4

INTRACRANIAL PRESSURE

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INTRODUCTION

The skull is a rigid, closed box and contains the brain, cerebrospinal fluid (CSF), arterial blood and venous blood. Brain function depends on the maintenance of the cerebral circulation within that closed space and arterial pressure forces blood into the skull with each heartbeat. CSF is being formed and absorbed and the result of these forces is a distinct pressure, the intracranial pressure (ICP). The difference between the mean arterial pressure (MAP) and the mean ICP is the pressure forcing blood through the brain, the cerebral perfusion pressure (CPP).

ICP is normal up to about 15 mmHg but it is not a static pressure and varies with arterial pulsation, with breathing and during coughing and straining. Each of the intracranial constituents occupies a certain volume and, being essentially liquid, is incompressible. In the closed box of the skull, if one of the intracranial constituents increases in size, then either one of the other constituents must decrease in size or the ICP will rise. Two of the constituents, CSF and venous blood, are contained in systems that connect to low-pressure spaces outside the skull, so displacement of these two constituents from the intracranial to the extracranial space may occur. This mechanism, then, compensates for a volume increase affecting any one of the intracranial constituents. The displacement of CSF is an important compensatory mechanism and is illustrated in the CT scan in Figure 4.1 where in response to the generalized development of cerebral oedema following head injury, the ventricles have been so compressed by the brain swelling that they are visible only as a slit. CSF absorption may increase as ICP rises and the CSF volume will be reduced.

The compensatory mechanism for intracranial space occupation obviously has limits. When the amount of CSF and venous blood that can be extruded from the skull has been exhausted the ICP becomes unstable and waves of pressure (plateau waves and B waves) develop.[1] As the process of space occupation continues, the ICP can rise to very high levels and the brain can become displaced from its normal position. High intracranial pressure can force the medulla out of the posterior fossa into the narrow confines of the foramen magnum, where compression of the vital centres is associated with bradycardia, hypertension and respiratory irregularity followed by apnoea.[2]

BRAIN

The brain weighs about 1400 g and occupies most of the intracranial space. The soft cerebral tissue is very susceptible to injury, although some protection is afforded by the skull and the CSF bathing the brain. Expanding mass lesions, such as a tumour, abscess or haematoma, increase the volume occupied by the brain. When such a space-occupying lesion develops, the brain can distort in a plastic fashion, allowing some compensation for the abnormal mass, but the distortion may produce neurological signs or CSF obstruction. Figure 4.2 shows a CT scan of patient with an extradural haematoma and also shows a considerable shift of the midline structures.

The symptoms and signs produced by a supratentorial tumour depend on its rate of growth and whether it is

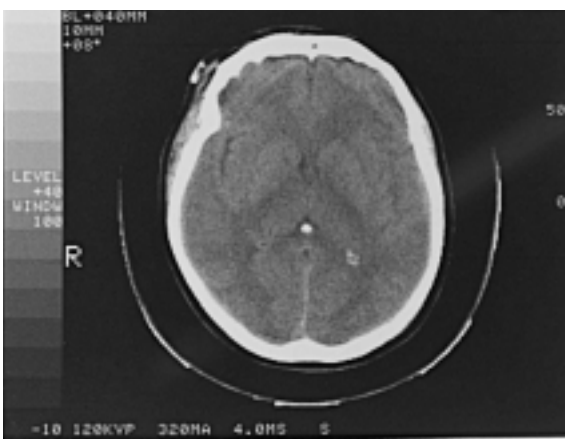

Figure 4.1 CT scan of a patient after head injury showing compression of the ventricles.

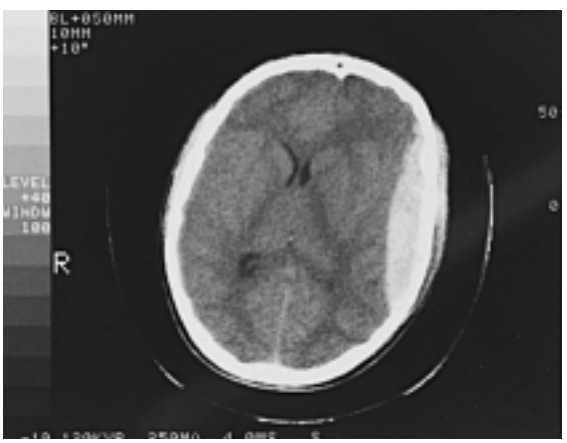

Figure 4.2 CT scan of a patient showing an extradural haematoma with considerable shift of the midline.

developing in a relatively silent area of the brain or in one of the eloquent areas, such as the motor cortex. A tumour developing in a silent area can achieve large size before presenting with symptoms and signs of raised ICP (Fig. 4.3). In this situation a major disruption of ICP dynamics may be present, with significant brain shift. A tumour may present rapidly if it is in an eloquent area, if it is a fast-growing tumour or if it causes CSF obstruction. Chapter 1 describes some of the common syndromes associated with tumour development.

Haematomas are usually fairly rapidly growing lesions and although they set in train the compensating mechanisms for intracranial space occupation, they will produce signs of raised ICP at an earlier stage.[3]

Space occupation in the posterior fossa has some characteristic features. The posterior fossa is a much smaller space than the anterior and middle cranial fossae and as tumours developing in the posterior fossa are growing in a more confined space, they tend not to grow to large size. The relatively small volume of the posterior fossa means that tumours tend to produce a rise in ICP early and this is accentuated by the fact that they frequently produce CSF obstruction. Distortion of the mid brain and compression of the lower cranial nerves may also be produced by posterior fossa tumours.

The bulk of the brain can also be increased by the development of cerebral oedema and frequently cerebral oedema is seen in association with a tumour (Fig. 4.4). The degree of space occupation produced by the oedema can be so great as to turn a relatively minor degree of space occupation from a small

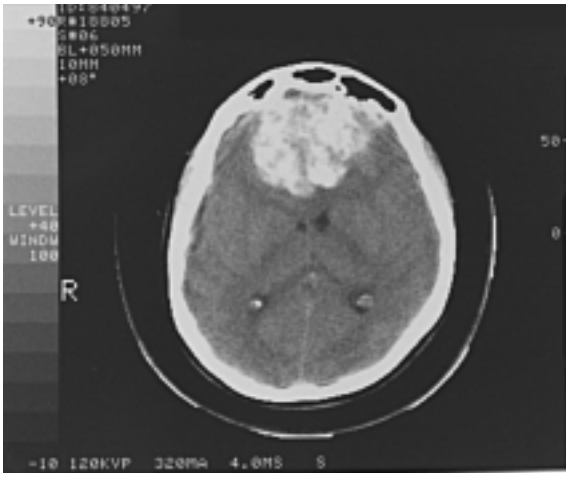

Figure 4.3 CT scan of a patient with a large, calcified frontal meningioma.

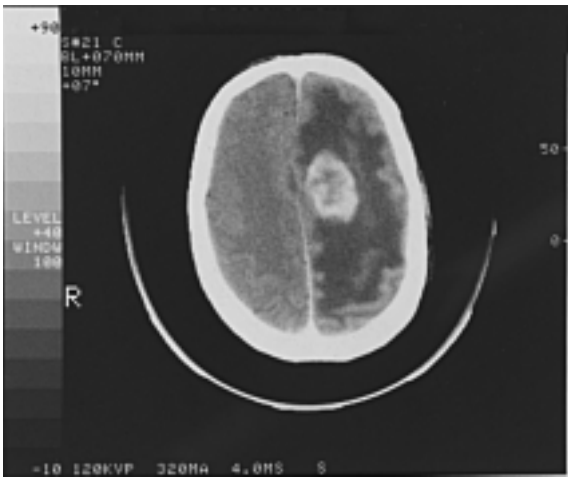

Figure 4.4 CT scan with contrast of a patient with a moderate sized glioma showing the extent of oedema formation.

tumour into a major problem requiring urgent treatment. Klatzo[4,5] provided a simple classification of cerebral oedema into two types: vasogenic and cytotoxic. In vasogenic brain oedema (VBO), the development of oedema results from damage to the blood–brain barrier, so that there is an increase in permeability of the cerebral capillaries and serum proteins leak into the brain parenchyma. The hydrostatic forces generated by the Starling balance at the capillary provide the impetus for the oedema fluid to spread through the brain; white matter, which has a less dense structure than grey, tends to offer less resistance. VBO may develop around neoplasms, haematomas and cerebral abcesses and in traumatized areas of the brain.

Once the primary lesion has allowed the initial formation of the protein-rich oedema fluid, several factors combine to spread the oedema and may be the result of arteriolar dilatation, increased systemic arterial pressure or a combination of both.[6] Increased intravascular pressure accelerates the rate of oedema spread. Eventually the fluid reaches the ependymal surface of the ventricles, where it passes into the CSF to be transported and absorbed by the mechanisms that regulate CSF outflow.[7] The production and maintenance of a low sagittal sinus venous pressure is important in allowing the resolution of cerebral oedema.

Cytotoxic brain oedema occurs after hypoxic or ischaemic episodes. The reduced state of oxygen delivery results in failure of the intracellular ATP-dependent sodium pump and therefore intracellular sodium accumulates followed by rapid increases in

intracellular water. In a pure form of cytotoxic oedema, the blood–brain barrier remains intact.

Other workers describe other types of oedema including hydrostatic, interstitial and hypo-osmolar. Hydrostatic oedema[8] is due to an increase in the intravascular pressure transmitted to the capillary bed. The combination of cerebral arteriolar vasodilatation and raised arterial pressure may lead to an outpouring of water, even though the blood–brain barrier is not necessarily damaged. Hypo-osmolar oedema can occur when the serum osmolality is less than that in the brain. Clinically it may develop following excessive intravenous infusions of glucose-water solution with associated hyponatraemia. Glucose penetrates freely into the brain and an osmotic gradient may develop, leading to an increase in brain water content. Hypo-osmolar oedema may also be associated with inappropriate secretion of antidiuretic hormone. Interstitial oedema is seen in patients with obstructive high-pressure hydrocephalus, occurring when CSF seeps through the ependyma, increasing the water content of the periventricular structures. Shunting reduces the ventricular pressure and the water content returns to normal.[9]

The ability of the brain to distort in a plastic fashion allows some accommodation for intracranial space occupation and it is not uncommon to see shift of the midline structures due to a supratentorial lesion on angiography or CT scan. If unrelieved, this displacement can cause part of the cerebral hemisphere, usually the temporal lobe, to become impacted beneath the falx cerebri or the tentorial hiatus. Jefferson[10] described the tentorial pressure cone and though it is classically associated with an extradural temporal haematoma, due to haemorrhage from the middle meningeal artery, it may be produced by any expanding supratentorial lesion. The development of a pressure gradient across the tentorium allows downward impaction of the medial part of the temporal lobe, the uncus, into the tentorial hiatus. Compression of the cerebral peduncles and oculomotor nerve at first causes pupillary changes and a contralateral hemiparesis but at a later stage respiratory irregularity and apnoea may ensue. Upward herniation of the cerebellum into the tentorial hiatus may also take place and be due to an expanding lesion in the posterior fossa.[11]

The serious nature of the medullary pressure coning has been mentioned earlier (p. 000) and the Cushing response[2] described. The mechanism of the response appears to be generated by brainstem ischaemia and Doba and Reis[12] demonstrated the existence of a receptive area for the Cushing response in the lower brainstem.

CEREBROSPINAL FLUID

There is about 140 ml of CSF in the adult, half in the skull and half in the spinal subarachnoid space. CSF is formed at about 0.4 ml/min, so that an amount of CSF equal to the CSF volume is produced in 4 h.[13] This is an energy-dependent active process requiring carbonic anhydrase and a sodium-potassium activated ATPase. Cutler et al[14] showed that the rate of CSF production was constant in the face of a raised ICP up to 200 mmHg. After formation from the choroid plexus in the lateral ventricles, CSF flows through the third ventricle, along the aqueduct and into the fourth ventricle, where it reaches the subarachnoid space through the foramina of Luschka and Magendie. CSF is also formed by the passage of brain tissue water across the ependymal lining of the ventricles and along perivascular channels into the subarachnoid space, so that the composition of CSF changes as it circulates through the ventricular system. Shapira et al[15] studied the rate of CSF production during hypotension with either adenosine or haemorrhage. They found that adenosine-induced hypotension did not affect the rate of CSF production, whereas haemorrhage-induced hypotension reduced CSF production. Adenosine is a cerebral vasodilator and haemorrhage will constrict the vessels of the choroid plexus, so CSF production falls as the choroid plexus perfusion falls.

Reabsorption of CSF takes place through the arachnoid villi into the sagittal sinus and requires a pressure gradient between the CSF and the sagittal sinus venous pressure. If the venous pressure is raised, then CSF reabsorption is slowed.[16] Normally CSF production is in balance with reabsorption and the CSF system is at equilibrium as regards both pressure and volume. If ICP increases, the rate of absorption of CSF also increases and ultimately the new CSF volume at equilibrium will be smaller. The stiffness of the brain will also affect the plot of CSF pressure against CSF volume, because when the tissues around the CSF are stiff, the plot of CSF pressure against volume will be steep and the equilibrium volume of CSF small. A slack brain will be associated with a flat pressure/volume curve (see Fig. 4.5) and a larger CSF equilibrium volume.

The circulation of CSF may be obstructed in a number of ways and this may result in raised intracranial pressure. Aqueduct blockage may follow head injury or subarachnoid haemorrhage, producing hydrocephalus. Tumours and other mass lesions may also distort or compress CSF pathways and, by causing ventricular dilatation, will increase the degree of intracranial space occupation. The passage of CSF from the fourth

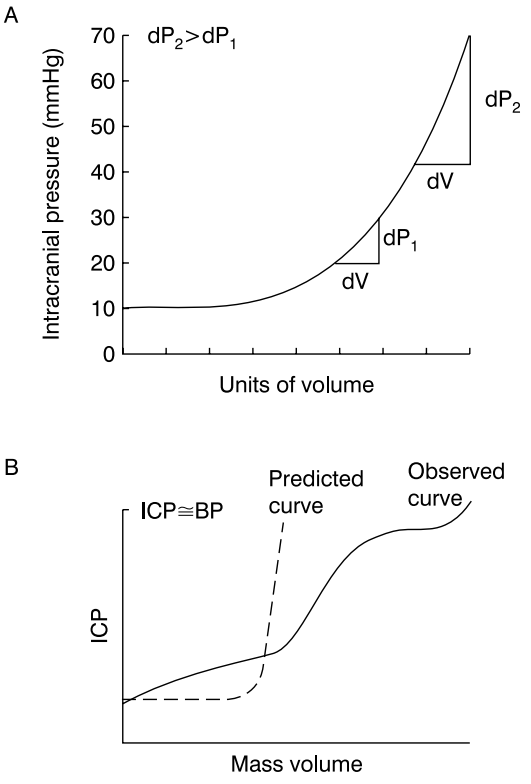

Figure 4.5 (A) Diagram of a volume/pressure curve. As the breakpoint is passed at 15 mmHg the curve becomes increasingly steep so that uniform increments of volume (dV) produce increasingly large rises in ICP (dp) (redrawn from reference[30], courtesy of the Editor). (B) ICP versus mass volume predicted by the Monroe–Kellie hypothesis for the curve observed during progressive epidural balloon inflation in animals. The observed curve is significantly different from the predicted curve in that its initial segment is not flat but increases slowly to a breakpoint. Beyond this breakpoint, the observed curve is not vertical but instead increases to a second plateau near the level of arterial blood pressure (redrawn from reference[55], courtesy of the Editor).

ventricle and through the foramen magnum may be impeded by congenital malformations.

Some elderly patients develop normal-pressure hydrocephalus, in which they present with dementia and incontinence and CT scans show the appearance of hydrocephalus, though ICP measurement may be normal. Continuous measurement of ICP reveals periods of raised ICP, especially during sleep.[17] These patients often benefit from CSF shunting.

Reabsorption of CSF is reduced in benign intracranial hypertension,[18] resulting in a greatly increased subarachnoid space. The condition tends to affect young women, particularly if they are obese. They present with headaches and the clinical picture includes marked papilloedema, which may be so marked as to affect vision. The ICP can reach very high values but without affecting consciousness. Once space occupation as a cause for the high ICP has been eliminated, lumbar puncture is safe.

ARTERIAL BLOOD VOLUME

The role of the arterial pulse in generating the ICP, along with the CSF, has been mentioned earlier (p. 000). Each arterial pulse produces a change in the level of ICP, with a rise in ICP during systole and a fall in diastole. Plum and Siesjö[13] suggested that CSF is able to absorb some of the energy in the arterial pulse wave because it transmits the pressure pulse out of the cranial cavity and into the more elastic spinal CSF space. Many workers have observed that as ICP rises, the pulse pressure of the ICP also increases.[19,20,21] Pickard and Czosnyka[20] suggest that two mechanisms may be active: first, the brain becomes stiffer (less compliant) as ICP rises and a given pulse volume load provokes a bigger pressure response; and second, the pulsatile component of cerebral blood flow (CBF) increases as the CPP is reduced.

The control of CBF is discussed in Chapter 00. If CBF rises, there will usually be an increase in ICP, produced by cerebral vasodilatation. Major changes in CBF and therefore ICP can be produced by $PaCO_2$ changes. There is a straight line relationship between CBF and $PaCO_2$: between the limits of 2.6 and 10.6 kPa (20–80 mmHg) $PaCO_2$, CBF changes 2 ml/100 g brain for every mmHg change in $PaCO_2$. The resultant change in cerebral blood volume (CBV) is 0.04 ml/100 g brain for every mmHg change in $PaCO_2$.[22]

When autoregulation is intact an increase in MAP will not normally be associated with an increase in CBF or ICP. If, however, the rise in MAP is so rapid or so great (as in the pressor response to intubation) as to exceed the capacity of the cerebral vessels to react, then an increase in CBF and ICP may occur. When autoregulation is impaired, as in diseased or damaged brain where local tissue acidosis produces local vasodilatation, then any change in MAP will produce a change in CBF and therefore ICP.[23] The blood supply of a vascular tumour is not under autoregulatory control and the tumour blood flow and therefore the size of the tumour will alter passively with changes in blood pressure.

The cerebral vasodilatation produced by disease or injury may be associated with blood–brain barrier

(BBB) damage, so that local cerebral oedema results in and increases the tendency to raised ICP. In the experimental animal in which brain injury has been produced, arterial hypertension can cause cerebral oedema and tentorial herniation in a few minutes.[24]

VENOUS BLOOD VOLUME

The volume of venous blood in the skull offers one of the compensating mechanisms for abnormal intracranial space occupation, because the thin-walled cerebral veins can be compressed as the space occupation proceeds and blood therefore lost from the skull to the great veins in the chest. Obstruction of the cerebral venous drainage, then, not only removes one of the compensating mechanisms but will also tend to increase ICP by holding venous blood back in the skull, distending the cerebral veins. The volume of the venous compartment of the skull also increases when there is cerebral arterial dilatation, because of the increased intravascular hydrostatic pressure.

Cerebral venous obstruction also tends to promote oedema formation. The increase in ICP resulting from the venous obstruction therefore will not be completely corrected when the obstruction is relieved, because the oedema will not resolve immediately.

Cerebral venous obstruction may be caused in a number of ways, including the use of the supine or head-down position and an incorrectly set lung ventilator, as well as coughing, straining or incomplete muscle relaxation in a ventilated patient. The effects on ICP of intubating an incompletely relaxed patient are demonstrated by studies which show an increase in anterior fontanelle pressure resulting from awake intubation.[25] Millar and Bissonette[26] reported no change in cerebral blood flow velocity during awake intubation and conclude that the observed increase in anterior fontanelle pressure could be attributed to a reduction in the venous outflow from the cranium.

The effect of positive end-expired pressure (PEEP) on ICP appears to depend on the degree of intracranial compression. Aidinis et al[27] described two responses to PEEP in cats: one in which the ICP rose less than the amout of PEEP which was applied and another in which the ICP increase was greater than the PEEP applied. In patients, it has been shown that most of those with significant intracranial compression display increased ICP when PEEP is applied.[28] Continuous positive airway pressure (CPAP) has been investigated by Hörman et al[29] in volunteers demonstrating a mean increase of 4 mmHg when CPAP of 12 mmHg was applied. They suggest that the changes were of only minor clinical significance.

QUANTIFYING THE DEGREE OF INTRACRANIAL SPACE OCCUPATION

The choice of an anaesthetic technique is helped if the anaesthetist is able to make an estimate of the degree of intracranial space occupation. The symptoms and signs of raised ICP may coexist with those due to the lesion producing the raised ICP and with those resulting from brain shift and cerebral ischaemia. Headache, vomiting, papilloedema and drowsiness are said to be the signs produced by raised ICP,[30] whereas other signs such as pupillary changes, bradycardia and hypertension result from brainstem distortion or cerebral ischaemia.

The headache may be paroxysmal in nature, sometimes relieved by sitting and worsened on straining or coughing. Some patients find that the headache is worsened by flexion of the neck and they lie in a position of hyperextension.

Bilateral papilloedema is the one sign that appears to be directly related to raised ICP but it takes a little time to develop. Pickard and Czosnyka[20] point out that optic disc swelling was found in only 4% of head injury patients, even though 50% had raised ICP on monitoring. They comment that many of the later signs of raised ICP are the result of herniation and that monitoring of ICP should detect raised ICP at an earlier stage so that treatment is started before irreversible damage occurs.

VOLUME/PRESSURE RELATIONSHIP

The degree of intracranial space occupation can be difficult to estimate from the clinical history and examination and much work has been done to quantify the relationship between intracranial space occupation and ICP. The simplest understanding of the relationship arises from the Monroe–Kellie hypothesis that within the closed space of the skull, a change in the volume of one intracranial constituent will be balanced by a compensatory change in another, the four constituents being incompressible. As space occupation develops, ICP shows little tendency to increase as long as compensation for the space occupation is available. CSF, for example, may be moved into the spinal subarachnoid space and venous blood displaced towards the great veins in the chest. ICP will only rise when no further CSF or venous blood can be lost from the skull. When ICP does rise, CSF production will continue at its normal rate but reabsorption of CSF will be accelerated[31] and the CSF volume will be further reduced. As the space occupation develops further, then CSF pathways will

become obstructed by the mass or by the brain shift it produces and distortion of veins, even collapse of veins around a mass, will begin to impede local venous drainage. Johnston and Rowan[32] showed that in such circumstances of high ICP, cerebral arteriolar dilatation occurs in an attempt to preserve CBF, adding to the already high ICP.

The exhaustion of the compensating mechanisms for intracranial space occupation implies that any further abnormal volume added to the tightly compressed intracranial state will produce a massive rise in ICP and clinically this may be associated with herniation of the brain through the tentorial hiatus or into the foramen magnum.

The process by which the intracranial space occupation gradually exhausts the compensating mechanisms is illustrated by the volume/pressure curve of the intracranial contents (Fig. 4.5).[21,33] At first the abnormal volume increase caused by a developing mass lesion produces little change in ICP. At a later stage, the same increase in volume produces a distinct rise in pressure. The steepest part of the curve represents the situation when the compensating mechanisms are virtually exhausted. The same volume increase at this point would produce a massive rise in ICP.

The addition of small volumes to the lateral ventricle while measuring ICP has been used to elucidate the patient's position on the volume/pressure response curve, the rise in pressure produced by the injected volume being called the volume/pressure response (VPR).[34,35] Leech and Miller[34,36] studied the relationship between the VPR and ICP in several conditions. At normal blood pressure they found that the VPR was unchanged by alterations in systemic arterial pressure but at raised arterial pressure, there was an increased VPR and a linear correlation between VPR and both arterial blood pressure and cerebral blood flow. They suggest that the clinical implication of this is that arterial hypertension in patients with raised ICP is likely to have a deleterious effect by increasing brain stiffness. They also studied the effect on the VPR of reducing ICP with hyperventilation or mannitol[37] and found that hyperventilation reduced ICP and VPR equally, whereas mannitol produced a greater reduction in VPR than ICP. They suggested that mannitol produced a more beneficial effect on intracranial compression than hyperventilation.

Measurement of the ICP, examination of the trace and measuring the VPR will yield useful information about the degree of intracranial space occupation but it is possible to obtain more information by infusion testing.[38] Pickard and Czosnyka[20] have suggested that close analysis of the ICP trace is able to reveal the mechanism responsible for the raised ICP and whether autoregulation remains intact.

Intracranial pressure waves

Episodes of very high ICP may occur when intracranial compression is advanced and the control of CBF has become unstable. These were first noted by Lundberg[1] who described A (or plateau waves), B and C waves occurring in patients in whom ventricular pressure was being continuously measured.

A waves represent considerable increases in ICP (up to 80 mmHg) and may persist for 15–20 min. Their appearance indicates the patient who is nearing the limits of compensation for intracranial space occupation. They are associated with cerebrovascular dilatation. During the plateau wave, the CPP may be greatly reduced, even though the systemic arterial pressure rises. In such periods of high ICP, the level of response may worsen with possible loss of control of the airway, exposing the patient to the further dangers of hypoxia and hypercarbia. A waves were observed in 18 out of 76 patients in one study of head-injured patients and 11 of the 18 died.[39] Tindall et al[40] showed that a transient rise in $PaCO_2$ often preceded the development of an A wave and Lassen and Christensen[41] suggested that painful stimulation could also produce an increase in CBF and initiate pressure waves. The increase in CBV[42] may in some cases be the result of inappropriate vasodilatation in response to a fall in CPP.

B waves are smaller in amplitude with an increase in ICP of 20–25 mmHg and a frequency of one per minute. They are of less serious import than A waves but do appear on occasion to be precursors of A waves. Cyclic variations in vascular resistance have been suggested as the cause of B waves[43] and transcranial Doppler (TCD) measurements of middle cerebral artery flow velocity have shown that MCA flow velocity increases during B waves.[44] The appearance of B waves during sleep in patients with normal-pressure hydrocephalus is said to be a helpful sign for a good outcome after shunting.[45] C waves occur six times per minute and are only just discernible on the pressure trace.

CT SCANS

CT scans give a valuable image revealing the size of a mass lesion and whether or not it is causing CSF obstruction, cerebral oedema or brain shift. Diffuse brain swelling can be evaluated by examining the size of both lateral and third ventricles and the perimesencephalic cisterns.

THE EFFECT OF RAISED ICP ON CEREBRAL BLOOD FLOW

Cerebral blood flow is controlled normally by cerebral metabolism. Autoregulation ensures that CBF remains constant even though the CPP may vary between 40 and 120 mmHg. Autoregulation is effective whatever the cause of the reduction in CPP, which can be either a reduction in the arterial pressure or an increase in ICP, or both. If CSF pressure is raised in experimental animals, CBF is maintained until CPP has been reduced to 30–40 mmHg; below this level, CBF falls rapidly.[46,47,48] Cortical electrical activity has been shown to remain normal in the face of experimentally induced intracranial hypertension to 40–50 mmHg.[49,50] The diseased or injured brain, where ischaemia may be part of the disease process, is less tolerant of high ICP.[51] There is frequently impairment of autoregulation, so that CBF becomes pressure dependent,[52] with the result that there may be a significant fall in CBF caused by a relatively small fall in CPP.

Other factors need to be taken into account. In the damaged brain there is frequently failure to observe an increase in cerebral perfusion despite an increase in CPP; that is, the hyperaemic brain may be suffering ischaemic damage. Langfitt et al[53] found that an induced rise in ICP produced arterial hypertension, followed by a secondary rise in ICP. Fitch et al,[54] studying the effects of expanding an artificial space-occupying lesion, showed that the arterial hypertension which was produced was not associated with any improvement in either CPP or CBF. Explanations include the fact that elevated blood pressure produces an increase in cerebral oedema which, by increasing tissue pressure, reduces perfusion at the capillary level.[55] In such circumstances, autoregulation is likely to be impaired or abolished and though an increase in CPP may not result in an improvement in cerebral perfusion, a fall in CPP will invariably cause a fall in CBF.[56]

DRUG EFFECTS

Anaesthetic agents alter cerebral function dramatically and it is possible to use some of their effects to benefit the patient undergoing neurosurgery. Some drugs have cerebral actions that may worsen the intracranial operating conditions, making the operation difficult or even impossible. The actions or side effects of drugs need always to be assessed in the light of the patient's clinical state. In the initial evaluation of Althesin, an intravenous anaesthetic, now withdrawn, which reduced $CMRO_2$ and CBF, Turner et al[57] showed that the fall in ICP produced by althesin in a group of patients with intracranial space occupation was proportional to the initial height of the ICP. That is, the patients most at risk from the space occupation showed the greatest fall in ICP with althesin.

INDUCTION AGENTS

The effects of thiopentone on $CMRO_2$ and CBF are well studied. There is a dose-dependent fall in $CMRO_2$ and a parallel fall in CBF until the electroencephalogram (EEG) is isoelectric.[58] At this point the $CMRO_2$ is about 50% of control values and no further fall in $CMRO_2$ occurs if the thiopentone dosage is increased. ICP falls with the CBF.

Propofol has similar effects to thiopentone on $CMRO_2$ and CBF.[59,60] 1.5mg/kg propofol has been reported to produce a 32% fall in CSF pressure 2 min after induction of anaesthesia.[61]

VOLATILE AGENTS

To a variable extent, all volatile anaesthetic agents cause an increase in CBF and therefore ICP. The magnitude of the effect is important but so is the patient's position on the volume/pressure curve. If serious degrees of intracranial space occupation exist, then even a small increase in CBF may produce a significant rise in ICP.[62]

Isoflurane

Isoflurane is frequently used as part of a neurosurgical anaesthetic and has been extensively investigated.[63,64] Though it can cause an increase in CBF and therefore ICP,[65,66] the effect is not large and Muzzi et al[63] suggest that at 1 MAC isoflurane did not affect CSF pressure. The effect of higher concentrations on ICP can be modified by the use of hyperventilation; indeed, Jung et al[67] comment that when an increase in CSF pressure has been reported during isoflurane anaesthesia, it was in the presence of normocapnia or moderate hyperventilation in patients with major intracranial space occupation. Matta et al[68] produced in humans an isolectric EEG by infusion of propofol and then added first 0.5 MAC and then 1.5 MAC of either halothane, isoflurane or desflurane. They showed that all the agents have intrinsic, dose-related effects producing cerebral vasodilatation and that at 1.5 MAC, isoflurane and desflurane have a greater effect than halothane. They point out that these effects are normally modified by the metabolic suppression produced by the drug resulting in an indirectly caused cerebral vasoconstriction. When metabolic activity is minimal

(here under the influence of the propofol infusion), the intrinsic vasodilatory action of the drug is revealed.

Desflurane

Desflurane has been shown to produce cerebral vasodilatation.[69] Clinical studies[68] have shown that the use of 1 MAC desflurane produced a rise in CSF pressure in patients with supratentorial mass lesions, whereas a group of patients receiving 1 MAC isoflurane showed no such rise. This last study showed that there was a gradual progressive increase in CSF pressure once desflurane was started and the authors suggested that the gradual increase in ICP could be due to either an increase in CSF production or a decrease in CSF reabsorption or a combination of both. Ornstein et al[70] measured CBF in patients with mass lesions, with both isoflurane and desflurane, and asserted that the two drugs are similar in terms of their effects on CBF.

Sevoflurane

Sevoflurane has been reported as causing an increase in ICP at high inspired concentrations, though the effect is much less at 0.5–1.0 MAC.[71] In a study[72] where 0.5, 1.0 and 1.5 MAC end-tidal concentrations of sevoflurane were compared with MAC-equivalent concentrations of enflurane and halothane, significant increases in ICP were found only with enflurane and halothane. Sevoflurane did not cause a rise in ICP but did produce a fall in MAP.

Enflurane[73,74]

Enflurane, like desflurane, appears to be associated with not only cerebral vasodilatation but also an increase in CSF production.

Nitrous oxide

The effect of nitrous oxide on CBF and ICP has been of interest for some time, not least because so many anaesthetics have been given for neurosurgery using nitrous oxide. As long ago as 1968, Theye and Michenfelder reported an increase in $CMRO_2$ with nitrous oxide[75] and Henriksen and Jørgensen[76] showed an increase in ICP when nitrous oxide was administered to normocarbic patients with intracranial tumours. More recently, Hansen et al[77] have demonstrated in rats that adding 0.5 MAC nitrous oxide to a background of 0.5 MAC halothane or isoflurane produced a greater rise in CBF than would be expected by increasing the concentration of the original agent to 1 MAC. Others have also shown a rise in CBF with nitrous oxide.[78]

ANALGESICS

The opioid analgesics have been extensively studied and some confusion exists. If ventilation is controlled, then morphine and pethidine have little effect on $CMRO_2$ and CBF.[79] Fentanyl used in combination with droperidol has been shown to have no significant effect on $CMRO_2$ and CBF[80] in man and, in a study measuring ICP in patients with space-occupying lesions, was shown either to have little effect on ICP or to produce a slight fall.[81] Other opioids seem to have different effects and there are many reports of opioid drugs increasing ICP.[82] Sufentanil was investigated in a study of brain-injured patients[83] in which great care was taken to analyse any ICP changes, relating them to changes in MAP. If there was a fall in MAP greater than 10 mmHg from baseline after sufentanil administration, then ICP was significantly increased. When MAP was constant, there was no increase in ICP. The authors suggest that sufentanil has no significant effect on ICP and that transient increases in ICP occur concomitantly with decreases in MAP, which they attribute to autoregulatory decreases in cerebral vascular resistance secondary to systemic hypotension. Sufentanil and fentanyl were compared in a similar study, which also showed no increase in ICP if MAP was controlled.[84] Alfentanil and remifentanil have been compared in hyperventilated patients with supratentorial space-occupying lesions receiving nitrous oxide and isoflurane; neither drug was associated with a significant increase in ICP, though both caused a fall in MAP.[85]

MUSCLE RELAXANTS

Non-depolarizing relaxants

The non-depolarizing relaxants generally have no effect on ICP (being highly polar molecules, they do not cross the blood–brain barrier) and this includes atracurium,[86,87] though it does have the potential to cause histamine release, and vecuronium.[88,89] The effects of rocuronium on ICP have been studied[90] because its relatively fast onset of action may be an advantage if a rapid-sequence induction is indicated. It was found to have no effect on ICP and not to cause histamine release. D-tubocurarine may increase ICP through its ganglion-blocking action[91] and also has the ability to cause histamine release.

Suxamethonium

Suxamethonium tends to cause an increase in ICP.[92,93] This is partly due to the muscle fasciculations which, by producing an increase in the intraabdominal and intrathoracic pressures, cause an

increase in the cerebral venous pressure. Some workers[63,94] have suggested that the increased afferent neuronal traffic resulting from the fasciculations produces a cerebral activation and therefore a local increase in $CMRO_2$ and CBF, so that CBV is increased.

HYPOTENSIVE AGENTS

Labetalol is used during neuroanaesthesia[95] as an aid to the production of hypotension. It appears not to affect CBF or $CMRO_2$ or to impair autoregulation.[96,97] Trimetaphan has no major effect on ICP but if there is a serious degree of intracranial space occupation, the ganglionic blockade produced by trimetaphan will cause a minor rise in CBF and CBV, which may be associated with a significant rise in ICP.[98] Sodium nitroprusside, a direct-acting vasodilator, causes a rise in ICP,[78] especially if the reduction in MAP is only moderate; when MAP is reduced to less than 70% of the patient's normal MAP, the effect on ICP is hidden. Nitroglycerine has also been used for hypotension but does produce an increase in ICP.[99] In one series, in which dogs had an artificial intracranial space-occupying lesion implanted, starting the infusion of trinitroglycerine produced not only a further increase in ICP but also pupillary dilatation, suggesting the development of transtentorial pressure gradients and coning.[100]

CONCLUSION

Intracranial pressure is only the result of many factors. Although an understanding of the ways in which ICP can be altered and controlled is essential for neuroanaesthesia and intensive care, it is important to remember that the primary cause for a high ICP must be sought and treated. Outcome studies for any treatment are necessary to improve standards of patient care.

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