Relationships Between Cerebral Perfusion Pressure and Regional Cerebral Blood Flow in Patients With Severe Neurological Disorders

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Abstract:

Three patients, one with a recurrent brain tumor, one with a severe brain contusion, and one with a brain abscess, are described who had continuous monitoring of the intracranial pressure with epidural and/or ventricular pressure transducers, continuous monitoring of the blood pressure, and periodic regional cerebral blood flow (rCBF) studies by the intra-arterial $^{133}$Xenon method. A fourth patient with a severe brain contusion is described who had only blood pressure monitoring and rCBF studies. By measuring the regional cerebral blood flow and by testing autoregulation through changes in cerebral perfusion pressure and arterial $P_{CO_2}$, it is possible to reveal critical levels of cerebral perfusion pressure in the supratentorial compartment. Such measurements allow more rational evaluation of methods for control of increased intracranial pressure. The data point out that monitoring of systemic cardiorespiratory parameters for signs of cerebral compression is generally inadequate. The fact that pressure gradients may exist within the craniospinal enclosure is discussed. For this reason, before valid conclusions can be made regarding brain stem circulatory impairment at the tentorium and in the posterior fossa, the present regional techniques must be applied to these compartments also.

ADDITIONAL KEY WORDS

$^{133}$Xenon intra-arterial method autoregulation intracranial pressure

Introduction

Cerebral dysfunction associated with increased intracranial pressure has been related to ischemic hypoxia. This explanation was implied by Leyden in 1866 in his first studies of the effects of cerebral compression and has been demonstrated experimentally in many studies since then. Kocher and Cushing were the first to stress that the focal brain stem ischemia which occurs in these conditions invokes systemic circulatory responses in an attempt to compensate for the hypoxia. However, Browder and Meyers showed many years ago that these systemic circulatory changes occur only at late stages of severe brain compression. More recent studies by Johnston et al., with continuous monitoring of the intracranial pressure and the systemic arterial pressure, have stressed the inconstant relationship between these two pressures and the inadequacy of the “Cushing” response. For these reasons monitoring the parameters of blood pressure, pulse and respiration is not sufficient to estimate the degree of circulatory impairment.

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Since it is now possible to measure routinely the intracranial pressure, the clinician can have a continuous measurement of the cerebral perfusion pressure as it can be easily calculated as the difference between the mean intracranial pressure and the mean arterial blood pressure. If the relationships of these pressures are then correlated with cerebral blood flow studies, one can better judge the degree of circulatory impairment of brain tissue.

Cerebral Blood Flow and Cerebral Perfusion Pressure

Past studies relating cerebral blood flow to intracranial pressure must be considered inadequate because the cerebral perfusion pressure was estimated by the systemic arterial pressure alone, or the lumbar cerebrospinal fluid pressure alone. The value of these studies, however, lies in the findings that the blood flow to the brain stayed relatively constant until high levels of intracranial pressure or low levels of arterial pressure were reached, a phenomenon commonly termed autoregulation. Noell and Schneider demonstrated in animals that cerebral blood flow decreased after the mean arterial pressure decreased to 60 to 70 mm Hg. Ryder et al. demonstrated that in some patients the lumbar spinal fluid pressure could be increased to 70 mm Hg without clinical symptoms occurring and without an effect on cerebral blood flow.

Zwetnow was the most recent worker to relate cerebral blood flow to quantitative measurements of the cerebral perfusion pressure which he calculated from simultaneous arterial and intracranial pressure recordings. He showed that when the intracranial pressure was raised uniformly by increasing the cerebrospinal fluid pressure, no decrease in flow occurred until the intracranial pressure reached 100 mm Hg and the cerebral perfusion pressure was narrowed to 30 to 50 mm Hg. His studies demonstrate very clearly that the normal brain does not lose its capacity for autoregulation until the perfusion pressure is narrowed markedly. Zwetnow also pointed out another very important factor about autoregulation. He demonstrated that the arterial $P_{CO_2}$ is a most critical factor in regulation of arteriolar tone and must also be considered in any definition of autoregulation abnormalities.

For example, at hypercapnia the arterioles will be dilated and will not be able to autoregulate flow even when the perfusion pressure is in a normal range. This phenomenon is clearly illustrated in figure 1 showing that at high $P_{CO_2}$ flow passively follows the perfusion pressure.

In pathologic states, particularly acute brain injuries, autoregulation is also impaired. The mechanism for this type of impaired autoregulation may be similar to the mechanisms in the hypercapnic state. The findings of an autoregulatory plateau have not
been uniform in the literature. The experimental studies of Langfit et al.\(^\text{18}\) and Baldy-Moulinier et al.\(^\text{19}\) showed that the blood flow decreased concomitantly with intracranial pressure increases. These findings are best explained by loss of autoregulation associated with brain lactoacidosis. Combinations of perfusion pressure, \(CO_2\) reactivity abnormalities, and focal changes in autoregulation explain the paradoxical flow changes around focal lesions. Brock\(^\text{20}\) and Reulen\(^\text{21}\) have demonstrated areas of both decreased and increased flow around focal cold or pressure lesions which cause combinations of tissue hypoxia with subsequent lactoacidosis, edema and impaired autoregulation. These studies also point out that the state of autoregulatory processes can be different in various areas of the brain. Moreover, the persistence of impaired autoregulation after an acute brain injury can vary.\(^\text{22}\), \(^\text{23}\), \(^\text{24}\)

It must also be pointed out that in many conditions low cerebral blood flow is found which is not associated with impaired autoregulation or \(CO_2\) reactivity. In conditions in which cerebral function is depressed, such as drug effects or states in which the brain has sustained past damage with loss of neuronal tissue, the metabolic rate of the brain will be low and the cerebral blood flow concomitantly depressed.\(^\text{24}\), \(^\text{25}\)

The context of the prior studies suggests that perfusion pressure affects cerebral blood flow when either the perfusion pressure is low or \(CO_2\) reactivity is absent. When autoregulation is impaired, control of the perfusion pressure is necessary to prevent decreases of the blood flow to levels which cause tissue hypoxia.\(^\text{26}\) This is particularly important in acute brain injuries in which it cannot be assumed that the cerebral blood flow is decreased due to a low metabolic demand.

The purpose of this report is to emphasize the necessity of monitoring the cerebral perfusion pressure and defining regional cerebral blood flow characteristics in neurosurgical patients. This is of increasing importance with the more prevalent use of controlled respiration in the treatment of central nervous system lesions.\(^\text{26}\)

**Methods**

The findings presented in this paper are selected from four of a series of 13 patients, all with severe brain disorders, 12 of whom were having the intracranial pressure monitored. The etiology of the central nervous system lesion was trauma, recurrent tumor, and brain abscess. Each of the patients had mechanically assisted respiration during part or all of the time he was studied. Two of the described patients died and two survived. The remaining nine patients are not described as the intracranial pressure was so high that the cerebral blood flow was unmeasurable. The intracranial pressure was monitored with a miniature pressure transducer which was introduced between the bone and the dura through a coronal perforator opening.\(^\text{27}\) The transducer was calibrated prior to insertion and recalibrated after removal. The time of recording varied from several hours to more than ten days. The maximum zero drift of the transducer was 5 mm Hg per 24 hours of recording. However, the zero drift over the longest recording time of ten days was only 15 mm Hg. Two of the four patients had the epidural pressure and ventricular pressure monitored simultaneously. Generally the epidural pressure was 5 to 15 mm Hg higher than the ventricular pressure. This has also been the experience in large series of comparisons except in a few cases where the two pressures are equal. The characteristics of the epidural or brain surface pressure have recently been discussed by Schettini et al.\(^\text{28}\) Other comparisons of ventricular pressure and epidural pressures have reported similar differences.\(^\text{29}\)

The normal intracranial pressure was established as 1 to 10 mm Hg in accordance with the large series of Lundberg.\(^\text{6}\) In patients with elevated intracranial pressure, the pressure recording showed an increase in the amplitude of the periodic changes which normally correspond to an integration of the arterial, venous and respiratory pulsations. When the intracranial pressure became markedly elevated, it directly followed changes in the arterial pressures. In this situation the brain tissue appears to act as a passive transmitter of the arterial pressure. This condition was defined as loss of regulation of intracranial pressure.

The mean intracranial pressure was determined by intermittent mechanical damping of the intracranial pulsations or calculated as one-half of the difference between the high and low peaks added to the height of the low peak. The arterial pressure was monitored by either the standard cuff technique or by an intra-arterial catheter in the radial or the internal carotid artery in patients who had reached a terminal state. The cerebral perfusion pressure (PP) was calculated as the difference between the mean intracranial pressure (ICP) and the mean arterial blood pressure (MABP).
The regional cerebral blood flow (rCBF), as measured by the $^{133}$Xenon method, has been described extensively in previous publications. In the patients who were not in terminal condition, the CBF study was performed in conjunction with cerebral angiography. A Teflon catheter, through which 2 to 3 mCi of $^{133}$Xenon dissolved in saline was injected, was placed percutaneously in the internal carotid artery by the Seldinger technique. The clearance was recorded with 14 NaI (TI) scintillation detectors placed over the cranial vault. In patients considered to be in a terminal state, the internal carotid catheter was left in place for up to 11 hours for continuous monitoring of the intracranial pressure and for multiple rCBF studies depending on changes in both the patient’s condition and the perfusion pressure. The rCBF was calculated by the height over the area method using the ten-minute clearance curve. The rCBF initial was calculated from the initial part of the clearance curve as described by Olesen et al., who have demonstrated the close correlation between the flow values calculated by ten-minute and initial slope methods. With each rCBF determination arterial blood was taken for determination arterial blood was taken for determination of the $P_{\text{CO}_2}$ and $O_2$ content. In several cases, jugular puncture was performed and jugular venous blood removed for determination of the $O_2$ content and calculation of the arterial-venous $O_2$ difference. When this determination was made, the oxygen utilization ($\text{CMRO}_2$) was calculated as the multiple of the mean rCBF and the ipsilateral A-V $O_2$ difference.

Generally each series of rCBF studies was followed or preceded by a cerebral angiogram.

**Case Reports**

**CASE 1**

This 52-year-old woman had a right frontal oligodendroglioma removed nine years prior to admission. She did well until one year before admission when she gradually developed marked mental changes. She was admitted in a state of stupor. Angiography and air encephalography showed evidence of a recurrent right frontal tumor. It was elected not to reoperate. The patient gradually deteriorated over 24 hours. The epidural pressure transducer was placed over the right hemisphere and a closed left ventricular puncture was performed, without removal of fluid, with a catheter attached to another pressure transducer. The left internal carotid artery was cannulated.

Clinical examination at that time showed an unconscious patient who reacted to noxious stimuli with purposeful movements of all extremities. Cranial nerve examination showed the pupils fixed and dilated with absent eye movements. Corneal and cough reflexes were present. Spontaneous respiration was present but was assisted with a volume respirator. The first flow study over the hemisphere opposite the tumor was performed two hours after pressure recording was started. At that time no cranial nerve reflexes could any longer be elicited although some spinal reflexes persisted. The EEG showed slow cortical activity. The PP was 70 mm Hg with the ICP elevated to 40 mm Hg and the MABP to 110 mm Hg. The rCBF was in average 21 ml/100 gm/min with no regional differences. The arterial $P_{\text{CO}_2}$ was reduced to 22 mm Hg and the A-V $O_2$ difference was 11.4 vol% showing a normal vasoconstrictor response to hypocapnia. In spite of this appearance of normal vessel $CO_2$ reactivity there was loss of regulation of ICP at this stage in that the intracranial pressure followed both the rapid and slow changes in arterial pressure. This finding suggested a pressure passive vascular bed. Over a period of two and one-half hours the ICP gradually increased to 80 mm Hg while the MABP showed a Cushing response and also increased, maintaining the PP at 50 to 60 mm Hg. This rise was followed by an abrupt fall of the MABP to 80 mm Hg. The ICP fell also but to a lesser degree so that the PP narrowed to 25 mm Hg and $^{133}$Xenon clearance started to increase. Removal of ventricular fluid further increased the PP to 80 mm Hg resulting in a further increase in flow as determined by increased $^{133}$Xenon clearance.

The MABP remained high but the ICP gradually increased over a period of two hours following which the MABP fell. It was again elevated with vasopressor agents but the PP remained narrowed at 15 mm Hg. At this stage $^{133}$Xenon was injected. The flow ($r\text{CBF}_{\text{initial}}$) averaged 9 ml/100 gm/min. Withdrawal of ventricular fluid twice, at three-minute intervals, resulted in increases of the PP to 25 mm Hg and 50 mm Hg followed by increases of $^{133}$Xenon clearance rate. The ICP continued to climb back up. When the PP reached zero, $^{133}$Xenon was injected again. The appearance of the clearance curve suggested that the $^{133}$Xenon did not enter the cranial vault, but refluxed into the external carotid system. Aortocervical angiography showed no entrance of contrast material into the cranial vault.

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*Values for initial portion of clearance curve—see case history.
Comment
This case illustrates the effect of perfusion pressure variations on blood flow in brain tissue subjected to increased ICP. The PP studied ranged from normal values to zero with most values in the interval where abolished autoregulation is expected from animal studies. As shown in figure 2, the changes in perfusion pressure were due both to fall in blood pressure and to increasing intracranial pressure. The absence of regional flow differences is probably explained by the fact that the tumor was located in the opposite hemisphere. However, global depression of flow was present at a time when the perfusion pressure was 70 mm Hg, i.e., a value which would allow a normal flow in healthy brain tissue. However, a significant factor in decreasing the flow to 21 ml/100 gm/min at this stage may have been the hyperventilation which lowered the arterial P_{CO_2} to 22 mm Hg. The high A-V O_2 difference of 11.4% resulting in oxygen utilization of 2.4 ml/100 gm/min, 73% of normal, tends to confirm the conclusion that the cerebral vessels at this point displayed a normal reactivity to hypocapnia. At two and one-half hours, the perfusion pressure was the dominant factor reducing flow. This is shown in figure 3. The systemic pressure fell precipitously, narrowing the perfusion pressure to 15 mm Hg. The initial clearance of ^133^Xenon was slow with a calculated rCBF initial of 6 ml/100 gm/min. The perfusion pressure was then increased first by raising the arterial pressure with a vasopressor, and second, by ventricular drainage. With both maneuvers, an increase in ^133^Xenon clearance occurred (evidence of an increase in flow).

CASE 2
This 26-year-old woman was admitted in coma following a suicide attempt in which she jumped from the third floor. Initial examination showed a comatose woman with marked nasopharyngeal bleeding. The blood pressure was 60/40, the pulse rate 130/min, and the respirations rapid. The ICP was not measured. Both pupils were dilated and

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**FIGURE 2**
*Case 1, illustrating the time course of cerebral perfusion pressure changes, CBF studies and aortocervical arteriography. The upper two solid lines illustrate the duration of cephalic and spinal reflexes. The third solid line illustrates the time of EEG recording and the interpretation.*
PERFUSION PRESSURE AND \( r \)CBF

\[ \text{FIGURE 3} \]

Case 1, illustrating the logarithmic display of the \( ^{133} \)Xenon clearance curves, from which the \( r \)CBF \(_{\text{initial}} \) is calculated, related to the cerebral perfusion pressure. CBF 1 shows the normal clearance curve with a stable perfusion pressure, while CBF 2 and CBF 3 show the increases in clearance which occur when the perfusion pressure is increased by ventricular drainage.

fixed and there were absent eye movements. Cough reflex was present. She repelled noxious stimuli with appropriate movements of all extremities and had normal tendon reflexes. An endotracheal tube was placed and multiple blood transfusions were administered. Skull films showed frontal comminuted fractures through the sinuses and orbital roofs. A chest film showed a fractured sternum and extremity films showed fractures of the left femur and the left radius. A right carotid arteriogram showed a small vertex epidural hematoma. Following angiography the CBF was measured. The MABP at the first CBF study was 40 mm Hg and the \( r \)CBF \(_{\text{10}} \) was 37.5 ml/100 gm/min. With rapid intravenous infusion of whole blood and balanced lactate solution over 30 minutes, the MABP raised to only 50 mm Hg. Nevertheless, the \( r \)CBF \(_{\text{10}} \) was increased to 49.7 ml/100 gm/min. Both studies showed focal areas of decreased flow frontally. The arterial \( P_{\text{CO}_2} \) was 42.5 mm Hg and 40.4 mm Hg at the first and second study, respectively. The A-V \( O_2 \) difference measured simultaneously with the second study was 4.2 vol %, yielding a CMRO \(_2 \) of 2.07 ml/100 gm/min. Following the CBF measurements a repeat chest film showed a left pneumothorax and a chest tube was placed. Her respirations improved slightly and the blood pressure rose to normal levels. The following day the pupils were small and reactive and dysconjugate eye movements were present. The patient could follow simple commands but was stuporous. She continued to have respiratory insufficiency and following a tracheotomy was treated with assisted ventilation for four days during which the arterial \( P_{\text{CO}_2} \) averaged 32 mm Hg. She gradually improved, and six weeks following the injury, she was alert with normal speech and good mentation. Bilateral dysconjugate gaze was still present. Her fractures were healing well. She was eventually discharged for rehabilitation.

Comment

This case illustrates most dramatically the critical range of perfusion pressure superimposed on an acutely damaged brain which has autoregulation abolished clearly on the basis of a low perfusion pressure but also possibly on the basis of tissue acidosis associated with trauma. With an MABP of 40 mm Hg the \( r \)CBF \(_{\text{10}} \) was 37.5 ml/100 gm/min. A minimal increase of the blood pressure to 50 mm Hg resulted in a flow increase to 49.7 ml/100 gm/min. If one considers that at this stage the ICP at the lowest would have been 10 mm Hg, one could assume that the PP was not more than 40 mm Hg. Although the flow was normal at this stage the A-V \( O_2 \) was decreased to 4.2 vol % with a CMRO \(_2 \) of 2.07 ml/100
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gm/mni, 63% of normal. With this evidence of subnormal oxygen extraction in the presence of normal flow, one can conclude that a "luxury perfusion state" existed presumably from tissue acidosis since the $P_{\text{CO}_2}$ was normal. The question can be asked if this high flow could in fact be deleterious, and once the blood pressure was elevated to normal, would the brain with presumably even higher flow be prone toward edema formation. Although the patient was improved on the second post-trauma day, her most marked improvement occurred during the four-day period of assisted ventilation. During this stage she was rendered mildly hypocapnic. Although no flow or A-V O$_2$ difference measurements were made during this treatment, one could presume that the relatively high flow state was counteracted, as she progressed to complete recovery except for mild ocular palsies.

Case 3

This 16-year-old boy was struck by an automobile while riding his bicycle. He had no severe complaints initially, but was found unconscious in his bed the next morning. After a right frontal epidural hematoma was removed through a burr hole at a local hospital, he was transferred to the neurosurgical service where the frontal lobe was further decompressed by hematoma removal through a craniotomy. Following surgery he remained unconscious with decerebrate posturing and active tendon reflexes. Cranial nerve examination showed the left pupil small, the right pupil dilated, both nonreactive, absent eye movements, and absent vestibular response to ice water. Corneal and cough reflexes were present. Spontaneous respirations were present but inadequate; he was hyperventilated with a volume respirator through a nasotracheal tube. Recording of the epidural and intra-arterial pressure was started 30

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**FIGURE 4**

Case 3, illustrating the time course of cerebral perfusion pressure narrowing, CBF studies and aortocervical arteriography. The upper solid lines illustrate the duration of cephalic and spinal reflexes. The third solid line illustrates the time of EEG recording and the interpretation. It can be seen that the perfusion pressure narrows to zero and remains negative two minutes after CBF 5 is started.
PERFUSION PRESSURE AND rCBF

hours after the injury (fig. 4). The first CBF study was performed one hour later, at which time the PP was 70 mm Hg. The average rCBF10 was 42 ml/100 gm/min. The P\textsubscript{O\textsubscript{2}} was 24 mm Hg. Marked interregional differences were present along with the decerebrate posturing and the evacuation of the hematoma. The average rCBF\textsubscript{initial} was 68 ml/100 gm/min in the frontal area and 31 ml/100 gm/min in the parietal area. The A-V \textsubscript{O\textsubscript{2}} difference was 3.7 vol % and the CMRO\textsubscript{2} was 1.55 ml/100 gm/min. These measurements suggested a "luxury perfusion" syndrome. His clinical condition did not change. However, it was considered that this respiratory activity was sufficient and the respirator assistance was stopped six hours later. An angiogram at that time showed absence of a hematoma. An early vein was noted in the frontal area. The second CBF study was performed 11 hours after the first. At that time his clinical condition was unchanged. The P\textsubscript{O\textsubscript{2}} had increased from 24 mm Hg to 36 mm Hg. The PP had decreased to 42 mm Hg to a decrease in the MABP rather than to a change in the ICP which remained at 40 mm Hg. The average rCBF\textsubscript{10} decreased minimally to 39 ml/100 gm/min. The regional differences were less marked in this study due to an increase in the rCBF\textsubscript{initial} to 44 ml/100 gm/min in the parietal region compared to a slight decrease in the frontal region to 62 ml/100 gm/min. This finding in conjunction with the first CBF study demonstrated hyperemia with impaired \textsubscript{CO\textsubscript{2}} reactivity and loss of autoregulation in the frontal regions and better preservation of autoregulation and \textsubscript{CO\textsubscript{2}} reactivity in the parietal area. The A-V \textsubscript{O\textsubscript{2}} was 5.85 vol % with the CMRO\textsubscript{2} 2.27 ml/100 gm/min. Although the patient's prognosis was poor, it was felt that his clinical condition had remained stable, and the intracarotid catheter was removed. Over the next two days the ICP remained unchanged. The clinical state did not change. However, it was considered that this respiratory activity was sufficient and the respirator assistance was stopped. The P\textsubscript{O\textsubscript{2}} had increased from 24 mm Hg to 36 mm Hg. The PP had decreased to 42 mm Hg to a decrease in the MABP rather than to a change in the ICP which remained at 40 mm Hg. The average rCBF\textsubscript{10} decreased minimally to 39 ml/100 gm/min. The regional differences were less marked in this study due to an increase in the rCBF\textsubscript{initial} to 44 ml/100 gm/min in the parietal region compared to a slight decrease in the frontal region to 62 ml/100 gm/min. 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Corneal reflexes were still present along with the decerebrate posturing and upper extremity tendon reflexes. The right internal carotid artery was recannulated. The ICP tended to follow the rapid variations in the MABP and slower variations in respiration, demonstrating the loss of regulation of ICP which occurs at increased ICP levels. When the PP narrowed to 40 mm Hg (ICP to 80 mm Hg) the third CBF study was performed. The mean rCBF\textsubscript{10} was 31 ml/100 gm/min with similar interregional differences recorded (as noted in the two earlier studies). No jugular blood was obtained for \textsubscript{O\textsubscript{2}} analysis. The fourth CBF study was performed 50 minutes later, at which time the MABP had fallen to 75 mm Hg narrowing the PP to 15 mm Hg. The mean rCBF\textsubscript{10} was 20 ml/100 gm/min. Interregional differences were no longer seen. The clearance curves appeared monoeponential. This finding was interpreted as a preferential decrease in the fast flow compartments as compared to slow compartments. The clinical state was unchanged. The EEG showed slow depressed cortical activity. The fifth CBF study was performed when the PP narrowed to 8 mm Hg. The mean rCBF\textsubscript{10} was 4.3 ml/100 gm/min. However, two minutes after the injection of \textsuperscript{189}Xenon, the perfusion pressure narrowed to zero and no further clearance of \textsuperscript{189}Xenon occurred over the next ten-hour observation period, implying that complete and permanent cessation of blood flow was recorded in this study. The EEG performed ten minutes after the \textsuperscript{189}Xenon injection was flat. No further corneal or cough reflexes were present and no movements were elicited with noxious stimuli. Upper extremity tendon reflexes persisted, however.

Aortocervical angiography showed no passage of contrast material into the cranial vault. One hour after the angiogram, with a negative PP of —10 mm Hg, no further \textsuperscript{189}Xenon could be injected into the cranial vault. Cardiac action ceased five hours later.

**Comment**

This case demonstrates a wide spectrum of abnormalities. There are regional differences in flow, autoregulation, and \textsubscript{CO\textsubscript{2}} reactivity when the perfusion pressure is above 40 mm Hg. However, when the perfusion pressure falls below the normal autoregulatory range, the flow in the whole hemisphere becomes dependent on the perfusion pressure. This is shown in figures 5 and 6. The first CBF study showed that in the right cerebral hemisphere, the one most directly subjected to compression by the epidural hematoma, the frontal and parietal areas had significantly different flow patterns. As the arterial P\textsubscript{CO\textsubscript{2}} was 24 mm Hg, one could conclude that in the frontal area loss of autoregulation and \textsubscript{CO\textsubscript{2}} reactivity was present, while in the parietal area the vessels were able to constrict to the hypocapnic stimulus. This conclusion was confirmed by the second study, at which time the P\textsubscript{CO\textsubscript{2}} was elevated to 36 mm Hg and the PP narrowed to 42 mm Hg and flow increased in the parietal area but decreased in the frontal area. At this PP and P\textsubscript{CO\textsubscript{2}} level the luxury perfusion condition was relatively improved with an increase of CMRO\textsubscript{2} to 2.27 ml/100 gm/min. In
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Case 3, illustrating the logarithmic display of the first two minutes of the regional \(^{133}\)Xenon clearance curves from which the rCBF\(_{\text{initial}}\) is calculated. In CBF 1 to CBF 3 the marked differences in the slope of the curves between the frontal and parietal areas are obvious. In CBF 4 the rate of clearance is decreased (lower flow) and no further differences are noted. The average rCBF\(_{\text{final}}\) of all channels, the average rCBF\(_{\text{initial}}\) in the frontal and parietal regions, and the MABP, ICP, PP, and P\(_{\text{CO}_2}\) are noted for each study.

Case 4

This 52-year-old man was admitted for evaluation of seizures. He showed the effects of chronic alcoholism and had received treatment for a seizure disorder with anticonvulsants for several years. He had chronic lung disease and had been hospitalized one year previously for a lung abscess. One week before the present admission he was noted to have left arm weakness. On admission he was afebrile and stuporous, with
poor respiration and a left hemiparesis. An angiogram showed a right posterior frontal mass and a lumbar puncture showed elevated pressure, clear fluid, 500 polynuclear cells and 258 mg % protein. Through a perforator opening an abscess was drained. The cavity was small and marked cerebritis was noted. Penicillin and Pantopaque were placed in the abscess cavity. He was treated with systemic antibiotics and anticonvulsants. The following day he was more alert but the hemiparesis was unchanged. Over a period of days he became more obtunded and respiratory insufficiency developed. The abscess cavity was repunctured and a brain scan showed a single lesion. Cultures produced no growth. A nasotracheal tube was placed and respiratory assist with a volume respirator was instituted. The following day, an epidural pressure transducer was placed in the right frontal area. Closed cannulation of the left ventricle was also performed for both pressure monitoring and control. A catheter was placed in the right internal carotid artery. Clinical examination showed a comatose patient unable to follow commands. The pupils were equal and the ocular movements were intact. A left central facial and left arm paresis were present with left hyperreflexia and Babinski response. At the first CBF study, the MABP was 115 mm Hg and the epidural pressure 78 mm Hg, resulting in a PP of 37 mm Hg. The arterial $P_{CO_2}$ was 27 mm Hg. The average $rCBF_{initial}$ was 14.5 ml/100 gm/min with the decreased flow more marked in the posterior frontal region. The PP was increased to 95 mm Hg by the removal of ventricular fluid, resulting in an increase in the average $rCBF_{initial}$ to 21.3 ml/100 gm/min, the most marked increase occurring in the area with the largest focal decrease. Even though an increase in flow occurred with ventricular drainage, all values remained markedly low. The ventricular fluid was clear and had 6 polynuclear cells/mm$^3$ and 45 mg % protein.

An angiogram following the flow study showed persistence of the mass effect and mild narrowing of the vasculature consistent with an infectious process. The high intracranial pressure was treated with periodic intravenous administration of mannitol and ventricular fluid drainage. Five days later the patient was awake; his respiratory status was improved but he still had a marked left hemiplegia. A CBF study and angiogram was again performed. At the first CBF measurement at this occasion the ICP was still elevated to 70 mm Hg but the MABP had increased to 136 mm Hg, raising the PP to 66 mm Hg. The arterial $P_{CO_2}$
was 19 mm Hg. The average rCBF was 17 ml/100 gm/min with persistent focal decreases. Raising the PP to 110 mm Hg by removing ventricular fluid resulted in an insignificant increase in the average rCBF to 18 ml/100 gm/min. An EEG the following day showed marked slowing and depressed amplitude over the whole right hemisphere. The patient continued to become more alert and was able to communicate and write. He was gradually taken from the respirator. The dense left hemiplegia persisted. A repeat angiogram showed marked diminution of the mass effect. He was discharged to a local hospital for rehabilitation.

**Comment**

This case illustrates the effect of PP as the brain disorder progresses from an acute to a chronic stage. This is shown in figure 7. The initial study showed markedly decreased flow in the whole right hemisphere greatest in the area of the abscess. The low PP of 37 mm Hg was a factor in the flow decrease, and increasing the PP by removing ventricular fluid resulted in a marked

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**SL 3-71 CBF and PERFUSION PRESSURE**

**FLOW 1**

- **mean rCBF**
  - 14.3 ml/sec/gm/min
- **MABP**
  - 115 mm Hg
- **ICP**
  - 78
- **PP**
  - 57
- **pCO<sub>2</sub>**
  - 27

**FLOW 2**

- **mean rCBF**
  - 21.3 ml/sec/gm/min
- **MABP**
  - 136 mm Hg
- **ICP**
  - 70
- **PP**
  - 60
- **pCO<sub>2</sub>**
  - 19

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**FIGURE 7**

Case 4, illustrating the first and second CBF studies. In the lower right is the brain scan performed one day after the first CBF study. Flow 1 shows the flow increase which occurs when the PP is increased from 37 mm Hg to 95 mm Hg, particularly in ischemic focus correspondent to the abscess. Flow 2 shows that no significant flow increase occurs with an increase of the PP from 66 mm Hg to 110 mm Hg.
PERFUSION PRESSURE AND rCBF

increase in flow. Five days later the situation had changed. During this period respiration was assisted with a volume respirator and marked hypocapnia had been maintained. Although the patient was awake and could follow simple commands, he had a dense left hemiplegia. By clinical examination one could estimate that the signs associated with marked increased pressure had subsided but that severe and possibly irreversible right cerebral hemisphere damage was present. The EEG at that time showed marked slowing and depression over the right hemisphere. The ICP had decreased only slightly, to 70 mm Hg. However, the MABP had increased to 136 mm Hg resulting in a PP of 66 mm Hg. The CBF study confirmed the severe hemisphere involvement with the flow still markedly decreased to 17 ml/100 gm/min. The arterial Pco₂ was 19 mm Hg. At this stage an increase in the PP to 110 mm Hg by removing ventricular fluid resulted in no significant change in flow, demonstrating that now autoregulation was present (at this low Pco₂).

Discussion

The data on intracranial pressure, systemic arterial pressure and cerebral blood flow from the four described patients show very clearly that concepts of the relationship of perfusion pressure to flow, that was demonstrated by Zwetnow1 in his animal studies, can be applicable to clinical situations. When the perfusion pressure falls below the normal autoregulatory range, by combinations of either intracranial pressure increases or systemic blood pressure decreases, both normal and damaged brain tissue reacts with a pressure passive flow response. This finding of critically low perfusion pressure was found in all four patients, two of whom progressed to zero perfusion pressure and cessation of flow.

With the perfusion pressure in the normal autoregulatory range, Zwetnow12 also demonstrated that when a state of hypercapnia exists then the cerebral arterioles are dilated and react passively to changes in perfusion pressure. This loss of autoregulation which occurs at hypercapnia resembles the loss of autoregulation which is seen with various types of acute brain injuries. This latter type of autoregulatory impairment has been related to tissue acidosis. Case 3 shows this type of autoregulatory loss in the damaged frontal area at the stage when the perfusion pressure is in a normal range. The observations in case 3 also offer an explanation for the paradoxical flow decrease during an increase in Pco₂ often found in space-occupying lesions. In the frontal area, the decrease in flow with an increase in Pco₂ was the result of the narrowing of perfusion pressure presumably caused by an increase in blood volume in the cranial cavity.

If one analyzes the relation of flow to perfusion pressure in all four patients (fig. 1), the flow values in the hypocapnic range follow the autoregulatory plateau. However, at normocapnia all of the flow values are associated with perfusion pressures which are below the autoregulatory range. This finding of lower perfusion pressures at normocapnia can also be explained by a Pco₂-induced cerebral blood volume increase.

The described measurements of blood pressure, intracranial pressure and perfusion pressure correlated to cerebral blood flow are therapeutically important because they allow more rational planning of techniques to control intracranial pressure, whether it be by surgical decompression, ventricular drainage, dehydrating agents or steroids.

It must be stressed that the present determinations do not allow estimation of adequacy of blood flow for cerebral tissue oxygenation. However, this may be provided in the future by regional oxygen utilization by the ³⁴Oxygen method.³⁴ The present method of measuring the cerebral perfusion pressure is open to criticism because it is based on the assumption that the pressures within the craniospinal enclosure are all equal.³⁵, ³⁶ Weinstein et al.³⁷ have shown that local pressure-creating factors act within local compartments and that single supratentorial pressure measurements are not completely relevant in a system which is not purely hydrostatic. All four cases suggest that this is true in that the supratentorial hemispheric circulatory impairment that was measured correlated poorly with the clinical findings of brain stem dysfunction. Kaufman and Clark³⁸ have demonstrated that the combination of supratentorial and cisterna magna pressure measurements can provide information about pressure gradients.

In conclusion, the relatively simple system of determining cerebral perfusion pressure used in this study of patients can be practically applied in all clinical situations with increased
intracranial pressure. However, it is only a start toward analysis of the complex effects of pressure gradients within the craniospinal enclosure.

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Relationships Between Cerebral Perfusion Pressure and Regional Cerebral Blood Flow in Patients With Severe Neurological Disorders
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