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A unifying theory for the definition and classification of hydrocephalus

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Abstract If the cerebrospinal fluid (CSF) is considered to be all the fluid (liquid), other than blood or the derivatives of its breakdown, that is normally contained within the brain, its cavities, and its spaces, this could be regarded as "brain fluid" in its most elemental form. "Pathological increases in intracranial CSF volume, independent of hydrostatic or barometric pressure", then, could be considered a definition of hydrocephalus. The observation of significant episodic variation in intracranial pressure (ICP) suggests the necessity of substituting the concept of "time-related pressure variations" for the older one of "level of pressure" in patients with defective ICP control mechanisms. It has been assumed that the subarachnoid channels are the first CSF compartment to dilate in response to the hydrocephalic process, reducing the CSF pressure and thereby establishing an equilibrium. When the equilibrium is disturbed, with progressive dilation of the subarachnoid channels, the increase in CSF pressure is transmitted to the ventricular system, resulting in its dilation (extraprenchymal hydrocephalus). Progressive ventricular dilation causes cerebral edema (intraparenchymal hydrocephalus) and obliterates the subarachnoid spaces as the hemispheres are compressed against the dura, resulting in apparent "internal hydrocephalus" in the absence of "external hydrocephalus". Thus, subarachnoid space or ventricular dilation occur as a result of intermittent increases in *extraparenchymal* CSF volume: *the primary pressure force emanating from the subarachnoid and subdural spaces and from the intraventricular compartment.* Hydrocephalus, therefore, may be present in a child who does not yet have dilated ventricles but in whom both CSF volume and pressure are increased. Thus, it becomes obvious that the term internal hydrocephalus is of little significance, since increases in intraparenchymal fluid – cerebral edema – cause the same volumetric changes as increases in intraventricular fluid volume. I suggest that hydrocephalus is a pathologic increase in intracranial CSF ("brain fluid") volume, whether intra- or extraparenchymal, independent of hydrostatic or barometric pressure. It may be classified as (1) intraparenchymal (cerebral edema) and (2) extraparenchymal, with the extraparenchymal types subclassified into subarachnoid, cisternal, and intraventricular forms.

Key words Hydrocephalus · Cerebrospinal fluid · Ventriculomegaly · Cerebral atrophy

Background

It is safe to assume that the anatomists and physicians prior to Vesalius were of the mind that the increased amount of fluid in hydrocephalus accumulated beneath the scalp. In his work, "*The Seats and Causes of Disease Investigated by Anatomy*", G. B. Morgagni, in 1761, called attention to the fact that the earlier investigators of increased cranio-cerebral size did not have any particularly clear ideas as to where beneath the skin the fluid present in hydrocephalus was located. Specifically, pathologist, anatomist, and clinical pathologist were dubious as to whether the fluid was located beneath the skin, beneath the skull, beneath the dura, or within the brain itself. The first to give a clear description of internal hydrocephalus, Vesalius, stated that:

> Galen declared that this shape of the skull may be imagined to come from another world but not to exist in the nature which surrounds us. A boy was seen by me in Venice, one deformed and insane, with an enormous and mis-shapened head. Also, there was a beggar in Bologna with a square head which is wider than it is long. A beggar-woman in Genoa carries about a little boy as she goes from door to door, and gives him to comedians who would use him in their show to illustrate a head which is larger than that of the two comedians' heads together! It is my own thought that the boy suffers the same disease I first observed in Augsburg in a little girl, who, at the age of seven months, had a head larger than that of any man I had ever seen. The disease I am describing was called hydrocephalus by the ancients because of the water which collected within the head but, in this child, the water did not collect outside of the skull and beneath the surrounding membranes nor did it collect within the skin – as most medical books teach – but, within the center of the brain itself, in the right and left ventricles of the brain. The depths and the breadths of these ventricles so increased, and the brain was so very swollen that they contained 9 lbs. of water, or 4 Augsburg wine measures (so help me God!). Just as the brain itself at the vertex was membrane-like in thinness indistinguishable from its own membraneous covering so was the skull membraneous, but the base of the skull was in harmony with that of the young child before her head took on abnormal proportions. The cerebellum and the brainstem were in their natural state, so were the nerves coming from the brainstem. I found water in no other place than in the ventricles of the brain: the girl was in control of all her senses until she died. When I examined her a few days before her death I noted that whenever her head was raised she coughed, her respirations became difficult, her face became red with the flow of blood, and tears dripped from her eyes.

This confirmed Vesalius' observation that the accumulation of fluid in hydrocephalus is within the ventricles and established the basis for his conclusion that hydrocephalus in infants causes an increase in head size, but that this macrocephaly does not occur in the adult with hydrocephalus.

Accentuating the fact that he had never encountered water between the dura mater and the brain, in the interhemispheral fissure, or over the corpus callosum in the children between the ages of 2 and 15 years that he studied at necroscopy, Robert Whytt first distinguished between internal and external hydrocephalus in 1768. The notable absence of subdural hygroma, subdural hematoma, and subdural effusion in this study may well be due to his exclusion of children under the age of 2 years. Despite its cursory form, his report definitely showed precisely that in the more common forms of hydrocephalus cerebral spinal fluid (CSF) accumulates within the ventricular system, dilating the ventricles and increasing head size.

At least six different disease categories have been identified over time, but no effort has been made to understand their single common denominator – increased amounts of CSF within the intra-cranial compartments – and to group them anatomo-pathologically. By and large, it has been assumed that (1) *external hydrocephalus* and subdural effusions were identical anatomic and clinical entities, characterized by accumulation of fluid within the subdural spaces, a much thinner cerebral mantle than normal, markedly enlarged subarachnoid spaces, and a dilated ventricular system. From a clinical point of view, therefore, until the present, external (over the cerebral hemispheres) accumulation of liquid and (2) *ventriculomegaly* (hyper-, hypo-, normotensive) have, respectively, been considered two distinct anatomopathological entities with different etiologies and both, in turn, separate from (3) *cerebral atrophy*. The entity characterized by pathological intraparenchymal accumulation of liquid, (4) *cerebral edema*, has been recognized in some cases as complicating hydrocephalus, in others as preceding it, but never (5) has *cerebral atrophy* been regarded as a form of hydrocephalus. Similarly, non-neoplastic (6) *parenchymal cysts* (arachnoid, porencephalic, etc.) have been looked upon as very distinct clinical entities, related neither temporally nor causally to "hydrocephalus".

We now know, however, that CSF can accumulate in pathological volumes within the subarachnoid spaces in the absence of ventricular dilation, and that it can pass freely across the arachnoid membranes into the subdural spaces. We also have evidence that the condition formerly referred to as external hydrocephalus and considered to be a distinct pathoanatomic entity, is in fact a variant of, or more precisely a stage, in the development of hydrocephalus.

These various anatomopathological flows of brain fluid are just that: pathological volumes shifting micro (intra and extracellular) and macro (subarachnoid and intraventricular) anatomical levels. The regulatory factors are complicated physical chemical and paracrine mechanisms which act via (1) osmotic feedback to produce a buffering effect and (2) an homeostatically controlled neuroendocrine system. The former prevents major fluid shifts in osmotic or pressure disequilibrium at the blood-brain barrier (BBB) within the four-compartment model of secretion of CSF at the BBB levels: bulk flow of interstitial brain fluid, regulation of intracellular volume, absorption of CSF. The extracellular fluid volume expands and contracts, allowing the brain to accomodate,

within variable limits, to such pathologic processes as neoplasias, inflammation, hydrocephalus, and thus permitting normal cell volume to remain constant. Unless these variations in extracellular space volume are such that either vascular or cellular structures are damaged, the process is reversible. The homeostatically controlled neuroendocrine system is equally active in brain volume regulation. It consists of a paracrine system secreting, among other peptides, vasopressin and atriopeptin, which are released by the brain into its brain water where they are totally independent of peripheral concentrations.

Changes in intracranial pressure (ICP) occur physiologically during the early stages of sleep and during REM sleep; they are episodic and rapid in onset and cessation, reflecting the fact that pathologic alterations in production or absorption of CSF are not the causative factors. Rather, alterations in cerebral blood flow (CBF), mediated by cerebral vasodilation and induced by neuronal or humoral mechanisms resulting from cerebral vasodilation, cause a greater increase in ICP (because of exponential relationship between intracranial volume and ICP) in children with defective CSF absorption mechanisms. These factors are thought to explain why normal pressure may be repeatedly recorded in patients who actually have progressive hydrocephalus. This observation of significant episodic variation in ICP suggested the necessity of substituting the concept of "time-related pressure variations" for the older one of "level of pressure" in patients with defective ICP control mechanisms. This is of particular significance in light of the fact that parenchymal damage results from the length of time that an increase in ICP has lasted, rather than the level the ICP has reached and/or presence of a space-occupying lesion. In fact, there is a point – not yet precisely identifiable clinically – at which the very increases in CSF volume become pathogenic.

Because liquids are not compressible, the Monro-Kellie doctrine was promulgated to offer a simple explanation for the pathoanatomic changes the brain undergoes in response to an intracranial space-occupying lesion: liquid changes in one intracranial compartment must be accompanied by simultaneous reciprocal changes in another. This is a neurobiological equivalent of $P = VT$, recognizing that within the physiologic variations compatible with life, temperature can be considered a constant. At this point, it is of value to state that the brain occupies approximately 93% of the intracranial space, and that the intracranial blood volume occupies 4% of this space.

Therefore, the concept that a differentiation between external hydrocephalus and cerebral atrophy is possible only when the child demonstrates the clinical picture of increased ICP, something considered (erroneously, I now believe) characteristic of all forms of hydrocephalus, but not present in cerebral atrophy, is no longer tenable.

Though the arachnoid villi along the superior longitudinal sinus are microscopically absent in the newborn and the infant, clinical and "experimental" evidence has been interpreted as indicating that the CSF is absorbed at these sites. Regardless of this observation, it has been presumed that the subarachnoid channels adjacent to the arachnoid are the first CSF compartment to dilate, reducing the CSF pressure and thereby establishing an equilibrium. When the equilibrium shifts to the right, with progressive dilation of the subarachnoid channels, the increase in CSF pressure is transmitted to the ventricular system, resulting in its dilation. Progressive ventricular dilation obliterates the subarachnoid spaces and the hemispheres are compressed against the dura, resulting in apparent "internal hydrocephalus" in the absence of external hydrocephalus.

In conditions characterized by variations in plasma osmolarity the brain does not "sop up" or "bleed" water; it cannot be likened to a sponge, which exerts purely mechanical forces. Rather, it shifts electrolytes into or from its bulk, thus re-adjusting itself slowly to a different overall volume. The relatively reciprocal volumetric relations between the interstitial and cerebrospinal extracellular fluids are therefore readily understood: cerebral edema/increased subarachnoid and/or intraventricular fluids. In fact, when the brain is osmotically dehydrated the Na^+/Cl^- volume regulatory influx is from CSF bulk flow. As there is an influx of Na^+/Cl^- at the BBB level there is an equivalent efflux of interstitial fluid, containing these ions, into the CSF. The extent to which there are variations between influx and efflux from the BBB level across the cerebral parenchyma and into the CSF-containing chambers determines the relative cerebral compartment volumetric alterations expressed clinically as cerebral edema (intracellular or extracellular), subarachnoid dilation, and ventriculomegaly: the continuum of increased brain fluid volume recognized grossly as hydrocephalus. Thus, dilation of the subarachnoid spaces or ventricles causing megacephaly occurs as a result of intermittent increases in *extraparenchymal* CSF volume: the primary pressure force emanating from the subarachnoid and subdural spaces in external hydrocephalus and from intraventricular compartment in internal hydrocephalus. Dilation of the subarachnoid spaces may therefore be present in an infant who as yet does not have dilated ventricles but in whom head circumference, CSF volume, and ICP are increased, with a bulging or sunken anterior fontanel. Similarly, cerebral edema or arteriovenous malformations also cause megacephaly, the result of increased *parenchymal* water. An infant's head may increase in size whether there is an increase in intraparenchymal or extraparenchymal liquid.

Overall brain volume, along with the control of ions that, in turn, regulate intra- and extracellular fluid flow, is regulated homeostatically by the brain itself through its own neuroendocrine system. The cellular elements re-

sponsible for this control are the same as are active in the BBB mechanism (capillary endothelium and astroglia) and secretion of most of the CSF (choroid plexus); the hormones secreted by the brain for the regulation (via a paracrine mechanism) of its fluid volume shifts and concentrations are vasopressin, angiotensin, and atriopeptin. These latter are conveyed to their targeted areas by the CSF flowing through the extracellular spaces, the ventricles, the subarachnoid spaces. Vasopressin facilitates the passage of water across the capillary endothelium, from the CSF into the vascular system, and increases ependymal permeability. Its antagonists not only block these physical chemical events but actually decrease brain bulk. Atriopeptin, on the other hand, is active in regulating liquid volume regarding ICP by decreasing brain water. Thus, via sodium and potassium activity coupled with chloride ions, brain-produced vasopressin is active in increasing brain volume, atriopeptin in decreasing it.

Proposed definition and classification

Until recently, the most commonly followed classification of hydrocephalus was put forth when it was assumed that there were neither compensatory pathways nor transependymal flow, when it was thought that CSF could not cross the arachnoid membranes to enter the subdural spaces, when the inter-relationships between CBF and CSF pressure were not understood, and when it was assumed that hydrocephalus necessarily entailed increased intraventricular pressure.

The connection of cerebral interstitial fluid though the subependymal, perimyelinic, and Virchow-Robin spaces is an essential component of brain and spinal cord volume regulation, and knowledge of it permits one to understand how, and though what anatomic pathways, the brain's *second* extracellular fluid (ECF), CSF, passes between the subarachnoid spaces and the ventricular system.

ECF and CSF are very similar, neither having the composition of a plasma ultrafiltrate and both being secreted at the BBB. The ECF drains into the CSF at both the subarachnoid and the intraventricular levels through a pressure-dependent mechanism – an extrachoroidal CSF source.

Because the brain has no lymphatics and brain capillaries, unlike peripheral capillaries, are impermeable to both proteins and salts, there is no anatomo-physiologic system to disperse excess ECF. It may, however, shift fluid from one compartment to another; for example, the gray matter may increase in volume by about 1–2%, the white matter by about 10–12%, and the ventricles by multiples of their total volume.

Most authors agree that the choroid plexus of the lateral, III, and IV ventricles serves as the driving force to propel the CSF through the ventricular system and into the basal cisterns. The water-hammer effect created by the pulsatile choroid plexus gives the CSF a to-and-fro movement within the ventricular system, allowing it to pass from one ventricular chamber to another, and from the IV ventricle into the cisterns. The circulation of CSF through the foramina of Luschka and Magendie and around the brainstem, and its percolation up through the basal cisterns and over the surface of the brain offered the basis for the conclusion that: (1) the CSF may circulate freely throughout the entire ventricular system and cisterns, but may not be adequately reabsorbed, in which case one spoke of communicating hydrocephalus; or (2) the passage of CSF from one ventricle into another or from the ventricular system into the basal cisterns may be obstructed totally or partially, causing obstructive hydrocephalus. These are valid observations, but not inviolate laws.

It is therefore necessary to consider critically whether hydrocephalus must necessarily be characterized by any one or all of the following: (1) an increase in intraventricular pressure; (2) an increase in intraventricular CSF volume; (3) increased, or increasing, subarachnoid/cisternal CSF volume; (4) increased intraparenchymal liquid. With the observations that imaging studies (CTT and MRI) have made available, namely that subdural, subarachnoid, or periventricular areas may hold pathological increases in fluid volume, the classification of hydrocephalus could be expanded to include cerebral edema, of either the vasogenic or cytotoxic varieties, and arachnoid or parenchymal cysts. The first of these (cerebral edema), permits the inclusion of metabolic disorders, arteriovenous fistulae, hormonal or humoral causes, and alterations in CBF: anatomic alterations and clinical conditions that have one common denominator, a pathologic increase in brain water. If we include the latter (cysts), it helps us to understand how entrapped CSF may act as a space-occupying lesion.

In order to define hydrocephalus, we must first define "brain water", since it is not reasonable to think in terms of a multitude of intracranial fluids:

- CSF – sulcal, cisternal, ventricular, perineural, central canal, spinal
- Extracellular – white matter, gray matter, areas without BBB
- Intracellular – ganglionic, glial, perivascular glial cells

Consequently, *if the CSF is considered to be all the liquid, other than blood or the derivatives of its breakdown, normally contained within the brain, its cavities, and its spaces... independent of its cellular or ionic composition, one may then consider "brain fluid" in its most elemental form.*

Such a definition of CSF makes it possible to think of it in terms of ion transfer and liquid medium permitting:

1. Transmembranous passage
2. Direct and reverse pinocytotic transport
3. Bulk flow across cellular layers or through extracellular spaces
4. Secretion and absorption
5. Changes in ionic concentrations and gas partial pressure, both over time and in different anatomic locations
6. Pulsatile intraventricular flow from one chamber to another
7. Percolation through the aqueduct and foramina
8. Pooling within basal and medial cisterns
9. Antigravitational rise through subarachnoid spaces, via capillary pressure

"Pathologic increases in intracranial CSF volume, independent of hydrostatic or barometric pressure", then, could be considered a definition of hydrocephalus that would be acceptable to both clinicians and basic scientists. It would permit basic scientists to establish criteria for determining whether the increase is a primary or a secondary event and to study the permutations and variations of each. It would also permit clinicians to evaluate volume increases as individual pathogenetic events, which could then allow them to identify the specific anatomopathologic entity concerned and to direct their treatment to the (vasogenic or cytotoxic) cerebral edema, aqueductal occlusion or obstruction of a foramen of Monro, high-flow arteriovenous shunt into the transverse sinuses, etc.

Accepting that the definition of *hydrocephalus implies a pathologic increase in intracranial CSF volume, independent of hydrostatic or barometric pressure,* it may be classified as follows:

I. Intraparenchymal (cerebral edema) (Fig. 1)

A. Intracellular
B. Extracellular

II. Extraparenchymal

A. Subarachnoid (Figs. 2, 3, 4)
   1. Transient, self-limiting
   2. Early stages of "communicating hydrocephalus"
   3. Transformation into regional or loculated arachnoid cysts
B. Cisternal
   1. Cyst of cisterna magna (Fig. 5)
   2. Cysts of basal or sagittal cisterns
   3. Cysts of cerebral fissures, with or without parenchymal dysplasia (Fig. 4)
C. Intraventricular (Fig. 6)
   1. Monoventricular (lateral)
   2. Biventricular (both lateral)
   3. Triventricular (III and both lateral)
   4. Tetraventricular (IV, III and both lateral)

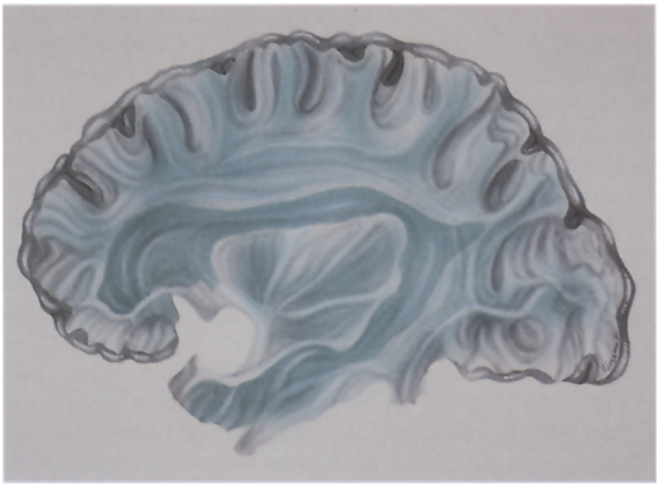
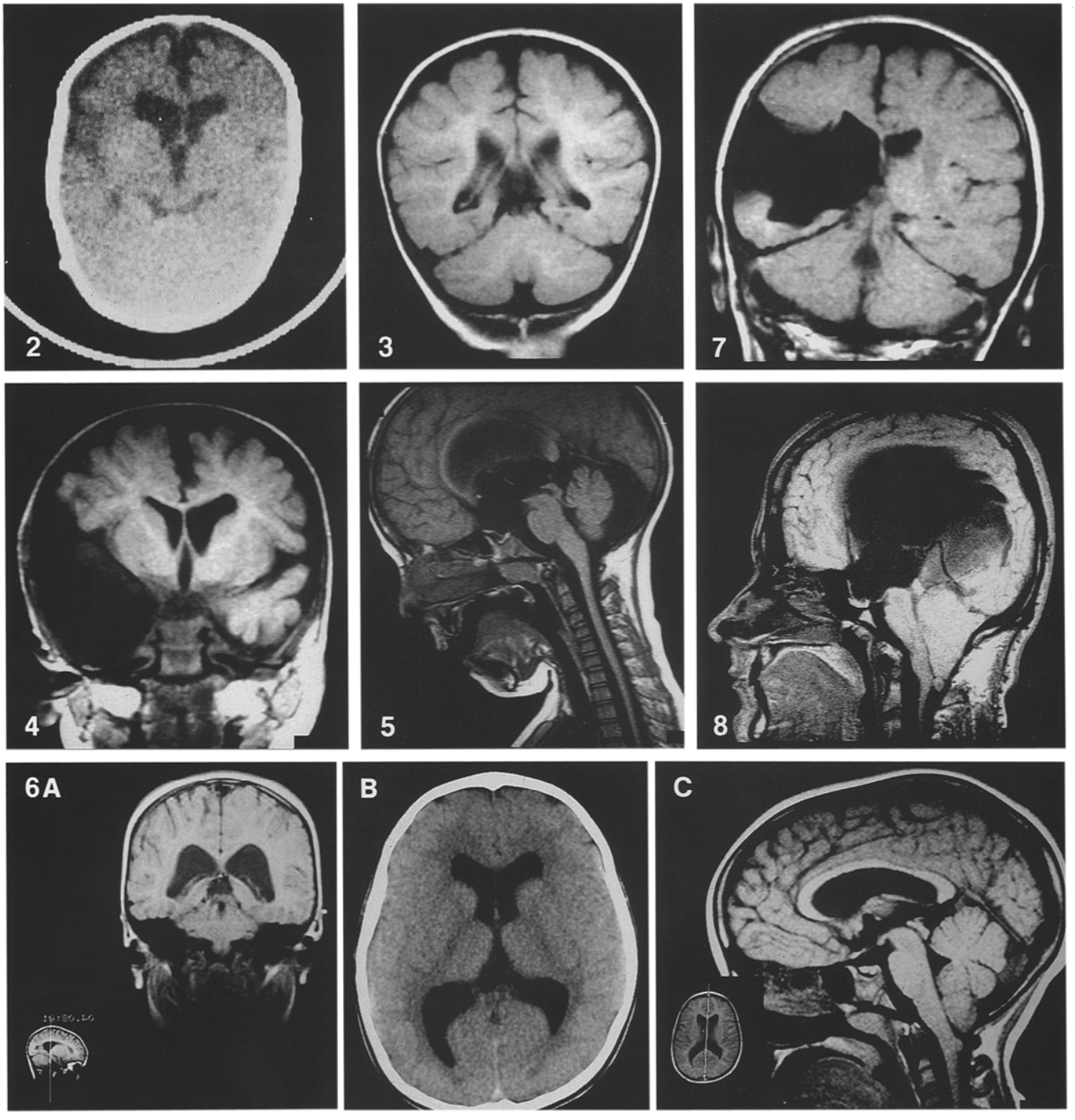


Fig. 1 Distribution of edema (*green*) within the cerebral hemisphere. Edema has accumulated and spread almost exclusively within the white matter, along the fiber bundle tracts connecting adjacent gyri, individual lobes of the hemisphere, cortical and subcortical nuclear masses, and the cortex within the brainstem and spinal cord. The gray matter (*black*), practically speaking, is only minimally involved by edematous change

Porencephalic or ependymal cysts must be considered anatomopathological complications of ventriculomegalic hydrocephalus.

I suggest that the anatomical natural history of hydrocephalus begins with an accumulation of fluid within the parenchyma, as *cerebral* edema. Subsequently, there are progressively disproportionate accumulations (shifts) of fluid within the subarachnoid spaces, the subdural spaces, the cisterns, and, lastly, the ventricles. This last, resulting in structural changes of the ependymal cells and the tight junctions that hold them together, permits pathologic amounts of fluid to pass into the cerebral parenchyma, first compounding cerebral edema and, ultimately, causing parenchymal destruction, porencephaly, or ependymal cysts. Occasionally, the parenchymal destruction is so massive as to result in fistulization between the ventricular system and the subarachnoid spaces (Fig. 7), a patho-anatomic process superficially referred to as a "compensatory mechanism".

For well over 65 years now, hydrocephalus has been considered in a purely mechanistic sense, following Dandy's classification of "external" and "internal," with the latter sub-divided into "communicating" and "obstructive" subtypes. During the past 15 years, the additional category of *constrictive* (as in the Chiari II malformation) hydrocephalus has been added (Fig. 8). It was observed that toxic substances, vitamins, nutritional disturbances, etc., could result in hydrocephalus, but such observations were not integrated into a new classification. Similarly we have not yet found a comfortable place for the hydrocephalus complicating arteriovenous mal-



Figs. 2–8 (for legends see p. 8)

Fig. 2 Computerized transmission tomography image of my first clinically documented case of extraparenchymal hydrocephalus characterized by accumulation of cerebrospinal fluid (CSF) within *both* the subarachnoid *and* subdural spaces, with early dilation of the ventricular system. At the reader's *right*, liquid accumulating within the subarachnoid spaces; at the *left*, liquid within both the subarachnoid, over the insula and medial surface of the frontal lobe, and subdural, over the lateral frontal lobe, spaces. Ventricular dilation is typical of that present during the early stages of communicating hydrocephalus

Fig. 3 Magnetic resonance (MR) image of a child with slowly progressive megacephaly and a flat to sunken anterior fontanel. Increase in volume of the subarachnoid spaces, especially along the parasagittal area, and the moderate ventriculomegaly can be fully appreciated. A very common observation in slowly progressive megacephaly secondary to increased volumes of CSF within the subarachnoid spaces and only moderate ventriculomegaly is the "opening up" of the cavum veli interpositi! When this constellation of signs is present, I suggest postponing insertion of a ventriculoperitoneal shunt

Fig. 4 MR image illustrating the presence of increased volumes of CSF within the subarachnoid spaces (over the cerebral hemispheres) and within the sylvian fissure at the reader's *right;* the conspicuously dilated arachnoidal cyst, occupying almost the entire middle fossa, is at the reader's *left*. It exerts a pressure force on the homolateral hemisphere. This arachnoidal cyst involves both the subarachnoid spaces over the insula and the sylvian fissure. There is also dysplasia of the temporal lobe, a common pathologic alteration when the sylvian fissure is involved

Fig. 5 Hydrocephalus in this child progressed clinically through stages of increasing subarachnoid space volume, dilation of the basal cisterns, cystic transformation of the cisterna magna, ventriculomegaly. This illustration shows the marked dilation of the basal cisterns and the cystic transformation of the cisterna magna with extension into the supraculminate and quadrigeminal cisterns

Fig. 6A–C Comparison of this illustration with Fig. 3 reveals various differences. **A** Relative diminution in volume of the subarachnoid spaces over the convexities and along the parasagittal plane, along with increase in volume of the lateral ventricles, dynamics common in the evolution of the hydrocephalic progress. The cavum veli interpositi is well visualized. **B** Almost complete obliteration of the subarachnoid spaces has occurred. The open cavum veli interpositi is clearly seen. **C** For comparison, note both the extension of the cavum veli interpositi in the anterior direction from the region of the quadrigeminal cistern, and the Chiari I malformation

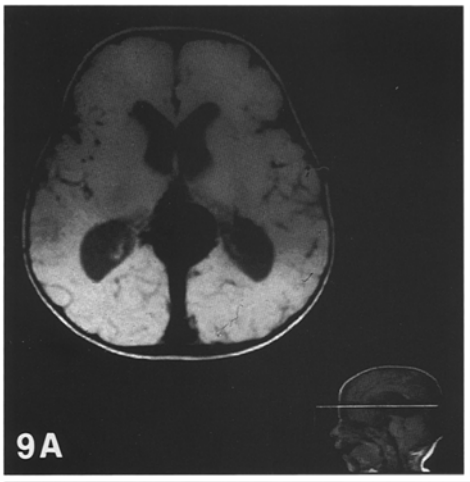
Fig. 7 This MR image study illustrates extensive parenchymal destruction and fistulization between the lateral ventricle and the subarachnoid spaces

Fig. 8 Chiari II malformation complicated by "constrictive hydrocephalus" resulting from incarceration of the inferior cerebellar hemisphere, vermis, medulla oblongata, and a portion of the pons within the cisterna magna. The striking ventriculomegaly, absence of the tentorium cerebelli and straight sinus, transformation of the IV ventricle into a tubular structure and polymicrogyria are well illustrated

Fig. 9 **A** MR image showing globular dilation of the great vein of Galen and straight sinus along the midline, accompanied by moderate ventriculomegaly, with the trigons being disproportionately dilated. This child had an arteriovenous malformation involving the galenic system, and suffered complicating hydrocephalus, which disappeared when the malformation was coagulated by the endovascular technique. No shunt was inserted. **B** In the same child, computerized transmission tomography permits evaluation of flow through the tentorial sinuses and of the conspicuous distention of the fistulous system at the torcula and transverse sinuses. **C** Diagram representing the pathogenesis of ventriculomegaly: shunting of arterial blood through the fistula and into the venous sinuses, cortical veins, and medullary venous system, resulting in remarkable increase in "venous pressure," obstructing CSF absorption and, therefore, causing both ventriculomegaly and dilation of the subarachnoid spaces. The arterial blood within the venous structures, schematically depicted in red, fills the great vein of Galen, straight sinus, torcula herophili, inferior sagittal sinus, posterior third of the superior sagittal sinus, and cortical veins draining into these last two sinuses. **D** Mid-sagittal MR transmission image performed in the same child as is shown in **A** and **B** before embolization of the arteriovenous fistula reveals that the volume of the "galenic" component is such as to obliterate partially the posterior portion of the III ventricle, and compress the culmen monticuli conspicuously, displacing the cerebellum downward and causing herniation of the cerebellar tonsils through the foramen magnum (Chiari I). It does not obstruct either the IV ventricle or the aqueduct of Sylvius. The arteriovenous malformation has been embolized and occluded. The cerebellar tonsil has returned to within the posterior fossa, and the ventricle dilation has diminished. Dilation of the subarachnoid spaces persists, most obviously noted where the retrograde flow of arterial blood through the venous system had been most severe: the posterior parietal and occipital lobes. The reversible pressure forces between the spinal fluid containing chambers and the vascular system and the disappearance of the hydrocephalic process after endovascular occlusion of the arteriovenous fistula (by Professor P. Lasjaunias) are all fully documented

Fig. 10 This computerized transmission tomography image is of a child with an arteriovenous fistula extending from the external and internal carotid arteries into the cavernous sinus, tentorium, and transverse sinus. There was no mass dilation anywhere along the midline structures, so that obstruction of the flow of CSF was not possible. Nonetheless, dilation of the subarachnoid spaces is seen bilaterally, with fluid also in the subdural spaces over the frontal lobes. The lateral ventricles are dilated. The hydrocephalus in this child is considered secondary to the arteriovenous fistula: the same dynamics as described in Fig. 9

Fig. 11 This arteriogram was performed before the era of computerized transmission tomography and MR imaging. It quite clearly reveals the striking changes in vascular anatomy and flow that occur secondary to ventriculomegaly and subarachnoid space dilation apart from stretching, narrowing, and flattening of primary and secondary branches of the cerebral arteries. Severe diminution of flow into the gyri is noted. The result is diffuse cerebral ischemia, most remarkable in the white matter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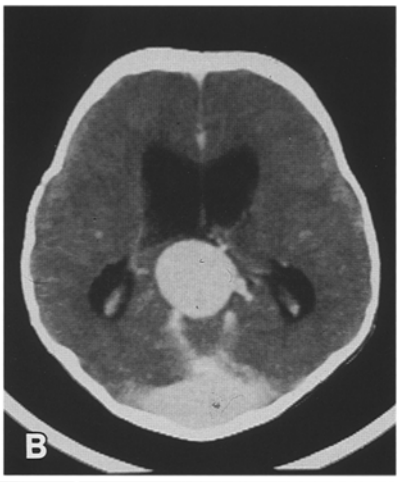
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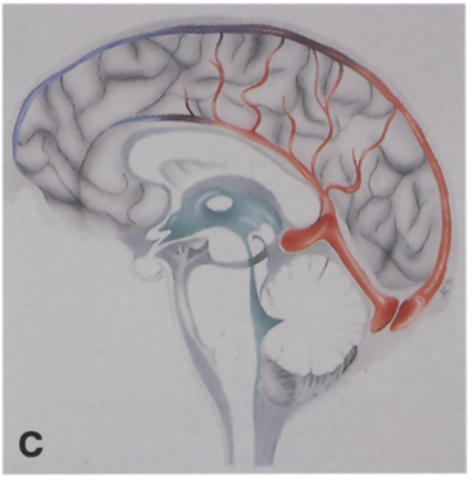
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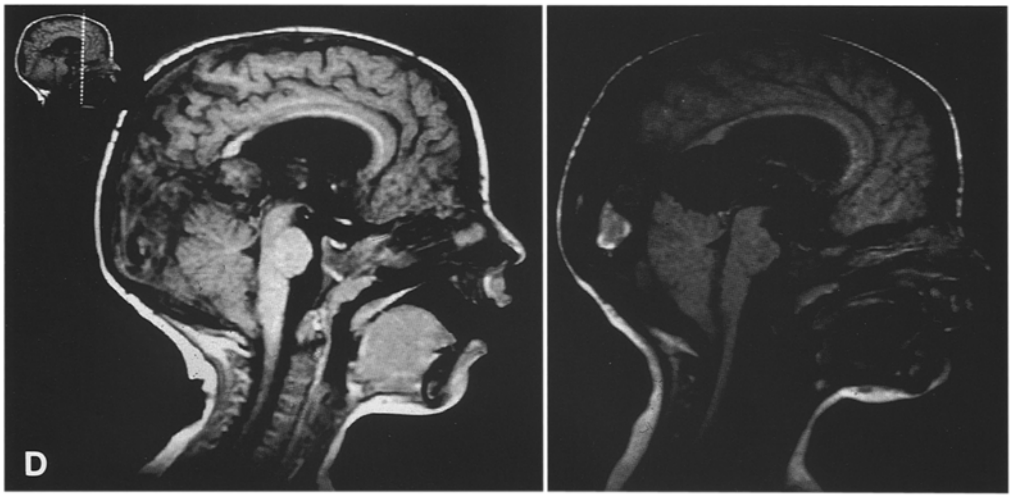
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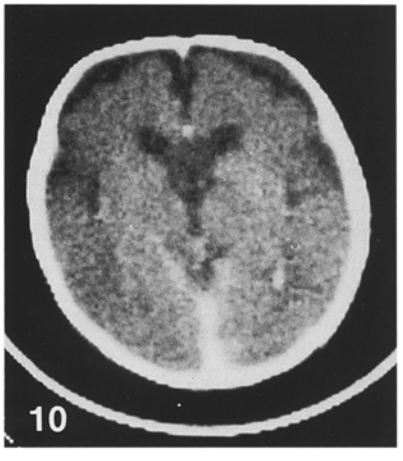
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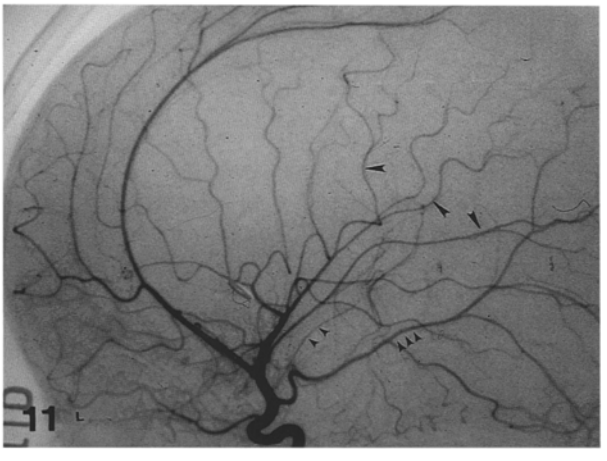
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formations and fistuale involving the galenic system or the dural sinuses, resorting generally to mechanistic explanations, e. g. compression of the aqueduct (Figs. 9, 10).

Hydrocephalus, then, is not a single disease entity; nor is it a syndrome. *It is, very probably, the final common pathway of the brain's response to various pathogenic events.* What we have heretofore interpreted as different nosologic types of hydrocephalus may well be simply different stages of this response. The various etiologic factors range from congenital malformations through neoplasms to meningitis.

Oversecretion of CSF and arterio-venous shunts

It has long been thought that such intraventricular tumors as the *choroid plexus papilloma* of the lateral ventricle are capable of producing increased amounts of CSF, and that, accordingly, this type of tumor causes communicating *hydrocephalus of the hypersecretory variety.* Certainly, it is true that children with choroid plexus papilloma show a clinical picture of both the space-occupying lesion and hydrocephalus. In addition, a large majority of these children require ventricular shunts after the choroid plexus papilloma has been totally removed. The reasons for this are not clear. Consequently, after a diagnosis of choroid plexus papilloma of the lateral ventricle has been made in either a newborn or an infant and the tumor removed, a medium- to high-pressure shunt may need to be inserted to ensure a smooth postoperative course and to diminish the possibility of progressive ventricular enlargement.

Milhorat et al. have shown that the rate of cerebral spinal fluid formation in a 5-year-old child who had undergone bilateral choroid plexectomy for communicating hydrocephalus during infancy was 0.35 (SD 0.02) ml/min, which is well within normal limits. This failure of choroid plexectomy as a treatment for hydrocephalus had previously been documented extensively in the world literature. The hypersecretory hydrocephalus that results from a papillary tumor of the choroid plexus may not necessarily be cured when the papilloma is resected, probably because of irreversible change at the sites of CSF absorption, changes which result from the extraordinarily high levels of protein secreted by the papillary tumor. Other intraventricular tumors, such as subependymal astrocytoma, tubers in association with tuberous sclerosis, ependymoma, and medulloblastoma, may be associated with permanent hydrocephalus after the tumor (whether obstructing or not) is totally removed.

The hydrocephalus that complicates an arteriovenous fistula may develop secondary to transcranial, dural, mixed dural-pial, or purely pial malformations involving major arterial and venous channels. The origin of blood supply depends, quite naturally, upon the type of arteriovenous malformation, but has no significance for the genesis of hydrocephalus. Increased venous pressure, with retrograde flow of aterial blood through major draining veins and sinuses and into the capillary bed, may well be the initial causative factor that results in communicating hydrocephalus. Very few documented cases of "obstructive hydrocephalus" resulting from arteriovenous fistuale have been reported, though we have all seen cases, which are generally characterized by enormous intracranial pools of blood occupying the tentorium, falx cerebri, galenic system or cerebral parenchyma. The same etiology – increased venous pressure at the torcular herophili and the resultant diminshed absorption of CSF – has been attributed to the hydrocephalus resulting from superior vena cava and/or internal jugular vein thrombosis or occlusion of one or both transverse sinuses (as seen in arteriovenous anomalies and aneurysmal dilation of the galenic system).

Genesis of parenchymal destruction

Irrespective of the etiology, pathogenesis, or type of hydrocephalus, micro and macro vascular changes in association with the cerebral edema are the direct cause of parenchymal destruction in infantile hydrocephalus. Ventricular enlargement causes displacement of primary cerebral arteries, followed by stretching and a decrease in the caliber of (arterial and venous) primary, secondary, and tertiary vessels (Fig. 11). Ultimately, there is a reduction in the number and caliber of the vessels in the microvasculature, resulting in diminished cerebral blood flow and cerebral edema. Tissue destruction ensues, leading to ependymal rupture, parenchymal cavitation, and the formation of porencephalic cysts within the edematous parenchyma. The ventricular enlargement occurs at the expense of the surrounding tissue, most notably the white matter, which becomes markedly thin. The most common end-stage changes found in the parenchyma of the hydrocephalic brain are atrophy, pallor and swelling, vacuolation and chromatolysis of nerve cells, hypertrophy of astrocytes, demyelinization and axonal degeneration, and a decrease in synapses. I suspect that synaptic function is permanently impaired to a greater or lesser degree, and that this plays an important role in the post-hydrocephalic psychomotor disturbances so common in children affected in this way.

It was suggested earlier that vascular changes are the result of an increase in ICP which induces a diminution in CBF in the hydrocephalic brain in either hypertensive or normal-pressure hydrocephalus. Early observations of the brain's vasculature in human hydrocephalus by Penfield and Elvidge in 1932 were contradictory. They stated that "There may be a decrease in the intramedullary capillary bed, but it seems likely that vascular obliteration begins in the smallest branches of the vascular tree and that further passage of blood through these branches is

prevented by their compression without thrombosis and congestion as in other forms of vascular occlusion." Hassler and De, working independently, found in studies of experimental hydrocephalus that there was a significant loss of smaller vessels (capillary and precapillary) around dilated ventricles, and concluded that ischemia was responsible for the associated changes in all structures along the ventricular surface. The variability of the cerebral damage observed in experimentally induced hydrocephalus is well known and probably results from lack of uniformity in species, of technique, and of reproducibility. Certainly, one must be very cautious in interpreting observations on changes secondary to experimentally induced, or even naturally occurring, hydrocephalus in "horizontal" (four-legged) experimental animals with extensive external/internal carotid anastomoses and attempting to extrapolate them to the hydrocephalus that can afflict man, a "vertical" animal with an "isolated" internal carotid system and dural sinuses.

In the hydrocephalic process it is possible to postulate a sequence of events leading to irreversible brain damage. After cerebral edema, the initial, remarkable dilation of the subarachnoid spaces and cisterns, ventricular dilation occurs and is, in turn, followed by periventricular lucency, recurrent cerebral edema, obliteration of the subarachnoid spaces, progressive cerebral edema, and aqueductal occlusion. The progressive cerebral edema first involves the white matter, but soon extends to the gray matter. Only in the very late, terminal, stages of hydrocephalus does edema occur within the basal ganglia.

Transependymal CSF perfusion, a compensatory mechanism that certainly also occurs in the normal state, is a response to high intraventricular hydrostatic or pulse pressure. The intraventricular CSF and ECF of the cerebral parenchyma act as one liquid medium, with bulk flow proceeding freely in both directions and across the ependymal barrier. The increased head of pressure both compresses and stretches the cerebral vasculature, displacing and deforming the vessels, causing their caliber to diminish, and resulting in changes in CBF.

The first vascular changes in the development and progression of hydrocephalus, as the edema progresses and the CSF containing chambers dilate, consist in a decrease in the caliber of cortical and white matter cerebral vessels, and not of the perforating branches going to the brainstem or basal ganglia. Subsequently there is a decrease in the number of the secondary and tertiary vessels, which begins in the white matter but rapidly involves the vasculature of the cortex. Then, the normal "palisade" pattern disappears, atrophy of the periventricular white matter follows, and ischemia occurs. The end-result is the following sequence of events, leading to irreversible brain damage: (1) accumulation of intraventricular CSF under either elevated hydrostatic pressure or increased pulse pressure; (2) increased transependymal flow; (3) parenchymal vascular compression; (4) ischemia; (5) increased/ECF and communication between intraventricular fluid and ECF; (6) cellular disruption and tissue destruction.

The onset of irreversible brain damage becomes obvious with the identification of porencephalic cavities and the disappearance of the tertiary branches of the anterior and middle cerebral arteries. Consequently, one may conclude that decompression of the intraventricular pressure head by a shunting device *after* parenchymal vascular compression has caused irreversible changes in CBF offers little hope of recovery of cerebral function. On the other hand, if one intervenes when early ventriculomegaly and/or edema of the white matter and enlargement of the extracellular spaces have only begun, and there is no more than a minimal decrease in the caliber of cerebral vessels with displacement of the primary and secondary vessels, drainage of the CSF has a benefical effect. In fact, a significant increase in caliber of the cerebral arteries after ventricular drainage, as evidenced by follow-up with cerebral MRI angiography, suggests that the increase in ICP associated with progressive hydrocephalus is transmitted from the ventricles to the extracellular spaces to compress, deform, and displace the cerebral vasculature and, therefore, results in diminished CBF. These changes are compounded by the progressive cerebral edema and may be directly correlated with the clinical observation that the earlier a hydrocephalic child is shunted, providing the shunt remains functional, the greater are the chances of the patient attaining or regaining normal intellectual and motor function.

Bibliography

1. Arantius, cited in [2]
2. Baker F (1909) The two Sylviuses. An historical study. Bull Johns Hopkins Hosp 20:329–339
3. Berengarious, cited in [2]
4. Buijs RM, Swabb DG, Dogterom J, Van Leeuwen FW (1978) Intra- and extrahypothalamic vasopressin and oxytocin pathways in the cat. Cell Tissue Res 186:423
5. Dandy WE (1918) Extirpation of the choroid plexus of the lateral ventricles in communicating hydrocephalus. Ann Surg 68:569–579
6. Dandy WE, Blackfan (1914) Internal hydrocephalus. An experimental clinical and pathological study. Am J Dis Child 8:406
7. Davidoff LM (1948) Hydrocephalus and hydrocephalus with meningocele. Their treatment by choroid plexectomy. Surg Clin North Am 28:416
8. De SN (1950) A study of the changes in the brain in experimental internal hydrocephalus. J Pathol Bacteriol 62:197–203

9. Deyo SN, Shoemaker A, Ettenberg A, Koob GF (1986) Subcutaneous administration of behaviourally effective doses of AVP change brain AVP content only in median eminence. Neuroendocrinology 42:260–266
10. Dóczi T, Bodosi M (1989) The central neuroendocrine regulation of brain water and electrolytes and reabsorption of cerebrospinal fluid (CSF). In: Gjerris F, Borgesen SE, Soelberg Sorensen P (eds) Outflow of cerebrospinal fluid. (Alfred Benzon Symposium 27) Munksgaard, Copenhagen, pp 282–292
11. Dóczi T, Szerdahelyi P, Gulya K, Kiss J (1982) Brain water accumulation after the central administration of vasopressin. Neurosurgery 11:402–407
12. Dóczi T, Szerdahelyi P, Joó F (1984) 5-Hydroxytryptamine, injected intraventricularly failed to increase brain water content. Neurosurgery 15: 165–169
13. Dóczi T, Joó F, Szerdahelyi P, Bodosi M (1987) Regulation of brain water and electrolyte contents: the possible involvement of central atrial natriuretic factor (ANF). Neurosurgery 21:454–458
14. Dóczi T, Joó F, Szerdahelyi P, Bodose M (1988) Regulation of brain water and electrolyte contents: the opposite actions of central vasopressin and atrial natriuretic factor (ANF). Acta Neurochir (Wien) [Suppl] 43:186–188
15. Dóczi T, Joó F, Vecsernyés M, Bodosi M (1988) Increased concentration of atrial natriuretic factor in the cerebrospinal fluid of patients with aneurysmal subarachnoid haemorrhage and raised intracranial pressure. Neurosurgery 23:16–19
16. Dóczi T, Joó F, Bodosi M (1990) Central neuroendocrine control of the brain water, electrolyte and volume homeostatis. Acta Neurochir (Wien) [Suppl] 47:122–126
17. Editorial (1991) Welcome to ouabain – a new steroid hormone. Lancet 338:543–544
18. Gardner DG, Vlasuk GP, Baxter JD, Fiddes A, Lewicki JA (1987) Identification of atrial natriuretic factor gene transcripts in the central nervous system of the rat. Proc Natl Acad Sci USA 84:2175–2179
19. Haddy FJ (1987) Endogenous digitalis-like factor of factors. N Engl J Med 316:621–623
20. Hassler O (1964) Angioarchitecture in hydrocephalus. An autopsy and experimental study with the aid of microangiography. Acta Neuropathol (Berl) 4:65–74
21. Johnson RT, Johnson KP, Edmonds ES (1967) Virus-induced hydrocephalus development of aqueductal stenosis after mumps infection. Science 157:1066–1067
22. Matson DD (1956) Prenatal obstruction of the fourth ventricle. AJR 76: 499–506
23. McGeer PE, Ecclers JC, McGeer EG (1986) Molecular neurobiology of the mammalian brain. Plenum Press, New York
24. Milhorat TH (1974) Failure of choroid plexectomy as a treatment for hydrocephalus. Surg Gynecol Obstet 193:505
25. Morgagni, cited in [38]
26. Nicholson C, Rice ME (1991) Diffusion of ions and transmitters in the brain cell microenvironment. In: Fuxe K, Agnati LF (eds) Volume transmission in the brain: novel mechanisms for neural transmission. Raven Press, New York, pp 279–294
27. Raichel ME, Grubb RL (1978) Regulation of brain water permeability by centrally released vasopressin. Brain Res 143:191–194
28. Raimondi AJ (1971) A critical analysis of the clinical diagnosis, management and prognosis of the hydrocephalic child. Yearbook Medical Publishers, Chicago
29. Raimondi AJ (1972) Pediatric neuroradiology. Saunders, Philadelphia
30. Raimondi AJ (1987) Pediatric neurosurgery – theoretic principles, art of surgical techniques. Springer, New York Berlin Heidelberg
31. Raimondi AJ, Samuelson GS, Yarzagaray L, Norton T (1969) Atresia of the foramina of Luschka and Magendie. The Dandy Walker cyst. J Neurosurg 31:202–216
32. Raimondi AJ, Clark SJ, McLone DG (1976) Pathogenesis of aqueductal occlusion in congenital murine hydrocephalus. J Neurosurg 45:66–77
33. Ransohoff J, Shulman K, Fishman RA (1960) Hydrocephalus. A review of etiology and treatment. J Pediatr 56:399
34. Steardo L, Nathason JA (1987) Brain barrier tissues: end organs for atriopeptins. Science 235:470–473
35. Sylvius, cited in [2]
36. Taggart JK, Walker AE (1942) Congenital atresia of the foramens of Luschka and Magendie. Arch Neurol Psychiatr 48:583–612
37. Vesalius (1543) De humani corporis labrica librorum epitome. Joannis Opporini, Baselieae
38. Whytt R (1768) Observations on the dropsy in the brain. Balfour, Edinburgh
39. Wozniak M, McLone DG, Raimondi AJ (1975) Micro and macrovascular changes as the direct cause of parenchymal destruction in congenital murine hydrocephalus. J Neurosurg 43:535–545