more than a generation, standard texts and teachings limited CSF drainage solely to the arachnoid villus.

The concept of CSF draining via the lymphatic system has been given additional support by a number of laboratory investigations in which it was indicated that a significant quantity of CSF, and under certain circumstances even the majority, can drain via lymphatic channels.⁷⁹⁻⁸⁰ Substances with different molecular weights infused into the lateral ventricles can be found in the same concentration in the deep cervical lymph, thus indicating that the process of transport is by way of bulk flow.⁷⁹ Additional studies have shown that elevations in interventricular pressure will increase the volume of CSF directed into the lymphatic pathways.^{74,88} Conversely, blocking access to the lymphatic pathways reduces CSF lymphatic drainage.^{28,99,100}

Lymphatic drainage declines with age but may relate to reduced CSF formation and thus turnover rate rather than increased resistance to drainage.¹⁰¹ At present, no studies show to what extent lymphatic drainage of CSF exists in humans, but some support of this concept comes from the clinical observation that parents of children with CSF diverting shunts will occasionally report nasal congestion and periorbital or facial swelling when their child's shunt becomes obstructed. With improved imaging techniques, it may be possible to visualize this pathway.

Absorption via the Brain

A question debated for some time is whether CSF can be absorbed by the brain. Penetration of substances into the periventricular region of hydrocephalic animals has been well documented.¹⁰²⁻¹⁰⁴ With the advent of computed tomography and MRI, periventricular hypodensity may be seen in the presence of acute hydrocephalus and has been shown to be the result of CSF migrating into the area surrounding the ventricles in the face of increased interventricular pressure.¹⁰⁵ CSF in

the parenchyma, indicative of migration, however, does not necessarily equate with absorption. Bulk flow of CSF is usually measured by the clearance of various reference macromolecules, such as radioiodinated serum albumin (RISA), which by necessity would have to enter the lumen of the blood vessel and be removed by the systemic circulation. It has been shown that the cerebral capillaries have low permeability to RISA and that most of any given quantity of RISA injected into the brain can be recovered from lymph and CSF with little being lost to blood.⁸⁰ Additional studies have found that HRP, which has nearly the same molecular weight as albumin, could penetrate into the basal lamina of the capillary endothelium but not beyond.¹⁰⁶ In addition to the impermeability of the capillaries to various reference markers, clearance of which is a measure of CSF absorption, Welch has pointed out that because absorption occurs in response to a drop in pressure, higher pressure would be required outside the lumen of the capillary than inside, which would obviously lead to its collapse and preclude absorption.²⁶ The ECS in the brain, which amounts to 15%, readily allows flow of fluid in the parenchyma. This flow of fluid within the parenchyma is present under normal physiologic conditions,¹⁰⁷ and its velocity and direction are responsive to changes in hydrostatic¹⁰⁸ and osmotic pressure gradients.^{107,109} Macromolecules injected into the CSF of the ventricles or SAS have been observed to readily penetrate the ECS of the parenchyma and vice versa.^{41,106,110} Evidence thus supports the contention that the brain, rather than absorbing CSF, is acting as a conduit for fluid to move from the ventricles to the SAS, there being no barrier at the pial surface, just as there is no barrier at the ventricular ependymal surface of the ventricles.⁹²

Absorption via Blood Vessels

As noted in the discussion on the absorption of CSF via the brain, there is no evidence to support CSF being absorbed by the capillary endothelium. However, this does not preclude net changes in water when disequilibrium in the blood-brain osmotic gradient occurs because there is no barrier in this regard. One experimental study found that carbon black injected into the parenchyma could later be traced to the SAS, the walls of cerebral blood vessels, the adventitia of the internal carotid artery outside the cranium, and the cervical lymph nodes.¹¹⁰ Two newer studies are at variance with this observation that macromolecules travel extracranially in the adventitia of the major cerebral blood vessels, for in these studies, RISA injected into the brain or SAS stopped abruptly when the blood vessels exited the SAS^{80,111}; however, a more recent study is inconclusive.¹¹² The parenchymal vessels appear to provide a passageway for macromolecules to reach the SAS, where absorption via the lymphatic system or arachnoid granulations occurs.

Absorption at the Nerve Root Sleeves

Drainage of CSF into the nasal submucosa was first postulated by Schwalbe,¹¹³ and this finding has been confirmed on many occasions since.^{72,73,114-118} Yoffey and Drinker noted that the best injections in the nasal submucosa were achieved by placing tracers in the cranial SAS.¹¹⁸ The nasal submucosa has a dense network of lymphatic channels that subsequently drain into the deep cervical nodes.^{72,73,113,114,116,118} The pathway of CSF into the nasal submucosa is via an extension of the SAS that surrounds each olfactory filament as it passes through the lamina cribrosa, and this pathway can be blocked if the continuity of the space is disrupted.^{83,119} The pia-arachnoid layer progressively thins

and blends into a perineurial sheath as the olfactory filaments pass through the cribriform plate. This perineurial sheath becomes but a single-cell layer in the submucosa. The perineural space between the filament and the sheath is in continuity with the SAS.^{114,118} A previous point of uncertainty has been whether open channels connect the perineural spaces (and thus the SAS) with the ECS of the submucosa. The presence or absence of open channels would mean basic physiologic difference in the manner in which CSF and its constituents drain, just as with the arachnoid villus. An electron microscopic study indicated that a tight junction endothelial membrane is not present, thus allowing passive escape of macromolecules via bulk fluid flow on a pressure-responsive basis alone (Fig. 188-4).⁸³ Two additional studies have shown that the SAS surrounding the optic nerve divides into numerous tortuous channels to form a "subarachnoid trabecular meshwork" containing "micro-canals" that allow the passage of ferritin to reach the posterior intraorbital connective tissue. Once again, the passageways were open and similar to those found in the olfactory region.^{84,91} A barrier present at the sclera prevented entrance of tracer into the choroidal interstitium.

A study looking at CSF drainage from the spinal nerve roots indicated that the same physiologic process operative at the cranial nerves occurs in the spinal nerves as well.^{80,93} Drainage of CSF from the spinal nerve root sleeves is yet to be studied from a morphologic standpoint, but the evidence thus far favors an open-channel passageway similar to that found in the optic and olfactory nerves.

Absorption from the Subarachnoid Space

Experiments have documented that CSF drains from the SAS surrounding the cranial and spinal nerves and enters the lymphatic system, but the question of egress of fluid from the membrane itself remains unsettled. Dandy and Blackfan contended that CSF absorption was a diffuse process from the SAS, with the arachnoid villi accounting for only a small percentage of the fluid drained.¹²⁰ Weed found that under normal physiologic conditions, the arachnoid membrane acted as a barrier but could readily be breached with cellular damage.¹¹ Bowsher injected radioisotope-labeled protein into the SAS of cats and found uptake at the arachnoid villi, around the blood vessels of the cortex, and along the cranial and spinal nerve root sheaths, but no penetration through the arachnoid membrane,¹²¹ thus confirming the work of Weed.

Electron microscopic studies have shown several layers of arachnoid cells between the SAS and the dura mater; the cells of the outer portion of these layers exhibit tight junctions with occlusion of intercellular clefts, thereby serving as an effective barrier to large molecules (i.e., they function as a blood-CSF interface or barrier at this location).¹²² Butler has noted that contrary to findings at normal pressure, the arachnoid barrier layer is disrupted at higher pressures and HRP can penetrate through the arachnoid membrane to reach the ECS of the dura mater and dural lymphatic channels.¹²³ Normally, it does not seem that much, if any, CSF drains through the arachnoid membrane, but at unphysiologically high pressures, disruption of the barrier may allow significant bulk flow.

CIRCULATION OF CEREBROSPINAL FLUID

CSF functions as a lymphatic system for the CNS. With rapid turnover of CSF, a concentration gradient or "sink" is produced for the clearance of metabolic waste products, including macromolecules.¹²⁴ The pressure gradient created between the

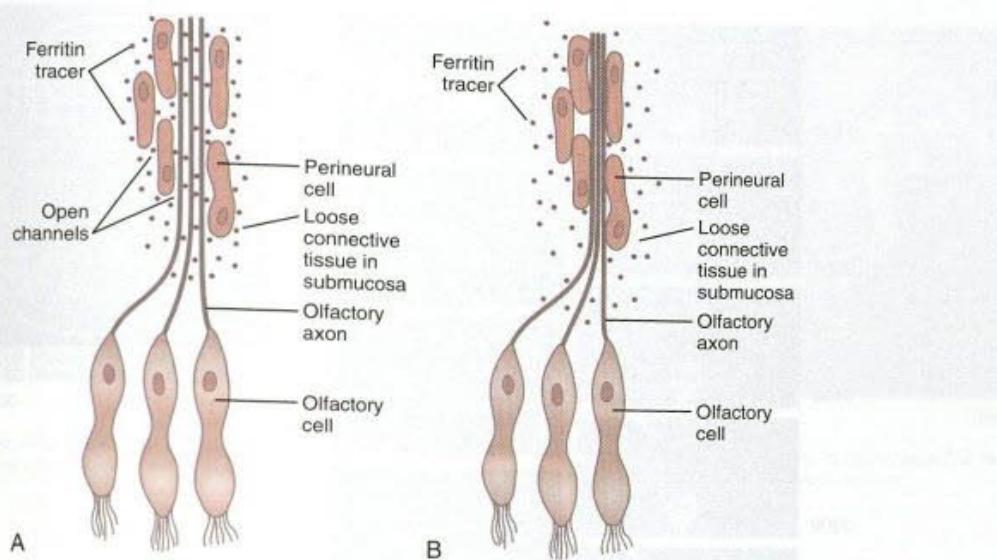


FIGURE 188-4 Schematic representation of the passage of macromolecules from the subarachnoid space (SAS) into the perineural space and then into the submucosal connective tissue. **A**, A positive hydrostatic gradient from the perineural space allows passive drainage of CSF and macromolecules via open channels. **B**, It is speculated that a negative hydrostatic gradient from the SAS to the nasal submucosa collapses the perineural space and acts as a one-way valve that prevents reflux into the SAS. (From Erlich SS, McComb JG, Hyman MS, et al. Ultrastructural morphology of the olfactory pathway for cerebrospinal fluid drainage in the rabbit. *J Neurosurg*. 1986;64:466.)

newly secreted CSF and that at sites of absorption produces the major force for bulk movement of CSF. Other factors that influence the circulation of CSF are the ciliary action of the ependyma and choroid plexus, pulsations induced by the arterial tree, and respiration. The newly formed CSF has a protein content of approximately 10 mg/dL; that from the lower spinal SAS is higher than 40 mg/dL. The difference reflects the rate of CSF turnover: the longer that CSF remains within the CNS, the more protein is added from the brain, spinal cord, and leakage from the blood-brain-CSF interface. That portion of the CSF produced in the parenchyma travels via the ECS to reach the SAS or joins the CSF made by the choroid plexus within the ventricular system. The lower pressure at sites of absorption draws CSF from the brain and spinal cord.

CSF circulation differs from the cardiovascular system in that no fluid returns to the starting point. Once produced, CSF is drained through the ventricular system and enters the SAS. If the ventricular pathways are obstructed, the increased resistance to flow can produce ventricular enlargement proximal to the site of blockage. Because CSF is still being formed and depending on the degree of ventricular obstruction, CSF will either continue to flow within the ventricular system or migrate through the ependymal lining of the ventricles into the ECS and cross the pia mater to enter the SAS, where it will drain via the usual pathways. The amount of CSF that drains via the transparenchymal route versus the ventricular system is dependent on the degree of resistance within each pathway at a given point in time.

Cardiac-gated phase-contrast MRI, until recently, was the only technique available to observe CSF flow noninvasively.^{125,126} This phase-contrast technique provides "to-and-fro" CSF flow velocity and direction during a period of a single cardiac cycle; however, this method is limited because of high variability of the

data, poor visualization of turbulent flow,^{127,128} and an inability to measure bulk flow.¹²⁶

Now available is a nonenhanced MRI technique, time-spatial labeling inversion pulse (SLIP), that can label or tag CSF in a region of interest. The tagged CSF is clearly visualized at inversion times of 1500 to 4500 msec after pulse labeling in both the intracranial and intraspinal compartments. Noninvasive visualization of CSF movement, including bulk and turbulent flow in normal and altered physiologic conditions, is possible with this time-SLIP technique (Figs. 188-5 to 188-7).¹²⁹ Impressive turbulent flow exists in the third and fourth ventricles and would aid in distributing various substances in the CSF, as well as in helping clear macromolecules from the parenchyma.^{130,131} The turbulent flow is markedly reduced with ventricular obstruction and readily reestablished with CSF diversion.

The time-SLIP technique shows significant movement of CSF within the SAS during respiration and increases in the mixing effect intraventricularly. One can observe "to-and-fro" flow of CSF, but no bulk flow from the sylvian SAS to the SAS over the hemispheric convexities leading to the superior sagittal sinus, the location of the arachnoid villi/granulations.¹²⁹ This lack of CSF flow over the dorsal surface of the hemispheres, in both normal and hydrocephalic individuals, adds additional support for the importance of nonarachnoidal granulation absorption of CSF.

Time-SLIP MRI can also be used to observe CSF movement in the spinal SAS. Rapid pulsatile CSF flow in the prepontine SAS is continuous with that in the ventral spinal SAS and progressively diminishes to almost nothing at the terminus of the thecal sac in the sacral region, as had been predicted.¹³² Imaging an individual turning from the supine to the prone position shows a position-related shift of the spinal cord with a concomitant change in CSF pulsatility from the anterior to the posterior SAS.

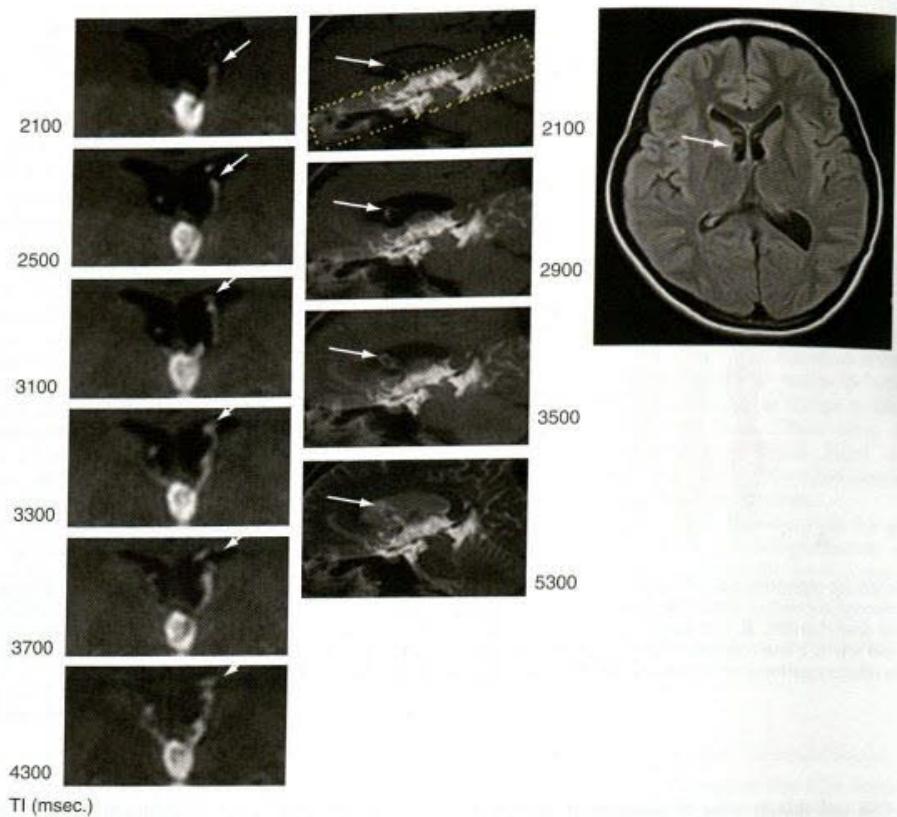


FIGURE 188-5 **Left**, Series of time-dependent coronal images acquired after a labeling pulse was placed on the third ventricle. **Middle**, Series of time-dependent sagittal oblique images acquired after a labeling pulse was placed on the third ventricle. The high signal intensity (yellow arrows) on these coronal and sagittal oblique images indicates turbulent CSF reflux flow from third ventricle into the lateral ventricles through the foramen of Monro. **Right**, This turbulent flow is frequently seen as a CSF flow artifact (arrow) on axial fluid-attenuated inversion recovery (FLAIR) images.

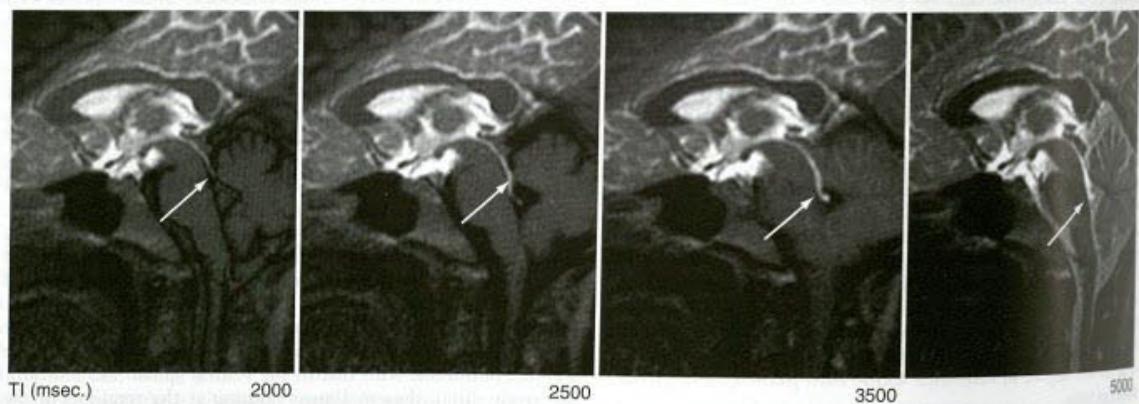


FIGURE 188-6 A series of time-dependent midsagittal images acquired after a labeling pulse was placed on the third ventricle. CSF flow from the third ventricle into the fourth ventricle through the aqueduct of Sylvius is seen (arrows).

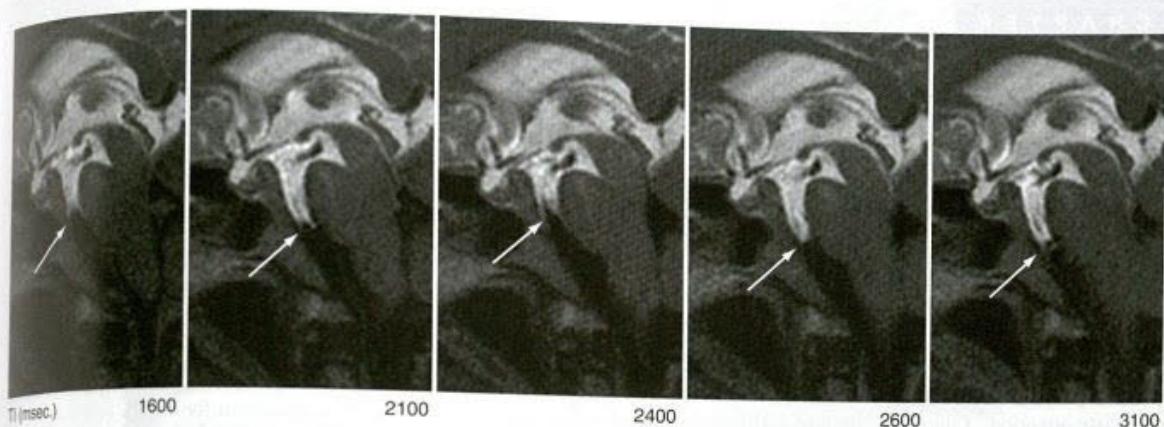


FIGURE 188-7 A series of time-dependent midsagittal images acquired after a labeling pulse was placed on the basal cisterns. Bulk CSF flow with rapid pulsatile motions was observed in the subarachnoid space anterior to the brainstem in the preoptine cistern (arrows).

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Experimental Hydrocephalus

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In the past 20 years our understanding of the pathophysiology of hydrocephalus has advanced significantly, yet critical gaps remain. A recent position paper identified 10 major areas that require immediate attention. Questions that are particularly amenable to experimental study include the following: How is cerebrospinal fluid (CSF) absorbed normally, and what are the causes of CSF malabsorption in hydrocephalus? Why do the ventricles dilate in communicating hydrocephalus? What happens to the structure and function of the brain when it is compressed and stretched by the expanding ventricles? What is the role of cerebrovenous pressure in hydrocephalus? What causes normal-pressure hydrocephalus? What causes low-pressure hydrocephalus? What is the pathophysiology of slit ventricle syndrome? What is the pathophysiologic basis for neurological impairment in hydrocephalus, and to what extent is it reversible? How is the brain of a child with hydrocephalus different from that of a young or elderly adult? It is difficult to address any of these important questions exclusively with clinical research, especially because of the wide variations in cause, onset, duration, and treatment complications that accompany hydrocephalus. Fortunately, animal models are available that approximate clinical conditions, and experimental hydrocephalus research is fundamental to promoting better treatments for this disorder. The recent white paper from a workshop sponsored by the National Institutes of Health bears witness to the importance of basic and clinical research in hydrocephalus.²

Unlike some neurological diseases or disorders, many mechanisms contribute to the pathophysiology of hydrocephalus. In fact, it is difficult to investigate these mechanisms individually because hydrocephalus is such a multifactorial disorder. Nevertheless, a clear distinction can be made between primary or causative mechanisms and secondary responses to ventriculomegaly. Primary mechanisms consist largely of developmental disorders that cause congenital hydrocephalus or pathologies such as intraventricular, subarachnoid, and intraparenchymal hemorrhage, meningitis and other infections, and tumors. Secondary mechanisms are far-reaching and include axonal damage, demyelination, cell death, gliosis and inflammation, biomechanical compression and stretch, edema, metabolic impairment, cerebrovascular effects and hypoxia-ischemia, synaptic and dendritic deterioration, neurotrophic changes, alterations of neurotransmitters and neuromodulators, and impaired clearance of toxins and metabolites. Often these secondary mechanisms overlap, making it difficult if not impossible to define the precise role of each. In spite of these obstacles, an emerging body of evidence is beginning to demonstrate that hydrocephalus (1) manifests, at least initially, as a disorder of periventricular white matter; (2) has a major impact on the structure and function of the cerebral vasculature; (3) involves metabolic and molecular changes that may not produce clinical symptoms but can have protracted effects on neurological function; (4) injures neurons in many ways but does not cause significant neuronal cell death unless ventriculomegaly is severe; (5) often follows a slowly progressive pathophysiological pattern, which may allow considerable plasticity; and (6) is more effectively (but not completely) treated when inter-

vention begins relatively soon after onset. A review by Del Bigio⁴⁻⁹ and several other summaries⁴⁻⁹ provide excellent introductions to the pathophysiology of hydrocephalus, and the reader is encouraged to consult these publications for details.

This chapter summarizes the basic science approaches to experimental hydrocephalus, focusing on new findings produced by such research and identifying promising new areas of research.

EXPERIMENTAL MODELS

Practically all the key questions listed earlier are best investigated, at least initially, in animals, and many *in vivo* models of hydrocephalus have been developed over the past 50 years.¹⁰⁻¹² In addition, there is renewed interest in the use of mathematical models that can be tested in animals. It is appropriate to review these models here because they all have advantages and disadvantages as well as specific relevance to different clinical applications.

Animal Models of Congenital and Transgenic Hydrocephalus

The rat congenital model most often used in experimental research is the H-Tx strain, which develops obstructive hydrocephalus from aqueductal stenosis in the perinatal period.¹³⁻¹⁵ From four chromosomes within a heterozygous background^{13,16,17} and incomplete penetrance,¹⁷ these animals develop hydrocephalus within several days of birth, which in rats corresponds to the third trimester of human brain maturation. In this model, ventriculomegaly becomes severe by the second postnatal week (Fig. 189-1), and the animals usually expire by 20 to 25 days of age if intracranial pressure (which does not rise until postnatal day 12) is not reduced by shunting. Drainage of CSF can be accomplished in H-Tx rats with either ventriculoperitoneal or ventriculosubcutaneous shunts, which are more effective when placed early (3 to 5 days of age) rather than late (12 to 14 days of age). Inbred strains of Wistar-Lewis (LEW/Jms) rats also develop aqueductal stenosis through non mendelian mechanisms as early as day 17 in a 21-day gestational period.¹⁸⁻²¹ The frequency of hydrocephalus and the ratio of affected males to females are significantly higher when the LEW/Jms parent is male. These rat models are excellent for studies of neonatal and juvenile hydrocephalus, especially that caused by aqueductal stenosis, because ventriculomegaly occurs naturally, the brain is large enough for customized shunting, the rats are amenable to behavioral testing, the cost is relatively low, and a wealth of data is available for correlation. Nevertheless, they are not ideal for long-term experiments unless shunting is performed, and their size restricts the use of clinical shunt systems and pressure probes.

Several interesting mouse models of hydrocephalus have provided valuable insights into the causes of ventriculomegaly.^{12,22-26} The most widely used models include the SUMS/NP,^{27,28} *hyh*,^{29,30} transforming growth factor (TGF)- β 1 overexpression,³¹ *hyh* with point mutation in α -SNAP and ependymal denudation³²



FIGURE 189-1 Examples of the H-Tx neonatal rat model of congenital hydrocephalus (**A** and **B**) and the adult rat model of basal cistern-dilated communicating hydrocephalus (**C-M**). **A**, T2-weighted magnetic resonance imaging (MRI) scans illustrating the progression of hydrocephalus at 4, 11, and 21 days of age. **B**, Skull changes correlating to the same ages in **A**; note the conspicuous doming of the head beginning at 11 days, when intracranial pressure begins to rise. **C-F**, T2-weighted images at four coronal locations in the brain of a hydrocephalic animal 4 weeks after kaolin injection. **G-J**, Corresponding images in a saline-injected control animal. Dilatation of all portions of the ventricular system are characteristic of all severely hydrocephalic animals. **K**, Cresyl violet-stained coronal section illustrating the location of kaolin deposits in the basal cistern. **L**, T2-weighted MRI at the same level as **K** showing patent foramina of Luschka (FL). **M**, Midsagittal T1-weighted MRI after gadolinium injection into the frontal horn of the lateral ventricle. Note tracer throughout the subarachnoid space, except at the location of the kaolin deposits in the basal cistern (asterisks). CA, cerebral aqueduct; FM, foramen of Monro. (**A** and **B**, Modified from Jones HC, Harris NG, Rocca Jr, Andersohn RW. Progressive tissue injury in infantile hydrocephalus and prevention/reversal with shunt treatment. *Neurol Res*. 2000;22: 89.)

that precedes aqueductal stenosis,⁴⁷⁻⁵¹ fibroblast growth factor (FGF)-2,⁵² L1-cell adhesion molecule deficient,^{27,53-55} aquaporin deficient,⁵⁶⁻⁵⁹ hpy,⁶⁰ members of the conserved forkhead-winged helix transcription factor gene (previously *Mft*),^{29,61-63} heparin-binding epidermal growth factor,⁶⁴ and collagen deficient.⁶⁵ Most recently, Sweger and colleagues⁶⁶ developed a double transgenic mouse model that allows expression of the G1-coupled R01 receptor exclusive to astrocytes. By controlling R01 expression

with a tetracycline-on promoter in drinking water, these mice develop enlarged ventricles, partial ependymal denudation, morphologic changes in the subcommissural organ, and obliteration of the cerebral aqueduct at designated times. This represents a powerful experimental model because the pathogenesis of hydrocephalus can be studied with neonatal, juvenile, and adult onset. The main disadvantage of these mouse models is that their size limits the use of CSF shunts and invasive physiologic sensors.

Animal Models of Acquired Hydrocephalus

Animal models of acquired hydrocephalus offer the advantages of precise timing, greater efficiency, and sometimes reduced costs. Kaolin, an inert silicate, is a well-accepted agent for inducing hydrocephalus in a wide variety of infant and adult animals (mouse, rat, rabbit, hamster, cat, dog) via injections into the CSF, with no evidence of direct pathologic effects on structures distant to the injection site. Although this induction method is mechanical (surgical) and produces hydrocephalus abruptly, which is not always the case clinically, it is useful when more "natural" models are not available.

Usually obstructive (noncommunicating or intraventricular) hydrocephalus is induced by kaolin injections into the cisterna magna or fourth ventricle, or both. In adult animals (cat, dog, rat, guinea pig, nonhuman primate), such intracisternal obstructions consistently produce a moderate degree of ventriculomegaly, presumably because the fused cranial sutures create a nonexpandable skull. In addition, the more mature brain, with well-developed myelin and less intercellular space, probably influences the extent of ventriculomegaly. In contrast, intracisternal kaolin injections in neonatal and juvenile animals consistently produce severe, rapidly progressing types of hydrocephalus. Skull enlargement always accompanies ventriculomegaly in these animals, and the severity of hydrocephalus is represented by Evans ratios of 0.5 to 0.9 (compared with 0.3 in nonhydrocephalic controls). The neonatal rodent models usually do not survive beyond 3 weeks of age unless treated by CSF drainage; those animals that do survive after this time typically exhibit mild forms of ventriculomegaly. A transitional model of obstructive hydrocephalus has also been used extensively by injecting kaolin into the cisterna magna of 3-week-old juvenile rats. This model remains "pediatric" because brain maturation is only about 50% complete (in rodents, neurogenesis and migration have concluded, myelination has peaked but not finished, and synaptogenesis continues for another 3 weeks), but the skull does not expand.

Communicating extraventricular hydrocephalus has been more difficult to achieve with acquired approaches. Attempts to produce communicating hydrocephalus with kaolin injections into the cortical subarachnoid space of adult rats^{67,68} and dogs⁶⁹⁻⁷⁴ or with silicone injections into the subarachnoid space^{75,76} have consistently produced only moderate ventriculomegaly and usually require a long time (several months) to develop. Likewise, Silastic has been infused into the basal cisterns of monkeys to produce mild forms of communicating hydrocephalus.⁷⁷ Recently, Li and colleagues⁷⁸ developed a novel model of communicating hydrocephalus by injecting kaolin into the basal cisterns of adult rats (see Fig. 189-1); these animals develop moderate ventriculomegaly within a week of induction and exhibit impairments in CSF absorption and pulsatility (see later).

Nonmechanical induction methods, such as viral⁷⁹ and bacterial inoculations,⁸⁰ have also been used to produce communicating hydrocephalus, but these procedures involve the additional influence of the induction substances on pathophysiology and thus are not true representations of the effects of hydrocephalus alone on the brain. Growth factors such as TGF- β and FGF-1 and -2,^{30,41,52} as well as neurotoxins,^{3,81} have all been successful to varying degrees.

An important advance in experimental studies has been the application of CSF shunting techniques.⁸²⁻⁸⁹ Initially, larger models such as feline,^{83,88} lagomorph,⁹⁰ and canine⁹¹⁻⁹⁷ were employed, and these still have the advantage of accommodating commercially available shunt systems. With improved neurosurgical techniques, smaller neonatal, infantile, and juvenile rats have been shunted successfully,⁹⁸⁻¹⁰⁴ but the catheters are usually custom made, and valves are seldom used. It is also important to realize that shunted animals, especially the youngest and smallest ones, develop shunt malfunctions at approximately the same rate

as human patients. Nevertheless, it is surprising that no studies have attempted to evaluate the effects of repetitive shunt malfunction.

Mathematical Models of Hydrocephalus

Several mathematical models have revealed possible mechanisms associated with hydrocephalus.¹⁰⁵⁻¹²² One of the prevailing hypotheses is that the mechanical properties of hydrocephalic brain tissue are fundamentally changed compared with healthy brain tissue. However, this change in material properties has not yet been quantified, so these models and others like them are not useful as predictive models. One particular mathematical model that has been reliable in matching patient outcomes describes the brain as a quasi-linear viscoelastic tissue,¹²³ which essentially means that there is an initial elastic response to ventriculomegaly, followed by a different long-term viscoelastic response. The flaw that prevents this model and all others from being predictive is that the material properties of the brain are not known precisely enough to be useful. CSF infusion tests are available to measure compliance (stiffness) of the brain by monitoring intracranial pressure changes during the injection of artificial CSF into the ventricles or the lumbar subarachnoid space.¹²⁴ These tests have shown that compliance decreases in the hydrocephalic brain.¹²⁴⁻¹²⁷ However, compliance is an extrinsic property of the entire contents of the cranial cavity and can be influenced by the amount of tissue, the amount and flow velocity of blood, the tension of the meninges, and the possible expansion of the skull. In contrast, the material properties needed to construct a predictive mathematical model, such as shear or elastic modulus, are intrinsic properties of brain tissue independent of the amount of tissue. Current tissue testing methods to acquire intrinsic properties typically involve the removal of brain tissue for mechanical tests, but this approach eliminates many structural and physiologic factors of the "living" brain, especially the mechanical support offered by blood volume and flow, that tend to hydraulically stiffen the tissue. Fortunately, a mechanical testing method has been developed that allows direct measurement of the initial elastic response as well as the long-term viscoelastic response of "living" brain tissue.^{134,135} This method uses a mechanical probe that displaces the surface of the cortical tissue inward slightly and holds the displacement for a period of time, which is an ideal way to investigate tissue properties without damaging the brain.

Magnetic resonance elastography^{136,137} measures the elastic properties of brain tissue *in vivo*, based on the propagation of waves through deformed tissue detected with magnetic resonance imaging (MRI). Tissues with different material properties conduct these waves differently. Although this method holds great potential for noninvasive tissue property measurement, the true material properties of the brain (healthy or hydrocephalic) have yet to be measured directly, so the accuracy of this method has not been verified. In addition, the device used to perform the mechanical perturbation of the tissue requires a flat surface,¹³⁸ so more developed gyral hemispheres are problematic, and the device is too large for rodent brains.

Nevertheless, once they are measured accurately, the intrinsic material properties of the hydrocephalic brain would be useful in the treatment of this disorder. Clinical decision making could benefit from knowing whether the relative stiffness of the brain increases with repeated shunt malfunction or at certain ages.

PATHOPHYSIOLOGIC MECHANISMS AND TREATMENT POSSIBILITIES

Several previous reviews have provided excellent summaries of the pathophysiology of hydrocephalus.^{2,4,5,138-140} In general, mechanisms of injury include morphologic and functional changes in

the cerebral vasculature, hypoxia-ischemia, gliosis and neuroinflammation, edema, axonal degeneration and impaired intracellular transport, demyelination and oligodendrocyte death, dendritic and synaptic degeneration and plasticity, altered levels of neurotransmitters and neuromodulators, and impaired protein clearance¹⁴¹ and lymphatic absorption. Exciting new data have revealed several novel mechanisms, dramatically broadening the view of the pathogenesis and secondary pathophysiology of hydrocephalus. These new findings are presented here rather than providing an exhaustive review of experimental studies.

Gliosis and Inflammation

Gliosis is a consistent finding in hydrocephalus, and inflammation and glial scar formation could play a major role in creating the chronic problems that plague hydrocephalic patients, but the time course and permanence of the reaction are not completely known.^{24,38,142-153} It has been suggested by many investigators that scar formation is a permanent fixture in hydrocephalic brains,^{90,144,152} even those that have been shunted successfully. Previous studies in both congenital and acquired models of hydrocephalus have shown that glial fibrillary acidic protein (GFAP) RNA and protein levels increase with the progression of hydrocephalus. Additionally, Mangano and colleagues¹⁵² illustrated that microglial cell proliferation and activation increased in regions distant from the cortical "lesion," suggesting that neuroinflammation is related to damage throughout the cortical pathways. Furthermore, GFAP-labeled reactive astrocytes surround cystic lesions in severely hydrocephalic H-Tx animals but are not present in the white matter surrounding the ventricles.^{154,155} Experimental models of hydrocephalus have demonstrated that shunting can reduce the amount of GFAP protein and RNA present in the cerebral cortex, but these levels begin to rise over time,⁸⁹ suggesting that reactive astrogliosis is highly sensitive to suboptimal CSF drainage. Clinically, increased levels of GFAP protein have been found in the CSF of patients with normal-pressure hydrocephalus and those who developed secondary hydrocephalus due to subarachnoid hemorrhage.¹⁵⁶⁻¹⁶⁰ The possibility of using GFAP protein levels as a diagnostic tool for hydrocephalus is currently being explored.^{158,161}

It is likely that gliosis may dramatically change the mechanical properties of the brain so that it becomes more rigid (less compliant) and resistant to increases in CSF pressure and flow.^{162,163} The importance of these properties in hydrocephalus is illustrated by the finding that reduced compliance, measured using the pressure-volume index, is a better predictor of shunt success than measurements of ventricular size.^{162,172,173} Unfortunately, no studies have directly examined the relationship between glial alterations and intracranial compliance. Compliance can be measured in animals using CSF infusion tests,¹⁷⁴⁻¹⁷⁶ and in hydrocephalus, resistance to CSF outflow is increased over a wide range of intracranial pressures.¹⁷⁶ Compliance is usually lower in hydrocephalic animals, but it varies depending on intracranial pressure.

Most recently, an interesting and potentially powerful relationship has been suggested between astrocytes and aquaporin channels, which can have major impact on CSF absorption. Aquaporins are cell membrane proteins, and most are permeable only to water.¹⁷⁷⁻¹⁸⁰ Aquaporin 4 (AQP4) is found primarily on the endfeet of astrocytes that contact microvessels in the periventricular white matter and the subpial region of the cerebral cortex,¹⁸¹ as well as in ependymal cells lining the lateral ventricles. These locations place astrocyte aquaporin channels in a good position to transport CSF from the brain to the vascular system, and several investigators have suggested that they may play a major role in CSF absorption.¹⁸² Aquaporin channels require connections to a basal lamina that specifically contains

collagen XVIII molecules; if these connections are not present, hydrocephalus ensues.^{65,183,184} One structural response of endothelial cells to chronic hypoperfusion is an abnormal basal lamina,¹⁸⁵ so it is not surprising that aquaporin changes have been reported in experimental hydrocephalus.^{56,186-188} More directly, expression of AQP4 (but not AQP1 or AQP9) increases in the cerebral cortex and hippocampus of rats with mechanically induced hydrocephalus, suggesting that this water channel plays a compensatory role in CSF absorption during ventriculomegaly.¹⁸⁶ Fibrosis in the form of reactive astrogliosis could therefore have an important impact on CSF absorption, which might not recover with ventricular shunting alone.

Minocycline has recently shown promise as a specific inhibitor of microglial cells,¹⁸⁹⁻¹⁹² one of the main elements of glial scar formation in hydrocephalus.^{89,152,193,194} Although the mechanism of action is still unknown, minocycline has multiple benefits in brain injury,^{191,195-227} and its promise as a neuroprotective agent is illustrated by the recent initiation of clinical trials in Parkinson's disease,^{228,229} Huntington's disease,²³⁰⁻²³³ amyotrophic lateral sclerosis,²³⁴ multiple sclerosis,^{235,236} and schizophrenia.^{237,238} Based on previous studies showing positive effects in white matter,^{195,203,215,239-242} Miller and McAllister²⁴³ initiated tests of minocycline's ability to inhibit gliosis in the H-Tx rat model of congenital hydrocephalus. Preliminary results are encouraging, in that both numbers of glia (astrocytes and microglia) and cortical mantle thickness were significantly reduced when minocycline was administered after hydrocephalus had progressed considerably (Fig. 189-2).

It should be noted that to date only a few other studies have attempted to protect the hydrocephalic brain by infusing nimodipine, a calcium channel antagonist, into the ventricles of juvenile hydrocephalic rats to reduce white matter damage, but these interventions produced only limited short-term success. Nevertheless, in the near future pharmacologic successes achieved in animal models of hydrocephalus have a strong likelihood of leading to supplemental clinical treatments for humans.

Intracranial Pulsatility

Thirty years ago, Di Rocco and coworkers²⁴⁴ showed that ventricular dilation can be caused by abnormal intracranial pulsatility in the absence of a physical obstruction to CSF flow. Abnormal intracranial pulsations are also clearly related to clinical hydrocephalus; intraventricular pulsatility, detected as CSF pulsations in the aqueduct on cine MRI, are often dramatically elevated in hydrocephalus²⁴⁵⁻²⁴⁸ and can be a useful diagnostic criterion in normal-pressure hydrocephalus. Although authors have posited theories on the cause of these elevated pulsations,²⁴⁹⁻²⁵¹ no study has provided a clear link between abnormal pulsations and the underlying pathophysiology of hydrocephalus.

Furthermore, the dissipation of cerebral arterial pulsatility, resulting in minimal (homeostatic) capillary and venous pulse pressure, is believed to be critical for normal cerebrovascular function.²⁵¹⁻²⁵⁴ Although dissipation is easily accomplished in other organs, the closed cranium requires a more complex system for this function; CSF and venous blood serve this purpose. The major arteries entering the cranium are located within the CSF-filled subarachnoid spaces, allowing the efficient coupling and transfer of pulsation. Pulsations can be transferred out of the cranium either directly via CSF flow through the foramen magnum into the compliant spinal subarachnoid space or indirectly via coupling to the sagittal sinus within the convexity. An important component of the pathophysiology of hydrocephalus is a change in intracranial compliance, which may lead to a redistribution of the pulsation dissipation mechanism.^{250,251} One potential pathway is directly into parenchymal capillaries. Thus, hydrocephalus may be caused by a breakdown in this pulse dissipation mechanism (or a failed windkessel),^{251,253,255-258} which

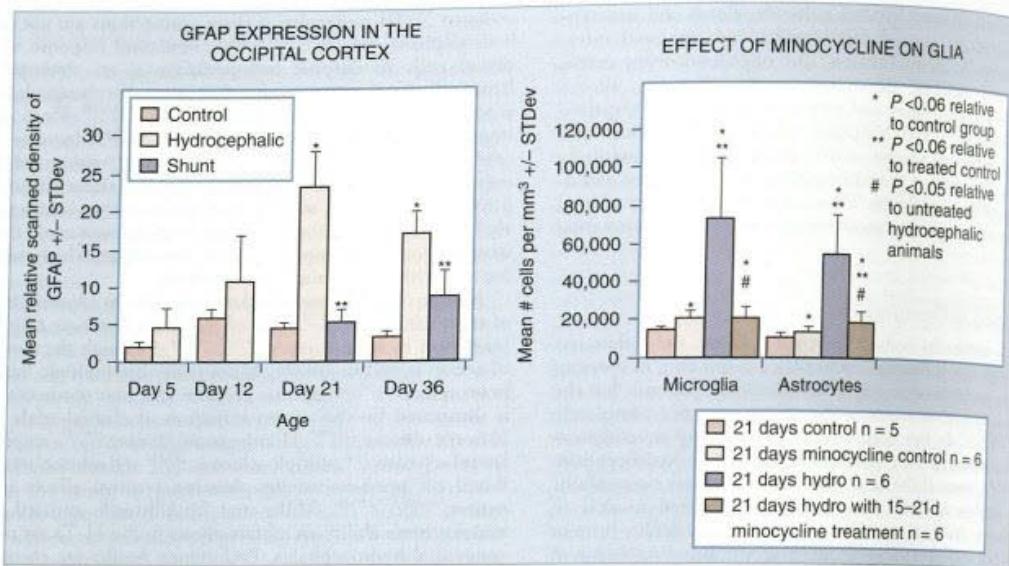


FIGURE 189-2 Stereologic analyses depicting changes in astrocytes in H-Tx rats with congenital hydrocephalus. The graph on the left shows the effects of progressive hydrocephalus on glial fibrillary acidic protein (GFAP) levels in the occipital cortex of control, untreated hydrocephalic, and shunted hydrocephalic H-Tx rats ($n = 5$ for each group). In untreated animals, increases began at 5 days (2.46-fold; $P = .08$), progressed at 12 days (1.81-fold; $P = .17$), and became significant by 21 days (5.26-fold; $P = .0008$). Ventricular shunting at 15 days of age significantly reduced GFAP levels within 6 days (5.23-fold; $P = .0003$). However, shunted animals with longer recovery periods exhibited higher GFAP levels than normal, suggesting that residual astrogliosis persists. $P < .05$ relative to control (*) and untreated hydrocephalic (**) groups. The graph on the right shows the effects of minocycline administered to H-Tx rats at 15 to 21 days of age with severe ventriculomegaly. Note that minocycline significantly reduced the density of both astrocytes and microglia.

normally protects the capillary bed from excessive pulsatile shear forces.

Increased capillary pulsatility may have several pathophysiological consequences. Structural responses may lead to the loss of parenchymal microvessels, and in fact, decreased capillary density has been shown in experimental hydrocephalus.^{4,159–264} In addition, the integrity of the blood-brain barrier is compromised in hydrocephalus.^{265–267} Both these effects might explain the marked loss of cerebral perfusion that has been well documented in clinical^{268–282} and experimental hydrocephalus.^{14,67,276,278,283–289} Importantly, it was recently shown that excessive pulsatile stress can impair hemodynamics through changes in endothelial cell homeostasis^{290–293} mediated by nitric oxide.²⁹⁶ A marked increase in nitric oxide synthase immunoreactivity has also been reported in a kaolin hydrocephalus rat model during the first few weeks of ventriculomegaly.²⁹⁶ These examples all provide a compelling case for the importance of pulsation dissipation in maintaining normal capillary function.

Zou and colleagues²⁹⁷ and Wagshul and associates,²⁹⁸ using two different types of analyses, recently showed that adult dogs normally exhibit a pulse dissipation mechanism termed a *notch* (because when intracranial pressure is graphed against frequency, it appears as a trough) and that this notch changes as pressure is raised. Further studies are needed to determine whether this change in intracranial hydrodynamics is causative or a secondary response to ventriculomegaly. One series of investigations that addressed this issue used the novel model of communicating hydrocephalus in adult rats described earlier.⁷⁸ Using high-field-flow MRI in this model, Wagshul and coworkers²⁹⁹ demonstrated that aqueductal pulsatility (stroke volume) increased within 24 hours of basal cistern obstruction, and the severity of ventriculomegaly was associated with the maintenance of high stroke volume. In contrast, only mild ventriculomegaly developed in

animals that exhibited an early but transient increase in aqueductal pulsatility. These experiments clearly indicate that pulsatility plays a role in the pathophysiology of experimental hydrocephalus (Fig. 189-3).

Cerebrospinal Fluid Absorption—Lymphatic, Arachnoid, Microvascular

The traditional view of CSF absorption exclusively via arachnoid granulations into the superior sagittal sinus or the veins adjacent to the spinal roots has been challenged by a series of experiments.^{300–310} Initially, the results of these experiments were challenged because they were performed on animals or human cadavers and consisted of latex Microfil infusions to reveal potential CSF pathways from the subarachnoid space. However, the latest *in vivo* studies clearly demonstrate that cranial lymphatics, most notably the nasal pathways surrounding the olfactory nerves, are capable of transporting large volumes of CSF. Most important, these pathways are impaired in adult rats with communicating hydrocephalus (Fig. 189-4).

CONCLUSION

In summary, the field of experimental hydrocephalus has grown dramatically in the past 20 years. It has evolved from early characterizations of the multifactorial pathophysiology of the disorder to current improvements in diagnostic evaluations and pharmacologic interventions to supplement CSF shunting. A wide variety of animal models are available for comprehensive, controlled studies, and CSF drainage procedures have been employed in many of these models. Most recently, advanced experimental approaches have identified novel, progressive

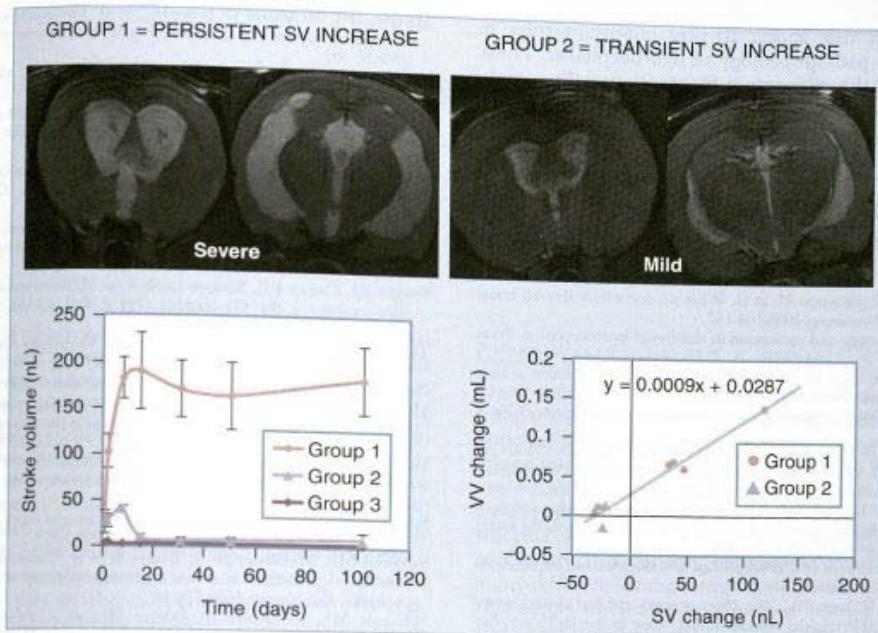


FIGURE 189-3 Aqueductal pulsatility (stroke volume [SV]) in adult rats with communicating hydrocephalus induced by kaolin obstruction of the basal cisterns. Based on the size of the pulsations and their temporal course, the animals clustered into three distinct groups: group 1 ($n = 5$) exhibited marked increases in aqueductal pulsation, rising mostly within the first 1 to 2 weeks and persisting throughout the entire study; group 2 ($n = 3$) exhibited modest initial increases in pulsations that persisted for the first week and then returned to near normal levels; and group 3 ($n = 7$) exhibited no changes in aqueductal pulsations compared with baseline values or intact controls. VV, ventricular volume.

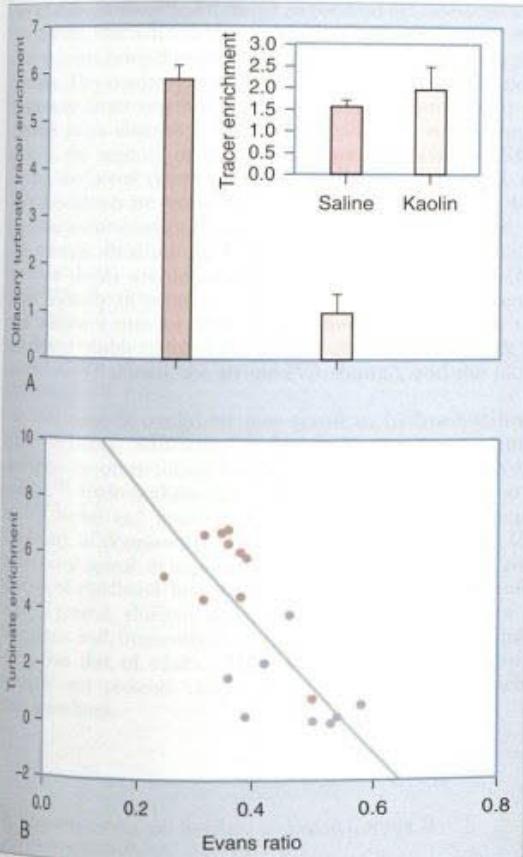


FIGURE 189-4 Absorption of cerebrospinal fluid by nasal lymphatics in adult rats with communicating hydrocephalus caused by basal cistern obstruction. **A**, Lymphatic absorption, measured by tracer levels in the olfactory turbinates following injection into the lateral ventricle, was significantly lower in hydrocephalic animals ($P < .0001$). The magnitude of ventriculomegaly is reflected in the Evans ratios (inset). **B**, The decrease in lymphatic absorption correlates well with the severity of hydrocephalus; hydrocephalic animals (red dots) with the most enlarged ventricles exhibited the lowest levels of absorption. (Modified from Nagra G, Li J, McAlister JP II, et al. Impaired lymphatic cerebrospinal fluid absorption in a rat model of kaolin-induced communicating hydrocephalus. Am J Physiol Regul Integr Comp Physiol. 2008;294:R1752.)

mechanisms of injury that appear to play important roles in the pathogenesis and pathophysiology of hydrocephalus. These studies have renewed the momentum for translational research, and future work will determine the roles of intracranial pulsatility, gliosis and neuroinflammation, and alternative CSF absorption pathways in hydrocephalus.

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Ventricular Shunting Procedures

Jeffrey P. Blount

The development of effective shunt procedures represents a landmark accomplishment in neurosurgery. Despite a somewhat notorious failure rate that has spawned a sinister reputation within neurosurgery, the fact remains that no other frequently performed neurosurgical procedure has saved more lives in western society than the placement and revision of ventricular shunts. Although comprehensive epidemiologic studies have never been performed, it is estimated that approximately 25,000 shunts are placed each year in North America and twice as many are revised (total of 75,000 shunt operations).¹⁻⁵ Shunt operations remain the most frequently performed operation by pediatric neurosurgeons, and they are the most common reason why children undergo any form of brain surgery.^{3,4} Even though endoscopic third ventriculostomy (ETV) has demonstrated promising and significant clinical utility, its overall role in managing hydrocephalus remains controversial; it appears fair to conclude that less than 50% of patients with hydrocephalus can be successfully managed over the long term with ETV.⁶⁻⁸ Accordingly, it appears that there will continue to be a significant role for ventricular shunts for the foreseeable future.

The word *shunt* is derived from the Middle English word *shun*, which indicates being pushed away or "to the side" and suggests diversion. This is appropriate because the fundamental role of shunts is to divert cerebrospinal fluid (CSF) from within the ventricles to an alternative location outside the subarachnoid space. In the majority of clinical situations in which CSF is diverted, the lateral ventricle is the initial source of CSF, and hence these shunts are ventricular shunts. The site to which CSF is diverted is characteristically added as a suffix. For example, the most common distal site for CSF diversion is the peritoneum, and these shunts are described as ventriculoperitoneal (VP) shunts. Virtually all anatomic sites have been tried as potential distal placement sites for ventricular shunts, but the ones that have proved reliably useful over time at many centers include the peritoneum (VP shunts), the atrium (VA shunts), and the pleura (VP shunts).

A wide range of conditions may result in hydrocephalus in adults, including subarachnoid hemorrhage, head trauma, meningitis (or other infections), and normal-pressure hydrocephalus.^{9,10} Hydrocephalus is more common in children (1 in 2000 births) and most often arises from intraventricular hemorrhage of prematurity, congenital anomalies of the CSF pathways, or spinal dysraphism/myelodysplasia or as a complication of childhood brain tumors, head injuries, or infections. In general, children are more absolutely dependent on their shunts and frequently have a more complicated clinical course than that of adults. This chapter reviews established principles and presents recent developments in ventricular shunt procedures.

COMPONENTS OF A SHUNT SYSTEM

Every shunt system consists of three central components—a ventricular catheter, a valve, and a distal catheter. Additional components such as tapping reservoirs, on-off devices, pressure transducers, and antisiphon devices may also be present, and there may be more than one ventricular catheter. *Simple* shunts have only a ventricular catheter, valve, and distal catheter, whereas *complex* shunts have more elaborate arrangements. Most commonly this consists of multiple ventricular catheters, but many different arrangements are possible. Loculated hydrocephalus occurs when fibrotic adhesions develop within the ventricles and cause isolated pools of CSF to arise that maintain independent capability of dilating and expanding. Before the development of contemporary endoscopic fenestration techniques, each of these loculated spaces required a ventricular catheter to ensure adequate drainage. Multiple ventricular catheters are still occasionally required for complex multiloculated hydrocephalus and are commonly required for some well-established congenital anomalies such as the Dandy-Walker variant or anomaly. Some commercially available systems have fused one or more of the aforementioned elements together to form a unishunt (to prevent potential disconnection²¹), but these systems still contain the same three conceptual components as all others.

Ventricular Catheter

The ventricular catheter is the component of the shunt that traverses the space from the ventricle to the valve. A variety of designs of ventricular catheters have been used over the years, but they share similar design principles. The rostral end of the catheter has a rounded tip and multiple holes along the proximal shaft of the catheter. Different design models have featured holes of different size. Proximal ventricular catheter obstruction is the most common cause of mechanical shunt failure, and the tissue implicated in such failure is an ingrowth of CP and gliotic neural tissue.²² Initially, it was thought that larger holes in the ventricular catheter would result in fewer shunt obstructions; however, experience with catheters with large holes showed that proximal obstruction still occurred. More importantly, the larger holes provided an opportunity for more robust ingrowth of CP and a secondary risk for hemorrhage when the catheters needed to be removed for revision. Other types of ventricular catheters were developed with mechanical adjuncts to keep CP away from the holes.²³ The Portnoy catheter had a series of Silastic ribs that gave it an appearance similar to a honey dipper and were designed to deflect the CP. Similarly, the Carrea cage had a series of four rib-like Silastic structures that laid in parallel with the shaft of the catheter and were designed to deflect CP away. Both systems were associated with higher rates of hemorrhage and revisions and did not prevent proximal catheter obstruction. As a result, most current systems have multiple rows of very small holes arranged concentrically along the axis of the ventricular catheter. The exact number of holes or volume necessary to ensure adequate flow has never been firmly established, and it appears to be

an area of modest investigation. Ginsberg and colleagues demonstrated that a single 500- μm -diameter hole permits flow and relieves the associated hydrostatic pressure.²⁴ However, these investigators were seeking to understand the minimum volume that needed to be opened to ultrasonically clean an obstructed catheter rather than determine the necessary or optimum criteria for shunt flow. Lin and associates demonstrated that approximately 60% of flow occurs through the first row of holes in a shunt catheter and that more than 80% flows through the first two rows. Further understanding of the mechanisms contributing to proximal catheter function may substantially reduce morbidity from proximal shunt malfunction.²⁵

Another important recent technologic advance in ventricular catheter design is the antimicrobial impregnation of ventricular catheters with antibiotics (antimicrobial-impregnated shunts). Two systems are commercially available. In the Codman Bac-tisite system, the catheter is impregnated with clindamycin and rifampin as part of the manufacturing process. This patented process results in the gradual release of antimicrobials over a period of approximately 4 weeks after implantation of the device. Clindamycin and rifampin are the preferred antimicrobials because of technical issues involving incorporation into the polymer, even though other antibiotics have greater effectiveness against organisms that commonly cause shunt infection. Results have varied widely, with some groups reporting nearly complete elimination of shunt infection after incorporation of antimicrobial-impregnated shunts. Other series have demonstrated a modest or nil impact of antimicrobial impregnation. The second

commercially available system is the Medtronic BioGide system, in which the ventricular catheter is impregnated with a polymer that gradually absorbs antibiotic when the device is soaked in a solution of antibiotic. The advantage of the system is that it affords the operating surgeon the choice of antibiotics to use. The disadvantages are that the catheter becomes very slippery and can readily be dropped or disconnected. Furthermore, the antibiotic migrates off the device more rapidly, and there is markedly less published experience with this system.²⁶

Future directions in ventricular catheter development are likely to center on efforts to prevent proximal obstruction and infection. Very limited numbers of papers and presentations have described preliminary experience with nanoparticles and varying hole size and distribution in catheter design. Further refinement of technique in antimicrobial-impregnated systems is likely, as well as properly designed and powered studies to determine the overall effectiveness of antimicrobial impregnation.

Shunt Valves

Since development of the first Spitz-Holter and Pudenz valves, valve design has received the greatest attention in the overall development of effective shunt systems (Table 190-1).²⁷ Although this empirically appears logical because the valve is mechanically the most complex (and hence potentially most vulnerable) part of the shunt, several important studies have shown that valve mechanics play a limited role in the overall rate of shunt failure or success. The first of these landmark studies was

TABLE 190-1 Shunt Valves

| Fixed-pressure valves | Flow-regulated valves | Programmable pressure valves |
|---|---|---|
| <ul style="list-style-type: none"> Hakim Microprecision <ul style="list-style-type: none"> • 0-5 cm H₂O outflow resistance • Siphonguard (ball and cone) can prevent overdrainage • Codman (Johnson and Johnson) Company  | <ul style="list-style-type: none"> Delta <ul style="list-style-type: none"> • Delta Chamber opens for free flow if ICP high • Elastomer diaphragm mechanism • 0.5, 1.0, 1.5, 2.0, 2.5 levels available • Medtronic  | <ul style="list-style-type: none"> Strata <ul style="list-style-type: none"> • Ball/spring mechanism with magnet • Programmable/noninvasive • Incorporated Delta chamber • Medtronic  |
| <ul style="list-style-type: none"> PS Medical <ul style="list-style-type: none"> • Injectable reservoir • Nonmetallic • Low-low, low, medium, and high pressure outflow available • Medtronic  | <ul style="list-style-type: none"> Orbit-Sigma OSV II <ul style="list-style-type: none"> • First flow-regulated valve • Three stage variable resistance mechanism • Magnet neutral/MRI safe • Integra  | <ul style="list-style-type: none"> Codman Hakim <ul style="list-style-type: none"> • Noninvasive programs among 18 preset levels • Ball/spring mechanism • Codman (Johnson and Johnson) Company  |
| <ul style="list-style-type: none"> Chhabra <ul style="list-style-type: none"> • Low cost—widely used in developing world • Made in India • Mechanism: Z flow system of three balls  | | <ul style="list-style-type: none"> Sophy <ul style="list-style-type: none"> • First adjustable valve • Silicone-coated polycarbonate chamber • Ball-cone mechanism with variable pressure spring • Sophysa  |
| | | <ul style="list-style-type: none"> Polaris <ul style="list-style-type: none"> • MRI compatible variable valve • Self-locking magnetic system • Sophysa  |

the Shunt Design Trial, a multicenter prospective survey of the effectiveness of different widely used shunt systems in the 1990s.^{30,31} In this trial the three most common types of commercially available shunts were compared with regard to shunt function. No difference was noted in the initial report, nor with longer term follow-up.³⁰ Other subsequent studies have repeated this finding.³¹

There has been an evolution in valve design over time that can broadly be classified into three conceptual approaches. The first of these was fixed-pressure valves, the second was flow-regulated or differential flow valves, and the third incorporates valves in which resistance to outflow of CSF can be altered or programmed noninvasively.

Fixed-pressure valves were the first valves developed for ventricular CSF shunts and overcame a significant barrier to successful CSF shunting, which was the development of low-pressure headaches. There are four different design styles of fixed-pressure valves: silicone rubber slit valves, silicon rubber diaphragm valves, silicon rubber miter valves, and metallic spring and ball valves. Each of these designs shares a common technical goal, which is to provide fixed resistance to outflow of CSF from the ventricle. If such resistance is not provided, the majority of patients will suffer from overdrainage, low-pressure chronic severe headaches. The resistance values are manufactured to three broad levels (low, medium, and high) that reflect different ranges within the normal spectrum of intracranial pressure. Examples of fixed-pressure valves that were widely used include the (first-generation) Hakim valves, the PS Medical (differential pressure) valve, the Denver valve, and the Chhabra valve, which is manufactured in India and still used widely throughout the world.^{32,33} Generally, these valves functioned well, but over time it became evident that debilitating overdrainage headaches still developed in up to 10% to 12% of patients with fixed-pressure valves. Clinically, this was manifested as an unyielding and life-altering headache that was accompanied by radiographic evidence of successful insufficient drainage (typically small or nonvisible ventricles on computed tomography [CT]).^{34,35} This led to the development of flow-regulated valves, which regulated the amount of flow through the system when they were functioning within the normal physiologic range. The two most widely used systems of this design are the PS Medical Delta valve and the Orbis Sigma valve.^{32,35}

Programmable valves can be adjusted noninvasively to vary resistance to outflow across a physiologically normal range. Two clinical observations drove the development of variable-pressure programmable valves. The first was that a significant (although smaller than with fixed-pressure valves) subset of patients treated with flow-regulated valves suffered from chronic headache. The second was the belief among selected groups of neurosurgeons that the ideal outflow resistance for an individual patient was a dynamic rather than a static system. Thus, the ideal outflow pressure for a patient varies with time, and periodic manipulation of outflow pressure ensures optimal function and the fewest symptoms of discomfort. For a persistently symptomatic patient plagued with endless headaches, outflow resistance can be varied to minimize or eliminate symptoms. Controversy still surrounds these ideas, and there are broad variations in clinical practice with regard to the utility of externally programmable valves. Proponents of the less costly flow-regulated valve systems contend (1) that the vast majority of pediatric patients do not require variable outflow resistance and the additional cost is unnecessary and (2) that manipulation of outflow resistance can distract one from the far more common problem of proximal catheter obstruction and can lead to delays in diagnosis of shunt failure. An additional vulnerability of programmable valves is the requirement that they be retested and reset after magnetic resonance imaging (MRI) because the magnetic field of the scanner characteristically affects settings of the programmable valve. Proponents of programma-

ble valves consider the capability of varying outflow resistance of the shunt an important and nearly essential tool in the armamentarium used in treating hydrocephalus.³⁶⁻⁴¹ The only prospective trial that compared programmable (Strata) and non-programmable valves showed similar survival across groups.⁴² Another important prospective study compared conventional flow-regulated valves with the markedly less expensive Chhabra system that is produced in India and found no difference in shunt survival in groups of shunted children in sub-Saharan Africa.⁴³

There appears to be greater consensus that programmable valves play a valuable role in treating adults with hydrocephalus. This is particularly so for older patients, who are at risk for the development of normal-pressure hydrocephalus and thereby at increased risk for the development of subdural hematomas.^{43,44} In this patient group, the programmable valve allows outflow resistance to be initiated at a higher level to prevent sudden ventricular decompression with concomitant ventricular collapse, cortical infolding, and tearing of the draining veins. Once an initial period of drainage is completed and a period of adjustment to ventricular shunting has occurred, outflow resistance can be decreased or adjusted as needed to optimize the clinical impact of ventricular drainage.⁴⁵

Distal Catheter

The distal catheter is by far the largest and longest component of a ventricular shunt, but it generally functions the best and has the fewest problems of all the shunt components. The most common problem related to distal catheter function is fracture of the catheter.⁴⁶ Fracture characteristically occurs at points where movement across the shunt is maximized. In practical terms, this means that most ventricular shunts that fracture do so between the mastoid and the clavicle. This is the region of greatest movement because the shunt is secured to and moves with the skull above and the chest wall and abdomen below. The distal catheter may also pull out of the atrium or peritoneum with growth of the patient, or an infected pseudocyst may develop around the distal catheter tip, but these are not problems in which the catheter itself can be implicated as being causative.⁴⁷ Hernia or varicoceles with migration of the distal catheter into the scrotum of a male patient have also been repeatedly observed and reported.^{48,49} Infection of the shunt may result in the development of an abdominal pseudocyst around the distal catheter. This was originally thought to be focal ascites, but focal distal CSF accumulation is now thought to strongly suggest infection.^{50,51} Tunneling for placement of the distal catheter can cause traumatic injury to adjacent structures.⁵² Very rarely, perforation of a hollow viscus may occur.⁵³⁻⁵⁵ Each of these complications has spurred innovative approaches in design that have resulted in a number of structural variations in distal catheter construction.⁵⁶

The proximal end of the distal catheter is always open to enable coupling with the shunt valve, but the distal end of the shunt catheter may be either open or closed with a distal slit.^{57,58} Other distal tip designs have incorporated basket-like projections around the distal tip to prevent obstruction to outflow from adjacent tissues (e.g., omentum) within the peritoneum. One system that was initially popular in the 1970s incorporated a spring into the distal catheter tip. The intent of the spring was to prevent distal kinking and obstruction, but an unfortunate side effect (which led to U.S. Food and Drug Administration [FDA] notification and virtual elimination from widespread use) was a pronounced increase in the incidence of viscus perforation.

The distal catheter may be homogeneously impregnated with barium or may have only a single stripe of barium within its wall. Barium impregnation allows the catheter to be visualized radiographically and fractures or placement problems (e.g., tight coiling within the abdomen, which may suggest preperitoneal placement) to be detected. Some authors contend that solid

barium catheters tend to leach barium salts over the extended life span of the shunt. The barium in turn is thought to precipitate locally within tissues as barium salts, which increases the focal tethering effect and risk for catheter fracture.⁵⁹ Catheters with single barium stripes leach less barium, are associated with a reduction in local tethering from the deposition of barium salts, and consequently appear to have a lower risk for fracture. The practical tradeoff is that catheters with barium stripes may be more difficult to see on routine radiographs, particularly in large or obese patients.

Distal catheters, like ventricular catheters, may also be impregnated with antimicrobials that are gradually released into the local tissue in the days or weeks after shunt implantation. Rifampin and clindamycin are the most commonly used antibiotics that are directly impregnated into the shunt system (Codman Bactiseal System R). Antimicrobial impregnation has appeared in many series to reduce shunt infection rates, but the results remain mixed.

COMMERCIALLY AVAILABLE SHUNT SYSTEMS

There are dozens of commercially available shunts on the market in the western world. The best choice for any given patient must be made on an individualized and admittedly subjective basis that takes into account the neurosurgeon's experience and confidence in a particular system, as well as circumstances unique to the cause and clinical history of the patient's hydrocephalus. Although many individual studies have claimed superior performance for a given system, there is no compelling concordance of findings that indicates the superiority of any given system or combination of components. There has been a general trend toward the use of flow-regulated valves, and the proponents and critics of programmable and antimicrobial-impregnated systems embrace and support their views fervently. However, no shunt system has been convincingly shown to be superior overall. Warf and colleagues³³ made this point most strikingly in a report that retrospectively compared overall shunt performance between groups of children in Uganda in whom the Codman-Hakim Micro-Precision shunt system from North America or the Chhabra shunt system manufactured in India was implanted. Despite the fact that the Chhabra shunt system costs a small fraction of the cost of the other shunt system, there was no statistically significant difference in overall performance. These findings, however, cannot be directly extrapolated to Western practice for several reasons. First, the groups were not identical and the review was retrospective and suffered from the inherent limitations of this design. Furthermore, the Chhabra system has not been subjected to evaluation by the FDA, which since 1976 has been granted authority by Congress to issue regulations requiring reporting of adverse events for marketed medical devices. Whether the progressively complex and expensive shunt systems that are being designed and released should be tested against existing equipment in head-to-head trials before release to the public appears to be a fair one in a progressively austere medical economic climate.

SHUNT INSERTION

Ventriculosubgaleal Shunts

Rationale and Indications

Ventriculosubgaleal (VSG) shunts have limited application and inherently limited duration of function. However, in appropriate circumstances (e.g., premature infants with very low birth weight), VSG shunts are extremely useful and safe.^{60,61} With this shunt,

CSF is diverted from the lateral ventricle to a small pocket that is gently dissected beneath the galea. From this location, CSF enters the cervical lymphatics and can be absorbed gradually for several weeks or months. These shunts are typically used as temporizing devices in very small premature infants in whom intracerebral hemorrhages of prematurity and posthemorrhagic hydrocephalus develop. These infants are often fragile and very ill and are uniquely sensitive to temperature and blood loss.^{62,63} Accordingly, the rapid and relatively avascular way in which these devices can be placed offers a decided advantage. Other temporizing uses of VSG shunts have been proposed.^{64,65}

A VSG shunt consists of a short (3.5 to 4 cm) segment of standard ventricular catheter that is connected to a shorter segment of distal catheter with a distal slit valve on its end. The connection typically occurs either via a right-angle connector or via a Rickham-style reservoir. The advantage of the Rickham reservoir is that the device can be tapped percutaneously; but its disadvantage is that the higher profile of the reservoir places tension on skin that is already thin and potentially compromised. Closing the skin on a macrocephalic neonate is typically the most challenging component of a shunt operation in neonates. As a result of the macrocephaly (which may at times be profound), the already thin skin become stretched to such a degree that multiple-layer closure becomes impossible.

The function of the distal slits in the subgaleal shunt is to ensure unidirectional flow. CSF leaves the ventricle, traverses the right angle connection and the distal slit valve, and accumulates in the subgaleal space. A subgaleal fluid collection of variable size will form, but the varying size of the pocket does not correlate with effectiveness of the pocket. At times, the accumulation of CSF can be sizable and can rarely be unsightly. However, VSG shunts offer a unique advantage over the alternative shunt system widely used for posthemorrhagic hydrocephalus of the neonate (the ventricular reservoir shunt): the VSG shunt drains continuously and does not have to be serially tapped. Another significant advantage of the VSG shunt is that its simple valve design does not appear to be sensitive to the presence of considerable amounts of blood or protein.

Infection and complication rates with VSG shunts are low.⁶⁶ Infection is typically manifested as shunt failure with rapid retraction of the pocket. More classic signs of infection such as erythema and fever are uncommon. Wound failure is a common problem with these procedures because of the delicate quality and inherent fragility of neonatal skin. In practical terms, VSG shunts take about 10 to 20 minutes to insert and optimally last about 8 to 12 weeks. Consequently, they do not represent an effective long-term treatment of hydrocephalus but may play a very valuable role in temporizing until more definitive treatment with a VP shunt can be accomplished when the child is a little older (and has more acceptable anesthetic risks and less risk for hydrocephalus).⁶⁸

Technique

The VSG shunt is typically inserted from a coronal approach. The patient is placed under general anesthesia and is positioned supine. Great attention is paid to the infant's temperature, and warming blankets and temperature are adjusted accordingly. A small curvilinear incision is planned and marked at the lateral edge of the fontanelle. After preparing the scalp and draping, the scalp is opened to the level of the dura. The shunt system is assembled on the back of the table in advance. Three to four centimeters of ventricular catheter is connected to a right-angle catheter, which in turn is connected to the terminal 2 to 3 cm of a peritoneal catheter with two distal slits. Connections are secured with silk sutures. The scalp is then gently elevated and broadly dissected with Metzenbaum scissors or a Kelly clamp to provide a distal pocket for CSF. The dissection should not extend beyond

the hairline to prevent potentially unsightly fluid collections over the face. Once the pocket is dissected, the dura is coagulated and opened sharply. The pia is coagulated and opened sharply as well. The ventricular catheter can then be advanced directly into what is usually a very large ventricle. CSF is forced out the distal slits, and the distal end is secured and sutured within the subgaleal pocket. The opening incision must then be closed meticulously because the wound must be watertight and neonatal infant skin is delicate and thin.

Signs and Symptoms of Failure

Subgaleal shunts typically demonstrate an abbreviated duration of function.⁶⁸ Characteristically, the subgaleal fluid collection will become smaller and tighter as the scalp galeal space shrinks. Occasionally, the fluid collection will be firm enough to inwardly reflect the malleable infant skull. Typically, a shrinking, progressively firm pocket indicates the end of useful utility of a subgaleal shunt. Conversion to a more permanent type of shunt is often necessary, but on rare occasion the subgaleal space can be re-opened (lifting up the skin). The other alternative by which VSG shunt failure can occur is with a pocket that never forms well. This cause of failure may be variable because good function is sometimes achieved with a small pocket. However, more often a VSG shunt in which a pocket never forms indicates impaired function and a need for revision or promotion to a more permanent type of shunt. If a subcutaneous collection of CSF does not form, the clinical course must be observed closely and a low threshold be given to re-exploration of the VSG shunt. If progress is good (fontanelle soft and flat, head growth arrested, sunken eyes resolved, ventricles small or stable on CT), the shunt need not be revised even in the absence of a significant subgaleal pocket.

One significant disadvantage that may accompany VSG shunts is that they may carry a higher burden of ultimate conversion to more inclusively permanently shunts than is the case with ventricular reservoirs. In recent series the rate of conversion of VSG to VP shunts was 90%, whereas in only about two thirds of ventricular reservoir systems was long-term CSF diversion required.

Ventricular Reservoirs

Rationale and Indications

A ventricular reservoir is typically used in two clinical situations. The first is for posthemorrhagic hydrocephalus of the newborn. Serial percutaneous taps are performed to control the hydrocephalus. This simple system is similarly resistant to obstruction from clots as the VSG shunt. Percutaneous taps are labor intensive, however, and introduce some possibility of infecting the device.⁷⁰ They are best performed by maintaining strict diligence to the skin over the reservoir. The skin must be gently but carefully prepared before puncture, and it must not be repeatedly punctured in exactly the same location. One technique that has proved useful is to designate an imaginary clock face on the skin outline of the reservoir. By designating a specific pattern for taps (12, 4, and 6 o'clock taps) on different days, the hazards of repeated taps are minimized. Many neurosurgeons insist that the device be tapped by members of the neurosurgery team, whereas others have trained neonatologists and house officers to perform taps, which are then performed serially.

The other less common indication for a ventricular reservoir is the need for serial examination or ongoing access to the CSF and the subarachnoid space. This usually occurs in the setting of an aggressive CNS neoplasm that requires intrathecal delivery of chemotherapy.

Technique

The ventricular reservoir is usually inserted through a coronal approach with the patient under general anesthesia. Because these devices are often placed in small babies, room temperature and patient temperature are closely monitored. The scalp is prepared in sterile fashion and the patient draped. A small curvilinear incision is made at the edge of the fontanelle. In adults, a location 9 cm above the inion and 3.5 cm laterally works well. A small bur hole is made in adults. Young children undergo coagulation and opening of the dura followed by puncture of the ventricle with a ventricular catheter. The reservoir is connected directly to the ventricular catheter either under the reservoir or via a side port. Meticulous closure is essential.

Signs and Symptoms of Failure

Because a reservoir is not purely a shunt system (in which CSF under pressure is diverted away), there are modifications for determining specific signs of failure. The tapping regimen is usually dependent on clinical criteria (fullness/firmness of the fontanelle, fussiness of the infant, and imaging criteria such as ventricular enlargement on ultrasonography or CT). Skin changes are important to note because repeated percutaneous taps traumatize the skin. The site of puncture can be varied by arbitrarily assigning the appearance of a clock face to the reservoir and varying the puncture sites according to an established protocol.

Ventriculoperitoneal Shunts

Rationale and Indications

VP shunts are the most commonly placed and most versatile shunts for long-term management of hydrocephalus. Historically, distal placement in the atrium occurred first. Yet, over time, the peritoneum proved to be a far better location because of the pronounced capacity of the (even injured or diseased) peritoneum to absorb fluid and the universally observed decreased severity of complications in comparison to atrial shunts.

Much has been discussed in the early parts of this chapter about the rationale for ventricular shunts, and this material applies most directly to VP shunts. VP shunts simply represent the best available treatment for patients with hydrocephalus who are not candidates for ETV. The choice of candidacy for ETV varies among surgeons and centers, and it should be actively considered an important treatment option for all children with hydrocephalus.⁶ Reported experience differs widely, but it appears fair to conclude that the incidence of acute complications is higher and more serious with ETV, yet successful ETV eliminates the need for long-term shunting and the attendant morbidity, cost, and suffering that come with shunt failures.⁵ Late failures with ETV are rare but definitely occur and must be watched for.^{71,72} Half of shunts fail within a year, and life with a shunt is typically one requiring multiple surgeries that arise at unpredictable times.⁷³⁻⁷⁵ There is concordance of data that babies have the highest incidence of failure of ETV and that patients with congenital aqueductal stenosis, tectal gliomas, or other "pure" obstructive causes of hydrocephalus are preferred candidates for ETV.⁷⁵ Patients with myelodysplasia, infections, and posthemorrhagic hydrocephalus have been reported in multiple series to have a higher incidence of complications with ETV. In the end, no single factor determines whether a patient is best served by a shunt or ETV, but rather the decision must be individualized by objective assessment of the patient's unique clinical situation, background, anatomy, social circumstances, and disease process in conjunction with the operating surgeon's experience with ETV and shunt placement.⁷⁶

**Technique** (See Video 190-1)

VP shunts are inserted and revised under general anesthesia. Typically, the patient is placed in the supine position, but occasionally a lateral position may be useful (Fig. 190-1). A lateral position with an occipital ventricular catheter and tunneling posteriorly over the scapulae to gain access to the peritoneum at the costal margin can be a particularly useful variation for children with birth prematurity and posthemorrhagic hydrocephalus. Such children often have percutaneous gastrostomy (PEG) tubes that exit in the subxiphoid region. The proximity of these incisions to shunt incisions at the time of shunt placement or if PEG revision or manipulation is required can create additional risk for infection.^{77,78} The supine position is otherwise preferred. The patient is positioned and bolstered to make the mastoid, clavicle, and xiphoid coplanar. This makes tunneling easier and safer regardless of whether it is performed rostrally (bottom up) or caudally (top down). All pressure points are carefully padded.

Appropriate prophylaxis against infection is critical. Virtually all shunt infections occur as a result of microbial inoculation of the shunt at the time of insertion.⁷⁹⁻⁸² Consequently, meticulous attention to the detail of prophylaxis is essential. Protocols differ among institutions, and there is some emerging evidence suggesting that adherence to a strict protocol may be more important than the specific components of the protocol (i.e., which antibiotic is chosen). Preparation of the scalp and the skin is the first step of infection prophylaxis. Selection of the site for insertion of the ventricular catheter must take into account the condition of the scalp and the potential for impaired healing (e.g., in situations of multiple previous shunt operations), in addition to considerations dictated by the ventricular anatomy. The scalp at the incision site must be carefully cleansed of any dander or eschar from previous wounds (Figs. 190-2 and 190-3). Removal of hair is another topic around which opinions and reported results vary, but most neurosurgeons placing ventricular shunts remove the hair in at least the region immediately around the shunt incision. Removal of hair from around the field also reduces the likelihood of hair that is unprepared or prepared only at its base and then pulled back across an operative field that is sterile. It is established that all surgical fields contain some small number of bacteria and that no field is absolutely sterile. Prophylactic measures are designed to minimize the number of bacteria in the field to as absolutely low a number as possible so that the immune system of the patient may eliminate them. Experience with shunt surgery would dictate that only a small number of bacteria need to be present in the field for shunt infection to result, and thus it would seem prudent to take all reasonable steps to reduce inoculation of bacteria into the field as much as possible. It is preferable to remove the hair in a gentle fashion with clippers



FIGURE 190-1 Patient positioning for a ventriculoperitoneal shunt.



FIGURE 190-2 Preoperative washing in preparation for surgery.

rather than with a razor because small nicks and cuts in unprepared skin can increase the risk for infection. The scalp is then prepared with an antimicrobial solution (Fig. 190-4), and great care is taken to ensure sufficient contact time before the placement of drapes or wiping of residual cleanser away so that maximum antimicrobial killing impact is realized. For iodine-based preparations, the solution must sit on the skin for several minutes after the agent has completely dried. Chlorhexidine-based preparations similarly require several minutes' contact time for optimal impact. Great care must be taken with these agents to avoid inadvertent contact with mucous membranes or sensory organs such as the eyes or ears because devastating toxicity with loss of end-organ function (e.g., blindness, deafness) has been reported. We generally prefer a meticulous but not overly vigorous scrub as a preparatory wash followed by careful and comprehensive multistep preparation (scrub and paint). The hair is clipped, the preparatory wash is performed, and the incisions are marked (Fig. 190-5). A preoperative time-out may then be taken in which all members of the operating team (surgeon, anesthesia, operating room nurses/technicians) cease their activities and all conversation, confirm patient identity, and sequentially review the planned procedure, including side and site, necessary equipment, and potential for additional items such as implants, blood for transfusion, or special tools needed for the procedure. When there is agreement, the remainder of the preparation ensues.

Additional measures for barrier protection include the use of iodine-impregnated adherent drapes directly over the skin to be incised and routine surgical drapes to isolate a sterile surgical field (Fig. 190-6). It has been demonstrated that wearing two pairs of gloves by all surgical team members provides important

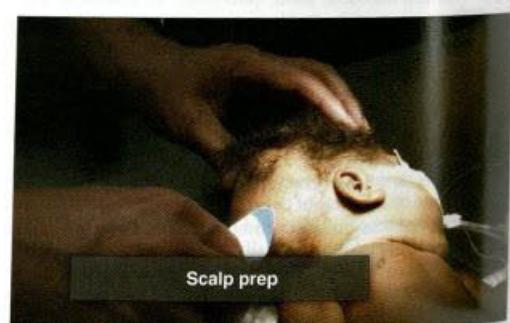


FIGURE 190-3 Scalp preparation.



FIGURE 190-4 Antiseptic skin preparation.

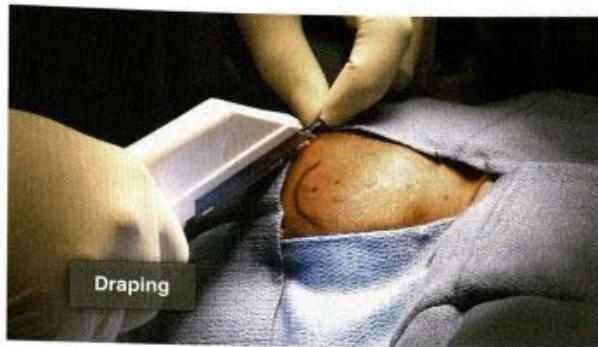


FIGURE 190-6 Draping.

protection against loss of glove integrity, which has been demonstrated to exceed 30% in at least one study.

Administration of a weight-appropriate dose of preoperative antibiotic has also been demonstrated to reduce infection rates.⁸³ The drug must be infused before any incision for optimum benefit. No single antibiotic has been shown to be superior, so many surgeons use a second-generation cephalosporin because of its low toxicity, broad coverage, and low cost. Many surgeons prefer to continue antibiotics postoperatively for one dose or 24 hours, but this has not been shown to lower infection rates.

The cranial incision is chosen so that the ventricle is approached from either a coronal or an occipital trajectory. Individual contradictory papers have suggested that one approach or the other is associated with longer shunt survival, but this has not been supported over time and repeated studies.⁸⁴ The choice of approach is based on subjective, individual factors related to ventricular size and configuration, condition of the scalp, presence of any other drainage catheters such as external ventricular drains, and surgeon preference and experience. In general, a coronal approach is preferred when the ventricles are small. A suitable entry point for a coronal catheter in an infant is at the far lateral corner of the anterior fontanelle. For a larger child and adult, the ideal coronal entry point is 11 cm above the nasion and 4 cm off midline. A trajectory that targets the medial canthus of the ipsilateral eye will puncture the anterior horn of the lateral ventricle in a location that allows the foramen of Monroe to be visualized and traversed if endoscopy is performed and generally ensures that the catheter is anterior to the bulk of the CP.^{85,86} The potential to keep the ventricular catheter clear of CP is another potential theoretical advantage of coronal catheters. An occipital approach is often used for large ventricles in a young child, in whom it is advantageous

to reduce both the length of tunneling and the number of incisions that need to heal for successful placement of the shunt. The occipital entry point is placed on the flat portion of the occiput above the superior part of the pinna and approximately 4 cm from the midline (Fig. 190-7). The catheter should encounter the ventricle at a depth of 4 to 5 cm when passed along a trajectory that aims at the medial canthus of the ipsilateral eye. Occipital entry can also be measured from the inion. A suitable and safe corridor is obtained with an entry point that is 7 cm above the inion and 4 cm off midline. If loculated hydrocephalus is present, multiple catheters may be needed. After the cranial incision is made and a small flap turned, a small bur hole is made. In very young infants this can be accomplished effectively by using a knife with a No. 15 blade on a long handle and gently rotating the blade on the skull surface so that the edge of the blade scrapes the skull away (see Fig. 190-7). Care is taken so that downward pressure on the blade is minimized and active scraping of the side of the blade against the skull can be palpated by the surgeon's fingers. In this manner a small penetration will be made at the level of the tip of the blade into the epidural space. Once this occurs, a small surgical clamp can be used like a Kerrison rongeur to gently yet effectively remove a small window of bone and gain exposure to the dura. In older children (older than 6 months) and adults, a high-speed pneumatic drill or craniotome is used to make a small bur hole. The intended trajectory of the ventricular catheter must be carefully and constantly considered when making the bur hole. This is particularly important for patients with thick skulls because a small, improperly directed bur hole may limit or impair a proper trajectory and prevent proper ventricular puncture.

The usual sequence of VP shunt insertion is that cranial and abdominal exposure are obtained, peritoneal entry is ensured,

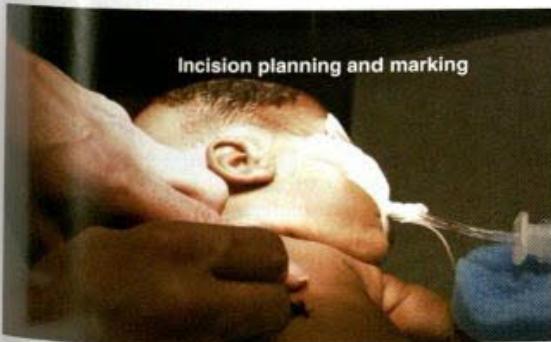


FIGURE 190-5 Incision planning and marking.



FIGURE 190-7 Scalp incision/flap.



FIGURE 190-8 Abdominal incision/approach.

tunneling is completed, and the shunt is assembled, tested, and placed into subcutaneous tissue before ventricular puncture. This ensures that the system can be assembled efficiently and the procedure completed once CSF access is obtained, and it minimizes the length of exposure of CSF to skin.

Placement of the peritoneal catheter may be performed either endoscopically or through a small open laparotomy.^{87,88} Again, the choice is based on individual patient characteristics, including a history of abdominal surgery, injury, or illness such as necrotizing enterocolitis of the newborn, which may have an impact on intraperitoneal anatomy and the consequent risk for complications. The assistance of a general surgeon may be useful if the abdominal history is significant. If a laparotomy is to be performed, a subxiphoid incision is the easiest and most straightforward approach because only the skin, the transverse rectus fascia, and the peritoneum need to be identified and opened (Fig. 190-8). A paramedian subcostal incision may be used, and the surgeon must be attentive to whether the rectus abdominis is traversed before the oblique muscles are encountered. Once encountered, the oblique muscles are gently dissected along their fibers to minimize bleeding and the peritoneum is grasped with a small forceps or curved clamp. Each layer is identified and tagged during the opening so that a layered meticulous closure may be performed reliably. A ventricular shunt procedure is only as good as its weakest step, and it is entirely possible for an imperfectly closed abdominal wound to compromise or doom an otherwise successful operation.

Trochar exposure of the peritoneum is achieved by sharply opening the transverse abdominal fascia and drawing it upward between two surgical clamps. In so doing, the anterior abdominal wall is lifted away from the underlying omentum and bowel and secured. In a single brisk, yet smooth motion the trocar is advanced downward and toward the umbilicus while upward tension is maintained on the anterior abdominal wall. The trocar punctures the peritoneum, and the sheath provides protection to structures within it. The laparoscope may be useful to confirm intraperitoneal localization.^{87,89-91}

Once the peritoneum has been grasped, it is gently but firmly elevated so that it can be drawn out to a thin layer. A second clamp is used to regrasp the peritoneum immediately adjacent to the first clamp while the tissue is gently drawn between the blades of the clamp. This technique, along with careful visual inspection, ensures that no mesentery or bowel has been drawn up with the peritoneum. The first clamp is then used to regrasp the peritoneum several millimeters away, and a final visual inspection is performed. If the tissue transilluminates, it is very unlikely to contain bowel or omentum. The peritoneum is opened sharply and the peritoneal cavity identified and maintained with a surgical probe (e.g., Penfield No. 4 dissector), and the same clamps used to grasp and hold the peritoneum upward are used to secure the

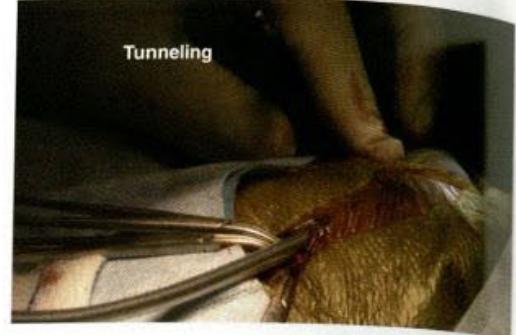


FIGURE 190-9 Tunneling.

edges of the peritoneum. Once the peritoneal edges are secured, any abdominal retractors are released to prepare for and facilitate tunneling.

Tunneling may be performed in either direction, but most neurosurgeons always tunnel in the same direction. Advantages of tunneling rostrally include a low risk of injuring the skin at the tunneling site, a reduced risk for chest or lung puncture, and a fixed target (skull) that can be cautiously used to backstop tunneling efforts. Advantages of tunneling caudally include a larger distal incision that can be manipulated to capture the tunneler as it descends and no risk of intracranial penetration in young children. Regardless of the direction of tunneling, great care must be taken to avoid a trajectory that allows the tunneler to pass under the ribs, under the clavicle, deep in the neck, or across the skull base. Meticulous attention to positioning so that the mastoid, the clavicle, and the xiphoid are coplanar will facilitate tunneling and make it safer (Fig. 190-9). The tunneler is a surgical steel rod that either is covered with a clear plastic sheath or has a robust silk thread tied through its tip. A slight bend similar to the shape of a hockey stick can be placed in the distal end to impart greater maneuverability and control. The skin at the site where tunneling commences is gently held up with forceps, and the tunneler is introduced into the fatty subcutaneous tissue. It is gently advanced with back-and-forth small rotatory movements of the tip that allow the tip to be visualized and palpated as it traverses the subcutaneous tissue. There is often significant resistance at the posterior nuchal line at the junction of the cervical and cranial skin. Great care needs to be exercised when traversing this region so that the chest or the skull base is not inadvertently punctured from a rebound phenomenon. Once the two incisions have been connected, the steel rod is removed and the peritoneal catheter is advanced through the sheath to the distal incision.

A small pocket is dissected at the proximal incision to allow the valve to sit neatly beneath the skin (Fig. 190-10). It is common for this pocket to initially be dissected insufficiently, but rarely does it happen that the pocket is not wide enough. Rather, inexperienced shunt surgeons will fail to recognize a web of galea at the distal end of the pocket that is restricting the size of the pocket as it enters the track through which the peritoneal catheter passes. Repeated robust dissection that massively widens the pocket but does little to extend it is a common error. Instead, it is preferable to use a headlight and look down the track, identify the offending band, and open the distal end of the pocket to allow the valve to sit neatly within the pocket.

Before the shunt system is inserted into the subcutaneous pocket and tunneling sheath it must be assembled and tested. Some systems come preassembled. Again, attention to detail is important, and each connection that is not made at the factory should be supported with a retaining ligature that is tied tightly.



FIGURE 190-10 Developing the subgaleal pocket.

and neatly cut short. Ensuring that the knots are on the under-surface of the device is an important technique in tiny babies that can avoid a focal point of skin pressure, which can lead to skin breakdown and infection. Once assembled, the shunt system should be flushed carefully with lactated Ringer's solution to reduce the likelihood of an air lock preventing good flow through the new system. Another option that is conceptually appealing but as yet unproven to reduce infection is intrathecal instillation of antibiotics directly into the shunt system at the time of shunt insertion.

Once the assembled shunt system is in the subcutaneous space and easy free flow through the system has been demonstrated, the ventricle is punctured. The dura is coagulated with bipolar cautery and opened as a pinhole just large enough to admit the bipolar tips (Fig. 190-11). The pia is then coagulated and opened sharply with a No. 15 blade or needle. The ventricular catheter is advanced deliberately approximately 5 cm. This distance will reach the ventricle from either trajectory if the ventricles are enlarged, and it is unlikely to injure deep subcortical structures if the trajectory is mistaken (Fig. 190-12). With experience, ventricular puncture becomes straightforward for all cases except small ventricles.

Adjuncts that can be used for the positioning of ventricular catheters include endoscopy, ultrasound, and frameless navigation.^{93,94} Small-diameter (1.2 mm) endoscopes have been developed by several manufacturers and are widely used by many neurosurgeons for the placement of VP shunts. The Shunt Placement Study was a multicenter prospective trial that examined whether shunts placed under endoscopic guidance exhibited longer survival than did those placed freehand.⁹⁴ The results showed that survival of endoscope-placed shunts was no better



FIGURE 190-12 Ventricular puncture.

and that the infection rate for endoscopically placed shunts was higher. There were significant limitations in this study, however, and many neurosurgeons continue to widely use endoscopy to ensure that the shunt is placed properly within the ventricle.

Ultrasound has been embraced by some neurosurgeons as being a very useful adjunct for the placement of ventricular catheters.⁹⁵ The development of bur hole ultrasound probes of high quality was a significant step in increasing the utility of ultrasound. Previously, significant enlargement of the bur hole was needed to gain access to the epidural space for placement of the ultrasound probe. In infants, the fontanelle could be used. There is definitely a learning curve in the use of intracranial ultrasound, but advocates claim that the technique is highly useful in providing real-time anatomic feedback that ensures proper ventricular placement with a fraction of the cost or potential risk for infection associated with endoscopy. Further prospective studies are under way that will continue to investigate the role of ultrasound in the placement of ventricular catheters.

Once ventricular puncture has been accomplished successfully, the ventricular catheter is cut off and connected to the valve or reservoir (Fig. 190-13). CSF flow should be vigorous and pulsatile and, with experience, can be recognized as ventricular. The catheter should not need to be longer than 7 cm from a coronal approach or 11 cm from an occipital approach. Need for a longer ventricular catheter may suggest placement that crosses midline or is either too deep or anatomically suboptimal.

Once connected, distal flow is ensured and the peritoneal catheter is inserted directly into the peritoneum. The edges of the peritoneum are held up and the distal catheter is introduced. Resistance or failure of the peritoneal catheter to advance is suggestive of either preperitoneal placement or intraperitoneal



FIGURE 190-11 Coagulating and opening the dura.

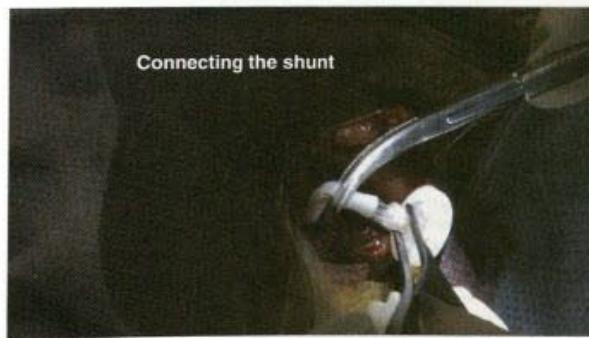


FIGURE 190-13 Connecting the shunt.



FIGURE 190-14 Peritoneal catheter placement.

adhesions causing loculations. Either event should prompt careful examination of the peritoneal exposure and consideration of an expanded exposure to ensure accurate and sufficient peritoneal placement (Fig. 190-14).

Meticulous closure and placement of sterile dressings complete the operative procedure (Fig. 190-15). Some have advocated that dressings are unnecessary, but the majority of neurosurgeons performing shunt operations still prefer to place a dressing for at least 24 to 48 hours postoperatively.

Ventriculoatrial or Ventriculocardiac Shunts

Rationale and Indications

VA shunts preceded VP shunts historically but have evolved to be infrequently placed because of the potentially higher morbidity and mortality with them.^{96,97} Complications of VA shunts may include endocarditis, cor pulmonale, shunt nephritis, and the potential for propagation into the heart or pulmonary artery of a blood clot on the distal catheter (pulmonary embolus) or the distal catheter itself in the event of a disconnection.^{98–100} Another significant liability of VA shunts is the predictable failure that accompanies natural growth of the child as the fixed-length distal (atrial) catheter is gradually pulled out of the heart.

In a VA shunt the distal end of the catheter resides at the junction of the superior vena cava and the right atrium. Because of the considerable effectiveness of VP shunts and ETV in managing hydrocephalus, VA shunts are progressively being used less commonly; however, they remain an absolutely essential option for a small but significant subset of patients with hydrocephalus. The primary indication for a VA shunt in contemporary practice



FIGURE 190-15 Closure.

is peritoneal insufficiency in a child who is not a candidate for or who has failed ETV. Peritoneal insufficiency may result from a variety of conditions, such as necrotizing enterocolitis of infancy, multiple VP shunt infections, omphalocele, or intraperitoneal infections, which may arise from bowel perforation or because of intra-abdominal surgery such as bladder augmentation in the spina bifida population. As a result, VA shunts remain an important but uncommon shunt option.

Technique

All of the techniques described for VP shunts are applicable to the placement of VA shunts. The patient is placed under general anesthesia in the supine position, the hair is clipped, and the skin is cleansed meticulously. Given the potential severity of infection, we advocate preoperative showers or cleansing with chlorhexidine. We prefer C-arm fluoroscopy with the use of iohexol (Omnipaque) contrast medium to ensure optimal catheter positioning. Others have advocated ultrasound. The C-arm is draped and positioned so that it can readily be swung in once the catheter is in position.

After the patient is anesthetized, positioned, prepared, and draped, the jugular vein is accessed. The most common and preferred way to accomplish this is to isolate and expose the common facial vein. A landmark for this vein is the anterior border of the sternocleidomastoid muscle 3 cm inferior and anterior to the angle of the mandible. Once the vein is identified, the proximal end is sewn off and the distal end is secured with a stay suture. The distal catheter is then measured carefully, advanced to the junction of the right atrium and the superior vena cava, and flushed with heparinized saline. The T7-8 interspace is a good practical target to approximate the appropriate site. The ventricular part of the shunt is placed as described in the previous section on VP shunts. Once the shunt is in place and exhibits good spontaneous egress of spinal fluid, it is connected (at the distal end of the valve) to the proximal end of the atrial catheter. Final shunt position is confirmed with fluoroscopy and then closure commences. We typically obtain a postoperative chest radiograph to confirm the position of the catheter tip.

An alternative technique involves direct puncture of the internal jugular or subclavian vein percutaneously in the same manner in which a central venous catheter is placed.^{101–103} In children it is useful to have the assistance of an experienced pediatric surgeon because the incidence and severity of complications with central venous access are significantly elevated in children. Once the jugular vein is cannulated, the Seldinger technique is used to secure access to the vein and allow dilation of the tract and venotomy to permit entry of the distal (atrial) catheter. A J-wire is introduced and the track is dilated. The distal catheter is manipulated and measured under C-arm fluoroscopy to ensure that its tip resides in the right atrium (T7-8). Another technique that is selectively performed for confirmation of atrial positioning of the distal catheter is to use the tip of the catheter as an electrocardiographic lead and observe for a change in polarity of the P wave on the electrocardiogram. Catheter length is adjusted and cut appropriately before attachment at the distal end of the valve.

Signs and Symptoms of Failure

In addition to the symptoms of elevated intracranial pressure that typify VP shunt failure (headache, emesis, progressive decline in alertness and mentation), VA shunts may show signs of a more generalized infection or symptoms from complications at other end-organs. The more generalized infection arises from bacteremia and is usually clinically manifested as recurrently spiking fevers, malaise, and irritability. Multiple blood cultures may be

necessary to confirm infection and identify the species of the offending organism. A high index of suspicion for shunt infection must be present any time that a patient with a VA shunt is encountered with recurrent fever and malaise. Removal of the hardware and institution of antistaphylococcal antibiotics may be indicated even before speciation of the infecting organism is confirmed.

VA shunts are sufficiently rare in the West now that children with shunt nephritis, cor pulmonale (of shunt etiology), and distal catheter propagation are infrequently encountered. Shunt nephritis is typically accompanied by hematuria, but fever, rash, and hepatomegaly/splenomegaly may also be present. Shunt nephritis arises from deposition of immune complexes in the glomerular wall. Long-standing low-grade bacteremia is generally implicated, and the deposition of immune complexes activates complement and leads to direct glomerular injury and to hematuria and proteinuria. Blood and CSF cultures confirm infection, and removal of hardware with administration of antibiotics remains the mainstay of therapy.

Distal propagation of either emboli or distal catheters usually causes dyspnea, tachypnea, or cardiac arrhythmia. A routine chest radiograph will typically demonstrate a catheter embolus, but more advanced imaging, including CT, MRI, or catheter angiography, may be necessary to diagnose a thrombus. Therapy may involve anticoagulation, endovascular lysis, or retrieval of the embolus.

Ventriculopleural Shunts

Rationale and Indications

VPI shunts are never used as first-line procedures to control hydrocephalus. This has largely resulted from the limited and variable capacity of the pleural cavity to reabsorb fluid, particularly in infants and small children. However, a VPI shunt can be a useful temporizing intervention if intra-abdominal infection or peritoneal insufficiency prevents distal catheter placement in the peritoneum, and several series have reported long-term success in a significant percentage of patients.¹⁰⁴ Contraindications to implantation of the catheter in the chest include active chest infection, compromised pulmonary reserve, and a history of thoracic surgery, which would increase the risk for adhesions. A preoperative chest radiograph is important in ruling out pneumonia, pleural effusion, or congenital anomalies, which may have an impact on patient risk and hence candidacy for VPI shunt implantation.

Technique

The proximal (ventricular) portion of the system is implanted identical to that for a VP shunt. The distal catheter is placed in the pleural space at the midaxillary line typically between T4 and T6. The patient is usually positioned supine with a chest roll beneath the ipsilateral scapula to elevate and rotate the chest wall. It has sometimes proved very helpful to use an occipital approach to the ventricle and position the patient in the lateral decubitus position. Tunneling over the scapula with gradual deviation to the midaxillary line can readily be accomplished. It is essential to work closely with the anesthesia team during placement of the pleural catheter to minimize the likelihood for and size of pneumothorax. The corridor for the approach goes immediately over the rib. After the skin incision, a muscle-splitting approach over the rib is made. The parietal pleura will be visualized. All other components of the procedure should have been done at this point, and the distal catheter should be in place and dripping CSF. The thickness of the chest wall can be measured from preoperative chest CT or estimated on the basis of patient age

and body habitus. We prefer to implant approximately 8 to 10 cm of catheter into the pleural space and routinely cut the distal catheter accordingly. Once the parietal pleura is visualized, the patient is preoxygenated and then maintained on positive pressure Valsalva respiration while the pleura is sharply opened and the distal catheter is gently introduced. It is essential that the catheter be directed in a tangential fashion so that it does not enter in a perpendicular manner and tend to invade the lung parenchyma. The catheter is advanced while positive pressure is maintained. Once the catheter is in place, we prefer to fill the wound with irrigation fluid and close the superficial fascia over the intercostal muscles while respiration is continued for the patient. Rapid and careful closure that incorporates a purse-string stitch around the catheter and careful closure of the fascia over the intercostals reduce the likelihood for and size of any associated pneumothorax. We have not found a chest tube necessary unless the mandatory postoperative chest radiograph indicates a sizable pneumothorax.

Postoperatively, a chest radiograph is obtained daily and respiratory status is closely observed. An effusion is common and confirms shunt flow and function. The presence of an effusion is not a problem, but progressive effusion must be watched diligently and careful consideration given to shunt removal if any signs of respiratory compromise ensue. If a progressive effusion occurs, it is necessary to remove the pleural shunt catheter. Aspiration from the pleural space via the shunt catheter is a very important step in any subsequent operation that is necessary because of pulmonary insufficiency from progressive effusion.

As with other shunt systems, infections and disconnections with distal catheter propagation may occur. Infections are characteristically associated with fever and may cause local pain along the chest wall. Rarely, more pronounced infections may result in empyema.

Alternative Distal Shunt Sites

Historically, placement of shunts in many alternative distal sites has been described.^{105,106} Some remain enthusiastically supported by limited numbers of surgeons and authors to the present time; however, broad utility is sufficiently lacking to discuss these systems at length in a general text of this nature. Interested readers are referred to primary papers describing ventricular-gallbladder and other novel distal site shunts.¹⁰⁷

CONCLUSION

Treatment of hydrocephalus with ventricular shunting procedures represents a paradox in neurosurgery. Technically, ventricular shunting procedures remain among the most challenging operations in neurosurgery. No other procedure has a progressive failure rate of 50% 2 years after the operation.¹⁰⁸ Indeed, few if any other neurosurgical operations can be completely ruined at any point up to and including the last stitch. Yet ventricular shunting procedures are relegated by the less experienced to be “easy” operations that lack the glamor or respect conferred to complex intracranial or spinal procedures.

Ventricular shunting procedures are similarly paradoxical from an outcomes perspective. On the one hand, ventricular shunts represent a great success that offers a life of hope and promise to literally thousands of patients who could not have been treated two generations ago. Patients who are treated successfully and maintained with ventricular shunts can achieve developmental outcomes that allow highly functional living and normal independence and prosperity.¹⁰⁹ Without treatment, patients may die or suffer profound developmental delay.

By contrast, treatment options remain limited for the majority of children in the developing world, in large part because of the failure profile of ventricular shunts.

Furthermore, little substantive progress has been made in extending overall shunt survival in the last 35 years despite extensive clinical experience and a sizable literature. Complications from ventricular shunting procedures are unequivocally multifactorial.^{74,110,111} Recently, cooperative multicenter investigations have been initiated that are using properly designed trials with validated instruments to measure outcome. Such studies will have greater power and should yield far more powerful evidence to address the difficult challenges that surround the management of patients with ventricular shunts.

Age at the time of shunt placement and time since previous revision are important predictors of shunt survival.⁷⁵

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Neuroendoscopy

Yin C. Hu ■ Alan R. Cohen

Deep-seated pathology in the intracranial compartment can provide a difficult challenge to the neurosurgeon. The adaptation of neuroendoscopy from urologic procedures now provides a realistic treatment alternative for a variety of intraventricular lesions as well as other lesions situated at the base of the skull. Advances in endoscopic technology and miniaturization of surgical instruments have expanded the application of neuroendoscopy. The current popularity of endoscopic neurosurgery arises from its ability to permit effective therapy in the depths of the brain with minimal disruption of eloquent neural tissue.

HISTORY

Endoscopic neurosurgery began in the early 20th century as an effort to diagnose and treat hydrocephalus. Surgeons realized that the same instruments used in urologic procedures could be inserted into the cerebral ventricles. In 1910, Victor Darwin Lespinasse, a urologist in Chicago, cauterized the choroid plexus of two infants with hydrocephalus using a rigid cystoscope. The results were not published but were presented locally. One child died immediately; the other lived for 5 years.¹ Lespinasse subsequently abandoned the procedure, calling it an "intern's stunt."

Walter Dandy is considered to be the father of neuroendoscopy. In 1918, he attempted to treat hydrocephalus in four infants by using a thin-bladed nasal speculum to gain access to the ventricles.² He extirpated the choroid plexus by avulsing it. Only one infant survived. Later in 1922, in a one paragraph landmark article in the *Johns Hopkins Hospital Bulletin*, Dandy coined the term *ventriculoscope* and described his use of a rigid cystoscope to gain access to the ventricles and fulgurate the choroid plexus in two hydrocephalic infants.³ Using electrocautery and long-handled scissors, Dandy was able to extirpate the choroid plexus under endoscopic guidance (Fig. 191-1). Subsequently, using similar techniques, he successfully removed choroid plexus tumors in three patients.⁴

Although Dandy performed the first third ventriculostomy through an open procedure, it was in 1923 when W. Jason Mixter reported the first successful endoscopic third ventriculostomy (ETV) using a flexible urethroscope.⁵ The operation was considered a success in that postoperatively indigo carmine dye instilled into the lateral ventricle could be recovered by a needle in the lumbar subarachnoid space. This recovery could not be demonstrated preoperatively, purportedly because of the patient's non-communicating hydrocephalus.

For years, the main surgical treatment of hydrocephalus was either ETV or endoscopic coagulation of the choroid plexus. Ultimately, neuroendoscopy fell out of favor because of the high rate of complications related to the primitive nature of the instruments and the advent of successful extracranial ventricular shunting. The first successful ventricular shunt procedure was performed by Frank Nulsen and Eugene Spitz in 1919 and reported in *Surgical Forum* in 1951.⁶ Extracranial ventricular shunting revolutionized the treatment of hydrocephalus and quickly became the procedure of choice for treating hydrocephalus.

However, ventricular shunts have remained troublesome devices, and despite clever advances in shunt design, ventricular shunting remains burdened by problems related to infection and malfunction. Thus, the search for improved methods for treating hydrocephalus has continued. With the introduction of improved optics, miniaturization, and computer technology, there has been a resurgence of interest in ventriculoscopic techniques.

INSTRUMENTATION

There are two classes of neuroendoscopes: rigid and flexible. The modern endoscope would not have been possible without the innovations of a British optical physicist, Harold Hopkins.⁷ Rigid endoscopes have optics that are superior to flexible fiberoptic endoscopes. Karl Storz adopted the solid rod lens developed by Hopkins and used it in his rigid endoscope systems. Hopkins and Storz developed the SELFOC lens, which is still used in modern rigid endoscopes and is more efficient than earlier lens models.⁸ The SELFOC lens has a refractive index that varies with the radial dimension of the lens, whereas the conventional lens has a uniform refractive index.^{8,9} The lens expands the field of vision and eliminates the need for a relay lens while preserving light transmission.^{8,10} The Hopkins lens system could also be made with a significantly smaller diameter than the earlier, more primitive lenses designed by Nitze for urologic use. Adding a series of angled rod lenses to the 0-degree straightforward lens system enhanced the maneuverability of the instrument.

The development of fiberoptic technology enables a flexible endoscope to be steered. The improved maneuverability of the flexible endoscope comes with a cost: the quality of the image and the amount of light transmitted are inferior to those provided by the rigid system. In addition, the flexible endoscope is more fragile than its rigid counterpart and requires meticulous care in handling.

There are devices designed for cutting, grasping, aspirating, and sampling lesions (Fig. 191-2). Balloon catheters and rigid and flexible probes are available for fenestration of cystic lesions, the septum pellucidum, and the floor of the third ventricle. Small catheters introduced through working channels in the endoscope sheath can provide irrigation and suction. It is important to keep the operative field clear by irrigation because even a small amount of blood can impair visualization. It is imperative that there be an escape route for irrigating fluid to prevent ventricular dilation and increased intracranial pressure (ICP) in a closed system.

The energy sources for neuroendoscopic dissection include monopolar and bipolar electrocoagulators and a number of fiber-optic lasers. Two of the most commonly used lasers are the neodymium-doped yttrium-aluminum-garnet (Nd:YAG) laser and the potassium titanyl phosphate (KTP) laser. Nd:YAG lasers emit light that is invisible and require a visible helium neon pilot beam. Pigmented tissues have a preferential absorption of the light emitted by the Nd:YAG laser. Thus, ventricular cyst walls and the whitish septum pellucidum require higher power settings for fenestration. KTP lasers emit a green light and do not require a pilot beam. Other, less commonly used lasers include argon and

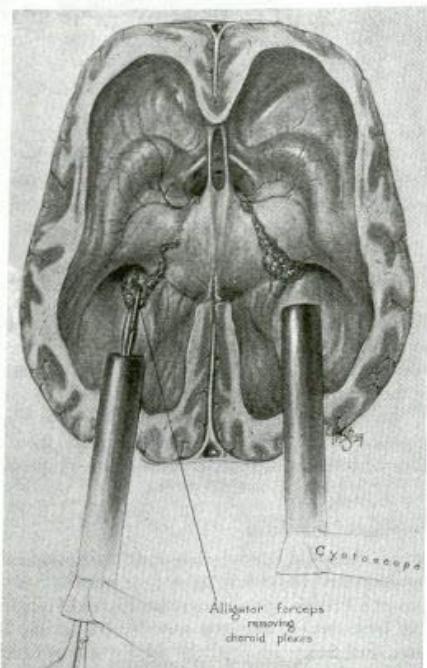


FIGURE 191-1 Dandy's ventriculoscope. The choroid plexus of the lateral ventricles was removed using two Kelly cystoscopes. (From Dandy WE. *Surgery of the Brain*, Hagerstown, MD: WF Prior, 1945:245.)

holmium sources. We have used endoscopic laser dissection for various lesions such as third ventricular colloid cysts, but prefer not to use the laser during ETV for fear of injuring the basilar artery. Oertel and colleagues have shown promising results in selected patients with a water jet system for dissection with preservation of nearby vessels.¹¹

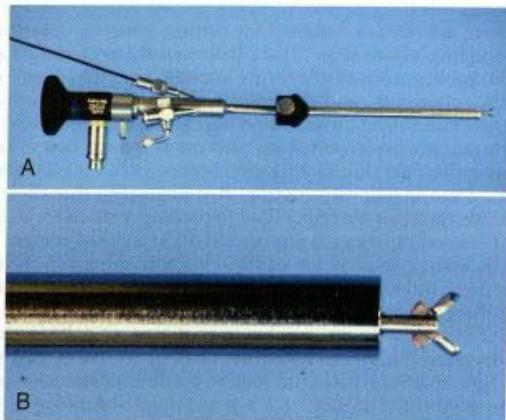


FIGURE 191-2 Rigid ventriculoscope (Karl Storz, Culver City, CA). **A**, Flexible grasping forceps introduced through working channel in the endoscope sheath. **B**, Close-up view.

STEREOTACTIC ENDOSCOPY

Frame-based or frameless stereotactic guidance can aid in tracking the endoscope in three dimensions. Freehand cannulation of the lateral ventricle can be difficult for selected cases, for example, in approaching an intraventricular lesion in the absence of hydrocephalus. In cases of complex, loculated hydrocephalus, stereotaxy can aid the operator in moving from one cystic compartment to another. Endoscopic navigation at the skull base can also be enhanced by stereotactic guidance.

Both rigid and flexible endoscopes can be used with stereotactic guidance.¹²⁻¹⁷ Standard frame-based stereotaxy is useful to guide an endoscope to the proximity of a lesion with small ventricles. Visual anatomic clues, once the endoscopist has accessed the ventricle, can further guide the operator in dissecting closer to the lesion. In addition, the frame itself can serve as a mount for the endoscope. However, frame-based endoscopy is not applicable to infants and young children. Frameless stereotaxy defines a three-dimensional coordinate space for a preoperative imaging modality and translates it to the three-dimensional coordinate space of the operative field. Articulated mechanical arms, sonic or optical digitizers, and electromagnetic systems are substituted for the frame (Fig. 191-3).¹⁸⁻²¹

ENDOSCOPIC ANATOMIC CONSIDERATIONS

The ventriculoscope is introduced into the cerebral ventricles through a bur hole. The position of the bur hole through which the ventriculoscope is introduced varies with the location of the pathology. A standard anterior shunt trajectory can be used to access the third ventricle. The bur hole is placed just anterior to the coronal suture just medial to the mid-pupillary line. Under direct visualization, the endoscope is passed through the foramen of Monro after the lateral ventricle is cannulated. The technique can be fine-tuned by using stereotactic guidance with preoperative planning, especially with small ventricles. We use image guidance to fine-tune ventricular cannulation for most operative cases independent of ventricular size.

After the orientation of the image on the monitor is concordant with the position of the patient, standard intraventricular landmarks are identified.^{22,23} The foramen of Monro is usually identified first,²⁴ given that it is in line with the trajectory of the



FIGURE 191-3 Image-guided ventriculoscopy. Rigid endoscope (Aesculap AG, Tuttlingen, Germany), frameless stereotactic navigation (BrainLab, Feldkirchen, Germany), and nitrogen-powered pneumatic articulated Mitaka Point Setter arm with micromanipulator (Karl Storz, Culver City, CA).

ventriculoscope from a coronal approach. The septum pellucidum is located medially, and the head of the caudate nucleus is situated laterally. The choroid plexus is always projected posterior to the foramen of Monro. The posterolateral thalamostriate vein joins the anteromedial septal vein to form the internal cerebral vein. The caliber of these veins increases as they approach the foramen of Monro. A pair of white C-shaped structures, the fornices, are seen as they curve ventrally and inferiorly to define the medial and anterior borders of the foramen of Monro.

A clear view of the anterior floor of the third ventricle is achieved after passing through the foramen of Monro from a standard coronal trajectory. The paired mamillary bodies appear as whitish prominences at the posterior inferior aspect of the endoscopic field. The optic recess is seen anterior to the infundibular recess as the endoscope is swept anteriorly along the third ventricular floor. The tuber cinereum forms the floor of the third ventricle from the mamillary bodies posteriorly to the infundibular recess anteriorly. In the setting of hydrocephalus, the tuber cinereum is often thin and translucent and can provide a glimpse of the basilar apex in the interpeduncular cistern below.

Structures of the posterior third ventricle may be difficult to see because they are often hidden from the endoscope from a standard precoronal bur hole approach. A more anteriorly located bur hole may be required to view these posterior third ventricular structures. Another option to view the posterior third ventricle is to replace the 0-degree rod lens with a 30-degree angled lens. By rotating the angled lens around its axis, the operator can have a panoramic view of structures situated medially, laterally, and posteriorly. A flexible steerable endoscope is another viable option to gain visualization of the posterior third ventricle.

ENDOSCOPIC PROCEDURES

Endoscopic Third Ventriculostomy

Despite Mixter's first successful ETV in 1923,⁵ the procedure did not gain early popularity because of poor illumination, primitive and bulky instruments, inconsistent results, and high complication rates. After the introduction of valve-regulated shunts in the early 1950s, ETV fell out of favor for some time. However, ventricular shunts are troublesome devices and pose lifelong problems for shunted patients. The significant improvement in endoscopic technology in recent decades has led to a renewed interest in ETV.

Candidates for ETV should have symptomatic noncommunicating hydrocephalus with a patent subarachnoid space. A classic example is acquired aqueductal stenosis with resulting proximal dilation of lateral and third ventricles. Neuroimaging, in particular magnetic resonance imaging (MRI), is useful in diagnosing noncommunicating hydrocephalus (Fig. 191-4). The ideal candidate for ETV has enlarged lateral and third ventricles, including a third ventricular floor that is thinned and bowed inferiorly. Preoperative planning with MRI delineates the anatomy of the third ventricle of Sylvius and the location of the basilar artery on the sagittal view.

Safe fenestration of the floor of the third ventricle requires the procedure to be performed in the midline and anterior to the mamillary bodies and the underlying basilar artery apex (Fig. 191-5). Fenestration of the floor of the third ventricle can be performed by blunt penetration with the endoscope or a rigid probe, electrocoagulation, balloon catheterization, water jet fenestration, or laser coagulation. Our preference is to use a rigid probe introduced through a working channel in the endoscope sheath to puncture the floor of the third ventricle. A Fogarty balloon catheter with its stylet in place is also an effective means of puncturing the third ventricular floor. The balloon catheter is then repetitively inflated and deflated to widen the fenestration

(Fig. 191-6). Both the ependyma and underlying arachnoid are opened. Bleeding from the edges of the opening can be tamponaded by keeping the balloon inflated for a slightly longer period. Fluctuation of the margins of the fenestration indicates cerebrospinal fluid (CSF) flow. The basilar artery complex can be visualized through the fenestration without inserting the endoscope into the basal cisterns (Fig. 191-7).

The reported success rate of ETV ranges from 50% to 95%.²⁵⁻³³ There are conflicting studies that have described the outcome after ETV to be dependent on age,^{25,26,34-36} independent of age,^{37,38} or dependant mainly on etiology.^{28,35,39,40} In a multivariate analysis, Drake and associates reported a higher failure rate for younger patients, particularly neonates and infants.²⁶ Similarly, Kadrian and coworkers have shown a higher failure rate for patients younger than 6 months.³⁵ The procedure is less likely to be successful if there is any history of communicating hydrocephalus.^{24,41} For example, patients with aqueductal stenosis who have prior evidence of ventricular hemorrhage, shunt infection, or meningitis are less likely to have a good result.^{36,42,43} However, this is not uniformly the case because ETV has been reported to be successful in some patients with hydrocephalus and associated ventricular shunt infections.^{44,45} The success of an ETV procedure is determined mainly by clinical evaluation, not postoperative imaging, because the ventricular system may not change significantly in size.

Although ETV is an effective treatment for selected cases of noncommunicating hydrocephalus, it is not without risks. The reported complication rates range from 0% to 20% in different series,⁴⁶⁻⁴⁸ with a mortality rate of less than 1%.^{30,47,49} Complications can be categorized as intraoperative, early postoperative, and late postoperative. Intraoperative complications include neurovascular injury and bradycardia with cardiac arrest.^{42,50-54} Massive subarachnoid bleeding from perforation of the basilar artery or its branches has been reported.⁵⁵⁻⁵⁹ The Canadian cooperative study reported a 1.4% bleeding rate in 368 patients who underwent endoscopic ETV.²⁶ Other authors have reported both arterial and venous bleeding during their procedures.^{28,60-62}

Intraoperative hemodynamic changes have been documented in different series. El-Dawlatly and coworkers experienced a 41% rate of intraoperative bradycardia during perforation of the third ventricular floor in their patients.⁶³ A proposed mechanism for intraoperative hemodynamic changes suggests Cushing's response from elevated ICP from aggressive irrigation and stimulation of the preoptic area or posterior hypothalamus resulting in bradycardia or tachycardia, respectively.⁶⁴ Handler and associates documented an intraoperative cardiac arrest during ETV in a patient with aqueductal stenosis.³² The patient required cardioversion. This case demonstrates the danger of infusing a high-flow fluid irrigation in a closed system.

Early postoperative complications include subdural hematoma, CSF leak, infection, and endocrinologic disorders. A large corticotomy draining into the subdural space or sudden excessive CSF drainage during ETV is a possible risk factor for the development of subdural hematomas.^{61,65,66} Restoration of CSF absorption by the arachnoid granulations may not be immediate in the early postoperative period. The increased ICP can lead to the development of a CSF collection under the incision or leakage of CSF resulting in meningitis or ventriculitis. Several investigators have reported electrolyte and endocrinologic abnormalities following ETV.^{51,67-69} Abnormalities include the syndrome of inappropriate antidiuretic hormone secretion (SIADH), diabetes insipidus, and secondary amenorrhea.^{51,68,69} Other early postoperative complications include transient memory loss and personality disorders from injury to the fornices as well as cranial nerve palsies and seizures.^{26,33,46,47,54,61,70,71}

Late postoperative complications consist mainly of delayed failure from closure of the ETV stoma. The reported rate of delayed failure ranges from 2% to 15% in different series.^{26,28,72-74}

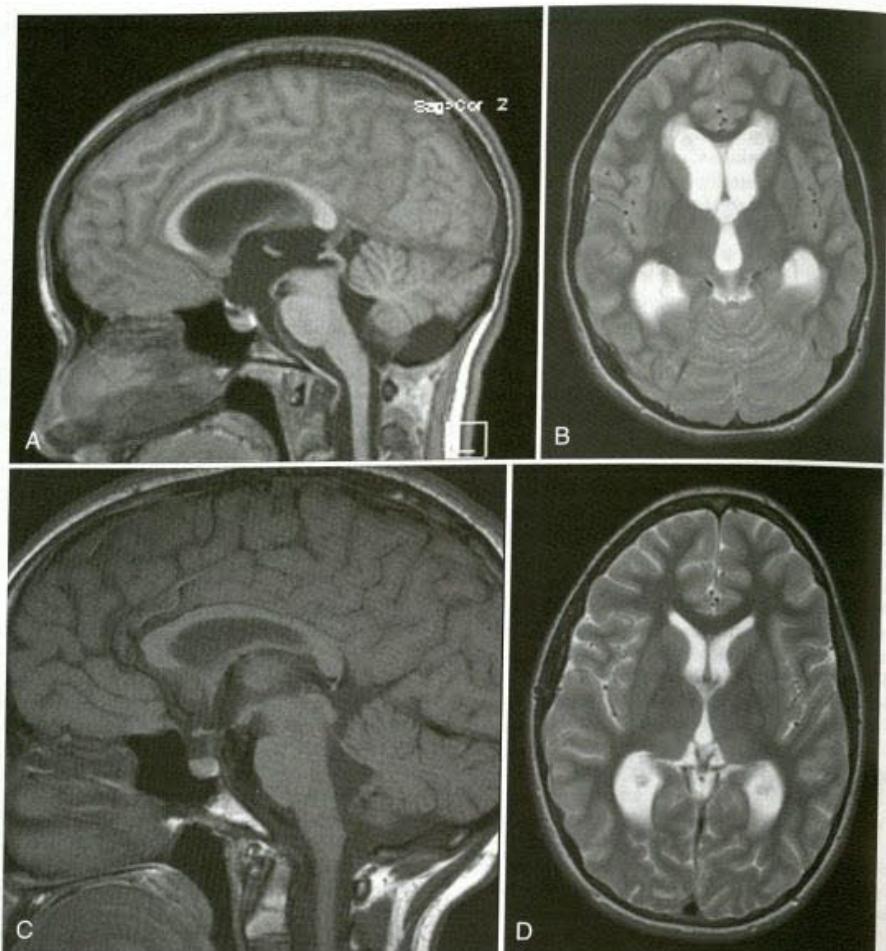


FIGURE 191-4 Noncommunicating hydrocephalus in a child with aqueduct stenosis undergoing endoscopic third ventriculostomy. **A**, Preoperative T1 sagittal magnetic resonance image (MRI) showing stenosis of the caudal aqueduct with inferior bowing of the third ventricular floor and a retrocerebellar cyst. **B**, Preoperative T2 axial MRI showing enlargement of the lateral and third ventricles. **C** and **D**, Postoperative T1 sagittal MRI and T2 axial MRI showing resolution of ventriculomegaly.

Late failure leading to rapid clinical deterioration and death are rare but real occurrences.^{38,72,75} The mechanism of ETV failure may be multifactorial. Causes include inadequate size of the initial fenestration, underappreciated secondary membranes, reduced or no CSF flow through the fenestration, narrowing or closure of the stoma due to hemorrhagic obstruction, elevated CSF protein and fibrinogen, postoperative infection with CSF obstruction at the fenestration site or inadequate CSF absorption by the arachnoid granulations, and tumor progression resulting in blockage.

Endoscopic Aqueductoplasty

The first aqueductal reconstruction was performed by Dandy in 1920.⁷⁶ In cases of hydrocephalus caused by membranous occlusion or short segment stenosis of the aqueduct of Sylvius, endoscopic aqueductoplasty (EA) with and without stenting has been reported.⁷⁷⁻⁸¹ The bur hole for EA is placed more anteriorly than the one for standard ETV. The tip of the Fogarty balloon cath-

eter may be shaped with a gentle curve given that the aqueduct is not straight. The catheter is then gently slid into the lumen of the aqueduct and the balloon is carefully dilated. A flexible endoscope may be useful for perforating membranous obstruction, especially if the obstruction is in the distal aqueduct, which is not well visualized by a rigid endoscope. Stenting of the aqueduct may be performed for patients at high risk for aqueductal restenosis or patients with a trapped fourth ventricle.^{76,82-85} The stent is usually a ventricular catheter with additional holes.^{76,82,86}

Shunted patients with a trapped fourth ventricle often have slit-like lateral ventricles, making them poor candidates for the standard EA.⁸² A suboccipital approach for retrograde aqueductoplasty and stenting can be performed.⁸² The entry point is usually just lateral to midline. These patients are at some risk for aqueductal restenosis; thus, aqueductal stenting has been advocated.⁸²

Success rates of EA have been reported in the 69% to 76% range in the largest two series.^{80,81} Other, smaller groups have also reported high rates of success.^{78,79} Most of the failures in

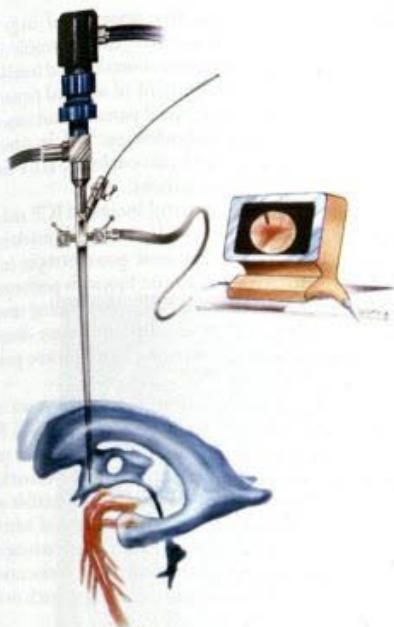


FIGURE 191-5 Endoscopic third ventriculostomy. (From Cohen AR. Images in clinical medicine. N Engl J Med. 1993;328:552.)



FIGURE 191-7 Endoscopic view of basilar artery in the preopticine cistern after third ventriculostomy.

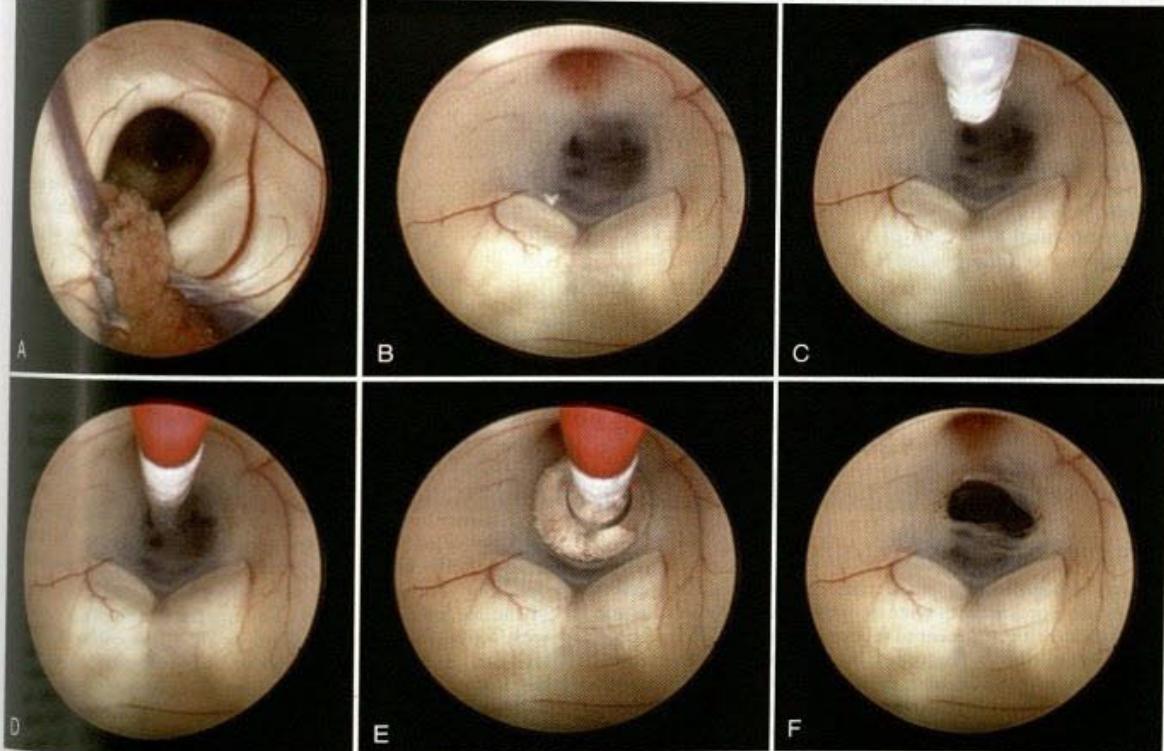


FIGURE 191-6 Endoscopic third ventriculostomy carried out through right precoronal bur hole. **A**, Foramen of Monro. **B**, Third ventricular floor. **C**, Balloon catheter introduced through working channel in endoscope sheath. **D**, Balloon puncture of floor anterior to mammillary bodies. **E**, Inflation of balloon to enlarge fenestration. **F**, Fenestration in third ventricular floor, with mammillary bodies posteriorly and infundibular recess anteriorly.

these studies were restenoses, and reoperation with stenting was performed to correct this problem. Proponents of EA have illustrated the advantages of the procedure compared with ETV.⁸¹ EA restores the physiologic CSF pathways and eliminates the risk for basilar artery injury. There are no arachnoidal adhesions around the aqueduct to interfere with CSF flow. The risk for injuring the hypothalamus is avoided, especially during cases when the floor of the third ventricle is thickened and a considerable amount of force is required to perforate the floor. Strictures at the aqueduct are usually not as tough to penetrate; thus, less force is required for fenestration.

A major risk of EA is injuring the periaqueductal gray matter and the floor of the fourth ventricle.⁷⁷ Other complications reported, especially in long stenoses, include midbrain injury causing transient or permanent dysconjugate eye movements, Parinaud-syndrome, and cranial nerve palsies.^{77,79,81} In cases with long stenoses, ETV may be a more appropriate procedure.

Septostomy

In 1991, Heilman and Cohen⁸⁷ reported neuroendoscopic septostomies that were performed using a "saline torch." In the largest published series of endoscopic septostomy by Aldana and associates, 53% of the procedures were thought to be successful.⁸⁸ Repeat septostomy was performed in 10 patients, with improvement noted in 81% at follow-up.⁸⁸

Fenestration of the septum pellucidum is indicated when there is an obstruction of one foramen of Monro causing the ipsilateral ventricle to dilate from trapping. The endoscope is inserted through a coronal bur hole. Image guidance allows the operator to place the bur hole somewhat lateral to the mid-pupillary line, thereby enhancing face-on visualization of the septum.

Foraminoplasty

Although rare, membranous obstructions of the foramen of Monro causing unilateral hydrocephalus have been reported in the literature.^{86,89-91} Endoscopic foraminoplasty can be carried out in such patients. When solid brain parenchyma is blocking the foramen of Monro, the risk for closure from foraminoplasty may be high. Schroeder and colleagues have suggested inserting a 10-cm ventricular stent from the lateral ventricle through the foraminoplasty and into the aqueduct to prevent closure.⁸²

VENTRICULAR TUMORS AND CYSTS

Neuroendoscopy has improved the diagnosis and treatment of selected third ventricular tumors and cysts. Endoscopic biopsy of third ventricular tumors was first reported by Fukushima.⁹² Both rigid and flexible endoscopes have been used to sample the tumors.^{12,93} In the setting of associated hydrocephalus, placement of a ventricular catheter, ETV, or septostomy may be performed simultaneously, if indicated.

PINEAL TUMORS AND CYSTS

Optimal management of pineal tumors remains controversial. Patients often present with acute symptoms of hydrocephalus and require immediate treatment to relieve increased ICP. Traditionally, hydrocephalus is controlled by placement of an external ventricular drain (EVD) or a ventricular shunt. The disadvantages of an EVD include infection and malfunction. Additionally, shunts have been implicated in extraneuronal dissemination of some pineal tumors.⁹⁴⁻⁹⁹

Standard methods to obtain tumor diagnosis include stereotactic biopsy and open microsurgical procedures. Stereotactic biopsy of pineal tumors is limited by the sampling errors secondary to frequent tumor heterogeneity and by the risk for

intraoperative bleeding due to the presence of large midline veins. Microsurgical resection is often the treatment of choice but carries a reported postoperative mortality and morbidity rate of 5% to 15%.¹⁰⁰⁻¹⁰² The management of selected pineal tumors, including germ cell tumors and pineal parenchymal tumors, often includes chemotherapy and radiotherapy.¹⁰³⁻¹⁰⁶ In patients who present with pineal tumors and hydrocephalus, ETV and tumor biopsy are a useful first-line treatment.

ETV can be performed to control increased ICP and establish a tissue diagnosis. Cytologic samples and CSF markers such as α -fetoprotein and β -human chorionic gonadotropin can be collected simultaneously. An endoscopic biopsy is performed unless the tumor appears hypervascular. The surrounding neural structures also can be examined to identify malignant dissemination that may not be seen on neuroimaging. A diagnostic yield of 75% to 100% has been reported.¹⁰⁶⁻¹⁰⁹

Approaching the pineal region requires a more anteriorly placed bur hole than the one used for standard ETV. Both rigid and flexible endoscopes can be used to perform the procedure. The rigid endoscope provides superior optics and working channels. It also allows larger tissue sampling. The flexible endoscope improves access to a greater area at the expense of inferior optics. The flexible endoscope may minimize the stretching of periforaminal veins and other neural structures. A combination of rigid and flexible endoscopes may enhance the approach to the posterior third ventricle.

COLLOID CYSTS

Colloid cysts are benign lesions constituting 0.5% to 2% of all brain tumors.^{110,111} They arise from the anterior aspect of velum interpositum or the choroid plexus of the third ventricle adjacent to the foramen of Monro. These lesions can lead to rapid clinical deterioration and even death from increased ICP. The natural history of the lesions is variable, and patients with small cysts are often asymptomatic. When symptomatic, colloid cysts usually cause hydrocephalus secondary to obstruction of both foramina of Monro (Fig. 191-8).

The numerous existing surgical approaches reflect the technical difficulty inherent in removing these lesions with minimal morbidity. Previous studies of stereotactic aspiration of colloid cysts showed a high recurrence rate of 30% to 80%.¹¹²⁻¹¹⁴ It is imperative that colloid cyst patients be followed over the long term because many recurrences can occur in a delayed fashion, sometimes after many years. Other problems associated with stereotactic aspiration include neural and vascular injury; difficulty puncturing small, thick-walled lesions; and difficulty aspirating viscous cystic contents (Fig. 191-9). Open microsurgical approaches may be associated with hemiparesis from venous infarction, seizures, and even death.¹¹⁵⁻¹²⁰ Memory deficits have been reported in up to 26% of microsurgical cases.^{115,121-123}

Neuroendoscopy provides a useful modality for the management of colloid cysts. Image guidance is useful in helping to place the bur hole more lateral and anterior than the standard shunt bur hole. This permits a face-on view of the surface of the cyst in the foramen of Monro. The operator can open the cyst wall with a fiberoptic laser and empty the cystic contents. The cyst wall can be shrunk by the laser or by bipolar coagulation, and the residual cyst can be excised. Horn and associates compared their patient groups in the transcallosal versus endoscopic approach to colloid cysts.¹¹⁹ In the transcallosal group, they found a higher rate of infection, longer operative times, longer hospital stays, and more patients who required ventricular shunts. The endoscopic group had a higher rate of residual cysts on follow-up neuroimaging studies. There was no significant difference in neurologic outcome between the two groups. Other published

FIGURE 191-8
Image C, Sagit

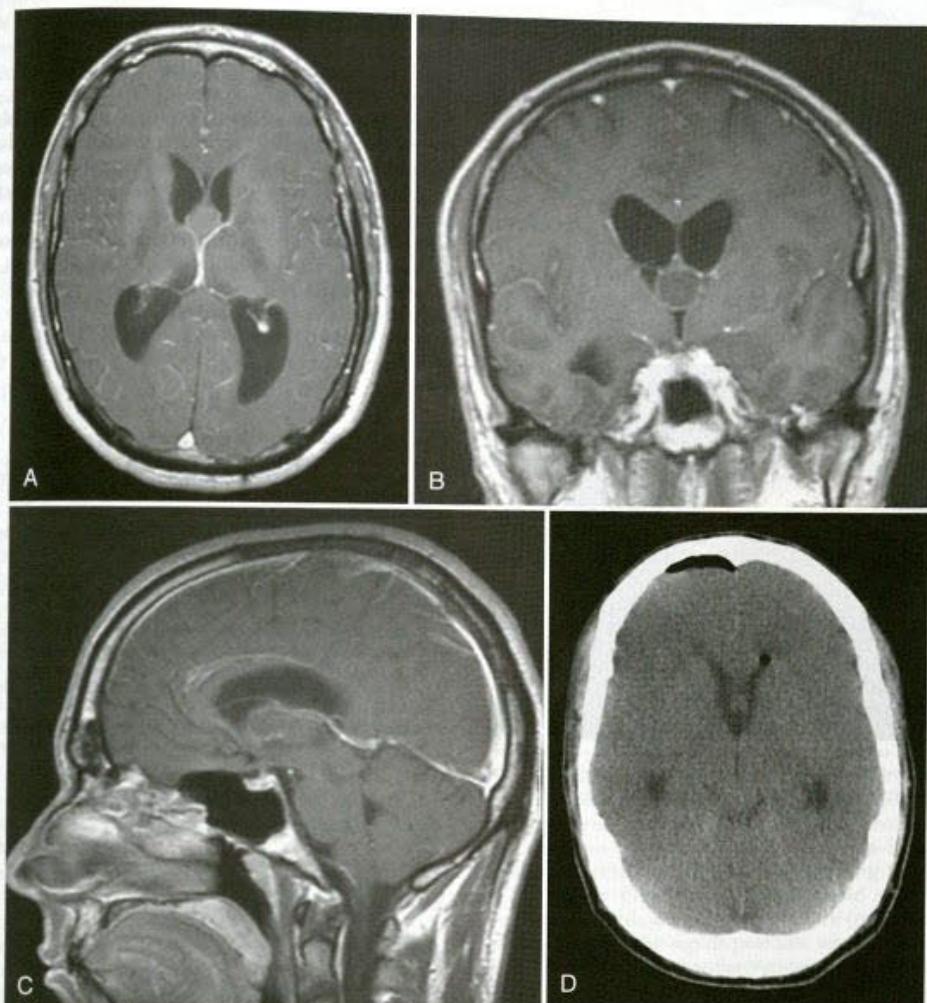


FIGURE 191-8 Preoperative contrast-enhanced T1 MRI showing colloid cyst obstructing both foramina of Monro. **A**, Axial image. **B**, Coronal image. **C**, Sagittal image. **D**, Postoperative computed tomography after ventriculoscopic resection through a right precoronal bur hole.

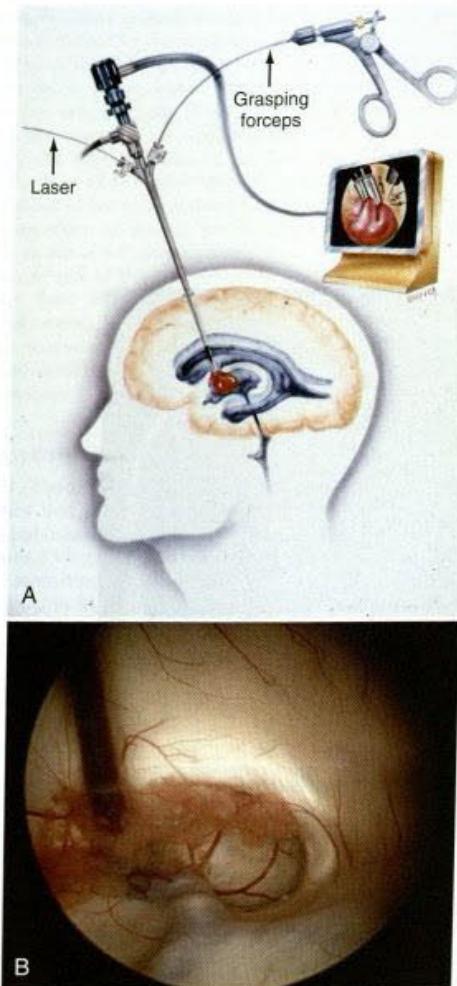


FIGURE 191-9 **A**, Ventriculoscopic resection of colloid cyst. **B**, Cyst in foramen of Monro approached from right lateral ventricle.

data show similar results.¹²⁰ In the largest series with the longest follow-up, with median of 88 months, Greenlee and associates reported only one recurrence in 34 patients treated purely endoscopically.¹²⁴ Thus, endoscopic resection of colloid cysts represents a safe and effective modality and may be considered a first-line treatment of symptomatic colloid cysts.

Endoscopic colloid cyst resection is not without risks. Some patients experience persistent low-grade headaches and fever that can last for a few weeks.^{41,125} This may be related to aseptic ventriculitis provoked by spilled cystic contents. The spilled contents can cause obstructive hydrocephalus in the aqueduct, even after the colloid cyst has been removed.^{116,126,127} Other complications include mechanical injury to neural or vascular structures.

CONCLUSION

Endoscopic neurosurgery has evolved and revolutionized treatments of certain intracranial pathologies, including hydrocephalus and tumors. Skull base lesions, once considered major surgical challenges, are now enhanced with endoscope-assisted microsurgery. Difficult angles inherent to the skull base can be visualized with the endoscope. Its applications in microsurgery have expanded to include endonasal tumor resection, cerebral aneurysm clipping,¹²⁸⁻¹³⁰ basal encephalocele repair,¹³¹⁻¹³⁴ diskectomy and other spinal procedures.¹³⁵⁻¹⁴¹ The role of endoscopy in minimally invasive neurosurgery will continue to expand as technologic advances improve the quality of the optics and instrumentation.

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Cerebrospinal Fluid Devices

Richard J. Edwards ■ James Drake

insertion of cerebrospinal fluid (CSF) devices for the management of hydrocephalus is one of the most common procedures performed in neurosurgery. A daunting array of CSF shunt components are available on the market, but there is a paucity of clinical evidence available to determine which devices, if any, are the best for a given indication. No single shunt or catheter design is suitable for all patients, and neurosurgeons should have a range of shunt devices at their disposal to minimize the risk for complications because of inappropriate selection of hardware. A good understanding of the principles of shunt physiology and design is necessary to allow informed decision making when selecting shunt hardware.

HISTORY OF CEREBROSPINAL FLUID SHUNT DEVICES

Before 1900, treatment of hydrocephalus was often uninformed and usually ineffective. Head bandaging, intraventricular injection of a strong iodine solution, exposure of the head to bright sunlight, and irradiation of the choroid plexus were among the more extreme procedures advocated.¹ Direct ventricular puncture and repeated lumbar puncture were rarely sufficient to control hydrocephalus, and efforts were directed toward internal diversion of CSF. In the 1890s, Miculicz developed a gold, tapered hollow tube that diverted CSF from the ventricle to the subdural space, but this valveless device was only rarely effective. Other valveless CSF diversion techniques involving the use of glass, rubber, or silver tubes and linen threads in the subdural or subgaleal space were all equally unsuccessful and carried high mortality. Attention then turned to the choroid plexus, with Walter Dandy promoting the technique of extirpation of the choroid plexus in an attempt to reduce production of CSF.² Before 1950 this was probably the most common procedure undertaken for infantile hydrocephalus,⁴ but success remained limited,^{5,7} and it was largely abandoned by the 1970s after reports of high failure rates.^{8,9} Interestingly, there has been a recent resurgence of interest in ablation of the choroid plexus, the efficacy of which may have been underestimated.¹⁰⁻¹² In 1914, Heile described the first diversion of CSF from the lumbar subarachnoid space to the peritoneum with the use of a valveless rubber tube, but this too was unsuccessful.¹³ In 1939, Torkildsen described a shunt from the lateral ventricles to the cisterna magna for obstructive hydrocephalus that was modestly successful.¹⁴ In 1949, Matson described a shunt from the lumbar subarachnoid space to the ureter, which became popular in the 1950s.¹⁵ The procedure necessitated nephrectomy and was often complicated by hypochloremic alkalosis, which was frequently fatal, and with the introduction of valved shunt systems, the technique was abandoned.

The advent of the "modern" era of CSF shunt devices was heralded by the publication of Nulsen and Spitz's ventriculolumbar shunt with a ball and spring differential pressure valve.¹⁶ The first shunt to use silicone was the Spitz-Holter valve, a slit valve designed by engineer John Holter for his son who had

hydrocephalus.¹⁷ At around the same time, Robert Pudenz also designed both a distal-slit and a sleeve valve, both differential pressure silicone valves for use in ventriculoatrial shunts.¹⁸ Silicone has since become the material of choice for implanted shunts. Although the initial preferred site for shunt placement was the vascular system, the risks, particularly infection and associated shunt nephritis or pulmonary hypertension,^{19,20} and identification of the peritoneal cavity as a suitable site for CSF absorption²¹ led to the peritoneum becoming the preferred site for distal catheter placement. Despite several new shunt and catheter designs over the past 50 years, many of the problems associated with shunts, such as blockage, overdrainage, and infection, still persist. The search for the "ideal" shunt system or an alternative, more efficacious treatment continues.

CEREBROSPINAL FLUID SHUNT HYDRODYNAMICS

To understand the mechanisms behind the multitude of shunt designs available, a basic knowledge of hydrodynamics, or the physics of fluid flow, is necessary. Three important physical concepts must be understood: pressure, flow, and resistance.

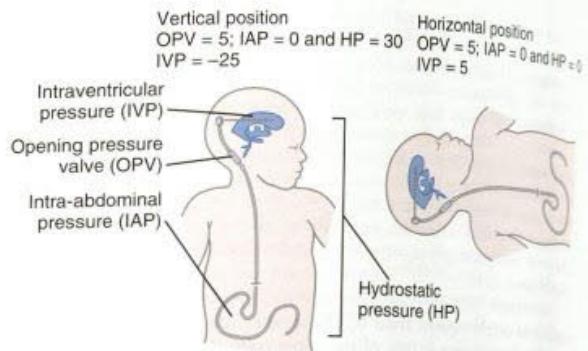
Pressure

Pressure is force (*F*) per unit area (*A*). For a cylindrical column of fluid, such as in a shunt tube, the pressure at the base of the tube is equal to the weight divided by the tube's surface area, which equates to the height of the column (*h*) times the density of the fluid (ρ) and the force of gravity (*g*): $P = \rho \cdot h \cdot g$. In vivo and in shunt systems, pressure is generally measured relative to atmospheric pressure, which we call zero. Pressure is usually expressed in millimeters of mercury (mm Hg) or millimeters of water (mm H₂O), with 1 mm Hg equaling 13.65 mm H₂O. If the CSF in the craniospinal subarachnoid space is considered a column of fluid, atmospheric pressure (zero) is at the level of the right atrium in the supine position; when sitting or standing, zero is at the level of the jugular venous pulse, and the pressure in the head is slightly negative and that in lumbar CSF is positive. The pressure in the abdominal cavity, the most common site for distal catheter placement, varies according to body habitus and abdominal wall tone but can generally be considered to approximate atmospheric pressure. In the pleural cavity, respiratory movements of the chest wall generate negative intrapleural pressure. With shunt systems we refer to the "differential pressure," or the difference in pressure between the two ends of the shunt that is responsible for flow in the shunt.

Flow and Resistance

Flow (*Q*) in a tube is defined as the volume of fluid (*V*) passing a point during a given time (*t*) (e.g., mL/min). Flow from one end of the shunt system to the other is defined by the equation $Q = \Delta P/R_t + R_v$, where ΔP is the difference in pressure between

FIGURE 192-1 Illustration of compartment pressures and the effect of position. Hydrostatic pressure predominates in the upright position. (From Drake JM, Sainte-Rose C. *The Shunt Book*. New York: Blackwell Science; 1995:23.)



the ventricle and distal catheter location and R_T and R_V are the resistance of the tube and valve, respectively.

Resistance to the flow of fluid through a shunt system ($R_T + R_V$) depends on a number of factors. Because flow of fluid through catheters is laminar (smooth), resistance of catheters (R_T) is defined by Poiseuille's law:

$$R_T = \frac{8L\mu}{\rho r^4}$$

where r is the radius of the tube, L is the length of the tube, μ is the viscosity of the fluid (CSF), and r the diameter of the tube.

Laboratory studies have demonstrated that a 90-cm-long distal catheter provides an additional resistance to flow that is roughly equivalent to that provided by a differential pressure valve.^{22,23}

The increase in CSF viscosity (e.g., proteinaceous CSF) seen in patients with optic pathway gliomas does not have a great impact in that even the most proteinaceous CSF reduces CSF flow by only around 7%.^{24,25} More importantly, CSF viscosity decreases with increasing temperature, with flow rates at body temperature some 30% higher than at room temperature, which has important implications for in vitro testing of new shunt designs, particularly those in which CSF flow occurs through a very small orifice, such as in the flow-controlled Orbis Sigma II valve.

Shunt catheter resistance rises as a fourth power of the radius, and this has been exploited in designing valveless shunt systems such as the "Mexican shunt," which has an internal diameter of 0.51 mm as opposed to a standard catheter diameter of 1.0 to 1.6 mm.²⁶ The relationship of shunt catheter resistance to radius has also been exploited as a means of reducing excessive drainage through lumbar shunt catheters.

Although R_T has linear pressure-flow characteristics, flow through the narrow orifices of valves, despite being laminar at low flow rates, may become turbulent at higher rates of flow. Therefore, the resistance of the shunt valve (R_V) is not constant in the range of physiologic flow rates, and a nonlinear pressure-versus-flow relationship is seen. Debris and air bubbles in the shunt valve or catheter will significantly increase turbulence and restrict the diameter of the lumen, both of which will significantly increase resistance to flow; although this does not necessarily occlude the shunt, it may have a major impact on shunt performance.²³

The pressure gradient driving CSF flow in a ventriculoperitoneal shunt system is determined by the formula $\Delta P = IVP + phg - OPV - IAP$, where IVP is intraventricular pressure, phg (h being the difference in vertical height between the head and distal drainage site) is hydrostatic pressure, OPV is the opening pressure of the valve, and IAP is intra-abdominal pressure. Thus, in the upright position, the predominant influence on the pressure gradient (and therefore CSF flow) is hydrostatic pressure, not OPV (Fig. 192-1).

SIPHONING

With differential pressure valves (see later), once the patient moves to the upright position and the valve opens, the hydrostatic forces acting on the shunt system will predominate and result in excessively high flow rates despite negative intracranial pressure (ICP). In a valveless system, ICP would continue to fall until IVP equals negative phg to balance the siphon effect (Fig. 192-2). Such a drop in ICP does not occur in a normal brain because there is no posture-related change in the CSF-sagittal sinus pressure gradient.²³ The exception occurs in patients who have undergone a wide decompressive craniectomy, in which the head is essentially exposed to atmospheric pressure. In these patients in the upright position, CSF will continue to siphon until the ventricles are emptied and the craniectomy is maximally sunken, which may result in marked shift and deformation of the underlying brain tissue and have significant neurological sequelae, the "sinking skin-flap syndrome."²⁷

The excessively negative pressures generated by siphoning are surprisingly well tolerated by the majority of patients, but around 10% of patients will experience low-pressure symptoms.²⁸ Other serious sequelae include ventricular collapse with tearing of bridging veins and subdural hematoma formation, premature

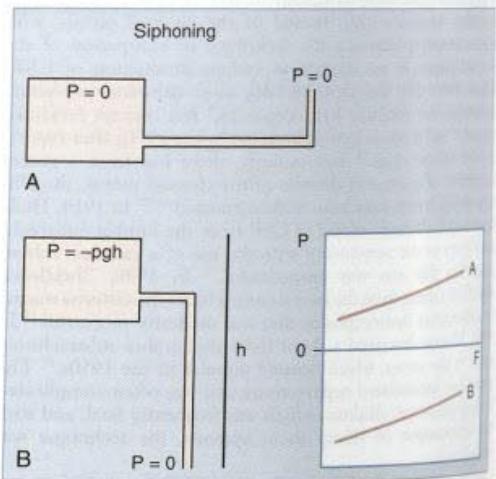


FIGURE 192-2 Changes in intraventricular pressure that occur with siphoning. Pressure (P) and flow (F) in horizontal (A) and vertical (B) position are shown. (From Drake JM, Sainte-Rose C. *The Shunt Book*. New York: Blackwell Science; 1995:21.)

closure, acquired aqueductal stenosis, Parinaud's syndrome, and slit ventricle syndrome.^{28,30-33}

It should be remembered that raising the opening pressure of the valve will decrease the magnitude of the negative IVP generated by siphoning but will not prevent siphoning or its clinical sequelae from occurring because the dominant influence of hydrostatic forces will persist.

PROXIMAL AND DISTAL SHUNT CATHETERS

All shunt catheters (both proximal and distal) are made of artificial silicone rubber or polyurethane. The catheters are stiff enough to resist kinking but compliant enough to minimize the risk of brain injury as the ventricles reduce in size and the catheter comes in contact with the ependyma. Catheters are available in a range of internal and external diameters, the smaller internal diameters being used in neonates or valveless shunt systems to add further resistance to CSF flow. Most modern catheter designs are impregnated with tantalum or barium to facilitate radiologic identification. The latter is associated with an increased rate of distal shunt catheter deterioration and host reaction leading to calcification and loss of elasticity and strength of the catheter tubing.^{34,35} The catheters then become tethered, typically in the neck, and are prone to fracture, particularly in growing children.³⁶ To mitigate this complication, some manufacturers now produce catheters with a barium strip or coating of pure silicone to reduce host reaction to the tubing.

Packaged catheters carry a static charge and, when opened, can attract airborne dust particles carrying microorganisms; accordingly, non-antibiotic-impregnated catheters should be soaked in sterile saline solution immediately on opening to reduce the risk of contamination. To reduce the risk for shunt infection, manufacturers have introduced specialized catheters, some of which are impregnated with antibiotics, such as the Leiseal catheter system, which is impregnated with clindamycin and rifampicin (Codman, Johnson & Johnson, Inc., Raynham, MA) and releases the antibiotics in the weeks after implantation to potentially reduce the risk for shunt infection by preventing biofilm-forming organisms from colonizing the catheter. Other manufacturers have developed catheters that are impregnated with silver nanoparticles (Silverline, Speigelberg, Hamburg), which have antibacterial properties,³⁷ or coated with antibiotics to reduce the risk for shunt infection. It should be noted, however, that to date, no prospective multicenter randomized controlled trials have been completed that demonstrate an overall reduction in infection rates with any of these catheters. Some retrospective studies have shown promising results in high-risk populations,³⁸⁻⁴⁰ but other series have not demonstrated a benefit,⁴¹ and a relative increase in more severe gram-negative infections may offset any benefit from an overall reduction in infection rates. Other measures such as the intraventricular administration of antibiotics at the time of shunt implantation may be of similar efficacy.⁴²

The proximal shunt catheter is usually placed in the lateral ventricle. Occasionally, catheters are placed within the subarachnoid space, arachnoid cysts, syrinx cavities, and subdural hygromas. The most common cause of shunt malfunction is blockage of the proximal catheter, which is usually secondary to ingrowth of choroid plexus. Attempts to identify a preferred site for catheter placement remote from the choroid plexus have been unsuccessful.⁴³ Even endoscopically assisted placement of proximal catheters does not reduce blockage rates,⁴⁴ although post hoc analysis of the data suggested that if catheters could be accurately positioned away from the choroid plexus, shunt failure could be reduced. A variety of proximal catheter designs with baskets, flanges, or recessed holes, as well as the "J"-shaped Hakim catheter with holes on the inside curve of the "J," have been produced in an effort to reduce mechanical obstruction by the choroid plexus, but none have been successful in reducing ventricular

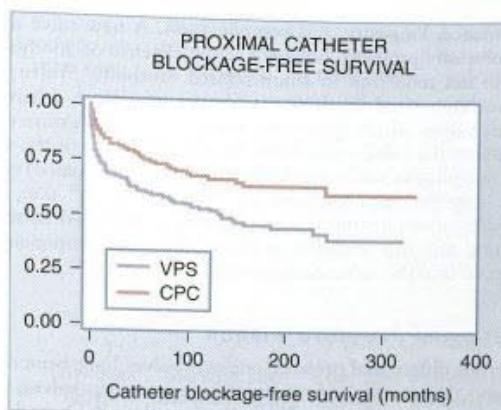


FIGURE 192-3 Proximal catheter blockage-free survival in shunted patients who had previously undergone endoscopic choroid plexus coagulation (CPC) versus those with no previous choroid plexus coagulation (VPS).

catheter blockage rates. Endoscopic coagulation of the choroid plexus itself on the side of the shunt may be the most effective means of reducing proximal catheter obstruction (Fig. 192-3).⁴⁵

The size and number of drainage holes in the tip of the catheter vary, but most holes are redundant. Laboratory studies have shown that even if only a single hole remains patent, there is no significant increase in the total resistance of the shunt system.⁴⁶ Ventricular catheters come with a stylet to facilitate passage of the catheter through the brain parenchyma. Hollow stylets to allow visualization of CSF when the ventricle is cannulated are now available. A number of devices can be used to facilitate proximal catheter placement, including the Ghajar guide, a tripod designed to ensure a perpendicular trajectory to the ventricle from a coronal approach,⁴⁷ as well as ultrasound probes and intraluminal ventriculoscopes.^{44,48} All these devices can assist in either accessing the ventricle or confirming position within the ventricular system (or both). Recently, frameless, image-guided neuronavigation has been used to facilitate catheter placement,⁴⁹ and the advent of electromagnetic navigation technology has enabled the use of such neuronavigation in infants.⁵⁰ When contoured or cylinder valves are used, external right-angle guides are used to reduce the risk of shunt migration, but in very small infants these guides may be unduly prominent and increase the risk for scalp breakdown. A variety of rigid connectors (either polyethylene or titanium) are available, either straight, right angled, or "Y," "X," or "T" shaped to facilitate the assembly of complex shunt systems. Bur hole reservoirs that redirect the flow of CSF 90 degrees can also be used in conjunction with contoured valves, particularly if the valve has no integral reservoir of its own.

Distal shunt catheters may have a distal slit or a single open-ended lumen. The latter is associated with a significantly lower rate of distal catheter occlusion,⁵¹ and we advocate removal of any distal slits before intraperitoneal placement. When the distal catheter is placed in the vascular system, a distal slit valve is required. Recently, distal catheters have been placed with laparoscopic assistance. This may be useful when cosmesis is a major consideration or when coexistent intra-abdominal pathology such as adhesions or obesity may compromise optimal placement, and it allows confirmation of the implanted functioning shunt system.⁵²⁻⁵⁷

SHUNT VALVES

There are an enormous number of shunt valves available on the market today. This is a reflection of the failure of any single device to demonstrate functional superiority in terms of valve

performance, longevity, and complications. A new valve design may solve one problem, but only at the expense of another and with no net reduction in shunt-related morbidity. Valve types may be categorized by their mechanism of action: differential pressure valves, which open when the differential pressure of the fluid across the valve exceeds the opening pressure of the valve; flow-controlled valves; and gravitational (gravity-actuated) valves. Valves may be fixed pressure or "programmable" (i.e., have adjustable valve opening pressure). Devices intended to reduce siphoning are also available as either separate components or integrated into the valve design itself.

Differential Pressure Valves

Numerous differential pressure one-way valves have been developed and they consist of four broad categories: slit valves, miter valves, diaphragm valves, and ball-in-cone valves.⁵⁸ These devices all attempt to achieve the same goal of keeping IVP from climbing too high or falling too low. Differential pressure valves are defined by their opening or closing pressure. As IVP rises, the differential pressure across the valve increases. When this exceeds the valve's opening pressure, the valve opens to allow egress of CSF at a rate determined by the resistance of the entire shunt system; once the pressure falls below the closing pressure, however, flow of CSF ceases. Although it has not been demonstrated *in vivo*, it is possible that the valve opens and closes with each cardiac cycle, and valves may act by damping the ICP pulse wave, which has been implicated in ventricular enlargement in hydrocephalus.⁵⁹⁻⁶¹ The valve's opening pressure is not necessarily the same as its closing pressure because of the phenomenon of hysteresis. Hysteresis occurs because of a slight change in the mechanical properties of the valves, depending on whether they are opening or closing, and occurs most frequently with silicone slit and miter valves. It can have a significant impact on valve performance and potentially lead to overdrainage, even in the absence of siphoning (e.g., during nocturnal vasogenic pressure wave activity or exercise).⁶² Pumping valve reservoirs can further affect performance, particularly with silicone diaphragm valves.⁶³

Most manufacturers provide differential pressure valves with various opening pressure ranges in categories such as very low, low medium, medium high and high. These ranges are usually coded by radiopaque markers on the valve housing. Unfortunately, there is no industry standard, and the exact pressure characteristics vary considerably between manufacturers. Some manufacturers classify valves according to closing pressure and others according to pressure at a particular flow rate. Most differential pressure valves will allow flow rates far in excess of what would be considered physiologic. Opening pressure is not everything, however; as shown earlier, two different differential pressure valves may have the same opening pressure but completely different resistance values and therefore behave differently. Manufacturers' descriptions of valves can be confusing; for instance, the PS Medical Flow-Controlled Valve is a differential pressure valve not a "flow-controlled" valve (see later).

Slit valves may be placed at the proximal end (Holter-Hausner valve) or at the distal end (Codman Unishunt) of a shunt. Simple distal slit valves offer the lowest resistance to flow, and in fact no significant difference in resistance can be measured between a tube with a distal slit valve and an equally long open-ended tube.

The diaphragm valve, such as the PS Medical Flow-Controlled Valve, is probably the most commonly produced type of differential pressure valve. Generally, these valves involve deflection of a silicone membrane in response to pressure to allow flow of CSF. Most of these valves contain an integral reservoir that may be either proximal or distal to the valve mechanism. It is important, for each shunt type, to understand the relationship between the reservoir and valve when examining an implanted shunt and when considering administering antibiotics intrathecally via the valve

reservoir, for example. Valves may have proximal and distal occluders to facilitate percutaneous flushing of the valve, *in vivo* testing, or drug administration.

Flow-Regulated Valves

Flow-regulating devices such as the Orbis Sigma II valve (NMT Medical, Inc., Boston) are designed to increase hydrodynamic resistance as the pressure gradient increases in an attempt to keep the flow rate constant.⁶³ It is in fact the differential pressure that controls the resistance, and perhaps these valves should be called pressure-controlled, variable-resistance, constant-flow valves. The valve is composed of a contoured synthetic ruby flow control pin that fits inside a movable synthetic ruby ring (Fig. 192-4). These devices produce pressure-flow curves with a sigmoid shape; at low pressures the valve behaves as a differential pressure valve until flow rates reach about 20 mL/hr. As the pressure increases, the ruby ring is deflected downward, and because the ruby pin is tapered, the flow aperture decreases, which increases resistance and reduces flow. This will tend to maintain flow at a constant level over a range of physiologic pressures (8 to 35 cm H₂O). If the pressure increases further, beyond a predetermined threshold, typically around 35 cm H₂O, the ruby ring is deflected further downward beyond the pin, thereby increasing the aperture for CSF flow and lowering resistance to allow "venting" of CSF for mitigating any pathologic rise in CSF pressure. At this point the valve behaves as a differential pressure valve and gives rise to a sigmoid curve. Flow-regulating valves are less likely to be associated with siphoning and overdrainage and have been shown to improve symptomatic low ICP in shunted individuals.⁶⁴ However, flow-regulated valves typically have very small orifices, which makes the valve itself a probable site of obstruction.^{65,66} In addition, the high resistance has a propensity to cause fluid collections under the scalp in young children unless they are nursed upright with a compressive dressing. A randomized controlled trial failed to demonstrate a reduction in revision rates with flow-controlled valves when compared with other conventional differential pressure valve types.⁶⁵

Antisiphon Devices

One strategy developed to avoid the complication of overdrainage is the siphon-resistive or antisiphon device (ASD). Several devices are available that can be broadly grouped into three different categories: those using a subcutaneous membrane, those using a gravitational mechanism, and those regulating CSF flow

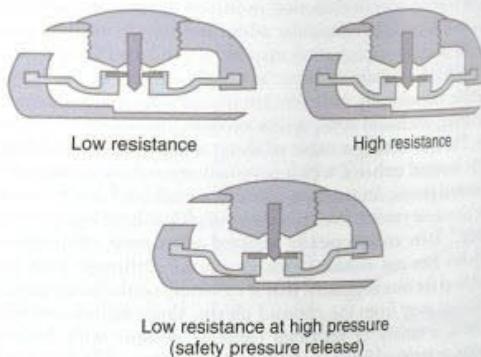


FIGURE 192-4 Schematic diagram of the Orbis Sigma valve. (From Drake JM, Sainte-Rose C. *The Shunt Book*. New York: Blackwell Science; 1995:98.)

The most widely used is the PS Medical Delta Chamber (Medtronic PS Medical, Goleta, CA), which also comes integrated with a differential pressure valve: the Delta valve. This device is typically placed under the scalp and has a small diaphragm that reduces the flow of CSF when the pressure inside the shunt falls below atmospheric pressure. Drake and coworkers demonstrated that raised tissue compartment pressure from scar tissue overlying an ASD can lead to functional obstruction.⁶⁷ Bench testing suggests that the Delta valve probably works predominantly in the horizontal position because in the upright position, the physiologic value of the ICP is sufficiently negative to close the ASD.⁶⁸ The SiphonGuard ASD (Codman and Shurtleff, Inc., Raynham, MA) is designed to reduce siphoning by having two alternative pathways for drainage of CSF. During normal flow, both the primary and secondary pathways are open. In high-flow states, the primary pathway closes and flow is diverted to a high-resistance secondary pathway. The device can be positioned anywhere along the shunt system. The main criticisms of this device derive from bench test data suggesting that in patients with small or slit ventricles, CSF may not be available to produce flow at a high enough rate to activate the high-resistance pathway. Furthermore, children or adults who spend significant time in a semirecumbent position (the elderly) may fail to generate sufficient "siphoning" to trigger the high-resistance pathway but may have flow rates sufficient to cause overdrainage, and there is also a theoretical risk of the valve "locking" in the high-resistance state.⁶⁹ These risks remain theoretical, and further clinical studies are required to evaluate this device. Gravitational ASDs are discussed in the next section.

Gravitational Valves

Gravitational (or gravity-actuated) valves (e.g., Cordis Horizontal-Vertical Lumboperitoneal valve; Miethke paedIGAV valve) attempt to prohibit or reduce siphoning by increasing opening pressure with the assistance of gravity when a patient sits or stands. All fixed gravitational valves are differential pressure valves but operate at two different opening pressures that is dependent on whether the patient is in the horizontal or vertical position. They are typically composed of a "ball-in-cone" unit, which is a simple differential pressure valve that acts in the horizontal position coupled with a "gravitational unit" composed of free-moving balls that "drop" into a cone in the upright position. In the upright position, the opening pressures of both valve mechanisms must be overcome. Because the hydrostatic pressure to be overcome is dependent on the height of the patient, these valves come in a range of opening pressures (both horizontal and vertical), and the most appropriate valve depends on the height of the child. Since movement of the balls within the gravitational unit determines the opening pressure, it is extremely important to ensure that gravity-actuated valves are secure and in the proper vertical position. The valves are usually in a cylinder-shaped, titanium housing and should therefore be used with a side inlet bur hole reservoir, both to prevent shunt migration and to facilitate *in vivo* testing of the shunt. The "gravitational unit" is also available as a standalone ASD, the Miethke "Shunt Assistant."

Programmable Valves

Programmable valves are more appropriately called *externally adjustable differential pressure valves*. They act in the same fashion as nonadjustable differential pressure valves, except that the surgeon has the option of altering the opening pressure with an external device, thereby obviating the need for surgical shunt revision. This increases convenience and marginally decreases risk, but it is not clear whether this benefit outweighs the increased cost of using these valves in all patients. Programmable valves include the Codman Medos Hakim Programmable Valve

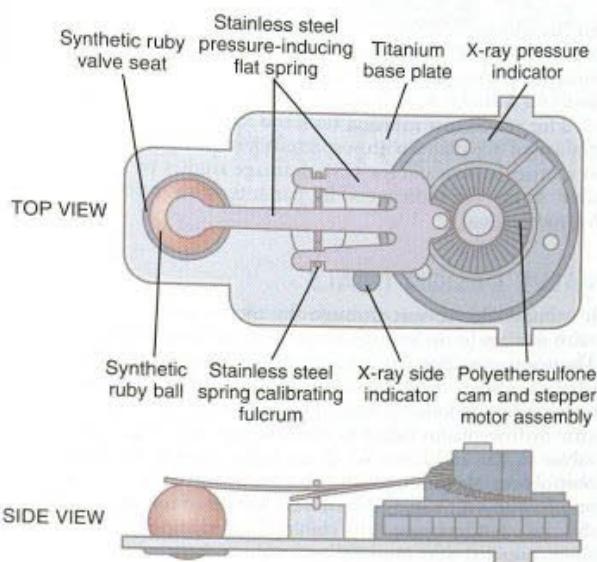


FIGURE 192-5 Schematic diagram of the Codman Medos programmable valve. The valve has an adjustable ball-spring mechanism. A cam and stepper motor assembly (akin to a spiral staircase) is used to adjust the tension on the spring. The motor assembly is adjusted with an externally applied magnetic field from the valve programmer. (From Drake JM, Sainte-Rose C. The Shunt Book. New York: Blackwell Science; 1995:94-95.)

(an adjustable "ball-in-cone" valve with 18 settings from 30 to 200 mm H₂O [Fig. 192-5]), the PS Medical Strata Valve (an adjustable, 5-setting Delta valve; also available as a 5-setting differential pressure valve without an ASD, the Strata-NSC), and the Sophy Programmable Pressure Valve (adjustable spring-ball valve). Most valves are adjusted with an external magnet, and some are disposed to inadvertent reprogramming in the presence of strong magnetic fields.^{68,70} Patients with these valves require reprogramming after magnetic resonance imaging (MRI) and should also be advised to avoid close proximity to strong magnetic fields (some stereo headphones, magnetic toys, televisions, electricity substations, etc.).⁷¹⁻⁷⁴ Several authors have reported clinical success with these devices,⁷⁵⁻⁷⁷ but to date no adequately powered randomized controlled trials designed to compare efficacy have been undertaken. It has been suggested that this type of shunt is well suited for difficult-to-manage cases of overdrainage (e.g., slit ventricles, subdural collections) or underdrainage (e.g., persistent symptoms of hydrocephalus).⁷⁸⁻⁸⁰ It has also been suggested that externally adjustable shunts are particularly useful in gradually decreasing the size of arachnoid cysts and in reducing the incidence of symptomatic subdural hygromas in patients with normal-pressure hydrocephalus.^{79,81,82} It is important to note that programmable valves that do not incorporate an ASD are also susceptible to siphoning.

VENTRICULAR ACCESS DEVICES

Ventricular access devices such as the Ommaya reservoir allow percutaneous access to ventricular CSF. They were initially developed to permit intrathecal administration of chemotherapy.⁸³ These devices can be used for the *in situ* treatment of CSF shunt infections.⁸⁴ Because they do not tend to become blocked with choroid plexus, they are now increasingly being placed in patients with CSF shunts to allow emergency ventricular access in the event of shunt blockage.^{85,86} They have also been advocated after endoscopic third ventriculostomy⁸⁷⁻⁹⁰ when there is a risk

for late blockage, which may be fatal, but this indication remains contentious.⁹¹ They are useful in facilitating ventricular taps in infants with posthemorrhagic ventricular dilation who are too small for a shunt. In addition, ventricular access devices may be used for ventricular infusion tests and monitoring of ICP for the evaluation of patients with suspected shunt failure but no increase in ventricular size and for CSF drainage studies to evaluate possible shunt responsiveness in patients with normal-pressure hydrocephalus.^{92,93}

VALVE DESIGN TRIALS

It is impossible to sort through the merits of the various shunt valve designs by attempting to evaluate uncontrolled case series. These series are frequently reported by proponents of the devices, who sometimes have financial interests or other incentives. A multicenter randomized trial of CSF shunt valve design for pediatric hydrocephalus failed to demonstrate any difference among valves in the incidence of shunt failure resulting from shunt obstruction, overdrainage, loculations of the cerebral ventricles, or infection over a minimum 1-year period of follow-up.^{65,94,95} In this trial, 344 hydrocephalic children undergoing their first CSF shunt insertion were randomized to one of three valves: a standard differential pressure valve, a Delta valve, or an Orbis Sigma valve. A randomized trial comparing a conventional valve and a Codman Hakim programmable valve with respect to shunt failure and valve explantation also did not demonstrate any significant difference between the valves.⁹⁶ It is clear that further prospective randomized controlled trials are required to evaluate the new generation of programmable and gravitational valves. Studies evaluating shunt selection for specific patient subgroups such as those with normal-pressure hydrocephalus are also required. Data from prospective national shunt registries such as the U.K. Shunt Registry, which now has more than 50,000 procedures logged, may also provide valuable insight into long-term valve outcomes.⁹⁷

IN VIVO SHUNT ASSESSMENT

Neuroimaging plays a major role in the assessment of suspected shunt malfunction. A plain radiographic shunt series can identify shunt fracture or migration and allow identification of the shunt valve type.⁶⁵ Computed tomography and MRI are particularly useful in the assessment of ventricular size, particularly when a "well baseline" scan is available for comparison. Radioisotope studies, the "shuntogram," can provide qualitative information on shunt patency. Pumping the shunt reservoir alone does not have sufficient predictive power to detect shunt malfunction.⁹⁸ Tapping the shunt with a butterfly cannula can confirm proximal catheter patency, and assessment for "siphoning" with the patient inclined 45 degrees can evaluate distal catheter function, but care should be taken to ensure that the assessor understands the relationship between the valve and integral reservoir for any individual shunt system when tapping a shunt. A more elaborate quantitative invasive test is the ventricular infusion study, which can be performed via either a separate ventricular access device or, for shunts in which the reservoir lies proximal to the valve, the shunt reservoir itself. Czosnyka and colleagues have established threshold pressures for different valve types, and this information is extremely useful when evaluating equivocal shunt failure or overdrainage.⁹² Accessing the shunt carries a risk for infection, so strict asepsis is essential.

FUTURE DEVELOPMENTS

Further advances in technology, such as nanocoatings for shunt components, should increase the biocompatibility of shunt systems, thereby prolonging life span.⁹⁹ Simple measures such as not using barium-impregnated catheters and removing distal shunt valves should also prolong shunt survival. Techniques such as percutaneous ultrasonic cavitation may enable recanalization of blocked ventricular catheters.¹⁰⁰ Efforts should be directed to establishing the efficacy and cost-effectiveness of existing technology in large randomized multinational controlled trials. Key areas of focus should include comparisons of novel valve types, including gravitational valves and new-generation programmable valves. Novel proximal catheters designed to reduce rates of obstruction with choroid plexus should be compared with other techniques such as choroid plexus coagulation. The development of telemetric ICP monitors will facilitate the diagnosis of shunt failure. Functioning prototype devices have been tested successfully in animal models.¹⁰¹ Unfortunately, the high cost of developing these products and bringing them to market may hamper translation from the laboratory to the bedside. Shunt systems with integrated thermistor sensors that can monitor flow are likely to be marketed in the near future and may be useful for diagnosing shunt blockage. Intelligent shunt systems with servo-controlled feedback mechanisms to regulate CSF flow remain elusive more than 35 years after they were first proposed¹⁰² and the goal of a single shunt that provides physiologic control of ICP and lasts a lifetime is some decades away.

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Shunt Infections and Their Treatment

Nalin Gupta

Hydrocephalus is a common neurological condition in children and accounts for approximately 2% of all pediatric hospital admissions.¹ The real costs of these admissions are substantial, with total hospital charges estimated to be between \$1.4 billion and \$2 billion annually.¹ Although shunt insertion greatly mitigates the long-term disability caused by hydrocephalus, the complications associated with shunt insertion are a challenge in the long-term management of these patients. One shunt-related complication is the postoperative occurrence of infection, which leads to increased hospital stays, additional negative impacts on the patient's developmental progress, and increased mortality.² This chapter summarizes the clinical features of shunt infection, its treatment, the benefits of preventive measures, and the long-term outcomes of shunt infection in the pediatric population.

INFECTION RATES

General

Shunt infection rates differ among reported studies.^{2,3} Borgbjerg and associates³ studied 884 individuals (440 of whom were younger than 14 years) who underwent placement of a new shunt from 1958 to 1989. The infection rate in this group was 6.2% for the first postoperative month, with an overall rate of 7.4%. Robust data are available from randomized clinical trials evaluating shunt designs in patients recruited from several medical centers. In one study, 344 patients were prospectively randomized to receive three different shunt designs.⁴ Nearly 40% of newly inserted shunts failed in the first year, with a shunt infection rate of 8.1% over the follow-up period of 1 to 3 years. These data reflect the shunt infection rate following a single shunt procedure. If patients are followed for longer periods, the cumulative likelihood of shunt infection related to multiple shunt procedures ranges from 19% to 38%.^{5,6} Despite the presence of a self-reporting bias, the Hydrocephalus Association database demonstrated that nearly 40% of patients who had hydrocephalus for at least 10 years experienced at least one shunt infection.⁶ Although preventive measures (see later) may reduce shunt infection rates, a reasonable conclusion is that the overall infection rate for new shunts is between 3% and 8%. Compared to historical data, it seems that there has been a gradual decline in shunt infection rates.⁷ It is not entirely clear what factors have contributed to this decline, although greater attention to sterile technique, preoperative antibiotics, and improved surgical technique may all play a role.⁸

Timing of Infection

Among pediatric patients, the majority of shunt infections occur relatively soon after operative placement of the shunt. In one of the larger series of pediatric patients with extended follow-up, Casey and colleagues⁹ reported that among children with shunted hydrocephalus who underwent a first shunt revision for infection, 92% of infections occurred within 3 months of the initial shunt placement. Similarly, in infants, who appear to have higher shunt

infection rates, the majority of infections occurred in the first 3 months after surgery.⁹ However, in a longer term analysis from a randomized trial, there appeared to be delayed shunt infections that occurred 2 to 3 years after shunt insertion.¹⁰

Risk Factors

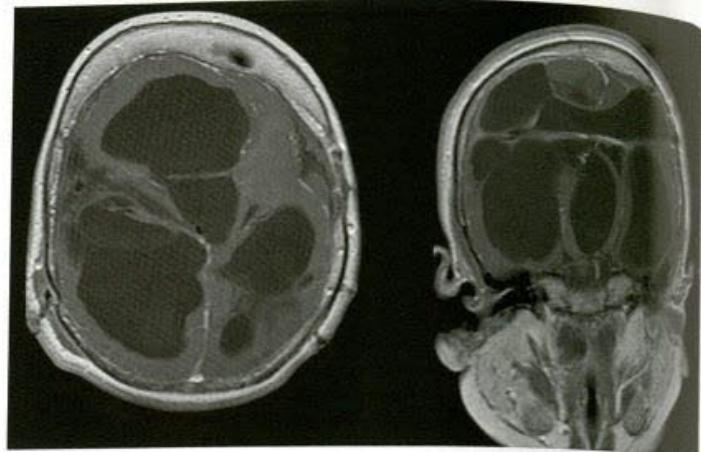
Although many variables are proposed to affect shunt infection rates, the most consistent factor is patient age, with neonates and very young children at greatest risk.^{5,11} In one cohort study, children 6 months or younger had a 19% rate of infection, versus 7% among older children; this finding is similar to the reports of other groups.⁵

A variety of explanations accounts for the increased shunt infection rate in very young children, including the presence of age-related changes in the density and identity of bacterial populations on the skin of neonates, as well as increased susceptibility to pathogens due to the relative deficiency of the neonatal immune system. Although maternal breast-feeding has been associated with the maintenance of immunoglobulin G levels in neonates, no data exist on the potential role of breast-feeding in reducing the risk of shunt infection. Some data suggest that more highly adherent strains of coagulase-negative *Staphylococcus*, the most prevalent organism in shunt infections, occur in neonates.¹²

Along with age, numerous other factors have been examined for their role in shunt infection, including the timing of shunt placement, educational level of the surgeon, length and time of surgery, use of antibiotics before and after surgery, surgical method for placement of the distal catheter, type of shunt, reason for shunting (e.g., posthemorrhagic versus congenital hydrocephalus), previous shunt history, spinal dysraphism, number of early revisions, and concurrent infection. In some studies, the reason for shunt placement^{5,9} and the presence of spinal dysraphism were associated with increased rates of infection.¹¹ Two studies reported that patients with congenital hydrocephalus had lower rates of infection than did patients with either postinfectious or posthemorrhagic hydrocephalus. One study reported that half the children in the postinfectious and posthemorrhagic group had at least one episode of shunt infection by the end of 1 year.⁹ Although earlier studies suggested that the type of shunt affected infection rates, more recent randomized studies examining shunt types have not confirmed this finding. A caveat with regard to these results is that the findings are not consistent across individual studies, suggesting that other variables are leading to an observed bias.

With respect to surgical factors, there is a paucity of convincing data. Shunt infection requires the exposure of shunt hardware to an infectious agent, usually bacteria, that subsequently leads to an inflammatory response of varying severity. An infection can result from several sources: colonization at the time of surgery, skin breakdown and subsequent colonization, hematogenous spread, and retrograde infection involving either a perforated viscus or coincident peritoneal infection. The timing of shunt infection and the predominance of skin organisms suggest that colonization from the patient's skin is the likely cause of most

FIGURE 193-1 Axial and coronal T1-weighted magnetic resonance images of the ventricular system and surrounding brain of a 5-year-old boy with bilateral schizencephaly and multicompartmental hydrocephalus caused by severe ventriculitis.



shunt infections. However, some data suggest that the patient's own skin flora may not be the primary source of these bacteria.^{13,14} A postoperative cerebrospinal fluid (CSF) leak leads to a very high risk of shunt infection (odds ratio of 19), presumably by allowing a direct path from the patient's skin to the shunt hardware.¹⁵

CLINICAL EVALUATION

Signs and Symptoms

Fever, headache, and pain in the setting of a recent shunt procedure are the usual symptoms reported to occur with infection. The actual presentation can vary and is dependent on the virulence of the organism and the location of the infection. It is useful to consider shunt infections as being present in three locations: within the ventricles and shunt, in the abdomen, or around the shunt hardware in the subcutaneous tissues. With low-virulence organisms, a shunt infection causes a pleocytosis and subsequent shunt obstruction, with corresponding symptoms such as headache and vomiting. Absence of a fever does not exclude shunt infection. More important, repeated shunt failure is sometimes caused by very low virulence organisms that may not be identified using routine culture techniques. Infections within the peritoneal cavity usually present with abdominal pain and shunt failure. Finally, wound infections at either the cranial or abdominal end may not affect shunt function but can result in wound dehiscence, cellulitis, and erosion of the skin over the hardware.

Symptoms and signs of shunt infection are also age dependent. Infants may present with increased irritability or, in more severe cases, apnea and bradycardia. Other clinical features include fever, gait disturbances, seizures (particularly in patients with a baseline seizure disorder, although new-onset seizures are possible), and visual disturbances, including upward gaze palsy and papilledema. The clinical presentation can also be affected by the type of infecting organism. For example, patients with shunt infection caused by gram-negative bacilli such as *Escherichia coli* frequently present in a relatively acute fashion with severe abdominal pain or septicemia, whereas shunt infections caused by skin organisms such as *Staphylococcus epidermidis* tend to be more indolent in nature. *Staphylococcus aureus* infections may be associated with erythema along the shunt tract. Individuals with ventricular-vascular shunts may present with subacute bacterial endocarditis as well as shunt nephritis, an immune complex disorder of the kidneys that is similar to glomerulonephritis.

Imaging Studies

Imaging studies play an indirect role in the diagnosis of shunt infection. Plain radiographs are used primarily to determine whether a shunt system is in continuity. Rarely, plain radiographs demonstrate a specific finding, such as air within the peritoneal cavity, that is strongly suggestive of a shunt infection.

In many cases shunt infection causes some degree of shunt obstruction and results in findings consistent with that diagnosis, such as increased ventricular size. This is usually easily determined on an ultrasound study if the fontanelle is open or with computed tomography (CT) or magnetic resonance imaging (MRI). Complex shunt infections, associated with multicompartmental hydrocephalus, severe ventriculitis, or resistant or virulent organisms, result in dramatic findings (Fig. 193-1). Imaging studies are needed in these situations to determine whether cystic collections should be fenestrated or multiple catheters are required for effective CSF drainage.

Peritoneal infections usually result in the formation of localized fluid collections that can be detected by sonography or CT. Formation of an abdominal "pseudocyst" is usually caused by a localized reaction of the omentum and progressive accumulation of fluid within that space (Fig. 193-2). Drainage of the pseudocyst is rarely needed unless there is strong suspicion of a true abscess or the collection fails to resolve after treatment. Antibiotic treatment usually results in rapid improvement. It is our practice to confirm resolution of the fluid collection with sonography or CT before placement of a new shunt.

Laboratory and Bacteriologic Studies

Shunt infection is a recognized complication of shunt insertion, and clinical suspicion should guide the investigations performed to either confirm or exclude the diagnosis of infection. If there is an obvious skin infection directly over the shunt hardware, or if the hardware becomes exposed owing to skin breakdown, infection should be assumed and antibiotic treatment should be started, along with removal of the device. Skin swabs are rarely helpful in isolating the exact organism because cross-contamination invariably occurs. In most other situations, confirmation of a shunt infection and identification of the causative organism require a CSF sample. This is most commonly obtained by percutaneous aspiration of the shunt through the cranial reservoir. Even if there is some degree of proximal shunt obstruction, CSF can usually be obtained. If the proximal portion of the shunt is completely obstructed and symptoms are suggestive of shunt



FIGURE 193-2 Sagittal ultrasonographic view of an abdominal fluid collection in a 7-year-old child with a ventriculoperitoneal shunt infected with methicillin-resistant *Staphylococcus aureus*.

infection, there are two options. If there is no evidence of raised intracranial pressure, a small-volume lumbar puncture (2 mL) can be done. It should be noted that a negative lumbar puncture result does not completely exclude a shunt infection. If the patient has symptoms of raised intracranial pressure, shunt exploration is required. An intraoperative Gram stain and cell count may clarify the issue. If there is sufficient doubt and the CSF analysis is inconclusive, the shunt should be externalized until final cultures are obtained.

CSF obtained from a shunt tap is tested for glucose, protein, and cell counts, and a separate specimen is sent for culture. Low glucose, high protein, and high nucleated cell counts are generally indicative of infection. Depending on the initial event causing hydrocephalus, CSF cell counts can remain elevated for weeks or months. A differential count can help clarify the origin of an elevated white cell count, with lymphocytes representing the predominant population after intraventricular hemorrhage or craniotomy. CSF cultures may also be positive for infectious organisms, although negative cultures can occur and should not be considered proof of absence of a shunt infection. Repeated shunt failure is sometimes a warning that an indolent shunt infection is present.

CSF ventricular shunt catheter infections occur via three routes: contamination of the shunt material with skin organisms at the time of surgery, contamination from the bloodstream, and contamination along the shunt tubing from an abdominal source (generally associated with bowel perforation, although in some cases, no gross disruption of the bowel is observed). The source of the infection is reflected in the causative bacterial agent. The most common organisms found in shunt infections are typical skin flora such as coagulase-negative *S. epidermidis*,^{5,9,16} followed by *S. aureus* in a roughly 2:1 ratio. Interestingly, data suggest that in addition to its easy access by virtue of being a skin contaminant, *S. epidermidis* secretes a mucoid material that enhances its ability to adhere to foreign bodies such as shunt material.¹⁷ Shunt infections in which enteric organisms are isolated, including gram-negative bacteria such as *E. coli*, *Proteus*, and *Klebsiella*, are also common. Delayed infections with anaerobic diphtheroids such as *Propionibacterium* are particularly difficult to assess and treat because cultures may remain negative for more than a

week.¹⁸ In the setting of repeated shunt failure, an indolent infection with *Propionibacterium acnes* should be considered, and CSF cultures should be followed for at least 1 week. Fungal infections are reported but are less common than bacterial infections. These often lead to repeated shunt failures and are notoriously difficult to treat, often requiring prolonged administration of antifungal agents.

TREATMENT

Most shunt infections caused by staphylococcal species do not cause significant tissue damage or a severe inflammatory response. Intravenous antibiotic treatment usually results in rapid bacteriologic clearance, with resolution of the CSF pleocytosis. Persistence of viable bacteria in or around the shunt hardware usually precludes the use of antibiotics as the sole treatment for shunt infections. The majority of shunt infections require surgical removal of the shunt, placement of an external CSF drain, and several days of intravenous antibiotics. A new shunt is usually not placed until CSF cultures are negative for bacterial growth. The recommended interval between shunt removal and reinsertion averages approximately 10 to 14 days, with at least 48 hours between the final negative CSF culture and reinsertion. A survey of centers to determine variations in practice patterns noted that the treatment time for shunt infection varied widely from 4 to 47 days.¹⁹

In the interval between shunt removal and reinsertion, a variety of methods can be used to support shunt-dependent patients, including shunt externalization or placement of external ventricular or lumbar drainage catheters. In patients for whom temporary external drainage systems are not appropriate, such as premature infants with very low birth weight, intermittent lumbar punctures or ventricular taps can be performed. Patients who might require these methods include those with high CSF protein levels and hence an increased likelihood of valve malfunction and those with repeated shunt infections, for whom the temporary removal of all foreign material may be necessary to clear material from the CSF. Replacement shunts are frequently placed at a new location relative to the old shunt.

CSF culture results are used to guide the selection of antibiotics during the interval between removal of the infected shunt and replacement of a new shunt. Given the preponderance of skin organisms such as *S. epidermidis* and *S. aureus* that are identified as infectious agents, intravenous vancomycin is frequently used initially, with rifampin occasionally added for increased coverage. Once the cultures have returned, antibiotics can be selected based on the identified organism and drug sensitivities. For example, in the absence of methicillin-resistant *S. aureus* organisms or penicillin-allergic patients, both *S. epidermidis* and *S. aureus* can be treated with oxacillin or nafcillin, with good results.

An alternative to surgical replacement of the infected shunt is the use of antibiotics alone. Although there have been cases of shunt infection eradicated by this method,^{20,21} purely medical treatment, administered either intravenously or by a combination of intravenous and intrathecal routes, appears to be less effective than surgical treatment.^{2,17,22} In the sole randomized trial to compare medical versus surgical treatment of shunt infection, 30 patients with ventriculoperitoneal shunts were randomized to one of three treatment arms: (1) removal of the shunt, accompanied by the use of systemic antibiotics and an interim period of external ventricular drainage or ventricular taps; (2) immediate surgical replacement of the infected shunt, along with antibiotic treatment; and (3) antibiotic treatment only. All study subjects were treated with intravenous and intraventricular antibiotics. The cure rates, as measured by negative CSF cultures 48 hours and 1 to 4 months after treatment, were 100%, 90%, and 30% for the three groups, respectively. In addition to lower rates of cure, medically treated patients had a mean hospital stay of 47

days, versus 33 and 25 days for the two surgical groups, respectively.¹⁷

In general, studies reporting high rates of cure from the use of antibiotics alone are limited by small sample sizes or the failure to randomize patients in treatment groups. Although it is likely that some shunt infections can be treated by antibiotic therapy alone, there is often doubt about the organism's identity at the time of diagnosis and a desire to avoid progression of a CSF infection. Prudence usually prompts the surgeon to proceed with shunt removal and broad-spectrum antibiotic coverage. Clearly, for resistant or recurrent infections, the intrathecal administration of antibiotics leads to increased antibiotic levels within the ventricular system; however, the role of routine intrathecal antibiotics in addition to intravenous antibiotics is unclear.²³

OUTCOME

A primary concern is the success of treatment. Kestle and colleagues¹⁹ noted that the reinfection rate in their study was 26%. Two thirds of the reinfections were caused by the same organism, suggesting a failure to completely eradicate the original infection. Surprisingly, the reinfection rate was not affected by the duration of antibiotic therapy. This suggests that other factors such as resistance or lack of antibiotic penetration may account for reinfection.

An important question is whether patients with shunt infections have a poorer health-related quality of life as well as higher overall medical morbidity and mortality. Although some studies report no difference in the rate of death in children with infected versus noninfected shunts,⁵ the data from other studies suggest an increased mortality risk in the former. In a series of 108 infants presenting with hydrocephalus at birth and operated on from 1971 to 1981, the 10-year mortality rate was 71% in children who had a shunt infection, compared with 51% in children who did not.²⁴ Similarly, Walters and colleagues² reported a mortality rate of 34% among infected patients, versus 18% in a group of shunted patients without infection.

Few studies include data on the long-term outcomes for patients with shunts, and those that do provide conflicting results. Casey and colleagues⁵ followed 155 shunted hydrocephalic children for 10 years and found no evidence that the number of infection-related episodes affected the final intellectual outcome, with a good outcome defined as the child's ability to attend school. Renier and associates,²⁴ however, found that shunt infection was associated with poor functional results; the mean "late" postoperative IQ was 40 among children who had at least one shunt infection, versus an IQ of 60 among children without infection. There has been no examination of the possible correlation between intellectual outcome and clinical or demographic patient characteristics, such as the severity of infection or the age at which a child suffers an infection. Future studies are needed to examine these relationships in greater detail.

PREVENTION

The overwhelming preponderance of skin flora as the causative organisms in shunt infections suggests that minimizing contact between shunt equipment and the skin and strict adherence to sterile technique may reduce colonization by organisms. Specific intraoperative factors contributing to shunt infection were analyzed, with only postoperative CSF leak, prematurity, and a possible breach in the surgeons' gloves reaching statistical significance.¹⁵

Data regarding the use of prophylactic antibiotics are strongly suggestive, but confirmation is lacking. Meta-analyses from pooled data suggest a 50% reduction in infection rates when prophylactic antibiotics are used.^{25,26} In one study, the benefit of prophylactic antibiotics was lost if the baseline infection rate

was below 5%. A recent systematic review noted that although there was a trend toward a reduction in infection rates with the use of antibiotics, there was no support for continuing antibiotics beyond 24 hours after surgery.²⁷ All these analyses are limited by variations in technique and treatment of shunt infections.¹⁹

Recently, antibiotic-impregnated shunt (AIS) components have been introduced for use as temporary external ventricular catheters and implanted shunts.²⁸ The antibiotics found in AISs include rifampin, clindamycin, and minocycline. A number of studies have shown a reduction in infection rates, but these studies are usually observational or cohort studies without the benefit of randomization to control for other changes in surgical technique. Nevertheless, some of these results are particularly compelling. For example, using AIS components in a population of very young infants, Sciumba and associates²⁹ reported a shunt infection rate of 4.6% (5 of 74 patients) with at least 9 months' follow-up. This represents a substantial reduction when compared with historical controls. A similar finding was noted by other investigators who compared groups of patients receiving AIS components with their own historical cohorts.^{30,31} A particular benefit was noted in the neonatal subgroup receiving first-time shunts. In contrast, an observational study of mainly adult patients did not find any reduction of shunt infection rates using AIS components.³²

CONCLUSION

Infection remains a life-threatening and costly complication of ventricular shunt catheter placement. Although an extensive literature exists on the topic, few preventable risk factors have been identified, and no consensus exists regarding the best treatment, making it difficult to develop and implement standardized guidelines. Despite these limitations, the prevalence of shunt infections appears to have decreased in the past few decades, and some general recommendations can be made. Surgeons should strictly adhere to surgical technique, minimize contact between the shunt hardware and the skin, and routinely use prophylactic antibiotics. The duration of prophylactic antibiotic use is not well defined, but use longer than 24 hours after surgery is not supported by data. In clinically stable neonates with hydrocephalus, there may be some advantage to delaying shunt placement until the child is older. Finally, the use of AIS components appears to reduce shunt infection rates, although this may be restricted to subgroups prone to higher infection rates. At an individual level, each surgeon should track his or her shunt infection rates and implement all possible preventive measures if they are elevated.

There is a need for additional prospective studies of patients with ventriculoperitoneal shunts. Future studies testing new treatment regimens or devices need to incorporate ideal clinical designs such as randomization, consistent outcome measures, and adequate patient numbers to allow robust data to be obtained, which will allow improvement in clinical care.

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Geriatric Neurosurgery

EVALUATION OF ADULT HYDROCEPHALUS 3a

CHAPTER 33

Production and Flow of Cerebrospinal Fluid

Conrad E. Johanson

Continually generated and flowing cerebrospinal fluid (CSF) is vital for brain homeostasis.¹ Day and night, the choroid plexus pumps out fluid into the ventricles. CSF formation is about 0.4 mL/min per gram of choroid plexus. Nascent CSF is more than a passive ultrafiltrate of plasma.² Active secretion by choroidal epithelium is exquisitely modulated so that intracranial pressure (ICP) is stable if CSF absorption is normal. A tenth of the choroidal blood flow of about 4 mL/min per gram^{3,4} becomes new CSF in the ventricular spaces.

Multisource evidence indicates that 70% to 80% of CSF is formed by the plexuses in the lateral, third, and fourth ventricles. Human CSF elaboration is mechanistically similar to that in many mammalian species. Extrachoroidal formation of a CSF-like fluid occurs at the cerebral capillary wall,⁵ but it is less efficient compared with choroid plexus generation. A lavish turnover of fluid at the blood-CSF interface (choroidal epithelium) is engendered by a high blood flow to the plexus, substantial activities of Na⁺,K⁺-ATPase^{6,7} and carbonic anhydrase,^{8,9} and a plethora of ion transporters. Stable composition is the hallmark of CSF. Extracellular pH stability is essential to neurotransmission.

INTRICATE FLUID BALANCE WITHIN THE CENTRAL NERVOUS SYSTEM

To preserve sound ICP and volume, the central nervous system (CNS) relies on a battery of choroidal and extrachoroidal fluid-regulating mechanisms.² Orderly CSF percolation depends on simultaneous, precisely controlled solute and water fluxes at several transport interfaces among blood, CSF, and brain.¹⁰ The choroid plexus at the blood-CSF border is at the heart of fluid dynamics in the CNS. This industrious secretory epithelium provides a steady fluid output that has an impact on the biochemical and biophysical integrity of the brain. Disturbance of CSF flow disrupts extensive exchange between large-cavity CSF and brain interstitial fluid.¹¹ Accordingly, the diminution of CSF formation and turnover rate in disease¹² and senescence sets into motion many pathophysiologic cascades.

VARIATION IN CEREBROSPINAL FLUID PRODUCTION

Because CSF dynamics have an impact on brain metabolism, it is important to assess optimal CSF formation rate in health. Adult humans normally form CSF at about 0.35 mL/min.^{1,2}

Nocturnally elevated CSF production¹³ may relate to altered cerebral metabolism during sleep. CSF formation also fluctuates in disease.¹⁴ Neurosurgeons face pathophysiologic situations in which the choroid plexus forms too much or not enough fluid. With hypersecreting choroid plexus papillomas,^{15,16} surgical excision often reduces ICP. With hyposecreting choroid plexus, as in normal-pressure hydrocephalus (NPH) and Alzheimer's disease (AD), the stagnated CSF turnover rate^{17,18} may contribute to cerebral dysfunction. Disease-modified fluid formation by the choroid plexus can thus harm CSF dynamics and the extracellular environment of neurons.¹¹ Accordingly, imbalanced CSF formation necessitates surgical or pharmacologic remediation.

MECHANISMS OF CEREBROSPINAL FLUID FORMATION BY CHOROID PLEXUS

Penetration of ions and water into the CNS occurs predominantly across the choroid plexus.² Control of brain fluid balance therefore starts with a thorough knowledge of choroidal transport mechanisms. Fluid secretion into the ventricles is mediated by an array of ion transporters asymmetrically positioned at the blood- and CSF-facing membranes.² Structurally and functionally, the choroid plexus epithelium resembles the kidney proximal tubule.¹⁹ Renal-like organs are designed to transfer a copious volume of fluid.

CSF production is directly proportional to the net transfer of Na⁺ and Cl⁻ from blood to ventricles.²⁰⁻²² Conversely, when CNS-inward Na⁺ and Cl⁻ transport across the choroid plexus is reduced, CSF formation is attenuated.^{23,24} The driving force for ion movements across choroid plexus membranes is a downhill (energetically speaking) concentration or electrochemical gradient. For the external limiting membranes of the choroid plexus, the direction of the gradients for Na⁺, Cl⁻, K⁺, and HCO₃⁻ is given in Figure 33-1. Na⁺ entry into choroid plexus epithelium is downhill (gradient-wise) from plasma across the basolateral membrane. At the other side of the choroid cell, K⁺, Cl⁻, and HCO₃⁻ move downhill across the apical membrane into CSF. However, both basolaterally and apically, these downhill ionic movements are facilitated by uphill active transport (requiring chemical energy as ATP) by the primary Na⁺ pump (Fig. 33-2). Active Na⁺ pumping into CSF keeps choroid cell Na⁺ concentration relatively low,² thereby establishing a basolateral inward driving force for Na⁺ from plasma into epithelium.²⁵

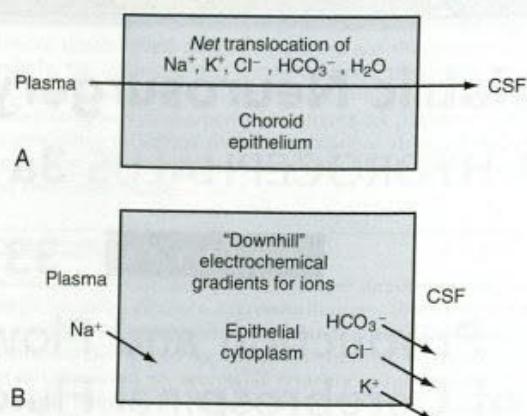


FIGURE 33-1 Ionic gradients across choroid plexus membranes that drive secretion of CSF. The continual streaming across the choroid plexus of the CSF, a fluid rich in Na^+ , K^+ , Cl^- , and HCO_3^- (**A**), is the result of regulated transport and permeability to various ions and water. As the result of active extrusion of Na^+ by the choroid plexus into CSF, a downhill gradient for Na^+ is set up across the opposite basolateral membrane (**B**). This inward Na^+ gradient promotes transfer of plasma-derived Na^+ into the choroid plexus epithelium through ion cotransport or exchange. Cl^- , HCO_3^- , and K^+ ions that are loaded into the choroid plexus are subsequently released through channels or cotransporters down their respective electrochemical gradients into ventricular CSF. (From Johanson CE, Duncan JA 3rd, Klinge PM, et al. Multiplicity of cerebrospinal fluid functions: new challenges in health and disease. *Cerebrospinal Fluid Res* 2008;5:10.)

Epithelial transport polarity is fundamental to fluid formation. Polar distribution (sidedness) of specific active transporters and passive channels enables net fluid movement from blood to CSF (see Fig. 33-2). Basolateral (vascular) and apical (CSF) transporters and channels thus mediate the streaming of ions and water. Directionally, the fluxes are mainly from interstitium to parenchyma to ventricles. Figure 33-2 schematizes the polar distribution of primary and secondary active ion transporters. Channels allow passive diffusion of K^+ and Cl^- (apical efflux) into nascent CSF.²⁶ Many ionic species are involved in CSF production (e.g., K^+ , Mg^{2+} , and Ca^{2+}). However, fluid formation is primarily (quantitatively) generated by net secretion of Na^+ , Cl^- , and HCO_3^- . Water osmotically follows ion transport across the apical membrane (see Fig. 33-2). Such transfers occur by stepwise and parallel processes described in the following sections.

Sodium

Energetically, the pivotal initiating step in CSF formation is the primary active transport of Na^+ from choroidal epithelium to ventricle.²⁷ Na^+ - K^+ -ATPase activity empowers this Na^+ pumping by generating ATP (see Fig. 33-2). To stabilize choroid pH and epithelial volume,^{25,28} while CSF is elaborated, the Na^+ efflux (apically) is balanced by continual Na^+ influx (basolaterally) through Na^+ - H^+ exchange and Na^+ inward transport coupled with HCO_3^- .^{29,30}

Chloride

As the main anion in CSF secretion, Cl^- is actively transported across the basolateral membrane in exchange for cellular HCO_3^- .³¹ This pulls plasma Cl^- into the epithelium for accumulation above electrochemical equilibrium.³² Under some conditions, intraepi-

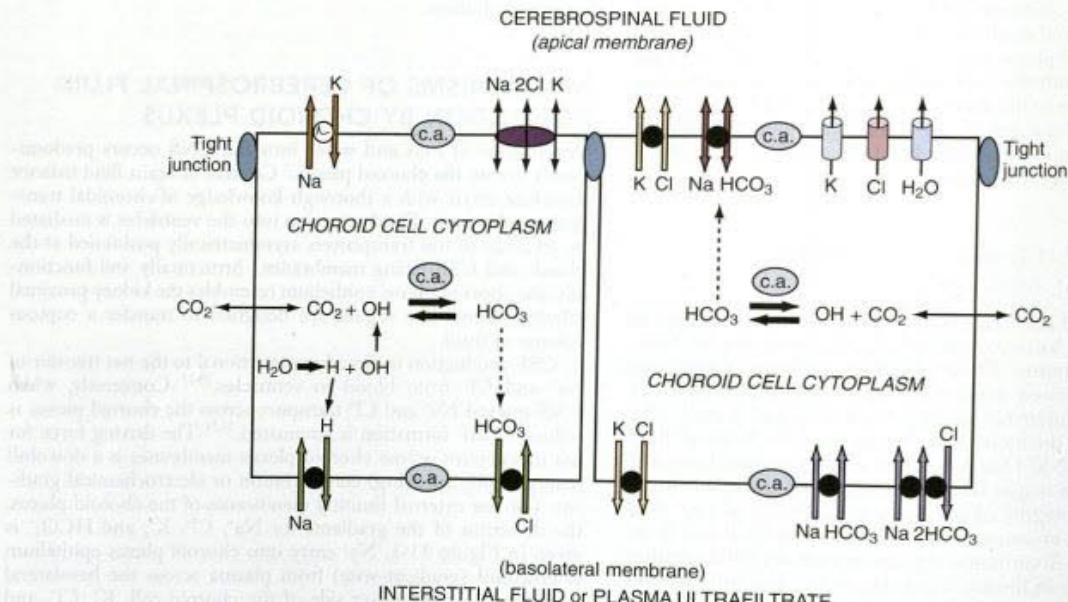


FIGURE 33-2 Choroid plexus basolateral and apical membrane transport mechanisms that are involved in CSF formation and homeostasis. Interstitial Na^+ , Cl^- , and HCO_3^- are actively accumulated by choroid plexus epithelium by transporters in the basolateral membrane. Additional HCO_3^- is generated intracellularly by carbonic anhydrase. K^+ , Cl^- , and water diffuse through channels down their gradients from cytoplasm into CSF. Na^+ and HCO_3^- move into the ventricles by apical membrane cotransporters. Na^+ is also actively extruded into CSF by the Na^+ pump, which cycles K^+ across the apical membrane. K^+ - Cl^- cotransport helps stabilize cell volume as CSF is formed. CSF production is essentially the net transport of Na^+ , K^+ , Cl^- , HCO_3^- , and water from blood to ventricles. (From Johanson CE, Duncan JA 3rd, Klinge PM, et al. Multiplicity of cerebrospinal fluid functions: new challenges in health and disease. *Cerebrospinal Fluid Res* 2008;5:10.)

distal Cl^- diffuses into CSF through the efflux arm of the Na^+ - Cl^- cotransporter.³³ However, the downhill diffusion of Cl^- into CSF by way of apical Cl^- channels is likely to be the main pathway by which Cl^- accesses the ventricles to sustain fluid formation.³⁶

Bicarbonate

HCO_3^- in choroid plexus has a dual source. First, carbonic anhydrase catalyzes the hydration of CO_2 to form H^+ and HCO_3^- ions in choroid plexus epithelial cells.⁸ In addition, HCO_3^- is pulled from plasma into the epithelium by Na^+ -coupled HCO_3^- transport.³ On accumulation, the HCO_3^- is available for release across the CSF-facing membrane by two mechanisms. Through one, HCO_3^- in the epithelium diffuses downhill through an anion channel into CSF.¹⁴ By another putative route, HCO_3^- is transferred by an electrogenic Na^+ -coupled HCO_3^- cotransporter at the apical membrane.^{28,35} HCO_3^- -rich nascent CSF reflects facilitated movement of this anion into ventricles as CSF is produced.³⁶

Water

CSF is 99% water. The watery medium of CSF enables multiple buffering, distributive, and excretory functions.¹ Therefore, it is important to thoroughly characterize water movement across the blood-CSF interface. After Na^+ , Cl^- , and HCO_3^- transport into CSF, water chases these osmotically active ions into the ventricles by diffusing down its chemical potential gradient through aquaporin 1 (AQP1) channels in the apical membrane.³⁷ AQP1 channel involvement in CSF formation is deduced from AQP1 knockout mice displaying substantially reduced fluid movement into the ventricles.³⁸ As a result, ICP is lowered.³⁹ Transcellular water diffusion across the choroid plexus is potentially a drug target in modulating CSF dynamics.

REGULATION OF CEREBROSPINAL FLUID FORMATION

CSF formation rate adjusted downward or upward is relevant to management of CSF disorders, such as elevated ICP and ventriculomegaly.^{1,40} Manipulation of choroid plexus ion transporters and channels is the key to achievement of finer control of epithelial fluid output. From a cellular physiology standpoint, there are multiple loci where CSF formation can be regulated. Two main targeting sites or strategies attempt to modulate choroid plexus secretory function: (1) manipulation of the concentrations of neurotransmitter and neuropeptide ligands that have receptors on choroid epithelial membranes that interface with the extracellular fluid and (2) use of diuretic-type agents to interfere with membrane-bound transporter proteins that effect ion-water fluxes. Many studies focus on reduction of CSF formation because both nature and clinicians try to prevent rises in ICP.

Neurohumoral Ligands and Receptors

Apical and basolateral membranes of choroid plexus contain receptors for biogenic amines and fluid-regulating peptides. Neurogenic tone on CSF formation is commonly inhibitory in nature.⁴¹ Adrenergic regulation of choroid plexus epithelium is substantial, including modulation of the activities of Na^+,K^+ -ATPase and carbonic anhydrase. The superior cervical ganglion innervates the lateral ventricle choroid plexuses. Sympathetic nerve stimulation or resection, respectively, decreases or increases CSF production by 30%.⁴² Pharmacologic and biochemical evidence indicates that sympathomimetic lowering of CSF forma-

tion results from a combined β -receptor inhibition of epithelial secretion and α -receptor stimulation (vasoconstriction and reduced plexus blood flow).⁴³ Cholinergic agents exogenously administered also decrease CSF production, indicating muscarinic receptor inhibition of the choroid plexus. Both sympathetic and parasympathetic tone autonomically regulate CSF formation.

Serotonin 5-HT_{2C} receptors in choroid plexus are highly expressed and therefore widely used in pharmacologic investigations,⁴³ including those of CSF formation. Serotonin and serotonergic agonists perfused through the ventricles reduce CSF production.⁴⁴ Localization of 5-HT_{2C} receptors to choroid plexus apical membrane points to control of CSF formation by centrally released serotonin. CSF serotonin derived from 5-HT fibers coursing through the ependymal wall⁴⁵ is a potential source of biogenic amine released into the ventricles for convection to the choroid plexus. Such binding of 5-HT to choroid plexus apical receptors would inhibit CSF formation.

Fluid-modulating peptides such as arginine vasopressin (AVP), angiotensin II, and atrial natriuretic peptide (ANP) reduce CSF formation when they are exogenously placed on the ventricular side. This fits with central neuroendocrine-like control of CSF mediated by receptors for these neuropeptides at the apical membrane.² Moreover, the CSF concentration of many neuropeptides, including AVP and ANP, is regulated independently of plasma. This implies neuroendocrine regulation of CSF dynamics by stimulation of receptors at the central or apical side of the choroid plexus.

Peptides figure prominently in transport, permeability, and synthetic and modulatory phenomena at the blood-CSF interface.^{46,47} Neuropeptide regulation of choroid plexus fluid output helps adjust ICP elevation. Both AVP and ANP induce dark, neuroendocrine-type choroid epithelial cells that inhibit CSF production, especially in hydrocephalus.^{48,49} AVP modulation of CSF formation includes complex functional interactions in the choroid plexus with basic fibroblast growth factor⁵⁰ and angiotensin II.⁵¹ AVP directly inhibits epithelial ion transport and constricts choroid plexus vessels, thereby reducing choroidal blood flow, which can be rate limiting for CSF formation.

ANP is the focus of substantial interest in the peptidergic control of CSF dynamics. Autoradiographic mapping of choroid plexus binding sites provides solid evidence for plasticity of ANP receptors⁴⁹ in response to hydrocephalus and CSF fluid shifting (as in space flight). In humans, the ANP concentration in CSF is independent of plasma levels⁵² and rises in proportion to increments in ICP.⁵³ Interestingly, intracerebroventricular ANP reduces the CSF formation rate in animal models⁵⁴ in the face of increasing plexus blood flow. Systemically, ANP unloads expanded plasma volume by inducing natriuresis. ANP may also unload CSF excess. ANP thus deserves more attention in the CNS as a regulator of CSF pressure and volume by feedback servomechanistic effects on ion transport (through cGMP) and fluid production by the choroid plexus.

Diuretic Agents and Ion Transporters

Both weak and high-ceiling diuretics reduce CSF production. The strategy is to suppress fluid formation without altering CSF composition by interfering with choroid plexus ion transporters at apical or basolateral membranes. One desirable clinical outcome is to lower ICP pressure by decreasing fluid input to the ventricles. To interpret hydrophilic drug effects, a significant factor is whether the inhibiting agent is administered on the blood side (intravenously or intraperitoneally) or the CSF side (intracerebroventricularly). Tight junctions between choroid epithelial cells limit penetration of water-soluble agents by diffusion across the blood-CSF barrier. Hydrophilic agents such as ouabain, a potent inhibitor of apical Na^+,K^+ -ATPase, therefore

do not inhibit CSF formation when they are presented on the blood side of the barrier.⁷ Drug access to the transporter target is critical.

Dual apical transporter targets are the Na⁺ pump and the Na⁺-K⁺-Cl⁻ cotransporter. Directly inhibited Na⁺ pumping is accomplished with cardiac glycosides. Intraventricular ouabain reduces CSF formation,⁵⁵ but it elevates the CSF K⁺ concentration⁷ and is not therapeutically feasible. Digoxin, more lipid soluble, permeates the blood-CSF barrier to reach target sites at the CSF. Patients treated with digoxin have a decline in CSF formation of about 25%.⁵⁶ Geriatric patients receiving digoxin may have a neurotoxicity risk due to reduced CSF turnover added to an already low baseline CSF production in senescence.¹⁸ Another apical target is Na⁺-K⁺-Cl⁻ cotransport, which is bumetanide sensitive.⁵⁷ Bumetanide acts on the kidney to reduce swelling and fluid retention. It has also been tested on the choroid plexus, the "kidney" of the CNS.¹⁹ When it is presented intraventricularly (0.1 mM) in dogs, bumetanide curtails CSF production up to 50%.⁵⁸ Bumetanide administered intravenously, however, affects CSF formation negligibly,⁵⁹ presumably because of poor systemic access to choroid plexus apical membrane. Furosemide, another high-ceiling diuretic, also reduces CSF formation and ICP.⁶⁰ At high doses, furosemide alters choroid plexus blood flow and carbonic anhydrase activity as well as Na⁺-K⁺-Cl⁻ cotransport. A third pharmacologic target on the CSF-facing membrane is the Na⁺-HCO₃⁻ cotransporter.⁵⁷ Awaiting elucidation is the role of this HCO₃⁻ cotransporter in CSF formation as well as the use of novel agents to access it after systemic administration.

Basolateral membrane targets for choroid plexus fluid production are the Na⁺-H⁺ (NHE) and Cl⁻-HCO₃⁻ (AE) exchangers as well as newly identified HCO₃⁻-loading transporters. Amiloride, a diuretic agent, inhibits Na⁺-H⁺ exchange, but relatively high doses are needed to lower CSF formation rate.⁶¹ Acetazolamide, used clinically to suppress CSF formation,⁶² indirectly slows Na⁺-H⁺ exchange by reducing availability of cellular protons for basolateral exchange with interstitial Na⁺.⁸ With regard to Cl⁻-HCO₃⁻ exchange, the disulfonic stilbene agent DIDS interferes with Cl⁻ uptake by the choroid plexus and reduces CSF formation,⁶³ but its experimental use is complicated by ion-CO₂ imbalances in the periphery. Recently delineated expressions of HCO₃⁻-loading transporters on the plasma side of the choroid plexus epithelium^{64,65} need to be assessed physiologically in relation to CSF dynamics. Finer pharmacologic control of fluid formation⁴⁰ promotes better management of disease-induced changes in CSF pressure, volume, and flow.²

CEREBROSPINAL FLUID FORMATION RATE IN HYDROCEPHALUS

Structurally and functionally, the choroid plexus is markedly altered in hydrocephalus.⁴⁸ There is a decrease in choroidal solute fluxes⁶⁶⁻⁶⁸ and CSF formation rate^{12,49} in congenital and adult chronic hydrocephalus, which is in response to augmented CSF volume and pressure. Reduced choroid plexus blood flow, epithelial cell shrinkage or damage, and diminution of blood-CSF surface area for transport contribute to reduced fluid turnover in hydrocephalus.^{48,66,69}

Two non-mutually exclusive mechanisms, physical and physiologic, explain how elevated CSF pressure reduces fluid formation by the choroid plexus.

- Physically, the rise of ventricular pressure in hydrocephalus opposes and thereby decreases net fluid filtration across the plexus capillaries,⁷⁰ the initial step in CSF formation. This physical factor by Starling's law reduces fluid (water, ions, and other substrates) availability to the plasma-facing membrane

of the choroid plexus. Consequently, as the choroidal perfusion pressure gradient (mean arterial blood pressure minus ICP) is lowered, the plasma ultrafiltrate feeding CSF formation is compromised by the reduced hydrostatic pressure gradient across capillary walls.

- Physiologically, a servomechanism operates such that as ICP is increased, there is a consequent release of neurohumoral agents that initiate a choroid plexus epithelial receptor-mediated inhibition of CSF production. The large number of endogenous systems or agents inhibiting CSF formation, which are activated by incremental pressure and volume, gives weight to this model.^{49,71}

In humans with NPH, the CSF formation rate decreases 40% as estimated by the Masserman technique.¹² In adult rats injected with kaolin, an NPH-like model, the CSF formation at 3 weeks is also reduced by 40%.⁷² Overall, the elevated CSF pressure in human NPH and kaolin models devastates the CNS interior (i.e., choroid plexuses, ependyma, and periventricular zones). Therapeutic agent stabilization of gradually increasing CSF pressure in adult chronic hydrocephalus, or in later progression to AD,⁷³ may minimize deterioration in the aged, dementia-prone CNS.

CEREBROSPINAL FLUID FLOW

Freely flowing CSF is biophysically necessary for efficient CNS absorption of the arterial pressure pulse.⁷⁴ Biochemically, the uninterrupted flow of CSF sustains an optimal level of substrate to stabilize metabolism and neuronal functions.² Overall, CSF flow rate complexly depends on upstream choroidal, mainstream ventriculocisternal, and downstream arachnoidal fluid throughput. Slowing of CSF flow disturbs both trophic and excretory functions in the CNS.¹¹ CSF flow characteristics and effects have been studied less than pressure and volume phenomena. Substantial brain injury incurred from severely attenuated CSF flow is prompting research on regional ventricular CSF interactions with nearby interstitial fluid and cerebral blood flow.⁷⁵

CSF flow is neither laminar nor constantly unidirectional. Pulsatile CSF movement during each cardiac pumping cycle occurs as anterograde caudal flow is followed by retrograde cranial flow. This cyclic forward and backward fluid motion, as commonly monitored in the aqueduct, is a rhythmic passive response to arterial pulsations and brain compliance. Thus, the cyclic flow of CSF is driven by a dynamically changing hydrostatic pressure gradient, which is superimposed on the static pressure gradient driving continuous bulk flow of CSF (volume transmission¹) from the proximal choroid plexus origin to the distal arachnoidal drainage sites.

Cine phase-contrast magnetic resonance imaging (MRI) is useful for quantifying CSF flow noninvasively and rapidly. It is convenient to assess peak CSF flow velocity in the cerebral aqueduct. Typically with MRI, the velocity sensitization (often referred to as velocity encoding) for the aqueduct is twice that of the cervical subarachnoid space. The velocity of CSF flow increases as it courses through the relatively narrow aqueduct of Sylvius. In addition to the size of the "pipe," the driving force associated with the pressure gradient across the aqueduct is another factor determining CSF flow.

Various methods have been employed for measurement of hyperdynamic pulsatile flow in the aqueduct, the most common being average flow rate (in milliliters per minute) and stroke volume (i.e., net caudal flow during one cardiac cycle, in microliters). Average flow rates greater than 18 mL/min can be considered a good criterion for diagnosis of NPH; an average flow rate of 27 mL/min has been reported in chronic hydrocephalus. Although early studies using aqueductal stroke volume as the flow measure reported favorable outcome from shunt surgery (i.e., improvement of the Hakim triad of NPH symptoms) for patients

with stroke volume greater than 42 μL , more recent studies have questioned this assumption.^{76,77} In general, although hyperdynamic flow greater than 18 mL/min may be considered diagnostic of NPH, patients with mild or normal pulsatile flow in the cerebral aqueduct cannot be excluded from this diagnosis.^{76,77} Other regions that can be assessed with this method include the third ventricle floor (third ventriculostomy context⁷⁸), the cervical (C2) subarachnoid space,⁷⁹ and the prepontine cistern.⁸⁰ Although questions persist, hyperdynamic CSF assessment may become increasingly valuable for diagnosis and management of CSF diversion in hydrocephalus. Phase-contrast balanced steady-state free precession, with its higher signal-to-noise ratio and insensitivity to turbulent (nonlaminar) fluid flow, improves CSF flow quantitation.⁸¹

CSF flow is tightly and intricately coupled to cerebral blood flow. Analyses of hydrodynamic and hemodynamic relationships provide differentials in disease diagnosis. Throughout the cardiac cycle, a typical MRI-generated CSF flow curve has separate and opposing phases covering flush and fill periods. Mechanical coupling of the CSF and vascular circulations is revealed by analysis of peak and latency phenomena during each cardiac cycle. Peak latencies on MRI-generated flow curves, for CSF and cerebral blood flow, are expressed as points over the cardiac cycle (0% to 100%). In healthy individuals, CSF flow follows a regular pattern (Table 33-1). At the start of systole, there is increased cerebral blood volume and thus elevated ICP. The consequent flushing of cervical CSF relieves subarachnoid space pressure, thereby reducing jugular venous peak flow. There is then peak CSF flow (downward flushing) through the third ventricle-aqueduct that helps equilibrate cerebral pressure. Following this sequence of flow distributions in systole, there are successive reverse phases during diastole to refill the aqueduct. CSF flushing phenomena in systole have been precisely timed (see Table 33-1). Such control data enable diagnostic evaluation of altered CSF-blood dynamic relationships in disease and aging.⁸¹

To delineate fluid dynamics in health versus neurodegeneration, it is advantageous to measure parameters in the aqueduct and subarachnoid space (C2-3) concurrently. The ratio of stroke volumes, cervical to aqueductal, is about 15:1 in adults. More information is needed to confirm the clinical impression that the cervical-aqueductal stroke volume ratio decreases with age. With disease-induced variations in compliance, in particular intracranial compartments, it may be clinically instructive to assess diseased cervical-aqueductal stroke volumes. In deciding on shunts for NPH, with putative imbalances in aqueductal-cervical functional relationships, the stroke volume ratio may be more mean-

ingful than a single CSF compartment determination of stroke volume.

CSF flow data from phase-contrast cine MRI are also useful for noninvasive analysis of intracranial compliance.⁸² With aging, neurodegenerative disease, and CSF overloading, the CNS becomes less compliant, that is, it is not as able to adjust to stressful increases in pressure and volume. A compliance index (Ci), defined as $\Delta \text{volume}/\Delta \text{pressure}$, is calculated with data for intracranial volume changes (derived from CSF and blood flows during a cardiac cycle) and the CSF pressure gradient (derived from CSF flow data). Ci values in NPH from subarachnoid hemorrhage are lower than those in patients with brain atrophy or asymptomatic ventricular dilation.⁸³ MRI flow analysis at the C2 subarachnoid space⁸³ can thus be used along with net blood flow determination (carotid and vertebral arteries and jugular veins) to assess brain compliance in NPH diagnostics.

INTERRUPTION OF CEREBROSPINAL FLUID FLOW AT VARIOUS LOCI

In chronic adult hydrocephalus,⁸⁴ CSF flow can be compromised at several anatomic locations along the neuraxis. To specify NPH conditions, it is important to elucidate the differential impact on brain and ventricular functions caused by flow disruption at sequential points in the pathway: sylvian aqueduct, basal cisterns, and subarachnoid space.

Aqueduct

Cerebral aqueduct narrowing enhances the resistance to CSF flow through the brain interior, often inducing an NPH-like syndrome. Late-onset idiopathic aqueductal stenosis usually presents with chronic onset; younger patients present with headache, and older ones have NPH symptoms.⁸⁵ Late-onset idiopathic aqueductal stenosis is relieved by endoscopic third ventriculostomy,⁸⁶ especially when CSF outflow resistance is assessed by test infusion of an indwelling ventricular catheter. In both animal and human models, late-onset idiopathic aqueductal stenosis has been linked to venous malfunctions: elevated venous pressure and greater collateral flow.⁸⁶

Basal Cisterns

MRI-viewed enlargement of the basal cisterns supports the diagnosis of shunt-responsive idiopathic NPH.⁸⁷ Kaolin injection into

TABLE 33-1 Dynamic Fluid Flow Throughout the Systolic Phase of Each Cardiac Cycle

| PHASE NUMBER | PERCENTAGE OF CARDIAC CYCLE | DESCRIPTION OF FLOW PHENOMENA IN VARIOUS CNS COMPARTMENTS |
|--------------|-----------------------------|---|
| 1 | 0 | Systolic arterial fill flow peak occurs in internal carotid arteries, which causes instantaneous increase in the cerebral blood volume. |
| 2 | 5 | The cervical CSF initially responds to brain expansion by flushing through the subarachnoid spaces. |
| 3 | 11-20 | In response to the cervical CSF displacement, there is a fall in subarachnoid space pressure, leading to peak flow (flush) through jugular veins. |
| 4 | 20-25 | In response to subarachnoid space pressure decrease, the third ventricle-aqueductal CSF surges distally (downward). |
| 5 | 25-35 | Cerebral pressures equilibrate as arterial and venous flows equalize, and the cervical CSF flow becomes negligible. |

Data are recapitulated from Stoquart-ElSankari et al.⁸¹

TABLE 33-2 Cerebrospinal Fluid Dynamics and Volume in Aging and Neurodegeneration

| | HUMAN DISEASE* | | | RAT AGING† | | |
|--------------------------------|----------------|------|------|------------|---------|---------|
| | Normal | NPH | AD | 3 mo | 19 mo | 30 mo |
| CSF formation rate (mL/min) | 0.40 | 0.25 | 0.20 | 0.00121 | 0.00148 | 0.00065 |
| CSF volume or space (mL) | 150 | 300 | 250 | 0.156 | 0.196 | 0.308 |
| CSF turnover rate‡ (volumes/d) | 4 | 1.2 | 1.2 | 11 | 10.8 | 3.0 |

*CSF formation rate and volume were determined by the Masserman method.

†CSF dynamics in rats were quantified by dilution of indicator perfused through the ventriculocisternal system.⁹²

‡CSF turnover rate = formation rate/volume.

AD, Alzheimer's disease; NPH, normal pressure hydrocephalus.

basal cisterns⁸⁸ creates communicating hydrocephalus that allows CSF outflow across the more proximal fourth ventricle–cisterna magna interface (foramen of Luschka). Thus, the more distal CSF blockage experimentally in the basal cisterns (compared with standard kaolin injection into cisterna magna) allows the modeling of extraventricular, nonobstructive hydrocephalus clinically observed in children. Tracking of the progression of the basal cistern destabilization is important in understanding how early-life “decompensating” hydrocephalus might evolve to NPH.

Cortical Subarachnoid Space

There is a paucity of systematic analyses of abnormal flow in the cortical subarachnoid space during NPH and AD.⁸⁹ In animal models, intrathecally injected kaolin disrupts orderly CSF flow in the subarachnoid space. Kaolin administration into the cortical subarachnoid space induces backstream ventriculomegaly, but the degree and rate of expansion of the lateral ventricles are not as great as with injection into basal cisterns.⁸⁸ Slower dilation of the ventricles after cortical subarachnoid space injection therefore provides a model that mimics the protracted development of NPH in adults. In aging, NPH, and AD, the structural changes in the subarachnoid space and arachnoid membrane increase the impedance to CSF flow.^{90,91}

CEREBROSPINAL FLUID TURNOVER RATE

CSF turnover rate is distinguished from CSF formation rate and flow. Defined as CSF formation rate divided by CSF volume, the turnover rate measures the frequency of total CSF renewal. With advanced aging comes markedly compromised CSF dynamics.¹⁴ Senescence is characterized by a decreasing formation rate even as the ventricular system becomes more voluminous. Ventriculomegaly is the cardinal feature of chronic hydrocephalus (NPH). In older animals and humans, the reduced choroid plexus formation of fluid, accompanied by expanding ventricles, is manifested by curtailed CSF turnover rate.^{18,92} Moreover, as AD progresses, the deepening sulci on the brain surface represent an enhanced volume of subarachnoid space. This increment in extracellular fluid volume places even more stress on the choroid plexus management of CSF composition.¹⁷

CSF circulation viewed from the standpoint of turnover rate is compromised in senescence, NPH, and AD.¹⁸ Table 33-2 summarizes CSF turnover rates, human versus rodent. CSF turnover rate is lower in humans than in rats but declines in both species substantially in late life. Relative stasis of CSF in aging is problematic for the brain, which lacks a lymphatic drainage system. Devoid of true lymphatic capillaries, the CNS is highly dependent on the quasi-lymphatic CSF sink action. The CSF sink effect is akin to drainage that removes proteins and harmful

catabolites from interstitial fluid. Sink clearance action is feasible because of the low concentration of proteins and neural catabolites in nascent CSF. This sets up a concentration gradient for macromolecules and parenchymal catabolites, directed from brain interstitial fluid into ventricles and subarachnoid space. This downhill concentration gradient facilitates diffusion of harmful substances from neural tissue to CSF, which are subsequently convected to lymph and venous blood.

Stagnated CSF bulk flow in aging and hydrocephalus⁹³ is problematic for brain clearance of peptides such as A β_{1-42} . With advancing age, there is reduced outward clearance of interstitial fluid A β peptide across cerebral capillaries. This places a burden on CSF to clear amyloid from CNS, but unfortunately, the bulk flow clearance capacity also diminishes in senescence because of less fluid production by the choroid plexus.^{17,94} Reduced interstitial clearance of A β promotes amyloid plaque deposition, creating additional metabolic effects that eventually destabilize the neuronal cytoskeleton. Given that brain interstitial fluid convection is interdependent with CSF dynamics, the latter need preservation to support healthy neuronal networks.

Pharmacologic strategies can be directed at stabilization of choroid plexus function throughout life to maintain or even increase the rate of CSF formation.⁴⁰ Consequently, improved CSF turnover rate curtails neurodegeneration by providing a cleaner, less oxidatively stressful environment for neurons. Brain well-being depends on a balance of CSF formation, flow, and turnover. Maintenance of fluid percolation through the ventricular–subarachnoid spaces also contributes to homeostasis of CSF pressure, volume, and composition.

TRANSPORT PHENOMENA IN HYDROCEPHALUS: CEREBROSPINAL FLUID–BORDERING CELLS VERSUS BLOOD-BRAIN BARRIER

To prevent or repair dwindling fluid turnover rates in the degenerating CNS, attention should be directed to the transport interfaces at the internal brain surface.⁴⁰ In the aging choroid plexus,⁹⁴ progressive interstitial fibrosis² and deposition of immune complexes interfere with efficient fluid movement across the blood-CSF barrier.⁹⁵ Also contributing to disrupted ventricular hydrodynamics is the senescence- and NPH-associated breakdown of the ependymal wall.⁹⁶ Denudation of ependymal cells in some regions and fibrillary (rosette) formation at other CSF–brain loci⁹⁷ contribute to modified fluid movement between ventricles and CSF. In the brain proper, untoward ischemic effects on the arteries and arterioles^{98,99} cause downstream destruction of human capillaries in NPH and AD,^{96,99} presumably leading to inefficient generation of interstitial fluid by microvessels. Kaolin-induced hydrocephalus mimics accelerated aging, thereby

informing on the evolving pathologic changes of the blood-brain barrier, blood-CSF barrier, and ependymal wall from aging or NPH⁹⁵ to dementia. Stabilization of chronic hydrocephalus therefore entails therapeutic targets at CSF transport interfaces² as well as the neural tissue and cerebrovasculature.^{96,100}

CEREBROSPINAL FLUID DIAGNOSTIC AND MANAGEMENT ISSUES IN ADULT CHRONIC HYDROCEPHALUS

Refined diagnosis and management of NPH, both idiopathic and secondary, are being driven by the burgeoning geriatric population and improving evidence-based medicine. Diagnostic categories of NPH have been presented as *possible*, *likely*, and *definite* and therefore reflect intensification of stages. Along with ventriculomegaly, new MRI biomarking approaches emphasize dilation of the sylvian fissure and high convexity tightness.¹⁰¹ Ependymal peak CSF flow velocity and the lumbar CSF tap are useful analytic measures to corroborate the clinical diagnosis of NPH.¹⁰² Maximal systolic flow through the sylvian aqueduct has also been useful in differentiating NPH from aged control patients.¹⁰³ Although CSF hydrodynamic data usefully distinguish non-NPH from NPH,¹⁰⁴ these MRI flow parameters do not always predict favorable response to surgical shunting.⁸⁶

Unstable CSF stroke volumes, which increase during early NPH progression but then decrease precipitously 3 to 4 years after onset, point to irreversible NPH. Regressing CSF-brain function in patients refusing shunting provide insight into the natural course of aqueductal dynamics in surgically untreated NPH. After NPH onset, the aqueductal stroke volume typically increases for 18 months or longer.¹⁰⁵ This progressive hyperdynamics is followed by a plateau in stroke volume and then a slight decline for another 18 months before a precipitous reduction in aqueductal flow. The continual fall in CSF flow in unshunted NPH, eventually decelerating rapidly, is attributed to worsening cerebral ischemia and irreversible hydrocephalus.¹⁰⁵

Pathophysiologic overlapping of altered CSF dynamics between NPH and AD creates a challenge to pinpoint differences among NPH, AD, and NPH-AD hybrid patients and to manage them by shunting versus medical regimens. Although the brain amyloid burden follows a continuum from aging to NPH to AD, the CSF hydrodynamics do not necessarily proceed in a progressive pattern. In one study of intracranial hydrodynamics and compliance, AD patients had aqueductal stroke volumes midway between those of NPH and controls.⁸⁶ In assessing NPH flow characteristics, the hydrodynamics of AD in comorbid patients thus complicates stroke volume interpretation.

CHALLENGES IN RECTIFYING DISTORTED CEREBROSPINAL FLUID DYNAMICS

What is the nature and potential reversibility of altered CSF flow coupling to brain metabolism? Multiple central mechanisms, including recruitment of alternative CSF outflow pathways, partially cope with failing CSF dynamics in chronic hydrocephalus. As CSF turnover rate decreases substantially, however, brain metabolism is severely affected. At some juncture, then, brain metabolic impairment is decoupled from CSF flow in that metabolic neuropathy is not improved after correction of fluid dynamics.¹⁰⁶ The best animal model for NPH (i.e., intrathecal kaolin) can be used to evaluate the time course of shunting improvement in chronic hydrocephalus intensifies. Earlier identification of cerebral metabolic distortions, by way of novel biomarkers in CSF,¹⁰⁷ will likely help stave off dementia development in advanced adult hydrocephalus. Another important dimension in treating NPH is the discovery of new agents⁴⁰ to more finely

adjust CSF formation as well as outflow. Overall, a combination of improved biomarking¹⁰⁷ and shunt technology, as well as pharmacologic advances, will help remediate flow disorders in the adult CSF system.

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Clinical Evaluation of Adult Hydrocephalus

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Diagnosis and management of adult patients with hydrocephalus continue to be challenging. Too often, management of hydrocephalus has been restricted to thinking about drainage of a balloon—the cerebral mantle is equally important and much less forgiving. Research has focused on the underlying pathophysiological concepts leading to ventriculomegaly with or without raised intracranial pressure (ICP). Refinements in neuroimaging tools and assessment of physiologic measures have greatly contributed to the understanding of this complex subject.

CLASSIFICATION AND ETIOLOGY

The term *hydrocephalus* is derived from the Greek: *hydro* meaning water and *kephale* meaning skull. Its classification still provokes controversy and often reflects outmoded methods of investigation. Commonly, hydrocephalus indicates dilated ventricles and hence increased volume of intracranial cerebrospinal fluid (CSF). However, this definition does not exclude cerebral atrophy caused by various neurodegenerative disorders ("hydrocephalus ex vacuo"). Hence, it is preferable to define hydrocephalus as the state of excessive intracranial accumulation of CSF that results from excessive production, circulation, or absorption of CSF. It is frequently, but not always characterized by ventriculomegaly. Similarly, the presence of excess CSF in the subarachnoid or subdural spaces over the brain convexity may or may not be a result of true hydrocephalus. Hydrocephalus is the consequence of active secretion of CSF by the choroid plexus—active CSF secretion continues even though ICP increases (see Chapter 33).

The following specific types of hydrocephalus are generally recognized, but there are challenging patients who defy such labels, and their clinical and pathophysiologic features may change over time.¹

Communicating Hydrocephalus

Communicating hydrocephalus is characterized by panventricular dilation and occurs as a result of obstruction to the flow of CSF in the subarachnoid space, distal to the foramina of Luschka and Magendie. Therefore, there is communication between the ventricles and the subarachnoid space. This condition is commonly caused by infection or hemorrhage or is idiopathic. Lumbar puncture is generally safe. Table 34-1 lists the types of communicating hydrocephalus.

Noncommunicating or Obstructive Hydrocephalus

Noncommunicating hydrocephalus is characterized by a pattern of ventricular dilation that reflects the site of obstruction. The term *noncommunicating* denotes obstruction within the ventricular system or at the level of the outlets of the fourth ventricle. Examples of obstructive lesions include giant pituitary adenoma or a colloid cyst at the level of the third ventricle, aqueduct ste-

nosis, basilar artery ectasia, and congenital causes such as Arnold-Chiari malformation. Noncommunicating hydrocephalus may develop after multiple shunt revisions. Lumbar puncture may be dangerous.

Long-Standing Overt Ventriculomegaly in Adults

This form of hydrocephalus develops during childhood, with symptoms being manifested during adulthood. Severe ventriculomegaly in adults is associated with macrocephalus measuring greater than 2 SD in head circumference or neuroradiologic evidence of a significantly expanded or destroyed sella turcica, or both. Aqueduct stenosis is present but may be secondary because it may develop after third ventriculostomy. A spectrum of patients ranging from those with symptoms and signs of increased ICP to those with dementia, gait disturbance, and urinary incontinence may be encountered (see the section on normal-pressure hydrocephalus [NPH]). There is a major risk with surgical intervention for subdural hematomas. The challenge is the timing of intervention—the point at which the significant risk for surgical complications outweighs the slow but inexorable natural history of decline.

Normal-Pressure Hydrocephalus

NPH is a syndrome characterized by gait apraxia, dementia, and incontinence with normal CSF pressure and dilated ventricles. The designation "normal" is misleading because continuous intracranial monitoring has demonstrated the presence of waves of increased ICP, particularly during rapid eye movement (REM) sleep.² It has been suggested that these abnormal CSF pressure spikes, called *B waves*, slowly increase ventricular size by exerting intermittent high pressure on the brain parenchyma that results in ischemic damage. Abnormalities of the aging brain parenchyma may make it more susceptible to these forces.³ However, the exact pathogenesis of NPH is still a matter of debate. Theories regarding the underlying pathophysiology of NPH are discussed in a later section. Despite the uncertainty regarding its evolution, NPH is a syndrome that is treatable by CSF diversion (i.e., shunt insertion).

Arrested Hydrocephalus

Some patients with hydrocephalus reach a state in which ventricular size remains unchanged in the absence of a shunt or in the presence of a nonfunctioning one. It is well accepted that careful follow-up is still required, particularly in children, because of reported cases of sudden death, sometimes years after the initial diagnosis. Neuropsychological testing may be useful in identifying subtle cognitive deterioration, which may precede the return of active symptoms. In adults, this may simply reflect an underlying pathologic process that may have spontaneously resolved, such as posttraumatic or posthemorrhagic hydrocephalus.

TABLE 34-1 Types of Communicating Hydrocephalus**DEFECTS OF FLOW IN THE SUBARACHNOID SPACE**

Leptomeningeal inflammation

Infection

Hemorrhage

Meningitis

Carcinomatosis

Foreign matter

Tonsilar elongation/prolapse or basilar impression

Masses (neoplastic and non-neoplastic)

Masses

Tonsilar elongation/prolapse or basilar impression

Masses (neoplastic and non-neoplastic)

DEFECTS OF ABSORPTION OF CSF AT THE ARACHNOID GRANULATIONS

Congenital deficiency, i.e., absence of arachnoid granulations

Raised cerebral venous sinus pressure

ABNORMALITIES IN CSF

Excessive production of CSF or abnormally high CSF volumes

Raised intraventricular CSF pulse pressure, e.g., in the presence of a choroid plexus papilloma

Increased CSF viscosity secondary to high protein content, e.g., in the presence of spinal neurofibromas

IDIOPATHIC

(CSF, cerebrospinal fluid).

From Pidard JD. Adult communicating hydrocephalus. *Br J Hosp Med*. 2002;27:35.**PATHOPHYSIOLOGY** (see also Chapter 33)**Formation, Circulation, and Reabsorption**

The total volume of CSF in the cranial-spinal axis is approximately 150 mL, distributed equally between the two compartments. However, net CSF production is about 0.35 mL/min (500 mL/day), which results in a CSF turnover rate of approximately three to four times per day. Intracranially, CSF is produced mainly by the choroid plexus of the ventricles (70% to 80%).⁴ The remaining amount is produced by the ependymal lining of the ventricles, by the brain's capillary bed, and by metabolic water production. The proportion of CSF produced in the ventricular system is unequal; the vast majority of CSF produced by the choroid plexus is from the lateral ventricles, although small amounts are produced in the third and fourth ventricles. CSF is formed by filtration of plasma through fenestrated capillaries and active transport of water and solutes through the epithelial cells of the choroid plexus at the blood-CSF barrier.

CSF circulates through the ventricular system and exits through the foramina of Luschka and Magendie into the cerebellomedullary cistern and onward to the spinal cavity and the subarachnoid spaces of the cerebral convexities. Circulation of CSF is thought to be driven by hydrostatic pressure generated by cerebral arterial pulsation and changes in venous pressure secondary to respiration, change of posture, and other mechanisms.^{5,6} CSF is resorbed by arachnoid villi that protrude from the subarachnoid space into the lumen of the dural sinuses. Solutes pass via one-way bulk flow into the venous circulation. The exact mechanism of this process has not been fully elucidated but may involve differential pressure between CSF and the venous system and one-way valves formed by overlapping endothelial cells lining the arachnoid villi.⁵ Figure 34-1 illustrates the concepts just discussed.

Isolated Fourth Ventricle Syndrome

The term "entrapped fourth ventricle" has also been used to describe the situation in which the fourth ventricle no longer communicates with the third ventricle, as well as the basal cisterns. Patients with prolonged infection or multiple shunt operations are particularly at risk for this syndrome. It is thought that secondary aqueduct stenosis from adhesions, obstruction of the foramina of Luschka or Magendie, or infective debris pooling in the basal cisterns may be responsible for this condition. Patients may have the typical symptoms and signs of hydrocephalus or more atypical symptoms such as lower cranial nerve dysfunction. Occasionally, an entrapped fourth ventricle is an incidental finding on imaging.

Slit Ventricle Syndrome

The lateral ventricles may collapse in some patients secondary to overdrainage or remain at a fixed size because of subependymal gliosis. This may lead to intermittent or complete shunt malfunction. Patients may experience raised ICP without ventricular enlargement, and therefore imaging findings may be falsely reassuring in such cases (unresponsive ventricles). Symptomatic patients may respond to a change in valve setting if a programmable valve is in situ or to revision surgery (change of valve or incorporation of an antisiphon device to prevent overdrainage). Patients with progressive neurological deterioration secondary to raised ICP may require subtemporal decompression. When the ventricles are slit intermittently, endoscopic third ventriculostomy may be possible during periods of relative ventricular dilation. Please see Chapter 186 for a discussion of these issues in children, including shunt removal.

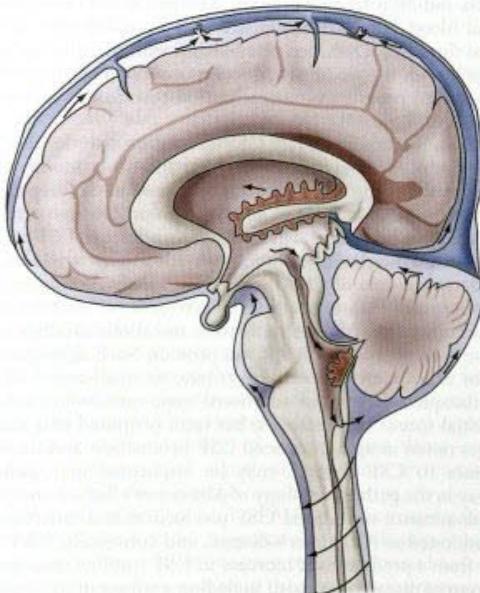


FIGURE 34-1 Circulation of cerebrospinal fluid.

Cerebrospinal Fluid Obstruction and Sequelae

Experimental models of acute ventricular obstruction have provided an understanding of the pathophysiologic processes occurring after disruption of the CSF circulation. Initial rapid ventricular dilation is followed by effacement of the cerebral sulci, fissures, and basal cisterns. Transependymal passage of CSF occurs through either an intact or disrupted ependymal lining and results in periventricular edema. Absorption of CSF occurs in the edematous white matter via alternative pathways, such as direct absorption into blood via the blood vessels.⁷ Destruction of tracts secondary to edema and subsequent gliosis of damaged tissue are believed to occur within the periventricular white matter, with relative sparing of gray matter.⁸ The resulting white matter damage and reduction in cerebral blood volume may progress to cerebral atrophy. This concept may explain the persistence of neurological deficits in some patients despite successful reduction of ventricular volume after shunt surgery. As a result of some or all of these processes, pathologic compensation for raised ICP may be reached. In a minority of cases, CSF production is reduced because of atrophy of the choroid plexus.⁷

Progressive Ventriculomegaly in the Context of Normal Pressure and the Concept of Combined Dementia

The confounding situation of progressive ventricular dilation in patients with NPH has led to many theories regarding the underlying pathophysiologic processes occurring in this condition. Hakim and Adams originally proposed that as ventricular enlargement progresses, the biomechanical forces required to maintain the ventricles in a dilated state are smaller.⁹ Distortion of tissue, including white matter tracts and blood vessels, may lead to damage and ischemia. Loss of elasticity within the brain parenchyma may result in a pressure gradient between the ventricles and periventricular tissue. The resulting excess fluid in the interstitial space may lead to failure of drainage of toxic metabolites. There is also evidence of disruption of cerebral blood flow or distortion of blood vessels, which is believed to lead to watershed ischemia and deep lacunar infarcts. The pattern of disruption of cerebral blood flow in white matter has been demonstrated to take the form of a U-shaped relationship with distance from the ventricles, with the maximal reduction occurring adjacent to the ventricles and progressive normalization toward the subcortical white matter.¹⁰

NPH is also thought to be a CSF circulation disorder resulting from an imbalance between production and absorption. Abnormalities in the aging brain may make it uniquely susceptible to intermittent spikes of B waves and result in progressive ventriculomegaly. It has been demonstrated that resistance to CSF outflow increases in a nonlinear fashion with advancing age despite a decrease in the rate of CSF production, which also occurs with increasing age.¹¹ Failure of efficient CSF turnover may also result in an accumulation of potentially toxic metabolic products, such as β -amyloid peptides ($A\beta$) and tau protein. Such aggregates are thought to be neurotoxic and contribute to small-vessel damage and subsequent leakage of additional toxic metabolites into the interstitial space.¹² Moreover, it has been proposed that the two changes noted in aging, reduced CSF production and increased resistance to CSF outflow, may be implicated in a common pathway in the pathophysiology of Alzheimer's disease and NPH. A predominance of reduced CSF production and turnover may be manifested as Alzheimer's disease, and conversely, NPH may result from a predominant increase in CSF outflow resistance. A spectrum of disease may exist, including a subset of patients who either have both conditions or have risks for the development of both even if one process is predominant.¹³

TABLE 34-2 Common Initial Features of Acute versus Chronic Hydrocephalus

ACUTE—RAISED INTRACRANIAL PRESSURE

| |
|--|
| Headaches |
| Nausea and vomiting |
| Deterioration in gait or balance |
| Papilledema |
| Upgaze palsy—setting sun sign |
| Parinaud's syndrome—pressure on the suprapineal recess |
| Abducens palsy—long intracranial course |

CHRONIC

| |
|---|
| Headaches |
| Deterioration in gait or balance |
| Urinary incontinence |
| Cognitive and attention deficits (subcortical dementia) |
| Personality changes (e.g., aggression, apathy) |
| Empty sella |
| Impingement or atrophy of the corpus callosum |

INITIAL FEATURES OF HYDROCEPHALUS

Both communicating and obstructive hydrocephalus may give rise to the same symptoms and signs (i.e., those of hydrocephalus or raised ICP). Alternatively, both types may be associated with normal CSF pressure or spontaneously arrest. The initial features specific to NPH are discussed in the following section. Table 34-2 lists the common symptoms and signs in patients with acute versus chronic hydrocephalus.

NORMAL-PRESSURE HYDROCEPHALUS

Clinical Findings and Differential Diagnoses

The concept of a “symptomatic occult hydrocephalus with ‘normal’ CSF pressure” was described by Hakim and Adams in 1965 in their landmark paper of observations based on three cases, two secondary and one idiopathic.⁹ Current guidelines deal primarily with idiopathic as opposed to secondary NPH, which occurs after trauma (such as the two patients in 1965), subarachnoid hemorrhage, intracranial surgery, or meningitis. The manifestations of secondary NPH may be delayed, sometimes many years after the incident in question. Most cases seen by clinicians are of the idiopathic variety. Despite advances in the diagnosis and management of this condition, the exact pathogenesis of NPH remains uncertain. The classic finding in patients with NPH is a clinical triad of symptoms—gait disturbance, dementia, and urinary incontinence. Patients may or may not have the complete triad of symptoms. In addition, many other symptoms have been reported, such as lethargy, apathy, impaired wakefulness, and visuospatial disturbances.

Gait Disturbance

Gait disturbance is the most common initial symptom and occurs in almost 90% of patients.⁷ Ojemann and colleagues in 1969 noted that gait disturbance could be an initial manifestation of NPH,¹⁴ thereby changing the emphasis from earlier descriptions of cognitive disturbance being the primary initial symptom. Fisher subsequently presented a series of 16 patients with shunt-responsive hydrocephalus in which gait disturbance was the initial manifestation in 12 of them.¹⁵ In that series, dementia

preceded gait disturbance in 1 patient and occurred at the same time in 3 patients. However, in 11 cases of shunt failure, dementia came first in 9 patients and gait disturbance was relatively less severe or was absent.

Common initial symptoms include unsteadiness, recurrent falls, shuffling, and reduced walking speed. More advanced symptoms include difficulty initiating gait and imbalance on turning. Gait in patients with NPH is described as being "magnetic" in nature, characterized by a broad base and slow, small steps with reduced height clearance as though the feet are "stuck to the floor." Patients may have difficulty rising from a chair or complain of their legs "giving way."¹⁶ Patients may have disturbances in stance with a tendency to lean forward and imbalance exacerbated by eye closure.^{14,17}

The gait disturbance may be difficult to distinguish from other types of frontotemporal pathology. The gait abnormality is often confused with Parkinson's disease because patients with NPH may appear to have features of lower limb parkinsonism such as rigidity, shortened stride length, and difficulties in balance and turning. This is particularly applicable in patients in whom other hallmarks of Parkinson's disease are not present, such as tremor, lead pipe rigidity, and a mask-like facies. However, unlike patients with Parkinson's disease, who are able to increase their stride length and walking cadence with the aid of external cueing such as counting, patients with NPH have a gait apraxia that does not respond to such aids. In addition, patients with NPH tend to ambulate with a relatively preserved arm swing.

Increased tone and brisk tendon reflexes in the legs are unusual in patients with shunt-responsive NPH, and there is absence of weakness or dysdiadochokinesia. The presence of upper motor neuron signs or lower limb weakness may be indicative of cervical myopathy and lumbar canal stenosis, respectively. Other structural lesions of the brain and spine should be considered, such as tumors or cerebrovascular ischemic damage. Poor balance may reflect an underlying sensory neuropathy, and in such instances, diabetic neuropathy and autonomic dysfunction should be considered. However, these conditions are common in the age group of patients seen with NPH. The finding of comorbid pathologies might be significant but may not exclude patients from having a favorable outcome from shunt surgery if NPH accounts for a major proportion of the initial symptomatology.

The anatomic basis for gait disturbance in patients with NPH remains controversial. In 1947, Yakovlev proposed a theory that paraparesis in patients with hydrocephalus is caused by compression of the internal capsule fibers by the distended third ventricle. However, the general lack of upper motor neuron signs and upper limb involvement in NPH would suggest that such a theory may not account for the characteristic gait apraxia seen in this condition. Indeed, a study using motor evoked potentials and central motor conduction time in both the upper and lower limbs in patients with NPH did not demonstrate any evidence of major pyramidal tract dysfunction or subclinical upper limb involvement in patients who responded to shunt surgery. Prolonged central motor conduction time was seen in the lower limbs of patients who did not improve after surgery.¹⁷ However, such methods may be insufficiently subtle to detect small lesions or reversible white matter damage occurring as a result of tissue distortion from hydrocephalus. Pyramidal tract damage may represent progression of these lesions to an end-stage phase of NPH that cannot be reversed by surgery.

Urinary Incontinence

Urinary incontinence may be a separate symptom or may be a consequence of gait disturbance or cognitive impairment. Some patients have urinary frequency rather than true incontinence. This symptom is thought to be due to involvement of the sacral fibers of the corticospinal tract.¹⁸ Because urgency of micturition

and incontinence are both common problems in older age, the clinical finding may be that of a change or worsening of urinary symptoms rather than a new problem.

Cognitive Impairment

NPH is estimated to account for less than 5% of all cases of dementia. It is essential that patients undergo neuropsychological testing to distinguish the pattern of dementia in NPH from other conditions such as age-related cognitive decline as a result of neurodegenerative processes, including Alzheimer's disease. The pattern of NPH appears to be a subcortical frontal dysexecutive syndrome.^{19,20} Cognitive deficits in patients with NPH typically include memory loss, reduced attention, difficulty planning, slowness in thought, and apathy. There may be speech disturbance because of dysexecutive or motivational problems.¹⁶ This pattern differs from the cortical deficits of aphasia, apraxia, and agnosia seen in patients with Alzheimer's disease.²¹

The most difficult differential diagnosis to consider in the context of NPH is Binswanger's disease, a form of subcortical vascular encephalopathy. Patients with this condition exhibit a predominantly frontal cognitive deterioration and gait disturbance (ataxia or motor dysfunction, or both), although focal neurological signs may be present. The pathologic changes occurring in patients with Binswanger's disease are believed to be the result of small-vessel ischemia and subsequent extensive white matter damage. Neuropsychological testing demonstrates features consistent with a frontal subcortical type of dementia, which is similar to the pattern noted in NPH. Similar magnetic resonance imaging (MRI) features may be seen, including ventriculomegaly and the coexistence of MRI white matter changes, such as deep white matter hyperintensities and subcortical lacunar infarctions. Table 34-3 summarizes the list of differential diagnoses for the clinical triad in NPH, aside from other hydrocephalus disorders.

Neuroradiologic Features

Guidelines published by the Idiopathic NPH Study Group¹⁶ include a set of imaging criteria required to justify the diagnosis of idiopathic NPH. Imaging in the form of computed tomography (CT) or MRI is required to establish the diagnosis of NPH. Important differential diagnoses to rule out include obstruction of CSF pathways as a result of tumor or similar pathology, significant cerebral atrophy, and evidence of cerebrovascular ischemia. Ventricular enlargement not entirely attributable to cerebral atrophy or congenital enlargement (Evans' index >0.3 or comparable measure) should be present. Evans' index is defined as the maximal width of the anterior ventricular horns divided by the maximal width of the calvaria at the level of the foramen of Monroe. An alternative measurement is the bicaudate ratio, which has been demonstrated to have excellent interobserver agreement and is more sensitive to changes in ventricular size.²² This is the minimal intercaudate distance divided by the brain width along the same line. Significant ventriculomegaly is defined as a ratio of 0.25 or greater with this method.

There should also be one of the following supportive features: enlargement of the temporal horns of the lateral ventricles not entirely attributable to hippocampus atrophy; callosal angle of 40 degrees or greater; evidence of altered brain water content, including periventricular signal changes not attributable to microvascular ischemic changes or demyelination; or aqueductal or fourth ventricular flow void on MRI. Other imaging findings were acknowledged to be supportive of the diagnosis but not required, including a brain imaging study performed before the onset of symptoms demonstrating the absence of ventriculomegaly or smaller ventricles, a radionuclide cisternogram showing delayed clearance of the radiotracer over the cerebral convexities

TABLE 34-3 Differential Diagnoses for the Clinical Triad in Normal-Pressure Hydrocephalus, Aside from Other Hydrocephalus Disorders

GAIT DISTURBANCE

Vascular
Cerebrovascular disease
Stroke
Multi-infarct dementia
Binswanger's disease
Neurodegenerative
Parkinson's disease
Alzheimer's disease
Progressive supranuclear palsy
Frontotemporal dementia
Miscellaneous
Peripheral neuropathy
Cervical myelopathy
Lumbar canal stenosis
Diabetic neuropathy
Autonomic dysregulation
Spinal neoplasm

DEMENTIA

Vascular
Cerebrovascular disease
Stroke
Multi-infarct dementia
Binswanger's disease
Cerebral autosomal dominant arteriopathy, subcortical infarcts, and leukoencephalopathy
Neurodegenerative
Parkinson's disease
Alzheimer's disease
Progressive supranuclear palsy
Frontotemporal dementia
Corticobasal degeneration

URINARY INCONTINENCE

Structural
Bladder outflow obstruction
Benign prostatic hypertrophy
Bladder innervation
Autonomic dysregulation
Lumbar canal stenosis
Miscellaneous
Medications—anticholinergics, diuretics

Data from Idiopathic Normal-Pressure Hydrocephalus Guidelines; Relkin N, Marmarou A, Klinge P, et al. Diagnosing idiopathic normal-pressure hydrocephalus. *Neurosurgery*. 2005;57:S4; and expert opinion.

after 48 to 72 hours, cine MRI showing an increased ventricular flow rate, or a single-photon emission computed tomography (SPECT)-acetazolamide challenge showing decreased periventricular perfusion that is not altered by acetazolamide.¹⁶

The imaging finding of deep white matter hyperintensities in a patient with NPH has been shown to be inversely correlated with shunt responsiveness.²³ Such white matter hyperintensities are probably a marker of comorbidity, with patients being more prone to general complications of surgery when they are present.

However, other studies have demonstrated that the presence of these lesions may not be predictive of a poor outcome after shunt surgery. This was the subject of an MRI study by Tullberg and colleagues, who used conventional MRI sequences to examine these lesions and other MRI variables in a group of NPH patients undergoing surgery.²⁴ The authors found no correlation between the presence of these parameters and poor outcome after surgery. Akiuchi and associates further demonstrated that there was improvement in ventriculomegaly and mean total scores for white matter lesions in patients who clinically improved after surgery, thus implying that these white matter lesions may be reversible.²⁵ In this patient cohort the majority had parkinsonism (71%), but other coexisting comorbid conditions, such as small-vessel disease (29%), hypertension (41%), and diabetes (35%), were also found. Eighty-eight percent of patients had white matter lesions noted on CT or MRI. These contradictory findings illustrate the continuing debate regarding the presence of deep white matter hyperintensities and their correlation to small-vessel disease.

Supplementary Prognostic Testing

Guidelines on the value of supplementary tests conclude that a single standard for the prognostic evaluation of patients with idiopathic NPH is lacking. However, supplementary tests can increase the prognostic accuracy to greater than 90%.²⁶

Three supplementary tests are currently recommended as options:

- Lumbar puncture “tap test”
- External lumbar drainage
- Measures of CSF outflow resistance

The method of choice depends on local experience and the availability of equipment. Direct ICP measurement may be useful to exclude other more acute causes of hydrocephalus but does not contribute to prognostic assessment. Radionuclide cisternography is no longer a favored option because this technique does not improve the diagnostic accuracy of combined clinical and CT criteria in patients with presumed NPH.²⁷

A lumbar puncture “tap test” has been shown to produce a specificity of 100% with a sensitivity of 26%,²⁸ provided that it is performed at a high volume (i.e., withdrawal of 40 to 50 mL of CSF). Symptomatic improvement after removal of CSF has a high positive predictive value (73% to 100%) of a probably favorable outcome with shunt placement.²⁶ It has to be remembered that improvement after a shunt is often delayed in many patients, so a simple tap test would not be expected to reveal all patients who might benefit from a shunt. However, the low sensitivity of the “tap test” precludes using this method as a diagnostic tool for exclusion. Nonetheless, a lumbar puncture is often used as a first-line investigative tool to establish that CSF pressure is within the normal range (5 to 18 mm Hg/7 to 24 cm H₂O) and that no biochemical or microbiologic abnormalities are present. Prolonged external lumbar drainage in excess of 300 mL is associated with high sensitivity (50% to 80%), specificity (80%), and positive predictive value (80% to 100%).^{26,28} However, this method requires inpatient stay and carries a risk for the complications of nerve root irritation, hemorrhage, and CSF infection.

Measurement of CSF outflow resistance, thought to reflect the CSF absorption pathways, is well established. Fluid is injected into a CSF space (e.g., ventricles or lumbar sac) either by bolus or infusion. CSF outflow resistance can then be calculated with a pressure-volume study and used to assess the CSF circulation for signs of disturbance.²⁹ The advantage of this technique is that it requires only day attendance and can also be performed through a preimplanted ventricular reservoir device. In the Dutch NPH study, outflow resistance greater than 18 mm Hg/mL per minute had a specificity of 87% and a sensitivity of 46%.³⁰



FIGURE 34-2 Measurement of ventriculomegaly on axial CT. Evans' ratio = 0.46. (Significant ventriculomegaly is an Evans index of 0.3 or greater.)

Current guidelines recommend that all patients suspected of having idiopathic NPH be considered for supplementary tests with one or more of the three methods.²³ Prolonged external irrigation has the highest sensitivity and positive predictive value but is associated with a higher complication rate. The other two methods can be considered in an outpatient setting, but measurement of CSF outflow resistance requires specialist equipment and interpretation of results. However, measurement of CSF outflow resistance can also be used as a method of comparing CSF hydrodynamics before and after shunt insertion to investigate the shunt responsiveness of a patient in the context of deterioration or failure to respond to intervention.

It should also be noted that alternative methods are available, such as the lumbar subcutaneous shunt proposed by Mendelow's group.¹¹



FIGURE 34-4 Example of dilation of the temporal horns (arrows)—axial CT.

NEURORADIOLOGIC FEATURES OF HYDROCEPHALUS

Figures 34-2 to 34-13 illustrate key features of hydrocephalus seen on imaging.

PHYSIOLOGIC TESTING OF CEREBROSPINAL FLUID DYNAMICS

When the clinical and radiologic features clearly reveal hydrocephalus and raised ICP, no further investigations are required unless a mass lesion is the cause of the hydrocephalus. However, there are many patients with chronic forms of ventriculomegaly in whom the clinical and radiologic features overlap with other

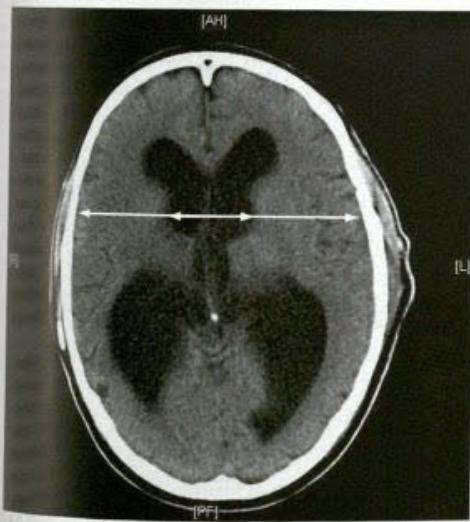


FIGURE 34-3 Measurement of ventriculomegaly on axial CT. The bicaudate ratio is 0.35. (Significant ventriculomegaly is a bicaudate ratio of 0.25 or greater.)



FIGURE 34-5 Example of dilation of the third ventricle (arrow)—axial CT.



FIGURE 34-6 Example of a patient with a Dandy-Walker malformation—axial CT.



FIGURE 34-7 Example of a patient with stenosis of the aqueduct (arrow)—sagittal T1-weighted magnetic resonance imaging.

FIGURE 34-8 Example of patient with a third ventricular arachnoid cyst (arrows). **A**, Sagittal T1-weighted magnetic resonance imaging (MRI). **B**, Axial T2-weighted MRI.

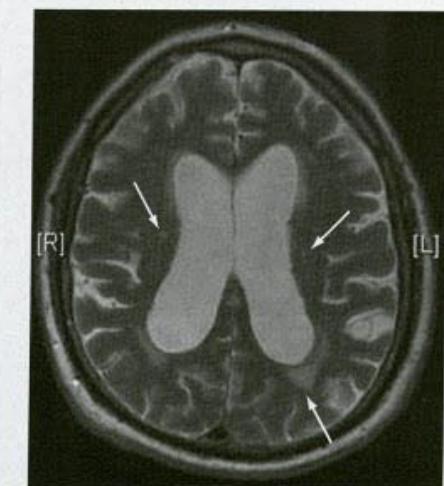
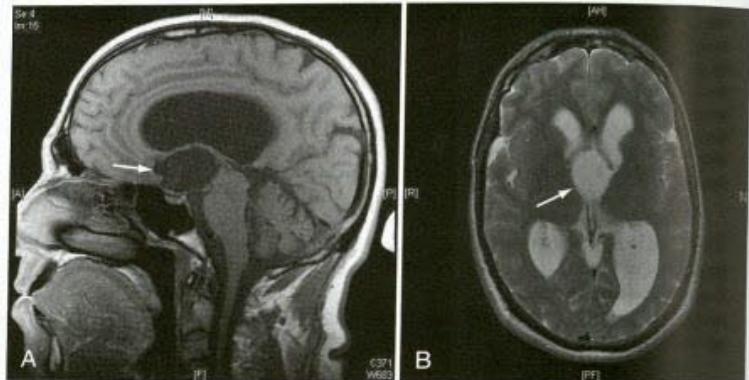


FIGURE 34-9 Example of a patient with normal-pressure hydrocephalus—ventriculomegaly, periventricular lucency (inferior arrow), and white matter hyperintensities (see text for debate regarding white matter hyperintensities (superior arrow))—T2-weighted magnetic resonance imaging.

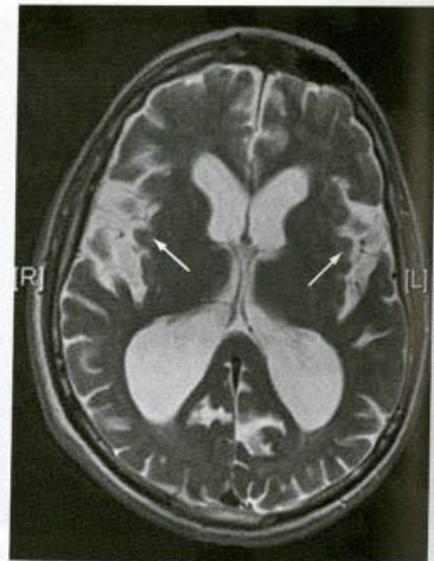


FIGURE 34-10 Patient with normal-pressure hydrocephalus and enlarged perisylvian fissures (arrows) without generalized atrophy—T2-weighted magnetic resonance imaging.

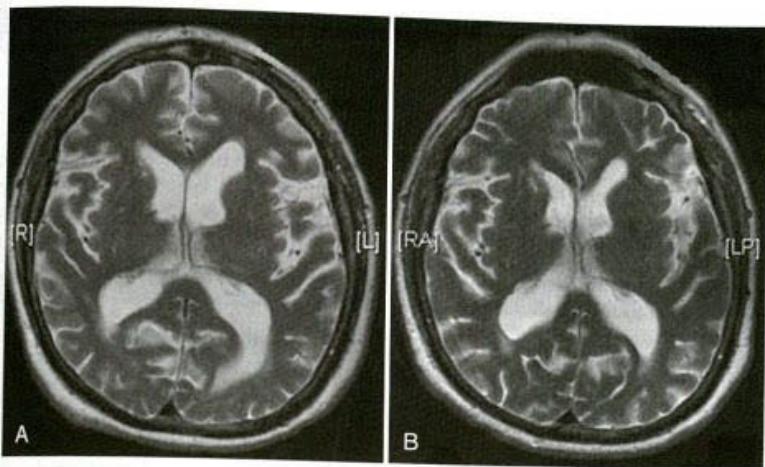


FIGURE 34-11 **A**, Example of a preoperative scan in a patient with normal-pressure hydrocephalus (NPH)—T2-weighted magnetic resonance imaging. **B**, Example of a postoperative scan in a patient with NPH and a good outcome (ventricular catheter not well demonstrated at this level).

conditions. The study of CSF dynamics, although invasive, may help in the diagnosis, be of assistance in decisions regarding surgical intervention, and provide a baseline for the long-term management of a shunted patient in whom shunt malfunction may develop. Despite early enthusiasm, such physiologic testing has not been widely adopted.³²⁻³⁶ More recent systematic studies have led to the first guidelines for the management of NPH,^{30,37-40} which recommend the inclusion of some forms of physiologic measurements.³⁶

Cerebrospinal Fluid Drainage and Dynamics

Drainage of CSF into the cerebral venous system is described in Chapter 33. The pathophysiologic processes of CSF obstruction and ventriculomegaly are described in the section “Pathophysiology.” In communicating hydrocephalus, intrathecal injection of

radioisotopes has previously demonstrated little passage of these markers over the convexity (i.e., a convexity block). Accumulation within the ventricles may persist for more than 48 hours as indeed reentry of CSF (ventricular stasis or reflux). This is thought to cause reversal of the normal flow of interstitial fluid from the brain into the ventricles so that there is net flow into the brain parenchyma. The mechanism of absorption of such fluid remains a subject of conjecture. Experimental studies suggest that perivascular absorption may occur in the opposite direction of cerebral blood flow with absorption thereafter into the cervical lymphatics via the olfactory mucosa. There is no direct evidence for such a mechanism in humans.

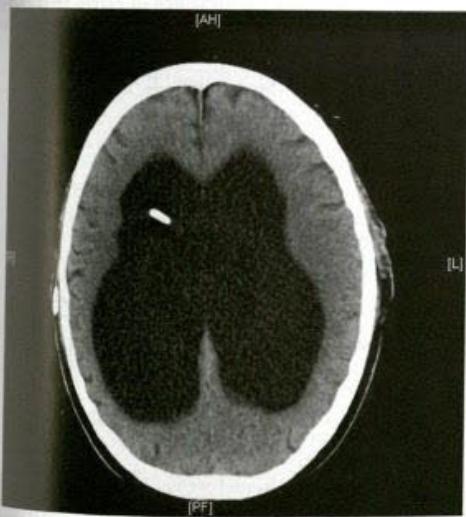


FIGURE 34-12 Axial CT of a postoperative patient with normal-pressure hydrocephalus demonstrating persistent ventriculomegaly despite a working shunt (note the absence of periventricular lucency). This patient made only a small improvement.



FIGURE 34-13 Fluid-attenuated inversion recovery magnetic resonance image of a postoperative complication—bilateral chronic subdural hematomas secondary to shunt insertion. Outward-facing arrows indicate the bilateral haematomas. Note the persistence of areas of periventricular lucency (arrows). This patient with normal-pressure hydrocephalus continued to improve postoperatively despite the complication. He was managed conservatively by resetting of his programmable valve.

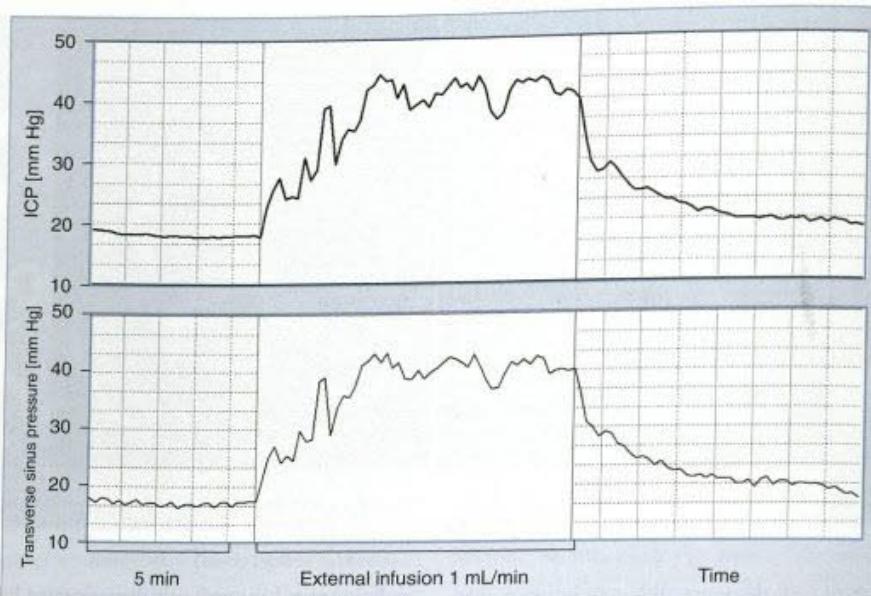


FIGURE 34-14 Simultaneous recording of lumbar cerebrospinal fluid (CSF) pressure (intracranial pressure) and transverse sinus pressure in a patient with idiopathic intracranial hypertension and documented narrowing of the venous sinuses (by magnetic resonance imaging). An increase in CSF pressure caused by infusion at a constant rate (delimited by two vertical lines) caused a simultaneous increase in transverse sinus pressure.

Mathematical Modeling of the Cerebrospinal Fluid Circulation—a Platform for Interpretation of Pressure-Volume Tests of Cerebrospinal Fluid Dynamics

Davson and coworkers⁴¹ demonstrated the passive nature of CSF absorption such that

$$P_{\text{CSF}} - P_{\text{ss}} = I_f \times R_{\text{out}}$$

where I_f is the CSF production rate and R_{out} is outflow resistance. R_{out} has been assessed in normal subjects and found to range from 6 to 10 mm Hg/mL per minute.^{35,42} The inverse of R_{out} is termed the *conductance to CSF reabsorption or outflow*.³⁶

Sagittal sinus pressure (P_{ss}) is considered to be a constant parameter that is determined by central venous pressure. However, it is not certain that interaction between changes in CSF pressure and P_{ss} does not exist in all circumstances; in patients with benign intracranial hypertension, P_{ss} is frequently elevated because of stenosis of the lateral sinuses.⁴³ Direct measurement of venous sinus pressure along with ICP reveals strict coupling between both pressures (Fig. 34-14).⁴⁴

Davson's equation reflects the steady state, but experimental and clinical recording have demonstrated vasogenic responses occurring during CSF infusion studies, thus suggesting that the Davson equation should be expanded:

$$P_{\text{CSF}} - P_{\text{ss}} = I_f \times R_{\text{out}} + \text{"Vasogenic component"}$$

Furthermore, if a bolus of CSF is injected, acute changes in the cerebral venous compartment occur together with displacement of CSF through the foramen magnum, so the compliance properties of the CSF circulation are brought into play. It is widely believed that many of the difficulties posed by patients with hydrocephalus may reflect ill-defined changes in the compliance of their cerebral mantle and CSF circulation. For example,

overdrainage after a shunt may render some patients vulnerable to minor changes in CSF pressure as though the brain has become stiffer.

The Pressure-Volume Curve

It is known that as CSF pressure increases, the compliance of the brain decreases. The electrical model of CSF compensation adapted from Marmarou⁴⁵ is presented in Figure 34-15. Storage of CSF is proportional to cerebrospinal compliance C (mL/mm Hg):

$$\text{Storage} = C \frac{dp}{dt}$$

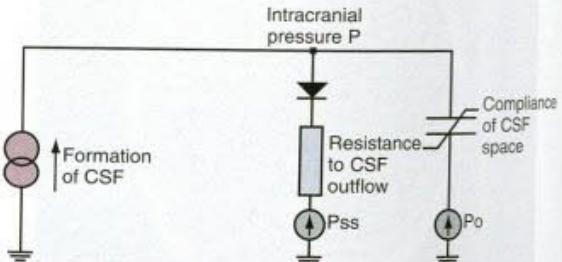


FIGURE 34-15 Electrical model of cerebrospinal fluid (CSF) compensation. The current source reflects the formation of CSF. Resistor with diode, unilateral absorption of CSF to the sagittal sinuses; capacitor and voltage source, nonlinear compliance of the CSF space and reference pressure P_{ss} . (Adapted from Marmarou A. A Theoretical Model and Experimental Evaluation of the Cerebrospinal Fluid System. Philadelphia, PA: Drexel University; 1973.)

Compliance of the cerebrospinal space is inversely proportional to the gradient of CSF pressure p and the reference pressure p_0 .

$$C = \frac{1}{E \times (p - p_0)}$$

The biologic significance of p_0 remains a matter of debate. Through various mathematical manipulations, it is possible to derive equations that

1. Replicate a CSF infusion study.
2. Replicate the effects of a bolus injection of CSF.
3. Demonstrate the variation in compensatory parameters such as RAP* and the pressure-volume index, which is independent of resting CSF pressure. A full account of this point has been presented elsewhere.⁴⁷

More sophisticated models have been formulated but have yet to become useful in clinical practice.⁴⁸⁻⁵²

Monitoring of Intracranial Pressure

ICP monitoring is relevant in patients with chronic forms of hydrocephalus and in some patients with possible shunt malfunction or confusing symptoms and signs. Although isolated measurements of CSF pressure in patients with communicating hydrocephalus and NPH may be in the normal range, overnight monitoring may reveal dynamic phenomena such as increased Lundberg "B waves."⁵³ B waves are slow waves of ICP lasting 20 seconds to 2 minutes. These waves are almost universally present in ICP recordings, probably even in healthy volunteers.^{54,55} The presence of B waves for more than 80% of the period of ICP monitoring is thought to indicate that it is much more likely than not that shunting would be helpful. Various attempts at more precise quantification have yet to be generally accepted.

Monitoring of ICP can be performed safely with intraparenchymal probes. ICP monitoring via lumbar puncture or a needle inserted into a preimplanted reservoir is used less frequently. Connection of the pressure monitor to a computer performing

real-time analysis is very helpful. The best results can be derived from overnight ICP monitoring. If this is impossible, a minimum of 30 minutes of ICP monitoring is required. Instant manometric lumbar CSF pressure measurements may be helpful but are known to be misleading⁵⁶ (Fig. 34-16). In patients with normal CSF dynamics, baseline pressure should be normal (i.e., <15 mm Hg) on overnight monitoring. Vasogenic waves of ICP, particularly intensive during the REM phase of sleep, are probably also present in normal conditions. The presence of vasogenic waves greater than 25 mm Hg for a period of around 10 minutes should be classified as intermittent intracranial hypertension. The average overnight RAP index should be less than 0.6 in patients with good compensatory reserve.^{57,58} The overnight magnitude of slow waves is considered increased when their average value is greater than 1.5 mm Hg. The presence of plateau waves is always a bad prognostic sign. An example of pathologic overnight ICP recording is presented in Figure 34-17.

During the recording, detection of pulse amplitude proves that the ICP waveform is properly being transmitted to the transducer. Lack of amplitude implies an invalid pressure recording in most cases.⁵⁹ In our own material there is no evidence that pulse amplitude is a strong predictor of outcome after shunting as reported by other authors.⁵⁹ Analysis of a subgroup of idiopathic NPH patients with a stable follow-up assessment suggested that when the pulse amplitude is large (>3 mm Hg), improvement is very likely (>90% patients improve). When the pulse amplitude is less than 2 mm Hg, improvement is as equally probable as lack of improvement.

There is no difference in amplitude between males and females. Pulse amplitude increases slightly with age but does not show any correlation with the duration of symptoms of NPH or their severity. However, pulse amplitude is lower in patients with idiopathic NPH and no any evidence of coexisting cerebrovascular disease than in patients with clear evidence of vascular problems.⁶⁰ After shunting, pulse amplitude decreases. Differences are significant both at baseline and during infusion studies.⁶¹ In shunted patients, pulse amplitude is lower in the context of normally functioning shunts than in patients with blocked shunts.

Clinical Tests of Cerebrospinal Fluid Dynamics

Measurement of the resistance to CSF outflow (R_{CSF} or R_{out}) is useful both in evaluating nonshunted patients with chronic forms

*RAP is the correlation coefficient between changes in mean CSF pressure and its amplitude over the period of 3 to 5 minutes. RAP close to 0 signifies good compensatory reserve and RAP close to +1 indicates compensatory reserve failed.

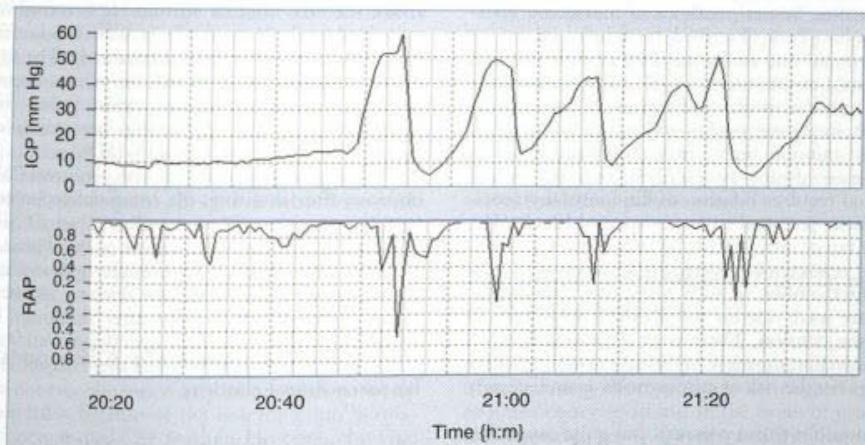


FIGURE 34-16 Example of recording of intracranial pressure (ICP) in a patient after subarachnoid hemorrhage with moderate ventricular dilation and normal baseline pressure (10 mm Hg). The computer recording indicated a regular pattern of plateau waves up to 60 mm Hg. The patient had previously undergone a series of manometric lumbar cerebrospinal fluid measurements with very mixed results: some measurements indicated normal pressure, and some indicated acutely elevated pressure.

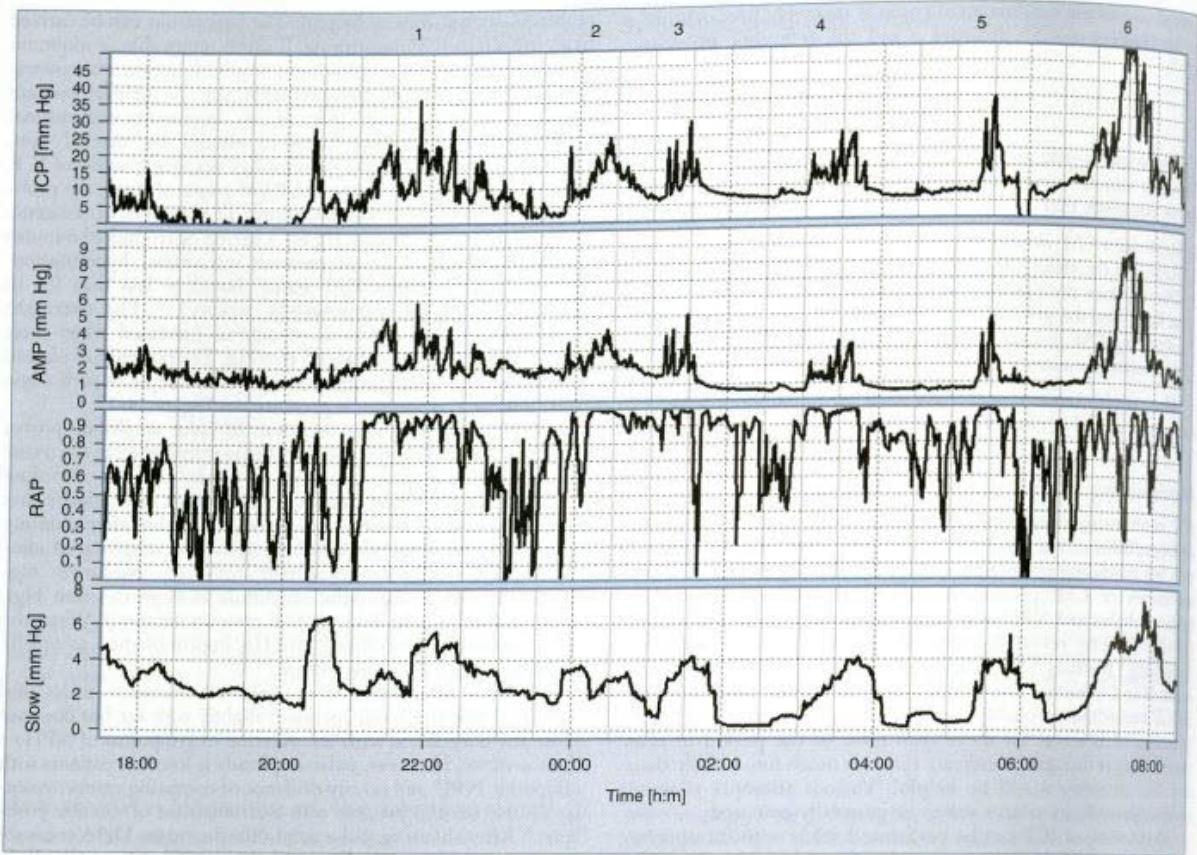


FIGURE 34-17 Example of overnight intracranial pressure (ICP) monitoring. Baseline pressure was normal (around 12 mm Hg) with periodic increases (probably during the random eye movement phase of sleep; they are indicated by numbers above the frame). Slow waves increased their power in these periods, and the compensatory reserve was worse (the RAP index increased to +1). During episodes 1 and 5, ICP increased above 25 mm Hg for only a short period (<5 minutes), but during episode 6 it increased to up to 50 mm Hg for 20 minutes. Overall cerebrospinal fluid dynamics was assessed as being disturbed. AMP, pulse amplitude.

of hydrocephalus and in assessing patients who are suspected of having shunt malfunction. Several methods of measuring resistance to CSF outflow have been described, from bolus injections into the CSF space (rapid but confounded by compliance and vasogenic phenomena), to servocontrolled constant-pressure tests, or controlled infusion studies (lumbar as in the original Katzman-Hussey test, lumboperitoneal, and ventricular).

The computerized infusion test^{62,63} is a modification of the traditional constant-rate infusion as described by Katzman and Hussey.⁶⁴ The method requires infusion of fluid into any accessible CSF compartment proximal to any suspected block. The options are a lumbar tap or intraventricular infusion via a subcutaneously positioned reservoir connected to an intraventricular catheter or shunt antechamber. In such cases, two hypodermic needles (25 gauge) are used: one for the pressure measurement and the second for the infusion. There is an approximate 0.5% risk of introducing infection during CSF infusion studies, which has to be weighed against the risk of misdiagnosis or unnecessary shunt revisions.

During the infusion, the mean pressure and pulse amplitude readings over time are calculated (Fig. 34-18A and B). Resistance to CSF outflow can be calculated by simple arithmetic as the difference between the value of the plateau pressure during infusion and the resting pressure divided by the infusion rate. Precise measurement of the final pressure plateau is not possible when

strong vasogenic waves arise or excessive elevation of pressure above the safe limit of 40 mm Hg is recorded. However, computerized analysis produces results even in difficult cases when the infusion is terminated prematurely. The algorithm uses time series analysis for retrieval of volume-pressure curves (Fig. 34-18C), least-mean-square model fitting (Fig. 34-18A), and examination of the relationship between pulse amplitude and mean CSF pressure (Figure 34-18D).

Although not all patients with abnormal CSF circulation may improve after shunting, the computerized infusion test is important because it provides a baseline value of CSF dynamics, which is useful in further management of the disease. Such testing can be invaluable in cases of chronic hydrocephalus in which the architecture of the ventricles remains unchanged (i.e., striking ventriculomegaly is present after shunting). Examples include stiffening of the ventricular ependymal wall from prolonged subacute infection and NPH when there may be loss of periventricular parenchymal elasticity.

Differentiation between Brain Atrophy and Normal-Pressure Hydrocephalus

CSF dynamics in patients with NPH is characterized by a normal baseline pressure (ICP <18 mm Hg). Resistance to CSF outflow

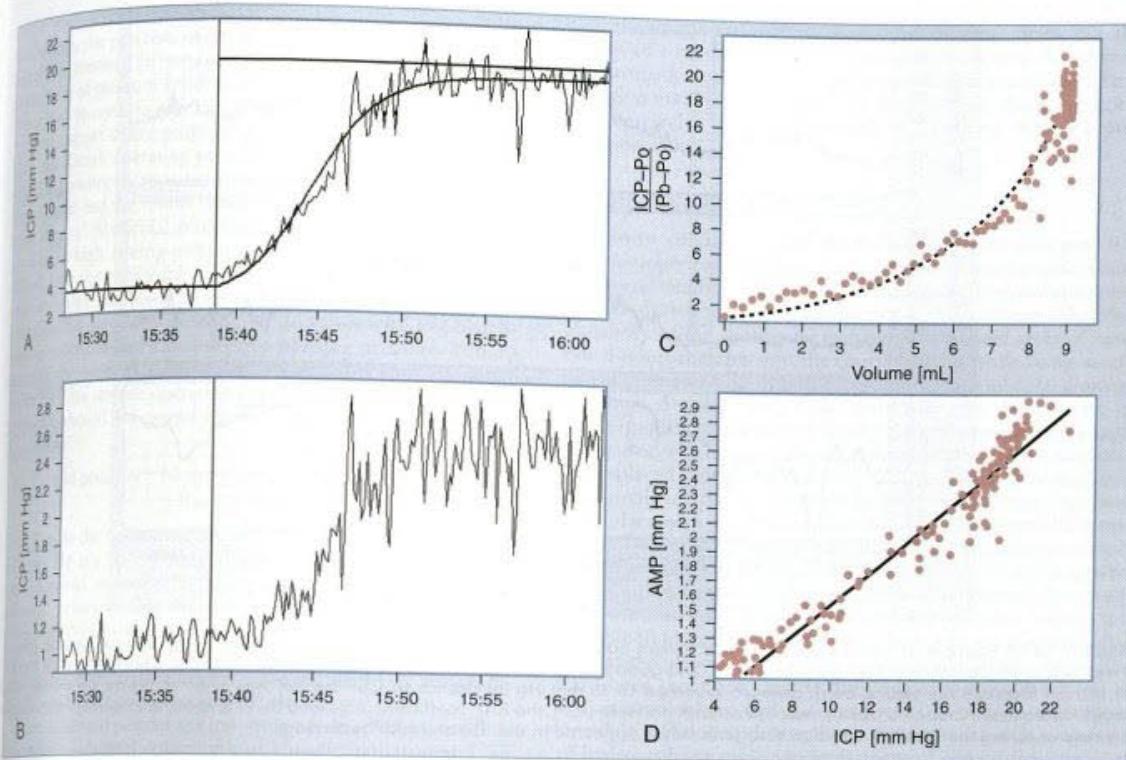


FIGURE 34-18 Methods of identification of the model of cerebrospinal fluid (CSF) circulation during infusion at a constant rate. **A**, Recording the CSF pressure (intracranial pressure [ICP]) versus increasing time during infusion with an interpolated modeling curve.⁷ Infusion at a constant rate of 1.5 mL/min starts from the vertical line. **B**, Recording of pulse amplitude (AMP) during infusion. It is customarily presented as different variables, in addition to mean ICP. The rise in AMP is usually well correlated with the rise in ICP. **C**, Pressure-volume curve. On the x-axis, an effective increase in volume is plotted (i.e., infusion and production minus reabsorption of CSF). On the y-axis is the increase in pressure measured as a gradient of the current pressure minus the reference pressure P_0 relative to baseline pressure P_0 . **D**, Linear relationship between pulse amplitude and mean ICP. The intercept of the line with the x-axis (ICP) theoretically indicates the reference pressure P_0 .

>13 mm Hg/mL per minute) is increased. The B waves recorded during infusion studies are regular. Pulse amplitude is well correlated with mean ICP. Compensatory reserve at baseline is usually good (RAP index <0.6), and the elasticity coefficient is usually slightly increased ($E > 0.2 \text{ 1/mL}$)—see Figure 34-19.

Patients suffering predominantly from brain atrophy have normal CSF circulation. Infusion studies in these patients typically demonstrate low opening pressure, resistance to CSF outflow, and low pulse amplitude ($ICP < 12 \text{ mm Hg}$, $R_{CSF} < 13 \text{ mm Hg/mL per minute}$, amplitude <2 mm Hg). Compensatory reserve at baseline is very good (RAP <0.5) as a result of the low elasticity of the atrophic brain ($E < 0.2 \text{ 1/mL}$). Vasogenic waves are rather limited during the period of the recording. Mean ICP increases smoothly during the infusion and decreases in a similar fashion after infusion, similar to the inflation and deflation of a balloon (Fig. 34-20).

Noncommunicating and Acute Hydrocephalus

Lumbar infusion is not recommended in patients with noncommunicating hydrocephalus because of the risk for brain herniation in the event of uncontrolled CSF leakage. However, this type of hydrocephalus may not always be easy to detect by imaging. In the few cases in which lumbar infusion is performed, resistance to CSF outflow may be normal (noncommunicating hydrocephalus) because the lumbar infusion is not able to detect the proximal narrowing in CSF circulatory pathways. In acute hydrocephalus,

resistance to CSF outflow, resting pressure, and pulse amplitude are elevated, whereas paradoxically, elasticity is relatively low ($ICP > 15 \text{ mm Hg}$, pulse amplitude >4 mm Hg, $E < 0.20 \text{ 1/mL}$).

Obstructive hydrocephalus can be safely assessed by ventricular infusion (via a reservoir). Typically, high intracranial resting pressure and high resistance to CSF outflow are demonstrated ($ICP > 15 \text{ mm Hg}$, $R_{CSF} > 13 \text{ mm Hg/mL per minute}$). Elasticity is high (>0.20 1/mL), RAP is elevated above 0.6, and the pulse amplitude is high (>4 mm Hg), findings indicative of poor compensatory reserve. Acute communicating hydrocephalus has a similar pattern of parameters, with frequent deep vasogenic waves (including plateau waves⁵¹).

Testing of Cerebrospinal Fluid Dynamics in Shunted Patients

Evaluation of CSF dynamics in shunted patients may prove very helpful in those with suspected shunt malfunction. The 0.5% risk of introducing infection has to be weighed against the avoidance of unnecessary revisions. In the event of proven shunt malfunction requiring revision surgery, CSF infusion studies may allow certain components to be targeted, such as a suspicion of valve malfunction or distal blockage. Infusion studies may be performed as previously described. Many shunts have accessible antechambers or have had reservoirs inserted within the shunt circuit. However, bur hole valves are generally unsuitable for

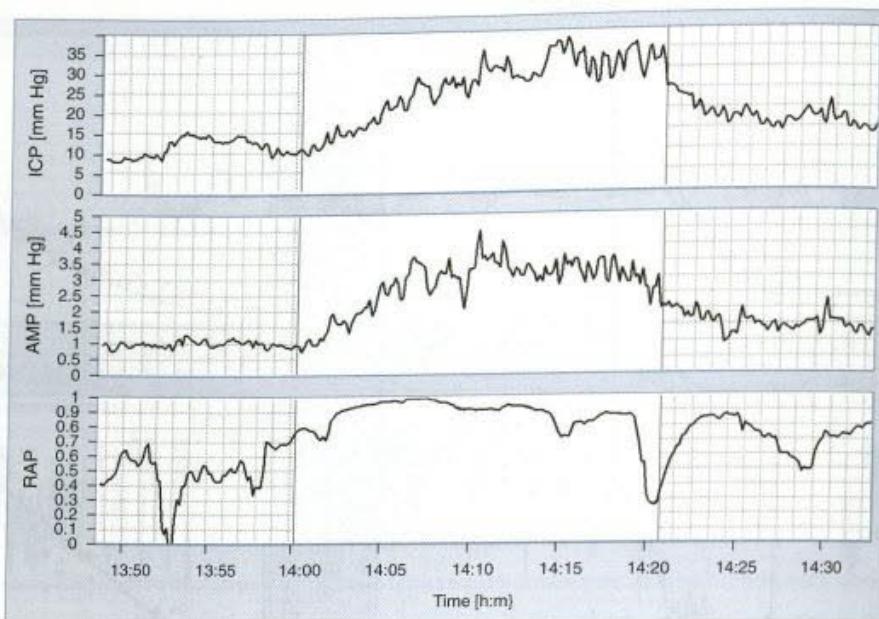


FIGURE 34-19 Example of an infusion study in a patient suffering from normal-pressure hydrocephalus with a normal baseline pressure (9 mm Hg), normal baseline pulse amplitude (AMP), and good compensatory reserve (RAP index at baseline <0.6). During infusion at a rate of 1.5 mL/min (between the vertical bars), pressure increased to 35 mm Hg (resistance to CSF outflow was 17.8 mm Hg/mL per minute), pulse amplitude increased proportionally to mean intracranial pressure (ICP), the RAP coefficient increased to +1 (indicating a decrease in compensatory reserve during the infusion), and slow vasogenic waves appeared in the ICP and AMP recordings.

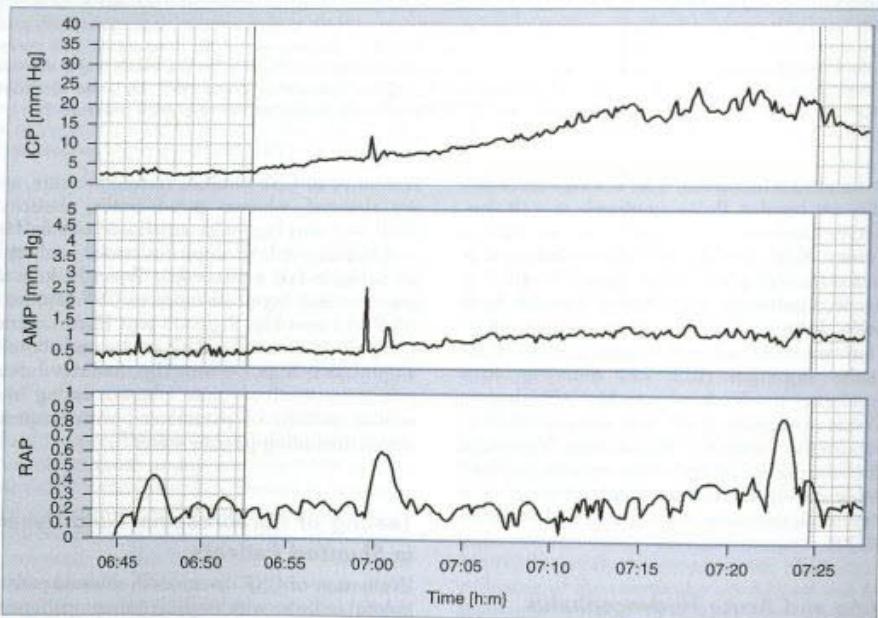


FIGURE 34-20 Example of an infusion study in a patient with atrophy predominantly. Baseline pressure was low (3 mm Hg) and increased only slightly to 18 mm Hg during infusion at a rate of 1.5 mL/min, which resulted in a normal value of resistance to CSF outflow (10 mm Hg/mL per minute). Compensatory reserve was good, even during infusion (RAP did not increase), pulse amplitude (AMP) increased very modestly in response to rising ICP, and there were very few slow waves in the recording.

infusion study access. With pressure measurement via the shunt antechamber, the presence of a CSF pressure pulse wave and an increase in pressure in response to coughing should indicate transmission of pressure between the needle and the CSF space. This is used to confirm patency of the ventricular catheter.

When a shunt drains properly, resting pressure remains at or below the shunt's operating pressure. Infusion studies or overnight ICP monitoring repeated with a shunt *in situ* should always be considered and the results compared with the tests performed before surgery. Abnormal cerebrospinal compensatory parameters, such as high resting pressure, increased resistance to CSF outflow, low compensatory reserve, increased activity of slow waves, or a high amplitude of the pulse waveform, should return to normal after successful shunting.^{61,65} In valves with low hydrodynamic resistance and a well-defined opening pressure, a sharp plateau of the pressure trend is seen about 1 to 5 mm Hg above the level of the shunt's operating pressure.⁶⁶ The magnitude of this plateau should not exceed a value as derived from the following equation:

$$\text{Critical pressure} = \text{Shunt operating pressure} + \\ + R_{\text{shunt}} \times \text{Infusion rate} + 5 \text{ mm Hg}$$

where R_{shunt} is the hydrodynamic resistance of the opened shunt and 5 mm Hg is a "safety margin" and a credit for possible non-zero abdominal pressure (in patients with possible increased abdominal pressure, this value should be increased to 10 to 15 mm Hg). When shunt operating pressures and R_{shunt} are measured in the laboratory, these parameters provide invaluable guidelines for shunt testing *in vivo*⁶⁷; see Figure 34-21 for examples of a working (A) and blocked (B) shunt.

When a shunted patient has low-pressure headaches, small or slit ventricles, subdural collections, or chronic hematomas, CSF overdrainage should be considered. Overdrainage related to body posture may be assessed with a tilting test. When the baseline pressure measured in the horizontal body position is low (usually negative), overdrainage is possible. A change in posture to sitting generally produces a further decrease in pressure. If the pressure decreases to a value lower than -10 mm Hg (the 95% confidence limit for ICP in the upright position in nonshunted patients is around -8 mm Hg), overdrainage is likely (Fig. 34-22).

The majority of contemporary valves usually have low hydrodynamic resistance,⁶⁸ a feature that may result in overdrainage from periodic oscillations in cerebrovascular volume. The expanding cerebrovascular bed acts like the membrane of a water pump with a distal low-resistance valve.⁶⁹ Early morning headache should not be always assumed to be "high pressure." It may be a consequence of the low pressure caused by nocturnal overdrainage.

In shunted patients with slit ventricles, baseline pressure recorded from the shunt antechamber may not demonstrate a pulse waveform. In this situation, collapse of the ventricular walls around the proximal catheter results in the lack of pressure transmission. A pulse waveform often appears after infusion starts as the buildup of pressure opens up the ventricular cavity (Fig. 34-23).

MANAGEMENT

Surgical management is required for patients with symptomatic acute or chronic hydrocephalus. Surgery is recommended for patients with idiopathic NPH and a favorable risk-to-benefit ratio.⁷⁰ Medical therapies, such as acetazolamide and repeated lumbar puncture, do not have a role in longer term management but may be used as temporizing measures before definitive treatment. Surgical management of any obstructive lesion, such as a tumor, may be required in addition to CSF diversion. The two main forms of surgical management for hydrocephalus are shunt insertion and endoscopic third ventriculostomy. Endoscopic

choroid plexus coagulation is favored in some units, but the results of a randomized controlled trial are awaited. Relief from symptomatic hydrocephalus and prevention of neurological deterioration may be achieved with or without a significant reduction in ventricular size, particularly in patients with chronic hydrocephalus.

Shunt Insertion

The most commonly used shunt in modern neurosurgery is a ventriculoperitoneal shunt. A ventricular catheter is placed into the lateral ventricles, usually from a frontal or occipital approach, and connected to the remainder of the shunt system. The ideal trajectory of the ventricular catheter would avoid areas of functional neuroanatomy and the choroid plexus while being at sufficient depth for CSF drainage to occur through all distal drainage openings despite changes in ventricular size. Stereotactic or image-guided placement of ventricular catheters is increasingly being used with normal or small ventricles to reduce the incidence of misplaced ventricular catheters. When raised ICP is associated with small ventricular size, such as benign intracranial hypertension, placement of a lumboperitoneal or lumbopleural shunt may be the preferred option. Ventriculoatrial shunts were previously in common use and may still be the treatment of choice in patients with significant truncal obesity, extensive abdominal abnormalities, or a history of multiple abdominal procedures. Indeed, it is possible to place the distal end of a shunt into any visceral cavity, such as the pleural cavity. Other more unusual shunt options that have been described include the Torkildsen shunt (ventricle to the cisternal space) and the Sinushunt (ventricle to the venous sinus). In addition to shunts placed within the ventricle, treatment of hydrocephalus may involve drainage of one or more cystic or subdural cavities, such as an arachnoid cyst or subdural hygroma.⁷¹

It is usual practice to incorporate a valve mechanism into the shunt circuit at the time of insertion. CSF drainage can be regulated either by pressure or by flow. Antisiphon devices to prevent overdrainage can be attached to the shunt circuit if required. Some valves incorporate such devices. Reservoir devices can also be fitted to allow access for subsequent CSF analysis or interrogation of CSF hydrodynamics. Some valves have separate reservoir chambers within their design. Many modern valves are programmable and allow subsequent adjustments in differential pressure after implantation. This permits changes to be made in the valve setting after insertion, often on an outpatient basis. The type of valves selected for patients with acute hydrocephalus is based on local experience, published data, and available supplementary information, such as drainage requirements assessed by external ventricular or lumbar drainage. In patients with NPH, no series has demonstrated a significant benefit with a particular type of shunt or valve, although there is a trend favoring low-pressure valves.⁷² Patients with low-pressure hydrocephalus may require a valveless shunt system. Shunt devices are discussed in greater depth later.

Endoscopic Third Ventriculostomy

Patients with obstructive hydrocephalus may benefit from endoscopic third ventriculostomy rather than shunt insertion (see Chapter 36). This technique involves passing an endoscope (rigid or flexible) through the lateral ventricles (usually via one of the frontal horns) directly into the third ventricle. If the floor of the third ventricle can safely be visualized, a stoma can be created within it to allow fluid to drain directly into the basal cisterns. The advantage of this procedure over a shunt is that it avoids the potential morbidity of shunt infection and lifelong risk for revision. This procedure has little role in the management of true communicating hydrocephalus. However, some patients with NPH have a late-onset form of relative aqueduct stenosis. In

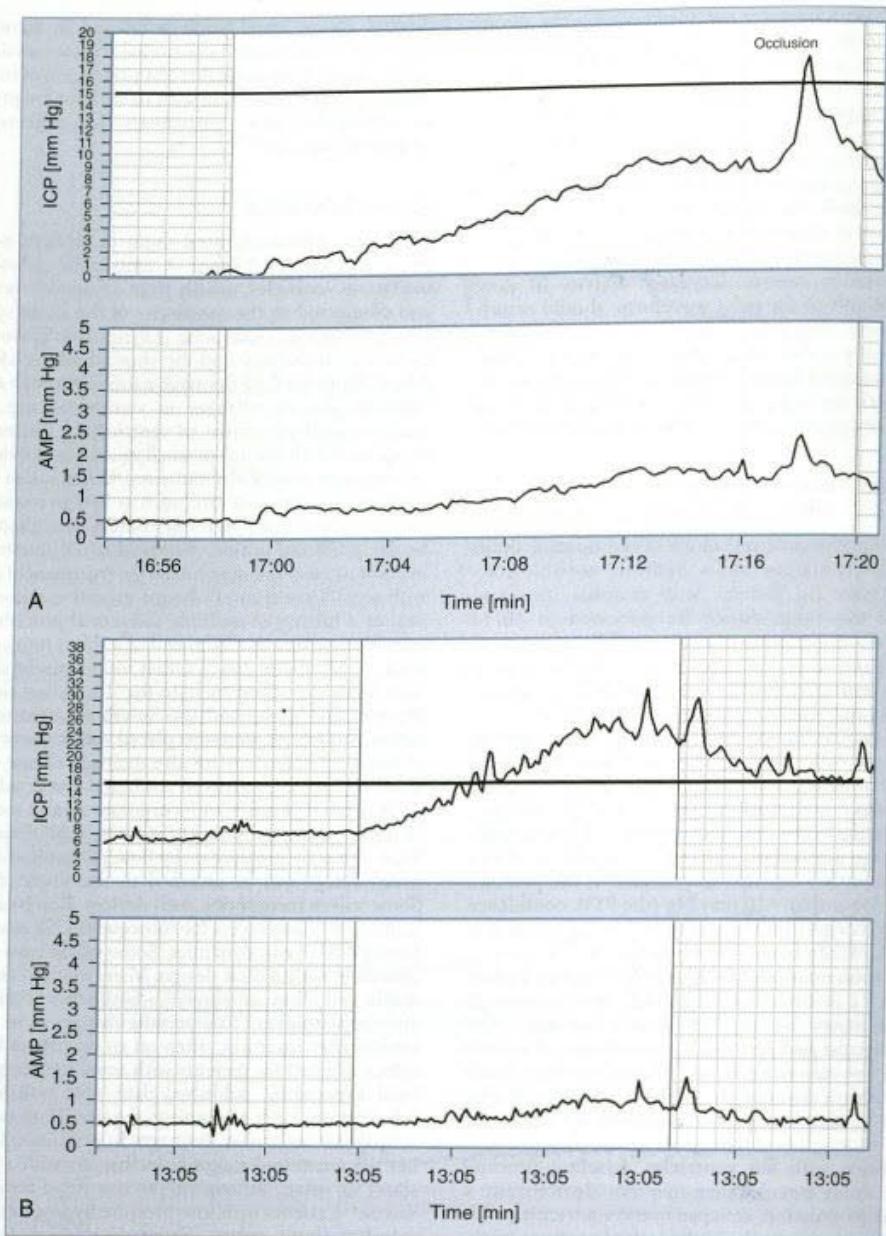


FIGURE 34-21 Examples of infusion studies performed in shunted patients through a shunt prechamber with a working and blocked shunt. **A**, Patient with a Strata Valve set for 1.5 in situ. Pulse amplitude (AMP) was low but clearly recordable, thus confirming the patency of the ventricular drain. Opening pressure was low, and during infusion the pressure increased to a value below the “critical threshold” for this valve (thick horizontal line). During infusion, transcutaneous occlusion (external compression of the siphon control device) was performed. Such a compression stops drainage through the valve. Pressure started to rise immediately, thus confirming that shunt system was patent. **B**, Patient with a Hakim Programmable Valve set at 100 mm H₂O. Pressure increased well above the “critical threshold” (horizontal line). Spontaneous vasogenic waves were recorded during the test. A pulse waveform was present on the recording. Distal obstruction of the shunt system was confirmed during revision of the shunt. ICP, intracranial pressure.

these patients, there is a mismatch between the degree of ventriculomegaly in the lateral ventricles and third ventricle and between the aqueduct of Sylvius and the fourth ventricle. This implies that the hydrocephalus has an obstructive element (although the hydrocephalus is still “communicating” in terms of

the chronic signs and symptoms). In this situation, endoscopic third ventriculostomy may be considered. Gangemi and coauthors reported improvement in 72% of NPH patients with this technique and a relatively low complication rate (intracerebral hemorrhage in 4%).⁷³



FIGURE 34-22 Overdrainage test showing an excessive decrease in intracranial pressure (ICP) during sitting up at the time point indicated by the vertical line (below -14 mm Hg). During sitting up, pulse amplitude (AMP) may not change.

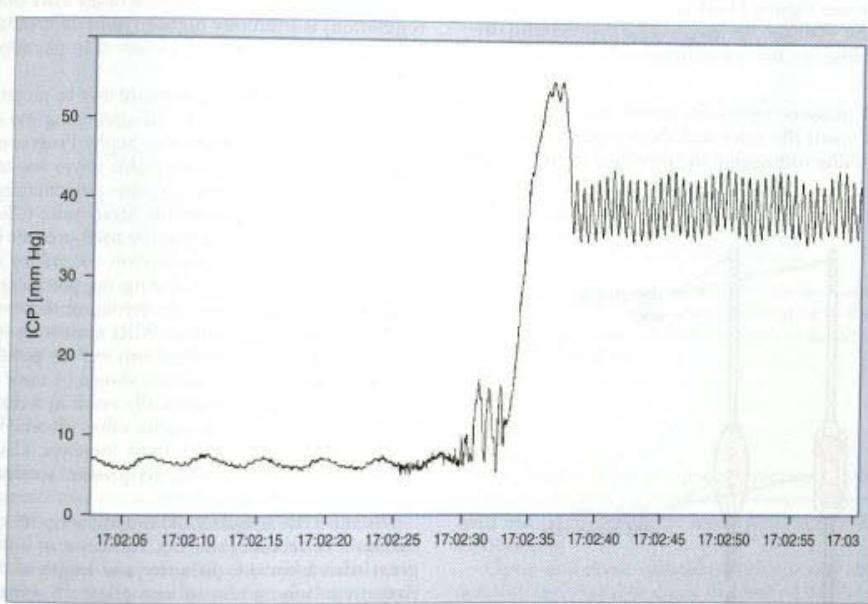


FIGURE 34-23 In patients with slit ventricles, the pulse amplitude (AMP) of intracranial pressure (ICP) is rarely visible on the recording. During infusion into the shunt prechamber, all fluid is drained distally—recorded pressure is equivalent to shunt operating pressure plus the pressure gradient along the distal tube plus abdominal pressure. A respiratory wave may be visible; it is commonly transmitted from the abdominal space. In patients with a membrane siphon-preventing device, occlusion of the device can be performed during infusion (17:02). Pressure increases suddenly to very high values (in this case >50 mm Hg), collapsed ventricles open within a relatively short time, and pressure stabilizes at a lower level with a pulse wave clearly visible. The "stabilization pressure" is elevated, because in slit ventricles syndrome an intraparenchymal ICP is very high. Ventricles may stay open for a longer time, but more frequently they collapse again after the end of the infusion.

SHUNTS

The ability of a shunt system to drain CSF continuously in a repetitive manner over a long-term period is crucial in the management of hydrocephalus. Contrary to popular opinion, a shunt constitutes a complex hydrodynamic system of highly nonlinear flow characteristics. A wide variety of shunt products (more than a hundred generic types, with numerous subtypes and performance levels—not including some homemade devices in use in developing countries) are manufactured. There is little systematic knowledge available with which their comparative cost-effectiveness can be judged by the practicing surgeon. Similarly, there is very little knowledge of whether a specific type of shunt can be matched to an individual pattern of disturbed CSF circulation.

An operating flow pressure of around 0.3 mL/min marks the range of ICP that can be measured in a patient with a properly functioning shunt in a horizontal body position. In ball-on-spring valves, this pressure is very stable over time but is sensitive to dynamic changes in ICP. This type is in contrast to silicone membrane valves, in which the operating pressure may vary within a range of 4 to 6 mm Hg in low, medium, or high ranges. Randomized trials have failed to demonstrate the superiority of different types of valve construction.⁷⁴ It is well recognized that physiologic ICP is variable within the limits of 0 to 15 mm Hg. Artificial attempts to set a constant ICP by using valves with minutely determined opening pressure and very low hydrodynamic resistance may not be useful.

Generally, a shunt consists of three parts: inlet tubing (ventricular or lumbar drain), which is a thin short tube with an inner diameter of 0.9 to 1.2 mm; a valve; and a distal drain, a longish silicone rubber tube—see Figure 34-24.

Contemporary CSF drainage devices may be divided into different groups according to the mechanism of CSF drainage control:

1. Fixed differential pressure valves, in which the inlet-outlet pressure gradient opens the valve and then controls the flow of fluid through tubing connecting the proximal (ventricles or

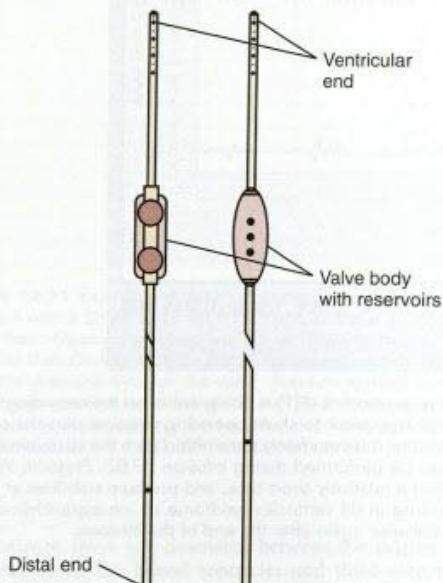


FIGURE 34-24 Components of a shunt system: proximal drain, valve, and distal drain.

lumbar subarachnoid space in most cases) and distal (e.g., peritoneal or atrial) spaces.

2. Adjustable differential pressure valves, which work similarly but allow the opening pressure to be externally adjusted via magnetic programming. Differential pressure (fixed or adjustable) valves are aimed at control of ICP.
3. Flow-regulating valves, in which flow is stabilized, irrespective of the differential pressure.
4. Accessory devices, which control flow and prevent overdrainage in the upright position (antisiphon devices).

Valves can be classified according to their construction:

1. Silicon membrane—flow is controlled by an elastic membrane that changes the area of the outlet orifice.
2. Ball-on-spring—flow depends on compression of a spring (flat or helical) supporting a ball moving along the cone that constitutes the outlet orifice.
3. Miter valve—flow depends on deflection of the silicon miter controlling the diameter of the outlet orifice.
4. Proximal or distal slit valves—flow depends on the area of a slit in soft silicone rubber.
5. Moving diaphragm—flow is stabilized within a certain fixed range of pressure.

Examples of pressure-flow curves of differential and flow-regulating valves are shown in Figure 34-25. Differential pressure valves are characterized by opening/closing pressure (pressure above/below the point at which flow starts/ceases) and an inverse of the slope of the curve within the range of full drainage (≥ 0.3 mL/min), which is termed the *resistance of the valve*. In flow-regulating valves, the resistance of the valve (within the range of regulation) is infinitely high. In most differential pressure valves, the resistance is very low (lower than physiologic resistance to CSF outflow).⁶⁸

Opening and closing pressure may be programmed externally in some models. Magnetic programming was used for the first time in a French model—the Sophy Programmable Valve. The next generation of programmable valves was designed by S. and C. Hakim. Much more precise programming (18 steps) was achieved. The programmable Strata valve followed, a programmable equivalent of the popular fixed-pressure Delta Valve, integrated with a membrane siphon controlling device.⁷⁵ Patients should be counselled regarding the possibility that some magnetic fields may modify the setting of these valves under some circumstances, such as in an MRI scanner. Some valves are more prone to this problem than others.⁷⁶ In pediatric patients with programmable valves, parents should be made aware that strong magnetic toys could potentially result in a change in the setting of the valve. Newer adjustable valves (Pro-GAV [B. Braun, Melsungen, Germany] and Polaris [Sophysa, Orsay, France]) offer mechanisms that are able to prevent accidental readjustment, even in a 3-T MRI scanner.

Because the majority of contemporary valves have low hydrodynamic resistance, the net resistance of a shunt depends to a great extent on the diameter and length of the distal drain. In patients in whom clinical complications related to overdrainage are likely to develop, implantation of an antisiphon device should be considered. However, the risk for overdrainage related to vasomotor nocturnal waves may still be high.⁷⁹ A standard peritoneal open-end catheter (usually around 90 cm long, 1.1 to 1.2 mm in diameter) provides a resistance of 2.5 to 3.5 mm Hg/mL per minute. This may amount to 100% to 200% of the overall resistance of the valve itself. It must be recognized that shortening of a drain decreases overall shunt resistance, thus making it potentially more susceptible to overdrainage.

The hydrodynamic resistance of the drain is inversely proportional to the fourth power of its diameter. Therefore, many thin lumboperitoneal shunts with a small internal diameter (0.9 mm)

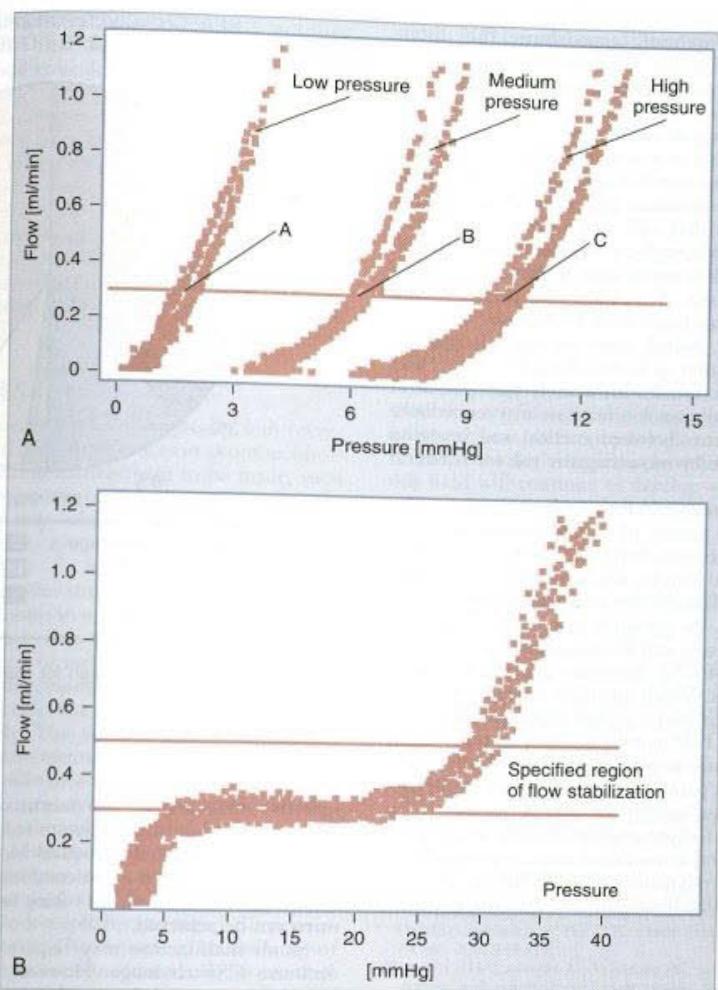


FIGURE 34-25 Pressure-flow curves for two types of shunt. **A**, Differential fixed-pressure shunt at three performance levels: low, medium, and high. Points A, B, and C denote operating pressures (i.e., pressure with a flow of 0.3 mL/min). **B**, Flow-regulating valve that is able to stabilize drainage rate within a wide range of differential pressures (from 7 to 27 mm Hg). Such a valve would perform as an overdrainage-preventing device, both related to posture- and vasocycling-mediated changes in cerebral blood volume.

in very high resistance (25 mm Hg/mL per minute). Moreover, the low internal diameter may result in susceptibility to blockage from small particles. All shunts are subjected *in vivo* to the constant presence of small particles in CSF. They can be as large as erythrocytes or even larger protein particles, choroidal debris, or other particulate matter. All shunts can be permanently clogged with larger debris. In addition, membrane and ball-on-spring valves can be permanently opened by particles the size of erythrocytes (as illustrated by experiments with graded-diameter microspheres or blood).

All accessory siphon-preventing devices have some drawbacks. Membrane devices (such as in the Delta chamber), in which the mucinous membrane is designed to stop drainage when its outer pressure is negative, could also impede CSF flow when compressed by tense skin or external pressure through the skin. A flow-regulating (Siphon Guard) device such as that used in the Holm programmable valve limits excessive flow but may permanently increase the hydrodynamic resistance of the shunt system

to very high values and cause intracranial hypertension. A gravitational device (Shunt Assistant) is potentially free of major problems but is still unable to limit overdrainage caused by nocturnal vasocycling.

Open-end distal catheters perform very differently from slit-opening catheters (or distal slit shunts). Hydrodynamic resistance depends dramatically on whether the end is wet or dry and on positioning. This illustrates the historically established belief that the distal slit valve may become partially or completely obstructed, depending on its environment in the abdominal space. In some cases, the very high hydrodynamic resistance is an attribute of the valve itself, as in the Orbis-Sigma valve, and this may prevent posture-related overdrainage. However, contrary to low-resistance valves, this valve stabilizes flow, not differential pressure. Therefore, patients suffering from high vasogenic pressure waves but with a normal baseline pressure level may not improve because the shunt cannot suppress the magnitude of the pressure oscillations. In differential pressure valves, the average operating

pressure (which should theoretically approximate the distal-proximal pressure gradient after implantation) can be lowered in the presence of pulsations of proximal pressure (pulse or respiratory waveform of ICP).

Despite the advances in shunt technology, many challenges remain. Shunts are still unable to restore physiologic pathways of CSF circulation. The long ventriculoperitoneal tubing produces a hydrostatic pressure gradient that despite some ingenious technologic advances, may still constitute an important source of secondary clinical complications. In normal conditions, ICP is always coupled to and a little higher than venous pressure in the sagittal sinuses. Ventriculoperitoneal shunting disturbs this coupling and can result in ICP that may be intermittently much lower than sagittal sinus pressure. It may be noticeable in an upright position, as well as during coughing and other body movements associated with acutely raised central venous pressure. Theoretically, such situations may contribute to excessive pressure gradients between cortical and bridging veins and CSF pressure, thereby increasing the risk for subdural or epidural bleeding.

Therefore, the ideal shunt should restore the normal circulation of CSF and the normal pattern of extrachoroidal fluid flow within the brain, prevent excessive buildup of ICP, and encourage restitution of the cerebral mantle, which consists of both gray and white matter. After shunting, the hydrodynamic performance of the shunt interacts with the patient's own CSF circulatory pattern. The result of shunting can be forecasted by a parallel connection of the model of CSF dynamics and pressure-flow characterization of the shunt. When a patient does not improve after shunting or deteriorates after a period of improvement, an infusion study or overnight ICP monitoring may confirm shunt malfunction if the hydrodynamic performance curve of a shunt is known.^{58,77,78} Many of the parameters of shunts are never disclosed or are disclosed insufficiently or even inaccurately by manufacturers. Programs of shunt evaluation have created an opportunity to understand and demonstrate some important phenomena related to the hydrodynamics of CSF flow in shunted patients and generate guidelines for "more physiologic" valves.^{67,68,79}

COMPLICATIONS

Surgical approaches to NPH are associated with relatively low morbidity and mortality rates. The general risks related to shunt surgery include infection, bleeding, CSF leakage, seizures, and neurological deficit. There is an estimated 3% to 4% risk for intracerebral hemorrhage^{73,80} and an estimated 1% to 2% risk for catastrophe, including coma or mortality. The risk for mortality can be greater for an individual NPH patient with multiple comorbid conditions. More commonly occurring complications are listed in the following paragraphs.⁷¹ Shunt surgery for other types of communicating or acute hydrocephalus is associated with similar risks. Revision or multiple reoperations for hydrocephalus can be challenging to manage. Figure 34-26 lists reasons given for shunt revision in adults (17 years and older) obtained from the U.K. Shunt Registry. It is important to note that these data have been derived purely on an intention-to-treat basis.

Both overdrainage and underdrainage of CSF can occur with any type of shunt system. Excessive CSF drainage from the ventricles is thought to increase the risk for subdural hematoma, the reported incidence of which varies from 2% to 17%.⁷⁰ The resulting hematoma can lead to neurological deficits, coma, or death. It may be useful to perform a postoperative CT scan to verify the accuracy of catheter placement and exclude new subdural hygromas into which hemorrhage may occur. Subdural fluid collections have a wide spectrum, from CSF subdural hygromas to frank hematomas. Strategies for treatment include con-

REASONS GIVEN FOR SHUNT REVISION IN ADULTS \geq 17 YEARS

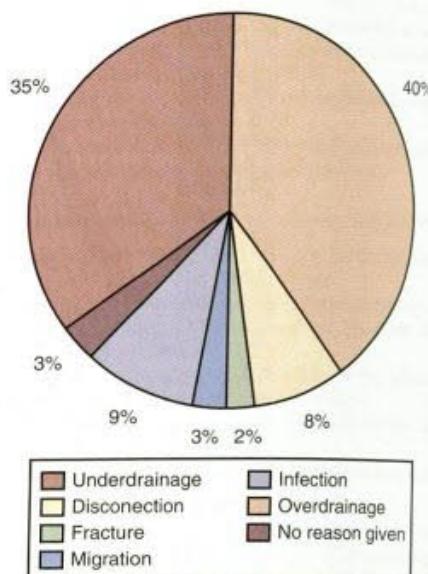


FIGURE 34-26 Reasons given for shunt revision in adults (17 years and older).

servative management by means of serial scanning with or without resetting of the valve to reduce CSF drainage. Symptomatic acute or chronic subdural hematomas require evacuation by either bur holes or a minicraniotomy. Severe cases may necessitate ligation of the shunt tubing until resolution of the hematoma can be achieved.

Shunt malfunction may require formal revision surgery to optimize CSF drainage. However, good long-term outcomes have been reported despite the need for multiple shunt operations in the case of shunt blockage.⁸¹ Malfunction can occur within any part of the shunt system, from blockage of the drainage openings of the ventricular catheter, to valve dysfunction, to distal blockage. The distal end of a ventriculoperitoneal catheter may become kinked or malpositioned because of shifting and peristalsis of abdominal contents. A clot or emboli may form as a result of a ventriculoatrial catheter. Disconnection or breakage of one or more shunt parts may occur, particularly in patients with epilepsy or other movement disorders or in patients prone to falls. Iatrogenic shunt dysfunction as a result of malpositioning of the shunt during insertion may necessitate revision surgery. Shunt systems can intermittently malfunction because of positional reasons. Strategies to reduce this complication include meticulous planning of placement of the various shunt components, such as antisiphon/antigravity devices, which work best in a true vertical position. Careful handling of any excess tubing during shunt insertion or revision surgery is required to avoid unintentional kinks in the shunt circuit.

Shunt infections represent a serious complication. Strategies to reduce this complication include rigorous adherence to intraoperative aseptic technique during shunt insertion and the use of shunt tubing coated with antiseptic or antibacterial agents. Repeated shunt infections secondary to skin breakdown may be indicative of an underlying silicone allergy and should necessitate formal testing. Other serious infective sequelae from shunts include meningitis and peritonitis. Subacute bacterial endocardi-

It is a known complication of ventriculoatrial shunts and may become apparent many years after the original shunt insertion. Encephalitis, adhesions, and radiculopathy have been reported with lumboperitoneal shunts.

It is also possible for shunt hardware to have an adverse effect on surrounding tissue. Shunt components can extrude through the skin, particularly after multiple operations, migrate, or penetrate into different cavities or viscera. Intestinal obstruction or ulcers can occur in cases of tethered or kinked distal peritoneal catheters. Wound breakdown, CSF leakage, and hernias can occur at incision sites and may require further surgical intervention. In cases of shunting for hydrocephalus secondary to tumors, there is a theoretical risk of extracranial seeding of metastases.

PATIENT OUTCOMES

Hydrocephalus can be successfully treated surgically with reversal of the initial neurological deficits. Advances in shunt technology have allowed refinements in management to be made, such as revising the settings of programmable valves instead of revision surgery. However, patients may exhibit variable improvement after successful CSF diversion, even in the context of proven hydrocephalus and raised ICP.

A study of CSF dynamics after shunting by Petrella and colleagues investigated this dilemma in a cohort of 25 patients with NPH.⁸¹ Patients who still had some adverse symptoms, mainly headaches, slow improvement, or no improvement of ventriculomegaly after shunt insertion, underwent infusion studies to assess shunt function. In all cases the shunts were confirmed to be draining CSF adequately. The authors demonstrated that there were significant improvements in mean ICP, pressure-volume compensation, and resistance to CSF outflow, as well as a decrease in vasogenic pressure waves. Such a study demonstrates the usefulness of fitting shunt systems with built-in access ports for the interrogation of shunt malfunction. However, the return of disturbed CSF dynamics to normal values, even in patients with disappointing clinical or radiologic improvement, implies that management of hydrocephalus as a pure CSF circulatory disorder may be insufficient. The element of reversibility of damage to important white matter connections may be essential for the continued improvement of symptoms after successful CSF diversion.

Audit data from our home institution have shown that in patients with NPH who underwent insertion of a ventriculoperitoneal shunt after assessment in a multidisciplinary CSF clinic, formal neuropsychological testing, and infusion studies, 69% (110 of 161) demonstrated initial clinical improvement.⁸² Of the 31% of patients who were shunt nonresponders, most had potential overlap with other neurodegenerative conditions, including Parkinson's and Alzheimer's disease. At a 2-year follow-up, 54% of the patients reported continued or sustained improvement. Despite initial improvement and a working shunt, as determined by further testing, 15% of patients suffered a late decline in terms of gait or cognition, or both. These figures are similar to outcomes from other worldwide series. Published rates of improvement after surgical intervention range from 53% to 78.9%.^{27,30,83}

A prospective study by Malm and coworkers demonstrated improvement in gait and cognitive function in 72% and 67% of patients, respectively.⁸⁴ Raftopoulos and coauthors reported improvement in cognitive function in 66.6% of patients and improvement in bladder function and gait apraxia in more than 80% 1 year after surgery.⁸⁴ A study by Savolainen and associates demonstrated that the early benefits of surgery declined significantly over a 5-year period from 74% to 47%.⁸⁵

However, there is controversy over the relative contribution of concomitant comorbid disease to the outcome figures in longer term follow-up studies of NPH. In the published idio-

pathic NPH guidelines, Klinge and colleagues concluded that a standard for outcome assessment of shunt treatment of idiopathic NPH was lacking because of different criteria for selection of patients, postoperative assessment, and follow-up intervals.⁴⁰ The 1-year postshunt period was thought to be a potential determinant of shunt outcome; shorter term results are more likely to be influenced by shunt-associated risks and longer term results may be related to concomitant cerebrovascular and vascular diseases. Recommendations made included the following: follow-up at 3, 6, and 12 months; careful evaluation of nonresponders for shunt malfunction; and the use of objective scales for measurement of improvement.

CONCLUSION

Hydrocephalus remains a rich and rewarding subject area in which successful surgical management requires meticulous clinical assessment, direct physiologic testing, and careful interpretation of the underlying pathophysiologic processes. It is likely that this field will continue to develop with the evolution of neuroimaging tools and novel shunt technology.

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MANAGEMENT OF ADULT HYDROCEPHALUS 3b

CHAPTER 35

Shunting*

Marvin Bergsneider ■ Eric Stiner

Hydrocephalus is a commonly encountered disorder that occurs either as a primary condition or as the sequela to an intracranial hemorrhage, a space-occupying lesion, or meningitis. For more than a half-century, a cerebrospinal fluid (CSF) shunt has been the mainstay for treatment of hydrocephalus. Although many consider shunting a relatively simple procedure, problems with CSF shunts are common, costly, and sometimes debilitating. Within the first year, shunts fail at extraordinary rates of up to 4% and show nearly a 10% infection rate.¹⁻⁴ Thus, the shunt operation has one of the highest associated complication rates in neurosurgery. Furthermore, cases of hydrocephalus can be some of the most complex and challenging clinical scenarios facing a neurosurgeon.^{5,6}

The aim of this chapter is to help neurosurgeons choose the type of shunt, valve setting, and shunt location that will offer the highest probability of a good outcome while avoiding complications and revisions. Unfortunately, there are scant class I and class II evidentiary data on which to base guidelines pertaining to shunting methods and materials for adult hydrocephalus patients. Our recommendations are therefore derived from personal experience (more than 6000 outpatient encounters and 700 surgical procedures on adult hydrocephalus patients during a 14-year period), insight drawn from our clinical studies,⁷⁻⁹ and information gleaned from the literature.

Although this chapter is entitled *Shunting*, neurosurgeons should reflexively consider endoscopic third ventriculostomy an alternative when appropriate.^{7,10} The “knee-jerk” response to proceed automatically with a shunt operation, particularly in patients presenting with shunt failure, robs the patient of an opportunity to live shunt free. Clinicians should investigate the etiology and ventricular anatomy in every case of hydrocephalus. In some cases, even patients whose physicians previously said that they had “communicating” hydrocephalus in fact have a ventricular obstruction that clinicians can readily visualize by modern high-resolution magnetic resonance imaging (MRI) technology (such as the CISS [constructive interference in steady state] or FESTA [fast imaging employing steady-state acquisition] sagittal sequences^{7,11,12}). Adult patients shunted in early childhood have a particularly high incidence of noncommunicating (intra-ventricular) hydrocephalus in our experience.

KEY POINT

In the initial evaluation of a newly diagnosed hydrocephalus patient or a previously shunted one, an essential component of the evaluation is to determine whether an endoscopic third ventriculostomy (or related procedure) is appropriate.

VALVE DESIGN AND TERMINOLOGY

Probably the most important component of a shunt system is the valve. Neurosurgeons can choose from more than 125 commercially available valves.¹³ During the past 50 years, the predominant theme in the evolution of valve design has been the goal of preventing CSF overdrainage. This includes the introduction of anti-siphon devices, flow-restricting elements, multistage valves, and adjustable valves. It is important to understand that manufacturers have little or no direct *in vivo* intracranial pressure or CSF flow data to back up advertised claims, such as “preventing excessive flow while allowing constant physiological drainage” or “regulates flow through the valve at a rate close to that of CSF secretion, therefore minimizing the risks of underdrainage or overdrainage.” Our studies⁸ demonstrate that the *in vivo* behavior of even the simplest shunt, the ventriculoperitoneal shunt with a standard differential pressure valve, is poorly predicted by the first-order, steady-flow equations that are the basis of the many valve designs.

In our opinion, there is no single valve mechanism, design, or arrangement that is clearly the “best,” nor one that will be adequate for every hydrocephalus patient. There are some valves and valve settings, however, that are poorly suited for adult hydrocephalus and will likely result in a higher complication rate. Hydrocephalus is a heterogeneous disorder, with a wide range of intracranial pressures, ventricular compliance, and CSF profiles across patients. It is somewhat fortunate that many valve designs work satisfactorily, at least in the short term, in the majority of patients. The main challenges arise from problematic patients, such as those suffering from headaches, subdural hematomas, repeated shunt obstructions, slit ventricle syndrome caused by chronic overdrainage, and so on. Shunt management is often a trial-and-error process, one in which knowledge of valve design and function can greatly help in the selection of a better choice should a revision be necessary.

The following is a primer on shunt valve design and characteristics with which every neurosurgeon placing shunts should be familiar.

*The senior author (M. B.) has received travel stipends from Codman & Shurtleff, Medtronic, and Sophysa. The senior author has served on Advisory Boards for Codman & Shurtleff and Medtronic. Clinically, the UCLA Adult Hydrocephalus Center uses Codman, Medtronic, Sophysa, Aesculap, and Integra products.

Differential Pressure Valve

The basic building block of most shunt valves is a differential pressure "check valve" mechanism. The basic design of John Holter continues in some form more than half a century after its development.¹⁴ In most current valve designs, it consists of a tiny ball situated on a ring, with a spring pushing the ball downward on the ring. CSF passes through the ring, elevating the ball if the pressure exceeds the pressure exerted by the spring. This creates a one-way flow mechanism because reverse flow will not occur as the ball sits down onto the ring.

Opening of this valve mechanism depends on the *differential pressure* across the ring. For example, if the spring is exerting downward pressure of 100 mm H₂O, CSF will flow if the difference between the inlet and outlet pressures is greater than 100 mm H₂O, regardless of whether the inlet pressure is positive or negative.

A common misconception is that the valve opening pressure must be lower than the ventricular pressure (as measured at the time of surgery) for CSF to flow down the shunt. Our studies demonstrate that this is clearly an invalid assumption. In a study of patients with normal-pressure hydrocephalus (NPH), intracranial pressure was statistically lower at all head-of-bed elevations compared with preoperative values, even with the valve set at 200 mm H₂O opening pressure. For example, despite a mean preoperative intracranial pressure of 164 ± 64 mm H₂O, the mean postoperative intracranial pressure was 125 ± 69 mm H₂O ($P = .04$).⁸

The finding that an intracranial pressure reduction occurs even with a very high valve opening pressure might appear counterintuitive and physiologically untenable, but this misconception arises from a perpetuated oversimplification of intracranial pressure and CSF flow hydrodynamics. The concepts of CSF opening pressure (which, by default, is a mean pressure) and bulk CSF flow have been the standards of hydrocephalus pathophysiology teaching for decades. In reality, the intracranial pressure waveform is pulsatile, with significant elevations of intracranial pressure occurring because of coughing and Valsalva maneuvers as well as intrinsic vasomotor changes. The interaction between pulsatile intracranial pressure and the one-way valve mechanism (inherent to differential pressure valves) is poorly studied. Our continuous intracranial pressure recordings demonstrate that peak intracranial pressures often exceed 200 mm H₂O among patients with a mean intracranial pressure of 164 mm H₂O.⁷ Even taking into account distal intra-abdominal pressure, one-way CSF egress occurs during these peaks, thereby lowering the mean intracranial pressure. The one-way flow check-valve phenomenon results in the shunt's draining CSF even with opening pressures exceeding the mean intracranial pressure. This demonstrates that use of a low-pressure valve setting is not necessary and results in excessive CSF drainage in many patients.

Most commercially available CSF shunt valves contain a differential pressure valve mechanism in one form or another. For some, it is the sole valve mechanism, whereas in others, it is the first in-series component of the valve assembly. Examples of ball-spring valves are the Medtronic Strata valve, the Codman Hakim programmable and Precision valves, and the Aesculap proGAV valve. A simpler, less accurate mechanism consists of a valve mechanism derived from two apposing semirigid membranes. These valves, which include the Medtronic, Pudenz, and Codman distal slit valves, are manufactured and then individually tested to determine the approximate opening pressure. They are then segregated into different bins covering a range of pressures. For example, the "medium-pressure valve" bin would contain valves ranging from 50 to 90 mm H₂O opening pressure.

KEY POINT

There is a basic misconception that the valve opening pressure must be lower than the mean ventricular pressure for the shunt to flow.

Adjustable ("Programmable") Valves

A "programmable" or adjustable valve is created by adding a mechanism that enables precise changes of the spring tension of a differential pressure valve. There are several competing designs enabling this—all incorporating a magnetic actuation of a rotor. Strictly speaking, these valves are not truly programmable and are better considered as merely *adjustable* valves. Adjustable valves arose from the realization that fixed-pressure differential pressure valves result in either overdrainage or underdrainage in a significant number of adult patients. The overdrainage side of this argument is supported by data from the Dutch Normal-Pressure Hydrocephalus Study,¹⁵ one of the few prospective, randomized studies performed in adult hydrocephalus. This study demonstrated that subdural hygromas occurred in 71% of patients with low-pressure valve shunts versus 34% of patients randomized to medium-pressure shunts. Given the likelihood that expanding or large subdural hygromas are a risk for subdural hematoma, this is one example that there is clearly a risk of selecting too low of an opening pressure. The analysis of our series of 114 consecutive idiopathic NPH patients, each treated with an initial valve opening pressure of 200 mm H₂O, revealed a subdural hygroma incidence of 4%.⁷ As shown in Figure 35-1, combining the results of the Dutch Normal-Pressure Hydrocephalus Study with our experience suggests a direct relationship between subdural hygromas and valve opening pressure.

Another justification for the routine use of adjustable valves is based on the range of "final" valve opening pressures when these valves are used. In our retrospective evaluation of 114 consecutive NPH patients surgically treated with a CSF shunt,

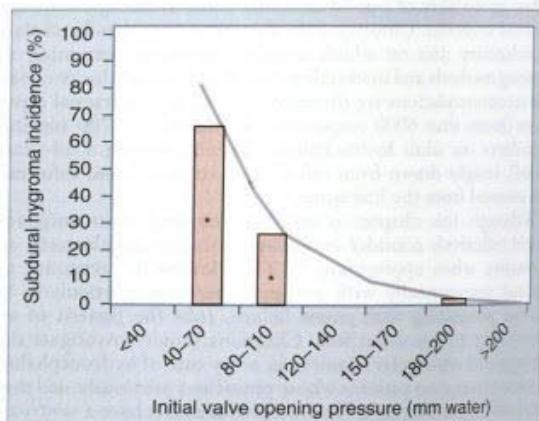


FIGURE 35-1 Estimated risk of subdural hygroma formation with idiopathic NPH. The Dutch Normal-Pressure Hydrocephalus Study¹⁵ documented a subdural hygroma (effusion) incidence of approximately 70% and approximately 30% with low- and medium-pressure differential pressure valves, respectively (data signified with an asterisk). We encountered a 4% incidence among patients with an initial valve setting of 200 mm H₂O. Combining these data sets results in a direct relationship between valve opening pressure and subdural hygroma incidence. The hygroma incidence for other valve designs and arrangements has not been well documented. (From Bergsneider M, Miller C, Vespa PM, Hu X. *Surgical management of adult hydrocephalus*. Neurosurgery. 2008;62:SHC643-660.)

the histogram distribution of the final valve opening pressure revealed a roughly gaussian distribution, with most patients in the range of 120 to 140 mm H₂O (Fig. 35-2).⁷ This finding closely agrees with that of other large NPH studies.¹⁶ With the wide distribution of final valve pressures shown in Figure 35-2 (from <40 to >200 mm H₂O), it is difficult to fathom how a fixed-pressure valve could adequately serve this population unless there is a way of selecting the appropriate valve pressure preoperatively. Although some have suggested algorithms to do so,^{16,17} none has been independently evaluated or validated.

Some neurosurgeons remain reluctant to use adjustable valves as a routine basis (or at all). On their side are the results of a prospective, randomized trial comparing the Codman Hakim adjustable valve and a standard differential pressure valve that failed to demonstrate a difference in shunt failure rates.⁴ This study, however, was primarily a pediatric study and, in our opinion, not conclusive with regard to adult hydrocephalus. Arguments that these valves are unreliable, or malfunction more frequently than fixed valves do, are not supported by any clinical study (or our clinical experience with the implantation of more than 400 of these devices). There is a fear that in certain patients, particularly in patients with chronic headache or with particular psychosocial issues, the clinician will be plagued with continued requests for valve adjustments. In our experience, this has not materialized to any significant degree. Perhaps the biggest drawback is cost. Currently, adjustable valves are two to three times more costly compared with fixed-pressure valves, and there is no clinical study comparing cost-effectiveness. A direct comparison of cost utilization would have to factor in the morbidity associated with repeated operations and associated operative risks when fixed-pressure valves are used.

Another drawback of adjustable valves has been MRI compatibility. Because the rotors harbor permanent magnets, there is an inherent susceptibility to large magnetic fields, especially MRI scanners. To date, two manufacturers (Sophysa Polaris and Aesculap proGAV) have designed a locking mechanism that in theory prevents resetting of the valve when the patient is brought

in and out of the MRI scanner. The first-generation adjustable valves (Sophysa Sophy, Codman Hakim, and Medtronic Strata valves) are all susceptible to high magnetic fields, and therefore the valve setting must be verified after an MRI scan. In our practice, we specifically use valves with locking mechanisms in patients in whom it is anticipated that future MRI studies are required (such as any patient with a brain tumor).

Commercially available adjustable valves have different opening pressure ranges. Because of physical limitations and spring properties, the maximum and minimum valve opening pressures are constrained. The best example is the Sophysa Polaris valves, which come in the following ranges: 10-140, 30-200, 50-300, and 80-400 mm H₂O (SPVA-140, SPVA, SPVA-300, and SPVA-400, respectively). The Codman Hakim and Medtronic Strata valves are available in only one range of pressure settings. There are no evidence-based guidelines for selection of the most appropriate valve pressure range for any given patient. In our practice, we have some adult patients who require a pressure setting of 10 mm H₂O and others who do best at 400 mm H₂O. See our recommendations on valve pressure selection later.

Both the Aesculap proGAV and Codman Hakim adjustable valve have multiple, smaller discrete settings (from 0 to 200 mm H₂O or 30 to 200 mm H₂O, respectively). Both the Medtronic Strata and Sophysa Polaris valves have only five settings, thereby necessitating a larger jump between steps. We are not aware of any clinical study demonstrating an advantage of smaller steps, although changes as small as 10 mm H₂O can result in clinical responses.¹⁶ Our current management algorithm typically involves making valve adjustments of 30 mm H₂O; only in uncommon scenarios are smaller adjustments apparently beneficial.

Siphon-Control and Anti-Siphon Devices

We refer to these collectively as anti-siphon devices (ASDs), although there are mechanical and marketing differences between them. ASDs are add-on devices, meaning that they are used in conjunction with (immediately distal to) a differential pressure valve mechanism. These devices have been used clinically for more than 30 years.¹⁸

In general, the device is based on a membrane that is mechanically coupled to the subcutaneous tissue overlying it.¹⁸ The pressure differential between the internal valve lumen and the atmosphere, transmitted across the skin and ASD membrane, determines the flow-pressure characteristics of the ASD device. When the intraluminal pressure becomes significantly negative (relative to atmospheric pressure), the membrane is drawn inward—interacting with other fixed components of the ASD and thereby creating an increased pressure gradient. The original ASD was a separate component (Heyer-Schulte) that had to be inserted into the shunt. The Heyer-Schulte ASD fell into disfavor because of a variety of reasons, typically underdrainage, and has been largely supplanted by a more advanced design marketed by Medtronic.¹⁹ The Medtronic Delta chamber is found in the Delta valve (fixed-pressure apposing membrane differential pressure valve with integral Delta chamber) and Strata valve (adjustable ball-ring differential pressure valve with integral Delta chamber).

ASDs were developed on the basis of the premise that “siphoning” is the etiology of shunt-related CSF overdrainage. Shunt overdrainage has existed since the inception of the shunt.^{13,20-22} This phenomenon, better termed gravity-dependent drainage, occurs as the result of gravity-driven CSF flow down the distal catheter when the patient is in the upright position. Early studies²⁰ documented significantly negative intracranial pressures in shunted patients in the upright position. At the time, it was natural to assume that overdrainage complications (such as subdural hematomas) were due to this gravity-dependent drainage.

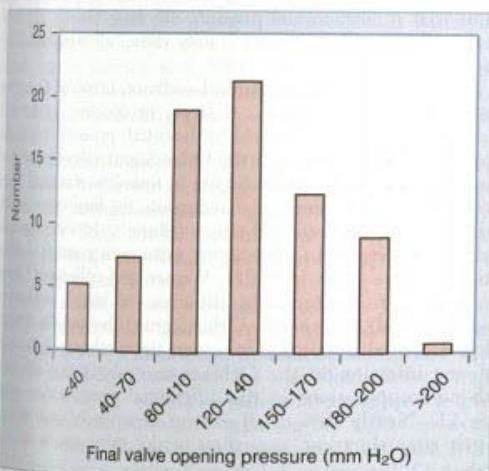


FIGURE 35-2 Range of valve opening pressures in the treatment of idiopathic NPH. Histogram of final differential valve opening pressure values shows a gaussian distribution centered at approximately 140 mm H₂O. The wide range of valve opening pressures required indicates that no single valve opening pressure is appropriate for the treatment of idiopathic NPH. (From Bergsneider M, Miller C, Vespa PM, Hu X. Surgical management of adult hydrocephalus. Neurosurgery [in press]. 2008;62:SHC643-660.)

Our intracranial pressure studies in idiopathic NPH patients,⁸ as well as those of others,¹⁵ suggest that gravity-dependent drainage is likely to play a lesser role in the etiology of overdrainage complications. As any person assumes an upright position, intracranial pressure decreases whether they have a shunt or not. As a matter of fact, in the standing position, most people have a slightly subatmospheric intracranial pressure. When you place a shunt with a differential pressure valve, the curve of intracranial pressure versus head-of-bed elevation in shunted patients nearly parallels that of the pre-shunt state (Fig. 35-3).⁸ In other words, a shunt with a differential pressure valve essentially lowers the intracranial pressure nearly equally across the head-of-bed angulation range. The degree of intracranial pressure reduction is largely a function of the valve opening pressure.

KEY POINT

In vivo intracranial pressure data suggest that the etiology of shunt "overdrainage" with differential pressure valves is in many cases, if not most, a result of too low of a valve opening pressure selection, rather than so-called siphoning.

There is little clinical evidence to support the contention that ASDs prevent overdrainage. A large, prospective, randomized study comparing a standard differential pressure valve, the Medtronic Delta valve, and the Orbis-Sigma valve found no statistical difference in the rate of ventricular reduction, the final ventricle size, or the incidence of clinical shunt failure.¹²³ A follow-up single-armed prospective study³ to the prospective, randomized trial comparing the Codman Hakim adjustable valve with a standard differential pressure valve⁴ similarly revealed that the programmable Strata valve also failed to show any benefit in pediatric patients.

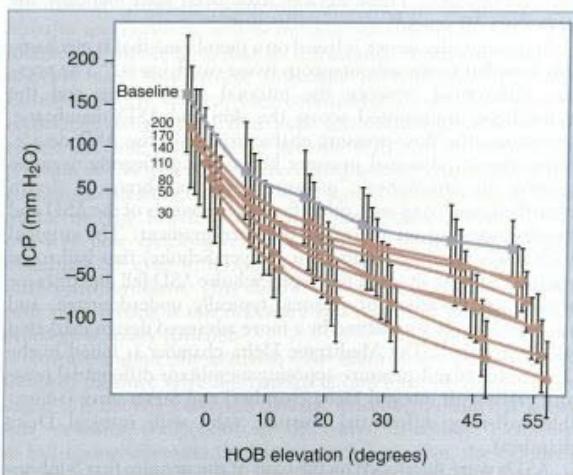


FIGURE 35-3 Intracranial pressure (ICP, mean \pm standard deviation) versus head-of-bed (HOB) elevation curves through the full range of differential pressure opening pressures (200, 170, 140, and so on) measured in idiopathic NPH patients treated with a ventriculoperitoneal shunt.⁸ The pre-shunt baseline curve (gray line, filled gray square) was obtained from the same group of patients. Note that the preoperative and postoperative curves roughly parallel one another, demonstrating the limited role of "siphoning" as the cause of overdrainage in idiopathic NPH patients.

For some hydrocephalus patients, the presence of an ASD is detrimental.²⁴⁻²⁶ This so-called low-pressure hydrocephalus syndrome, of which the incidence has not been quantified but is presumed to be less than 5%, occurs both in childhood and in adults. Given the low incidence of low-pressure hydrocephalus, we do not think that this "risk" constitutes a contraindication to the general use of products with ASDs. For clinicians who routinely use ASD devices, however, it is important that they become familiar with the signs and symptoms of low-pressure hydrocephalus.^{7,24} In our experience as well as that of others,¹⁶ the addition of an ASD can be effective in patients with clinically symptomatic overdrainage.

KEY POINT

A patient who fails to improve clinically (or deteriorates), a patient who remains with significant ventriculomegaly that did not change, a patient who has low measured intracranial pressure, or a patient with an ASD should not be written off as a nonresponder. The diagnosis of low-pressure hydrocephalus should be considered.²⁴

Flow Restriction Devices

Another approach taken to counteract shunt overdrainage is the incorporation of a CSF flow restriction mechanism. The premise is that shunt overdrainage occurs as a result of an excessive rate of CSF drainage. It follows that by limiting the maximum CSF flow rate, overdrainage should be averted.

There are several different design approaches to achieve flow restriction. The Integra Orbis-Sigma II valve was designed to directly address flow restriction by use of a multistage needle-valve design. Depending on the differential pressure, a needle is raised or lowered through a small orifice. The diameter of the needle at any given point will determine the cross-sectional area through which the CSF can flow. The manufacturer claims that in stage I, it functions as a low-pressure differential pressure valve to minimize underdrainage complications. When conditions "favor postural or vasogenic overdrainage," the needle moves to stage II, and the valve functions as a flow regulator to maintain flow within "physiological limits." Last, the manufacturer claims that if intracranial pressure elevates abruptly, the valve opens widely to function as a "safety valve," allowing rapid CSF flow.

There is scarce in vivo clinical evidence, however, to support these manufacturer claims. A large, prospective, randomized study comparing a standard differential pressure valve, the Medtronic Delta valve, and the Orbis-Sigma valve (the original design, predating the Orbis-Sigma II) found no statistical difference in the rate of ventricular reduction, the final ventricle size, or the incidence of clinical shunt failure.¹²³ In a retrospective study comparing the Orbis-Sigma valve with a standard differential pressure valve in NPH, Weiner and colleagues³¹ found no significant difference in the time to initial malfunction (shunt survival) between the Orbis-Sigma valve and the differential pressure valve shunts. There were three subdural hematomas and one infection in the Orbis-Sigma valve group compared with no complications in the differential pressure valve group ($P = .11$). Nearly 90% of all patients experienced improvement in gait after shunting, regardless of the valve system that was used.

Remarkably, there exist some in vivo data of measured CSF flow rate through shunts. Miyake and associates³² created an externalized loop connected to an indwelling ventriculoperitoneal shunt and measured CSF flow rates in patients with NPH. They assessed the Codman adjustable (differential pressure valve) and Orbis-Sigma valves. They demonstrated that shunt flow differed across patients, but in general, flow increased as the adjustable valve setting was lowered regardless of whether the patient was

recumbent or sitting. At higher opening pressures of the adjustable valve (140 to 200 mm H₂O) in the recumbent position, the flow was intermittent, whereas at the lowest setting of 30 mm H₂O, the flow rate was 100 to 200 µL/min. In the sitting position, the shunt flow rates were higher, ranging from 200 and 600 µL/min. For the Orbis-Sigma valve, the flow rates were very similar to the adjustable valve set at 200 mm H₂O in both the recumbent and sitting positions. This actual *in vivo* flow data would appear to contradict the Orbis-Sigma manufacturer's concept that in stage I, it functions as a low-pressure differential pressure valve. There are no in vivo data available either to confirm or to refute the manufacturer's claims regarding stage II and stage III activity.

The Orbis-Sigma II valve was studied in a single-armed, prospective, multicenter clinical study that included 270 adult hydrocephalic patients.¹² Shunt obstruction occurred in 14% of patients. The probability of having experienced a shunt failure-free interval was 71% at 1 year and 67% at 2 years; no difference was observed in shunt survival in pediatric versus adult groups. According to the authors, "overdrainage" occurred in only 2% of patients, although their definition of overdrainage was very narrowly defined. Clinical underdrainage was not assessed.

Another approach to flow restriction is the incorporation of a high-resistance element. The Codman Siphonguard is a coiled helical device that is placed immediately distal to a differential pressure valve (adjustable or fixed pressure). Unlike some ASDs, the Siphonguard device is unaffected by scar tissue encapsulation or external pressure. According to the manufacturer, the mechanical design "detects the difference between the normal and excessive flow and closes the primary pathway only when excessive flow occurs. The secondary pathway is always open and allows for the slow release of CSF when the primary pathway is closed." To our knowledge, to date, there are no published clinical studies evaluating the Siphonguard device. In vitro bench-top testing from an independent laboratory¹³ demonstrates that switching between the primary and secondary pathways was initiated at a fluid flow rate between 700 and 1800 µL/min. On the basis of the data of Mykle and associates,¹⁷ presented earlier, in which measured flow did not exceed 600 µL/min, it is unclear whether the flow-restricting circuit would be activated at all in NPH. Similar flow data do not exist for younger hydrocephalus patients to our knowledge, although presumably the flow rates may be higher than in patients with NPH. Unlike gravity-dependent valves, both the Orbis-Sigma and Siphonguard designs potentially mitigate overdrainage that may occur in the recumbent position.

In our anecdotal experience, we have found that the Siphonguard appears to alleviate or to prevent the transient headaches our shunted patients complain of after sneezing, coughing, or leaning over. These headaches, which are common in shunted patients, are rarely problematic and therefore typically do not require surgical intervention.

Medtronic manufactures a peritoneal catheter with a smaller internal diameter, which also achieves a fixed added flow resistance. This catheter is intended to be used in conjunction with a valve. To date, there have been no published clinical studies addressing the clinical efficacy or pitfalls of this approach. Interestingly, Sotelo and coworkers¹⁴ reported the use of a valveless shunt that instead incorporated a peritoneal catheter with a highly precise cross-sectional internal diameter of 0.51 mm. At the end of the observation period of 44 ± 17 months, the failure rate of the shunting device was 14% for the high-resistance valveless shunt compared with 46% for controls ($P < .0002$). Shunt incidence was 88% for patients with the valveless shunt and 60% for patients with conventional valve shunts. Signs of overdrainage developed in 40% of patients treated with valved shunts but apparently were not observed in patients with the high-resistance valveless shunt.

Gravitational Devices

As discussed earlier, gravity-induced CSF flow (commonly referred to as siphoning) is considered by many to be the primary cause of overdrainage. To offset the negative pressures generated by the long hydrostatic column, the gravitational (also termed hydrostatic) device interposes a very high differential pressure valve while the patient is in the upright position. This is accomplished by a mechanical mechanism that diverts the CSF into one of two parallel differential pressure valves. When the patient is in the recumbent position, a low (lower) opening pressure is operational. CSF is diverted to the high-pressure valve in the upright position.

This approach is not new (the Integra horizontal-vertical valve has been marketed for more than two decades), but recent improved designs have offered a graded transition (Aesculap proGav and shunt-assist valves) as well as a wider selection of the low- and high-pressure (fixed) valve settings. If used alone without a series adjustable differential pressure valve, gravitational devices do not prevent overdrainage or underdrainage clinical conditions.¹⁵ It was subsequently recommended that these gravitational devices be used in series distal to an adjustable differential pressure valve, although this too has been beset with technical problems.¹⁶ Our preliminary experience with the add-on Aesculap shunt-assist valve is that like the Delta ASD device, it is effective in alleviating overdrainage headaches.

Other Valve Characteristics

There are other practical considerations to valve selection. One is the physical profile of the valve—particularly with adjustable valves. A high-profile (prominent) valve housing can have significantly negative cosmetic consequences, especially in alopecia patients. Moreover, prominent housings are more likely to cause overlying skin breakdown in susceptible patients (chronic steroid use, elderly patients, incisions overlying the valve). Another consideration is length of the valve assembly. For occipitally placed ventricular catheters, multiple series devices (such as adjustable valve plus gravitational device) may result in the latter situated in the neck region rather than overlying the skull.

Most valve assemblies have an integrated reservoir (also known as a tapping chamber), although some require a separate component to be added on proximally. It is our opinion that every shunt system should have a tapping chamber for access to CSF (for either CSF sampling or shunt patency assessment).

SHUNT OVERDRAINAGE AND UNDERDRAINAGE DEFINED

Overdrainage

This term means different things to different people. In our view, it is a condition that is (1) caused by excessive CSF drainage or intracranial hypotension and (2) of clinical significance. Overdrainage typically is manifested as either postural headaches (with or without nausea or other ill feelings) or imaging evidence of pathological subdural fluid collections.

Overdrainage symptoms are equivalent to a post-lumbar puncture or "spinal" headache. We know from the lumbar puncture literature that depending on needle size and design, the incidence of post-dural puncture headaches is 1% to 30%.¹⁷ Presumably, most subjects after lumbar puncture experience some period of intracranial hypotension, but only a minority are sensitive to the state. This means that the mere presence of negative intracranial pressure is not pathognomonic of overdrainage. In fact, our studies and those of others^{8,20} document that some degree of intracranial hypotension is the norm in shunted patients.

(data exist primarily for differential pressure valve shunts), but only a small percentage complain of postural headaches.

KEY POINT

In shunted patients undergoing continuous intracranial pressure monitoring, the finding of negative intracranial pressures in the upright position is not diagnostic of shunt overdrainage—there must be accompanying symptoms to establish this diagnosis.

The determination of postural headaches is straightforward in most cases. The patient will have clearly recognized that the headache or other symptoms occur within minutes of assuming an upright position and are alleviated immediately with recumbency. Intracranial pressure monitoring is not needed in such cases. Furthermore, postural headaches can occur in the setting of unchanged ventricle size, with a reduction in ventricle size, or with the presence of subdural fluid collections. Increasing the valve opening pressure (by at least 30 mm H₂O) usually alleviates postural headache symptoms within 1 hour of the intervention. The use of adjustable valves obviates the need for a shunt revision in most of these cases. In the situation in which the patient is already at the maximum valve opening pressure of an adjustable valve (or has a fixed pressure or other valve), a shunt revision is typically required either to add an ASD or gravitational device or, with the latter scenario, to change the valve to an adjustable valve with a higher range of pressures. If postural headaches are mild, conservative measures such as hydration can often bide the patient over until the body re-equilibrates and the symptoms abate spontaneously.

Less commonly, headache may not be the main symptom of shunt overdrainage. Some patients complain of only nausea, whereas others have difficulty concentrating. For patients who have new-onset headaches not present before the shunt operation, there should be a clinical suspicion of overdrainage even if there is no clear postural relationship.

In general, overdrainage headaches do not occur in a delayed manner. In other words, a patient who has been doing fine for months will not spontaneously present with overdrainage symptoms. Exceptions to this rule might include new subdural fluid collection and inadvertent shunt adjustment (such as with an MRI).

The development of subdural fluid collections is a second possible manifestation of shunt overdrainage. Subdural hygroma (also known as effusion) formation is relatively common in the shunted NPH population. Small subdural hygromas (<5 mm) are usually asymptomatic¹⁷ and are often associated with improvement in NPH symptoms because they occur only in conjunction with reduction of the ventricular system. As a result, the presence of a subdural hygroma is not by itself diagnostic of shunt overdrainage. Expanding or large subdural hygromas are more worrisome and, many would agree, are risk factors for the development of acute hemorrhage (subdural hematoma). A non-trauma-related subdural hematoma in a shunted patient is obviously an overdrainage presentation.

It is our observation that shunted patients undergoing a contrast-enhanced MRI study sometimes show diffuse pachymeningeal enhancement—the same finding that is used to diagnose spontaneous intracranial hypotension. Given that most shunts generate some degree of intracranial hypotension, this enhancement pattern is not necessarily indicative of clinical overdrainage. If postural symptoms are present, however, the finding may support an overdrainage diagnosis.

"Slit" or collapsed ventricles are typically a manifestation of chronic overdrainage. Clearly, not all patients with slit (or unilateral slit) ventricles are symptomatic, but it is generally agreed that this state increases the risk of ventricular shunt obstruction. The apposition of the ventricular catheter to the ventricular wall

increases the chance of ingrowth of ependymal cells or choroid plexus. The adult slit ventricle syndrome is an ill-defined disorder, but the key components are "slit" or "collapsed" ventricles seen on computed tomography or MRI in a symptomatic, shunted patient. The incidence is unknown but represents about 5% of the non-NPH evaluations in our clinic.⁷ Although relatively few in number, these patients represent a disproportionate amount of clinical effort expended with frequent emergency department visits and requests for office visits. The syndrome occurs more commonly in patients who have been shunted for many years, either as an adult or in childhood. In addition, it is our observation that a significant proportion of patients with adult slit ventricle syndrome have previously unrecognized noncommunicating hydrocephalus.

Common symptoms of adult slit ventricle syndrome include intermittent headaches that become more frequent and intense over time. The etiology of these intermittent headaches has been unclear but may be related to periods of insufficient CSF drainage. In addition, collapse of the ventricular system lowers intracranial compliance, further amplifying elevations in intracranial pressure during shunt underdrainage. At shunt revision, the typical intraoperative finding is nearly total but not complete obstruction of the ventricular catheter (typically only one or two holes are patent). Left untreated, the symptoms may progress to more continuous headaches, presumably due to completed mechanical obstruction of the shunt system. Therefore, the slit ventricle syndrome is actually an underdrainage syndrome created by a preceding period of overdrainage.

Underdrainage

In many cases, shunt underdrainage is easy to recognize. This includes patients who were obviously symptomatic from hydrocephalus and then fail to improve after shunt surgery or see a return of their symptoms with clinical deterioration. Similarly, interval enlargement of the ventricles is diagnostic of underdrainage.

It is the patient in whom the association between clinical findings and ventriculomegaly is uncertain and fails to improve after shunt surgery (or only minimally improves) who represents a clinical challenge. This is especially problematic in NPH patients because there always exists some doubt in the diagnosis. As a result, the failure to improve might be attributed to an incorrect diagnosis (an underrecognized weakness of many NPH clinical studies).

For example, what if there is no clinical improvement in a patient with suspected NPH despite the valve's being brought down to its lowest setting? After confirming shunt patency, many might consider such a patient a "nonresponder" and therefore by inference misdiagnosed. For patients in this scenario who remain with significant ventriculomegaly, the low-pressure hydrocephalus state should be considered.^{25,29} For these patients, clinical improvement strongly coincides with reduction in the ventricular size, and only with significant negative intracranial pressure does reduction in the ventricular size occur. Not surprisingly, this state occurs with higher incidence in patients with ASDs.^{24,29}

In NPH, if imaging reveals a reduction in ventricular size, a patient should be considered a nonresponder if no clinical improvement occurred. Downward adjustments in valve opening pressure are unlikely to benefit the patient and instead increase the risk of subdural hematoma.

If underdrainage is suspected, shunt obstruction is always a consideration. Based largely on the experience with pediatric hydrocephalus, many neurosurgeons use nuclear medicine isotope studies to determine shunt patency.³⁸⁻⁴¹ At our center, however, we have found fewer indications for this study, and it is now rarely ordered. The primary reason is that the results of the study seldom alter the clinical decision tree. As noted before,

many cases of shunt malfunction are readily identified on the basis of the history or imaging findings, and a "confirmatory" patency study is not needed and perhaps is relatively contraindicated. In more clinically challenging cases, the question of shunt patency arises in association with the possible nonresponder. If the patient remains with unchanged (large) ventricle size and has not improved clinically (with a reasonable suspicion of clinical hydrocephalus), the results of a nuclear medicine study will unlikely alter the management plan. If no flow is found (which could be a false-positive finding because CSF drainage may occur only if the patient is allowed to assume the upright position for some time), the patient needs a shunt revision. Even if shunt flow is documented, one should pursue other interventions. For example, if there is an ASD, remove it. If the patient has a fixed-pressure valve or a flow-restricting valve, change it to an adjustable differential pressure valve (no ASD). It is our observation that ventriculoatrial shunts provide more drainage than ventriculoperitoneal shunts do, and therefore we offer a shunt revision to a ventriculoatrial shunt as well. It is only the case in which the patient has a ventriculoatrial shunt with a differential pressure valve set to 30 mm H₂O or less that an operative intervention is recommended. Therefore, the results of a nuclear medicine study (positive or negative) likely would not obviate a shunt revision for these selected patients.

KEY POINT

In NPH, documentation of shunt patency with a nuclear medicine study is not diagnostic of a shunt nonresponder. Functional underdrainage must be considered.

VALVE SELECTION

There are no evidenced-based guidelines to support any recommendations. If the prospective pediatric hydrocephalus valve studies^{13,42,43} are extrapolated to the adult population, no one valve design would appear to hold an advantage. Most would agree that NPH is clearly a distinct entity from pediatric hydrocephalus forms, and therefore the relevance of these studies can be challenged. On the basis of peer-reviewed published clinical studies and our large experience, we see no reasonable justification for not using an adjustable valve for NPH. Although adjustable valves are not the panacea, the use of a nonadjustable valve for the treatment of NPH exposes the patient to an unacceptable underdrainage or overdrainage risk.

In our view, the more difficult question pertains to the younger adult age group (18 to 65 years). Our routine practice includes the use of an adjustable valve for all adult patients, although admittedly, there are fewer published data to support this practice. What is not known is whether the added cost can be justified relative to the selective benefit in this cohort. Because we have no way of differentiating which patients might or might not benefit from the use of an adjustable valve, we do not think that the cost of the device should dictate the decision because an adjustable valve will be equivalent to or better than a standard fixed differential pressure valve for any given adult patient.

The next concern is whether an adjustable valve should be used alone or in conjunction with another device. There is no evidence demonstrating that valve designs incorporating an ASD, a flow-restricting device, or a gravitational device lower the incidence of overdrainage complications. In our opinion, what is important is that the clinician understand the potential pitfalls and risks of each valve type (including the stand-alone differential pressure valve) and be able to recognize possible shunt overdrainage or underdrainage states.

The second decision in valve selection is choosing the initial opening pressure. Our experience during the past decade is largely limited to the use of an adjustable, stand-alone differential

pressure valve. For NPH, it is our experience that approximately 96% of patients are aptly treated with a valve pressure range between 30 and 200 mm H₂O. About 2% will have clinical overdrainage despite a valve pressure setting of 200 mm H₂O, and the other 2% will have underdrainage at a setting of 30 mm H₂O. An adjustable valve with a range from 10 to 240 mm H₂O would meet the needs of more than 99% of NPH patients on the basis of our experience. In our practice,^{7,24} the valve pressure for all NPH patients is initially set at 200 mm H₂O, and the opening pressure is then sequentially lowered to effect.

We recommend that younger, non-NPH patients receive even higher opening pressure settings (upper opening pressures of 300 or 400 mm H₂O) or, alternatively, that an ASD, flow-limiting device, or gravitational device be incorporated in series with the "standard" adjustable valve (30 to 200 mm H₂O).

SHUNT CONFIGURATION

Cerebrospinal Fluid Access

For routine shunt placement, we prefer a frontal (precoronal) ventricular puncture shunt rather than a posterior or occipital shunt. A retrospective analysis of shunt operations from the U.K. Registry study demonstrated that frontal catheters were adequately placed in 67% of cases, whereas occipital catheters were adequate in 52%.⁴³ Moreover, we typically use frameless stereotaxis for the shunt ventricular catheter placement in patients with a bifrontal distance (maximum distance of lateral frontal horns) of less than 40 mm to increase the chances of optimal catheter placement. The tip of the catheter should reside just anterior to the ipsilateral foramen of Monro to keep it away from the choroid plexus. If the ventricles are large, the catheter is first positioned orthogonal to the skull, then angled slightly about 5 degrees anteriorly before the freehand insertion. The ideal depth is typically 6 cm of catheter at the dura.

As a general rule, every shunt incision should be carefully planned so that it does not directly overlie a shunt component. Failure to do so increases the risk of skin breakdown. We routinely place a modified titanium bur hole cover (one sector removed) over the frontal bur hole site after the catheter is situated. This prevents dimpling of the skin into the bur hole, which can result in poor cosmesis and sometimes discomfort.

Some neurosurgeons routinely use ventricular endoscopy to assist ventricular shunt placement. A multicenter trial demonstrated no benefit from this strategy.⁴⁴ In our opinion, endoscopy is not a substitute for stereotaxis. A poor initial trajectory may not be remediable by attempted endoscopic catheter placement.

Distal Site

During the past decade, our center has performed a similar number of ventriculoperitoneal and ventriculoatrial shunts. We have found a nearly identical complication rate between the two techniques.⁷ We use a pragmatic decision-making process. If the patient is not obese and has no history (or probability) of peritoneal adhesions, a ventriculoperitoneal shunt is offered. Otherwise, a ventriculoatrial shunt is recommended. There is a growing literature on laparoscopy-assisted peritoneal catheter placement for obese patients and patients with peritoneal adhesions.⁴⁵⁻⁴⁹ For the very cases in which laparoscopy is indicated, a ventriculoatrial shunt can usually be performed instead. As a result, we have used laparoscopic assistance in only two cases during a 14-year period.

Ventriculoatrial Shunt Technique

We routinely use a modified percutaneous technique.⁵⁰⁻⁵² With use of a sterile intraoperative ultrasound unit⁵³ to visualize the

needle cannulation of the internal jugular vein (Fig. 35-4), only a 5-mm incision is needed. We use an 8 French peel-away vascular access kit and fluoroscopic visualization to place the tip of the catheter at the distal superior vena cava (we still use the term *ventriculoatrial shunt* for simplicity). We avoid placement of the catheter in the atrium to minimize the risk of sinus arrhythmias.

There continues to be reluctance for ventriculoatrial shunt placement. The perception that the infection rate is higher with ventriculoatrial shunts in comparison to ventriculoperitoneal shunts is not supported by the literature.^{7,54} One concern is shunt nephritis, an immune complex-mediated glomerulonephritis that results from long-term, subacute bacteremia (typically an indolent species, such as *Staphylococcus epidermidis*).⁵⁵ During the last 15 years, with placement of more than 250 ventriculoatrial shunts, we have seen one case of documented shunt nephritis. This condition is not unique to ventriculoatrial shunts, having been reported in ventriculoperitoneal shunts as well.^{56,57} Patients present with fever of unknown origin and microscopic hematuria. It underscores the importance of a shunt tap in shunted patients in whom another obvious source of infection cannot be identified. Shunt cultures should be kept in the incubator for at least 5 days to identify indolent bacterial forms.

The percutaneous ventriculoatrial shunt approach is performed in a specific order. Once the components are tunneled and situated, the patient is placed in Trendelenburg position for the ultrasound-guided placement of the distal ("atrial") catheter. Once this has been accomplished and the table returned to the neutral position, the dura is incised and the ventricular catheter is inserted. This order eliminates CSF loss while the patient is in the Trendelenburg position. The final assembly of the ventriculoatrial shunt is at the retroauricular incision site, where the distal valve is connected to the proximal portion of the atrial catheter. This has to be done last because the atrial catheter has to be cut to the correct length based on the localization of the distal tip.

Ventriculoperitoneal Shunt Technique

For most cases, we mark an incision about 4 to 5 cm below the costal margin and centered at the lateral border of the rectus musculature (Video 35-1). Typically, the mini-laparotomy can be accomplished easily with a horizontal incision of 3 cm or less. The (appendectomy) retractor is used for exposure in the pre-

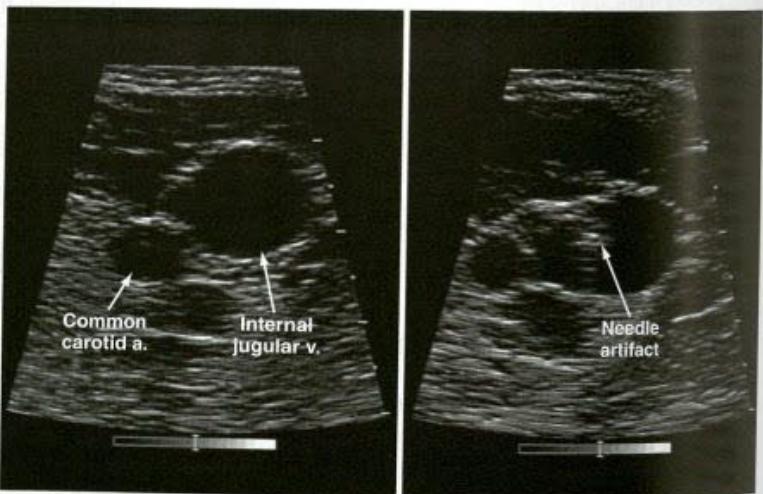
rectus fascia space only. After the superficial rectus fascia is opened transversely, the rectus muscle separated vertically in a muscle-sparing fashion, an open Cushing forceps is all that is needed to provide exposure of the deep rectus fascia. This fascia is picked up with two Crile hemostats, and a 3- to 4-mm incision is made with Metzenbaum scissors. Pulling up on these hemostats brings this deep fascial plane superficial to the rectus muscle, thereby allowing the approach by such a small skin incision. In about half the cases, the peritoneum is adherent to this fascial layer, and the peritoneal cavity will be encountered. In the other cases, the peritoneum can be picked up with two mosquito hemostats and incised with the Metzenbaum scissors; the peritoneum cavity can then be confirmed by gently probing with the Penfield 4 instrument. Closure is performed in layers, with a single 3-0 absorbable suture reapproximating the deep fascia (we do not use a purse-string suture) and interrupted 3-0 absorbable sutures in the superficial fascia and dermis layers. We do not use skin sutures, staples, or subcuticular sutures, but instead only use Steri-Strips and Mastisol for maximal cosmesis.

 Video 35-1 can be found on Expert Consult @ www.expertconsult.com

Challenges occur when a thick preperitoneal fat layer is encountered or if the omentum is large and it is difficult to confirm entrance into the peritoneal cavity. More troublesome is encountering peritoneal adhesions. If this occurs, a larger exposure may be required to be able to digitally explore the peritoneal space. As noted before, a ventriculoatrial shunt is a better choice in patients suspected of having peritoneal adhesions.

As noted before, our center has extremely limited experience with laparoscopy-assisted placement of peritoneal catheters. It is our experience that with the approach described, the incision is small and not a cosmetic issue. Therefore, the rationale of using laparoscopy for cosmetic purposes is difficult to justify in our opinion. One of the known complications of ventriculoperitoneal shunts is retraction of the peritoneal catheter into the subcutaneous pocket underlying the wound. In this case, a laparoscopic technique proposed by Nfonsam and coworkers⁵⁸ is appealing in that the shunt tunneler penetrates the peritoneum under laparoscopic visualization away from the open incision sites.

FIGURE 35-4 Image captures taken from an intraoperative 7.5-MHz portable ultrasound unit (Site-Rite, Bard Access Systems, Salt Lake City, Utah). Left, Normal tranverse plane anatomy, clearly demonstrating the common carotid artery and internal jugular vein. Right, Real-time ultrasonography allows visualization of the needle insertion into the vein (usually about 1.5 cm below skin surface), avoiding the artery and inadvertent puncture of the lung.



INFECTION AVOIDANCE

Nearly every prospective pediatric population shunt study has reported an infection rate of approximately 8%.^{1,3,4,44} Less information is available about infection rates for adults. There are clearly multiple contributing factors for shunt infections, but given the highest incidence within the first month of surgery, the "contamination" most likely occurs at the time of the shunt surgery. A study by Kulkarni and associates⁵⁹ suggested that many infections are iatrogenic, identifying surgical glove breaks as one of the likely and common culprits.⁶⁰

KEY POINT

Double gloving by all surgical staff and surgeons should be considered the standard of care for all shunt operations.

Meta-analyses support the routine use of perioperative intravenous antibiotics.^{61,62} We routinely use cephazolin (Ancef), although an argument could be made for an antibiotic with better central nervous system penetration.

We routinely remove the hair (with clippers) over the surgical area once the patient is under anesthesia. Our rationale is that there is greater assurance that the surgical preparation solution will cleanse and make contact with all surfaces exposed after trimming if the hair has been removed. Although thorough cleansing of the hair may be achievable in young children with fine hair, we do not believe that this is achievable in most adults with thicker hair. The same argument applies to "minimal" hair-clipping approaches. A stray hair strand (which may not have been prepared) that protrudes into the surgical field and touches the shunt will likely increase the risk of shunt infection. We routinely clip the hair enough to create at least a 1-cm margin around all wounds. Use of a razor to shave the scalp is not necessary and possibly contraindicated because it causes microabrasions that expose more skin flora.

For "healthy" patients undergoing a primary, uncomplicated shunt operation, we basically employ only these measures. For other patients, we use a tailored approach. Before every shunt operation, we investigate the risk factors for shunt infection. This includes any of the following: malnourishment, diabetes mellitus, open sores or wounds, hospitalization of more than 24 hours, shunt revision within 3 months, and immunosuppression (including steroids). If possible, a shunt operation should be postponed for patients with active infection, such as a urinary tract infection, until the infection is resolved. In many cases, it is prudent to elicit the aid of an infectious disease consultant.

Certain "high-risk" patients undergo more extensive preoperative skin preparation. These patients include intensive care unit patients with an external ventriculostomy, patients with a history of a shunt operation within 30 days, patients with a tracheostomy, and patients with a history of problematic skin infections. After clipping of the hair as described earlier, all adhesive residues along the track are removed with an adhesive remover agent. This is particularly important in neurosurgical intensive care unit patients who have had ventriculostomies, electroencephalographic leads, or recent craniotomies. These adhesive residues are not removed by the standard sterile preparation, and in our opinion, the space underlying them may be contaminated by virulent nosocomial organisms. Once the adhesive residue is removed, we gently cleanse the skin with a mild detergent before final surgical "sterile" preparation with Betadine or chlorhexidine.

Whether antibiotic-impregnated catheters reduce the incidence of shunt infections remains undetermined. A small prospective, randomized study assessing a catheter impregnated with clindamycin found a reduced infection rate, although the control arm had a high rate of 16%.⁶³ Arguments pertaining to creation of resistant organisms may have some merit, although

this has not been documented to date with the use of special catheters. An analysis by Eymann and colleagues⁶⁴ suggests that despite the incremental implant costs associated with the use of antibiotic-impregnated catheters, the overall reduction in infection-related costs made their use cost-beneficial. We routinely use antibiotic-impregnated catheters for all higher risk shunt operations (as defined earlier).

A third tier of antimicrobials is the instillation of intrathecal (intraventricular) antibiotics at the time of the shunt operation.⁶⁵ This better addresses the possibility of CSF "contamination" at the time of surgery. Many of the common skin bacteria associated with shunt infections, such as coagulase-negative staphylococci and *Propionibacterium acnes*, are highly sensitive to antibiotics; therefore, giving a high concentration of intraventricular antibiotics at the time of the presumed contamination sounds reasonable to us. During the last 2 years, we have routinely used intrathecal antibiotics for all higher risk shunt operations (as defined earlier). The antibiotic solution (tobramycin, 8 mg, and vancomycin, 10 mg, in 6 mL of saline) is prepared by the hospital pharmacy in a sterile hood.

A wound breakdown or CSF leak increases the risk of (or is a sign of) shunt infection.⁵⁹ The importance of planning the incision sites and configurations so as not to overlie any shunt hardware cannot be overemphasized. We do not use monopolar electrocautery (and avoid any coagulation) on skin incisions. Meticulous closure of the wounds is also important. For scalp wounds, following an interrupted layer of absorbable galeal sutures, we routinely close the skin with a 3-0 (or 4-0) running vertical mattress suture to best appose and align the skin edges.

Although it is usually straightforward, shunt placement carries one of the highest complication rates among neurosurgery operations. Attention to detail and careful planning and surgical technique can mitigate many risk factors.

KEY POINT

Patient morbidity related to a shunt infection (or a poorly placed shunt) is high; therefore, the operation deserves the same attention to detail as any major neurosurgery operation.

Shunt Allergies

True shunt allergies are rare. CSF often demonstrates persistent eosinophilia (3% to 36%), with negative cultures. Recurrent shunt failure is a common presentation. Pathologic examination of the ventricular catheter often demonstrates mechanical obstruction by inflammatory debris consisting of eosinophils and multinucleated giant cells. There are documented cases of immune responses to unpolymerized silicone in the literature.⁶⁶⁻⁶⁹ There are several management strategies. One is to consider an endoscopic third ventriculostomy and to remove the offending shunt. A second is to use a shunt system devoid of silicone, such as a polyurethane shunt system (Medtronic, Goleta, CA). We favor the use of hyperextruded silicone components (Medtronic). According to the manufacturer, many shunt allergies arise from a reaction to the oils used during the silicone manufacturing. A second extrusion cycle apparently effectively removes these oils that are otherwise present in trace amounts.

RECOMMENDATIONS FOR SPECIFIC CHALLENGING SCENARIOS

High Protein Concentration or Cell Count in the Cerebrospinal Fluid

High CSF protein concentration alone does not appear to increase the incidence of shunt obstruction.⁶⁹ It is the cell count

(which is often associated with a high protein concentration) that is more problematic. Ideally, the fewer the total cells (specifically white blood cells) the better. Issues such as pleocytosis chronicity must be considered; therefore, it is not possible to assign an arbitrary cutoff point for cell number. For example, in a patient with coccidioidomycosis meningitis, you may have to accept CSF cell counts in the hundreds.

Patient Undergoing Anticoagulation or Antiplatelet Therapy

We make every effort to normalize the clotting profile before shunt implantation. Aspirin is stopped at least 8 days before surgery, whereas clopidogrel (Plavix) is stopped 14 days before surgery. Warfarin (Coumadin) therapy is reversed and, if necessary, enoxaparin (Lovenox) is temporarily prescribed and then discontinued 24 hours before surgery. A normal partial thromboplastin time and international normalized ratio are documented before skin incision. After surgery, warfarin can be restarted as early as 3 to 5 days postoperatively.⁷⁰ It is critical to maintain a tightly controlled international normalized ratio. Aspirin or clopidogrel is restarted 7 to 10 days after surgery. In our opinion, combined aspirin-clopidogrel is contraindicated after shunt surgery because of the high risk of subdural hematoma.

The Hemicraniectomy Patient

Management of hydrocephalus in a patient with a hemicraniectomy is challenging. This hypercompliant state is prone to both shunt underdrainage and overdrainage situations in the same patient, depending on body position. If possible, it is advisable to perform the cranioplasty before the shunt placement or as soon

as possible if a shunt is already present. During this cranioplasty, we place multiple central dural tack-up sutures every 2 cm. Failure to do so greatly increases the risk of an epidural hematoma once the shunt is placed (or if it is already present).

Shunt Operations Associated with Other Procedures

For patients undergoing a lengthy craniotomy (such as for tumor resection), we avoid placing a shunt at the same operation. There is typically a higher CSF cell count at the time, and the longer operative time increases the risk of shunt infection.

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Full references can be found on Expert Consult @ www.expertconsult.com

Adult Hydrocephalus: The Role of Endoscopic Third Ventriculostomy

Jay Riva-Cambrin ■ James M. Drake

There is little doubt that the surgical world and its accompanying literature have seen an overwhelming trend toward the use of minimally invasive techniques; however, these depend on the parallel development of state-of-the-art technologies for the creation of new tools or improvement of existing tools. Unfortunately, many great surgical techniques have fallen to the wayside because they outran the necessary technologic advances needed to sustain them. There is not a better example in the surgical literature than third ventriculostomy. Endoscopic third ventriculostomy (ETV) emerged as a potential "cure" for hydrocephalus, but its initial use was fraught with complications because the breakthrough was not accompanied by the parallel development of microinstrumentation and high-resolution illumination and image projection.

The history of the neurosurgical use of third ventriculostomy is fascinating and filled with ebbs and flows of popularity. This history has been elegantly detailed by both Hellwig and colleagues¹ and Enchev and Oi.² It is not the intention of this chapter to reiterate these previous accounts; instead, we urge readers to refer to these references.

COMPARISON OF ADULT AND PEDIATRIC HYDROCEPHALUS

Epidemiology

A close examination of the current literature on pediatric and adult hydrocephalus highlights the paucity of scientific data, especially in the adult hydrocephalus arena. There are approximately 10 articles dealing with pediatric hydrocephalus for every publication on adult hydrocephalus. Therefore, much more is known about the incidence, prevalence, epidemiologic factors, patient hospitalization, health care costs, and mortality associated with the treatment of hydrocephalus in children. Simon and associates estimated that there are approximately 38,000 to 39,000 admissions for hydrocephalus each year in the United States, with approximately 400,000 hospital days and \$2 billion per year in charges for admissions alone for the care of pediatric hydrocephalus.³ The authors found that pediatric hydrocephalus accounts for more than three times the inpatient utilization but less than 4% of the National Institutes of Health (NIH) funding for a comparable chronic disease such as cystic fibrosis. Studies such as this help quantify potential impediments to the progress of pediatric hydrocephalus research in the hope of bringing this disparity to the attention of the NIH.

Tisell and coworkers conducted a cross-sectional study in Sweden to evaluate the incidence of adult hydrocephalus from 1996 through 1998.⁴ During that time, they found 891 new adult patients in whom hydrocephalus was diagnosed and treated. This represents an incidence of 3.6 per 100,000. They also found that the incidence was increasing over the 3 years of study. In a North American setting, Patwardhan and Nanda used the Nationwide Inpatient Sample database to determine that 8305 new cases of pediatric and adult hydrocephalus were treated in 2000 in the

United States.⁵ This study also estimated an inpatient mortality of 2.7% for hydrocephalus and an overall cost to the health care system of \$1.1 billion in 2000. Bondurant and Jimenez used a similar database to estimate the overall prevalence of hydrocephalus in the United States to be 125,000 in 1988, with 36,000 cerebrospinal fluid (CSF) shunt operations being performed each year.⁶ Neither of these studies, however, addressed adult hydrocephalus specifically because the pediatric cohort was intermingled with the adult cases.

One common theme between the pediatric and adult hydrocephalus populations is that they both include a heterogeneous group of hydrocephalus subtypes; however, the causes and incidences of these subtypes differ vastly between children and adults. Unpublished data from the Hydrocephalus Clinical Research Network, which is a five-center network dedicated to studying pediatric hydrocephalus, indicate that the five most common causes of pediatric hydrocephalus are intraventricular hemorrhage (IVH) resulting from premature birth (22%), myelomeningocele (14%), posterior fossa tumor (9%), aqueductal stenosis (8%), and congenital communicating hydrocephalus (8%). These prospective data represent only new diagnoses of hydrocephalus and will be published in detail in the near future. In contrast, Tisell and associates found that the most common causes of adult hydrocephalus were normal-pressure hydrocephalus (NPH) (47%), acquired communicating high-pressure hydrocephalus from bleeding such as after subarachnoid hemorrhage (15%), adult-onset aqueductal stenosis (10%), other noncommunicating hydrocephalus (e.g., tectal glioma) (9%), and acquired communicating hydrocephalus from trauma (5%).⁴ However, these incidences are not stagnant. Technologic advances to improve the care of pediatric patients with hydrocephalus have begun to translate into diminished mortality. Thus, many hydrocephalic children reach adulthood, which makes treatment of the adult cohort perhaps more complex.³

Use of Endoscopic Third Ventriculostomy

Another major difference between pediatric and adult hydrocephalus is that ETV is much more commonly used and therefore much more frequently described in the literature in the pediatric context. For instance, Drake reviewed the cases of 368 patients who had undergone ETV in Canada during a 15-year period.⁷ Analysis of this cohort demonstrated that younger age was associated with ETV failure whereas other factors, including etiology, surgeon experience, previous surgery, and center volume, were not. No similar studies have been conducted in the adult cohort, although there is a burgeoning literature on the role of ETV in patients with NPH. This specific issue is explored later in this chapter.

PATIENT SELECTION AND OUTCOMES

In general, the idea of third ventriculostomy for hydrocephalus is much more appealing to neurosurgeons than placement of CSF shunts for two main reasons: (1) it renders the patient "hardware

free," and (2) it is technically a more elegant challenge. Nevertheless, neurosurgeons have learned that ETV is far from a "silver bullet" for hydrocephalus.

The overall success rate of ETV lies somewhere between 50% and 90% at 1 year,⁷⁻¹⁰ primarily because hydrocephalus has such a heterogeneous compilation of causes, which vary with the age of the population being studied. For example, ETV in children with hydrocephalus secondary to tectal glioma has a success rate of 88%,⁹ but ETV performed in the context of IVH associated with prematurity succeeds just 0% to 33% of the time.^{11,12} Therefore, careful patient selection is absolutely essential in maximizing the chance of success and minimizing the complications inherent in ETV.

Young age (<6 months) has been shown to be associated with a lower success rate independent of etiology; however, this age effect either plateaus or diminishes after the patient reaches the age of 2 years, perhaps because of cranial maturation.^{7,13} The literature indicates that in patients older than 2 years, the success rate of ETV is high for noncommunicating hydrocephalus caused by such conditions as aqueductal stenosis, tectal glioma, and posterior fossa tumors.^{7,9} In contrast, there appears to be a lower success rate in patients with hydrocephalus caused by IVH associated with prematurity or in those with postinfectious hydrocephalus, thus leading to some controversy regarding its use in these populations.^{11,12,14} Who are the best candidates for ETV in the adult setting? What are the factors that matter in making the decisions?

Because the surgery is associated with a slightly higher complication rate and is longer and more involved than placement of a CSF shunt, patients must be relatively healthy. Primarily, they should be devoid of a coagulopathy. The patient must also be willing and able to return for follow-up care. It is folly to think that ETV is a "cure" because ETV can and will fail over time.¹⁵ It is significant to note that these failures can rarely result in sudden death.¹⁶

Patient selection for ETV is inescapably linked to outcome, and therefore one cannot be discussed without the other. The most important factor in selecting adult patients for ETV is the subtype of hydrocephalus itself. Treatment with ETV appears to offer the most benefit for late-onset idiopathic aqueductal stenosis (LIAS), secondary noncommunicating hydrocephalus, NPH, and conversion of a shunt in a patient who was treated for hydrocephalus as a child.¹⁷

Late-Onset Idiopathic Aqueductal Stenosis

LIAS, also known as *delayed* or *compensated* aqueductal stenosis, is a triventricular hydrocephalus with little or no flow through the aqueduct of Sylvius and a normal to small fourth ventricle. This form of hydrocephalus occurs in adult patients in the absence of space-occupying lesions or previous central nervous system insults (e.g., previous meningitis). LIAS is the cause of approximately 3% to 10% of all adult cases of hydrocephalus.^{18,19} In a meta-analysis of 190 patients, Tisell found that the clinical symptoms included headaches (70%), cognitive impairment (55%), urinary incontinence (40%), gait disturbance (28%), diplopia (15%), and endocrine dysfunction (12%).¹⁹ Fukuura and Luciano evaluated 31 patients and added papilledema, swallowing difficulty, Parinaud's syndrome, and seizures to this list.¹⁸ Interestingly, patients tended to dichotomize into either a younger cohort (mean age of 33 years) who had primarily headache and signs and symptoms of raised intracranial pressure or an older cohort (mean age of 63 years) with larger ventricles and NPH-like symptoms (cognitive impairment, urinary incontinence, and gait disturbance).¹⁸

Patients with LIAS respond to ETV if properly selected on the basis of signs and symptoms, radiologic findings of triventricular hydrocephalus, and minimal subarachnoid spaces. Success

typically results in complete or nearly complete resolution of preexisting signs and symptoms and no need for further CSF diversion procedures. The preponderance of the literature suggests that the success rate of ETV in these patients is 50% to 86.5%, with most authors reporting a success rate of approximately 80% with 6 to 22 months of follow-up.^{10,17,18}

Secondary Noncommunicating Hydrocephalus

Secondary noncommunicating adult-onset hydrocephalus is defined as obstructive hydrocephalus resulting from a lesion impeding the CSF pathway.¹⁷ The first choice for such lesions is removal or partial resection to reestablish CSF flow; however, in many cases this is not possible or warranted. In such cases, ETV may provide an alternative.

Pineal region tumors, tectal gliomas, and posterior fossa tumors are the most common types of mass lesions causing secondary noncommunicating hydrocephalus in adults. Rare entities such as thalamic masses, cerebellar infarction, and neurocysticercosis have also been described.^{20,21} Dusick and colleagues reviewed a series of 108 adult patients who underwent ETV for the treatment of hydrocephalus and found that a mass lesion was an indication for the procedure in 47 (43.5%).²² Their overall success rate for this indication was 76.6%, although the 8-month median follow-up was short. In their study, pineal region masses were the most prevalent indication for ETV, and the success rate in these cases was 71%. These results are compatible in both incidence and success rates with other similar studies.²³⁻²⁵ Even higher success rates of 81% to 88% are seen for ETV performed to treat patients with tectal gliomas, although 18% of these patients may require a second ETV for ostomy blockage.²⁶ Tectal gliomas are uncommon and, in general, are the indication for only about 4% of all ETVs—both pediatric and adult.²⁶ Arachnoid cysts, especially those found in the suprasellar, prepontine, third ventricle, or posterior fossa region, can often cause obstructive hydrocephalus. Dusick and associates found that ETV was successful in treating this cause of hydrocephalus in 86% of patients.²²

Frequently, ETV performed for tectal and pineal region masses is paired with endoscopic biopsy of the lesion through the third ventricle. Despite a high success rate of the ETV procedure itself, diagnostic rates for the masses are generally lower (69% to 90%). Complication rates associated with the biopsies are typically documented at approximately 18%.^{8,23} Common complications of these types of biopsies include intracerebellar and intraventricular hemorrhage, upgaze palsy, ventriculitis, and disturbances in sodium balance.²³

Normal-Pressure Hydrocephalus

NPH is a very controversial subject in the neurosurgical literature in both its diagnosis and its treatment. It is characterized by gradual blockage of the drainage of CSF, which causes a slow buildup of fluid and a less dramatic increase in fluid pressure. Patients with NPH are, in general, elderly patients with a triad of clinical signs and symptoms, including gait abnormalities such as a "magnetic" or "festinating" gait, bladder incontinence, and cognitive impairments or dementia. Findings on magnetic resonance imaging (MRI) include ventriculomegaly, focal enlargements of the subarachnoid space, and an open aqueduct.¹⁷ Most authors use an open aqueduct as a necessary criterion for the diagnosis of NPH. A normal-sized fourth ventricle is seen in 35% of patients with an open aqueduct, whereas it is slightly enlarged in 37% of patients and grossly enlarged in 27%.¹⁷

The diagnosis of NPH can be supported by formal neuropsychological testing, gait testing, clinical improvement after a lumbar CSF tap test¹⁸ or an external CSF lumbar drainage test,¹⁷ or a high-pressure steady-state plateau found on a lumbar infu-

test.²⁸ There is as yet no consensus on which of these tests either defines the diagnosis or predicts good outcomes after CSF diversion.

The use of ETV is relatively new and controversial for the management of NPH. Detractors of its use in this context note that CSF shunts have a high success rate in patients with NPH^{29,30} and ETV does not lower intracranial pressure enough to maximally improve clinical outcomes. Proponents emphasize that use of ETV will enable these patients to be free of hardware and point out that CSF shunts cause frequent complications in these patients, including infection, overdrainage symptoms, a need for revision, and subdural hematomas.²⁹

Reported success rates of ETV in patients with NPH have varied considerably from 21% in a study of 14 patients³⁰ to 87% in a study of 15 patients with 27 months of follow-up.²⁹ However, in a recent study by Gangemi and coworkers, 110 patients with NPH were treated by ETV at four centers and monitored for a minimum of 2 years; the success rate in these patients was 69%.²⁷ A successful procedure was defined as resulting in a significant improvement in clinical symptoms. Another 22% of these patients had no change clinically and 9% deteriorated. Potential predictors of success included a shorter duration of symptoms and milder symptomatology, but neither patient age nor size of the fourth ventricle predicted response.

Secondary Endoscopic Third Ventriculostomy for Revision of Pediatric-Onset Hydrocephalus

As noted earlier, the most common causes of pediatric hydrocephalus are IVH secondary to prematurity, myelomeningocele, posterior fossa tumors, aqueductal stenosis, and congenital communicating hydrocephalus (authors' unpublished data). Many patients with aqueductal stenosis, previous posterior fossa tumors, or IVH secondary to prematurity underwent placement of a shunt as children because their diagnosis preceded the recent emergence of ETV or because they required treatment before the age of 1 year, for which ETV has been demonstrated to have a poor success rate.⁷ If these patients are seen with a shunt malfunction as adults, ETV with shunt removal is a viable option in lieu of shunt revision. Most studies show a 70% success rate in these patients at a median follow-up of 36 months.^{15,35} It is important to consider that success rates will always vary with each study's selection criteria (the underlying cause for performance of ETV). This may explain why other studies show similar initial success rates that diminish rapidly to 25% at 2 years.³¹ Another consideration when assessing adult patients for possible ETV who have previously placed shunts is that a much higher complication rate (31%) has been demonstrated for ETV performed after shunt malfunction than for ETV performed as a primary procedure (8%).³²

Special consideration should be made for patients with myelomeningocele who have an implanted shunt. ETV is rarely used as a primary procedure for treating hydrocephalus in these children because it can be technically challenging and has poor rates of success (11% to 37%).^{11,33} However, when ETV is undertaken in the setting of shunt malfunction in older children or adults with myelomeningocele, the success rate increases to 63% to 93%.¹⁵ Therefore, ETV is a viable option in adult myelomeningocele patients with shunt failure even if they were not candidates for the procedure as children.

PREOPERATIVE IMAGING

Although many clinicians recommend ETV based solely on findings on computed tomography (CT) such as a small fourth ventricle, we recommend performing MRI preoperatively. The

MRI sequence of most value is a high-resolution sagittal T2-weighted image. This sequence allows visualization of the floor of the third ventricle so that thickness, bowing, and proximity to both the clivus and basilar arteries can be identified. T2-weighted imaging can help identify when membranes beneath the floor, such as the membrane of Liliquist, are thickened and require fenestration. The sagittal view also demonstrates whether there is obstruction or flow through the aqueduct. Other factors that should be examined include the relative size of the fourth ventricle, the presence of ventricular or compressive lesions, and the presence of blood products or other debris in the ventricular system.

Some authors also rely on the sagittal kinematic, or CINE, phase-contrast sequence to identify absence of flow through the cerebral aqueduct for selection of patients for ETV.³⁴ Although we are not fervently against this sequence, we do not place much emphasis on the kinematic sequence because we have found it to overestimate the level of CSF flow through the aqueduct. In these cases, ETV candidates who might otherwise have benefited from this procedure might not be offered the treatment.

RADIOLOGIC OUTCOMES

In general, the success of ETV is measured by resolution of the clinical signs and symptoms and absence of the need for a repeat procedure—either ETV or CSF shunting. The diminution in ventricular size after ETV is usually considered a much smaller factor for determining success, if it is used at all; however, there are growing concerns that persistently enlarged ventricles, even without signs of raised intracranial pressure, may have chronic cognitive consequences.^{35,36} In a study that included both children and adults who underwent ETV, Fukuhara and associates demonstrated that only 25% of patients' ventricles diminished in size the next day, with 52% being diminished at 6 months and 58% at 1 year.¹⁴ Other authors have found a significant correlation between diminution of ventricular size and clinical improvement.³⁷ Despite these improvements in ventriculomegaly, however, in most cases the ventricles remain larger than normalized correlates for age and sex, which is contrary to the findings from patients with shunts.³⁸

OPERATIVE TECHNIQUE FOR ENDOSCOPIC THIRD VENTRICULOSTOMY

Operating Suite

Ideally, the patient on the operating table should be in the center of the operating suite. The endoscopy tower should be placed at the patient's feet facing the patient's head and the surgeon. This is critical to ensure surgeon comfort and monitor visibility at all times while the surgeon is facing the operative field. We have found that placing the light source at 40% intensity seems to be ideal for optimizing anatomic visualization and minimizing glare off the ventricular walls. Determination of the proper focus aperture and white balancing should also occur at this time. Any equipment problems should be detected and corrected before induction of anesthesia or at least skin opening.

Irrigation is a very necessary and useful tool for neuroendoscopy that serves to clear the operative field, maintain ventricular volumes/working space, and stop low-pressure venous bleeding if necessary. Irrigation can be used in either a continuous or intermittent manner with the scrub nurse controlling the flow or delivering boluses through a 50-mL syringe. We recommend

continuous irrigation with 1-L bags of lactated Ringer's solution heated to 37.5°C and hung on an intravenous drip pole next to the monitor with tubing tracking along the patient's body. In this setup, the flow of irrigation can be controlled by either the scrub nurse with a stopcock or the circulator, who can also raise or lower the intravenous drip pole or place a pressure bag around the intravenous solution to increase flow. We use intraoperative ultrasound in every case. It is also positioned beside the endoscopy tower with the probe's wires tracking along the patient to the operative field.

The patient is placed in the supine position with the head on a horseshoe head frame. The head is slightly flexed in a sniffing position to maintain proper cerebral venous drainage and kept in a midline position to help the endoscope operator maintain orientation at all times.

Operative Techniques

A curvilinear incision is usually made around a point 2 to 3 cm off the midline to the right and 1 cm in front of the palpated coronal suture; however, if the right ventricle has distorted anatomy, a left-sided approach may be used. An extended bur hole is made to a diameter of approximately 2 cm to allow the use of an ultrasound probe, as well as to provide a large enough dural area to make a linear incision. Options for opening include a cruciate dural opening or a small (3 to 4 cm) craniotomy to allow definitive dural closure.

The cortical surface is coagulated, and a brain needle is placed in the right lateral ventricle under ultrasound guidance. The use of ultrasound for entry into the ventricle ensures a precise trajectory aimed at the foramen of Monro. A proper trajectory allows access to the third ventricle with minimal torsion on the cortical mantle and the thalamic and fornical aspects of the foramen of Monro. The brain needle is then removed and ultrasound guidance is used to place the endoscope sheath/trocarr down the tract. After the light source and irrigation are activated, the endoscope is then placed into the sheath.

Anatomic Considerations

A knowledge of ventricular anatomy is paramount and should be reviewed with the assistants before the operation. The venous anatomy of the lateral ventricle gives visual confirmation of which ventricle the endoscope has entered. The thalamostriate vein runs along the lateral wall and converges with the anterior septal vein before converging and entering the foramen of Monro as the internal cerebral vein. The choroid plexus together with the superior choroidal vein runs along the floor of the lateral ventricle (Fig. 36-1).

The foramen of Monro is entered while ensuring that traction is not placed along the margins. The anterior and medial circumference of the foramen of Monro is the fornix, and it should be carefully monitored for traction because this structure is particularly sensitive and short-term memory disturbance may be induced by traction. The posterior and lateral circumference represents the thalamus and choroid plexus, for which care must also be taken, although the thalamus is much more resistant to slight traction.

The floor of the third ventricle is generally thin and translucent in a hydrocephalic patient. After the third ventricle is entered, the paired mamillary bodies should be evident midway along the floor, with the basilar complex generally just anterior to them in the midline (Fig. 36-2). The infundibular recess is usually evident as a pinkish orange spot on the anterior midline floor. Slightly posterior to this recess is a white rectangular transverse band of the dorsum sellae. The ideal spot for fenestration is midway between the basilar complex and the dorsum sellae in the midline. The oculomotor and abducens (deeper) nerves can

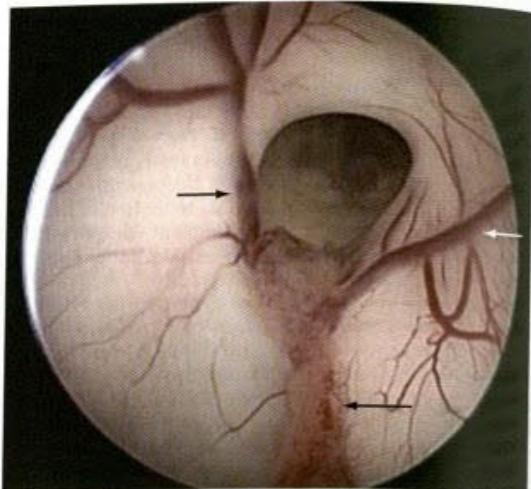


FIGURE 36-1 Endoscopic view into the right lateral ventricle. The thalamostriate vein (white arrow) runs along the lateral wall and converges with the anterior septal vein (short black arrow) before converging and entering the foramen of Monro as the internal cerebral vein. The superior choroidal vein (long black arrow) is also seen coursing through the choroid plexus. (Courtesy of T. T. Wong, M.D.)

at times be visualized laterally along the floor. Some patients have a thicker and somewhat opaque floor. In this scenario the infundibular recess, clivus, and basilar pulsations can usually be seen and the fenestrations then directed over the bony aspect of the clivus in the midline for maximal safety.

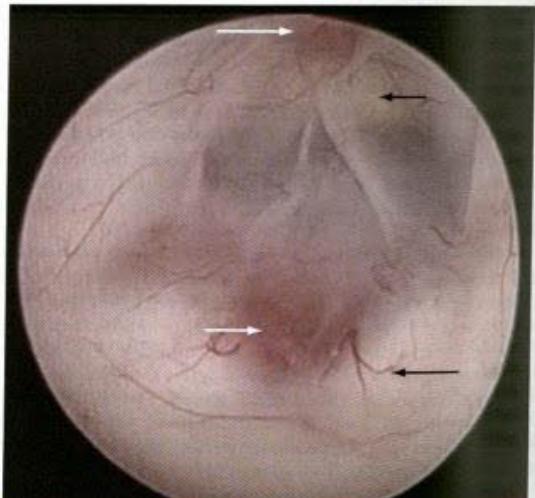


FIGURE 36-2 Endoscopic view of the floor of the third ventricle. The ideal spot for fenestration is in the midline, midway between the dorsum sellae (short black arrow) and the basilar artery (short white arrow). The paired mamillary bodies (long black arrow) and the infundibular recess (long white arrow) are also seen. (Courtesy of T. T. Wong, M.D.)

Third Ventriculostomy

The fenestration through the floor of the ventricle is made bluntly with a blunt trocar, closed forceps, or a laser wire. Sharp dissection and cautery are not recommended because both these techniques increase risk to the basilar artery complex, a disastrous scenario. Some authors maintain that fenestrations may create tension along the walls of the third ventricle and increase the risk for postoperative hypothalamic dysfunction,³² but we have not found this to be problematic. Others use a small Doppler probe to locate the basilar complex definitively before fenestration, especially in patients with opaque third ventricular floors.³³

The fenestration is then dilated to 4 to 6 mm in diameter by using a double-balloon catheter, Fogarty balloon, spreaders, or forceps. Next, the endoscope is perched atop the ostomy to inspect the subarachnoid spaces for membranes such as the membrane of Lillequist. These, too, must be carefully fenestrated or the operation will be at risk for failure. A rule of thumb is that if the endoscope can fit within the fenestration, it is large enough. After the fenestration, the floor of the third ventricle should pulsate and flap with the respiration and heart rates. These pulsations have been shown to be a strong predictor of ETV success.⁴⁰

Closure and Postoperative Issues

Once the procedure is completed, the endoscope should be withdrawn slowly to inspect for hemorrhage and contusions before final removal. Some authors use fibrin glue or Gelfoam sponge to occlude the tract through the cortex. This can potentially prevent subdural hygromas and leakage of CSF. We do not routinely occlude the tract but rather close the dura mater in a single dose watertight fashion.

The use of external ventricular drains postoperatively is a controversial topic. Many surgeons will use them to measure intracranial pressure postoperatively or as an emergency safety valve in the event of patient deterioration or ETV failure. However, detractors of the use of drains point out that the presence of an external drain can promote leakage and wound pseudomeningocele and, if open, may not permit the necessary pressure head to encourage flow through the ventriculostomy and thereby cause false-negative failures. Our goal is to limit the use of external drains except in select cases in which the patient is in a morbid state, is at a high risk for failure, or is at high risk for hemorrhage during and after the procedure.

Many centers encourage the use of subcutaneous bur hole reservoirs after ETV. These can be tapped in emergency or potentially infectious scenarios and can also be used postoperatively to measure intracranial pressure.^{39,41} However, ventricular reservoirs may encourage patency of the cortical tract and thus promote CSF leakage; their use may also disallow the possibility of rendering the patient hardware free.

As stated previously, ventriculomegaly in patients who have undergone ETV decreases at a much slower rate and to a much less extent than in patients with implanted shunts.³⁸ Therefore, we perform postoperative imaging (CT) at 6 to 8 weeks rather than on postoperative day 1 as is our practice in patients with shunts. Typical in-hospital stays for patients after ETV vary between 1 and 3 days, with most patients going home on postoperative day 2; this is longer than their counterparts with shunts.

COMPLICATIONS

Preoperative informed consent and postoperative patient monitoring require a detailed understanding of both the types and frequencies of complications associated with ETV. Despite allowing the patient to be hardware free and therefore invulnerable to shunt infection, ETV is certainly not without risk, espe-

cially in the short term. The risk for ETV failure was described earlier and ranges from 10% to 50% in most studies. This variation is a result of the wide range of causes of hydrocephalus. The overall complication rates for this procedure vary from 5.8% to 16% (Table 36-1). These rates vary primarily based on indications for or cause of the hydrocephalus, patient comorbidity, surgeon experience, and vigilance in reporting.

Major complications that should be disclosed to the patient before surgery include CSF leakage (1% to 6%), meningitis (1% to 5%), cranial neuropathies (1% to 2%), seizures (1%), and medical complications (2% to 9%). Overall hemorrhage rates vary from 1% to 3.6% and include intraventricular bleeding requiring either abandonment of the procedure or reoperation (hemorrhage blocking the ostomy), postoperative hematoma, or rare catastrophic basilar injury. Hypothalamic injuries are generally underreported, especially pathologic weight gain, and include diabetes insipidus, amenorrhea, and precocious puberty.⁴²

Hydrocephalic patients treated with ETV must be considered treated and not cured; therefore, they require follow-up just like their counterparts with shunts. This is especially important because rapid delayed deterioration has been reported in upward of 1 in 200 ETV patients.⁴³ Sixteen such cases have been reported, with a staggering mortality rate of 81%. All the survivors except 1 have been disabled as a result of the rapid deterioration.⁴²

REPEATED ENDOSCOPIC THIRD VENTRICULOSTOMY AFTER PRIMARY FAILURE

When hydrocephalic patients who have previously undergone ETV fail the treatment, they generally have the usual signs and symptoms of raised intracranial pressure and increased ventricular size on CT from their postoperative baseline. Persistent wound pseudomeningocele and delayed CSF leaks are also highly suspicious symptoms suggestive of ETV failure.

Such patients with ETV failure should undergo MRI with high-resolution T2-weighted sagittal sequencing. This sequence will allow the clinician to evaluate ventricle size, the presence or absence of an interruption in the floor of the third ventricle (ostomy), and whether a flow void exists through the opening. If the opening is present with or without a flow void, serial lumbar punctures to encourage flow through the ostomy can be considered.⁴³ If there is no resolution after two or three attempts, CSF shunting is mandated. In a patient in whom neither an opening nor a flow void is seen on MRI, re-exploration or repeated ETV is warranted. During re-exploration, if an opening is visualized and is of adequate size, conversion to a CSF shunt is suggested. In the event that the ostomy is occluded either by debris or by scar tissue, refenestration is warranted. Gangemi and coauthors reported that in 10 of 110 patients who worsened clinically after primary ETV, 4 were found to have occluded ostomies on MRI and agreed to undergo a repeat ETV procedure.²⁷ All 4 improved clinically.

CONCLUSION

ETV is a useful technique for treating adult hydrocephalus, with success rates varying from 50% to 90%. Patient selection is key to achieving clinical success. Causes of hydrocephalus most favorable for consideration of ETV in the adult population are LIAS, secondary (lesional) obstructive hydrocephalus, NPH, and secondary ETV revisions of patients with pediatric-onset hydrocephalus who have a shunt. Detailed knowledge of the intricacies of each of these causes and their success rates, awareness of the potential risks and complications, and expertise in normal and anomalous ventricular anatomy will allow successful performance of ETV.

TABLE 36-1 Reported Rates of Complications in Patients after Endoscopic Third Ventrilostomy

| PAPER | PATIENT POPULATION (AGE IN YEARS) | SAMPLE SIZE | CSF LEAK (%) | MENINGITIS (%) | HEMORRHAGE (%) | HYPOTHALAMIC INJURY (%) | CRANIAL NEUROPATHY (%) | SEIZURE (%) | RAPID DELAYED DETERIORATION OR DEATH (%) | WOUND INFECTION (%) | MEDICAL COMPLICATIONS (%) | OVERALL COMPLICATION RATE (%) |
|--------------------------------|--------------------------------------|-------------|--------------|----------------|----------------|-------------------------|------------------------|-------------|--|---------------------|---------------------------|-------------------------------|
| Drake ¹ | Pediatric (0-20) | 368 | 3.6 | 2.8 | 1.4 | 1.4 | 1.4 | 3.75 | 0.5 | — | — | 13.6 |
| Jenkinson et al. ¹⁵ | Adult (16-79) | 190 | 1.0 | 0 | 2 | — | 1 | — | 0 | — | — | 5.8 |
| Hader et al. ²⁷ | Pediatric and adult | 131 | 6.1 | 5.3 | 2.3 | 6.1 | 2.3 | — | — | — | — | 16* |
| Gangemi et al. ²⁷ | Adult NPH only | 110 | 1.8 | — | 3.6 | — | — | — | — | 1.5 | — | — |
| Dusick et al. ²² | Adult (17-88) | 108 | — | 1 | 1.9 | — | — | — | 0 | 1 | — | 6.4 |
| | | | | | | | | 1 | 1.9 | — | 8.3 | 14.8 |

*Eight percent for primary endoscopic third ventriculostomy and 31% for endoscopic third ventriculostomy in lieu of shunt revisions.

Zeros indicate that the authors clearly stated that they had no such complications; dashes indicate that such complications were not discussed or reported.

CSF, cerebrospinal fluid; NPH, normal-pressure hydrocephalus.

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