Clinical Advances in the Management of Patients with Severe Head Injury*

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Some of the physiological properties of the cerebral circulation, intracranial pressure and brain metabolism, as well as some of the pathophysiological alterations that we see with various types of brain injuries have been discussed in this series. We are going to see how we can apply some of this information clinically. I will begin with a patient.

A patient, comatose following a severe head injury, is brought into the emergency room. Our method of managing these patients has evolved over a number of years. Although I shall present the procedure to you sequentially, in fact, much is done virtually simultaneously. As always, the first thing that one must attend to is the airway. The majority of comatose head-injured patients, upon admission to the emergency ward, have a hyperventilation syndrome. It is of primary necessity, in this situation, to obtain an arterial blood sample for measurement of Pa_{O_2}, Pa_{CO_2}, and pH. Frequently, the patient is hypocapnic, with a Pa_{CO_2} of perhaps 30, and is hypoxic as well. In a large series from several clinical units, the average Pa_{O_2} of several hundred patients at the time of admission was about 65-70 mm Hg— somewhat hypoxic but generally not severely so.

How can the patient be hyperventilating, be hypocapnic, and hypoxic at the same time? Nearly all of these patients have some degree of pulmonary arteriovenous shunting but are able to eliminate the CO_2 with their relatively inadequate respirations, because CO_2 diffuses across the alveolar membrane at twenty times the rate of oxygen. At the same time, they are not able to get enough O_2 into the blood. Hypoxia and hypocapnia are a very common pulmonary syndrome in these patients.

If the patient looks as though he is severely brain injured and is not going to recover soon, we go straight to intubation after drawing the arterial blood gas. The patient's airway is cleaned and he is then ventilated with an Ambu® bag. By now, someone is taking the blood pressure and the heart rate. If the patient has a mass lesion, then, in a majority of cases, he has a so-called Cushing response consisting of arterial hypertension. He may or may not have bradycardia; in fact, in our experience, in the acute brain injured patient, tachycardia is more common than bradycardia, except in those patients with acute extradural hematomas. A decision must be made now as to how to manage the patient over the next hour. We give dexamethasone (10 mg IV), although I am not at all convinced that the patients are benefitted by it. If the patient is in extremis, we give 1.5 mg/kg of hypertonic mannitol by IV push, in the hope of buying time for angiography. We like to have angiography for all of these patients as soon as possible. It must be remembered, however, that if done within an hour or two of the injury, one may miss the hematoma that is in the process of developing. If the neurosurgeon in charge feels that there is not time for an angiogram, the surgeon may perform exploratory burr holes. We avoid this operation if possible, since we feel that angiography gives so much information. (The technique mentioned in Dr. Vries' presentation of inserting a ventricular cannula, injecting some air, and then treating the patient immediately, depending

upon what that air study shows is impressive; if the patient has a shift, take him directly to the operating room.) If the patient does not have a mass lesion, a Scott cannula is placed through a twist drill hole into the anterior horn of the right lateral ventricle, in order to measure intracranial pressure continuously. If the patient goes to the operating room and has a mass lesion removed, the Scott cannula is put into the anterior horn of the lateral ventricle at the time of surgery.

The patient is then returned to the neurosurgical intensive care unit, where we go through a number of procedures which will constitute the bulk of my discussion. Figure 1 is simply an artist's sketch of the Scott cannula in the anterior horn of the right lateral ventricle at the level of the coronal suture. Again, Figure 2 is an artist's sketch of the patient in the intensive care unit with the head dressing and the Scott cannula. The transducer is wrapped in a sterile towel because there is a risk of infection from an inside-outside connection of CSF, and this requires meticulous technique. In 350 cases, we have had an infection rate of about 2%, which compares favorably with Lundberg's 1.6% infection rate in something

Fig. 2

over 1,000 patients with continuous recording of intracranial pressure. We would like to get rid of the intraventricular cannula, because we consider 2% to be still too high, but we do not feel, at this time, that there is an adequate solid state transducer for measuring intracranial pressure.

Figure 2 also shows a two channel strip chart recorder. One channel records the intracranial pressure and the other, systemic arterial pressure from a catheter in either the radial or the brachial artery.

At this point, we prepare to do regional cerebral blood flow and metabolism studies. We use the ^{133}Xe clearance technique, in order to measure regional cerebral blood flow (RCBF). Xenon is injected through a catheter placed under fluoroscopic control into the internal carotid artery and the xenon is then injected as a bolus. The xenon enters the brain, diffuses into the brain tissue, and is then cleared from the tissue over a period of about 15 minutes. The rate of clearance from each region under study determines the blood flow; therefore, the faster the rate of clearance, the faster the flow. There are a number of ways of examining and analyzing these clearance

Fig. 1

curves. We feel, for our purposes, that eight probes for measuring RCBF over each hemisphere are perfectly adequate. There are, however, extremely sophisticated systems in which it is possible to measure the RCBF from as many as 250 regions.

In addition, a second catheter is placed percutaneously into the jugular vein and passed well up into the intracranial space, into the sigmoid sinus, in order to obtain a cerebral venous blood sample. Periodically during the course of the clinical investigation, simultaneous samples of blood are taken from the artery (from the internal carotid artery, in this case) and from the jugular bulb, from which it is possible to calculate the cerebral metabolic rate of oxygen (CMR_{O_2}). Studies on the cerebral metabolic rate of glucose, lactate, and pyruvate have been done as well. In fact, if one's techniques are sophisticated enough, accurate enough, in theory at least, it is possible to measure anything that the brain utilizes by measuring the content in both the arterial blood and the cerebral venous blood. Here we shall discuss only CMR_{O_2}, oxygen utilization. First, we determine the O_2 content in both the arterial and venous samples; CMR_{O_2} is equal to the arteriovenous difference of oxygen content times the mean cerebral blood flow divided by 100.

Table 1 shows a selection of the normal values, such as CBF, approximately 50 ml/100 gm/min, systemic arterial pressure, about 85. We defined, as have others, normal intracranial pressure as less than 200 mm CSF or less than 15 mm Hg. The cerebral perfusion pressure, assuming an ICP of 10, is 75 mm Hg, the normal arterial-venous oxygen difference (AVD_{O_2}) is 7—a figure to remember. The CMR_{O_2} is 3.5 ml/100 gm/min and the normal values for arterial blood gases and pH are familiar to you.

For the sake of example, a single patient will now be described in detail.

A 50-year-old man had been found on the street and was brought into the emergency ward comatose; he had bruises about the head, indicating that he had been bludgeoned, and there were clinical signs pointing to a left hemispheric mass with evidence of transtentorial herniation. He was given dexamethasone and mannitol and was intubated and ventilated with the Ambu® bag. The resident who was caring for him felt that he was in extremis, that there was not enough time to do an angiogram, despite the administration of mannitol; therefore, the patient was taken to the operating room for burr holes. There was no evidence of an extracerebral

TABLE 1

Normal values of variables tested

Variable	Normal Value
cerebral blood flow (CBF)	50 ml/100 gm/min
systemic arterial pressure (SAP)	85 mm Hg
intracranial pressure (ICP)	15 mm Hg (200 mm CSF)
cerebral perfusion pressure (CPP)	75 mm Hg
cerebral vascular resistance (CVR)	1.70
arteriovenous blood oxygen content (AVD_{O_2})	7.0 vol %
cerebral metabolic rate (CMR_{C_2})	3.5 ml/100 gm/min
arterial carbon dioxide partial pressure ($PaCO_2$)	40 mm Hg
arterial oxygen partial pressure (PaO_2)	100 mm Hg
arterial blood acidity (pH)	7.35

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hematoma; the resident needled the brain one time and got no blood, and the Scott cannula was put in along with a solid state transducer to measure intracranial pressure. The patient was then taken to the angiography suite, where we also do the RCBF and metabolism studies. On angiogram, the patient had a huge, temporal and deep mass in the hemisphere. The Scott cannula was, in this case, placed through a burr hole in the lateral ventricle. While the angiogram was being developed, we carried out our first RCBF and metabolism study.

Figure 3 demonstrates one of the ways in which we display the data. You will note that this patient, during the control period, had a mean CBF of 10 ml/100 gm/min, one-fifth normal and far below that ordinarily required to maintain brain function. The patient's mean systemic arterial pressure was 135 mm Hg, and the mean intracranial pressure extremely high at 107 mm Hg, giving the patient then a cerebral perfusion pressure (CPP) of 28. Note that at this time, the Pa_{O_2} is quite adequate at 104 and the Pa_{CO_2} is slightly low. The value for CMR_{O_2}—0.71—is one-fifth normal. One can state as a general rule, with the occasional rare exception, that any patient with CMR_{O_2} less than 1.0 probably will not survive.

The angiogram showed the huge mass which had been missed in the operating room with the single pass of the needle. The needle was then inserted into the region of the mass and we obtained 70 cc of blood. A second postevacuation study was per-
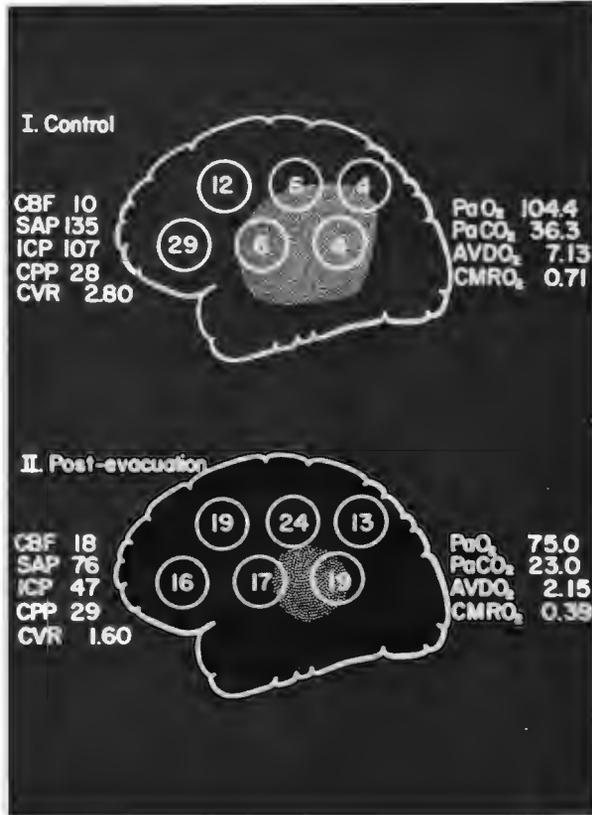
Fig. 3

formed, disclosing the reduced mass with the estimated increase in CBF from 10 to 18 ml/100 gm/min. In the region of the mass, where blood flow was virtually obliterated, we had a fourfold increase from 6 to 24 ml/100 gm/min. The intracranial pressure dropped from 107 to 47 mm Hg following evacuation of the mass. If we were measuring only the ICP, we might feel we had really accomplished something. The systemic arterial pressure, however, was being held up by a Cushing response, secondary to the intracranial hypertension. Although we markedly reduced the intracranial pressure, the blood pressure fell equally, and the perfusion pressure went only from 28 to 29; despite that, we did increase CBF by 8 ml/100 gm/min.

Now, however, another problem arose. The patient, comatose but showing slight evidence of arousal, went from flaccidity to some decerebrate posturing; he also began to hyperventilate, driving his Pa_{CO_2} from 36 down to 23, but, at the same time, he developed acute pulmonary edema. Even though he was hyperventilating and producing hypocapnia,

because of the edema, we now saw his Pa_{O_2} dropping also, from 104 to 75.

Despite the improvement in the CBF and some evidence of clinical improvement, the patient's CMR_{O_2} actually fell from 0.71 to 0.39, which is barely one-tenth of normal. We tried to raise his blood pressure, hoping to improve his perfusion pressure and further improve his CBF, then at 18. Figure 4 shows the response following angiotensin. We brought his SAP up to 129 from 76, but the CBF increased only from 18 to 23, because, with the arterial hypertension and the edema fluid, the intracranial pressure has gone from 47 to 74 mm Hg. In order to comprehend the pathophysiology of these patients, one must measure nearly all of these variables. Despite his marked hypocapnia and hyperventilation, his Pa_{O_2} is still only 67 because of his pulmonary edema. We decided to give mannitol, and the patient, in terms of CBF, responded dramatically; CBF went from 23 to 38, perfectly adequate for a normally metabolizing brain, and ICP dropped from 74 to 48.
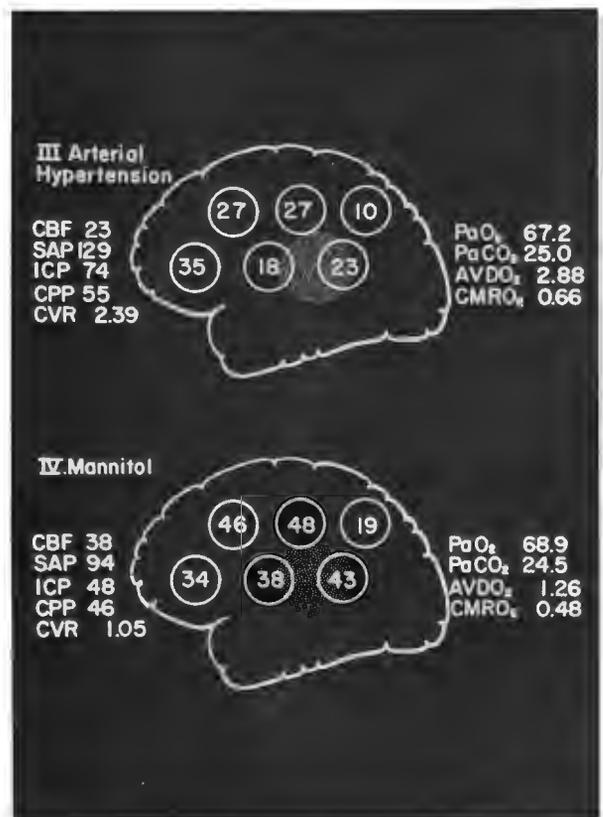

Fig. 4

Marked improvement in CBF occurred, despite the fact that the patient's perfusion pressure dropped from 55 to 46. A change in flow, of course, will occur with a change in perfusion pressure or a change in resistance or with a change in both, and, in this case, it is quite clear that the mannitol has reduced the edema, thereby opening up the microcirculation and permitting a marked improvement in CBF, despite there being no significant change in the patient's CPP. The Pa_{O_2} and Pa_{CO_2} were the same; the CMR_{O_2} was fluctuating somewhat.

We continued to battle his intracranial pressure, which, however, continued to rise, and finally, as is the rule in these cases, the intracranial pressure equaled the blood pressure. At this point, the phenomenon of nonfilling of the cerebral circulation upon angiography or injection of ^{133}X became evident. In this situation, if one injects radio-opaque media into the carotid artery, it will rise up into the internal carotid (sometimes to the level of the siphon) and then stop. A film taken 30 seconds or a minute later will show the opaque dye still sitting in the carotid artery, none having entered the intracranial space, due to the fact that ICP equals SAP and, therefore, CPP is zero. When this occurred in our patient, we decided he obviously had all of the clinical criteria of brain death. We decided, however, to manipulate the blood pressure with a vasopressor agent, Levophed®, to see whether we could possibly reestablish a perfusion pressure. These primary changes in systemic arterial pressure, produced by altering the rate of drip of a vasopressor agent, produced precisely equal changes in the ICP. There was no way to reestablish perfusion pressure by manipulating the arterial pressure. In this patient who had a severe and, as it turned out, irreversible brain injury, we were, by various types of manipulations, able to raise his CBF to something approaching a normal range, but too late, and the patient died shortly after this study.

Now, just a few comments on intracranial pressure. Until the publication of Lundberg's landmark monograph from the University of Lund in Sweden in 1960, we generally thought of ICP as being a steady phenomenon; intracranial pressure had been measured only through the lumbar subarachnoid space in the vast majority of patients. In 1963, we demonstrated in experimental animals (using a slowly expanding extradural balloon in the monkey), that when the intracranial pressure rises by virtue of expansion of a mass, a dissociation occurs invariably, between the supratentorial pressure and the pressure of the lumbar subarachnoid space. Finally, with the slow expansion of the balloon, when the intracranial pressure reached the level of the blood pressure in the monkey, lumbar subarachnoid pressure was normal. We demonstrated that this also occurs in man. The higher the intracranial pressure, the greater the brain swelling, the less likely it is that the lumbar subarachnoid pressure will reflect that increased intracranial pressure. Many times in man, lumbar subarachnoid pressure is normal when the intracranial pressure is from 50–100 mm Hg. It follows, therefore, that one cannot use lumbar subarachnoid pressure to determine the actual pressure within the intracranial space. All pressure measurements today are done directly from the intracranial space by one method or another.

Lundberg then demonstrated that in many patients, intracranial pressure is not a steady phenomenon; in fact, there are tremendous fluctuations in pressure. He described what he called "A waves or plateau waves, B waves, and C waves." For the most part, these waves appear to be rather innocuous, there being, usually, no indication of neurological deterioration. With the extremely dangerous plateau wave, the intracranial pressure is reasonably steady, at first, but then fluctuates, and finally, inexorably rises—a terminal pressure wave.

Figure 5 summarizes work that we did some 10 or 11 years ago. It is a very simple figure but quite important. This is the volume pressure graph within the
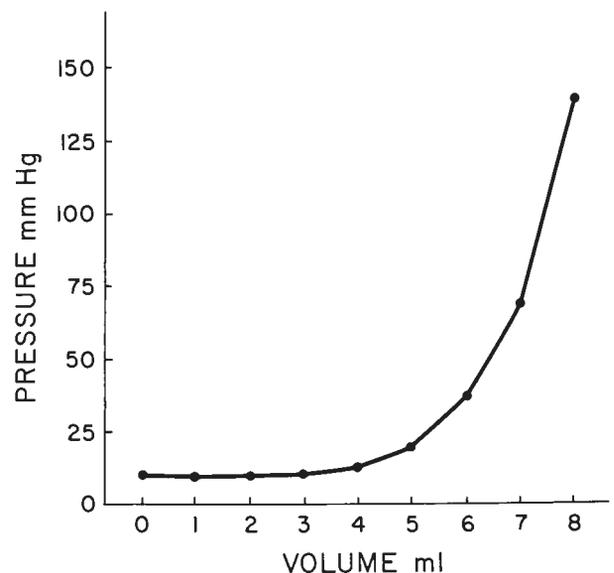

Fig. 5

intracranial space, actually taken from a series of monkeys. We put in an extradural balloon, and then slowly inflate it at a rate of 1 ml/min, while we measure the intracranial pressure. Up to a volume of about 5 ml in the balloon, there is no significant change in intracranial pressure. Why is this? Because the intracranial space contains displaceable fluid, mainly in the form of CSF but also, to some extent, in the form of intravascular blood. Since we are dealing with a cavity that is nondistensible, which is filled to capacity with a noncompressible fluid and solid material, it follows that if indeed we had a completely closed system, that is, if we had a sphere made of bone filled to capacity with water, and we attempted to inject additional water into that cavity, we could probably inject no more than 0.1 ml, in the case of the monkey; we would get a tremendous rise in intracranial pressure, simply because we cannot stretch the shell. We cannot compress the fluid. That is not the case in life. We can actually put 5 ml of fluid into this monkey's skull (total capacity of 100 ml), because of spatial compensation. It means that up to a value of about 5 ml, for every 1 ml that we are putting into the balloon, we are expressing 1 ml of CSF or blood. Then we pass from this period of spatial compensation, the horizontal portion of the volume pressure graph, onto the vertical portion. Note here that between a balloon volume of 7 and 8 ml, the intracranial pressure rises 75 mm Hg. Thus, in the case of those patients with pressure waves, those who have any kind of mass lesion or brain edema, the bulk of them are somewhere on the vertical part of the graph. The pressure waves are due to spontaneous alterations in cerebral blood volume. The pressure waves are reflecting alternating vasodilatation and vasoconstriction of the cerebral vascular bed. We do not know the reason for this. The vasodilatation produces a slight increase in cerebral blood volume. That slight increase, however, when the patient is on the vertical portion of the volume pressure graph, will produce a tremendous change in pressure. The patient who presents with a longstanding space-occupying mass, chronic subdural hematoma or meningioma, who has now reached the limits of his period of spatial compensation, therefore, may have few signs or symptoms, but he is sitting on a time bomb as it were. When he goes to sleep, for example, he becomes a little hypoxic and hypercapnic. We recorded many of these patients in sleep, and indeed, their intracranial pressure may rise astonishingly during sleep, simply because of a little bit of vasodilata-

tion from the hypercapnia. It follows as well, that if one is treating a patient who is on the vertical portion of the curve, it is necessary to remove only a small portion of any one of the volumes within the intracranial space in order to drop the pressure. We have many patients who have had pressure of 80–90 mm Hg. The removal of no more than 2 ml from the ventricle will drop the pressure down to 20–30 mm Hg, because they are falling on an extremely sharp vertical portion of the curve.

What constitutes a critical level of intracranial pressure for brain function? I have no idea, because it varies so much from patient to patient. The more the brain itself is damaged, that is, the more the edema, the more contusion, then the less tolerant that patient is of intracranial hypertension. We have many patients, for example, who would not tolerate an ICP above 25–30 mm Hg; they would obtund, develop a hemiparesis. When we then lowered the pressure to 10–15 mm Hg, they would improve. Patients who do not have brain damage but, nevertheless, have intracranial hypertension, will often tolerate extremely high levels of intracranial pressure. We have seen a young woman with severe hydrocephalus from a cerebellar hemangioblastoma. She was neurologically normal, except for minimal ataxia and some papilledema—her brain was normal. We recorded her intracranial pressure continuously through the Scott cannula and then slowly drained the ventricles over a period of two or three days, as we always do before doing posterior fossa surgery in these people. We also recorded and checked the systemic arterial pressure from the catheter in the the radial artery. For very long periods of time, the patient had a CPP as low as 6 mm Hg, the mean intracranial pressure, 85, and the mean arterial pressure, 91; this particular time, she was in the intensive care unit, sitting up reading a magazine, completely asymptomatic. This is an indication of the phenomenal degree of autoregulation that can be seen clinically.

If a hypertonic solution such as mannitol has been given to a patient without causing reduction in his intracranial hypertension, we might conclude that mannitol has been of no benefit, and not give it to that patient again. We might say that the patient is refractory to mannitol.

Often this is not the case, and the patient improves despite no major ICP fall. How can this be? We postulate that mannitol has reduced edema. Reduction of the water content in the brain alone, obviously, should result in decrease in intracranial

pressure, but if one has compression of the microcirculation of the capillary bed in the venules by the edema, and one reduces the edema, what is going to happen to the cross-sectional area of the vascular bed? It will enlarge as the compression is relieved. Our guess is that as we remove the edema from the brain with the mannitol, the edema is being replaced by intravascular blood secondary to expansion of the cerebral vascular bed. The net intracranial volume remains the same, and intracranial pressure does not decrease. What these data clearly show is that one cannot use intracranial pressure alone to determine whether or not mannitol has had a beneficial effect on the patient; one must, unfortunately, measure CBF.

The first indication for the use of mannitol therapy, in our opinion, is for reducing brain bulk during craniotomy, and second, for reducing ICP to permit time for emergency cerebral angiography. The third indication for its use is control of ICP during *continuous recording of ICP*. I believe that the intermittent, or perhaps even the continuous, use of mannitol in these patients without continuous recording of intracranial pressure is very dangerous, because if the patient has a hemorrhage, a hematoma that is expanding, reduction of the intracranial pressure causes further expansion of the hematoma; then, as the osmotic gradient is reversed, fluid comes back into a space reduced by the enlargement of the hematoma. This kind of situation can kill the patient quickly.

I will conclude by saying that I think the continuous measurement of intracranial pressure in the proper management of patients not only with severe head injuries, but with severe brain insults as well,

has passed now from being a research tool to a virtual necessity. I cannot say the same thing, yet, about measurements of RCBF and cerebral metabolism, as we are now caught in an ethical bind. We have four or five RCBF runs, or consecutive studies, done on patients over several hours. Rarely have we been able to repeat these studies, because we did not feel justified in repuncturing the carotid artery, unless it was necessary to do an angiogram on the patient. My contention is that we would learn much more from one patient with severe brain injury who has ten CBF studies over a period of several days than we would learn from ten patients who have one study each. In order to prove that these techniques, which are expensive and time consuming, are really going to help us in the management of these patients, we now need to have a reliable noninvasive technique for doing RCBF. These techniques are now available, particularly in the form of either inhalation or intravenous injection of ^{133}Xe, but the mathematics are extremely complex and must be done with a laboratory computer, but I think they are promising. In our neurosurgical intensive care unit, we are just beginning to compare the carotid injection of xenon with the inhalation of xenon, to see how well the results correspond in our patients with severe brain injuries. If we obtain a reliable noninvasive technique and can repeat the RCBF studies every hour, day and night for as long as we wish, with no harm whatsoever to the patient, we will then be able to provide the intensive treatment for these patients and the evaluation of the therapy to which we have looked forward for so long.