

# 19 MANAGEMENT OF INTRACRANIAL PRESSURE AND CEREBRAL PERFUSION

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## 19.1 Introduction

The treatment of traumatic brain injury is based on the conceptual distinction between primary and secondary injury. Primary injury comprises the immediate effects of impact. Secondary injury is due to factors other than the direct impact and may begin almost immediately or some time later. The distinction is of course, not so sharp. It is increasingly clear that the impact initiates a series of events, including an evolving axonal injury and release of mediator substances, which cause injury over minutes to hours after impact, suggesting that it may become possible to intervene therapeutically in the evolution of these processes initiated by the primary injury.

Secondary injury, on the other hand, may begin at or very close to the impact. Asphyxia or massive blood loss may cause overwhelming ischemic–hypoxic secondary damage, irrespective of the severity of the primary injury.

However the model of primary and secondary injury has clinical value and this chapter will concentrate on the two of the main end points in managing the secondary effects of injury, cerebral perfusion pressure (CPP) and intracranial pressure (ICP).

*The major cause of raised ICP, apart from hematomas, is brain swelling. The factors responsible for post-traumatic brain swelling are not clear. There is convincing evidence for both cytotoxic and ischemic–hypoxic influences, and specific means of combating them are now emerging from the laboratory into clinical trial. However, until brain swelling can be prevented the primary goals in preventing secondary brain injury will be to provide adequate cerebral perfusion and oxygenation and to prevent brain shift (herniation).*

Ideally, treatment should be based on direct knowledge of regional CBF, metabolism and function. Although this may soon be possible, at present ICP

and CPP, which can be measured easily and continuously, provide the best indirect measurements of tissue perfusion. ICP and CPP are however, global measurements and this has implications in defining treatment goals for a heterogeneous injury. This will be discussed later. Indirect indices of CBF and metabolism, such as jugular venous oxygen saturation ( $P_{jvO_2}$ ), transcutaneous Doppler (TCD; Chapter 14), electrical function (Chapter 13) and near-infrared spectroscopy (Chapter 11) may assist in defining adequate cerebral perfusion and oxygen delivery and in selecting the most appropriate treatment.

## 19.2 Intracranial pressure

Some aspects of ICP pathology relevant to the management of head injury will be reviewed briefly. (This subject is covered in greater detail in Chapter 6.)

*Our understanding of the relationship between intracranial volume and pressure has its origin in the appreciation of Monro (1783) and Kellie (1824) that cranial volume remains constant after sutural fusion and that the intracranial contents are incompressible. Burrows (1846) subsequently made the important additional observation that, while total volume remains constant, CSF volume could interchange with blood volume. Hence provided that a change in volume in one compartment is balanced by near-equal change in another, ICP will remain constant.*

*The major intracranial volumes are brain parenchyma (1200–1600 ml), blood (100–150 ml) and CSF (100–150 ml; Figure 19.1). These latter two constitute about 20% of total intracranial volume and part of each is capable of rapid extracranial displacement. Therefore they are of prime importance in the volume equilibration of an expanding mass.*

The extracellular fluid component of brain parenchyma is also capable of change, both pathologically and in response to treatment. Therefore

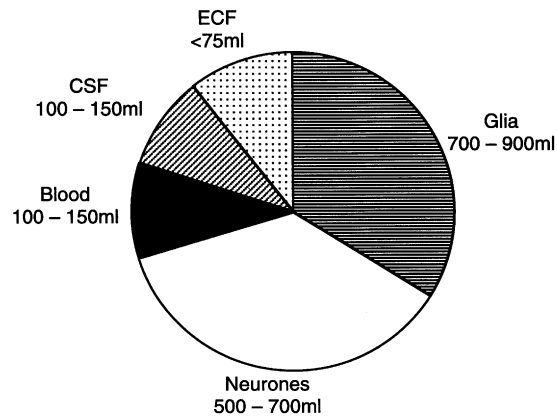


Figure 19.1 The major intracranial contents by volume.

manipulation of these volumes underlies the treatment of raised ICP after head injury.

Since the landmark study of Lundberg (1960) on the clinical value of ICP monitoring, many studies have drawn attention to the importance of raised ICP after severe head injury.

*In one major trauma center, ICP was found to be elevated (to greater than 10 mmHg) in 82% of patients with severe head injury. Of those with raised ICP, one-third (16% of the entire series) developed uncontrolled intracranial hypertension and died. Conversely, in about 50% of those who died, raised ICP was the major cause. In survivors, moderately raised ICP was a major cause of morbidity (Miller et al., 1977; 1981).*

In the multicenter Traumatic Coma Data Bank (TCDB) study from the USA, ICP was found to be an important independent variable, significantly related to outcome (Marmarou et al., 1991). Although in some patients intracranial hypertension may simply be a sign of an overwhelming and irrecoverable brain injury, the evidence for actively treating raised ICP derives mainly from the observation that mortality is lower in those patients in whom ICP can be controlled (Eisenberg et al., 1988).

#### 19.2.1 INTRACRANIAL PRESSURE AND CEREBRAL PERFUSION PRESSURE

The relationships between ICP, CPP and brain function are complex. However certain points can be made.

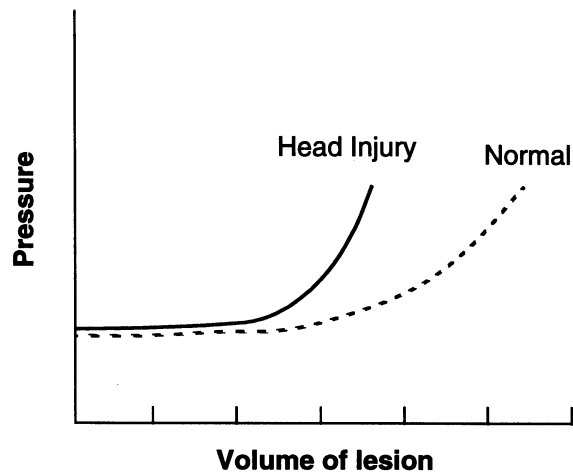
- It is doubtful whether raised ICP itself directly alters neuronal function. Although it has been suggested that the effects of raised ICP on cellular metabolism and membrane integrity may not be entirely related to CPP (Chesnut and Marshall, 1993), it seems likely that the absolute level of ICP is not as important as its effect on CPP and its relationship to brain herniation.

- Reduced CPP and brain herniation are principal mechanisms of secondary brain damage following severe head injury (Johnston, Johnston and Jennett, 1970; Rosner and Daughton, 1990). In support of this, raised ICP, even over 60 mmHg, without displacement and with adequate CPP may produce no neurological deficit. This is seen quite dramatically in benign intracranial hypertension.
- In the absence of herniation, ICP measured in one brain region will reflect the pressure of the entire cranial cavity (Langfitt, Weinstein and Kassell, 1964a, b). Even so, its effects on regional perfusion may be heterogeneous. Perfusion in and around areas of injury may be reduced further by an increase in regional tissue pressure creating regional pressure gradients, by vessel distortion or by regional loss of autoregulation. ICP and therefore global CPP may thus overestimate regional perfusion.
- The viscoelastic properties of the brain as measured by compliance tests are altered by brain injury (Figure 19.2(a)) and by the standard methods of treating raised ICP (Figure 19.2(b)). Mannitol compared with hyperventilation increases compliance at the same pressure level (Leech and Miller, 1974; Rowed et al., 1975).

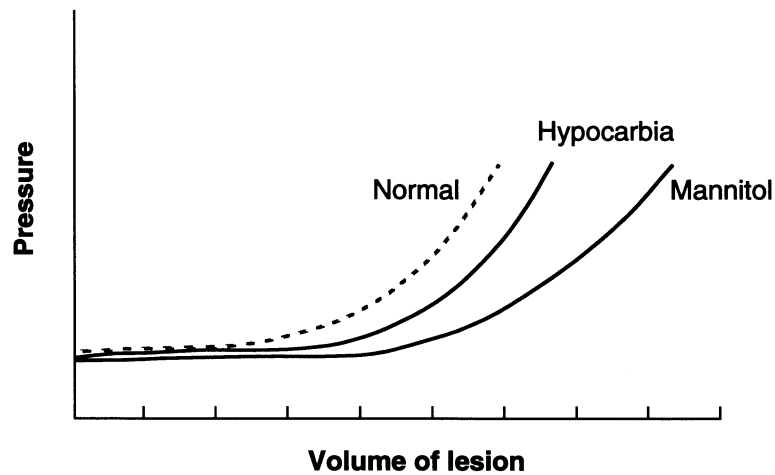
#### 19.2.2 INTRACRANIAL PRESSURE GRADIENTS

Interhemispheric pressure gradients are not observed in patients with diffuse injury but can occur in patients with focal lesions and midline shift and may last several hours (Sahuquillo et al., 1994). In this latter group, ICP might best be measured from the side of the focal lesion.

The relationship between ICP and cerebral herniation is variable. Herniation is the result of a pressure gradient between anatomical compartments generated by an expanding mass, but the speed of development depends on anatomical factors and determines the functional significance of the herniation. Temporal lobe masses can only expand medially and posteriorly, being constrained anteriorly, laterally and inferiorly by bone. They will therefore result in more tentorial herniation at lower ICP than will occipital or frontal masses. The lateral displacement of deep brain structures may itself be an important basis for loss of consciousness through the shearing effect on small perforating vessels to deep diencephalic structures (Andrews et al., 1988; Ropper, 1986, 1989; Marshall et al., 1983). Herniation is a form of volume compensation for high ICP and once herniation and brain-stem compression have occurred, the inter-compartmental pressure gradients will disperse and ICP may even be low for a short time (Johnston and Jennett, 1973).



(a)



(b)

**Figure 19.2** The influence of viscoelastic changes on the volume pressure curve. **(a)** Edema and hemorrhage reduce compliance, as well as take up volume. Hence pressure begins to rise sooner and more steeply. **(b)** Mannitol reduces brain volume and shifts the curve to the right. The brain is more compliant, hence the initial curve is flatter. Hypocarbica reduces blood volume and also shifts the curve to the right but does not alter compliance (the slope of the curve).

### 19.2.3 THE GENESIS OF RAISED INTRACRANIAL PRESSURE

Marmarou, Shulman and LaMorgese (1975) developed a theoretical model of ICP based on a constant production of CSF independent of pressure, circulation through a compliant storage space and absorption via pressure-dependent outflow pathways at the arachnoid villi. Dural sinus pressure was defined as the exit pressure of the system. The steady state relationship may be expressed as:

$$ICP = I_f \times R_o + P_D$$

where  $I_f$  = formation rate;  $R_o$  = outflow resistance;  $P_D$  = dural sinus pressure.

In this model, steady state ICP is proportional to:

- rate of CSF formation;
- resistance to CSF absorption;
- dural sinus pressure.

The factors leading to raised ICP can be considered as being of CSF or vascular origin.

The CSF component of ICP derives from the product of CSF formation and outflow resistance. Pathological events that increase the CSF component are associated with an increase in brain water. This may take the form of ventricular dilatation or brain edema.

The vascular component of ICP under normal physiological conditions is equivalent to dural sinus pressure. Pathological events that affect the vascular component are associated with dilatation of the vascular bed and congestive or hyperemic brain swelling. The contribution of these two components to raised ICP can be determined by analysis of pressure-volume relationships. In head-injured patients, vascular factors are twice as common as non-vascular factors and make the major contribution to raised ICP, probably from compression of compliant veins (Marmarou *et al.*, 1987). Hyperemic swelling is particularly common in children (Muizelaar *et al.*, 1989)

### 19.3 Cerebral perfusion pressure

*Perfusion pressure across any vascular bed is the mean systemic arterial pressure minus venous outflow pressure. Intracranial venous outflow pressure at the dural sinuses (the pressure in the cerebral veins within the subarachnoid space) remains slightly above and is linearly related to CSF pressure over a wide range, so in practice cerebral perfusion pressure (CPP) = mean BP – mean ICP (Rowan et al., 1972). Normally, within a CPP range of 60–160 mmHg, CBF remains constant. However, in brain injury this autoregulatory relationship may be altered by a number of factors.*

*CPP is equivalent to the transmural pressure across the cerebral vessel walls. CPP at the arteriolar level is the stimulus for the autoregulatory response and, at the capillary level, is the driving force for fluid exchange.*

### 19.4 Intracranial volumes

#### 19.4.1 CEREBRAL BLOOD VOLUME

Some 70% of cerebral blood volume (CBV) resides in the capacitance vessels. As CPP falls, arteriolar dilatation occurs in an attempt to maintain constant CBF. CBV will vary with these autoregulatory adjustments in vessel diameter. Within the autoregulatory range, as CPP rises, arteriolar constriction leads to a fall in CBV and hence in ICP. Below the autoregulatory range, maximal vasodilatation has occurred but, if CPP falls further, CBV will fall paradoxically as a result of vasocollapse (Kontos et al., 1978)

*Hence, although CBV and ICP are directly related, the relationship between CBF and CBV depends on the status of autoregulation and the level of CPP.*

Hypoxia causes cerebral vasodilation at  $P_{aO_2}$  levels below 50 mmHg. The stimulus for vasodilatation is reduced oxygen delivery and therefore depends on Hb, CBF and  $O_2$  saturation.

*CO<sub>2</sub> is also a cerebral vasodilator probably acting through H<sup>+</sup> concentration in smooth muscle cells of the cerebral vessels (Gotoh, Meyer and Takagi, 1965). The relationship between  $P_{aCO_2}$  and CBF is sigmoid (Harper and Glass, 1965). Within the range of 30–50 mmHg CBF bears a linear relation to  $P_{aCO_2}$  (Hayes and Tindall, 1969; Paul et al., 1972). The CO<sub>2</sub> response is very robust and is usually at least partly preserved after severe head injury, even when pressure autoregulation is lost.*

Indeed the absence or severe reduction of the CO<sub>2</sub> response has serious prognostic significance (Shalén, Messeter and Nordström, 1991; Cold, Jensen and Malmros, 1977; Enevoldsen and Jensen, 1978; Overgaard and Tweed, 1974; Yoshihara, Bandoh and

Marmarou, 1995). It may also predict failure to respond to barbiturates (Nordstrom et al., 1988) since the ability of these drugs to reduce ICP depends upon the capacity of the cerebral vessels to respond by vasoconstriction to reduced metabolic demand.

#### 19.4.2 CEREBROSPINAL FLUID VOLUME

Some 70% of CSF is produced by the choroid plexus and 30% enters the ventricles across the ependyma from brain parenchyma as excess extracellular fluid ('brain lymphatic fluid'). CSF production involves active transport, particularly of Na<sup>+</sup>, and may be reduced by the carbonic anhydrase inhibitor acetazolamide (Rubin et al., 1966; Sahar and Tsipstein, 1978), by frusemide (furosemide) and steroids (Sato et al., 1973). The rate of production is constant at about 0.35 ml/min (20 ml/h or 500 ml/d) giving a fivefold turnover per day. Production is not influenced by ICP except at very high levels (Børgesen and Gjerris, 1989).

Total CSF volume in an adult is approximately 140 ml, of which 30 ml is spinal and 20 ml in the ventricles (Davson, Welch and Segal, 1987).

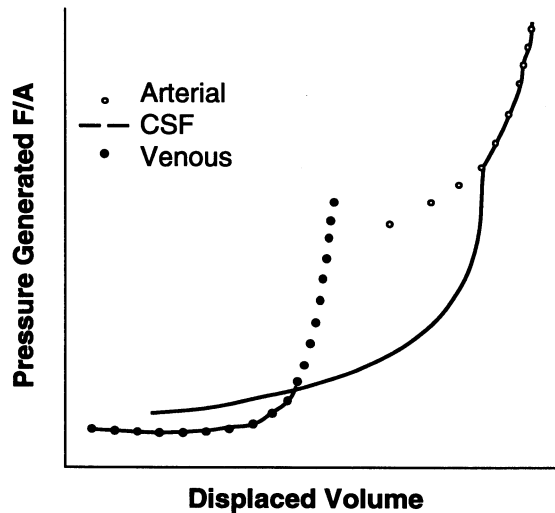
A total of 80% absorption occurs via the arachnoid granulations, particularly those related to the dural sinuses, and at normal pressures is determined both by the pressure gradient across the granulations and by active transport. The other 20% is absorbed via spinal nerve root sheaths and the Virchow–Robin perivascular spaces. Hence CSF absorption increases with ICP. It can be inhibited by obstruction in any part of the CSF pathways or at the arachnoid villi.

#### 19.4.3 BRAIN VOLUME

Brain volume contributes about 70% of intracranial volume and is normally constant. Traumatic brain swelling may be due to an increase in one or more of the three brain fluid compartments – blood, intracellular or extracellular fluid – and is the major cause of raised ICP after head injury. (See Chapter 7 for a detailed discussion of traumatic brain swelling.) Brain is the least displaceable of the intracranial volumes. Displacement or herniation of brain is a limited and final form of accommodation of an intracranial mass.

### 19.5 Volume–pressure relations

The initial, nearly horizontal part of the exponential volume–pressure curve represents the phase when intracranial (venous) blood and CSF can be readily displaced to accommodate an increase in another



**Figure 19.3** The contribution of CSF, venous and arterial blood volume displacement to the volume pressure curve. Pressure is defined here as the 'force necessary to displace contents'. The volume pressure curve is seen as the resultant of curves derived from the pressure necessary to displace CSF, venous and arterial blood. (Source: reproduced from Rosner, 1993, with permission)

volume or the addition of a new volume, without rise in pressure. Further volume additions ( $\Delta V$ ) cause increasingly steep rises in ICP as the force needed to displace compensating fluid volumes increases. The relative contribution of the two chief displaceable volumes, blood and CSF, are represented in Figure 19.3 (Rosner, 1993).

CSF can be displaced readily into the spinal sub-arachnoid space. A total of 70% of the CSF buffering capacity is contained in the intracranial compartment and 30% in the spinal compartment, where dural expansion can occur by compression of epidural veins (Marmarou, Shulman and LaMorgese, 1975). Blockage at the foramen magnum by tonsillar herniation prevents this compensatory displacement and accelerates further rapid rises in ICP.

CBV within the venous (capacitance vessels) can be readily and passively displaced to the extracranial venous system. A smaller volume of blood is contained on the arterial side but the reactivity of the arterioles (autoregulation) has a major influence on CBV and hence on ICP as already outlined.

#### 19.5.1 INTRACRANIAL PRESSURE WAVES

Lundberg (1960) first recognized the significance of pressure waves occurring under conditions of reduced intracranial compliance. Of the three main waves he described, A waves (Plateau) and the shorter duration B waves are of greatest clinical relevance. Rosner

(Rosner and Becker, 1984a) has attributed them to a reduced CPP, which leads to a vasodilatory cascade.

*Providing CPP is within the autoregulatory range and autoregulation is preserved, a fall in CPP will induce vasodilatation, an increase in CBV and a parallel increase in ICP. This will further reduce CPP and tend to perpetuate the circle.*

The process may be terminated by a rise in BP (Cushing response) – the increase in CPP will then lead to vasoconstriction and a fall in CBV – or by hyperventilation, which reduces ICP by vasoconstriction.

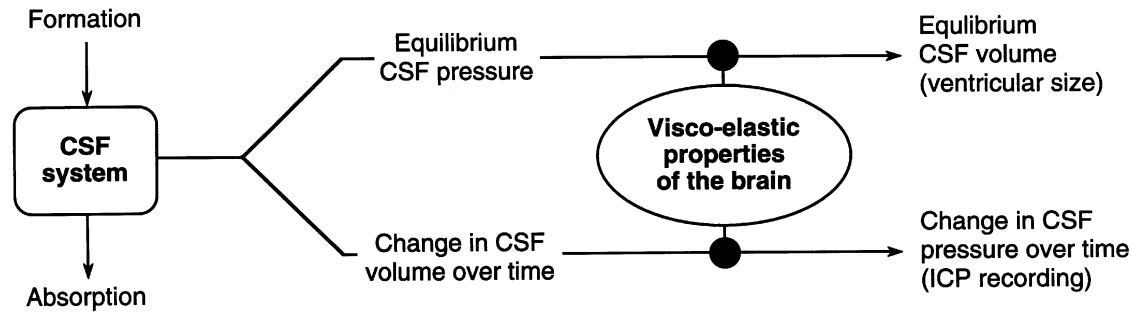
#### 19.5.2 MEASURING INTRACRANIAL VOLUME RESERVE

Theoretically, measurement of intracranial volume reserve would allow treatment of brain swelling before ICP rises (Marmarou, 1986). However compliance measurements (the pressure rise associated with a given volume increase) have not gained a place in routine clinical practice and it is not known whether such a 'pre-emptive' approach would make the treatment of brain swelling more effective. However, compliance measurements have given some insights into the effects of head injury and various treatments. Following head injury, compliance increases, altering the shape of the volume pressure curve so that it rises more steeply, and the 'breakpoint', the point at which ICP begins to rise, may be moved to the left, indicating a reduced buffering capacity (Figure 19.2(a)).

Treatments used to reduce ICP may also affect compliance. Hyperventilation moves the breakpoint to the right, increasing the intracranial buffering capacity, but does not change its slope (Rowed *et al.*, 1975). Yoshihara, Bando and Marmarou (1995) found that the PVI, and hence the slope of the volume-pressure curve did not change with moderate changes of  $P_a\text{CO}_2$ . Mannitol appears to shift the breakpoint and also to change the slope of the curve, so having the additional advantage of rendering the brain more compliant (Leech and Miller, 1974; Figure 19.2(b)).

#### 19.5.3 VISCOELASTIC PROPERTIES

As indicated by the changing slope of the volume-pressure curve under different circumstances, the viscoelastic properties of the brain, the skull and the dural sac affect the equilibrium relationship between ICP and intracranial volume. If the brain is 'tight' (high elastance, low compliance), a small volume addition will produce a marked rise in ICP. Hence pathological processes, such as brain edema, will affect volume-pressure relationships both by the increase in volume of tissue water and by altering the



**Figure 19.4** The relationship between CSF inflow and outflow and viscoelasticity. The viscoelastic properties of brain affect the equilibrium relationship between CSF pressure and volume (the starting point of the volume pressure curve) and also the dynamic relationship, i.e. the effect of a small volume addition. (Source: reproduced from Miller, 1985, with permission.)

viscoelastic properties of the brain The relationship between CSF inflow and outflow and viscoelasticity are represented in Figure 19.4 (Miller, 1985).

#### 19.5.4 IDENTIFYING THE CAUSES OF RAISED ICP AFTER HEAD INJURY

After mass lesions (e.g. hematomas) have been excluded and extracerebral factors such as raised intrathoracic pressure or hyperthermia have been rectified, persistently raised ICP is likely to be due to brain swelling.

*Brain swelling may be due to hyperemia (vascular engorgement, mainly venous) or edema (an increase in brain water content). Brain edema has been further classified as cytotoxic, vasogenic or hydrostatic (Chapter 7).*

Ways of identifying the vascular and non-vascular factors contributing to raised ICP by a combination of ICP wave form analysis, cerebral electrical function monitoring and continuous monitoring of jugular venous oxygen saturation have been suggested (Piper, Dearden and Miller, 1989; Dearden and Miller, 1989). Jugular venous oxygen saturation combined with arterial oxygen saturation measurements will indicate cerebral oxygen consumption and so identify ischemic and hyperemic states.

*It must always be remembered that the pathology of head injury is both heterogeneous and dynamic, and that the dominant cause of raised ICP may vary with time. Brain injuries do not produce simple or 'pure' forms of brain swelling.*

Indeed one form of brain swelling may inevitably lead to the development of another. For example, an increase in ICP due to extravascular fluid increase (brain edema) may lead to ischemia and vasodilatation, a 'vascular' cause for increased ICP. Conversely, ischemic cytotoxic swelling may later damage the blood-brain barrier and cell membranes, leading to vasogenic brain swelling.

Swelling that is predominantly due to increase in blood volume may respond to vasoconstriction and hence to barbiturates or to hyperventilation (Yoshihara, Bandoh and Marmarou, 1995). Indeed, the initial effect of the osmotic diuretic mannitol may also be through vasoconstriction induced by lowering blood viscosity, and therefore dependent on intact vascular reactivity.

Mannitol also increases brain tissue specific gravity, most probably by reducing brain tissue water; hence non-vascular swelling may also respond to osmotic therapy (Nath and Galbraith, 1986).

## 19.6 Principles of management

### 19.6.1 EVIDENCE-BASED GUIDELINES

The many and often conflicting reports and reviews on aspects of head injury pathophysiology and treatment have supported a range of different plans of management (Gahjar *et al.*, 1995; Fearnside *et al.*, 1993). There is now an emphasis on forming guidelines for treatment based on a rigorous assessment of the available evidence. It is inherent to such a process that the guidelines be constantly updated in the light of new evidence. *Guidelines for the Management of Severe Head Injury* was published in 1995 by the Brain Trauma Foundation and the American Association of Neurological Surgeons and forms an excellent precis of present knowledge.

Because of the clear relationship between ICP and outcome, most treatment protocols have focused on avoiding high ICP. Others have argued that the primary objective of treatment should be to maintain an adequate CPP, i.e. above the lower limit of autoregulation, as far as it can be judged in the head-injured patient. Rosner suggested that a falling CPP may set in train a vasodilatory cascade. As CPP falls, vasodilation occurs to maintain CBF. The consequent increase in CBV raises ICP and further reduces CPP.

The cascade is halted by increasing CPP. The consequent vasoconstriction will reduce ICP (Rosner and Coley, 1986).

Initial reports of the use of CPP-based protocols suggest improved outcome compared with the TCDB (Rosner, Rosner and Johnston, 1995). However, the principal benefit of focusing on CPP may be to reduce the incidence of hypotension, one of the commonest causes of secondary insult after head injury (Chesnut *et al.*, 1993a). No particular management protocol has yet had the benefit of a controlled trial.

It seems clearer now that, although ICP and CPP are interrelated, both need to be taken into account.

In treating ICP and CPP the following questions need to be addressed.

- What is the likely cause of increased ICP or reduced CPP?
- What levels of ICP and CPP should be maintained in this patient?
- What methods of treatment should be applied and in what order?
- What effects might the treatment of ICP or CPP have on cerebral oxygenation and metabolism?

Since ICP and CPP are indirect indices of brain oxygenation, treatment goals must allow for the anticipated but usually unmeasurable variability in CBF and metabolism resulting from the head injury. For example, pericontusional CBF may be borderline ischemic (18 ml/100 g/min), while whole-brain CBF is high. CBF is generally reduced in the first 24 hours after injury but in the first 4–6 hours both very low flows and hyperemic flows (i.e. greater than metabolic requirements) are found (Salvant and Muizelaar, 1993; Bouma *et al.*, 1991; Chapter 5).

#### 19.6.2 CLINICAL SIGNS OF RAISED ICP

The traditional clinical signs of raised ICP and of a mass lesion are in fact quite unreliable (Chapter 8) Furthermore Chesnut *et al.* (1994) reported that pupillary asymmetry was a poor indicator of either the presence or the side of an intracranial lesion. They found pupil asymmetry of 1 mm or more in only 40% of patients with a mass lesion of 25 ml or more and only 33% of patients with pupil inequality of 3 mm or more had an ipsilateral mass lesion. This study emphasizes the importance of early CT scanning of all patients with severe head injury.

Nonetheless, it is important to watch for clinical signs of brain-stem compression, in so far as this is possible. Signs of herniation demand treatment whatever the level of ICP, and indeed may not be reliably related to the level of ICP or to the degree of midline shift (Marshall, Toole and Bowers, 1983).

#### 19.6.3 WHO IS MONITORED?

*Some 80% of patients with severe closed head injury (GCS < 8) will have some degree of raised ICP when first monitored. In about 40% ICP is greater than 20 mmHg at some time after injury, despite therapy (Miller et al., 1979).*

CT features will identify most patients who have or are likely to have raised ICP (Chapter 9).

The most important features are:

- midline shift;
- obliteration of CSF cisterns around the brain stem (Eisenberg *et al.*, 1990; Marshall *et al.*, 1992).

Even in a patient who is able to talk, a midline shift of greater than 1.5 cm due to an acute traumatic lesion will invariably predict later deterioration (Marshall, Toole and Bowers, 1983).

Patients with severe head injury and a normal initial CT scan have a 10–15% chance of developing raised ICP later (Eisenberg *et al.*, 1990; Narayan *et al.*, 1982).

Risk factors for later onset of high ICP in this group were:

- age over 40 years;
- BP less than 90 mmHg;
- unilateral or bilateral motor posturing.

If none or one of these factors was present, the incidence of raised ICP was only 4%, whereas if two or more were present it rose to 60%.

However, those with a normal initial scan who were not monitored should have a repeat CT scan at 12–24 hours (Narayan *et al.*, 1982).

In another study, seven of eight patients with severe head injury (GCS < 8) whose initial CT scan was normal developed intracranial hypertension of more than 20 mmHg for 5 minutes, and five of these developed ICP greater than 30 mmHg. CPP was reduced below 60 mmHg in five patients (O'Sullivan *et al.*, 1994).

Hence, in severely head-injured patients with a normal initial CT scan, there is an incidence of raised ICP and critically reduced CPP, which will only be apparent if they undergo close and continuous monitoring of ICP and CPP or, if they have low risk factors, close clinical monitoring and repeated CT.

It is our practice for all patients in coma, defined as a GCS of 8 or less after resuscitation, to be ventilated for CT scanning. If the CT scan is normal and there are no other adverse features, then sedation will cease within 24 hours and their neurological status is reviewed. Patients who have been transferred from another hospital by retrieval team are usually intubated and ventilated for stability during transfer and their initial neurological status may be in doubt

(Chapter 8). A decision about continuing monitoring will also depend on the CT and, if that is normal, on neurological status after reversal of sedation.

The criteria for ventilation and ICP monitoring are:

- GCS  $\leq$  8 after resuscitation with an abnormal scan, or with a normal scan and at least two adverse features – i.e. age  $>$  40 years; BP  $<$  90 mmHg after resuscitation; unilateral or bilateral motor posturing;
- GCS  $\leq$  10 and abnormal CT scan;
- a tight brain at operation following removal of a clot;
- ventilation necessary for other injuries, especially chest injuries.

#### 19.6.4 TREATMENT GOALS

##### (a) ICP levels

A number of studies have considered the level of ICP that should be treated.

Patients were found to have a higher morbidity when ICP exceeded 20 mmHg (Miller *et al.*, 1981) and improved outcome was reported when ICP was maintained below 15 mmHg (Marshall, 1980; Saul and Ducker, 1982). Saul and Ducker (1982) suggested that early and aggressive treatment of modest rises of ICP might avoid more significant rises late. *Contant et al. (1993) found that critical values independently related to outcome were ICP more than 25 mmHg, BP less than 80 mmHg and CPP less than 60 mmHg.*

The safe level of ICP in a particular patient may depend on the accompanying CPP and on the pathology.

Miller (1992) recommended treatment when ICP exceeded 25 mmHg in the first 2 days and 30 mmHg thereafter, providing there were no signs of brain herniation.

As stated earlier, signs of herniation may occur at only moderately elevated ICP, e.g. less than 20 mmHg, particularly with bifrontal or temporal contusions (Andrews *et al.*, 1988), and these signs demand immediate treatment whatever the pressure level (Johnston and Jennett, 1973, Marshall *et al.*, 1983). For this reason Chesnut, Marshall and Marshall recommended always treating ICP greater than 20 mmHg lasting more than 20 minutes but, with lesions in the temporal fossa or deep inferior frontal lobes, treating ICP greater than 15 mmHg (Chesnut, Marshall and Marshall, 1993).

It is our present practice to aim for ICP below 20 mmHg but on occasion to accept higher pressures if CPP can be held over 70 mmHg and there are no signs of brain-stem herniation.

##### (b) CPP levels

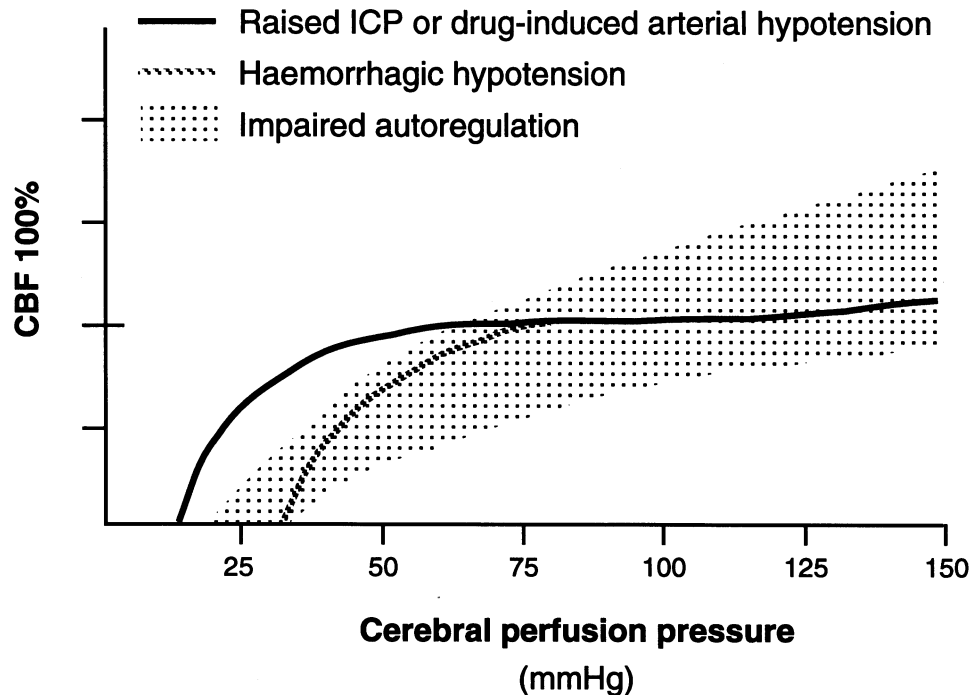
*CPP should be maintained above the expected lower limit of autoregulation, that is above the level at which CBF will be expected to fall.*

*In a particular patient, this level will depend upon a number of factors.*

- **Pre-existing hypertension.** *In chronically hypertensive patients the upper and lower limits of autoregulation are raised, so they tolerate hypotension poorly; i.e. CBF will begin to fall at a higher level of CPP than in normotensive patients (Strandgaard and Paulson, 1992). Conversely they will tolerate higher levels of systemic hypertension without increase in CBF.*
- **Susceptibility of injured brain to additional injury.** *Prior injury may reduce brain tolerance to hypotension and hypoxia (Jenkins et al., 1989) Hence, more severe injuries may be more susceptible to the effects of secondary injury.*
- **Mechanism of reduction of CPP.** *CBF will begin to fall at a higher level of CPP when CPP is reduced by hemorrhage hypotension rather than by raised ICP or hypotensive medication (Figure 19.5).*
- **The pattern of brain injury.** *CPP is a global measurement and brain injury is typically inhomogeneous. There may be brain regions where perfusion is marginal even though global CPP and CBF are adequate. CBF may be reduced around contusions or beneath subdural hematomas (Salvant and Muizelaar, 1993), by compression of vessels due to brain shift or by vasospasm. In areas of ischemia, tissue acidosis may cause maximal vasodilatation so that any fall in global perfusion will result in a fall in regional blood flow.*

Without direct measurement of CBF, the lower limit of autoregulation can be estimated from changes in middle cerebral artery flow velocity measured by transcutaneous Doppler (TCD). As described in Chapter 13, below a CPP of 70 mmHg, pulsatility index may rise and jugular venous oxygen saturation fall, indicating the onset of hypoperfusion (Chan *et al.*, 1992). Increasing CPP above 70 mmHg did not improve cerebral oxygenation further, suggesting that a CPP of 70 mmHg was adequate.

Hence although ICP and CPP are inter-related, both must be taken into consideration in setting treatment goals. Brain swelling may progress despite an adequate CPP and in this situation steps must be taken to reduce ICP. However, providing there is no midline shift or evidence of other brain herniation, and CPP is maintained, moderate increases in ICP can probably be accepted (Miller, 1992).



**Figure 19.5** The lower limit of autoregulation under different conditions. (Source: reproduced from Miller, 1985, with permission)

## 19.7 Treatment

### 19.7.1 CONTROLLING ICP AND CPP DURING TRANSFER

#### (a) From the accident site

Apart from intracranial hemorrhage, the major early risks to the patient with a head injury are hypoxia ( $P_{aO_2} < 60$  mmHg) and hypotension ( $BP < 90$  mmHg; Fearnside *et al.*, 1993; Chesnut *et al.*, 1993b). Cardiopulmonary resuscitation is always the first priority, as set out in the ATLS program in Chapter 15. The patient with a severe closed head injury should be presumed to have raised ICP and factors that may further increase ICP should be avoided. Urgent attention to airway, breathing and circulation will reduce cerebral hypoxia and hypoperfusion (Chapter 15). Normoxia and normocarbica or moderate hypocarbica ( $P_{aCO_2} = 28$ – $32$  mmHg) should be achieved as soon as possible. ICP can be dangerously increased by overperfusion, hypertension, hyperpyrexia, inadequate sedation and inappropriate anesthetic agents. Intubation and endotracheal suction cause sharp although usually transitory increases in ICP. In patients with reduced volume reserve, however, these stimuli may initiate a prolonged rise in ICP.

Pressure waves may be avoided by adequate fluid resuscitation to maintain CPP. Sedation should be sufficient to prevent coughing or gagging during transport (Chapter 17).

#### (b) During transfer between hospitals

Patients who have been intubated and ventilated for transfer are usually moderately hyperventilated ( $P_{aCO_2} = 28$ – $32$  mmHg). If lateralizing signs or pupillary asymmetry develop, signs that are highly suggestive of a mass, then mannitol may be given. At the same time, the neurosurgeon at the receiving hospital should be alerted. However, mannitol should not be given routinely as it may interfere with volume resuscitation and furthermore mask the signs of a developing mass lesion.

### 19.7.2 DEFINITIVE TREATMENT

Following the initial assessment, CT scanning and treatment of immediate causes of raised ICP such as intracranial clots and enlarged ventricles, a decision must be made as to whether to institute continuous ventilation in order to treat brain swelling. Basic monitoring consists of ICP, CPP and central venous pressures. In some institutions it will also include jugular venous oxygen monitoring and continuous transcranial ultrasonic Doppler examination.

*Raised ICP is treated by removing mass lesions and/or increasing the volume available for expansion of injured tissue.* This may be achieved by:

- reducing one of the other available intracranial fluid volumes:

- CSF by ventricular drainage;
- cerebral blood volume by hyperventilation or mannitol;
- brain tissue water content by mannitol;
- removing swollen and irreversibly injured brain;
- increasing cranial volume by decompression.

#### (a) CSF drainage

A ventricular catheter is the most accurate method of measuring ICP and also permits CSF drainage. Since reliable, safe and robust pressure-tip catheters that can be placed easily in the subdural space or within the brain parenchyma have become available, ventricular catheters are being used less often. Certainly, when ventricles are compressed or displaced, they may be impossible to catheterize, even with ultrasound guidance. However, outcome was reported to be better in patients in whom ICP was controlled by ventricular drainage alone (Gahjar, Hariri and Patterson, 1993).

Ventricular catheterization should be used whenever possible and particularly if the ventricles are enlarged. Drainage of even small amounts of CSF produces an immediate fall in ICP and a rise in CPP. However if systolic BP has been increased by a Cushing response, then sudden release of ICP may precipitate a fall in BP and CPP. This can be minimized by i.v. fluid preloading.

CSF drainage pressure should be set at about 20 cmH<sub>2</sub>O since continuous drainage at a low pressure may lead to collapse of the ventricles and loss of this avenue for ICP control.

#### (b) Hyperventilation

*Hyperventilation will reduce ICP by vasoconstriction induced by alkalosis. The fall in ICP parallels the fall in CBV.*

The relationship between  $P_a\text{CO}_2$  and ICP is exponential and follows the volume–pressure curve. By measuring the change in ICP induced by change in  $P_a\text{CO}_2$ , vascular reactivity to  $\text{CO}_2$  can be calculated. In one study (Yoshihara, Bandoh and Marmarou, 1995), patients with severe closed head injury (GCS < 8) were studied within 24 hours of injury.  $\text{CO}_2$  reactivity to hypocapnia was reduced by 50% compared with hypercapnia, indicating that at this phase after injury resistance vessels were in a state of persistent vasoconstriction, possibly due to vasospasm or compression. The volume of blood needed to increase ICP was estimated from the position on the volume–pressure curve, i.e. on the baseline ICP and the compliance measured as the pressure volume index (PVI). The PVI is derived from the slope of the semilogarithmic transformation of the exponential pressure–volume curve and is the theoretical volume necessary to

increase ICP tenfold. At a baseline ICP of 15 mmHg, only 2.5 ml of blood were needed to increase ICP to 20 mmHg. This was equivalent to a  $P_a\text{CO}_2$  increase of about 3 mmHg. When PVI was less than 15 ml, only 4 ml of blood were needed to raise ICP by 10 mmHg, whereas if the PVI was greater than 15 ml then twice that amount was necessary. As the brain became swollen, so the amount of intracranial blood necessary to increase ICP also fell, as predicted by the exponential volume pressure curve. This study also confirmed that impaired blood vessel reactivity was associated with a worse outcome.

Apart from reducing ICP rapidly, hyperventilation may have other beneficial effects.

- It may correct brain and CSF lactoacidosis which is commonly present and associated with poor outcome from head injury (DeSalles, Muizelaar and Young, 1987).
- It may restore pressure autoregulation (Paulson, Olesen and Christensen, 1972) and increase global  $\text{O}_2$  metabolism (Obrist *et al.*, 1984; Gennarelli *et al.*, 1979).
- It may reverse post-traumatic hyperemia, reduce the associated raised ICP and normalize cerebral glucose uptake (Cruz, 1995).

Cerebral resistance vessels are most sensitive to  $P_a\text{CO}_2$  around the normal level of 40 mmHg. Even in severe injury where pressure autoregulation is impaired or absent, cerebral vessels usually retain some responsiveness to  $P_a\text{CO}_2$ , although it may be less than normal (Enevoldsen and Jensen, 1978; Muizelaar *et al.*, 1991; Newell *et al.*, 1996). Hyperventilation is the most rapid method of reducing ICP other than ventricular drainage. Yoshihara, Bandoh and Marmarou (1995) noted a 15-second delay between initiating respiratory change and fall in ICP. The peak effect occurs in about 30 minutes.

Since hyperventilation has its maximal vasoconstrictor effect on normal vessels, it has been suggested that it may cause a favorable redistribution of blood from less injured to more injured or ischemic areas where the vessels are already fully dilated and unresponsive to hypocapnia ('reverse steal'). Any redistribution, however occurs within the context of an overall reduction in CBF and indeed it was suggested some time ago that prolonged hyperventilation might be harmful (Jennett *et al.*, 1977). This has been now been supported by a randomized trial, which found that prophylactic hyperventilation applied to a consecutive group of patients with severe head injury was associated with a worse outcome. Prophylactic hyperventilation ( $P_a\text{CO}_2$   $25 \pm 2$  mmHg) was applied for 5 days to patients with a GCS of 8 or less, 14% of whom had an ICP of more than 20 mmHg on admission. Hyperventilated

patients with a GCS of 4 and 5 had worse outcomes at 3 and 6 months. The bad outcome did not occur in a similar group treated by hyperventilation and the base tromethamine (THAM). Ischemic levels of CBF were not recorded in any group either by xenon CT or by AVDO<sub>2</sub> measurements. However, fluctuations in ICP were most marked in the hyperventilation-alone group, perhaps because of vessel hypersensitivity to CO<sub>2</sub>. It was speculated that these fluctuations and the time spent at ICP greater than 20 mmHg were the determining factors in the increased mortality in hyperventilated patients, but that the deleterious effects of hyperventilation might be avoided by using THAM (Muizelaar *et al.*, 1991).

Cruz (1995) recommended profound hyperventilation ( $P_{aCO_2} < 25$  mmHg), with continuous monitoring of cerebral oxygen uptake, in patients with raised ICP and diffuse swelling on CT, and found that in most patients oxygen and glucose uptake was optimal under these conditions.

Other clinical studies have, however, reported a fall in global AVDO<sub>2</sub> to potentially ischemic levels in some patients during hyperventilation to  $P_{CO_2} = 25$  mmHg (Sheinberg *et al.*, 1992; Lewis, Myburgh and Reilly, 1995).

Once hyperventilation is initiated, CSF begins to compensate for the systemic alkalosis immediately. In a study of non-injured rabbits, vessel diameters and arterial and CSF pH returned to baseline by 24 hours, despite continued hypocapnia (Muizelaar *et al.*, 1988).

CBF measured within 6 hours after head injury by xenon CT was below the threshold of infarction ( $CBF \leq 18$  ml/100 g/min) in one-third of patients (Bouma *et al.*, 1991) and is generally below normal in more than 50% of patients. This early ischemia may be worsened by hyperventilation or by a fall in BP. Hyperventilation might also increase the potential for ischemia in patients with vasospasm, which is an increasingly recognized complication of head injury (Cold, 1989; Yoshida and Marmarou, 1991; Turner *et al.*, 1984).

Hence, hyperventilation to  $P_{aCO_2}$  less than 28 mmHg should be avoided, especially in the first day after injury, unless all other measures to control ICP have failed. If profound hyperventilation is undertaken, the return to normocarbica needs to be slow because the increase in  $P_{aCO_2}$  will now act as a vasodilatory stimulus and cause a rise in ICP (Havill, 1984). ICP must be monitored carefully during this phase.

*The present view is that  $P_{aCO_2}$  levels below 28 mmHg are acceptable only as an emergency, for about 30 minutes, or when all other means of ICP control have failed.*

If prolonged hyperventilation is necessary because other ICP control measures have failed, then its potentially harmful effects may be overcome by the use of THAM. However, the effects of THAM on renal function must be monitored carefully.

Marked hyperventilation and vasoconstriction, particularly in young patients, may reduce venous return and cardiac output (Muizelaar *et al.*, 1991) and it is important to ensure that CPP is maintained, particularly if the patient is nursed head-up (section 19.9.1).

In summary, hyperventilation is an effective method of ICP control. However, it is best reserved as specific treatment, e.g. following initial resuscitation until CT scanning, and as short-term treatment for acute ICP rises, rather than prophylactically. If profound hyperventilation is used ( $P_{aCO_2} < 28$  mmHg), CPP and  $P_{jvO_2}$  should be monitored carefully and ventilation titrated to keep the  $P_{jvO_2}$  above 60–65 mmHg, or AVDO<sub>2</sub> below 6 ml. However, it is safer to keep the  $P_{aCO_2}$  at 30–35 mmHg, thus avoiding the potential for ischemia.

#### *Ventilation parameters*

Hyperventilation for rapid control of ICP can be achieved by increasing stroke rate and tidal volume. However high ventilatory rates and tidal volumes may also reduce systemic arterial pressure and hence CPP. This may also occur with vigorous hand ventilation or 'bagging', often a very effective way of rapidly reducing ICP. However, this may be dangerous because  $P_{aCO_2}$  is not controlled and may fall to 15–20 mmHg.

Positive end-expiratory pressure (PEEP) improves oxygenation without the need for a high inspired oxygen fraction ( $F_{iO_2}$ ). It has been suggested that the higher end-expiratory pressure of PEEP might raise venous pressure and hence ICP. However, studies in patients have suggested that ICP is not affected, even with intrathoracic pressures of up to 40 cmH<sub>2</sub>O sustained for up to 18 hours (Frost, 1977; Shapiro and Marshall, 1978; Cooper, Boswell and Choi, 1985). Others have reported that PEEP is associated with increased ICP in patients with reduced compliance (Apuzzo *et al.*, 1977; Burchiel, Steege and Wyler, 1981). Hence the effects of PEEP are hard to predict and, if it is used, ICP and CPP should be carefully monitored. For a more extensive discussion on ventilation in head injury, refer to Chapter 17.

#### **(c) Osmotic agents and diuretics**

Osmotic agents have been one of the principal means of treating raised ICP for many years (Weed and McKibben, 1919), yet their principal modes of action are still debated

*Mannitol*

Mannitol, a six-carbon hexhydric alcohol of the sugar mannose, molecular weight 182, is a powerful osmotic diuretic and draws fluid into the vascular compartment, thereby increasing circulating blood volume and reducing blood viscosity. It is not metabolized and the intact blood–brain barrier is relatively impermeable to it, although in high concentrations or after prolonged use the normal blood–brain barrier may ‘open’, allowing it or other large molecules to enter the extracellular space.

It was originally proposed that the principal action of mannitol was to reverse the blood–brain osmotic gradient, thereby drawing water from the brain extracellular space. On this premise the aim of treatment has been to maintain an osmotic gradient of 10–20 mosmol. This requires repeated doses of mannitol with consequent problems of progressive dehydration, hypotension and prerenal failure. CVP and urine output need to be carefully watched, particularly if mannitol is combined with the renal loop diuretic frusemide. Serum osmolarity needs to be checked and hypokalemia corrected with potassium supplements. Normovolemia should be maintained (Chapter 17).

Evidence of a cerebral dehydrating action has come from clinical studies. MRI studies have suggested that mannitol reduces tissue water in edematous but not in normal brain (Bell *et al.*, 1987). In a group of patients with traumatic intracerebral hematomas and contusions, mannitol increased the specific gravity of white matter, probably by reducing brain water content (Nath and Galbraith, 1986). On the other hand, in non-injured cats there was no change in brain water content after mannitol and it was suggested that mannitol acted by reducing CSF volume (Takagi *et al.*, 1983). Also in non-injured cats, pial artery constriction was observed and taken to indicate autoregulation to change in viscosity (Muizelaar *et al.*, 1983).

In patients with severe head injury, when autoregulation was intact, mannitol reduced ICP by 27.2% without changing CBF. However, when autoregulation was defective ICP fell by only 4.7% and CBF increased. This strongly suggests that vasoconstriction, as well as cerebral dehydration, is a major action of mannitol (Muizelaar, Lutz and Becker, 1984). In another study of patients with severe head injury, mannitol consistently reduced ICP and increased CBF and CPP, the greatest increases in CBF after mannitol being seen in patients with low initial CPP and very high ICP, i.e. those most likely to have impaired autoregulation (Mendelow *et al.*, 1985).

***It is probable that the initial rapid reduction in ICP is due to plasma expansion and decreased blood viscosity which leads to constriction of the cerebral vasculature to maintain constant CBF. This rapid***

***response is more likely with bolus injection rather than infusion. The more prolonged reduction in ICP may be due to the osmotic effect.***

Mannitol may have other possible beneficial actions.

- It may reduce red blood cell rigidity, thus allowing them to penetrate small vessels and areas of marginal perfusion more easily (Burke *et al.*, 1981).
- It may scavenge free radicals, which have been implicated in ischemic brain damage.
- It may reduce CSF production (Sahar and Tsipstein, 1978) and a reduction in CSF volume has been reported experimentally (Tagaki *et al.*, 1983). However, as argued by Nath and Galbraith (1986), this is unlikely to be an important mechanism for reducing raised ICP when CSF has already been displaced.

Treatment based on the dehydration theory aims at providing a constant osmotic gradient. However, treatment based on the theory of viscosity autoregulation employs the opposite strategy – i.e. fluid losses are replaced accurately to maintain normal osmolality and normovolemia (Rosner, 1993).

*Mannitol dose*

***Mannitol is usually given in a 20% solution in bolus doses, rather than as a continuous infusion. ICP falls within 5–10 minutes. The maximum effect occurs in about 60 minutes and the total effect may last 3–4 hours (James et al., 1977).***

Bolus administration minimizes hemoconcentration and prolongs the effects. Boluses of 0.25–0.5 g/kg (given over 10–20 min) may be used and repeated depending on the response. A dose of 0.25 g/kg seems as effective as 1 g/kg in reducing ICP but may not act as long (Marshall *et al.*, 1978). A Foley catheter should be inserted and fluid losses should be replaced. Central pressures should be carefully watched and the patient kept euvoletic. Even so, mannitol may become less effective with repeated doses because:

- replacing the diuresis becomes increasingly difficult and hemoconcentration develops; at serum osmolality of greater than 320 mosmol/l there is a risk of uremia and prerenal renal failure (Stuart *et al.*, 1970);
- as osmolality rises, the increase in blood viscosity causes a fall in CPP, which will lead to cerebral vasodilatation and hence to a rise in ICP;
- mannitol may enter the extracellular space by opening the normal blood–brain barrier or where it is disrupted, taking fluid with it and cause a ‘rebound’ rise in ICP (Kaufmann and Cardoso, 1992). In practice this was seen more often with urea and is uncommon with mannitol (James *et al.*, 1977).

However the gradual increase in extracellular fluid osmolality reduces the osmotic gradient and renders mannitol less effective. This change will occur more slowly if mannitol is given in boluses rather than as an infusion.

It is our practice to avoid osmolality above 320 mosmol/l. Calculated osmolality may be significantly less than measured osmolality in the presence of mannitol.

#### *Complications of mannitol*

- Hyperosmotic prerenal renal failure (Cottrell *et al.*, 1977; Feig and McCurdy, 1977).
- Electrolyte disorders. Hypokalemia usually occurs after a few days of treatment and requires potassium supplements.
- Dehydration and hypotension. Reduced vascular volume leads to hypotension and the added risk of cerebral ischemia due to a fall in CPP. This is a particular risk in those with multiple injuries, the aged and those with pre-existing cardiac disease. These patients need careful monitoring of central pressures (Chapter 16).
- Expansion of an intracranial hemorrhage. By shrinking the brain, osmotic diuretics may assist the continued expansion of an intracranial clot. When the effects of mannitol wear off, there may be an acute deterioration. This risk is not proven and the acute deterioration under these circumstances may simply represent the inevitable enlargement of the clot temporarily masked by the effects of the mannitol. In a patient who may harbor a clot, mannitol is very effective in allowing time for transfer, CT scanning and surgical treatment.

#### *Renal diuretics*

Furosemide (furosemide) and other renal loop diuretics such as ethacrynic acid increase plasma osmolality by diuresis (Cottrell *et al.*, 1977; Cottrell and Marlin, 1981). They may reduce CSF formation directly (Sahar and Tsipstein, 1978). In combination with mannitol, furosemide produces a slightly greater reduction in ICP and increases the duration of its effect (Pollay *et al.*, 1983; Wilkinson and Rosenfeld, 1983). Given alone, furosemide and other renal diuretics do not reliably reduce ICP.

*The combination of furosemide and mannitol increases the risk of hypovolemia and renal failure and should be reserved for patients with actual or incipient cardiac failure or pulmonary edema. When used it is important to avoid excessive dehydration and sodium loss.*

**Dose:** furosemide 20–40 mg i.v.; **monitoring:** serum and urinary electrolytes and fluid balance.

#### **(d) Barbiturates**

High doses of barbiturates will frequently lower ICP even when osmolar therapy and hyperventilation have failed. Barbiturates and the other hypnotic drugs (such as etomidate and propofol), act by reducing cerebral metabolic rate for oxygen (CMRO<sub>2</sub>) and producing a coupled reduction in CBF. The consequent reduction in CBV leads to a parallel fall in ICP (Michenfelder, 1974). Some degree of retained vascular reactivity to CO<sub>2</sub> (Nordstrom *et al.*, 1988; Messeter *et al.*, 1986) and brain electrical activity must be present for barbiturates to act. The maximum effect has been correlated with EEG burst suppression, again underscoring the relationship between reduced metabolic rate and fall in ICP.

Anesthetic equivalent doses of hypnotics are necessary and hence ventilation and ICP monitoring are mandatory. Systemic hypotension and pulmonary failure may occur. *Cardiovascular status, including central venous and pulmonary artery wedge pressures, must be carefully monitored.*

If BP falls and cannot be maintained by volume transfusion then CPP must be maintained by inotrope infusion. It is safest to set up an inotrope infusion in anticipation whenever barbiturates are given.

Barbiturate therapy is generally reserved for the 12–15% of patients in whom other forms of intensive medical therapy for raised ICP have failed. Two uncontrolled trials reported an improved outcome with barbiturates (Marshall, Smith and Shapiro, 1979; Rea and Rockswold, 1983). In one trial about half those patients who failed to respond to other ICP therapy responded to barbiturates. The mortality in the barbiturate responders was 33% compared with 75% in the non-responders: 69% of survivors were classed as good recovery/moderate disability at follow-up (Rea and Rockswold, 1983). Similar results were reported in the earlier study (Marshall, Smith and Shapiro, 1979). In a controlled trial, patients were randomized to barbiturate therapy after other medical management for raised ICP had failed. ICP was controlled in about 30% of the barbiturate group compared to 16% of those treated with conventional therapy (Eisenberg *et al.*, 1988). Thus, in each trial, barbiturates were able to control ICP in some patients, even when all other medical means had failed and failure to respond to barbiturates carried a high mortality and morbidity. In contrast to these studies, when barbiturates were given prophylactically, i.e. to all patients, no benefit was found (Ward *et al.*, 1985; Schwartz *et al.*, 1984).

*Thus there appears to be a small subgroup of patients with severe head injury in whom barbiturate treatment is beneficial.*

*At present barbiturates are generally used in the following situations:*

- *as part of a stepwise protocol for ICP control, once other medical management has failed (see Figure 19.6).*
- *for acute intraoperative brain swelling (Shapiro et al., 1973; Bricolo and Glick, 1981).*

It has been suggested that hypnotic therapy, using barbiturates and other anesthetic drugs, may be specifically indicated in patients in whom ICP is elevated by vascular or hyperemic brain swelling, as indicated by decreased arteriovenous oxygen difference ( $S_{jv}O_2 > 75\%$ ) and preserved electrical activity (Dearden and McDowall, 1985; Miller, Piper and Dearden, 1993). Miller *et al.* have recommended that in this group of patients, hypnotic therapy should be given early, since barbiturate and other hypnotic agents will only work if vascular reactivity to arterial  $CO_2$  is still present (Nordstrom *et al.*, 1988) and brain electrical activity is preserved (Bingham *et al.*, 1985).

Hyperemic diffuse brain swelling is found most often in young patients, who usually show an ICP trace in which the amplitude of the arterial pressure oscillation is more than twice that of the respiratory oscillation (Miller, 1992; Dearden and Miller, 1989; Aldrich *et al.*, 1992). Chesnut, Marshall and Marshall (1993) have also suggested that young patients with markedly increased ICP and CT grade 3 or 4 swelling (Chapter 9) may sometimes benefit from early barbiturate treatment. However, they emphasized that the evidence for such a specific benefit is anecdotal and early aggressive barbiturate treatment cannot be generally recommended.

#### *Actions of barbiturates*

The actions of barbiturates include:

- *a decrease in metabolic rate with coupled reduction in CBF;*
- *free radical scavenging and reduction in lipid peroxidation;*
- *a direct increase in vasomotor tone.*

#### *Complications and contraindications*

- **Hypotension.** This is the main complication of barbiturate therapy and is due to reduced systemic vascular resistance and myocardial depression. Existing cardiovascular instability, hypotension and hypovolemia increase the risks of barbiturate therapy, lowering the safe dose that can be given and therefore reducing the likelihood of ICP control. Consequently patients must be euvoletic before barbiturates are started.
- **Anergy,** so that infection may occur without leukocytosis or fever.

- **Hypothermia.** Moderate hypothermia may be beneficial. However, below a core temperature of  $32^\circ C$  the risk of cardiac complications increases markedly.
- **Complications of prolonged coma** such as decubitus ulcers and venous thrombosis.
- **Gastric stasis.** This usually necessitates parenteral feeding.
- **Inability to diagnose brain death by clinical criteria** for 24 hours or more after treatment has stopped.

#### *Monitoring*

Barbiturate coma should only undertaken in an experienced Intensive Care Unit. Monitoring should include ICP, BP via an arterial line, CPP, central venous and pulmonary artery catheters and core temperature.

#### *Pupillary responses*

*Moderate levels of barbiturates cause small pupils that are sluggish or non-reacting. They may still dilate in response to brain-stem pressure. Larger doses may produce mid-position to 5mm non-reacting pupils (Chapter 8), which may produce a state indistinguishable from brain death (Chesnut, Marshall and Marshall, 1993). Widely dilated pupils, particularly if unequal, should always suggest the possibility of a mass lesion. During reduction of barbiturate dosage, pupil reactions are the first neurological function to recover and motor responses are the last (Chesnut and Marshall, 1993).*

#### *Endpoints*

- **ICP control:** *this is the principal endpoint;*
- **EEG:** *EEG burst suppression is a useful guide to optimal barbiturate dosage; there is no benefit in achieving higher barbiturate levels;*
- **Serum barbiturate levels:** *most authors advocate serum levels of about 30–40 mg/dl for optimal ICP control; however it is doubtful whether routine serum levels are really necessary except to determine when clinical tests of brain function are likely to be valid.*

#### *Dose and duration*

- **Thiopentone.** An i.v. bolus of thiopentone (e.g. 250 mg) will reduce ICP within seconds, but the effect will last for only 15–20 minutes. This may be a useful test to see whether a patient is likely to respond to prolonged barbiturate therapy. Once tissue levels have built up after continuous or repeated doses, the half-life is similar to that of the longer-acting barbiturates more commonly used.

● **Pentobarbitone.**

- Loading dose 10 mg/kg over 30 min or 5 mg/kg hourly for 3 hours;
- Maintenance 1 mg/kg/h or adjusted to serum level of 30–40 mg/dl or to burst suppression (Eisenberg *et al.*, 1988).

*Reducing barbiturate therapy*

Once ICP control has been achieved for 24–36 hours barbiturates may be reduced. Despite their long half-life it is preferable to reduce them slowly in order to prevent ICP overshoot.

(e) **Other agents**

*Hypertonic saline*

A 15% solution of sodium chloride was the first agent used experimentally to reduce raised ICP. It was presumed to act by osmosis but the effect was found to be short-lived and it gained no place in clinical practice (Weed and McKibben, 1919). However hypertonic saline has more recently been found to be useful in patients who no longer respond to mannitol and are developing uremia. Intravenous hypertonic saline (30% or 5 mmol/ml) over 10 minutes may produce a prolonged reduction in ICP without diuresis and improve renal function in dehydrated patients (Worthley, Cooper and Jones, 1988). Small amounts of hypertonic saline may help to prevent hypovolemia in patients requiring large amounts of mannitol (Ropper, 1993). In animal models of focal brain injury and hemorrhagic shock, resuscitation with hypertonic saline increased CBF at a lower ICP than did Ringer's solution (Walsh, Zhuang and Shackford, 1991).

**Dose:** hypertonic saline (5 mmol/ml) – up to 50 ml over 10–15 min; **monitoring:** serum Na<sup>+</sup>; urinary output.

*Steroids*

*Because of their effectiveness in treating the brain swelling associated with brain tumors and abscesses, steroids were at one time widely used in traumatic brain swelling. However, several trials, some using very high-dose steroid regimes, have failed to identify a benefit (Saul *et al.*, 1981; Dearden *et al.*, 1986; Gudeman, Miller and Becker, 1979; Cooper *et al.*, 1979).*

The was a single exception (Gobiet, 1977). However when this study was reanalyzed the changes after steroids were found not to be statistically significant (Cooper *et al.*, 1979). Steroids probably have no place in the routine management of closed head injury. However a non-glucocorticoid, the 17 amino steroid

(tirilazad), has shown promise in experimental head injury and is presently undergoing phase 3 clinical trials (Hall *et al.*, 1988). The present status of this and other neuroprotective agents is discussed in Chapter 21.

*Gamma hydroxybutyrate*

Gamma hydroxybutyrate is an analog of the inhibitory neurotransmitter gamma-amino butyrate acid (GABA) and is used as a short-acting anesthetic agent. It is a potent vasoconstrictor and reduces cerebral metabolic rate. When given as a bolus it has been shown to be as effective as sodium thiopentone in reducing ICP and with a longer duration of action. As with sodium thiopentone it will reduce systemic blood pressure and CPP must be carefully monitored (Leggate, Dearden and Miller, 1986).

**Dose:** 60 mg/kg body weight; **monitoring:** cerebral perfusion pressure, since it may reduce systemic blood pressure.

*Indomethacin*

Indomethacin, a prostaglandin inhibitor, may reduce raised ICP even though other medical treatments, including barbiturate therapy, hyperventilation and mannitol have failed (Jensen *et al.*, 1991; Biestro *et al.*, 1995). Indomethacin may act by restoring the capacity for autoregulation and hence the response to hyperventilation and to mannitol. If indomethacin infusion is withdrawn suddenly there may be a rebound rise in ICP (Biestro *et al.*, 1995).

**Dose:** bolus – 50 mg in 20 min; infusion – 10–30 mg/h.

*Lidocaine*

Lidocaine is a local anesthetic which may be given as an endotracheal aerosol to prevent ICP rises during intubation (Yano *et al.*, 1986). It may also be given intravenously for the same purpose (Donegan and Bedford, 1980). This may cause myocardial depressant and requires ECG monitoring. Lidocaine has been used to treat refractory status epilepticus, but high doses may lower the seizure threshold. There is some evidence that it will lower raised ICP refractory to other methods but it has not been widely used because of the potential complications. At the doses used preintubation, such complications are unlikely.

**Dose:** 1–1.5 mg/kg i.v. within 60–90 s of intubation, or as a 4% intratracheal aerosol; **monitoring:** ECG.

*Tromethamine (THAM)*

The base tromethamine has been proposed as a means of correcting the lactic acidosis frequently found in

patients after head injury (Rosner and Becker, 1984b). In a randomized trial of the effects of prophylactic hyperventilation, Muizelaar *et al.* (1991) found that the potentially adverse effects of hyperventilation were prevented and that ICP was more stable. In a further prospective, controlled study, the addition of THAM to conventional treatment resulted in better ICP control. However there was no improvement in outcome (Wolf *et al.*, 1993). Hence, THAM may be useful in controlling raised ICP but its place needs to be more clearly defined in further studies. THAM may impair renal function and this needs to be carefully monitored.

**Dose:** 1 mg/kg/h of 0.3 mmol/l solution; **monitoring:** renal function.

#### (f) Hypothermia

*Moderate hypothermia (core body temperature 30–34°C) was recommended many years ago in the treatment of head injury (Sedzimir, 1959) but after some initial interest it was little used. However, recent experimental evidence suggests that moderate hypothermia is cytoprotective after severe global ischemic insults. Hypothermia reduces the effects of global ischemia in head injury. It reduces glutamate release and prevents the depletion of high-energy phosphate compounds (Chopp *et al.*, 1991; Busto *et al.*, 1989). A significant improvement in recovery was found following fluid percussion injury in rats when hypothermia was initiated up to 15 minutes after the injury (Clifton *et al.*, 1991). Similarly, cerebral damage following epidural compression was reduced in a canine model (Pomeranz *et al.*, 1993).*

Recent clinical studies have suggested a benefit from moderate hypothermia used prophylactically for 24–48 hours following severe head injury (Marion *et al.*, 1993), or when ICP is not responding to medical therapy, including high-dose barbiturates (Shoizaki *et al.*, 1993). In both studies there was a reduction in ICP, CBF and CMRO<sub>2</sub> and a trend towards improved outcome in the hypothermic groups, more evident in a later report (Marion and Carlier, 1995). There has been no greater incidence of significant complications with moderate hypothermia in the head injury studies reported so far. Hypothermia is well known to cause coagulopathy, but Resnick, Marion and Darby (1994) found no greater incidence of measurable coagulopathy or of delayed intracerebral hemorrhage in a small study. Metz *et al.* (1996) found that platelet count fell during 24 hours of hypothermia and for up to 24 hours after rewarming, but there was no significant change in coagulation tests. Four of ten patients developed signs of pancreatitis, which reversed with rewarming. Thus hypothermia may be a safe additional treatment in patients with high ICP. Currently, a

large multicenter placebo-controlled trial of prophylactic moderate hypothermia (32 ± 2°C) is under way in neurosurgical centers in the USA to test its effects upon outcome and ICP control.

#### (g) Hyperbaric oxygen

Hyperbaric oxygen reduces CBF and ICP by vasoconstriction while preserving a high oxygen delivery to the tissues. Those who respond to hyperbaric oxygen are also likely to respond to hyperventilation, which has fewer logistical problems. Hence, even where pressure chambers are available, hyperbaric oxygen is rarely used in the management of patients with head injury. In one prospective study, hyperbaric oxygen reduced mortality after severe head injury by nearly 50%, but did not increase the favorable outcome rate among survivors (Rockswold *et al.*, 1992).

## 19.8 Surgical treatment

### 19.8.1 INDICATIONS (Chapter 20)

When there is clear evidence of neurological deterioration and a CT scan shows an intracranial mass lesion, the need for urgent removal is clear. The results of surgery for a mass lesion are directly proportional to the neurological state at the time of evacuation (Becker *et al.*, 1977; Mendelow *et al.*, 1983). Unnecessary delay in achieving surgical evacuation and lowering ICP must be avoided under any circumstances. Rarely, if deterioration is rapid and there are clear localizing features, then the CT scanner may be bypassed and the patient taken directly to surgery (Chesnut *et al.*, 1994).

In comatose patients with hemispheric or diffuse swelling and a small surface clot the need for surgical removal may be less clear. However the removal of even a small surface clot 3–5 mm thick, extending over several cuts, may improve compliance and make ICP management easier. Moreover, duraplasty and craniotomy itself may reduce ICP dramatically in these circumstances. These potential advantages must be balanced by the risk of brain herniation, venous compression and increased swelling, even with duraplasty. When the patient is stable, there is only moderate brain shift, i.e. 5 mm or less, and ICP is less than 20 mmHg it may be reasonable not to treat small surface clots by surgery initially. However, such patients need careful ICP monitoring and CT scans should be repeated routinely. In general we believe that it is better to err towards removing too many clots rather than to tolerate high ICP. Knuckey, Gelbard and Epstein (1989) noted that patients with small extradural hematomas were more prone to late deterioration if the hematoma was diagnosed within 6 hours of

injury than if it was diagnosed later. Deterioration in the latter group was therefore most often due to other factors.

#### *Delayed intracerebral hemorrhage*

Delayed intracerebral hemorrhages have been recognized for many years. However, the CT scan has enabled more precise definition and distinction from swelling around or enlargement of a previous hemorrhage (Gentleman and Macpherson, 1989). A delayed intracerebral hemorrhage is defined on CT as a lesion of increased attenuation occurring in a previously normal area. They are uncommon, being only 2.6% of traumatic intracranial hematomas in the series of Gentleman and Macpherson, and developed within hours to days. Some 80% were detected within 48 hours of injury. Less than half needed surgical evacuation. Their potential occurrence makes repeat CT scan mandatory whenever there is an unexplained clinical deterioration, failure to improve or a rise in ICP, even if the initial scan was normal. It was suggested many years ago that delayed hemorrhage occurred in areas of focal injury where vasoparalysis, congestion and increased capillary permeability resulted in multiple areas of diapedetic hemorrhage (Evans and Scheinker, 1946). Delayed hemorrhage has been associated with clotting abnormalities, in particular disseminated intravascular coagulation (Kaufman *et al.*, 1980), hypotension and hypoxia (Ninchoji *et al.*, 1984).

### 19.9 Plan of management of raised ICP and reduced CPP

Although the evidence for certain components of head injury management is sufficient to provide management guidelines, there is no controlled study of any particular combination of treatments that would constitute a recommended protocol or 'critical pathway'. The treatment plans outlined here are those of two separate institutions and represent somewhat different approaches to the same problem.

It must be recognized that head injury is a dynamic process that varies in its pathophysiology between patients, with time, and in its regional distribution. The usual practice of using a single protocol of management for all patients is not ideal. However at present it is difficult to measure cerebral blood flow and metabolism directly and treatment tends to be based on probabilities rather than on specific information. Furthermore there are still few effective treatments available for brain swelling and increased ICP.

In order to tailor the treatments that are available to the specific and evolving pattern of injury in a particular patient, continuous bedside monitoring of brain metabolism and substrate delivery are required. Methods of providing this information are becoming available but until it is possible to distinguish specific causes for raised ICP and reduced CPP in individual patients, treatment regimes will remain sequential.

Despite these limitations it is important that a generally consistent plan of approach be adopted. The goals of management should be:

- to identify the dominant pathology;
- to target treatment to the cause;
- to avoid secondary insults.

There are three levels of observation upon which treatment is based:

- clinical;
- continuous multimodality monitoring;
- imaging.

#### 19.9.1 NURSING POSITION

Patients are usually nursed 30° head up after intracranial surgery and head injury in order to reduce 'venous congestion' and 'brain swelling'. In most patients ICP is lower in this position.

Rosner and Coley (1986) found that in many patients, although ICP fell with head elevation, there was also a significant fall in CPP. A fall in CPP was less likely when circulating volume was adequate. However this variable response to positional change highlights the need for adequate fluid replacement and for CPP monitoring (Chapter 17).

#### 19.9.2 EXTRACRANIAL CAUSES OF RAISED ICP (Table 19.1)

ICP may be increased by a number of extracranial factors, including nursing procedures such as endotracheal suction and physiotherapy. Before concluding

**Table 19.1** Factors that affect intracranial pressure

Increase	Decrease
Hypercarbia	Hypocapnia
Hypoxia ( $P_{aO_2} < 50$ mmHg)	Hyperoxia
Epilepsy	Hypothermia
Hyperthermia	Barbiturates
Venous congestion due to intrathoracic pressure; fluid overload	

that raised ICP is due to intracranial factors, a checklist should be considered.

- **Airway and head position.** Ensure that there is no venous obstruction.
- **Arterial blood gases.** Ensure that  $P_a\text{CO}_2$  is  $32 \pm 2$  mmHg.
- **Core temperature.** A rise of  $1^\circ\text{C}$  can increase metabolic rate by 10%, thus increasing ICP by several millimeters of mercury. Core body temperature must be kept below  $38^\circ\text{C}$ .
- **Occult seizures.** Anticonvulsants have been recommended in all ventilated patients with severe closed head injury because seizures occurring in heavily sedated and paralyzed patients are difficult to detect without EEG monitoring, yet they can lead to marked increases in CBF and ICP (Marienne, Robert and Bagnet, 1979)
- **Sedation level.** Consider whether the patient is becoming more conscious and 'fighting the ventilator'.

### 19.9.3 TREATING RAISED ICP AND REDUCED CPP

Treatment protocols should begin with simple nursing procedures and proceed stepwise to more complex methods, depending on the response at each stage. Recent studies from Edinburgh and other centers have helped to define what constitutes a significant secondary insult and hence to set treatment goals (Jones *et al.*, 1994). When methods of reliably monitoring cerebral oxygenation and metabolism become available, these parameters can be taken into account.

Treatment endpoints should take into account the time since injury and nature of the pathology. There also needs to be a balance between treating every change in ICP or CPP from normal and using up the available and limited methods of treatment prematurely.

Treatment should be on the background of:

- cardiopulmonary homeostasis and euvolemia;
- adequate sedation.

These aspects are covered in Chapters 16, 17 and 18.

Table 19.2 indicates the changes in the emphasis of treatment that have occurred in recent years.

#### *First-tier therapy*

If ICP rises the first steps are:

- check blood gases to ensure normoxia and normocarbida;
- drain CSF;
- administer mannitol;
- institute moderate hypothermia.

**Table 19.2** Changing emphasis in management of acute head injury:  $S_{jv}\text{O}_2$  = jugular venous oxygen saturation; PEEP = positive end-expiratory pressure; ICP = intracranial pressure (Source: adapted from Myburgh and Lewis, 1996.)

<i>Previous strategies</i>	<i>Current strategies</i>
Reduce intracranial pressure	Maintain cerebral perfusion pressure and reduce intracranial pressure
Elective dehydration	Euvolemia
Routine osmotherapy	Selective osmotherapy (< 300 mosmol/l)
Routine hyperventilation: ( $P_a\text{CO}_2 < 30$ mmHg)	Normocapnia: acute hyperventilation to control rises in ICP prior to imaging, maintain $S_{jv}\text{O}_2$ above 55%
Routine barbiturates	Limited barbiturates
Routine corticosteroids	No corticosteroids
Avoid sedation, use muscle relaxants	Avoid muscle relaxants, ensure sedation and analgesia
Avoid PEEP	Use PEEP to maintain $P_a\text{O}_2$
ICP monitoring – intraventricular or subdural fluid-filled catheters	ICP monitoring – intraventricular or intraparenchymal solid-state systems

#### *Refractory intracranial hypertension*

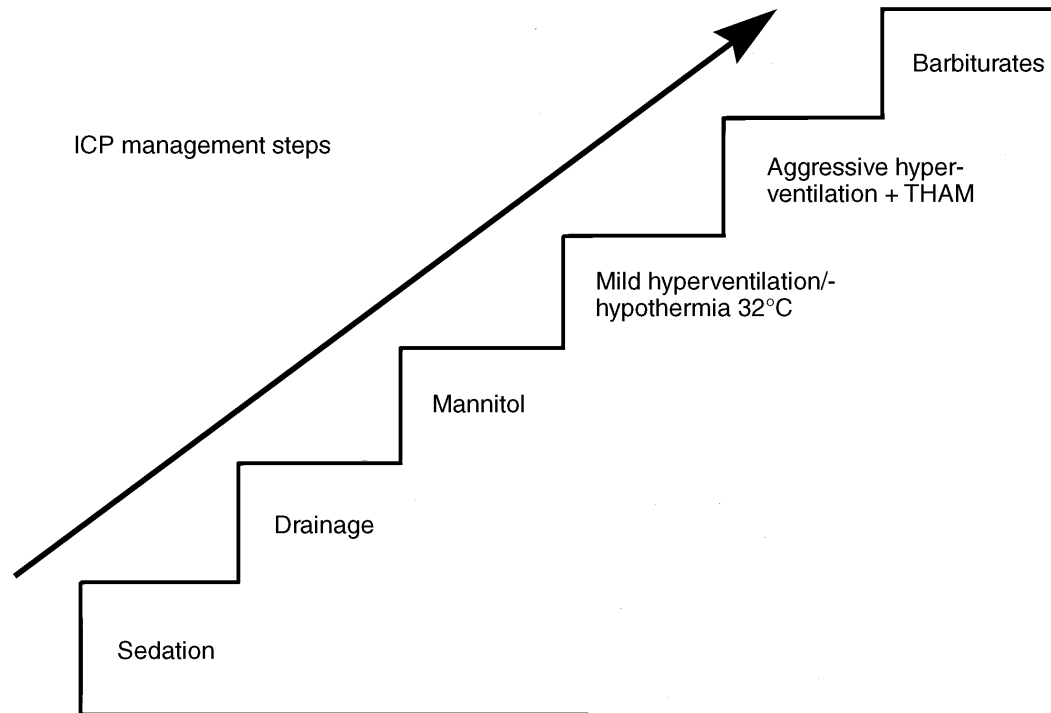
If ICP rises above the desired treatment level and CPP falls despite first-tier therapy, the second-tier therapies to be considered are:

- induced hypertension;
- barbiturate therapy;
- decompressive craniotomy;
- hypothermia;
- marked hyperventilation (Guidelines for the Management of Severe Head Injury, 1995).

Before proceeding to more complex treatments it is always important to recheck for easily reversible causes of raised ICP, as set out in section 19.9.2, and to consider repeating the CT scan.

#### *Treatment algorithms*

The 'staircase' protocol used at the Medical College of Virginia is shown in Figure 19.6. The indications for decompressive craniotomy within this protocol are summarized in Chapter 20. The protocol currently used at the Royal Adelaide Hospital (Figure 19.7) is based on maintaining ICP below 20 mmHg and CPP above 70 mmHg. However, it also takes into account  $S_{jv}\text{O}_2$  and TCD data in distinguishing hyperemia and



**Figure 19.6** The 'staircase' approach to management of ICP and CPP at the Medical College of Virginia. Treatment is initiated when ICP > 20 mmHg or CPP < 70 mmHg for more than 10 minutes. Inotropes are used at any time, aiming to keep CPP above 70–80 mmHg.

determining the lower limit of autoregulation in order to define the optimal level of CPP (Lewis, Reilly and Myburgh, 1996). If jugular bulb oximetry is used, a careful protocol must be observed to minimize false readings.

#### *Duration of monitoring*

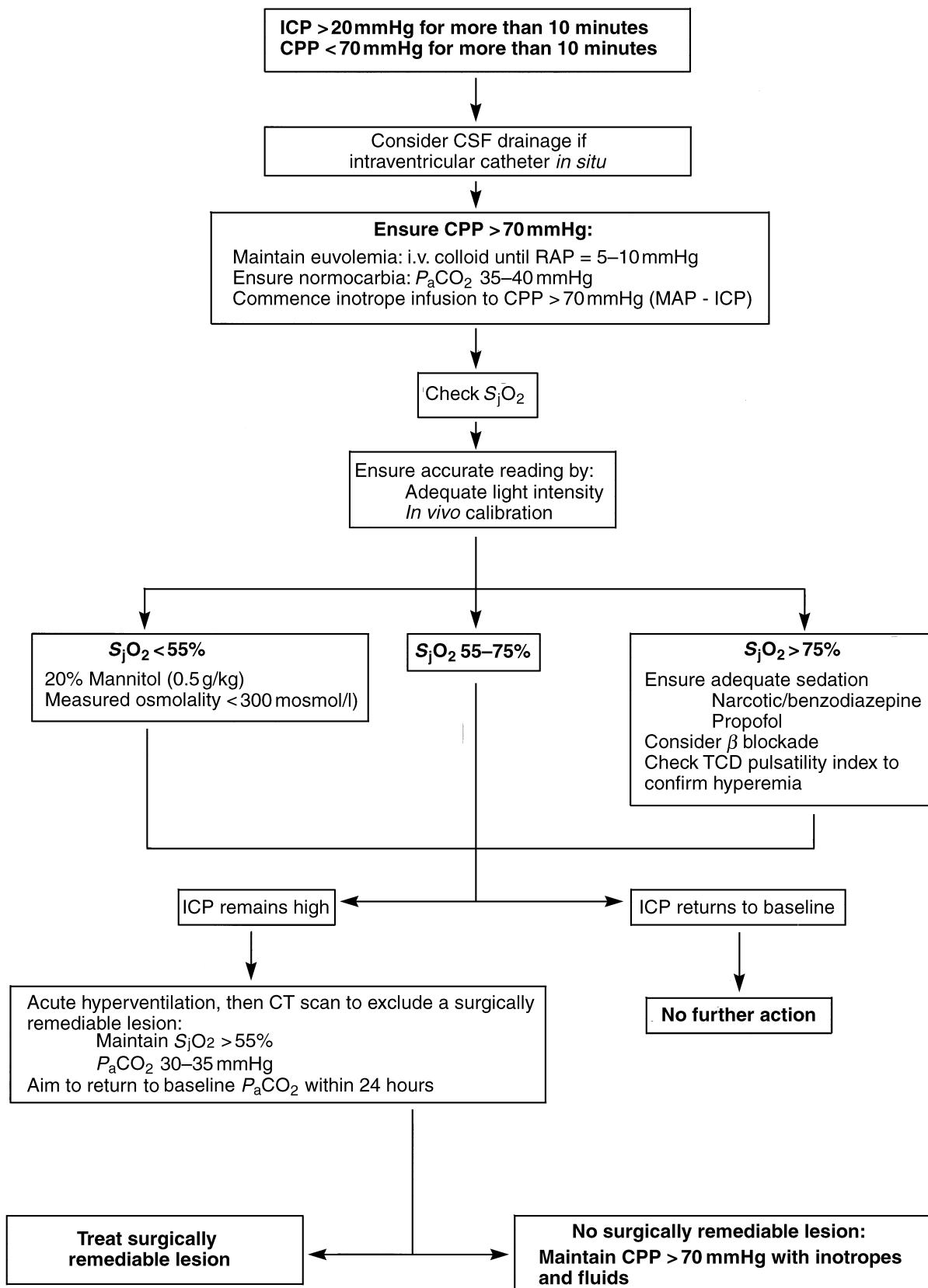
ICP and CPP monitoring should continue until the patient is stable without treatment and the risk of a later deterioration is low. The period of vulnerability to secondary insults may be up to two weeks after injury. Studies from Edinburgh found two peaks of reduced CPP. The first, within 24 hours, was most often due to hypotension. The second occurred 5–6 days after injury, usually as a result of increased ICP (Cortbus *et al.*, 1995). Unterberg *et al.* (1993) reported the peak incidence of high ICP to be 1–3 days after injury. Late rises occurred after 3–10 days, particularly in patients with multiple contusions, and coincided with a marked leukocytosis. These reports suggest that patients with severe head injury and abnormal scans should be monitored for at least 6 days, and that weaning from the ventilator should occur slowly.

If the ICP is low from the outset or has been low without treatment for 24 hours, and the CT scan does not show a mass lesion or diffuse swelling, then it is reasonable to cease sedation. If ICP and CPP remain

satisfactory, then monitoring may be withdrawn. As noted earlier, it is important to withdraw barbiturate therapy slowly.

#### *Intractable ICP: who manages the patient?*

One of the most important advances in the management of head injury in recent years has been the formation of integrated multidisciplinary services that extend from the accident site to the trauma hospital and indeed beyond to the phase of rehabilitation. The intensive care specialist has played a key role in all stages of acute care. With the emphasis on intensive care management for patients, the intensivist needs, in addition to expertise in cardiorespiratory care, a detailed knowledge of the pathophysiology of head injury and the effects of drugs – knowledge that needs to be shared by the neurosurgeon. The neurosurgical role extends beyond removing hematomas. The neurosurgeon should be involved in determining treatment protocols, assessing and deciding the treatment plan for each patient and continuing care after the acute phase. During the acute phase neurosurgeons and intensivists should work in cooperation in determining treatment steps and in counseling relatives. This is particularly important when the question of withdrawing treatment arises, which is discussed in more detail in Chapter 21.



**Figure 19.7** Algorithm for the management of acute head injury based on CPP and ICP and taking into account  $S_jO_2$  and TCD measurements. ICP = intracranial pressure; CPP = cerebral perfusion pressure; CSF = cerebrospinal fluid; RAP = right atrial pressure; MAP = mean arterial pressure;  $S_jO_2$  = jugular venous oxygen saturation; TCD = transcranial Doppler. (Source: reproduced from Myburgh and Lewis, 1996, with permission)

## 19.10 References

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