

A Contemporary Definition and Classification of Hydrocephalus

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This review focuses on the problems related to defining hydrocephalus and on the development of a consensus on the classification of this common problem. Such a consensus is needed so that diverse research efforts and plans of treatment can be understood in the same context. The literature was searched to determine the definition of hydrocephalus and to identify previously proposed classification schemes. The historic perspective, purpose, and result of these classifications are reviewed and analyzed. The concept of the hydrodynamics of cerebrospinal fluid (CSF) as a hydraulic circuit is presented to serve as a template for a contemporary classification scheme. Finally, a definition and classification that include all clinical causes and forms of hydrocephalus are suggested. The currently accepted classification of hydrocephalus into “communicating” and “noncommunicating” varieties is almost 90 years old and has not been modified despite major advances in neuroimaging, neurosciences, and treatment outcomes. Despite a thorough search of the literature using computerized search engines and bibliographies from review articles and book chapters, I identified only 6 previous attempts to define and classify different forms of hydrocephalus. This review proposes the following definition for hydrocephalus: hydrocephalus is an active distension of the ventricular system of the brain related to inadequate passage of CSF from its point of production within the ventricular system to its point of absorption into the systemic circulation. Based on this definition (potential points of flow restriction) and on the view of the CSF system as a hydraulic circuit, a classification system is proposed. The acceptance of this proposed definition and classification schema would allow clinicians and basic scientists to communicate effectively, to share information and results, and to develop testable hypotheses.

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In 1914, Professor Walter Dandy began a multidecade study on the pathophysiology of hydrocephalus with observations on the clinical aspects and pathology of hydrocephalus.¹ By 1919, he had developed experimental animal models to study the pathophysiology of hydrocephalus and to develop potential treatments for this essentially fatal condition. Based on these studies, Dandy defined the choroid plexus as the site of cerebrospinal fluid (CSF) production and classified hydrocephalus into 2 types: “communicating” and “noncommunicating.”¹ Since then, this classification has been the accepted system and still forms the basis of the reimbursement system used in the United States.²

When Dandy’s work was published, the available tools were limited. Dandy used clinical observations and pathological dissections. However, testing in living animals was limited to the injection of a supravital dye into the ventricle and seeing if it could be recovered from the spinal subarachnoid space (SSAS). On the basis of these injection studies, Dandy defined communicating hydrocephalus as that form of hydrocephalus in which the injected dye could be recovered from the SSAS and noncommunicating hydrocephalus as that form of hydrocephalus in which the dye did not reach the SSAS.

Dandy’s work on experimental hydrocephalus, especially the dye studies, led to attempts to control hydrocephalus using internal bypasses such as third ventriculostomy. Originally, the bypasses involved the resection of an optic nerve. Dandy also attempted to treat hydrocephalus by extirpation of the choroid plexuses. Except in rare cases, these initial attempts were essentially unsuccessful.¹ In Dandy’s time, the diagnosis of hydrocephalus was limited to extreme cases because diagnostic studies were limited to physical examina-

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tions and later to radiographs after the injection of air. Dandy's story, however, emphasizes how important it was to classify hydrocephalus in studying this disease. Patients with noncommunicating hydrocephalus were thought to be candidates for a third ventriculostomy. Patients with communicating hydrocephalus were not candidates for internal bypass and had to be treated with a choroid plexectomy or some form of external bypass or shunt.

In the 1950s, the development of the valve-regulated shunt led to a marked increase in the desire to understand the condition.³ In 1960, an extremely important but mostly ignored study by Ransohoff et al reassessed Dandy's classification.⁴ Experiments in Ransohoff's laboratory and experiences gained from the treatment of hydrocephalus led him to revisit the classification based on communicating and noncommunicating forms of the disorder. Ransohoff believed that all hydrocephalus involved the obstruction of CSF flow between its point of production in the ventricular system and its point of absorption into the systemic circulation at level of the arachnoid villi. Consequently, Ransohoff renamed noncommunicating hydrocephalus as intraventricular obstructive hydrocephalus. Such patients could not be treated with shunts from the SSAS, which Matson⁵ had shown was an effective treatment for some forms of hydrocephalus.⁶ Communicating hydrocephalus was caused by an obstruction at the level of the basal cisterns or arachnoid villi and was therefore called "extraventricular obstructive hydrocephalus."

Classification Theory

Scientific classification relates to the naming and grouping of things into categories. Ideally, a classification would have groupings that would include all those things that share a set of characteristics and exclude all that do not share those characteristics. In mathematics, a classification theory is called a set theory. The goal of defining groups so that all examples fit into a single grouping with no overlap is an unfulfilled dream except in a limited number of small, simple systems. An obvious example of the value of classification is the classification of books and periodicals in libraries. Searching for a specific volume or learning about what has been written about a concept would be impossible without a classification system. In both the Dewey Decimal System and the now more commonly used Library of Congress system, works are linked to broad subject matter, then by more focused subject, and finally by title and author. This system allows readers not only to find needed work specifically but also to browse volumes in the vicinity that are likely related.

To some extent, the classification of biological systems is limited by the tools that are available to study the systems. Aristotle (384-322 BCE) proposed a system of classification of plants and animals based on observation and probably at least on a modicum of dissection. In this work, he divided the animal kingdom into those with blood (essentially the vertebrate world) and those that did not have red blood (invertebrates). This classification remained in place until the 16th century when new tools led to new understanding and a new classification. The effect of this early system and of subse-

quent classifications of biological systems was to allow analysis of the characteristics that led to an animal's inclusion into a specific genus and species. Perhaps the most important function of the process of classification was to be able to refine our ability as researchers to communicate with each other.

In scientific endeavors, the process of classification leads to careful study of the elements that successfully define the differences between sets of data. In the case of hydrocephalus research, these differences translate into defining why patients do not always respond to treatment paradigms in a predictable way. Does the important finding that a patient with an assumed pathology does not respond to treatment in the expected manner mean that the form of treatment was inappropriate for that pathology or does it mean that the treatment was unsuccessful as performed and if performed successfully that treatment would be successful? In this context, unexpected outcomes present opportunities to structure research to determine the limits of a classification scheme. The process of classification as it relates to hydrocephalus research would allow investigators to search and find studies and reports, to analyze observations in the context of the classification scheme, to communicate with each other so that each investigator is discussing the same sets of phenomena, to define specific hypotheses, and to structure research to challenge hypotheses.

The process of scientific classification is and must be an ongoing, dynamic process. As new tools for study evolve and as understanding of mechanisms improve, classifications also must be updated. New technology and more than a half century of increasingly successful management of hydrocephalus is not well served by a classification scheme developed almost a century ago. From the perspective of increasing the global fund of knowledge related to hydrocephalus, a contemporary classification system must be vetted and used as a structure on which basic science exploration can be directed and logical and effective treatment algorithms can be developed.

Modern Attempts to Classify Hydrocephalus

A search of the literature on computerized search engines (PubMed) in which the key words hydrocephalus and classification were used yielded 77 citations. Of these, only 5 actually discussed potential classifications of hydrocephalus.⁷⁻¹² Each of these potential classifications proposed a different approach with different goals.

Raimondi⁹ interpreted hydrocephalus literally as "water head" and considered all pathologies associated with excessive amounts of water in the intracranial compartment as hydrocephalus. Therefore, he included not only conditions that would normally be considered hydrocephalus (ie, intracranial cysts, brain atrophy, and hydrocephalus ex vacuo) but also both cytotoxic and vasogenic edema. Although clear and understandable, this classification has not received wide-

Table 1 Classifications of Hydrocephalus

Author	Concept	Controversial Areas
Raimondi ⁹	All intracranial fluids except blood found in excess	Includes vasogenic and cytotoxic edema includes brain atrophy and hydrocephalus ex vacuo
Mori ¹³	Definition of intractable hydrocephalus	In which case is intervention futile
Johnston and Teo ⁷	Includes all abnormalities of CSF pressure and volume	Includes arrested hydrocephalus and cysts
Beni-Adani et al ¹¹	Obstructive versus communicating forms limited to infants and small children	Classification devised to define babies who may be candidates for third ventriculostomy
Oi and Di Rocco ¹⁰	Classification of infantile and fetal hydrocephalus based on CNS developmental state	Prognosis is dependent on what is occurring at the time the pathology develops. May be a rationale for in utero surgery
Rekate ¹²	Based on point of obstruction and developed on a mathematical model	Assumes all hydrocephalus is obstructive

CNS = central nervous system.

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spread acceptance. It did not lead to testable hypotheses and did not improve understanding of enigmatic conditions.

The Ministry of Health and Welfare of Japan commissioned a study of hydrocephalus. One goal of this study was to determine which forms of hydrocephalus should be considered intractable (ie, treatment attempts would be futile). Mori et al^{8,13} studied 1,450 patients, excluding those with brain tumors. Many different mechanisms of classification were reviewed, and why each cause and effect involved variations in the pathophysiology of the hydrocephalus was discussed. An attempt was made to define futility of treatment. The premise of this extensive study was similar to the one discussed here. We should be able to use the information from contemporary neuroimaging to improve understanding of the causes of hydrocephalus and to choose the most appropriate treatment options.^{8,13}

In the year 2000, a conference was held in Martinique to update the state of the art of neurosurgery for the 21st century. One presentation related to a thorough discussion of the pathophysiology of hydrocephalus and other abnormalities involving intracranial pressure and CSF volumes. This presentation by Johnston and Teo⁷ led to a thorough review of the history of research on the production, absorption, and flow of CSF and included 192 citations. They concluded that the process of classification and understanding of hydrocephalus was still primitive and recommended that work be done to clarify the issues.

Interest in the prenatal management of spina bifida and other fetal anomalies increased, and Oi and Di Rocco¹⁰ produced a unique classification of hydrocephalus based on the stage of development at the time that the ventricles became dilated. They classified the various subtypes of fetal hydrocephalus as to the mechanism of obstruction to the flow of CSF to include primary or simple hydrocephalus with a single point of obstruction to flow, dysgenetic hydrocephalus to include complex abnormalities of the central nervous system such as the Arnold-Chiari malformation, and secondary hydrocephalus from tumor or bleeding. They cross-referenced this classification with the stage of fetal

development (ie, neuronal maturation, cell migration). This classification may prove useful in deciding when treatment may be futile if beyond the legal period for terminating a pregnancy in identifying potential candidates for early delivery or fetal surgery.

Most recently, Beni-Adani et al¹¹ in Israel attempted to develop a classification scheme for infantile hydrocephalus to improve the selection of small children and infants for endoscopic third ventriculostomy (ETV). This classification represents a variation on the theme of intraventricular versus extraventricular obstructive hydrocephalus as proposed by Ransohoff et al.⁴ This work emphasizes the obstructive nature of all forms of hydrocephalus. The Israeli system reminds readers that triventricular hydrocephalus is not synonymous with aqueductal stenosis, which is not the only condition that is treatable with ETV.

Table 1 is a summary of the classification schemes that have been published since contemporary neuroimaging in the form of computed tomography scans has been available.¹² Based on a review of previous attempts at classification, no classification is completely adequate for hydrocephalus at all ages. All authors agree that such a classification scheme that would help explain the pathophysiology and predict treatment outcomes is needed.

Proposed Definition

In preparation for a consensus conference related to research in hydrocephalus held in Hannover, Germany, in September 2008, I published a discussion on the definition and classification of hydrocephalus to stimulate a debate on these important issues.¹² This work was intended to be a “straw man” that would provoke discussion of the issues and would lead to research focused on assessing the validity of these concepts. This work is ongoing. The definition that I proposed at that time was as follows: hydrocephalus is an active distension of the ventricular system of the brain resulting from inadequate passage of cerebrospinal fluid from its point of production within the cerebral ventricles to its point of ab-

sorption into the systemic circulation. The definition was specific to hydrocephalus in that it excluded other abnormalities of CSF dynamics such as benign intracranial hypertension in which the ventricles are not enlarged. It excluded brain atrophy or hydrocephalus ex vacuo in which the ventricular dilatation is not an active process of distension. It does not specify the source of production or absorption of CSF and does not presuppose the mechanisms inherent in ventricular distension.

Ventricular Volume Regulation

Based on the definition proposed earlier, the process of classification focuses on the volume of the ventricles or fluid compartments within the central nervous system. For a ventricle to enlarge in a closed space like the fixed cranial cavity, the volumes of the other compartments of fluid or the volume of the brain must decrease to compensate for the change.

In 1977, I began working with the School of Engineering at Case Western Reserve University (Case Institute of Technology) to study the physics of the intracranial compartment and thus the pathophysiology of hydrocephalus. Over the course of several years of seminars, the engineers and I educated each other in the approach to the difficult problems associated with applying engineering principles to biological systems. Our initial goal was to develop a mathematic model of ventricular volume regulation with a computer simulation of this control system. We began by evaluating previous attempts to develop mathematic models of intracranial biophysics to see how applicable they were to our needs.^{14,15} Our first requirement of the model was that it must be able to account for the 2 most enigmatic conditions of CSF dynamics, normal pressure hydrocephalus (NPH), and benign intracranial hypertension.¹⁶

For this purpose, we visualized the CSF circulation as a circuit and the heart as analogous to a battery in an electrical circuit. Using hydraulic equations analogous to Ohm's Law of electrical circuits, we defined changes in the components of CSF volume in terms of rate of flow, resistance to flow among various resistive elements, and pressure changes from 1 compartment to another (Fig 1) CSF flow is a circuit parallel to cerebral blood flow. All the compartments, including the brain, are constrained by their position in a fixed skull. However, the SSAS is less constrained because the volume of the lumbar thecal sac is distensible when intracranial pressure increases.

Our intention had been to begin with a bulk flow model to see what could be learned before we attempted the much more difficult task of incorporating pulsations into the model. With more than 30 years of research effort based on this model, we have found no conditions of hydrocephalus or other abnormalities of CSF dynamics that have required the incorporation of pulsation to explain the phenomena, except for the experiments of Bering¹⁷ and those of Di Rocco et al,¹⁸ which stimulated our interest in this subject in the first place.

The first observation that we made in the formulation of the model was the untenability of expecting brain tissue to change passively with changes in pressure and flow, thereby

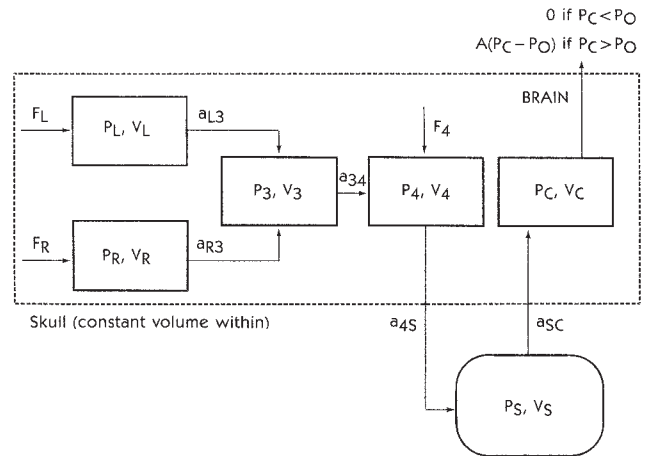


Figure 1 A diagrammatic representation of the compartments within the central nervous system as a circuit. This circuit is in parallel with the circuit of cerebral blood flow. In this circuit, the cerebrospinal fluid (CSF) compartments and blood volumes lie within the fixed volume of the skull. The only exception is the spinal subarachnoid space, which is not so constrained. (Reprinted from Rekate, HL, et al.³⁶ with permission from S. Karger AG, Basel.)

leading to changes in the volume of the ventricles. We realized that to understand benign intracranial hypertension and NPH, some property of the brain must be related to its resistance to distension. That viscoelastic property must be permissive to distortion in the case of NPH and resistant to distortion in the case of benign intracranial hypertension.¹⁶

Our first approach to this problem was to postulate that brain viscoelasticity was a constant for each person. The constant described the condition of the brain at a specific age and before or after an insult. We hypothesized that the brain softens with age and therefore resists distortion less easily. At this point, we incorporated a constant related to fixed brain viscoelasticity in the mathematic equations to account for brain viscoelasticity.¹⁹ Later we realized that the most important aspect of this term is venous blood volume. Brain viscoelasticity is a rapidly changing variable whose most important determinant is venous volume.

Subsequent work with the model has focused on defining the real physical properties and potential points of obstruction.²⁰⁻²² Except in the rather contrived experiment in which a small ventricle is drained to negative intracranial pressure, we were never able to define pressure differentials within the CSF pathways.²³ This work mirrors another experiment of ours that showed instantaneous transmission of undiminished pulses throughout the brain parenchyma as if the intracranial compartment were a homogeneous fluid compartment.²⁴ It is also reflected in the work of other researchers seeking to define a transmante pressure from the ventricle to the cortical subarachnoid space. Within the limits of resolution of pressure transducers available to these researchers, no transmante pressure was identified even though there must be such a gradient for the ventricles to expand.^{21,25}

There are 2 presumed reasons for these counterintuitive results. First, the resolution of our measuring devices (± 1 mm Hg) may be too gross to detect small variations in pres-

sure and time. The second potential explanation relates to the fluid nature of the brain. As soon as a pressure differential is created, the brain shifts to the point of lower pressure; therefore, the difference cannot be measured. Both explanations probably play a role.

A Contemporary Classification of Hydrocephalus

Beginning with the definition of hydrocephalus as a mismatch between CSF production and absorption and using the results from considering the CSF circulation as a circuit, a classification scheme that allows us to use contemporary tools of investigation can be constructed. Computed tomography studies, especially after the injection of iodinated contrast, can pinpoint actual points of obstruction to or restriction of the flow of CSF that leads to hydrocephalus with excellent accuracy. Magnetic resonance imaging also helps show precisely where flow is restricted and visualizes that flow in real time. Nuclear medicine studies provide evidence about the rate of flow and rate of clearance of radionuclide tracers, clarifying the process of CSF flow and CSF dynamics. Combining the use of these tools, which were unavailable to Dandy, with the results of more than 50 years of evaluating the success of treatments for hydrocephalus, it is now possible to develop a classification that can serve as a template for the study of hydrocephalus and its treatments.

I propose a classification structured around the circuit diagram of CSF flow. This classification is based on the effect of derangements of pressure flow characteristics of CSF dynamics anywhere within the circuit (Fig 1). In this paradigm, the rare case of overproduction of CSF by a large choroid plexus papilloma is the only communicating form of hydrocephalus. Because the absorption system can absorb a considerable amount of excess CSF, a component of obstruction is likely present in these conditions.²⁶

All other forms of hydrocephalus are obstructive. The differences associated with their appearance on neuroimaging depend on the point or completeness of obstruction. This classification (Table 2) can be tested easily using magnetic resonance imaging cine flow studies and confirmed with the intrathecal injection of contrast material and the visualization of its distribution.

In infants, particularly newborns with severe hydrocephalus, it is often difficult to show the actual point of obstruction. Some patients with complex malformations may have multiple sites of obstruction. There are 4 different potential points of obstruction in patients with a Chiari II malformation associated with spina bifida. Several or all of these points may be defined in a single individual.²⁷⁻²⁹ At the time of shunt failure or when treatment of a patient with hydrocephalus must be modified, injection studies are often valuable for determining the actual point of obstruction.

A complex example of the value of the approach is given related to the selection of patients for ETV. For most investigators, aqueductal stenosis is one of the most common forms of hydrocephalus and is synonymous with obstructive hydrocephalus and triventricular hydrocephalus. It is assumed that patients with aqueductal stenosis are excellent candidates for ETV. Unfortunately, it is not that simple.

Aqueductal stenosis as a primary problem is very rare. It occurs in the context of sex-linked dominant transmission with pathological forking of the aqueduct and other associated anomalies. Specific occlusion of the aqueduct later in life is often related to a small tumor of the midbrain. These patients are indeed excellent candidates for ETV.³⁰ Most patients with presumed aqueductal stenosis have triventricular hydrocephalus, and the cause of the hydrocephalus is not related specifically to the aqueduct.

In some species of both mice and rats, the ventriculomegaly occurs first, and inward pressure from the temporal horns leads to functional stenosis of the aqueduct.^{31,32} Nugent et al³³ first postulated that aqueductal stenosis was caused by the hydrocephalus and not vice versa. They showed that an aqueduct that was closed before treatment could be seen to open after implantation of a shunt. In reviewing the treatment of chronic compensated hydrocephalus, we showed that adults with longstanding triventricular hydrocephalus responded to ETV by opening the aqueduct. One such patient had persistent intracranial hypertension after successful ETV. This patient required treatment of high-grade stenosis of the transverse sinuses with venous stenting.⁵

ETV not only bypasses the aqueduct of Sylvius but also bypasses the outlet foramina of the fourth ventricle, which is a common cause of hydrocephalus associated with meningi-

Table 2 Proposed Classification of Hydrocephalus

Site of Obstruction	Pathology	Treatment
None	Choroid plexus papilloma	Removal
Foramen of Monro	Tumor, congenital anomaly, postshunt ventricular asymmetry	Tumor removal, septum pellucidotomy, ventricle shunt
Aqueduct of Sylvius	Congenital lesion, tumor secondary to extraventricular obstruction	ETV, ventricular shunting
Outlets of fourth ventricle	Chronic meningitis, Chiari II malformation	ETV, ventricular shunting
Basal cisterns	Meningitis, postsubarachnoid hemorrhage	ETV, ventricle shunt, spinal thecal shunt
Arachnoid granulations	Hemorrhage or infection in infancy	Ventricle or thecal shunt
Venous outflow	Skull-base anomalies, congenital heart disease	Ventricle or thecal shunt, treatment of vascular anomaly if possible

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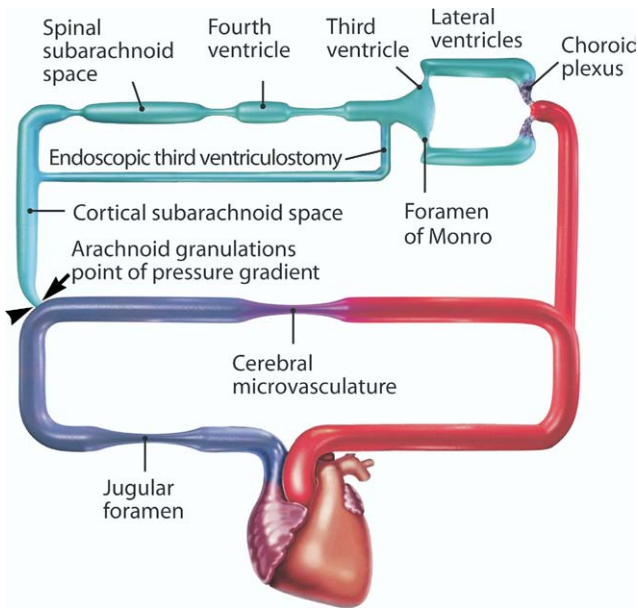


Figure 2 A diagrammatic representation of what an ETV accomplishes. ETV is an internal bypass of all potential points of obstruction with the exception of the actual absorption of CSF into the dural venous sinuses. (Courtesy of Barrow Neurological Institute.) (Color version of figure is available online.)

tis and tumor (Fig 2). ETV can also bypass obstruction to flow at the level of the basal cisterns.⁶ This is the specific mechanism for most patients with posthemorrhagic hydrocephalus such as those shunted in infancy for intraventricular hemorrhage of the premature newborn. It is also the cause of hydrocephalus in the case of hemorrhage related to trauma or aneurysmal subarachnoid hemorrhage. This is a common cause of secondary NPH and may be a factor in the pathophysiology of idiopathic NPH. This blockage between the SSAS and the cortical subarachnoid space leads to hydrocephalus, and it may underlie the successful management of intraventricular NPH with ETV.^{34,35}

Why Classification Matters

Hydrocephalus is not a unitary condition. It is the result of the effect of a wide variety of pathologies on a well-tuned system. In general, the prognosis in hydrocephalus relates more to the underlying cause of the obstruction than to the ventriculomegaly itself. Moderate ventriculomegaly is often detected during adolescence and young adulthood. Would these patients benefit from treatment at the time of recognition, or would their quality of life be diminished by treatment or complications related to treatment? We are now seeing patients with hydrocephalus treated during infancy who are reaching seniority in this most chronic of disorders. Clearly, not all degrees of ventriculomegaly need immediate treatment. However, it seems likely that deterioration can occur late in life, and chronic compensated hydrocephalus may be the underlying substrate of NPH.

The limited classifications now available place many completely different conditions in the same grouping. Therefore,

many researchers assume that all communicating hydrocephalus is the same and related to filtration difficulties at the level of the arachnoid villi. In fact, this condition is extraordinarily rare. Abnormalities of terminal absorption into the systemic circulation lead to ventriculomegaly only in infants with distensible heads.⁶ Except in the very young, the process of ventricular dilatation requires a disconnection between the ventricle and the cortical subarachnoid space. This disconnection suggests that most causes of hydrocephalus in adulthood lead to adequate management with ETV. Researchers cannot assume that they know the point of obstruction to flow in their animal models or study patients. Consequently, dye studies are often required to define that point of obstruction. With these strategies, we can be certain that we are all speaking the same language and studying the same condition.

Conclusions

The currently accepted classification of hydrocephalus is about 90 years old and greatly limited because it was developed when few tools were available to study the condition. Future research needs to be structured in a context that allows it to be focused and ensures that researchers from disparate fields reliably communicate with each other on the important aspects of the pathophysiology and treatment of hydrocephalus. However, a recognized definition for hydrocephalus is lacking. A consensus on the definition of hydrocephalus is needed as is a commitment to develop a consensus on a classification of hydrocephalus. This review postulates that the new classification should be based on the circuit diagram and the potential points of flow restriction in the CSF circuit.

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