History of hydrocephalus and its treatments

JASON I. LIFSHUTZ, M.D. AND WALTER D. JOHNSON, M.D.

Division of Neurosurgery, Loma Linda University Medical Center, Loma Linda, California

Hydrocephalus has amazed and challenged clinicians throughout the history of medicine. In reviewing the treatment of hydrocephalus, the integral relationship between basic science and therapy is reaffirmed. As we embark into a new millennium, it is appropriate to reflect on the past studies of this disorder, review various attempted and currently used, and finally speculate on possible future directions in its treatment.

KEY WORDS • hydrocephalus • shunt • cerebrospinal fluid • neurosurgical history

Hydrocephalus has amazed and challenged clinicians throughout the history of medicine. To trace the history of the treatment of hydrocephalus, in many respects, is to document the parallel development of medicine as a whole; when one reviews the treatment of hydrocephalus, the integral relationship between basic science and therapy is reaffirmed. As we progress further in this new millennium, it is appropriate to reflect on the past understanding and treatment of this disorder, review strategies to curb this disease process, and consider therapies and possibly cures that will be available in the future.

Prior to the late 19th century, treatment for "water on the brain" involved more observation than intervention. Hippocrates[13] (5th century B.C.), the father of medicine, is thought to be the first physician to attempt and document the treatment of hydrocephalus.[8,9] In fact, he is often cited as the first to have performed ventricular punctures, although this point is debated, as it is possible he was merely draining the subdural or subarachnoid space. Further description and delineation of this condition can be found in the works of Galen (130–200 A.D.);[9,10] however, he believed this condition was caused by an extraaxial accumulation of CSF rather than enlargement of the ventricles. This belief led to many erroneous diagnoses and treatments. He recounted examples and described the thinness of the brain and skull associated with this condition. He found the ventricles to be in communication with each other and believed that the "soul" contained within these structures underwent a purification process with the waste being deposited in the pituitary gland.[9,10] The Greeks reportedly treated hydrocephalus by twisting bark around the patient's head and inserting it into trephined openings.[9] In the Middle Ages, the Arabic surgeon Abul-Qasim Al-Zahrawi, known in the western medical literature as Abulcasis, wrote a 30-volume treatise on medicine in which he touched on many aspects of neurosurgery, including the diagnosis and treatment of hydrocephalus.[1]

Vesalius (1514–1564)[46] at the University of Padua clarified many of the anatomical and pathological characteristics of hydrocephalus, noting that in one of his patients, "the water had not collected between the skull and its outer surrounding membrane, but within the ventricles of the brain." Vesalius, however, upheld the Galenic view that the CSF was a vaporous substance, the "spiritus animalis," produced in the ventricles that provided energy and motion to all parts of the body.[9,24,38,46] Further clinical descriptions of the disease in the 16th century can be found in the work of Thomas Phayer[31] in his *The Boke of Chyldren*, one of the first comprehensive texts on pediatric medicine.[9]

In 1664 Thomas Willis[51] was the first to suggest that the choroid plexuses produced CSF, contrary to the major paradigm at that time, which held that the ventricles contained a vapor during life and, after death, condensed and gravitated to the spaces in and around the brain and spinal cord.[16,24] In 1701 Pachioni described the arachnoid granulations, which he falsely believed were the source of CSF production.[38] In 1761 Morgagni[27] wrote in *Seats and*

Abbreviation used in this paper: CSF = cerebrospinal fluid.

Causes of Diseases that hydrocephalus could occur without accompanying head enlargement; however, he did not know the source of the excess fluid in this disease process. It is of note that he is one of the first investigators to link hydrocephalus with myelomeningoceles.[23,24] In 1774 Cotugno[5] proved that the cerebral ventricles were filled with fluid during life and that this fluid could be successfully sampled by percutaneous aspiration.[5,24] Monro illustrated the presence of the paired intraventricular foramen.

In *Observations on the Dropsy in the Brain*, written in the middle 18th century, Robert Whytt[50] first described hydrocephalus as a disease, illustrating several cases of internal hydrocephalus caused by tuberculous meningitis. He warned of the high morbidity and mortality associated with ventricular drainage.[20,23,24,50] West[49] (1808) and, subsequently, Cheyne (1848), differentiated between acute and chronic forms of hydrocephalus, as well as recognizing and documenting both acquired and congenital causes of the disease.[24]

Because of the poor understanding of the pathophysiology of hydrocephalus, initial theraputic attempts were sporadic and generally resulted in failure.[20] Attempted treatments included multiple medications and purgatives such as rhubarb, jalop, calomel, and oil, as well as various diuretics, injection of intraventricular iodine, head wrapping, blood letting, and skull trephination.[20] The use of carotid artery ligation was also reported. One can speculate that cures were rare and treatment fraught with complications.[20]

In the 19th century, the understanding of the anatomy and physiology of the ventricles and the CSF was advanced remarkably. In 1825 Magendie, in several important papers, illustrated the medial cerebellar foramen and eloquently described the circulation of CSF within the brain.[24] Cushing paid tribute to this notable work, naming it the "third circulation." Luschka, in 1859, confirmed the presence of the foramina of Magendie and described two additional lateral foramina. A milestone in the understanding of CSF circulation was the classic anatomical atlas of Key and Retzius[16] in which they described in detail the meninges, the subarachnoid spaces and cisterns, the ventricles, and the arachnoid villi, virtually the entire circulation of the CSF from production to absorption.[24]

In the early 20th century, Weed[48] described the embryology of the choroid plexus and confirmed the absorptive capacity of the arachnoid villi. Concurrent with the physiological advances made during this period, a new understanding of this enigmatic disease process was further elucidated in the classic work *Observations on the Pathology of Hydrocephalus*.[39] In this work, Russell[39] provided an encyclopedic collection of hydrocephalic specimens. These descriptions were to have great influence on the future therapeutic modalities for this disorder.[23]

As the 20th century progressed, more defined investigations into the physiology of CSF dynamics and hydrocephalus became possible. The introduction of radioactive tracers in the 1950s allowed for the detailed analysis of the circulatory dynamics of CSF. Papenheimer's perfusion method helped establish the rates of CSF production and absorption, while elucidating the extrachoroidal formation of CSF.[40] Brightman and Reese showed that communication between the extracellular fluid and CSF was relatively free;[37,40] Klatzo, et al.,[17] demonstrated that this movement was caused by bulk flow. In 1970, Milhorat, et al.,[22,26] illustrated the increase in periventricular permeability and the concept of transependymal absorption in experimental hydrocephalus.[40] This was later found to correlate with periventricular low densities observed on computerized tomography scans obtained in patients with untreated hydrocephalus.[40] A further milestone in understanding hydrocephalus came with the discovery that acute hydrocephalus could develop within hours in contrast to weeks or months, which was the prevailing paradigm. In a work on the experimental treatment of rhesus monkeys, Milhorat, et al.,[22] demonstrated that inflation of a fourth ventricle balloon could produce hydrocephalus in as early as 1 hour, and by 3 hours these changes were already advanced.[21,22,26] They furthermore correlated this with a clinical example of acute obstructive hydrocephalus in a child presenting with hemorrhage into a posterior fossa medulloblastoma.[21,22,26]

In parallel with the advances in the basic sciences understanding of hydrocephalus, newer therapeutic interventions were initiated. This new knowledge provided impetus for more rational and substantive treatments. Quincke,[35] in 1891, first described the lumbar puncture as an effective treatment for hydrocephalus.[20] Keen is credited with the first description of continuous ventricular drainage.[15,20] Miculicz first attempted drainage from the lateral ventricle to the subgaleal, subdural, and subarachnoid spaces with the use of gold tubes and cat-gut strands.[8,9,20]

Whereas it was surmised that surgical removal of an anatomical obstruction as a primary treatment for hydrocephalus would reestablish normal CSF flow dynamics, permanent CSF diversionary procedures and the means to reduce CSF production were also investigated. Anton and von Bramann[3] introduced the "Balkenstich Method" in 1908, a procedure in which the corpus callosum was perforated with resultant drainage of CSF into the subdural spaces.[20] The procedure fell into disfavor because of high surgery-related mortality and low cure rates. Parkin[29] and Glynn[11] explored the effects of lysis of posterior fossa adhesions and achieved mixed success.[20] Attempts to drain CSF via the orbital roof (ventriculoorbitotomy approach) and from the temporal horn into the cheek fat pad were also explored but without resolution of the hydrocephalic process.[20] In 1908 Payr[30] introduced drainage into the vascular system by using vein grafts from the ventricle directly into the sagittal sinus and jugular veins.[20] In this same year, Kausch used a rubber conduit to drain the lateral ventricle into the peritoneal cavity.[14,24] This concept, however, did not receive much initial enthusiasm. During this time, Heile[12] attempted to perform spinal CSF drainage into the peritoneum by sewing the serosa of the bowel to the dura mater, connecting the subarachnoid space to the peritoneum by use of a silk suture, and by using other conduits such as veins or latex rubber tubes. He also was the first credited with CSF diversion to the urinary system.

Under the pioneering efforts of Cushing and his followers, neurosurgery emerged as a distinctive specialty. Cushing established the Hunterian Laboratory of Experimental Medicine at The Johns Hopkins University and with as-

sociates S. J. Crowe, James Bordley, Jr., Emil Goetsch, Walter E. Dandy, and Lewis Weed, began investigating, among other topics, hydrocephalus.[25] Cushing devised a technique in which the lumbar subarachnoid space was connected to the peritoneal cavity or retroperitoneum by using silver cannulas passed through apertures through the L-4 vertebral body.[20] Cushing can also be credited with the innovative idea (for that time) that as the "third circulation;" the CSF had unique function greatly more complex than simply providing buoyancy for the brain. In 1914, Dandy and Blackfan[7] developed a technique of producing experimental obstructive hydrocephalus in dogs by placing cotton pledgets at the distal aqueduct of Sylvius, thereby causing proximal ventricular dilation.[42] Dandy[6] also reported that with unilateral choroid plexectomy and obstruction of the foramen of Monro, the plexectomized ventricle would collapse while the contralateral ventricle would dilate; he concluded that CSF was produced exclusively by the choroid plexus. This in turn led Dandy[6] to introduce, in 1918, bilateral choroid plexectomy as a means of reducing CSF production.[20,23] Although technically challenging, this procedure remained for many years the most commonly performed surgery for infantile hydrocephalus in the United States. Putnam[34] and Scarff[41] expanded on this technique by including endoscopic cauterization of the choroid plexus in the late 1930s and early 1940s. Upon review, however, in the majority of patients the ventricles demonstrated progressive enlargement at the same or greater rate than that observed preoperatively with disappointingly poor results; thus, by the 1950s, these techniques had largely been abandoned.

The placement of intracranial shunts was also investigated. Third ventriculostomy was introduced by Dandy[9,20,24] to bypass aqueductal stenosis, and this technique was later refined by Stookey and Scarff. [9,20,24,43] In their procedure the lamina terminalis was approached via a subfrontal or subtemporal route through the interpeduncular cistern into the floor of the third ventricle. Although the mortality rate was somewhat high, the reported arrest of hydrocephalus in surviving patients was approximately 70%. This technique was further refined with the use of endoscopes. Torkildsen[9,20,23,24,45] devised a procedure in which a shunt was placed from the lateral ventricle to the cisterna magna (ventriculocisternostomy); initially the success rate was high but so too was surgery-related morbidity, which was subsequently reduced. This procedure, however, has been largely replaced by more current CSF diversion techniques.

Efforts to divert CSF to remote body cavities were also advanced. Ureteral diversionary procedures—from the ventricles and lumbar subarachnoid spaces—were reported by Matson and his collegues at Boston Children's Hospital.[9,18,19] Although it was associated with a very low mortality rate, this procedure did require a nephrectomy and was complicated by both infection and electrolyte abnormalities, particularly troublesome in infants.[9] The concept of valves and flow regulation was reinforced by this procedure (although the idea had its roots in the work reported by Payr[30] in which he used venous valves); Matson believed that the success of the technique lay in the natural valve function provided by the ureter.[9] Other attempted spaces included the heart, jugular vein, thoracic duct, pleural space, gallbladder, fallopian tube, ileum, and salivary ducts.[20] Over time, the right atrial and peritoneal spaces became the locations of choice for shunts.

Attempts at medical cures or symptomatic arrests were made during this period. Reports of thyroid extract, vital dyes, and various diuretics found their way into the clinical practice in the early part of the 20th century but lost favor because it became more apparent that hydrocephalus was primarily a disease best treated with surgery although it was without definitive cure.[20]

The development that ushered in the modern era of hydrocephalus surgery was the introduction of valve-regulated shunts and biocompatible synthetic materials in 1952.

In 1952 Nulsen and Spitz, working in conjunction with John Holter,[9,20] the father of a child with hydrocephalus, reported the successful use of a ventriculojugular shunt regulated by a spring and ball valve. At approximately the same time Pudenz, et al.,[32,33] produced a one-way slit valve made of silicone.[9] The development of the valve system combined with the application of new bioavailable materials allowed for the safe and reliable diversion of CSF without many of the complications of unregulated CSF drainage.[9] Ames,[2] and Raimondi and Matsumoto[36] resurrected the concept of ventriculoperitoneal procedures in which these new devices were used. In the 30 years since this resurgence, great advances and modifications in hardware have been realized. There are now literally hundreds of options for valves, proximal and distal catheters, antisiphon devices to prevent overdrainage, and, more recently, programmable valves for fine-tuning CSF flow rates.

Concomitant with the advance in shunt-related materials, progress in imaging technology has further allowed clinicians to treat hydrocephalus with greater success and safety. In the 1980s and 1990s the use of an endoscope again found a role in neurosurgery, the benefits of which include more accurate placement of ventricular catheters and a resurgence of the third ventriculostomy for aqueductal stenosis.[47] Stereotactic localization[47] has led to more functional forms of therapy and safer approaches for the drainage of CSF.

Furthermore, with the advent of prenatal ultrasonography, diagnosis of hydrocephalus in utero has led to attempts with intrauterine fetal surgery. The rationale for this intervention is that early surgery can prevent progressive injury from ongoing pathophyisiology or from secondary damage in the intrauterine environment. While the concept of fetal surgery is not new (the first experimental models appeared in the mid-1920s), its inception into clinical practice began in the 1970s under the direction of Michael Harrison.[44] The current focus of surgery in fetal patients lies in the treatment of life-threatening congenital anomalies such as lung and airway lesions as well as in twin–twin transfusions.[44] In the realm of neurosurgery, attempts had been performed in the late 1970s and early 1980s to treat hydrocephalus diagnosed in utero. Procedures such as ventriculoamniotic shunts and serial cephalocenteses were attempted to curb the ventriculomegaly.[44] High morbidity and mortality rates, however, marked these early attempts at treatment, and outcomes were generally worse than in those in whom shunting procedures

were performed in the neonatal and infant periods. Currently, there is a defacto moratorium on fetal surgery to treat hydrocephalus, as the issues of patient selection and surgical procedure remain in question.[28,44]

Fetal therapy for spinal dysraphism–associated hydrocephalus has seen an emergence in recent years, spurred on by advances in neuroimaging, better understanding of the pathophysiological nature of the disease, and the refinements of surgical techniques including endoscopy. Bruner, et al.,[4] have reported the first cases of intrauterine closure of a myelomeningocele in 1997. The suspected benefits of this early intervention include decreased hindbrain herniation, improvement of lower extremity function, and the decreased need for shunts.[4,44] Although the initial results seem promising, long-term follow-up examination of these patients is necessary to prove the efficacy of the therapy.

Whereas great advancements and achievements have been made over the course of medical history, clinicians in the new millennium will be required to continue face the challenges of presented by hydrocephalus. It appears that treatment up to this point and time has focused on the arrest of the disease process, with further therapy focused on the complications of these treatment modalities. With current research in molecular biology, gene therapy, and neural regeneration, the concept of a functional cure may become an achievable goal. As in the past, the integration of the discoveries in basic science and clinical innovation will continue to lead the path as it has in the past.

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Address reprint requests to: Walter Johnson, M.D., Loma Linda University Medical Center, Division of Neurosurgery, 11234 Anderson Street, Room 2562 B, Loma Linda, California 92354. email: wjohnson@ahs.llumc.edu.