

# Hydrocephalus and the heart: Interactions of the first and third circulations

**C**hronic hydrocephalus and cardiovascular disease are related, which may result in a dangerous cycle of pathophysiology in elderly patients. Evidence suggests that patients with chronic adult hydrocephalus, also referred to as normal-pressure hydrocephalus, have vascular disease. Studies have shown an increased incidence of arterial hypertension, cardiac disease (including ischemic heart disease, valvular disease, and congestive heart failure), and cerebrovascular atherosclerotic disease in patients with chronic adult hydrocephalus compared with age-matched controls.<sup>1-6</sup>

A major coordinating factor in the regulation of interactions between the cerebrospinal fluid (CSF) and the cardiovascular system appears to be cardiac impulse control. The CSF spaces of the cranium play a critical role in cardiac impulse absorption by surrounding the cerebral vasculature and controlling blood flow, allowing CSF circulation, when diseased, to reduce blood flow, and CSF manipulation to enhance blood flow. This article briefly reviews proposed mechanisms for interactions between the CSF circulatory system and the cardiovascular system.

## ■ CSF AND THE CARDIOVASCULAR CIRCULATION

CSF is produced mainly in the choroid plexus at a rate of about 400 mL/day. It flows through the ventricles of the brain, exits the brain, flows around the hemispheres, and eventually is absorbed through the venous system back into the circulation. This cycle can be obstructed within the ventricular system or outside the brain before absorption, which is termed “obstructive” or “communicating” forms of hydrocephalus, leading to dilation of the ventricles and compression of the brain.

Recent imaging technologies have revealed that CSF moves within the subarachnoid space in harmony with the cardiac cycle. The energy of this move-

ment is several times the energy of its movement through the circulation.

As formally described by Cushing in 1925, the first area of contact between the CSF and the cardiovascular circulation is at CSF secretion and absorption sites. A second contact zone is at the CSF space and cerebral vessels. A third site of interaction is at the brain regulatory nuclei, with expansion of the ventricular system.

## ■ CSF VENTRICULAR ENLARGEMENT

Pressure forces within the ventricles, the brain, and the subarachnoid spaces must be balanced for ventricles to retain their size. If these forces become imbalanced, either by an increase in ventricular pressure or a change in the resistance or compliance of the brain, the ventricles may enlarge. A canine model of obstructive hydrocephalus confirmed increased pressures with occlusion of the ventricle, resulting in ventricular enlargement. As chronic hydrocephalus developed, the brain became less compliant.<sup>7</sup> With acute decompression (CSF drainage), the hydrocephalic brain became more compliant.

### Hydrocephalic brain: A worn-out spring

To understand this phenomenon, we can apply mathematical spring constants in which compliance is dependent on intracerebral pressure and CSF volume. The hydrocephalic brain can be thought of as a worn-out spring in which the ventricles compress the brain against the skull, decreasing the brain's compliance. With acute CSF drainage, the spring is released and the brain becomes softer (more compliant).

### Changing the spring's constant

Chronic hydrocephalus changes the spring's constant; under conditions of large ventricles, the compliance is lower than normal, but under conditions of smaller ventricles, the compliance is higher.

### The brain as a sponge

The blood vessels within the brain, and not the brain itself, appear to be the compressible components that

\* Both authors reported that they have no financial relationships that pose a potential conflict of interest with this article.

allow for acute changes in volume and re-expansion. If this is so, then changes in blood flow should cause changes in brain compliance. When hydrocephalus is induced in animal models, a reduction in cerebral blood flow occurs, as measured using a microsphere technique, which permits observation of blood flow in any tissue.<sup>8</sup> With obstructive hydrocephalus, we found the same reduction of blood flow in cardiac tissue,<sup>8</sup> which suggests that hydrocephalus is not simply a local brain phenomenon but that blood flow in the brain is part of a response to the general cardiovascular blood supply. In this sense, cerebral blood flow is under the control of the heart. This phenomenon is confirmed by measuring cardiac output, which changes in a pattern similar to changes in blood flow.<sup>8</sup> This pattern of change indicates that cardiac output, and not simply expansion of the ventricles, is responsible for changes in cerebral blood flow.

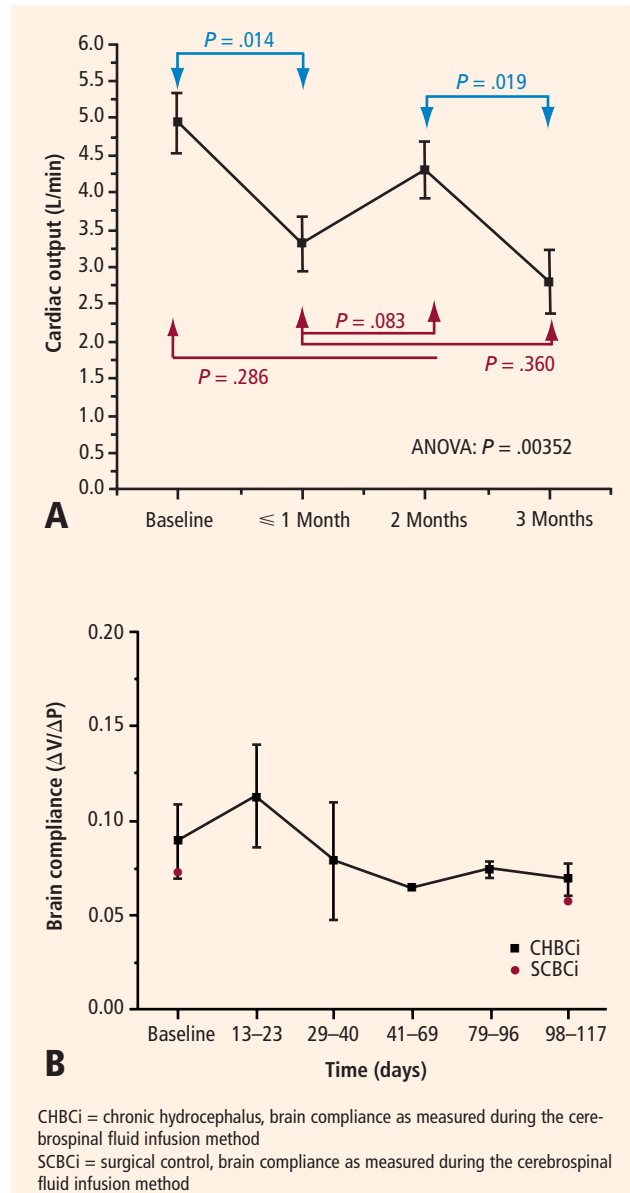
Brain compliance in these animals was found to be inversely correlated with cardiac output and vascular flow (**Figure 1**). The inverse correlation suggests that brain stiffness is governed by cerebral blood flow. Also, if the presence of cardiovascular disease decreases blood volume, then the brain may have a smaller vector to oppose the expanding ventricular system.

The amplitude of intracranial pulses serves as an indication of compliance. We found that in animal models of chronic obstructive hydrocephalus, the pulse amplitude is significantly reduced compared with normals, a finding that suggests a softer, more compliant brain (unpublished results). With CSF infusion, pulse amplitude increases to a greater degree in the hydrocephalic animal, indicating less tolerance to the infusion.

Research in the 1970s demonstrated that enlargement of CSF ventricles occurs because of an imbalance of pulsations between the CSF space and brain.<sup>9</sup> Di Rocco et al were able to cause ventriculomegaly by increasing pulsations within the ventricular system without changes in CSF absorption or secretion.<sup>9,10</sup>

#### ■ HYDROCEPHALUS AND CARDIAC DISEASE: A FEEDBACK LOOP?

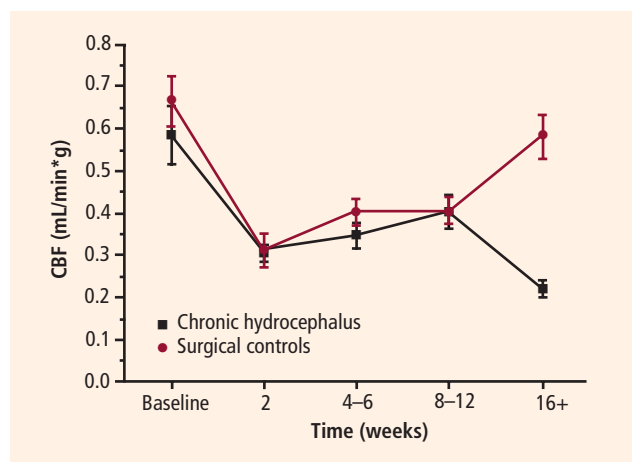
Chronic adult hydrocephalus may increase the risk of cardiovascular disease via compression of cardioregulatory nuclei near the hypothalamus, as already described. Early cerebral blood flow is no different in animal models with hydrocephalus compared with controls, but a divergence in cerebral blood flow between hydrocephalic animals and controls is observed with time (**Figure 2**).<sup>8</sup> Examination of cardiac output and central venous pressure shows simi-



**FIGURE 1.** (A) A significant decrease in cardiac output is observed after surgical induction of chronic hydrocephalus in dogs. (B) In the same animals, brain compliance increased over the same period that cardiac output decreased, indicating that brain compliance is inversely correlated with cardiac output and vascular flow.

larly late development of congestive heart failure in hydrocephalus.<sup>8</sup> Electrocardiographic data confirm signs of congestive heart failure in chronic hydrocephalus (unpublished results).

A strong relationship between ventriculomegaly and cardiac output was also observed, as was a relationship between cardiac output and cerebral blood flow.<sup>8</sup> Therefore, unlike the intuitive concept that the



**FIGURE 2.** Cerebral blood flow (CBF) is not different between control dogs and those with early hydrocephalus, but decreases significantly ( $P < .01$ ) over time in the dogs with chronic hydrocephalus (CH) compared with the surgical controls.

enlarged ventricles have a direct effect on cerebral blood flow, the link between ventriculomegaly and cerebral blood flow may instead be mediated to a great extent by general systemic blood flow and changes in cardiac output.

If changes in cardiac function can increase brain compliance and exacerbate hydrocephalus, and chronic hydrocephalus can result in congestive heart failure, then chronic hydrocephalus and chronic cardiac failure may represent a vicious pathophysiologic cycle in the elderly.

## ■ CSF AND CARDIAC IMPULSE ABSORPTION

The CSF spaces play a critical role in cardiac impulse absorption.<sup>11</sup> The direct contact between the CSF space and the cerebral vasculature, which exists in the subarachnoid space, is a dynamic place of CSF movement and pulse changes, and is also believed to be the place where the brain controls its impulses. Like every organ in the body, the brain receives cardiac impulses, and through the elasticity of the blood vessels, arterial pulsations are dampened to a more steady (ie, continuous) stream of blood. This vessel compliance, which makes blood flow more even, is called the Windkessel mechanism.

When an artery expands in the cavity of the rigid skull, some fluid needs to be displaced as a result. CSF fluid movement occurs at the cervical medullary junction into the spinal canal, compressing veins epidurally and within the CSF spaces. If movement of CSF decreases as a result of disease of the dura or the brain, an increase in CSF pressure, or occlusion, then these

arteries are less able to enlarge, blood inflow is compromised, and compliance of the vascular system decreases. In this way, cerebral vascular compliance is dependent, to some extent, on CSF space compliance.

## CSF: The brain's shock absorber

Patients with chronic hydrocephalus have abnormal compliance waves and abnormal intracranial pulsations, indicating that intracranial pressure is increasing because arteries are unable to expand. The CSF serves as the brain's shock absorber in that the impact of the blood is absorbed by CSF spaces, allowing intracranial pulsations to be absorbed by CSF spaces before they are able to reach the brain and capillary system. However, the spring constant of the hydrocephalus brain is changed, perhaps because the brain is stiffer in certain circumstances and softer in others, allowing dyssynchrony between expansion and contraction of these springs.

The constant of synchrony is important because arriving impulses must be met by an oscillating CSF space system, and this system has its own constant and its own preferred frequency. In control dogs without hydrocephalus, we found that the energy of the cardiac impulse is best absorbed at the normal cardiac frequency, which suggests that the brain and the heart are in tune at this frequency.<sup>12</sup> In dogs in which hydrocephalus is induced, the energy absorption trough at the cardiac frequency is much wider and shallower, which indicates that the hydrocephalic brain does not absorb the cardiac impulse as well as in normal situations.

Effective absorption of cardiac impulses and production of smooth blood flow through the capillary system via the Windkessel effect reduces vessel wall oscillation, capillary trauma, and blood inertial impedance, resulting in more efficient blood flow. Consequently, compromised absorption of cardiac impulses allows more of these impulses into the capillary system and brain, decreasing the efficiency of blood flow. In the future, alterations of the brain's ability to absorb cardiac pulsation may allow improvement in cerebral blood flow.

## ■ SUMMARY

Hydrocephalus is not always caused by blockage in absorption; it can result from an imbalance in cardiac impulse distribution that can cause a ventriculomegaly in chronic communicating hydrocephalus. Chronic ventriculomegaly may result in cardiac dysfunction, which may beget a pathophysiologic cycle in the elderly.

The CSF spaces play a critical role in cardiac impulse absorption: cerebral blood flow may be diminished in CSF disease and enhanced by its manipulation.

The interface between the CSF circulatory system and cardiovascular system is based on certain organizing principles, at least one of which appears to be the control and regulation of cardiac impulses that are reaching the brain tissue.

## ■ REFERENCES

1. Krauss JK, Regel JP, Vach W, Droste DW, Borremans JJ, Mergner T. Vascular risk factors and arteriosclerotic disease in idiopathic normal-pressure hydrocephalus of the elderly. *Stroke* 1996; 27:24–29.
2. Graff-Raford NR, Godersky JC. Idiopathic normal pressure hydrocephalus and systemic hypertension. *Neurology* 1987; 37:868–871.
3. Casmiro M, D'Alessandro R, Cacciatore FM, Daidone R, Calbucci F, Lugesesi E. Risk factors for the syndrome of ventricular enlargement with gait apraxia (idiopathic normal pressure hydrocephalus): a case-control study. *J Neurol Neurosurg Psychiatry* 1989; 52:847–852.
4. Earnest MP, Fahn S, Karp JH, Rowland LP. Normal pressure hydrocephalus and hypertensive cerebrovascular disease. *Arch Neurol* 1974; 31:262–266.
5. Bradley WG Jr, Whittemore AR, Watanabe AS, Davis SJ, Teresi LM, Homyak M. Association of deep white matter infarction with chronic communicating hydrocephalus: implications regarding the possible origin of normal-pressure hydrocephalus. *AJNR Am J Neuroradiol* 1991; 12:31–39.
6. Boon AJ, Tans JT, Delwel EJ, et al. Dutch Normal-Pressure Hydrocephalus Study: the role of cerebrovascular disease. *J Neurosurg* 1999; 90:221–226.
7. Johnson MJ, Ayzman I, Wood AS, et al. Development and characterization of an adult model of obstructive hydrocephalus. *J Neurosci Methods* 1999; 91:55–65.
8. Dombrowski SM, Schenk S, Leichter A, Leibson Z, Fukamachi L, Luciano MG. Chronic hydrocephalus-induced changes in cerebral blood flow: mediation through cardiac effects. *J Cereb Blood Flow Metab* 2006; 26:1298–1310.
9. Di Rocco C, Pettorossi VE, Caldarelli M, Mancinelli R, Velardi F. Communicating hydrocephalus induced by mechanically increased amplitude of the intraventricular cerebrospinal fluid pressure: experimental studies. *Exp Neurol* 1978; 59:40–52.
10. Pettorossi VE, Di Rocco C, Mancinelli R, Caldarelli M, Velardi F. Communicating hydrocephalus induced by mechanically increased amplitude of the intraventricular cerebrospinal fluid pulse pressure: rationale and method. *Exp Neurol* 1978; 59:30–39.
11. Raftopoulos C, Chaskis C, Delecluse F, Cantraine F, Bidaut L, Brotchi J. Morphological quantitative analysis of intracranial pressure waves in normal pressure hydrocephalus. *Neurol Res* 1992; 14:389–396.
12. Madsen JR, Zou R, Egnor MR, et al. Variation in the notch filter response of the ICP to arterial pulse pressure. *American Academy of Neurological Surgeons Abstract #29935*; 2005 Dec 1. Available at: <http://www.aans.org/Library/Article.aspx?ArticleId=29935>.

**Address:** Mark Luciano, MD, PhD, Department of Neurological Surgery, Cleveland Clinic, 9500 Euclid Avenue, S80, Cleveland, OH 44195; [lucianm@ccf.org](mailto:lucianm@ccf.org).