The problem isn’t with what we don’t know, the problem is with what we do know that isn’t so.

—WILL ROGERS

Hardly any other pathological condition has been accorded more determined attention on the part of the medical profession ... than has hydrocephalus. And in hardly a single other condition have cures been so elusive or so often wrecked on purely mechanical obstacles.

—LEO DAVIDOFF, 1929

Barely 25 years after Davidoff decried the lack of a cure for hydrocephalus, effective shunts came into existence. Since then, thousands of children and adults have received treatment for this disorder, often resulting in significant symptomatic recovery and improvement in development and functional ability. Nonetheless, Davidoff’s phrase “so often wrecked on purely mechanical obstacles” was prophetic. Fifty years later, the mechanical obstacle of shunt failure remains the rule, not the exception, in the management of hydrocephalus. More than 30% of new shunts fail within 1 year. Fewer than one third of new shunts survive 10 years without revision. In some large pediatric neurosurgery services, the ratio of shunt revisions to placement of new shunts is 2.5:1. Authors of a recent randomized controlled multicenter study have shown that a half century of research in shunt valve design has produced little if any improvement in the rate of shunt survival.

Perhaps the obstacles on which our cure for hydrocephalus has been wrecked are conceptual. Is there more to hydrocephalus than our long-held and oversimplified concept of it as a plumbing problem of mismatched CSF production and resorption treated by the insertion of shunts or the surgical diversion of CSF flow through ventriculostomies? Do we really understand how hydrocephalus and its treatment affect the brain? As neuroscientists, we must ask the following questions: what do we know about hydrocephalus, and how do we know it? And, perhaps more important, what don’t we know about hydrocephalus that we ought to know?

Working together with support from the Brain Child Foundation, an organization dedicated to conducting innovation in the field of neurosurgery and neurorehabilitation, we have identified critical gaps in our prevailing knowledge of hydrocephalus.

In an effort to identify critical gaps in the prevailing knowledge of hydrocephalus, the authors formulated 10 key questions. 1) How do we define hydrocephalus? 2) How is cerebrospinal fluid (CSF) absorbed normally and what are the causes of CSF malabsorption in hydrocephalus? 3) Why do the ventricles dilate in communicating hydrocephalus? 4) What happens to the structure and function of the brain when it is compressed and stretched by the expanding ventricles? 5) What is the role of cerebrovenous pressure in hydrocephalus? 6) What causes normal-pressure hydrocephalus? 7) What causes low-pressure hydrocephalus? 8) What is the pathophysiology of slit ventricle syndrome? 9) What is the pathophysiological basis for neurological impairment in hydrocephalus, and to what extent is it reversible? 10) How is the brain of a child with hydrocephalus different from that of a young or elderly adult? Rigorous answers to these questions should lead to more effective and reliable treatments for this disorder.

KEY WORDS • hydrocephalus • critical issues • normal-pressure hydrocephalus • treatment • pediatric neurosurgery

Abbreviations used in this paper: CSF = cerebrospinal fluid; ICP = intracranial pressure; NPH = normal-pressure hydrocephalus; SVS = slit ventricle syndrome.
Question 1: How Do We Define Hydrocephalus?

A rigorous definition of hydrocephalus is surprisingly difficult and is becoming more complicated. From a physiological perspective, the finding of enlarged ventricles combined with high ICP represents only one presentation along a spectrum of disorders ranging from pseudotumor cerebri to low-pressure hydrocephalus. From a clinical perspective, how should we classify patients with hydrocephalus, from truly asymptomatic to severely impaired individuals, and how do we measure recovery after treatment? From the anatomical perspective, given the success of endoscopic third ventriculostomy in patients with communicating hydrocephalus and shunt failure, does the concept of obstructive versus “communicating” hydrocephalus need to be reassessed?

Question 2: How Is CSF Absorbed Normally and What Are the Causes of CSF Malabsorption in Hydrocephalus?

Most surgeons do not question the dogma that hydrocephalus is caused by the mechanical obstruction of the absorption of CSF through the arachnoid villi, although there is considerable evidence that the arachnoid villi are not the principal sites of CSF absorption at normal CSF pressures.1,8,17 Do lymphatic or vascular pathways mediate CSF absorption? If CSF water can move freely, and bidirectionally across brain capillary membranes, is it time to reconsider the concept of CSF “absorption”?9,10 If we are to make progress, we must be willing to expand into an exciting, albeit more complex, scientific frontier of CSF physiology. The role and interactions of cerebrovenous pressure and blood volume in ICP pathophysiology and intractable shunt problems deserve further investigation.

Question 3: Why Do the Ventricles Dilate in Communicating Hydrocephalus?

The question asked by Dandy and Blackfan1 in 1914, and reiterated many times by others, has still not been answered: how can the ventricles dilate and the subarachnoid spaces be compressed when the subarachnoid and the ventricular CSF are in free communication? A static pressure gradient in communicating hydrocephalus would seem to violate the Pascal law. Fundamentally, do we understand the pathophysiology of communicating hydrocephalus as well as we think we do?

Question 4: What Happens to the Structure and Function of the Brain When It Is Compressed and Stretched by the Expanding Ventricles?

Why does the cortical mantle reexpand in most but not all patients when ventricular volume is reduced? Is brain reexpansion necessary for all patients to be successfully treated? And why do some patients with untreated hydrocephalus appear to have no neurological impairment? Although more details of the cellular pathology associated with hydrocephalus have been forthcoming,6,8 a true understanding of injury mechanisms, their multiple interactions, and the role of neural plasticity has escaped us. Thus, the reasons for reconstitution of the cortical mantle are still not clear. By gaining a complete understanding of the cellular basis for cortical reexpansion, we will no doubt discover many of the fundamental mechanisms that put the hydrocephalic brain at risk and provide the basis for recovery.

Question 5: What Is the Role of Cerebrovenous Pressure in Hydrocephalus?

Increased cerebrovenous pressure has been found in virtually all clinical and experimental studies of hydrocephalus, and cerebrovenous hypertension also plays a role in pseudotumor cerebri. Nevertheless, displacement of venous blood is the main source of rapid compliance in the craniospinal axis in response to expanding masses or hydrocephalus. The role and interactions of cerebrovenous pressure and blood volume in ICP pathophysiology and intractable shunt problems deserve further investigation.

Question 6: What Causes NPH?

It is not clear whether idiopathic NPH shares a common pathophysiology with secondary communicating hydrocephalus of known causes. Can the cause or causes of idiopathic NPH be discovered, and thus prevented? Are there critical relationships between NPH, degenerative dementias, and subcortical ischemic vascular disease, and how do they influence clinical presentation and outcomes? Understanding the cause of NPH may lead to preventive measures, risk factor-based screening, and better diagnostic tools and clinical outcomes.

Question 7: What Causes Low-Pressure Hydrocephalus?

Low-pressure hydrocephalus is an enigma. A clear view of this perplexing condition, in which patients with ventriculomegaly show symptoms of hydrocephalus and even signs of brain herniation despite zero or negative ICP, may provide a much deeper understanding of hydrocephalus.

Question 8: What Is the Pathophysiology of SVS?

Shunt overdrainage continues despite various valve designs specifically aimed to prevent it,11 and clinical experience suggests that the symptoms of SVS do not correlate with ICP.11 Furthermore, why does SVS appear to be associated only with shunts placed in infancy, whereas small ventricles can develop in adults with shunt-treated hydrocephalus who do not have symptoms of SVS?
What we don’t (but should) know about hydrocephalus

Question 9: What Is the Pathophysiological Basis for Neurological Impairment in Hydrocephalus, and to What Extent Is It Reversible?

Is it regional ischemia? Disruption of white matter pathways? Alteration of interstitial fluid volume or composition? What subcellular pathways are perturbed? What is the proportional role of neuronal and glial dysfunction? A more thorough understanding of injury mechanisms should lead to pharmacological treatments that can supplement CSF shunt placement.¹

Question 10: How Is the Brain of a Child With Hydrocephalus Different From That of a Young or Elderly Adult?

The clinical presentation of hydrocephalus differs with age.² Does this fact reflect different susceptibility and compensatory mechanisms that depend on the age and developmental or involutional status of the brain? Now that more and more children with hydrocephalus are becoming adults with hydrocephalus, their medical care requires a better understanding of the plasticity and age-related changes that accompany chronic hydrocephalus. The medical treatment also requires a change in the organization of healthcare services provided by neurosurgeons and neurologists so that the needs of adults with hydrocephalus can be met.

Conclusions

There are, of course, many other important questions, and this is not to say that we have not come a long way in research of hydrocephalus during the last 75 years. Nonetheless, our understanding of hydrocephalus is not nearly as sophisticated or complete as we might have imagined. Fifty years after the introduction of shunts for the treatment of this previously untreatable disorder, we must acknowledge that the shunt is not a cure for hydrocephalus; it is only a “patch,” and an unreliable one at that. We know a lot about hydrocephalus, but much of what is true about hydrocephalus is strange, and is not necessarily the same as what we think we know. There is surprisingly little scientific basis for many of our commonly held opinions.

Our intent is to instigate a new and vigorous dialogue among neurosurgeons, neurologists, neuroscientists, and research funding agencies that will promote needed advancements in the understanding of hydrocephalus. The recent symposium “Hydrocephalus: Myths, New Facts, Clear Directions,” sponsored by the National Institutes of Health (Bethesda, MD, September 29–October 1, 2005), underscores the need for this dialogue.

It is time to dispense with our presuppositions, to be clear about what we do and do not know, to ask the basic questions again, and to follow confidently where the answers lead us.

References


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