The clinical problem of hydrocephalus, and its many associated paradoxes, has focused new attention on the nature of the pulsatile pressures and flows in the brain. The physiology of hydrocephalus may teach us about intracranial pressure and dynamics more generally, so it is difficult for any neurosurgeon to escape the implications of this sea-change, which comes with a focus on waves. I would like to develop the idea of the intracranial pulsation absorber and, in homage to Dr. Cushing’s “third circulation” \(^1\), I would like to suggest that the passage of pulsations through the brain constitutes a kind of “fourth circulation.”

An impediment to progress has been the tendency to think of hydrocephalus as a solved problem since the invention of the shunt valve in the 1950s \(^2\) by Holter, a lay machinist who produced a one-way valve in his home shop in an attempt to help doctors save the life of his child who had spina bifida.\(^3\) Unfortunately, shunts have not completely solved the problem. Indeed, they have generated problems such as slit ventricle syndrome, chronic headaches, and other problems which did not occur before there were shunts. In fact, there has been a lag in interest in publications on hydrocephalus compared with other neurological problems \(^4\) (Fig. 6.2). In spite of this, the National Institutes of Health sponsored a conference to look at new thinking in hydrocephalus just a week before this Congress presentation. One of the trends voiced at the meeting was the increased focus and potential utility of pulsatile models.

I would like to discuss why we should pay attention to the pulsatile component of intracranial pressure and why we might think of this as a fourth circulation. Stated simply, cerebrospinal fluid (CSF) movements include both bulk flow (or, by analogy with electrical circuits, DC components), and rapidly pulsating, or AC, components in the CSF and in the circulation. Most of our thinking has focused on the DC components, but if the AC components can help us make predictions, understand pathophysiology, or improve treatment, we should pay attention to these as well. Recent investigators and contributors to this thinking include Dan Greitz,\(^17-21\) Michael Egnor,\(^2-4\) and Marvin Bergsneider,\(^2-4\) but much of it goes back to earlier workers, including Portnoy and Chopp,\(^11-13\) who, in the early 1980s, presaged some of the techniques that I will cover at the end of this talk.

### HISTORICAL BACKGROUND

**Cushing, Bering, and Pappenheimer**

Let us begin with Harvey Cushing and his very important work, “The Third Circulation” (1925) (Fig. 6.3). It was a lecture published in the *Lancet* in which he talked about the third circulation and its channels. It was called the third circulation, meaning that it was a circulation somewhat like the blood and somewhat like lymphatic flow, which, incidentally, has also received a great resurgence of interest of late. This is the flow of the bulk flow of water in the cerebral spinal fluid space, which was the topic of his talk. I would like to propose that we think of a fourth kind of flow through the intracranial cavity, which is the flow of pulsations. Pulsations, like CSF, come from the arterial blood, must traverse the brain, and come out the venous side, but they do not necessarily flow through the capillary bed. In fact, unless the capillary epithelia are highly resistant to very severe pulsatile shear stresses, it is highly desirable that they not flow that way.

There was a specific time in the history of CSF investigation when interest shifted to the bulk flow aspects and away from the effects of pulsatility. I would like to briefly tell you the stories of two investigators with very different views on CSF physiology and very different legacies. Both happened to be working within a few hundred yards of each other in laboratories on Longwood Avenue in Boston. The first, Dr. Edgar Bering (Fig. 6.4, left), a neurosurgeon at Children’s Hospital, was, in 1955, very interested in the role of pulsations in determining the ventricular size and shape in hydrocephalus. He was, in 1955, very interested in the role of pulsations in determining the ventricular size and shape in hydrocephalus. John Pappenheimer (Fig. 6.4, right), who is still alive and only recently stopped contributing to the literature, was at the same time a Professor of Physiology at Harvard Medical School. He was kind enough to advise me when I started to do CSF research about 20 years ago, and his major contribution was to precisely quantify bulk flow of CSF in the central nervous system.
Bering was very interested in pulsations in the CSF, which he thought came from choroids plexus vessels (which proves to be but one contributor to the vascular generation of pulsations). In one of his experiments, he modified an experiment of Dandy’s to examine unilateral removal of the choroid plexus in an animal model of hydrocephalus (Fig. 6.5). In this case, he removed the choroid plexus on one side and then induced hydrocephalus in a communicating model with saline injection into the subarachnoid space. He recorded the pressure from both lateral ventricles and what you see in the tracing is that the pressure in the right and the left ventricle have the same mean value in this preparation, but a very different amplitude of their pulsation. The DC pressure is the same. The AC component of the pressure is very different. He showed that the ventricle with the greater pulsations is enlarged. Later, in Rome, DiRocco buttressed and extended these results by showing that simply placing a balloon in one ventricle and making it pulsate with the arterial pulsation could make a ventricle larger without any change at all in the CSF, arguing for a role for pulsations.

Why did we neurosurgeons stop thinking about pulsations and their dynamics as important? I think much of the answer may be that Bering’s work was trumped by very important and, ultimately, seductive work by Dr. Pappenheimer. Now, Pappenheimer was a pure physiologist, a very eminent man who devised a method of measuring the production rate and a rate of absorption of the CSF fluid using a dye dilution technique, the same as could be used, for example, in the kidney to understand the different contributions to the fluid in different parts of the kidney. This allowed clinicians to concentrate on the bulk production and bulk absorption of CSF and for decades almost all of us learned and thought that hydrocephalus must be a disorder of the balance of these two stationary parameters. To his credit, Pappenheimer never asked clinicians to ignore pulsatile dynamics of the CSF—but his very beautiful papers showing how to measure the DC parameters pulled all interest away from pulsations.

Bering returned to the question after publication of Pappenheimer’s work and repeated the method in some hydrocephalic animals, and his conclusion was that “the hydrocephalic animals could not be distinguished from the normal in terms of the rate of production or absorption of CSF. The reason for this is that the intraventricular pressure has always been considered as if it were a constant when in fact it is changing constantly. The
problem of ventricular enlargement concerns small, but very rapid, changes in intracranial contents that occur with each beat of the pulse so we have to think of these small fluctuations and the frequencies at which they occur”.

An Engineering Approach: First Principles

Let us consider this problem as one in design engineering. If we think that it is good to have the brain in a rigid container for the purposes of protection, then the hemodynamics in the brain have some unusual characteristics that are different from what we would see in any other organ in the body. Specifically, there is going to be a highly pulsatile inflow of blood from the arterial side, highly pulsatile pressure wave, which will end up injecting about 12 cm³ every heart beat for over about one-third of a second, because almost all of that flow happens during systole. The venous flow in the CSF intracranially is equally pulsatile. It has to be because it has to exactly match this to maintain the same amount of mass in the brain but the problem is how do we make the capillary flow as non-pulsatile as possible. These very high rates of shear and changes in direction in the flow of blood in the capillary bed would be very deleterious to the delicate capillary supply of the brain. This becomes an engineering problem. An engineer would think of this as a problem in dampening a vibration, and illustrating the need for a vibration absorber or a pulsation absorber.

How could we imagine designing such a vibration absorber? If we allow a connection between the arterial side and the venous side by, for example, putting in a vein right next to an artery or, even better, in wrapping an artery entirely within a vein, that would be one way that high frequency pulsations can go directly from the arterial side to the venous side and not pass through the capillary bed. It is very easy for any neurosurgeon to think of this: this is the cavernous sinus, and if you wondered why the artery runs through a vein there, this by a physical mechanism which could benefit from that design. A more quantitative analysis of this design of a vibration absorber reveals it to be a low-pass filter. It lets the low frequencies through, but not the high frequencies, so it may not be ideal for separating out just the pulsations related to the cardiac rate.
A second engineering solution, though, would say let’s put a mass that has to be moved between the artery and the vein and that mass could be something like cerebral spinal fluid and the amount of that fluid could be a variable and could be changed as could the elasticity in the wall. This ends up giving us a model where we can have isolation of a very particular band of the frequency spectrum that can be taken out. This can be shown mathematically. Interestingly, Hugh Davson, in 1956, really had the anatomy relevant to this figured out and here we are showing some of these notch filters, or band-stop filters with different models of how the mass must relate to the resistance and the capacitance of this system.

Experimental Demonstration of a “Notch Filter”

We have been able to look at this filtering mechanism, i.e., the transfer between the arterial blood pressure wave form and the intracranial pressure wave form using a technique called time-varying transfer function, which has been adapted in my lab by Dr. Rui Zou. We will not highlight the mathematical rigors here. The important thing is that we will be thinking of the brain as a black box system capable of translating an input signal to an output signal, and it can have a different gain for a particular frequency component within this input signal in terms of how it ends up in the output signal. Figure 6.6 shows data taken from dogs in the laboratory of Michael Egnor at SUNY Stony Brook. In this experiment, the intracranial pressure is being monitored and transiently forced to go up rapidly with an injection of CSF into the lumbar subarachnoid space. The intracranial pressure (ICP) and arterial blood pressure were recorded with high fidelity recording.

The upper graph in Figure 6.6 plots the gain of the transfer function at different values of the frequency of the energy in the blood pressure (BP) and ICP tracings, and how far the experiment has progressed (therefore it is a time-

FIGURE 6.5. Results of a dog experiment reported by Bering.7 In a model of communicating hydrocephalus, as described by Dandy, unilateral choroid plexectomy diminishes the amplitude of pressure pulsations on the plexectomized side, but mean pressure is the same on the two sides. Ventricular dilation occurs primarily on the intact side (with greater pulsations). This favors a view that pulsatile pressure waves can alter ventricular size even when the average pressure is kept constant.

FIGURE 6.6. Time-varying transfer function analysis of canine arterial blood pressure and ICP, during an increase in ICP caused by infusion of excess CSF. The so-called gain of the transfer function relates how much of the amplitude of the signal in various frequency bands. Normally (as at the beginning and end of the experiment), there is a sharp “notch” at the frequency corresponding to the animals heart rate. By mechanisms suggested in the text, movement of CSF within the intracranial system could produce a “notch filter” which would decrease the relative amplitude swings of the ICP compared with the blood pressure. The experimental addition of excess CSF, like many pathological occurrences, may perturb the notch at the correct frequency.
frequency graph, and is shown as a three-dimensional [3D] surface). If we look at this transfer function over time, we clearly see a notch which has the same properties we predicted earlier in the hypothetical model of how the CSF dynamics work. The space here where we lose the notch is a portion where this perturbation was made and this is a recoverable, changeable difference in the system. This exercise is called by engineers “system identification,” and the change in the graph describes a change in the ABP to ICP system.

Implications for Clinical Management

So, would disorders of the pulsations cause pathology? We mentioned the experiments of Bering and DiRocco previously. There are several recent examples that suggest clinical correlates. Ed Oldfield showed a mechanism whereby pulsations in Chiari malformation in the spinal space account for the shearing. Dailey and others have correlated an increase in Chiari pulsations in the spinal space accounting for the shearing previously. There are several recent examples that suggest that this is related.

I would sum up by saying that the opportunity here is for us to pay more attention to pulsatility. At age 17, Galileo made one of his greatest discoveries. While bored listening to someone speak in a cathedral, he was watching a chandelier swing and timed it against his pulse. He discovered that the timing of the swing depended on the length of the arm of the pendulum and nothing else, and this became the principle model for the physics of harmonic oscillations and, indeed, everything discussed in this talk. The invention of the pendulum clock fostered our modern concept of time. The moral of the story is to attend to your pulse. We think that neurosurgeons can and will be doing more of this in the future.

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