

18 SEDATION AND ANESTHESIA

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18.1 Introduction

The patient with a severe acute head injury, often with other bone and soft-tissue injuries, presents a complex management problem involving a large number of medical and paramedical staff. A coordinated approach is essential, with clear and frequent communication between the involved personnel on all aspects of critical care, including initial resuscitation, anesthesia, radiological imaging, surgical intervention and intensive care management.

The anesthetist is an active member of this team and is involved in many stages of management. *Indeed, the anesthetist is often the one medical specialist in constant attendance from hospital admission through to the postoperative ward or intensive care unit. Furthermore, therapy instituted by the anesthetist, such as the choice of sedative agents, paralysis, intubation and fluid management, will directly impact upon other aspects of management, such as neurosurgical and intensive care treatment.*

The anesthetist must have a sound knowledge of cerebral pathophysiology and pharmacology and of the acute medical care of the multiply injured patient. Many of these aspects are covered in other sections of this book. The conduct of basic anesthetic techniques is well covered in general anesthetic texts. This chapter will therefore concentrate on the pharmacology of drugs in current use and aspects of anesthetic management specifically related to the patient with a severe head injury.

18.2 Cerebral pharmacology

There is a wide range of potent drugs available for sedation, analgesia, anesthesia, paralysis, anticonvulsant therapy, cardiovascular manipulation and fluid balance and most have actions that affect the injured brain and its treatment.

Knowledge of drug effects on cerebral oxygen consumption (CMR), cerebral blood flow (CBF), intracranial pressure (ICP), cerebral perfusion pressure

(CPP) and seizure activity are essential for planning the optimal drug regimen for each patient.

Partly because these parameters are quite difficult to measure both experimentally and in clinical practice, there is no agreed optimal drug regimen for anesthesia or sedation of the head-injured patient. Indeed, views are constantly changing as new information and new drugs come to hand. Examples of this include the recently described effects of nitrous oxide on CBF and CMR, the increases in CBF and ICP reported with the synthetic opioids and the introduction into clinical practice of the volatile agents desflurane and sevoflurane.

More difficult to resolve is whether a particular anesthetic technique or drug regimen with theoretical advantages – and perhaps significant financial cost – improves patient outcome. This was highlighted in a recent study where no differences in short-term outcome were found between three anesthetic drug regimens used during elective neurosurgery, even though each had very different pharmacological cerebral effects (Todd *et al.*, 1993). These difficulties were well summarized in an editorial on monitoring by Eichhorn (1993), where he stated: 'There will never be enough " $p < 0.05$ " scientific data on outcome of anesthesia to satisfy the staunch traditionalists. We will continue, however, to have practices based on a modern synthesis of the best information available at the time.'

18.3 Intravenous anesthetic agents

18.3.1 PROPOFOL

Propofol, a substituted phenol, is a relatively new intravenous induction agent. It has achieved widespread popularity, largely because it has a short effective half-life and hence a rapid onset and offset of action with a short recovery time. *Intravenous administration via bolus produces rapid onset of anesthesia and a dose-dependent coupled fall in CBF and CMR, effects similar to those well described following*

barbiturate administration (Ludbrook et al., 1996; Ramani et al., 1992; Eng et al., 1992; Figure 18.1).

The effects on CBF are probably secondary to a reduction in CMR, but the effectiveness of propofol in reducing raised ICP may be less if CMR–CBF coupling is impaired by the head injury itself. Hence cerebral vasoconstriction and a decrease in ICP could be demonstrated in patients receiving propofol during elective surgery (Ravussin et al., 1988) but not in a group of patients with severe head injuries, despite evidence of a reduction in CMR (Stewart et al., 1994).

CO₂ reactivity and autoregulation of CBF appear reasonably well preserved during propofol admin-

istration (Fox et al., 1992; Eng et al., 1992) and consequently, in the normal brain, CBF is not greatly affected by changes in CPP between approximately 50 and 150 mmHg. This may not be so in the patient with head injury if cerebral autoregulation is impaired (Bouma et al., 1992).

In the head-injured patient with raised ICP, rapid induction with propofol may reduce ICP and improve cerebral oxygenation. This may prevent or attenuate the marked, though relatively brief ICP increases that may occur with endotracheal intubation.

Propofol may cause dose-dependent cardiovascular depression and systemic hypotension especially when

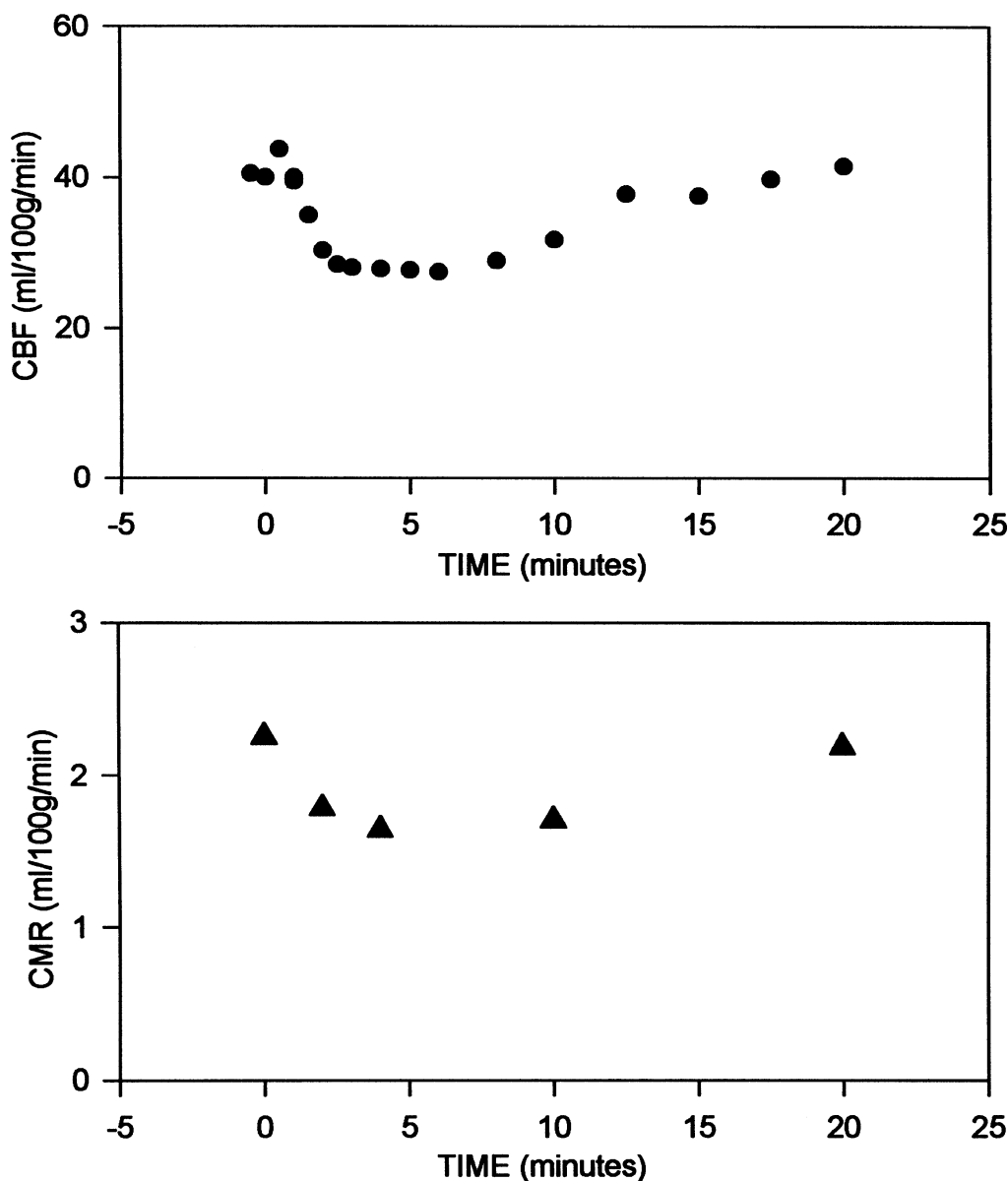


Figure 18.1 Changes in CBF and CMR in a sheep following a bolus dose of propofol, 100 mg i.v. (Source: reproduced from Ludbrook et al., 1996, with permission.)

anesthesia is rapidly induced by bolus drug administration. Hypotension is partly due to systemic vasodilatation (Pensado, Molins and Alvarez, 1993; Petros, Bogle and Pearson, 1993) but may also be due to direct myocardial depression and decreased cardiac output (Lindgren, 1993). This may induce cerebral ischemia by one of two mechanisms. If autoregulation is intact, a reduction in mean arterial pressure will produce reflex cerebral vasodilatation and risk further increase in ICP and fall in CPP; if autoregulation is impaired, hypotension may produce a critical decrease in CPP and CBF. The risk of hypotension is greater in the presence of hypovolemia due either to multiple injury or to deliberate dehydration for ICP control. Because of the cardiovascular effects and brief duration of action, propofol requires a careful choice of dose regimen for induction in order to avoid hypotension or raised ICP at laryngoscopy. A slow rate of administration may provide greater cardiovascular stability (Stokes and Hutton, 1991) and allow titration of dose against effect, but this is usually not possible in patients with head injury because of the risk of regurgitation in the unfasted patient and the dangers of hypoventilation and hypercarbia.

The potentially beneficial cerebral effects of propofol and its brief duration of action even after prolonged administration make it suitable for maintaining anesthesia or sedation by infusion. Thiopentone, opioids and benzodiazepines can be used in this manner, but they have a greater tendency to accumulate, which can delay recovery from anesthesia or sedation. This is particularly relevant if early or frequent postoperative neurological assessment is required.

Infusion regimens which will provide stable planes of anesthesia without prolonged recovery times have been developed for propofol, either alone or in combination with inhaled anesthetic agents (Valanne, 1992). For similar reasons, propofol infusion is becoming more popular for sedation of ventilated patients in intensive care (Roekaerts, Huygens and de Lange, 1993; Farling, Johnstone and Coppel, 1989). Whether used in anesthesia or for sedation, hypotension with propofol needs to be carefully avoided by aggressive fluid and/or pharmacological therapy.

There has been considerable debate about the effects of propofol on seizure threshold. This is clearly relevant in patients with head injuries where massive increases in CBF have been demonstrated during seizures, even during artificial ventilation (Meldrum and Nilsson, 1976). *The anticonvulsant properties of propofol are now well described. It reduces the duration of seizures during electroconvulsive therapy (ECT) when compared to more traditional barbiturate-based anesthesia (Simpson et al., 1988; Dwyer et al., 1988; although its effect on ECT efficacy is as yet unclear)*

and there are clearly documented examples of its efficacy in the treatment of status epilepticus (Melloni et al., 1992; Mackenzie, Kapadia and Grant, 1990). Excitatory movements and patient arousal have been described during induction with propofol but, rather than being true seizure activity, are probably related to light planes of anesthesia and are more akin to the excitation that frequently occurs during induction with methohexitone (Reddy et al., 1993). For a more complete discussion the reader is directed to recent reviews of the current evidence regarding propofol and convulsions (Bevan, 1993; Smith et al., 1994).

The clinical experience of this author is that propofol, when administered at both sedative and anesthetic doses by infusion, is effective in controlling seizures after neurosurgery. This adds to its potential benefits in the management of the head-injured patient during and after surgery.

18.3.2 BARBITURATES

Thiopentone has been one of the most commonly used induction agents in anesthesia for many years, and is frequently used in neuroanesthesia and intensive care. As with propofol, intravenous administration of thiopentone produces rapid induction of anesthesia accompanied by dose-dependent parallel falls in CBF and CMR (Michenfelder, 1974). The preserved coupling of CBF and CMR and the potential benefits on ICP led to the extensive use of barbiturates in the head-injured patient.

The cerebral vasoconstriction induced by barbiturates is effective in controlling raised ICP, even when it is refractory to mannitol or hyperventilation. Barbiturates may also improve blood flow to underperfused areas of the injured brain which have lost or reduced vasoreactivity ('reverse steal'; Levin et al., 1979; Marshall et al., 1978; Frost et al., 1981; Rockoff, Marshall and Shapiro, 1979). As with propofol, cerebral vasoconstriction is secondary to reduced CMR, and is dependent on the presence of coupling of CBF and CMR after injury. Messeter et al. (1986) found that beneficial effects on CBF and ICP could be demonstrated in patients with intact CO₂ reactivity, but there was no change in CVR and only a transient ICP reduction in patients in whom CO₂ reactivity was impaired.

The protective effects of barbiturates in experimental models of cerebral ischemia or hypoxia appear greater than can be explained by decreases in CBF and CMR alone, and other mechanisms including decreasing cellular calcium influx, inhibition of free radical formation, membrane stabilization and actions as a GABA agonist have been proposed (Blaustein and Ector, 1975; Smith et al., 1980; Yoshida, Inoh and Asano, 1983). *However, despite the evidence of cerebral protection in experimental models, there is little*

evidence that barbiturates improve outcome after severe head injuries (Ward et al., 1985; Chapter 19).

Thiopentone may cause hypotension, due primarily to myocardial depression (Azari and Cork, 1993). Hypotension and a fall in CPP is a particular risk in the hypovolemic patient and, as with propofol, careful choice of dose and aggressive use of vasopressors should be used to avoid this during induction of anesthesia. If barbiturate coma is used to control raised ICP concomitant use of vasopressors is often necessary.

To maintain anesthesia, thiopentone can be administered simply and successfully *via* continuous infusion (Crankshaw and Karasawa, 1989), avoiding inhaled anesthetic agents, many of which produce cerebral hyperemia and may increase ICP. However, thiopentone has largely been replaced by propofol for intravenous anesthesia because of reduced recovery times.

Barbiturates are very effective anticonvulsants. Thiopentone is probably the most effective agent available for the rapid control of seizures. For prolonged control, however, thiopentone must be given by continuous infusion. Hence if barbiturates are necessary for more than 24–48 hours, longer-acting agents such as pentobarbitone are usually substituted.

Methohexitone, a barbiturate, is widely used as an induction agent because it has a short duration of action allowing a more rapid recovery than thiopentone. Induction is frequently accompanied by excitatory movements which may resemble seizures (Dundee and Moore, 1961). For this reason it is not commonly used in neuroanesthesia.

Longer-acting barbiturates such as pentobarbitone (half-life 20–30 h) and phenobarbitone (half-life 30–90 h) are rarely used in anesthetic practice because of their delayed onset and long duration of action, but they may be considered for prolonged anticonvulsant therapy.

Ketamine, a phencyclidine derivative, is a useful induction agent, which may support or increase blood pressure because of a drug-induced increase in sympathetic activity, and it may induce postoperative confusion or nightmares. There is conflicting evidence regarding the effects of ketamine on CBF. *Early studies found marked increases in CBF, CMR and ICP and interference with autoregulation (Dawson, Michenfelder and Theye, 1971; Shapiro, Whyte and Harris, 1974; Whyte, Shapiro and Turner, 1972). In addition, the postoperative confusion which occurs particularly in the elderly, may complicate neurological assessment. For these reasons, ketamine was not recommended for neuroanesthesia by most clinicians.* Later studies have shown no change or falls in CBF and ICP (Bjorkman et al., 1992; Pfenniger and

Reith, 1990; Hougaard, Hansen and Broderson, 1974; Takeshita and Michenfelder, 1972). Furthermore, in some animal models a cerebral protective effect following cerebral ischemia and head injury has been reported (Church, Zeman and Lodge, 1988; Hoffman et al., 1992; Shapira, Artru and Lam, 1992; Shapira et al., 1994). Ketamine is an antagonist at N-methyl D-aspartate (NMDA) receptors, and this is one proposed mechanism behind this protective action.

Ketamine's popularity has recently increased in general anesthesia, where it may be given either by infusion alone or in combination with other hypnotic agents (Royblat et al., 1992) and, for the reasons outlined above, there is also some renewed interest in its use in neurosurgery.

18.3.3 ETOMIDATE

Etomidate is a hypnotic agent that will rapidly induce anesthesia after bolus intravenous administration. *As with propofol and thiopentone, onset of anesthesia is accompanied by parallel decreases in CBF and CMR (Milde et al., 1985; Renou et al., 1978). There is some evidence that etomidate provides protection against cerebral ischemia (Sano et al., 1993; Watson et al., 1992). CO₂ reactivity is preserved during etomidate administration (Renou et al., 1978). Accompanying cardiovascular changes are usually minimal (Criado et al., 1980) and it is therefore the induction agent that is most likely to reduce ICP and CMR with least compromise of CPP.*

These effects are likely to be most beneficial when inducing anesthesia in a head-injured patient, particularly in the presence of hypovolemia.

However, the onset of anesthesia is not uncommonly accompanied by myoclonic movements resembling seizures (Reddy et al., 1993). There have also been reports of adrenal suppression following even brief administration (Ellis et al., 1985; Fellows et al., 1983) limiting its usefulness for maintenance of anesthesia.

18.3.4 BENZODIAZEPINES

Benzodiazepines have sedative and anticonvulsant properties, making them potentially very useful for head-injured patients during anesthesia and intensive care treatment. They bind to benzodiazepine receptors linked to GABA-dependent chloride channels in the cell membrane and, as the actions of both propofol and the barbiturates are likely to be at least partially GABA-mediated, it might be expected that their cerebral effects would be similar.

Diazepam has been used extensively as an intravenous sedative/hypnotic agent but disadvantages include a long elimination half-life (20–50 h), irritant

effects on veins and incompatibility with a number of other agents. The use of a lipid emulsion carrier improves intravenous administration but its prolonged sedative and ventilatory depressive effects, especially after repeated or infusion administration, are a disadvantage.

Midazolam is a water-soluble short-acting benzodiazepine that has largely replaced diazepam for parenteral use because it has a shorter half-life, is miscible with most drugs and does not cause venous irritation. Midazolam produces a dose-dependent fall in CMR, CBF and ICP in both experimental animals and humans (Nugent, Artru and Michenfelder, 1982; Giffen, Cotrell and Schwirey, 1984; Fleischer et al., 1988; Forster, Juge and Morel, 1982; Hoffman, Miletich and Albrecht, 1986; Bjorkman et al., 1992). It is a potent anticonvulsant.

In line with most drugs that reduce CBF and CMR, there is some evidence of cerebral protective effects with both midazolam and diazepam (Nugent, Artru and Michenfelder, 1982). Midazolam is a safe and effective agent for sedating patients with head injury undergoing ventilation in intensive care, where it is often combined in an infusion with opioids such as fentanyl or morphine.

Midazolam is not as effective an anesthetic agent, since the onset of anesthesia is slow, although without excitation, and it has a less reliable dose-response relationship than many other hypnotic induction agents. It has a reputation for cardiovascular stability but the large doses required for induction of anesthesia (in the order of 0.2 mg/kg) may produce a critical reduction in CPP, especially in the hypovolemic patient or in the presence of raised ICP (Derbyshire et al., 1984; Forster, Juge and Morel, 1982; Papazian et al., 1993). Low doses of midazolam can effectively supplement anesthesia, allowing lower doses of volatile or hypnotic agents without reducing CPP.

Flumazenil is a specific antagonist to benzodiazepines that acts competitively at the benzodiazepine receptor (Hunkeler et al., 1981). Its half-life is significantly shorter than either midazolam or diazepam and repeated administration or infusions are necessary to avoid recurrent sedation. Given intravenously it rapidly reverses the sedative and anticonvulsant effects of benzodiazepines but not surprisingly it increases CBF and ICP and can induce seizures (Fleischer et al., 1988; Kumano et al., 1993). In two of 15 head-injured patients administered flumazenil, ICP increased to over 40 mmHg (Chiolerio et al., 1986). It cannot be recommended in patients with severe head injury. Rather, if a patient remains excessively sedated after benzodiazepine administration, ventilation and airway protection should be undertaken until benzodiazepines levels have fallen.

18.3.5 OPIOIDS

Opioids provide potent analgesia and are widely used intraoperatively to permit lower doses of volatile or hypnotic anesthetic agents and to provide cardiovascular stability. *Fear that ICP would be increased due to opioid-induced respiratory depression has frequently limited their use in head-injured patients.*

Morphine and **pethidine** (meperidine) were the main opioids in anesthetic practice prior to the introduction of the newer synthetic opioids. They have similar durations of action and produce identical respiratory depression in equipotent analgesic doses. They may be therefore be associated with similar ICP increases in self-ventilating patients. *However, if ventilation is controlled, they produce either a slight decrease or little change in CBF and CMR (Takeshita, Okuda and Sari, 1972; Jobes et al., 1977). They may be used safely with controlled ventilation for analgesia during anesthesia, or combined with hypnotic agents in ventilated patients in intensive care. However their use during anesthesia should be restricted if early postoperative extubation is anticipated.*

The newer **synthetic opioids** have relatively brief durations of action and high dose rates can be used to supplement anesthesia without causing excessive postoperative recovery times. Recent evidence suggests that synthetic opioids may cause CO₂-independent ICP increases. This has led to doubts about their safety in the presence of raised ICP. *Indeed there have been numerous recent studies of the effects of synthetic opioids on CBF and ICP during ventilation. The findings are somewhat inconsistent, but overall it seems likely that any increases in CBF due to the administration of synthetic opioids are insignificant.*

In fact, From et al. (1990) found that there were no detectable differences in intracranial operating conditions or in neurological outcome when fentanyl, alfentanil or sufentanil were used.

However despite their reputation for cardiovascular stability, they can induce hypotension and systemic arterial pressure must be maintained. Sufentanil and alfentanil can cause significant increases in ICP accompanied by marked decreases in blood pressure. It is possible that some of the adverse intracranial effects are due to cerebral vasodilatation induced by systemic hypotension. For an excellent summary of this subject the reader is directed to Mayberg and Lam, 1993.

18.4 Muscle relaxants

18.4.1 DEPOLARIZING RELAXANTS

Suxamethonium is the only depolarizing muscle relaxant in clinical anesthetic practice. Because of its short onset time, it is the relaxant most often used when rapid intubation is required.

Suxamethonium 1–1.5 mg/kg in an adult (1.5–2 mg/kg in a child) administered intravenously provides good intubating conditions in 30–60 seconds, thus minimizing the time between loss of airway protection and airway control. It is sometimes avoided in neuroanesthesia because of concern about increases in ICP.

There are several suggested mechanisms for the increase in ICP. The dominant view is that afferent signals from muscle spindles activated during muscle fasciculation produce cortical stimulation, a rise in CMR and CBF, and hence an increase in ICP (Lanier, Milde and Michenfelder, 1986). Other mechanisms of action, perhaps of lesser importance, are an increase in cerebral venous pressure due to fasciculations and a fasciculation-induced small but measurable increase in global metabolic rate leading to a slight rise in arterial CO₂ tension. These ICP changes are transient and usually quite small, even in the presence of a space-occupying lesion, especially when suxamethonium is given in combination with anesthetic induction agents known to reduce ICP (Ducey, Deppe and Foley, 1989). Indeed, Kovarik *et al.* (1994) were unable to demonstrate any significant changes in intracranial dynamics when suxamethonium was administered to sedated ventilated patients with neurological injuries.

*Suxamethonium can provide excellent intubating conditions rapidly with insignificant changes in intracranial dynamics. It is the relaxant of choice for rapid-sequence induction in the head-injured patient. Pretreatment with non-depolarizing relaxants has been advocated if ICP is raised, to ameliorate any further ICP increases without increasing the risk of aspiration (Stirt *et al.*, 1987), but is probably not necessary.*

18.4.2 NON-DEPOLARIZING RELAXANTS

Non-depolarizing relaxants in general have little direct action on the cerebral circulation but may affect it indirectly through effects on the systemic circulation and histamine release.

(a) Curare

This drug was the earliest muscle relaxant but has now largely been replaced in clinical practice. It can produce systemic hypotension and significant histamine release and has been reported to increase ICP (Tarkkanen, Laitinen and Johannsen, 1974). Therefore it is not generally recommended in the head-injured patient.

(b) Pancuronium

This amino steroid is a long-acting neuromuscular blocker that causes significant increases in blood

pressure and heart rate. While this may be an advantage for circulatory support in the hypotensive patient, it may produce prolonged increases in ICP if cerebral autoregulation is impaired. The excretion of pancuronium is dependent on renal function, which may be impaired in the presence of major trauma.

(c) Vecuronium

This analog of pancuronium has a shorter half-life, is cleared by the liver and has negligible direct effects on the systemic circulation. It does not adversely effect intracranial dynamics, but bradycardia and consequent hypotension due to its lack of vagolytic activity may present a problem when it is given in combination with drugs such as suxamethonium and synthetic opioids and ICP is raised.

(d) Atracurium

Atracurium is a relatively short-acting agent which is quite unique in that its offset is partially dependent on spontaneous degradation in blood. It is useful in neuroanesthesia because stable neuromuscular blockade can be easily achieved by infusion and intracranial dynamics are not adversely affected (Rosa *et al.*, 1986). Rapid bolus administration may produce significant histamine release and hypotension, but this can be ameliorated by slow i.v. injection. Although one of its metabolites (laudanosine) can induce seizure activity (Sheepstra *et al.*, 1986), sufficient levels are not achieved when atracurium is administered at clinically appropriate doses and so should not prevent its use in neuroanesthesia.

(e) Mivacurium

This is a newer agent, characterized by a brief duration of action of only 10–15 minutes, and degradation by plasma cholinesterases (Ali, 1988). It does not act as rapidly as suxamethonium and administration of larger doses in an attempt to reduce onset time is limited by histamine-related hypotension (Mangat *et al.*, 1993; Silverman and Brull, 1993). Although experience is still limited, infusion provides stable relaxation without risk of accumulation and it appears suitable for use in neuroanesthesia (Diefenbach, 1992).

(f) Rocuronium

This steroidal relaxant, has a rapid onset of action. It is a low potency drug and large doses can be given safely to decrease onset time without adverse hemodynamic effects (Kopmann, 1992; Puhlinger, 1992). However prolonged duration of action will result

because of its relatively long half-life. Suxamethonium, because of its faster onset, remains the drug of choice for rapid sequence induction in the head-injured patient.

18.5 Inhaled anesthetic agents

18.5.1 NITROUS OXIDE

Nitrous oxide (N_2O) has been widely used for many years to maintain anesthesia. *It has been considered to be an excellent adjunctive anesthetic agent with minor side effects. There are significant advantages using N_2O as an adjunctive agent in the head-injured patient. Its rapid onset and offset of action allows rapid control of the depth of anesthesia, thus minimizing the response to intubation and surgical stimulus early in the course of anesthesia and allowing rapid postanesthetic recovery for early assessment of neurological function. Furthermore, it does not contribute to postoperative respiratory depression.*

N_2O is also useful in a patient with multiple injuries because its effects on the cardiovascular system are minimal. Maintaining CPP in these patients in the presence of hypovolemia may be more difficult if high concentrations of volatile agents or intravenous infusions of drugs such as propofol and barbiturates alone are used.

However, with the advent of techniques such as transcranial Doppler there is now good evidence that N_2O can cause increases in CBF and ICP and this has resulted in a decline in its use (Lam and Mayberg, 1992; Sakabe et al., 1978; Jung et al., 1992; Henriksen and Jorgensen, 1973). Near-maximal vasodilatation occurs at relatively low inspired concentrations, suggesting an 'all or none' phenomenon at clinically useful doses. There is little doubt that N_2O can adversely affect CPP but its advantages in cardiovascular control and in allowing rapid changes in the depth of anesthesia must still be considered.

The exact mechanism behind the cerebrovascular effects is not clear. N_2O administration increased CBF in awake humans but pial vessel diameter did not change with direct exposure to N_2O *in vitro* (Reinstrup et al., 1994). It was suggested therefore that the increase in CBF might be due to increase in CMR. This was supported by a study in which addition of N_2O to propofol caused no change in CBF, suggesting that CMR depression by propofol negated any CMR or CBF increase due to N_2O (Eng et al., 1992). Studies of the effects of co-administration of isoflurane suggested an alternate explanation. In an elegant study Lam et al. (1994) showed that reducing the dose of isoflurane from 1.1 to 0.5 MAC and adding N_2O increased both CBF and CMR, whereas adding N_2O to 1.1 MAC increased CBF but not CMR. They suggested

that the CBF changes following N_2O may result directly from vasodilatation and indirectly from a decrease in CMR.

Co-administration of N_2O and volatile agents is clearly likely to increase cerebral blood volume and ICP in patients with head injury and should be avoided. Addition of N_2O to an anesthetic based on agents such as propofol or a benzodiazepine may augment anesthesia with minimal increase in ICP, but it should also be used cautiously in the head-injured patient. As previously discussed, the ability of these drugs to induce cerebral vasoconstriction will depend on the status of autoregulation and Matta and Lam (1995) have recently shown increases in CBF when N_2O is added to propofol anesthesia, which may be a result of increases in CMR.

Nitrous oxide is much more soluble than nitrogen in blood and will rapidly diffuse into gas-filled spaces. Consequently, when N_2O is administered during anesthesia, there will be expansion of compliant nitrogen-containing gas-filled spaces (such as the bowel or a pneumothorax) or an increase in the pressure within non-compliant spaces (such as the middle ear or a pneumocephalus). Therefore, in the head-injured patient with a pneumothorax or pneumocephalus, N_2O should be avoided.

Currently there is divided opinion on whether N_2O has any place in neuroanesthesia. Although it should not be used indiscriminately, it should also not be forgotten that N_2O has been used successfully in neuroanesthesia for many years. It can be administered safely and, as with any other drug, its risks and benefits should be carefully considered when planning an anesthetic.

18.5.2 VOLATILE AGENTS

Volatile anesthetic agents remain the mainstay for maintaining anesthesia despite a recent trend towards continuous administration of intravenous agents. Anesthetists are experienced with the dose regimens of volatile agents appropriate to achieve required depths of anesthesia and with the cardiovascular changes that are likely to occur. The equipment for their delivery is both readily available and familiar. However, their place in neuroanesthesia has been debated since halothane was first implicated in increases in ICP.

(a) Halothane

Halothane, used in neuroanesthesia for many years, is now rarely seen in the neurosurgery theater. It is the volatile anesthetic against which the effects of newer agents on intracranial dynamics are often compared; therefore its neuropharmacology remains relevant.

Halothane uncouples CBF and CMR in a dose-dependent manner, producing cerebral vasodilation and a simultaneous fall in CMR. This relative CBF excess (hyperemia) can readily be demonstrated by measuring the increase in cerebral venous oxygen content under halothane anesthesia.

At normocarbia the increase in CBV consistently results in increased ICP with the potential to critically reduce cerebral perfusion (McDowall, 1965, 1967). These ICP effects can be prevented, or at least ameliorated, by hyperventilation as the CBF response to changes in arterial CO₂ tension (CO₂ reactivity) is not abolished by halothane. However in order to prevent an increase in CBF, P_{CO₂} must be lowered prior to halothane administration (Adams *et al.*, 1972).

It is important also to recognize that both halothane administration, particularly at doses greater than 1 MAC, and head injury itself can impair cerebral autoregulation so that CBF is more directly dependent on perfusion pressure (Miletich, Ivankovich and Albrecht, 1976; Figure 18.2). Even minor degrees of hypotension may then reduce CBF, while hypertension can result in increased CBF and ICP.

(b) Enflurane

Enflurane was the successor to halothane in general anesthetic practice because of a more rapid onset and offset of action and a lower risk of volatile-anesthetic-induced hepatitis, a very rare but well publicized condition. *It is epileptogenic, however, and this has led to a decline in its use in neuroanesthesia.*

Its effects on intracranial dynamics represent some improvement over halothane. CBF and CMR are still

uncoupled but the increases in CBF are probably lower than with halothane at equivalent depths of anesthesia (Drummond and Shapiro, 1981). Carbon dioxide reactivity is well maintained; hence the CBF increases can be minimized with hyperventilation. As with halothane, at high doses autoregulation becomes impaired and CBF becomes more pressure-dependent (Miletich, Ivankovich and Albrecht, 1976).

(c) Isoflurane

Isoflurane is generally considered to be the volatile anesthetic agent of choice for neuroanesthesia. Of all volatile agents it causes the greatest dose-dependent fall in CMR (Todd, Drummond and Shapiro, 1982). Complete suppression of neuronal electrical activity, as demonstrated by an isoelectric EEG, is achievable at the clinically useful concentrations of 2–3 MAC (Newberg, Milde and Michenfelder, 1983). Like all volatile anesthetics, isoflurane is a cerebral vasodilator. However CBF and ICP increases are less marked with isoflurane than with other volatile agents at equivalent depths of anesthesia – one reason for its popularity in neuroanesthesia.

CO₂ reactivity is well preserved and CBF increases can be prevented by hyperventilation (Adams *et al.*, 1981). Simultaneous hyperventilation is sufficient to prevent increases in CBF and can therefore be used to control ICP. Furthermore, autoregulation is reasonably well preserved (McPherson and Traystman, 1987, 1988; Adams *et al.*, 1981). *Isoflurane may be neuroprotective, (a particular advantage over other volatile agents) and flows of only 10 ml/100 g/min may be sufficient to prevent ischemia under isoflurane anesthesia (Messick*

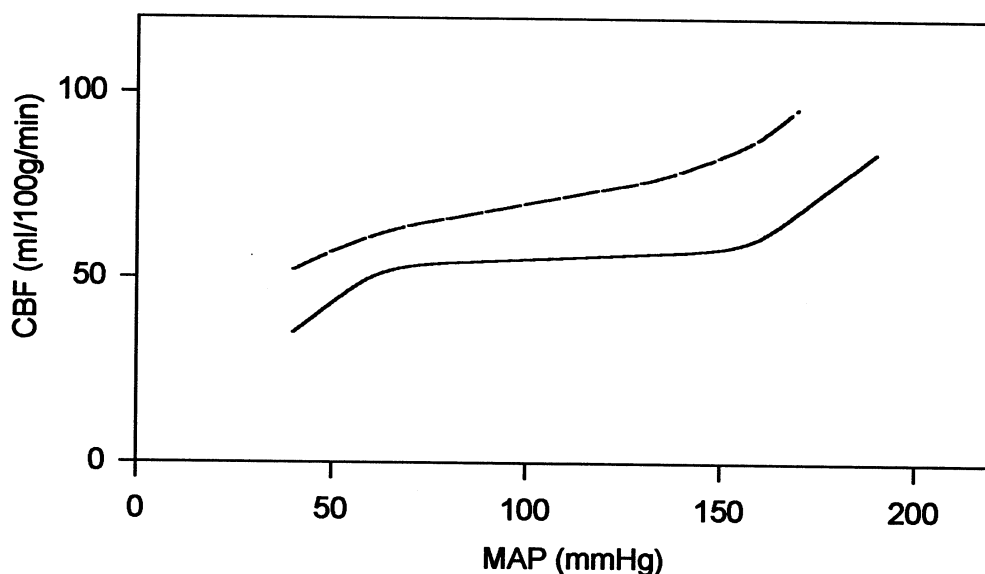


Figure 18.2 The relationship between blood pressure and CBF with autoregulation intact (solid line) and impaired (broken line).

et al., 1987). Increased seizure activity does not occur with isoflurane and indeed it may be used successfully to treat recurrent seizures. Even marked hypocarbia, which will potentiate seizures, does not induce seizures during isoflurane administration.

(d) Desflurane

Desflurane is a new volatile anesthetic agent of particular interest because of its physicochemical properties. It has very low partition coefficients, which results in rapid induction and recovery from anesthesia (Jones, 1990). It also has a low boiling point (23.5°C) and requires expensive, specifically designed heated and pressurized vaporizers (Graham, 1994).

It is structurally similar to isoflurane and it is not surprising that it has similar effects on the cardiovascular and cerebrovascular systems. With increased inspired concentrations it produces minimal myocardial depression and a fall in peripheral resistance and blood pressure. Increases in CBF are similar to those seen with isoflurane (Ornstein *et al.*, 1993) and ICP may increase in the presence of an intracranial mass lesion (Muzzi *et al.*, 1992). CO₂ reactivity appears to be well maintained (Lutz, Milde and Milde, 1991) hence increases in CBF and ICP may be avoided by hyperventilation.

Desflurane-induced hypotension can reduce CBF (Milde and Milde, 1991) but this can be avoided by pressor support. No EEG evidence of seizure activity has been detected at therapeutic concentrations of desflurane.

If inhaled anesthetic agents are to be used in neuroanesthesia, desflurane would appear to have many advantages. Intracranial dynamic changes are similar to those of isoflurane but its physicochemical properties allow more rapid control of depth of anesthesia and more rapid recovery. However it is a relatively new agent, and further clinical experience and laboratory research will be valuable.

(e) Sevoflurane

Sevoflurane is another new agent with physicochemical properties that, like desflurane, produce very rapid onset and offset. Cardiovascular effects are similar to those of isoflurane, producing a fall in peripheral resistance and hypotension but with less tachycardic response. Administration of either agent in concentrations up to 1.5–2 MAC produces similar changes in CBF and CMR (Scheller *et al.*, 1990).

Preservation of CBF under sevoflurane anesthesia during drug-induced hypotension has been demonstrated, suggesting that autoregulation remains intact (Kitaguchi *et al.*, 1992, 1993). CBF CO₂ response is also preserved (Kitaguchi *et al.*, 1993). In a study of

hyperventilated dogs, increase in ICP was seen with halothane and enflurane anesthesia but not with sevoflurane. Sevoflurane, however, caused significant hypotension (Takahashi, Murata and Ikeda, 1993). There is no evidence of seizure activity on EEG at therapeutic concentrations (Scheller *et al.*, 1990).

There appear to date to be few differences in the intracranial dynamic effects of sevoflurane, desflurane and isoflurane but experience with the two newest agents is still limited.

18.6 Other agents used in neuroanesthesia

18.6.1 MANNITOL

Mannitol is an osmotically active agent which has been used for many years as a diuretic and is now also now well established for the treatment of ICP (Chapter 19). For many years it was assumed that it acted primarily by increasing the osmotic gradient between blood and brain, producing a net movement of water out of the brain and a reduction in intracranial brain volume and pressure, an action that may be compromised by injury-induced blood–brain barrier defects (Shapira *et al.*, 1993). Recent evidence suggests that the initial rapid fall in ICP may be due to plasma expansion, with reduced blood viscosity. CBF increases and there is a compensatory vasoconstriction, which reduces blood volume. The more delayed and sustained fall in ICP may be due to the osmotic effects. Both of these actions are greater with bolus administration than with continuous infusion.

However, bolus administration can produce transient systemic vasodilatation and hypotension, particularly in a hypovolemic patient, with an acute fall in CPP (Cote, Greenhow and Marshall, 1979; Nissenson, Weston and Kleeman, 1979), and plasma expansion may precipitate cardiac failure in the patient with compromised cardiac performance.

Dosages from 0.25–2 g/kg of mannitol have been advocated. However the higher doses do not necessarily provide better ICP control and the side effects are increased (Smith *et al.*, 1986).

In the patient with a severe head injury and raised ICP, 0.25–0.5 g/kg given over 10–20 minutes will usually reduce ICP and provide improved operating conditions. This dose can be repeated 2–4-hourly as necessary with regular monitoring of serum osmolarity.

Co-administration of frusemide (furosemide) can decrease the onset time and increase the duration of ICP effects of mannitol (Wilkinson and Rosenfeld, 1983) but there is increased risk of hypovolemia and this combination should be avoided in patients with head injury.

18.6.2 CARDIOVASCULAR AGENTS

Numerous drugs are available for control of blood pressure and heart rate perioperatively. The merits of some of the more commonly used drugs will be described briefly.

Glyceryl trinitrate (GTN) is a short-acting vasodilator that can be given by infusion to control hypertension intraoperatively. It is not an ideal agent for use in the head-injured patient as it is also a cerebral vasodilator. A recent study using SPECT scanning and transcranial Doppler found that sublingual GTN produced a fall in cerebral blood velocity without a change in CBF (Dahl *et al.*, 1989). Not surprisingly, this cerebral vasodilatation with a resultant increase in cerebral blood volume has been shown to increase ICP (Hartmann *et al.*, 1989; Lagerkranser, 1992). *GTN administered for systemic hypertension in the presence of decreased intracranial compliance risks further increases in ICP. Hyperventilation may be less effective in reducing ICP than expected in these circumstances because GTN-induced vasodilation will reduce CO₂ reactivity (Hartmann *et al.*, 1989).*

Sodium nitroprusside (SNP) has a very rapid onset and brief duration of action, which allows very precise blood pressure control. Hamaguchi *et al.* (1992) found no change in CBF during SNP-induced hypotension under enflurane-N₂O anesthesia. This suggested a cerebral vasodilatory action but could not differentiate between direct SNP-induced vasodilatation and impairment of normal autoregulation. It has been associated with ICP increases in clinical practice, presumably due to increase in cerebral blood volume.

SNP produced greater increases in ICP than GTN in a baboon model at both normal and raised levels of ICP and reduced CO₂ (Hartmann *et al.*, 1989).

Hydralazine is a direct-acting vasodilator which acts directly on vascular smooth muscle producing delayed onset of action; the peak hypotensive effects occurring 15–20 minutes after intravenous administration. As with GTN and SNP, it can increase ICP by increasing cerebral blood volume (Herpin, 1989). This cerebral vasodilatation may be prolonged and appears to be a direct effect as it can occur in the absence of significant change in blood pressure (Figure 18.3). *Because of its prolonged action, hydralazine should be avoided in the presence of raised ICP.*

Beta-blockers may be the antihypertensives of choice for the treatment of perioperative hypertension in the presence of raised ICP, since they lower blood pressure by reducing cardiac output without reducing systemic or cerebrovascular resistance or increasing cerebral blood volume.

Esmolol is a relatively new selective beta-antagonist which has an extremely short half-life (8–10 min) due to rapid hydrolysis in blood. This allows rapid and readily reversible changes of blood pressure and it is therefore particularly useful for the control of brief periods of hypotension, such as those occurring at induction. It appears to have little effect on CBF when autoregulation is intact (Bunegin, Albin and Gelineau, 1987), but esmolol-induced hypotension may decrease CBF if autoregulation is impaired.

Inotropic or vasoconstrictor drugs under physiological circumstances can significantly increase blood pressure without altering CBF. Adrenalin (epineph-

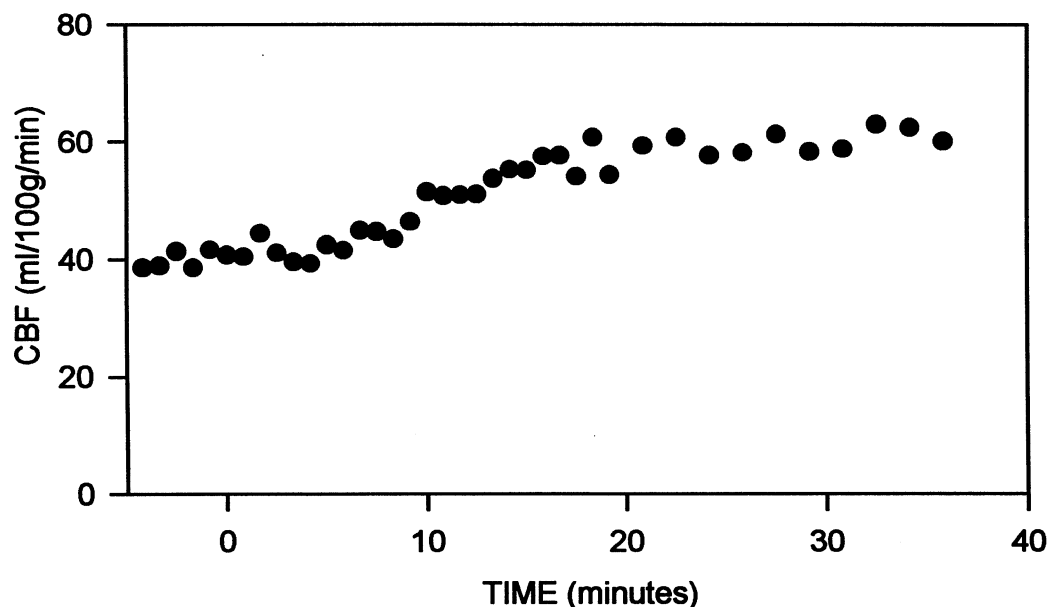


Figure 18.3 CBF in a sheep following low-dose bolus hydralazine administration, producing no changes in systemic arterial pressure (Source: reproduced from Ludbrook *et al.*, 1995, with permission.)

rine) has minimal effects on CBF in the normal brain (Olesen, 1972; King, Sokoloff and Wechsler, 1952). However, if the blood-brain barrier is disrupted, as may be the case after severe head injury, CBF may be significantly altered (Abdul-Rahman *et al.*, 1979). The reported success of therapeutic strategies that aim to maintain CPP with drugs such as phenylephrine, metaraminol and noradrenalin (norepinephrine) suggests that they have a place in management of the head-injured patient (Rosner *et al.*, 1994; Chapter 19).

18.7 Conduct of anesthesia in severe head injury

This section will concentrate on aspects of anesthetic practice that relate to the patient with an severe acute head injury, focusing particularly on preventing secondary injury.

18.7.1 PATIENT ASSESSMENT AND PREPARATION

Preoperative assessment is often brief because of the urgent nature of this condition, and management will usually have begun with the acute resuscitation team outside hospital or in the emergency room. This period of management is described in Chapter 15.

The anesthetist must often rely on limited information about the premorbid medical and anesthetic history of the patient. Relatives are often the most valuable source of this information. Details of the nature of the trauma involved (such as speed and direction of impact in the case of a motor vehicle accident) should be sought from the retrieving medical or paramedical staff, and detailed records of all treatment regimens and investigations performed should be available to, and studied by, the anesthetist at the outset.

Although a detailed examination should have been performed by other medical staff, the anesthetist must undertake a basic assessment of cardiorespiratory systems at least, with particular emphasis on traumatic injuries. The significance to the anesthetist of such basic findings as broken teeth may not be appreciated by non-anesthetic personnel.

Depending on the stage at which the anesthetist is involved in patient management, extensive investigations including radiological surveys may have already been performed. It is advisable for the anesthetist to check these results personally. The presence of pneumocephalus, broken ribs or a small untreated pneumothorax may not be emphasized by other attending staff and the experience of medical personnel reporting on investigations such as cervical spine X-rays is not always known.

Acute resuscitation may have commenced (Chapter 15). *Adequate intravenous access should be ensured,*

especially if blood loss from other injuries or for surgery is anticipated, and the anesthetist should check that blood is readily available for transfusion. Adequate patient monitoring should be begin pre-operatively. An arterial line should be sited, central venous access obtained for monitoring as well as drug administration, and a urinary catheter inserted.

18.7.2 INDUCTION OF ANESTHESIA

The aim of induction of anesthesia is to achieve an adequate depth of anesthesia and relaxation in order to rapidly and safely control airway and ventilation without patient awareness and to simultaneously improve intracranial dynamics. All this must be achieved in a patient who may have a full stomach, be hypovolemic and have other injuries or medical problems. Many of these factors place conflicting demands on the anesthetist – for example, whether to use a rapid large dose of sodium thiopentone in order to reduce the ICP response to intubation but risk hypotension. A diversity of techniques are used, according to the clinical setting and the preference of the anesthetist (Nakajama *et al.*, 1992).

The advantage of having an anesthetic plan, prepared equipment, adequate assistance, and a second anesthetist if particular difficulty is anticipated, cannot be stressed enough.

If aspiration of gastric contents is a significant risk, a rapid-sequence induction including the use of suxamethonium is necessary. A 'priming dose' of a non-depolarizing relaxant such as vecuronium may be considered to offset the ICP effects of suxamethonium (Stirt *et al.*, 1987) but is probably not necessary.

If hypovolemia or concomitant cardiovascular disease are not major concerns then an induction dose of sodium thiopentone (3–6 mg/kg) or propofol (2–3 mg/kg) will provide rapid onset of anesthesia while at the same time reducing CBF and ICP. However, depending on the dose regimen, these agents alone may be insufficient to ablate the cardiovascular responses to laryngoscopy and intubation (Giffen, Cotrell and Schwirey, 1984) and so adjunctive drugs may be necessary. Lignocaine (1–1.5 mg/kg) given approximately 3 minutes prior to intubation may cause sufficient cerebral vasoconstriction to further reduce the ICP response to intubation (Bedford *et al.*, 1980). Fentanyl (5 µg/kg) may be considered but to be effective should be given at least 3–5 minutes prior to intubation and unexpected loss of airway protection and muscle rigidity which compromises ventilation may occur in that time period. *Doses of all drugs should take into account the preanesthetic conscious state, which may have been affected by the head injury or both therapeutic and recreational drugs.*

If hypovolemia/hypotension and aspiration risk coexist, the challenge to the anesthetist is great. Hypovolemia should be corrected before, or if surgery is urgent, during induction by fluid replacement guided by central pressure monitoring. Etomidate (0.1–0.5 mg/kg) may provide cardiovascular support without reducing cerebral perfusion but can still precipitate hypotension, and furthermore is not available in a number of countries. The combination of an opioid such as fentanyl with small doses of midazolam or sodium thiopentone may avoid profound hypotension. Ketamine can be a useful induction agent in the presence of hypovolemia, but it cannot yet be recommended in a patient with a severe head injury because marked increases in ICP have been recorded following intravenous bolus administration.

The anesthetist must be prepared to treat hypotension rapidly and aggressively as episodes of hypotension following a severe head injury are associated with a worse neurological outcome. Adequate intravenous access to allow rapid infusion of fluid should be obtained, and vasopressors such as metaraminol should be drawn up ready for use. Simple maneuvers such as leg elevation (rather than the Trendelenburg position, which may do little to improve CPP) should not be forgotten in treating anesthesia-related hypotension.

Oral endotracheal intubation is usually preferred, especially as it allows the airway to be most rapidly secured with less trauma than nasal intubation. Nasal intubation, preferred in some centers if long-term ventilation is anticipated, should be avoided in the presence of a basal skull fracture or major maxillary trauma as passage of the endotracheal tube out of the airway and even intracranially is possible. The postoperative phase should be considered when selecting the endotracheal tube. Depending on the surgical approach and patient positioning, armored or preformed tubes may be most convenient intraoperatively but if postoperative ventilation is planned a straight plastic tube with a high-volume low-pressure cuff should be substituted after completion of surgery.

Cervical spine injury occurs in 10–20% of patients with severe head injury (Hills and Deanse, 1993; Heiden et al., 1987). There are differing opinions about the optimal intubation technique for these patients. However it is generally considered that oral intubation with head immobilization (rather than in-line traction) is a safe technique and does not compromise the spinal cord (Wood and Lawler, 1992; Suderman, Crosby and Lui, 1992).

As for any surgery, particularly when it may be prolonged, careful attention should be paid to patient positioning. This should be discussed with the surgeon preoperatively, so that the position of the anesthetic machine, endotracheal tube selection and

the position of monitoring lines and equipment can be planned in advance. Particular care should be taken with positioning of the patient before draping and the surgeons prevent access. A head-up posture (15–20°) has been shown to improve ICP and not adversely affect CPP or CBF, and is therefore recommended when practical (Durward *et al.*, 1983; Wilson, 1992; Feldman *et al.*, 1992). There must be no obstruction to venous drainage from the head by endotracheal tube tapes or other equipment.

18.7.3 MAINTENANCE OF ANESTHESIA

There are some aspects of neuroanesthesia for the severely head-injured patient that warrant specific mention.

(a) Anesthetic agents

The complex and variable pathophysiology of brain and systemic injuries makes a simple anesthetic 'recipe' impossible. For example, head injury can be associated with either high or low CBF and theoretically no one anesthetic technique is ideal for both situations. While sophisticated techniques to differentiate between the two states exist, this is rarely possible preoperatively, even in the few centers capable of such measurements.

There is in fact little outcome-based evidence that any particular anesthetic technique is superior to any other in neuroanesthesia in general. This is in part a result of the inherent difficulties of outcome-based studies in anesthesia (Eichhorn, 1993) as well as of the difficulties in performing well controlled trials in head-injured patients. Indeed, as pointed out earlier, even halothane, a drug with substantial theoretical disadvantages for neuroanesthesia, has not been proved to detrimentally affect patient outcome. The choice of i.v. anesthetic technique will depend largely on the personal experience of the anesthetist and an assessment of the particular case. For example, a total intravenous technique using propofol to reduce CBF may be an excellent choice for a patient who is normotensive or hypertensive and may have cerebral hyperemia, while an opioid–benzodiazepine technique may be preferred when postoperative ventilation is anticipated. Because of the risk of adversely affecting CPP, cerebral vasodilators such as the volatile agents should be avoided.

(b) CVS homeostasis

Maintaining adequate and sustained oxygen delivery is fundamental to avoiding secondary hypoxic injury, and cardiovascular homeostasis is a vital step in the oxygen delivery chain.

Hypotension is detrimental whether or not autoregulation is compromised. In the presence of impaired cerebral autoregulation, any degree of hypotension will produce a decrease in CBF and, although ICP may also decrease, cerebral ischemia may result.

This has been demonstrated in animal models where either hypotension or acute head injury alone did not impair CBF, but CBF fell significantly when both conditions occurred simultaneously (DeWitt *et al.*, 1992). As described by Bouma *et al.* (1992) cerebral ischemia may still occur following hypotension and head injury if autoregulation is preserved. Cerebrovascular resistance will fall in response to a fall in MAP, producing an increase in cerebral blood volume, a rise in ICP and a net fall in CPP. Hypotension has been associated with an increased morbidity and mortality (Pietropaoli, Rogers and Zhuang, 1992). Hypertension may or may not be detrimental. It may increase CBF and CPP and reduce ischemia due, for example, to cerebral vasospasm following traumatic subarachnoid hemorrhage (Martin *et al.*, 1992; Lang and Chesnut, 1994). However, in the presence of impaired autoregulation and hyperemia it may increase CBF, ICP and cerebral edema and thus ultimately increase cerebral ischemia.

It is apparent therefore that both hypo- and hyperperfusion must be avoided, but the difficulty lies in deciding what level of MAP is ideal.

*Because of the risk of increasing ICP with fluid overload (Hariri *et al.*, 1993), central pressure monitoring is mandatory to optimize intravascular volume. CPP should not fall below 60–70 mmHg and pharmacological support should be used to maintain this as necessary (Bendo, 1994).*

Oxygen-carrying capacity is another vital link in avoiding secondary hypoxic injury. Hematocrit should be measured regularly and kept between 30% and 35%, which probably gives the optimal balance between reduced blood viscosity and adequate oxygen-carrying capacity.

(c) Monitoring

Observation of the patient and equipment by an alert, skilled anesthetist once constituted an acceptable level of monitoring; however it is now generally recognized that correctly used specialized equipment provides more accurate measurements and an increased margin of safety.

Pulse oximetry

Pulse oximetry has been the most important advance in monitoring during anesthesia since the introduction of the sphygmomanometer. Not only can its waveform provide an index of peripheral perfusion

but it also continuously displays the saturation of the hemoglobin in arterial blood, thus providing valuable information about the cardiovascular and respiratory systems

Clinical acumen is notoriously unreliable in detecting cyanosis (Hanning, 1985) and pulse oximeters are now mandatory in anesthetic practice in many centers. They are reasonably accurate under most clinical circumstances (Webb, Ralston and Runciman, 1991); however, reduced tissue hypoperfusion in hypotensive, hypothermic or vasoconstricted patients – situations not uncommon in severe head injury – may give falsely low readings. If there is doubt about the accuracy of the pulse oximeter reading, measurement of arterial blood gas tensions is essential.

Capnography

Capnography to monitor endotracheal tube placement and ventilation is essential. It also provides a guide to changes in cardiac output. It must be recognized that large alveolar–arterial gradients in carbon dioxide tension can occur, especially in patients with traumatic injuries, and end-expired carbon dioxide tensions should be calibrated against blood gas measurements.

Electrocardiography

The electrocardiogram (ECG) may be used to measure heart rate, detect and characterize arrhythmias and conduction defects, monitor pacemaker function and provide some indication of myocardial ischemia. There are specific indications for its use intraoperatively (Ludbrook *et al.*, 1993) but it is an essential monitor for the head-injured patient because of the increased risk of dysrhythmias and the high incidence of ischemic changes in these patients (Kaufman *et al.*, 1993; section 17.3.3(b)).

Blood pressure measurement

*Blood pressure measurement is essential for determining CPP and must be continuously and accurately recorded during anesthesia. Indirect blood-pressure measuring devices such as blood pressure cuffs or oscillometric devices can be inaccurate by up to 30% (Raftery and Ward, 1968; Bruner *et al.*, 1981) and the degree of error may change with the patient's cardiovascular status (Rutten *et al.*, 1986). This is particularly relevant in the head-injured patient, where vascular tone and the accuracy of blood pressure measurement may change dramatically during an operation (Cohn, 1967). It is therefore essential that an arterial line be placed preoperatively and connected to a cannula–tap–pressure-tube–tap–transducer system, which will provide reasonable accuracy.*

Several systems in clinical use have surprisingly large errors (Gardner, 1981). In practice, a fluid-filled system comprising a 4 cm 20 gauge, non-tapered arterial cannula connected to a low-displacement pressure transducer by non-compliant pressure tubing and a three-way stopcock is sufficiently accurate to gauge mean and systolic pressures. Care must be taken to exclude all air bubbles and the amplifier-recorder system must have an adequate frequency response.

Central venous pressure measurement

This is a high priority. A catheter can usually be inserted quickly and safely to the junction of the superior vena cava and right atrium *via* the basilic vein from the cubital fossa. If time permits, however, a subclavian or internal jugular catheter inserted using a Seldinger technique is preferable, being more suitable for long-term use in intensive care. Pneumothorax following subclavian line insertion is uncommon in experienced hands (Eerola, Kaukinen and Kaukinen, 1985); nonetheless a chest X-ray should be taken prior to anesthesia. Monitoring pulmonary capillary wedge pressure and cardiac output may require a Swan-Ganz-type catheter. This is covered more extensively in Chapter 17.

Cerebral perfusion measurement

More specialized monitoring of intracranial perfusion developed for intensive care use has little application in the operating room at present.

Transcranial Doppler can be used to differentiate between low- and high-flow states and autoregulatory break points (Chapter 14; Chan *et al.*, 1992; Compton and Teddy, 1987; Mayberg and Lam, 1992) but this is frequently impractical intraoperatively.

Jugular bulb catheters incorporating oximetry to measure the saturation of cerebral effluent blood has proven useful in Intensive Care management (Sheinberg *et al.*, 1992; Robertson *et al.*, 1992; Matta, Lam and Mayberg, 1994) and there is now some experience of their use intraoperatively (Matta *et al.*, 1994).

Near-infrared spectroscopy has the potential to provide a continuous measurement of cerebral oxygenation intraoperatively but this promising technique requires further refinement before it can be accepted as a reliable monitor of brain mitochondrial oxygenation (Hazeki and Tamura, 1988; Brown, 1993; Lewis *et al.*, 1994).

Temperature

Core body temperature is usually tightly regulated by peripheral and central thermosensors, a central control system in the hypothalamus and effector mecha-

nisms operating largely *via* the sympathetic nervous system. The central control mechanisms can be disrupted through cerebral injury, or by anesthetic or vasoactive drugs (Morley-Forster, 1986). Severe hypothermia has been intentionally induced in neurosurgery when cerebral perfusion is likely to be compromised or even deliberately arrested for a short period (Silverberg, Reitz and Ream, 1981). The adverse systemic effects of profound hypothermia have largely limited its use in neurosurgery to operations such as clipping of giant cerebral aneurysms under circulatory standstill.

Mild hypothermia is almost inevitable during most surgery and considerable effort can be expended in trying to minimize this by using warmed intravenous fluids, warming blankets and temperature monitoring. Many of the adverse effects of severe hypothermia such as cardiac dysrhythmias, increased blood viscosity and coagulopathy do not occur with mild hypothermia, but there is a marked increase in oxygen consumption during rewarming.

There is renewed interest in the intentional use of mild hypothermia (33–35°C) during neurosurgical operations and in the intensive care management of patients with head injury (Baker *et al.*, 1994). The main advantage of hypothermia was initially considered to be the reduction in CBF and CMR (a reasonable rule of thumb equates each 1°C fall in temperature with an 8% fall in CMR and CBF), an effect similar to that following administration of barbiturates and propofol.

It is now apparent that even small reductions in brain temperature provide a greater tolerance to ischemia than can be explained by the predicted falls in CMR (Busto, Dietrich and Globus, 1987; Kader et al., 1992). A number of mechanisms such as reduced levels of nitric oxide or excitatory amino acids, or effects on ion transfer and lipid peroxidation, have been proposed.

Recent clinical trials of moderate hypothermia have demonstrated apparent improvement in the outcome following head injury. Clifton and coworkers (1993) found a significant reduction in seizure rate and some improvement in cerebral function during recovery when all patients with severe head injuries were treated with mild hypothermia. In another study, patients with large rises in ICP that did not respond adequately to dehydration, hyperventilation or intravenous barbiturates were treated with mild hypothermia. There were significant increases in CPP and reductions in ICP, CBF and CMR (Shiozaki *et al.*, 1993). Marion and coworkers (1993) also found reduction in CBF, CMR and ICP in head-injured patients after induction of mild hypothermia, but this reversed as patients were rewarmed. This form of therapy does not appear to significantly increase the incidence of

dysrhythmias and hypokalemia (Clifton and Christensen, 1992). Hypothermia (33–35°C) may therefore be advantageous in the treatment of the severely head-injured patient.

A major clinical trial is currently being conducted to test the ability of moderate hypothermia to improve outcome after severe head injury.

Hypothermia can often be relatively easily achieved as patients are frequently cold on arrival to hospital as a result of such factors as exposure, fluid therapy and alcohol (Luna *et al.*, 1987), and exposure to the cold theater environment and heat redistribution commonly leads to decreases in core body temperature between induction of anesthesia and beginning of surgery. Temperature can be reduced further by the use of cooling/heating blankets (air-circulating types are particularly effective) and cooled intravenous fluids. Lower esophageal probes give a reasonable estimation of core body temperature with a rapid response time. External cooling measures carry the risk of 'overshoot' during the initiation of hypothermia, and therefore active cooling should be discontinued before the target temperature is reached.

Shivering is an early response to hypothermia and can increase BP, ICP, respiratory effort and oxygen consumption; it should be avoided in severe head injury. Therefore, if hypothermia is induced intraoperatively, muscle relaxation should be used and temperature corrected before relaxation is reversed. Muscular relaxation may be continued postoperatively if ongoing artificial ventilation is planned.

While hypothermia may be beneficial, hyperthermia after trauma induced by loss of cerebral temperature autoregulatory mechanisms, drugs or infection may worsen outcome. Hyperthermia has been shown experimentally to increase neurological damage following cerebral ischemia. Hyperthermia should therefore be treated aggressively.

18.7.4 FLUID ADMINISTRATION

*Concepts of fluid administration in the patient with head injury have undergone significant change in recent years. In particular, the greater appreciation of the dangers of hypotension and cerebral hypoperfusion following head injuries have led to an emphasis on maintaining normovolemia. Care must still be taken to avoid fluid overload by aggressive fluid therapy, since this may increase ICP and reduce cerebral perfusion (Hariri *et al.*, 1993).*

Where possible, fluid resuscitation should be instituted before or during induction of anesthesia. The delicate balance between the risks of under- and over-resuscitation described above make monitoring of central pressures, or pulmonary artery pressures, a high priority.

The ideal fluids for resuscitation remains a subject of debate but there are some reasonable rules of thumb.

In general, hypotonic solutions should be avoided since they will reduce plasma osmotic pressure and this may worsen cerebral edema (Kaieda, Todd and Cook, 1989; Shackford, Zhuang and Schmoker, 1992).

Glucose-containing solutions should be used cautiously. Hyperglycemia has been linked to poor neurological outcome after traumatic and ischemic brain injury (Lam *et al.*, 1991; Araki *et al.*, 1992) and may be associated with a worsening of intracerebral acidosis. Although less common, hypoglycemia may compound cerebral damage. Hence if glucose-containing solutions are used, for example in the diabetic, hypothermic or intoxicated patient, serum glucose levels should be monitored closely.

The debate over colloids versus crystalloids for fluid resuscitation continues in most fields of anesthesia, including neuroanesthesia and in the management of head injury. However there appears to be little evidence that isotonic crystalloid solutions are harmful following head injury.

*Hypertonic saline solutions have recently been used for the resuscitation of hypovolemic patients since relatively smaller infusion volumes are required to achieve blood volume expansion. Studies have shown them to successfully increase CPP and perhaps reduce cerebral edema (Fisher, Thomas and Peterson, 1992; Prough *et al.*, 1985; Battistella and Wisner, 1991; Shackford, Zhuang and Schmoker, 1992).*

Some reservations remain about the possibility of adverse effects of large and prolonged rises in serum osmolarity, particularly renal failure, and further studies are required before they can be recommended for routine use in head injury.

18.7.5 VENTILATION

It is not surprising that hyperventilation during neuroanesthesia became widespread considering the marked reductions in ICP and brain tension noted intraoperatively with hypocarbia. It is now recognized that persistent hypocarbia may have significant side effects and there is a move towards using normocarbia or only moderate hypocarbia in neuroanesthesia (Chapters 17 and 19).

*In the head-injured patient, hyperventilation may be relatively ineffective as CO₂ reactivity may be impaired (Bouma *et al.*, 1992). Indeed for this reason hyperventilation may be the least effective in controlling raised ICP in the most severe injuries. Secondly, hyperventilation may induce cerebral ischemia. Cerebral injury is inhomogeneous and, in some areas of the injured brain, critical falls in CBF may be induced by hyperventilation (Cold, 1989; Obrist *et al.*, 1984).*

Furthermore, hypocarbia may lower MAP and CPP, particularly if there is concomitant hypovolemia, and it may induce dysrhythmias. Hyperventilation has been associated with increased morbidity after head injury (Muizelaar *et al.*, 1991).

Thus P_{aCO_2} during anesthesia should be maintained at 35 ± 2 mmHg and monitored with intermittent arterial blood gas analysis.

Despite the evidence against profound and sustained hyperventilation, temporary hyperventilation may be vitally important for the rapid control of raised ICP. If CPP is compromised by raised ICP, brief periods of hyperventilation may allow time for other measures such as surgical evacuation of a hematoma, osmotic or barbiturate therapy, to be instituted. Hyperventilation is only a temporary measure, however, as resetting of CBF occurs within hours. CSF pH returns towards normal and rebound increases in CBF and ICP may occur when normocarbia is resumed (Muizelaar *et al.*, 1988).

18.7.6 SEIZURE MANAGEMENT

Seizure management (Table 18.1) is an important aspect in the care of the head-injured patient, and involves treating and preventing seizures occurring early in the course of the injury, and preventing late seizures. There are recognized risk factors for the development of seizures after head injury. Patient factors include age (there being a higher incidence in the pediatric age group), a history of alcoholism, previous seizures and a family history of seizures (Yablon, 1993; Annegers, 1980). Injury factors include injury severity – patients with minor head injuries (PTA < 24 h) have a very low seizure rate and thus the occurrence of seizures in this group may signify a more serious cerebral injury than was originally believed (Feuerman *et al.*, 1988; Lee and Lui, 1992), and the pattern of injury. Patterns associated with an increased risk of seizures include intracranial

hemorrhage, linear and depressed skull fractures, focal or penetrating injuries and the presence of focal neurological deficit or prolonged amnesia (i.e. PTA > 24 h; Jennett, 1975). The presence of intracerebral blood or iron may be a trigger for late seizures (Lee and Lui, 1992).

Anticonvulsants are administered during the acute phase of head injury management to prevent or treat early post-traumatic seizures or to prevent the development of post-traumatic epilepsy. Seizures occurring during the acute phase can increase ICP and interfere with ventilation and airway control and the management of other injuries. *Indeed, there is a positive association between the occurrence of seizures and morbidity and mortality, although whether this simply reflects the presence of a more severe injury or is a result of the seizures is unclear (Yablon, 1993).*

That acute seizures should be treated immediately is clear. Prophylactic therapy has been more controversial and its effectiveness has been debated (North *et al.*, 1983; Temkin *et al.*, 1990; Hauser, 1990; Young *et al.*, 1983). However, it appears likely that anticonvulsant administration, carefully monitored to ensure therapeutic blood levels, is effective in reducing the incidence of seizures occurring early after head injury. They are most effective in the first week after an injury and less so in preventing delayed seizures (Temkin *et al.*, 1990).

The rationale for using anticonvulsants to prevent late seizures is based largely on the kindling model. This assumes that recurrent stimulation by seizures lowers the stimulus threshold for further seizures, eventually reaching the stage where spontaneous seizures may occur. Clinical trials, however, have not shown a convincing benefit (Temkin *et al.*, 1990; Young *et al.*, 1983) and the place of prophylactic therapy beyond the first week is still unclear.

What guidelines should therefore be used for the institution of anticonvulsant therapy?

Table 18.1 Seizure management in acute head injury

<i>Drug</i>	<i>Initial dose</i>	<i>Maintenance dose</i>
Initial treatment of a seizure		
Diazepam	0.05–0.15 mg/kg i.v.	0.1–0.2 mg/kg i.v.
Sodium thiopentone	1–4 mg/kg i.v.	1–5 mg/kg/h i.v.
Propofol	0.5–2 mg/kg i.v.	1–6 mg/kg/h i.v.
Clonazepam	0.003–0.01 mg/kg i.v.	0.002–0.004 mg/kg i.v.
Treatment of recurrent seizures		
Phenytoin	15 mg/kg i.v. over 20 min	3–12 mg/kg/24 h (titrated to therapeutic range of 10–20 µg/ml)
Diazepam	0.05–0.15 mg/kg i.v.	0.1–0.2 mg/kg/h i.v.
phenobarbitone		1–5 mg/kg/24 h (titrated to therapeutic range of 45–130 µg/ml)
Clonazepam	0.003–0.01 mg/kg i.v. or po	0.002–0.004 mg/kg i.v.

- *Any seizure occurring early in the course of the injury should be rapidly treated, and therapy should be continued because of the high risk of recurrence.*
- *Prophylactic anticonvulsant therapy should be instituted to those patients considered at high risk of seizures, but should be discontinued during the second week after injury. Those at high risk include patients with*
 - *intracranial hemorrhage;*
 - *linear and depressed skull fractures;*
 - *focal or penetrating injuries;*
 - *focal neurological deficit or prolonged amnesia (post-traumatic amnesia > 24 h).*

A seizure should not automatically be attributed to the recent head injury. Other causes, which may be treatable, should be excluded. A family or personal history of epilepsy should be sought and reversible conditions such as hypoglycemia, hyponatremia, hypoxemia and extreme hypocarbia should be excluded. Alcohol, antidepressant medication and recreational drugs have all been reported to cause seizures and a history of their use should be sought or a drug screen performed.

In the ventilated and paralyzed patient seizure activity may be disguised. Neuromuscular blockade should therefore be avoided unless it is essential for ICP control or because of severe lung pathology. In these patients consideration should be given to prophylactic anticonvulsant therapy. Ideally, continuous EEG monitoring should be instituted to detect seizures and monitor the effectiveness of therapy.

(a) Anticonvulsant therapy

Many of the hypnotic anesthetic agents in clinical use have anticonvulsant actions. Intravenous bolus administration of even small doses of sodium thiopentone or propofol provides rapid-onset, short-duration seizure control, but with the risks of loss of airway reflexes, neurological and respiratory depression and hypotension. They should only be used if personnel and equipment for airway management and artificial ventilation are available. Because of the cardiorespiratory depression, infusion administration for prolonged anticonvulsant therapy is usually restricted to the ventilated patient, where their sedative and cerebrovascular effects may be beneficial. Phenobarbitone has a longer onset time and more prolonged duration of action than thiopentone and is therefore more appropriate for prolonged therapy.

Intravenous benzodiazepines (diazepam and midazolam) are also effective but have a variable dose-response relationship and a more prolonged duration of action than the other sedative/hypnotic i.v. anesthetic agents.

Phenytoin, a diphenylhydantoin, is one of the most commonly used anticonvulsants in head injury. It does not cause significant CNS depression; it is effective both intravenous and orally; and it has a long duration of action. Its onset is considerably longer than that of barbiturates and benzodiazepines; hence it is relatively ineffective in the immediate treatment of seizures. Other agents should be used until therapeutic levels have been achieved. Dilantin levels should be monitored regularly to maintain concentrations in the therapeutic range of 8–20 µg/ml.

18.8 Emergence and recovery

A period of ventilation is often undertaken post-operatively and clear communication between anaesthetist and intensive care staff is essential. Transportation of the critically ill patient must be undertaken with great care. It requires continued adequate sedation and analgesia to prevent emergence during transportation. Sedative infusions, such as propofol or fentanyl/midazolam, administered *via* a portable syringe pump are one satisfactory solution. Ventilation and cardiovascular homeostasis must be continued, often with suboptimal monitoring.

If extubation is anticipated, there is a choice between extubation under deep anesthesia or 'awake', i.e. after reflexes have fully returned. In the non-fasted patient the 'awake' approach should be used to reduce the risk of postoperative aspiration, even if attempts have been made to empty the stomach with gastric tubes intraoperatively. With this technique it is difficult to avoid coughing and postoperative ventilation should be considered if ICP is still high. In the fasted patient, extubation while still deeply anesthetized reduces the risk of coughing or gagging, but is inevitably associated with some ventilatory depression and potential ICP increase.

18.8.1 ANALGESIA

Head-injured patients frequently experience moderate to severe pain due to associated soft tissue or bony injury. This is a common cause of restlessness and difficulty in managing and assessing. There may be some reluctance to prescribe analgesic agents because of the fear of drug-induced respiratory depression which may increase ICP, and because sedation may affect the neurological status.

If sedation, intubation and artificial ventilation are necessary early, opioids are indicated for analgesia and to assist in tolerating the endotracheal tube.

For the patient in whom control of ventilation or airway protection is not considered necessary (either pre- or postoperatively), but who has severe pain, the decision is more difficult. The practice of prescribing

mild analgesia with non-opioid analgesics in the presence of major injuries cannot be condoned. The restlessness, straining and systemic hypertension associated with severe pain increases ICP, makes nursing more difficult and hazardous and causes unnecessary suffering.

One solution is to administer short-acting opioids such as fentanyl or alfentanil intravenously and to titrate the dose according to analgesic effect. If there is a significant deterioration in mental state due to oversedation, the effect is likely to be short-lived or can be readily reversed with opioid antagonists such as naloxone. This may indicate a reduced intracranial compliance and ventilation or the use of pharmacological measures to reduce ICP need to be considered. If this technique is successful in producing adequate analgesia without significant change in the neurological status or respiratory function, equivalent doses of longer-acting opioids such as morphine, intravenously or subcutaneously, can then be considered.

Patient-controlled analgesia should be avoided in a confused patient.

Codeine phosphate has often been used as an alternative to drugs such as morphine but it should be recognized that codeine is an opioid (and in fact it acts mainly through metabolism to morphine) and will produce as much respiratory depression for the same degree of analgesia as any other opioid.

Regional anesthetic techniques in patients with head injury should be used whenever possible. If used appropriately, they have the advantages of excellent analgesia with little risk of cerebral side effects. For example, femoral nerve blockade can provide good pain relief for a fractured femur without affecting conscious state, and intercostal nerve or interpleural blocks may aid in analgesia for fractured ribs

Non-steroidal anti-inflammatory drugs, have gained popularity for perioperative analgesia, particularly now that parenteral preparations are available (Gillies *et al.*, 1987). For the patient with an acute head injury, they have the advantages of minimal respiratory depression and sedation, but their side effects include impairment of platelet aggregation and of renal function and have tended to limit their use in fields such as neuroanesthesia, when hemostasis is critical (Merry, 1994; Walker, 1991).

18.9 References

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