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**The Use of Local Analgesic Agents in  
Scoliosis Surgery**

**The Implications for Spinal Cord Monitoring**

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## **ABSTRACT**

The thesis examines the use of local analgesics as part of the anaesthetic technique for scoliosis surgery. Any agents used must have minimal interference with monitoring of spinal cord integrity.

The literature on the anaesthetic requirements for scoliosis surgery is reviewed and the various methods of monitoring spinal cord function are discussed.

The historical background and experimental rationale for the use of the somatosensory evoked potential (SEP) in scoliosis surgery is examined. The advantages of the epidural SEP over the scalp-recorded SEP are demonstrated. Spinal cord monitoring at many UK centres consists of measuring the SEP recorded from the C<sub>7</sub> - T<sub>1</sub> epidural space to stimulation of the posterior tibial nerve (PTN) at the popliteal fossa.

The effects of a lumbar epidural injection of different local analgesic solutions on the SEP to posterior tibial nerve stimulation were investigated. In the initial study, epidural lignocaine 2% 10 ml was evaluated. The next two experiments assessed the changes after epidural diamorphine 0.1 mg kg<sup>-1</sup> and epidural etidocaine 1% 10 ml respectively on the SEP. The final study compared the effects of epidural bupivacaine 0.25%, 0.5% and 0.75% 10 ml on the SEP.

These studies showed that 10 ml of lignocaine 2%, bupivacaine 0.5% or bupivacaine 0.75% depressed significantly the epidural SEP. Diamorphine 0.1 mg kg<sup>-1</sup> had no measurable effect. Etidocaine 1% caused a profound decrease, and in some cases an obliteration of the SEP. There was a clear concentration-dependent effect of increasing concentrations bupivacaine on the SEP.

The effects of the different local analgesic agents on the neurophysiological variables are considered in the light of their known physicochemical properties. The literature on the neural generators of the epidural SEP is reviewed. My studies are compared to similar experiments on the scalp-recorded SEP and the SEP to dermatomal stimulation. Possible differences in the epidural SEP between scoliosis and non-scoliosis patients are noted. The possible relevance of the changes in mean arterial pressure when assessing alterations in SEP is examined.

Etidocaine, and local anaesthetics of high lipid solubility, have no place in anaesthesia for scoliosis surgery. Furthermore, lignocaine 2%, bupivacaine 0.75% or bupivacaine 0.5% cannot be recommended because they interfere with monitoring of the SEP in the perioperative period. However, lower concentrations of bupivacaine such as 0.25%, together with diamorphine 0.1 mg kg<sup>-1</sup>, may be appropriate, since they have minimal effects on the SEP.

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## LIST OF PUBLICATIONS

The following is a list of publications on work which is described in the thesis.

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Loughnan, B.A., L.J. Murdoch, M.A. Hetreed, L.A. Howard, & G.M. Hall, 1990. 'Effects of 2% lignocaine on somatosensory evoked potentials recorded in the extradural space'. *Br. J. Anaes.*, v.65, pp.643-47.

Loughnan, B.A., K.W. Yau, A.O. Ransford, & G.M. Hall, 1991. 'Effects of epidural diamorphine on the somatosensory evoked potential to posterior tibial nerve stimulation'. *Anaesthesia*, v.46, pp.912-4.

Loughnan, B.A., S.M. McHale, K.R. Welsh, & G.M. Hall. 'Etidocaine and epidural somatosensory evoked potentials after posterior tibial nerve stimulation'. *Submitted to Br. J. Anaes.*

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## CHAPTER I

### INTRODUCTION

#### 1.1 Introduction

Dickson (1983) found the prevalence of scoliosis in the community was 15%. However, in only 10% of patients screened was the curve of the idiopathic variety. These are patients with no associated neuromuscular, cardiac or other abnormalities. By definition, the cause is uncertain and the scoliosis starts in adolescence. It is far more common in girls than in boys (relative incidence of female to male is 5 : 1). Rogala, Drummond & Gurr (1978) similarly found an incidence of idiopathic scoliosis of 4.5% and 2% where the curve was defined as greater than 5° or 10° respectively.

However Rogala *et al.* (1978) found that in only 2.75 per 1000 children screened was treatment required. A large proportion of the corrective surgery in this group is undertaken primarily for cosmetic reasons.

One of the major considerations in scoliosis surgery is the monitoring of spinal cord function. The incidence of paraplegia as a complication of corrective surgery is only around 1% (MacEwan, Bunnell, & Sriram 1975). But this is catastrophic in the individual and more particularly if the operation is performed for cosmetic reasons, as is the case in the idiopathic group.

Scoliosis can be divided into two groups: congenital (15%) and acquired - idiopathic group in 65% of cases; those secondary to neuromuscular disease account for only 20% of cases (Steward 1979). Initial assessment of each patient should include the determination of which group that individual belongs to, as this has an influence on the likelihood of intraoperative spinal cord damage. The presence of mental retardation is important because it is essential for the patient to co-operate with postoperative treatments such as physiotherapy.

The planned surgical manoeuvres are important in the context of the likelihood of neurological complications and therefore the requirement for spinal cord monitoring. Surgical opinion on this issue is divided. Previously operations such as posterior fusion with instrumentation, in which distractive forces were applied to the spine, were considered to be the main indication for some form of spinal cord monitoring. However, with the introduction of a greater variety of instrumentation, the criteria for spinal cord monitoring have widened to include many operations using the anterior approach. It has been suggested that all surgery involving the insertion of wires or pedicle screws warrants some form of monitoring, as it may result in direct cord damage. This has been made possible by the development of modern signal averaging techniques and the consequent availability of relatively simple monitoring devices.

## 1.2 **Methods of Monitoring**

In some centres no monitoring is performed but, with the advent of an increasingly litigious climate, this is probably unwise. Most surgeons performing this specialised surgery request some method of assessing spinal cord conduction intraoperatively.

### 1.2.1 **The wake-up test**

The wake-up test is still performed, particularly in departments lacking access to neurophysiological monitoring and advice. The disadvantages of this test are that it requires the patient's co-operation, it can result in an increase in blood pressure with consequent increase in blood loss and there is the obvious risk of endotracheal tube dislodgement. Furthermore, it cannot be adequately performed in the mentally retarded, it is difficult in emotionally labile adolescents and it can only be performed once, or at the most on two occasions, during surgery. It also has an incidence of false negatives. However, even when neurophysiological monitoring is employed, there is still a very small incidence of false negatives. Clinical assessment of the patient in terms of intact sensation and movement in their lower limbs is paramount.

### 1.2.2 **Somatosensory evoked potentials (SEP)**

Evoked potentials are the electrical potentials (voltages) generated by the nervous system in response to brief sensory stimuli. A large number of responses can be

averaged using electronic signal averaging devices, so that the stimulus-related portion only of the electroencephalogram (or electrospinogram) is seen. The evoked potentials in response to stimulation of a mixed peripheral nerve, such as the median or posterior tibial nerve, are termed a somatosensory evoked potential (SEP). The SEP may be recorded by using electrodes placed on the scalp in an area overlying the relevant area of the sensory cortex. It may also be recorded from electrodes on skin and other tissues overlying the spinal cord.

The use of the SEP to monitor spinal cord function was established by Brown, Nash and colleagues (Brown & Nash, 1979, Brown, Nash Jr, Berrilla, & Amaddio 1984, Nash, Lorig, Schatzinger, & Brown 1977a, Nash, Schatzinger, Brown, & Brodkey 1977b, Wilber, Thompson, Shaffer, Brown, & Nash 1984) and has been an accepted part of clinical practice for a number of years. It was noted that neurological complications were much more frequent in patients who received segmental instrumentation. SEP monitoring correctly predicted every occurrence of major neurological sequelae, usually by complete loss of the SEP. Loss of the SEP was followed by appropriate surgical intervention and the confirmatory use of the wake-up test.

Engler, Spielholz and colleagues were among the earliest groups to report a series of patients monitored while undergoing Harrington rod instrumentation (Engler, Spielholz, Bernhard, Danziger, Merkin, & Wolff 1978, Spielholz, Benjammin, Engler, & Ransohoff 1979). The SEP in the fifty-five patients remained stable and there were no neurological complications. A similar series of sixty-one patients was reported by Mostegl & Bauer (1984). In this series, the SEP disappeared during Luque wiring in two patients and loss of function was confirmed by the wake-up test. The surgeons modified their corrective instrumentation and the patients awoke later without any neurological deficit.

All the above series used the scalp-recorded SEP. These are known to be affected markedly by anaesthetic drugs, in particular the volatile anaesthetic agents (McPherson, Mahla, Johnson, & Traystman 1985, Sebel, Flynn, & Ingram 1984). Jones, Edgar, & Ransford (1982) were among the first to report the use of more

invasive forms of monitoring, namely the epidural recording of the SEP. They observed that there was little effect of the inhalational agents on the epidural SEP in 115 operations for scoliosis (Jones, Edgar, Ransford, & Thomas 1983). These workers recommended that an SEP attenuation of greater than 50% was an indication of impending neurological damage and that the surgeon should modify his instrumentation if this occurred. Although Jones and colleagues also recorded from the spinous process, they found epidural recording to be the preferable method because of its more stable baseline. In the original work a single recording electrode in the epidural space was used with a nearby reference electrode. However, this has been largely superseded by the use of bipolar recording electrodes. Japanese workers such as Tamaki and colleagues (Tamaki, Tsuji, Inoue, & Kobayashi 1981, Tamaki, Noguchi, Takano, Tsuji, Nakagawa, Imai, & Inoue 1984) routinely use epidural SEP monitoring, but in association with direct spinal cord stimulation via a fine epidural stimulating electrode.

In the United Kingdom at the present time, spinal cord conduction is usually monitored by the use of an epidural recording electrode. However, in some United Kingdom centres and in the United States, scalp recordings of the SEPs are employed. In these centres the application of a standardized anaesthetic technique, in particular the use of opiates rather than inhalational agents, renders this form of monitoring satisfactory (Pathak, Brown, Nash, & Cascorbi 1983, Pathak, Brown, Cascorbi, & Nash 1984). In cases of gross deformity of the spine, or severe kyphoscoliosis, cortical recordings are the only satisfactory method of obtaining the SEP, as placement of electrodes in the extradural space is not possible.

The principal advantages of intraoperative SEP measurement are that it is objective and does not require a co-operative patient, and that it can be performed on an almost continuous basis.

However, there is a small incidence of occasions where spinal cord injury has occurred without any accompanying change in the SEP (Lesser, Rauzens, Luders, Nuwer, Goldie, Morris, Dinner, Klem, Hahn, Shetter, Ginsburg, & Gurd 1986).

This may be due to disruption of motor function alone, without any changes in afferent conducting pathways and, therefore, no change in SEP. Currently, monitoring of motor pathways is being developed (Boyd, Rothwell, Cowan, Webb, Morley, Asselman, & Marsden 1986, Loughnan, Anderson, Hetreed, Weston, Boyd & Hall 1989b, Taylor, Fennelly, Taylor, & Farrell 1993).

### 1.3 The Effects of Arterial Pressure

There is likely to be considerable blood loss during spinal surgery, especially in patients undergoing posterior fusions. The haemoglobin may fall by as much as 5 g dl<sup>-1</sup>. As in all back surgery, it is important to try to decrease intraoperative blood loss. Hypotensive agents are often used as part of the anaesthetic technique. Agents used to lower the blood pressure may include high concentrations of the inhalational agents, such as enflurane, isoflurane or halothane, and drugs with a more specific hypotensive effect such as trimetaphan and labetolol.

Dommissie (1980) emphasised the importance of an adequate blood supply in the prevention of neurological complications of spinal surgery. Preservation of both the macro- and microcirculation are important as "under conditions of anoxaemia the delicate neurological structures cannot survive". Induced hypotension is a common feature of the anaesthetic requirements for scoliosis surgery. However, it should be used with caution because of the known importance of the blood supply on cord viability and the experimental evidence which suggests that the effects of hypotension and distraction may be additive in causing neurological damage (Yeoman, Gibson, Hutchinson, Crawshaw, Bradshaw, & Beattie 1989).

### 1.4 The Case for Epidural Anaesthesia

The analgesic requirements for scoliosis patients in the immediate postoperative period are great and administration of high-dose opiates by intravenous infusion is common. Frequently, a two-staged surgical procedure is undertaken with a fortnight between. The pain from a first-stage thoracotomy with an indwelling chest drain is often severe and poorly tolerated in the young.



The requirements of a hypotensive field and an awake, pain-free patient at the end of surgery suggest that general anaesthesia supplemented by epidural analgesia would be an appropriate technique for scoliosis surgery. Furthermore, the intraoperative use of local analgesics can be continued into the postoperative period.

Bromage (1952) recommended lumbar epidural supplementation of general anaesthesia for patients undergoing lumbar laminectomy. He found that an ischaemic field resulted from the combination of hypotension due to the epidural blockade and vasoconstriction from 1 : 150,000 adrenaline in the epidural solution. Reynolds, Dautenhahn, Fagraeus & Pollay (1986) used epidural analgesia successfully as the sole anaesthetic in twenty-two patients requiring lumbar disc procedures. They state that epidural analgesia is safe and reliable in spine surgery, even in the presence of abnormal anatomy. Furthermore, the technique provided intraoperative analgesia, muscle relaxation and, when combined with adrenaline, shrinkage of the epidural veins.

However, reports of the use of epidural analgesia in scoliosis surgery have been sparse. Jennings & Delaney (1979) successfully used epidural bupivacaine 0.25% in scoliosis surgery and the patients were able to move their hands and feet when woken during the operation. Purnell (1982) suggested that there were difficulties with this technique. He found that the block was more profound and persistent than expected, and was a confusing factor in the early postoperative assessment of his patient. But in this case bupivacaine was administered in a total dose of 4.3 mg kg<sup>-1</sup> to an eleven-year-old girl over a three-hour period.

It is well known that large volumes of high concentrations of local analgesics administered to normal patients can result in profound muscle paralysis and loss of sensation for prolonged periods of time. However, the judicious use of a low concentration of local analgesic agent, together with an opiate in the epidural space will provide satisfactory analgesia, but with preservation of the relevant motor power so that early postoperative assessment of limb movements remains feasible.

There is little data on the effect of local analgesic agents on spinal cord monitoring. In animal experiments on baboons (Cusick, Myklebust, & Abram 1980), it was shown that

the effect on any evoked response depended on the site of monitoring chosen, the location of epidural local analgesic administration, as well as the agent used. Cusick *et al.* (1980) found that chlorprocaine affected the dorsal root entry zone with minimal effects of the long conducting tracts. The opposite was shown for etidocaine, namely that the major effect was on the long conducting tracts of the spinal cord with minimal action on the dorsal root entry zone. Bupivacaine 0.5%, on the other hand, depressed conduction in both the dorsal root entry zone and the long tracts.

There are no studies in man assessing the effects of epidural analgesics on spinal cord monitoring (i.e. the SEP recorded using an electrode in the epidural space). The nearest approximation is the work of Kehlet and colleagues (Dahl, Rosenberg, & Kehlet 1992, Lund, Selmar, Hansen, Jensen, & Kehlet 1987a, Lund, Selmar, Hansen, Hjortsø, & Kehlet 1987b, Lund, Hansen, & Kehlet 1989, Lund, Hansen, Mogensen, Qvitzau, & Kehlet 1991, Saugbjerg, Asoh, Lund, Kühl, & Kehlet 1986) In a study using the SEP recorded from the scalp, Saugbjerg *et al.* (1986) showed that the administration of bupivacaine 0.5% into the lumbar epidural space resulted in a decrease in the P<sub>1</sub> component only. This is the only component of the scalp-recorded SEP that is thought to be representative of spinal cord conduction. Other studies by this group (Dahl, Rosenberg, Lund, & Kehlet 1990, Dahl *et al.* 1992, Lund *et al.* 1987a, 1987b, 1989, & 1991) utilised the scalp-recorded SEP evoked by stimulation of the L<sub>1</sub>, T<sub>10</sub> and T<sub>6</sub> dermatomes to assess any difference between the various analgesic agents. A further study (Lund, Hansen, Mogensen, Kehlet 1987c) evaluated the effect of a thoracic epidural injection site on the dermatomal SEP. However, the dermatomal SEP is difficult to reproduce, and has a high degree of individual variability (Slimp, Rubner, Snowden, & Stolov 1992). Moreover, this SEP may only measure nerve root integrity, rather than spinal cord conduction (Dvinch, Scarff, Bunch, Smith, Boscardin, Lebarge, & Ibrahim 1984, Katifi & Sedgwick 1986).

## 1.5 Conclusion

There is little doubt that during spinal surgery some monitoring of intraoperative spinal cord function is advisable and the most appropriate method is the SEP. However, the overriding consideration remains the early assessment of the patient postoperatively.

Because many of the surgical techniques require a relatively avascular field, hypotension is a frequent requirement for scoliosis surgery. Any changes in spinal cord function and/or the SEP caused by surgical intervention may be potentiated by hypotension. Hypotension is commonly produced using high inspired concentrations of inhalational agents, supplemented if necessary by alpha and/or beta adrenoceptor blocking drugs. The administration of high inspired concentrations of inhalational agents has the disadvantage that it may delay patient awakening and make early postoperative assessment of limb movements difficult. General anaesthesia supplemented by the judicious employment of epidural blockade with local analgesics would seem to be an appropriate technique for achieving a degree of hypotension. This would also offer the advantage of early postoperative assessment and perioperative analgesia. It is particularly important, however, that the local analgesic used has minimal effect on the intraoperative SEP.

#### 1.6 Objectives of the Thesis

The major aim of the following studies was to assess the effects of different local analgesic agents on the epidural SEP and make recommendations for their use in scoliosis surgery.

Because I wished to record the effects of the analgesic agents on the SEP in the absence of surgical stimulation, all patients were studied in the anaesthetic room, after induction of anaesthesia but prior to surgery.

The current series of studies used a lumbar epidural site of injection and stimulated a mixed peripheral nerve with lumbar origins. This permitted the maximal effect of the local analgesic on the SEP to be ascertained.

The studies were designed to assess the effects of a fixed volume (10 ml) of different local analgesic agents on the epidural SEP.

This thesis, in a small number of studies, makes recommendations about the use of local analgesic agents in scoliosis surgery. The first study investigated the effects of lignocaine on the SEP because this local anaesthetic agent is used as the standard. I next assessed the effect of diamorphine on the epidural SEP, because epidural opiates are commonly

used for perioperative analgesia. In the third experiment the effects on the SEP of etidocaine, a local anaesthetic with physical characteristics markedly different from lignocaine, was appraised. Finally I investigated whether there was an effect of increasing concentration and in the fourth study compared the effects of three different concentrations of bupivacaine on the SEP.

To summarise: the studies estimate the effect of the local anaesthetic agents on the epidural SEP. By assessing the effects of the different agents, I hope that clear recommendations can be made on the local anaesthetic agents appropriate for use in scoliosis surgery which will not interfere with spinal cord monitoring.

## CHAPTER II

### LITERATURE REVIEW

#### 2.1 Anaesthesia for Scoliosis Surgery

Little is written on the anaesthetic management of surgery for scoliosis in the standard textbooks. The authors deal mainly with the small number of patients who have pre-existing lung disease and muscular impairment (Atkinson, Rushman, & Lee 1987, Spencer 1978). Atkinson *et al.* (1987) discusses, albeit briefly, the wake-up test and the use of evoked responses to assess spinal cord integrity. This text mentions extradural anaesthesia in the context of decreasing the systemic blood pressure, but warns of possible danger to the cord consequent on the hypotension produced.

Zauder (1989) does a brief, but comprehensive, review of modern concepts in scoliosis surgery. He emphasises the fact that 80% of cases are of the idiopathic variety, with congenital scoliosis the second major group of importance to the anaesthetist. He stresses that the group most likely to have concomitant anomalies are the congenital group. Zauder discusses the need for preoperative respiratory assessment and suggests appropriate lung function tests. He mentions the different operative positions adopted for the various types of surgery. Moreover, he reviews comprehensively the various tests of spinal cord conduction, including the wake-up test, the SEP and the motor evoked potential. Zauder states that an epidural recording electrode may be used, thereby eliminating the effects of anaesthetic agents on the SEP, but at the expense of awake control data. Subsequent text in this chapter infers that the cortically recorded SEP is the mainstay of monitoring. He suggests the use of balanced anaesthesia with opioids, neuromuscular blocking drugs and nitrous oxide-oxygen mixture as the technique of choice. Although the blood loss may be considerable, the only recommended means of decreasing this is by positioning, rather than manipulation of the blood pressure. Hypotension, if employed, is recommended to be "moderate" only, but prior to distraction it should be normalised.

Steward (1979), in his textbook of paediatric anaesthesia, emphasises that numerically the idiopathic group is the most important. Contrary to current experience, he states that

respiratory function is usually impaired. Most of the discussion is centred on the anaesthetic management of the posterior approach. The anaesthetic technique suggested is dependent on the prone position required for the surgery. He warns that blood loss may be severe and even exceed 50% of estimated blood volume. Steward specifically advises against the use of induced hypotension on the basis that inadvertent obstruction of a major blood vessel may seriously reduce venous return, exacerbating the hypotension and even resulting in ischaemia of the cord. There is no mention of neurophysiological monitoring, although a description of an appropriate method of conducting the wake-up test is given. Steward states, however, the importance of checking movement of the legs and feet (as a confirmation of spinal cord integrity) both in the course of the wake-up test and in the immediate postoperative period. However, most of the emphasis is on the prevention and management of any respiratory dysfunction.

Spencer (1978) has a brief discussion on the management of severe scoliosis in the chapter on artificial ventilation. The discussion is confined to long term management of patients with scoliosis and the prevention of respiratory failure. Spencer does not deal with the anaesthetic management of these patients for corrective, or any other form of, surgery.

In summary, the standard anaesthetic textbooks mention little about the anaesthetic management of scoliosis except for concentrating on those patients who have major respiratory impairment. They do, however, state that there may be considerable blood loss, but do not recommend induced hypotension as a means of reducing this loss. There is very little discussion of spinal cord monitoring except for the use of the wake-up test or early post-operative assessment.

A search of the recent literature for the anaesthetic management of scoliosis is slightly more productive. Relton & Conn (1963) described the large blood loss found during such surgery. However, although they reviewed the various methods of reducing blood loss (including regional analgesia) they considered that induced hypotension was contraindicated because the patient's position was likely to compress the inferior vena cava, thereby resulting in decreased venous return. Relton & Conn considered that

epidural analgesia was contraindicated mainly because of technical difficulties and possible difficulties with neurological assessment.

An early review by Shin (1973) dealt mainly with patients with a severe degree of anatomical distortion. He emphasised the large possible blood loss, but made no suggestions about the use of hypotensive techniques or spinal cord monitoring.

Induced hypotension was suggested as a valuable anaesthetic technique by McNeill, DeWald, Kuo, Bennett, & Salem (1974). This technique was used in forty-four patients undergoing corrective surgery for scoliosis, and the blood loss in these patients was compared with that in a further twenty-two patients whose intraoperative management involved normotension. All patients underwent Harrington rod insertion and the anaesthetic technique was otherwise standardised in all cases. Despite the fact that the data was collected retrospectively, this study showed that blood loss could be reduced significantly by the use of induced hypotension and, provided monitoring was adequate, that the technique was safe. These workers recommended the use of a ganglionic blocking agent in association with an inhalational agent, rather than halothane alone. Paraplegia due to vascular impairment did not occur. They described one patient in the normotensive group who developed a postoperative paraplegia, which recovered after removal of the Harrington rod.

The data of Wong, Webster, Coleman, & Dunn (1980) supported the use of hypotensive anaesthesia for scoliosis surgery and described haemodilution and induced hypotension as an appropriate technique for reducing blood loss in a Jehovah's Witness patient undergoing Harrington rod insertion. Kafer (1980) reviewed the cardiorespiratory function and anaesthetic management of scoliosis and advised against the use of induced hypotension. This note of caution was repeated by Grundy, Nash Jr., & Brown (1981), who reported a patient undergoing correction of an adolescent idiopathic scoliosis curve where the intraoperative monitoring indicated a deficit. There was an improvement in the appearance of the trace on restoration of the arterial pressure to normotensive levels. She recommended that, when induced hypotension is used, some form of intraoperative spinal cord monitoring should be undertaken. A later paper by Bourreli, Pinaud, Passuti, Gunst, Drouet, & Remi (1988) investigated the haemodynamic and neuroendocrine

responses to induced hypotension for scoliosis surgery and showed that a combination of dihydralazine and enflurane or isoflurane anaesthesia resulted in a reduction of arterial pressure to 50-60 mm Hg. The hypotension was easy to control, permitted rapid intraoperative awakening and, despite concomitant increases in the plasma renin activity and aldosterone and noradrenaline values, the authors recommended this technique for spinal surgery.

Several papers on the anaesthetic management of scoliosis deal mainly with the use of the wake-up test. The earliest reference described the use of the wake-up test on 124 procedures with Harrington instrumentation performed from November 1970 to January 1972 (Vauzelle, Stagnara, & Jouvinroux 1973). When the wake-up test was performed, nitrous oxide was discontinued and oxygen in air was administered. These authors described, in detail, the anaesthetic management of three representative cases. A later paper by Abbott & Bentley (1980) described the wake-up test in greater detail; they used a relatively high total dose of morphine as premedicant and at induction in twenty children undergoing scoliosis correction. The wake-up test was administered by withdrawal of nitrous oxide and hand-ventilation of the patient with 100% oxygen in 5% carbon dioxide. No inhalational agent appears to have been used and there was no attempt to induce hypotension. A later paper by the same group (Dorgan, Abbott, & Bentley 1984) reported essentially the same findings, but in a larger group of 102 patients. In the review by Kafer (1980), a narcotic-nitrous oxide-relaxant technique with controlled ventilation supplemented as necessary by inhalational agents was recommended. Evoked potentials were mentioned, but the major emphasis was on the use of the wake-up test.

Hall, Levine, & Sudhir (1978) described the anaesthetic management for Harrington Rod instrumentation in 166 cases operated on between 1974 and 1976. Again a high-dose opiate technique was used. The wake-up test was administered by reversal of the neuromuscular blocking drug, turning off the nitrous oxide and administering 100% oxygen. Hypotensive agents were administered in this series (trimethaphan as a 0.01% solution) to prevent hypertension and maintain systolic blood pressure between 90 and 100 mm Hg of mercury.



Jennings & Delaney (1979) described the use of epidural analgesia as a method of providing hypotension, thereby avoiding high doses of opiates whilst still providing enough analgesia to allow the use of the wake-up test. In their anaesthetic management of five patients undergoing Harrington rod instrumentation, bupivacaine 0.25% 20 ml with adrenaline 1:200,000 was injected into the L<sub>3-4</sub> epidural space. They found that this concentration of bupivacaine provided sufficient sensory blockade, so that high doses of systemic analgesics were avoided. However, the low dose of the local analgesic meant that motor function, necessary for the wake-up test, was preserved.

## 2.2 Somatosensory Evoked Potentials

The main dangers of the wake-up test were described by Dorgan, Abbott, & Bentley (1984). They are:

- (1) extubation due to raising of the head;
- (2) air embolism due to aspiration of air into the open vessels in the wound;
- (3) dislodgement of the rod, or fracture of a lamina, due to sudden movement.

Youngman & Edgar (1985) stated that the test may result in surges of arterial pressure. Previous authors have not been concerned this with problem, but it is important in the context of modern practice, where induced hypotension is a standard part of the anaesthetic management. It also has the disadvantage that it can only be performed a limited number of times. Furthermore, it is not suitable in the very young or the mentally retarded.

Somatosensory evoked potentials have the advantages that they are objective and can be performed on an almost continuous basis. They can be used in association with induced hypotension and warn of any danger to spinal cord function when distractive forces are applied to the spine in association with hypotension.

### 2.2.1 **Experimental Background**

Several groups of workers have examined the neurophysiological and neurological effects of experimentally induced spinal cord compression in cats. D'Angelo, Van Gilder, & Taub (1973) used a controlled impact injury and found that, when a 100 g cm force weight was applied to the spinal cord, there were no changes in the somatosensory evoked potential (SEP) or pathological injury to the cord.

However, when 300 and 500 g cm forces were applied, there was an immediate loss of the SEP. Multiple petechial haemorrhages were found in the cord and, with the 500 g cm force, there was profound central cord damage. Croft, Brodkey, & Nulsen (1972) placed weights of 38, 48 and 58 g on an area of cord of 0.4 cm<sup>2</sup> and correlated changes in the SEP with later neurological changes. The 58 g weight abolished the SEP within 10 min and there was no return of the potential in the succeeding 60 min. The animal had a severe neurological deficit after operation. The 48 and 38 g weights resulted in an early decrease in the SEP but abolition did not occur for at least 15 min. Removal of the weights was associated with a return of the SEP within 20 min. Neurologically, the 48 g weight was associated with an immediate severe deficit from which the animal recovered rapidly, and the 38 g weight resulted in only minor changes. Therefore, both these classical studies have shown that, when increasing compressive forces are applied to the spinal cord, there is a loss of the SEP coincident with increased neurological damage, as assessed both histologically and neurologically.

However, the forces involved in spinal cord surgery are distractive rather than compressive, so that experimental data derived from studies using distraction are probably more relevant to clinical work. Nordwall, Axelgaard, Harada, Valencia, McNeal, & Brown (1979) applied distractive forces to adjacent lumbar vertebrae in cats and attempted to correlate changes in the SEP with impaired motor function as assessed by the "wake-up" test. No significant neurological deficit was found when the distractive forces produced less than a 50% attenuation of the SEP but, when further force was applied, severe impairment resulted. Therefore most recommendations made on the use of the intraoperative SEP to monitor spinal cord integrity have stated that a fall in overall SEP amplitude of more than 50% is a signal to the surgeon to evaluate recent surgical procedures.

### **2.2.2 Hypotensive Considerations**

Brodkey, Richards, Blasingame, & Nulsen (1972), using a feline spinal cord compressive model, found that when hypotension was induced this had an additive effect with compression on the SEP. This is an important observation for

scoliosis surgery, where Whittle, Johnston, & Besser (1986) showed that hypotension to a mean arterial pressure of 50 mm Hg did not alter the waveform of the SEP. Dolan, Transfeldt, Tator, Simmons, & Hughes (1980) used a spinal cord distraction technique in cats to cause a significant decrease in the SEP, at which time there was a 50% decrease in spinal cord blood flow. When distraction was continued further, 0.5 cm beyond the point of abolition of the SEP, there was virtually no blood flow up to 2 cm caudal to the site of distraction. This suggested that damage to the cord during distraction was more likely to result from ischaemia rather than mechanical deformation. It has been shown experimentally by Kobrine, Evans, & Rizzoli (1979a) that ischaemia *per se* results in the abolition of the SEP after only 10 min. When blood was reinfused, the SEP reappeared after a similar interval. More recently, Yeoman and colleagues (1989) used a distractive model similar to that of Nordwall *et al.* (1979) and recorded the SEP at the T<sub>11</sub> interspace. They found that the feline spinal cord was more sensitive to spinal cord distraction under hypotensive conditions (mean of 60 mm Hg).

The animal data, therefore, suggest that the SEP is an early indicator of spinal cord dysfunction and that such dysfunction is reversible if the force and duration of distraction do not exceed critical values. Also, hypotensive and distractive forces are additive in terms of their effect on the SEP, their effect on spinal cord blood flow and their potential for causing neurological damage.

### 2.2.3 Clinical Application

Correction of the spine using instrumentation was first described by Harrington in 1962. He considered that a greater degree of correction was obtainable using an implanted metal rod. However, the technique remained controversial for a number of years. Winter, Moe, & Lonstein (1984) reviewed the surgical management of 290 patients who underwent posterior spinal arthrodesis, with or without Harrington instrumentation, and concluded that the higher risk of paraplegia due to excessive distraction with the rod was unacceptable, and recommended posterior spinal arthrodesis. A survey by MacEwan, Bunnell, & Sirram in 1975 of eighty-seven patients with acute neurological complications

Sirram in 1975 of eighty-seven patients with acute neurological complications resulting from the treatment of 7,885 cases of scoliosis concluded that the incidence of these sequelae was 0.72%. However, he did point to certain procedures as carrying an increased risk of neurological injury, namely skeletal traction, spinal osteotomy and the use of Harrington instrumentation. To this must be added the later risk posed by the use of intralaminar wires (Wilber *et al.* 1984). The prognosis for recovery, in both complete and incomplete lesions, can be increased by removal of the Harrington rod in the early postoperative period, i.e. within three hours of diagnosis.

As stated previously, Brown and colleagues first established the place of SEP monitoring as a means of assessing spinal cord integrity (Nash *et al.* 1977a, 1977b, Brown & Nash 1979, Brown *et al.* 1984, Wilber *et al.* 1984). Engler, Spielholz and colleagues were among the earliest to report the use of the SEP in patients undergoing Harrington Rod instrumentation (Engler *et al.* 1978, Spielholz *et al.* 1979). However, all these series involved the use of the scalp-recorded SEP. This monitoring technique is known to be affected by high inspired concentrations of the inhalational agents (Sebel *et al.* 1984, Pathak, Amadio, Kalamchi, Scoles, Shaffer, & Mackay 1987). Investigators, such as Pathak *et al.* (1984), have sought to show that the effects of anaesthesia on the scalp-recorded SEP can be minimised by the use of a balanced anaesthetic technique consisting of nitrous oxide, narcotics and muscle relaxants. More recently, Kalkmann, Traast, Zuurmond, & Bovill (1991) have found that the early peaks of the scalp-recorded SEP to posterior tibial nerve stimulation are better preserved under alfentanil-propofol anaesthesia than when an alfentanil-nitrous oxide technique was used. Current evidence suggests, therefore, that when the scalp-recorded SEP is used for spinal cord monitoring, optimal conditions are provided by an anaesthetic technique with the minimal possible use of inhalational agents.

Jones and colleagues at the Royal National Orthopaedic Hospital, England (Jones *et al.* 1982) were the first investigators to use an epidural electrode for intraoperative SEP monitoring. They found that this was more stable than the scalp-recorded SEP particularly when inhalational techniques were used (Jones

Johnston, Besser, Taylor, & Overton 1984a, Whittle, Johnston, & Besser 1984b). In the United Kingdom at the present time, the epidural SEP is the normal method of assessing spinal cord integrity intraoperatively.

## 2.3 Effects of Local Analgesics on the SEP

### 2.3.1 Experimental studies

#### 2.3.1.1 In vitro studies of local analgesics

Gissen, Covino, & Gregus (1980) performed studies on different nerve fibres of varying conduction velocities and showed that the larger fast-conducting fibres (presumably representing "A" fibres) were more sensitive to the action of local anaesthetic agents than the smaller slow-conducting fibres (presumably representing "B" and "C" fibres). These authors showed that the local anaesthetic agents exhibited differential effects on the various nerve fibres. A larger variation in local anaesthetic concentration was required to block the differing fibres when lignocaine was used than when tetracaine was the agent. Etidocaine and bupivacaine behaved similarly and were intermediate in terms of their differing effects on nerve fibres. On this basis, they concluded that the larger fibres subserving motor function are more sensitive to local anaesthetic action, with lignocaine exerting the most powerful effect. In clinical practice, however, blockade of pain fibres precedes that of motor fibres. The apparent contradiction between *in vitro* results and clinical experience is explained by the observation that the local anaesthetic agent must penetrate the myelin sheath surrounding the motor fibres before exerting an effect. Therefore, some of the determinants of effect are physical, namely:-

- a) the presence or absence of a myelin sheath around the nerve, and
- b) the ability of the local anaesthetic agent to penetrate this sheath.

The speed of onset and duration of action of local anaesthetic agents is also related to their physical properties other than lipid solubility (Wildsmith, 1986), namely, chemical structure, protein binding, partition coefficient and the  $pK_a$  of the particular agent, which in turn determines the rate of diffusion through physical barriers such as nerve sheaths.

the rate of diffusion through physical barriers such as nerve sheaths. Previously, it has been thought that the "C" fibres were the most sensitive to the action of local anaesthetic agents and the "A" fibres least sensitive Reynolds (1984). However, *in vitro* studies performed by Wildsmith, Gissen, Takman, & Covino (1987) on the desheathed cervical vagus nerve of the rat showed that the reverse was true. Furthermore, he contended that the absolute and relative development of "A" fibre blockade was related to lipid solubility. Etidocaine is a highly lipid soluble agent and therefore diffused through myelin sheath rapidly and blocked the "A" fibres at a faster rate than the "C" fibres. Lignocaine however, because of its lower lipid solubility, took longer to penetrate the "A" diffusion barriers, so that the onset of blockade of these fibres was delayed.

Spinal or epidural blockade involves drug-induced blockade in the spinal canal. The anatomy of the dorsal root entry zone brings small-diameter fibres close to the nerve root surface, thereby shortening the diffusion pathway of a drug introduced into the spinal subarachnoid or epidural space. The diffusion pathway to the larger diameter fibres, which are situated deep in the nerve bundle, is longer. This makes it appear that the smaller diameter fibres are more susceptible to drug action than are the larger-diameter fibres. How the various local analgesics act, and the extent to which they exhibit a differential effect on the different fibre types, depends on their own physicochemical properties and the precise anatomy of the nerve or nerve roots.

#### 2.3.1.2 *In vivo* studies

The major animal *in vivo* work on the changes in evoked potentials in response to epidural injection of local anaesthetic agents, was performed by Cusick *et al.* (1980). This group performed a series of experiments on six monkeys, in which they assessed the differential effects of three local analgesic agents on neural conduction, as assessed by the SEP elicited from various sites.

The evoked potential responses measured from electrodes positioned along conducting pathways were investigated in these animals following epidural injections of 0.5% bupivacaine, 3% chloroprocaine and 1% etidocaine. The sciatic nerve (SN) was stimulated transcutaneously, using rectangular pulses of 0.2 msec duration at 4 Hz with intensities well above motor threshold. A similar stimulus was used for stimulation of the conus medullaris (CM) and sensorimotor cortex (SMC) via electrodes, previously positioned at these levels, which could act as both stimulating and recording electrodes. Responses evoked by SN stimulation were recorded from the cauda equina (CE), conus medullaris (CM), upper thoracic cord (CORD) and sensorimotor cortex (SMC). It was found that chloroprocaine depressed conduction in the dorsal root entry zone as indicated by the moderately decreased amplitude of the conus medullaris (CM) responses evoked by sciatic nerve stimulation (SN → CM). Responses recorded from the cauda equina (CE) evoked by SN stimulation (SN → CE) showed a smaller and less sustained latency increase and loss of amplitude. Responses conducted along the spinal cord white matter fibre tracts (CORD → CORD and SMC → CM) showed no significant change. Therefore, Cusick and colleagues argued that the main site of action of chloroprocaine was at the dorsal root entry zone. Utilizing this methodology, they inferred that the site of action of etidocaine was mainly on the spinal cord white matter with minimal effect on the dorsal root entry zone, whereas bupivacaine acted on both the spinal cord white matter and the dorsal root entry zone. The time course of this action was such that effects were seen at 15 min, were maximal at 60 min, and were beginning to wear off after 120 min. This study supported the concept that local anaesthetics in the epidural space have the spinal cord as their major site of analgesic blockade. Each agent showed selective regions of altered electrophysiologic activity within the spinal cord, with only bupivacaine producing significant conduction changes in both grey and white matter.

In a recent study Mitchell, Goad, Erwin, Camporesi, Moon, Watkins & Bennett (1989) investigated the effects of lignocaine 2% 5ml injected into the canine L<sub>2,3</sub> lumbar epidural space, and measured the evoked potentials in the thoracic epidural space in response to sciatic nerve stimulation. They found that the P<sub>1</sub>N<sub>1</sub> peak amplitude decreased with time and was completely obliterated after 25 minutes. This infers, in a different animal model, that lignocaine has a prominent effect on conduction in the spinal cord.

### 2.3.2 Clinical Studies

Studies assessing the effects of local analgesic agents on the SEP are limited to measurement of the scalp-recorded response. Almost all the work has been performed by Professor Kehlet's group (Dahl, Rosenberg, Lund, & Kehlet 1990, Dahl *et al.* 1992, Lund *et al.* 1987a, 1987b, Lund *et al.* 1989, Lund *et al.* 1991, Saugbjerg *et al.* 1986). However, in only two studies from the Kehlet group were scalp-recorded evoked responses to posterior tibial nerve stimulation measured (Lund *et al.* 1987a, Saugbjerg *et al.* 1986). In both these studies they found that the responses after lumbar epidural bupivacaine administration were identical to those obtained after thoracic epidural bupivacaine administration, that is suppression of the N<sub>1</sub> scalp-recorded response only. Assessment of spinal cord continuity by the scalp-recorded response to posterior tibial nerve stimulation has limitations, since only the N<sub>1</sub> component is thought to represent spinal cord conduction. In contrast, the SEP recorded from the epidural space shows cord activity only; there are 3 discrete peaks and there is negligible effect from the anaesthetic drugs.

Elsewhere Lund and colleagues (1987, 1989, 1991) and Dahl *et al.* (1990, 1992) used the scalp-recorded SEP to dermatomal stimulation. This method of stimulation is mainly of use in the assessment of lumbar radiculopathies prior to lumbar spine surgery (Dvinch *et al.* 1984). Even amongst its enthusiasts (Katifi & Sedgewick 1986), there is acknowledgement of an overlap between adjacent zones when dermatomal SEP are used to assess the various nerve roots.



## 2.4 Summary

In conclusion, there is little written in the standard textbooks about the modern management of scoliosis surgery. A review of recent anaesthetic literature is more productive. There is conflicting information on the need for hypotension as part of the anaesthetic technique. Many of the reports make recommendations about administration of the wake-up test.

The use of the SEP for intraoperative spinal cord monitoring is mentioned mainly in the recent anaesthetic literature. Most of the research investigating the effects of anaesthetic agents on the SEP uses the scalp-recorded response only. There has been little work on the effects of anaesthetic agents on the SEP recorded from the epidural space.

Epidural anaesthesia as part of the anaesthetic technique for scoliosis surgery would provide hypotension and permit the patient to wake earlier from the anaesthetic, thereby allowing early assessment of limb movements. However, there have been few studies of the effects of local anaesthetic agents on the scalp-recorded SEP. Those that have been performed deal mainly with the dermatomal stimulated SEP, and not the SEP to posterior tibial nerve stimulation used in monitoring for scoliosis surgery.

The only studies investigating the effects of local analgesic agents on the SEP recorded from the epidural space, have been performed on animals. If local anaesthetics are to be injected into the epidural space at the commencement of scoliosis surgery, it is important that they have a minimal effect on the spinal cord monitoring. The various local analgesic agents exhibit different properties *in vitro* and *in vivo*. It is to be expected, therefore, that they will have differing effects on the SEP recorded from the epidural space.

## CHAPTER III

### METHODS

The experimental work presented in later chapters of this thesis comprises four studies involving eighty-eight patients. Three of these studies were performed at the Royal National Orthopaedic Hospital, Stanmore and one at Northwick Park Hospital. Two complementary earlier studies had been carried out on a further thirty-two patients at the Royal National Orthopaedic Hospital. The aims of these studies, patient details and Chapters in which they are reported, are summarised in Table 3.1. Each study was approved by the local Ethical Committee. Informed consent was obtained from patients and/or their parents as appropriate.

#### 3.1 Patients Studied

##### 3.1.1 At the Royal National Orthopaedic Hospital

The patients studied at Stanmore were all suffering from adolescent idiopathic scoliosis. In total, five studies were performed at this hospital involving 104 patients. All were undergoing corrective surgery which required intraoperative monitoring. The insertion of a monitoring electrode preoperatively in the anaesthetic room by experienced anaesthetists was thought not to represent a significantly greater risk than intraoperative insertion of the electrode by the orthopaedic surgeon. No patient had any systemic disease or neurological abnormality. Specific syndromes such as Marfan's syndrome were excluded. Only patients with a curve of Cobb angle between thirty and seventy degrees as assessed by plain X-rays were studied.

Every patient studied had a major curve that was concave to the left. This was thought essential to ensure uniformity of patients. Also, Shukla, Sedgwick, & Doherty (1987) suggested that, in the intraoperative monitoring of such patients, any decrease in amplitude of the SEP was usually seen on the concave side of the curve. Other studies performed on scoliosis patients (Pathak *et al.* 1987), where one side only was studied, obscure this possible laterality of response.

### 3.1.2 At Northwick Park Hospital

After the studies on scoliotic patients, I felt sufficiently experienced in the technique to use it to assess spinal cord conduction in healthy gynaecological patients undergoing total abdominal hysterectomy. Again, all these women were ASA grade 1 or 2, with no neurological abnormalities. A very important reason for performing a study investigating the effect of epidural etidocaine on afferent conduction, was that animal studies by Cusick *et al.* (1980) indicated that etidocaine was likely to have a depressant effect on spinal cord conduction. If this drug was used in patients with adolescent scoliosis, it might not be possible to monitor satisfactorily spinal cord conduction intraoperatively. Therefore, the initial assessment of etidocaine was undertaken on gynaecological patients.

### 3.2 Equipment Used

In all studies, the electronic equipment, electrodes, and the stimulation and recording protocols, were identical to those used in the routine intraoperative SEP monitoring of adolescent scoliosis patients. The electrode used for measuring the epidural SEP is a bipolar electrode originally intended for cardiac pacing. It is manufactured by S-Pace Medical Ltd. and is available in 3 French Gauge (FG) and 2 FG sizes. The slightly larger 3 FG size was used throughout the studies, as this electrode was found to be more robust, gave a more consistent baseline and was associated with less background noise. The distal pole of the preamplifier of the recording apparatus was connected to the negative input of the recording electrode. Observations by Jones and colleagues (1982, 1983) utilised a unipolar wire electrode with a reference electrode placed in the nearby exposed muscle intraoperatively. However, this method was found to result in an unstable baseline and the unipolar electrode was abandoned for routine clinical use in favour of the bipolar one.

The recording and stimulating equipment used in this study was that incorporated in a Medelec MS-91 single-channel EMG recorder. The stimulus applied was a square-wave impulse of 0.2 ms duration, applied to the posterior tibial nerve in either popliteal fossa by means of skin-surface electrodes and stimulated at the rate of 20 pulses per second. The intensity was adjusted so that it was supramaximal in terms of the SEP response. In most cases this was less than 200 V.

The evoked potentials were routinely amplified over a narrow bandwidth of 200 Hz - 2 kHz, averaged and recorded on heat-sensitive paper. A minimum of 750 responses were averaged with a resolution of 0.033 ms.

### 3.3 Anaesthetic Protocol

All patients were premedicated with papaveretum 0.3 mg kg<sup>-1</sup> and hyoscine 0.006 mg kg<sup>-1</sup> 90 min prior to the induction of anaesthesia. Anaesthesia was induced with propofol 2.5 mg kg<sup>-1</sup> and tracheal intubation facilitated with pancuronium 0.08 mg kg<sup>-1</sup>. The lungs were ventilated with 67% nitrous oxide in oxygen. A bipolar recording electrode was inserted in the C<sub>7</sub>-T<sub>1</sub> interspace, connected to the preamplifier of the Medelec MS91 recorder and baseline responses to stimulation of each posterior tibial nerve were averaged.

Once baseline responses were obtained, anaesthesia was continued with 70% nitrous oxide in oxygen and a three-stage propofol infusion was started in all patients; 21 mg kg h<sup>-1</sup> for 5 min, 12 mg kg h<sup>-1</sup> for 10 min and thereafter 6 mg kg h<sup>-1</sup> for 35 min. Repeat SEP measurements were made at 30, 40 and 50 min after infusion commencement or lumbar epidural injection. Once the study period of 50 min was completed, patients were taken into theatre and surgery commenced. The extradural electrode was used for the routine monitoring of the SEP during corrective surgery in the adolescent scoliosis patients. In the gynaecological patients, it was removed just prior to the patient awakening.

The propofol infusion regimen was described by Vandesteene, Trempont, Engelman, Deloof, Focroul, Shoutens, & de Rood (1988) and is designed to give stable propofol values of approximately 4 µg ml<sup>-1</sup> between 30 and 50 min after infusion commencement. An initial study was performed at the Royal National Orthopaedic Hospital (Loughnan, King, Grundy, Young, & Hall 1989a). In the study group (n=6), increasing concentrations of halothane were administered and the "control" group (n=6) received no volatile anaesthetic agent, but only incremental doses of thiopentone as deemed appropriate clinically. The high total dose of thiopentone received by most of the "control" patients meant that many were very drowsy and unresponsive for some time after the end of surgery. This hindered early postoperative clinical assessment of these

patients' motor and sensory function. It was decided, therefore, that propofol as a continuous infusion was a more appropriate agent as it has a shorter elimination half-life (Adam, Briggs, Bahar, Douglas, & Dundee 1983). All studies subsequent to this initial one have used propofol in the regimen outlined above. In the first study using propofol (Loughnan *et al.* 1989b), plasma concentrations were measured using HPLC with fluorescence detection as described by Plummer (1987). Mean (SD) blood concentrations of propofol after 30, 40 and 50 min were 4.36 (3.65), 4.23 (1.90) and 4.54 (1.82)  $\mu\text{g ml}^{-1}$ , respectively.

### 3.4 **Epidural Analgesia**

Immediately after insertion of the epidural recording electrode, a 16-gauge Tuohy needle (Portex) was inserted into the L<sub>2,3</sub> epidural space using the loss of resistance to air technique as described by Bromage (1978). In the lignocaine, diamorphine and bupivacaine studies, a single bolus (10 ml) of the local analgesic agent was injected. In the etidocaine study, an epidural catheter was inserted 3 cm into the epidural space; the patient was then placed supine for baseline SEP recordings and local anaesthetic injection via the epidural catheter.

The local analgesic agent was administered only after satisfactory baseline SEP recordings were obtained. The three-stage propofol infusion was commenced at the same time as the local anaesthetic injection.

### 3.5 **Routine Monitoring**

All patients were monitored with an ECG and a calibrated end-tidal carbon dioxide analyser, and ventilation was adjusted to maintain an end-tidal concentration of 4.0-4.5% carbon dioxide. Rectal temperature was measured and remained greater than 35°C throughout the study period. Mean arterial pressure was measured at the same time as each SEP was measured. In the case of the adolescent scoliosis patients, arterial pressure was measured directly using cannulation of the radial artery. This was not considered appropriate in the case of the gynaecological patients at Northwick Park Hospital and non-invasive methods of arterial pressure measurement were used (calibrated Cardiacap).

### 3.6 **Intravenous Fluids**

In all patients, a 14G intravenous cannula was inserted in a peripheral vein and Hartmann's solution was infused slowly at first. After the epidural injection/infusion commencement, the rate of infusion was increased as deemed necessary to maintain systolic arterial pressure above 80 mm Hg.

### 3.7 **Positioning of Patient**

The positioning of the patient for the study period was dictated by the position required for surgery. In each study the position remained the same throughout. In those studies investigating the effects of lignocaine and diamorphine on the SEP, all patients were undergoing posterior fusion surgery and patients were placed prone on a Montreal mattress immediately after intubation. The electrode and lumbar epidural injection were inserted with the patient in this position.

In the bupivacaine experiment, most of the patients were undergoing surgery using the anterior approach. Therefore, they were placed in the left lateral position after intubation. Insertion of the epidural electrode and the lumbar epidural injection of local analgesic were performed with the patient in this position. The patients remained on their left side for the subsequent 50 min SEP recording period.

Finally, in the study investigating the effects of etidocaine, the patients were anaesthetised supine. Epidural electrode and lumbar epidural cannula placement were performed with the patient in the left lateral position. As the gynaecological surgery was to be performed with the patient in the supine position, this was adopted for the SEP investigation period.

### 3.8 **Description of the Traces**

A typical trace is shown in Fig. 3.1. Approximately 15 ms after stimulus administration (shown by an initial stimulus artifact) there is the appearance of the first downward deflection (described as a positive wave). Thereafter, there are three major negative peaks (or upward deflections) which occur at time intervals of approximately 15, 17 and 19 msec after stimulus administration. In their study on 115 scoliosis patients, Jones *et al.* (1983) showed that the overall amplitude of the response (i.e. the height from the highest peak to the lowest trough) ranged between 0.3 and 7 microvolts with a mean of

2.4 microvolt. Provided the electrode position was undisturbed, the waveform remained fairly constant within the individual during surgery. In my studies on adolescent scoliosis patients, the SEP amplitudes obtained are similar to those of Jones. However, in the gynaecological patients, the amplitude was smaller.

There is no definite agreement about the origin of the three negative peaks seen in the extradural SEP. However, it is believed at the present time that the short latency potentials are thought to represent post-synaptic conduction in the spino-cerebellar tract, while the asynaptic dorsal column fibres conduct more slowly and are responsible for the later potentials (Jones *et al.* 1982).

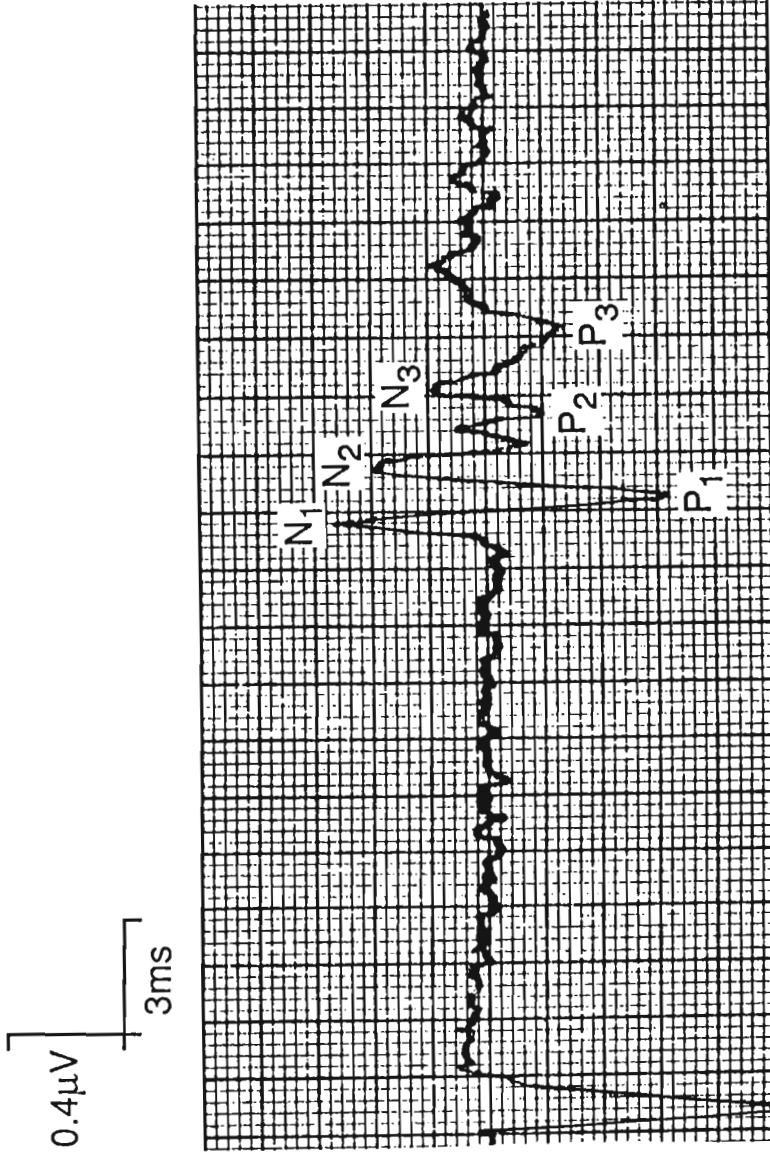
Although it is possible to obtain recordings of responses evoked by lower limb stimulation by a less invasive method, for example percutaneously over the vertebrae prominens, these are technically more difficult to obtain than extradural recordings. The impedance is high, there is more baseline drift and several thousand responses need to be averaged. More importantly, the waveform does not have the triphasic configuration of the extradural potential and is not considered to be representative of spinal cord conduction (Jones and Small, 1978).

### 3.9 **Statistical Analysis**

The amplitudes measured in addition to the overall amplitude were the first peak amplitude ( $P_1N_1$  in Fig. 3.1), the second peak amplitude ( $P_2N_2$  in Fig. 3.1) and the third peak amplitude ( $P_3N_3$  in Fig. 3.1). The latency, from stimulus to the onset of the first positivity, was also noted.

The above-mentioned data were recorded and found not to conform to a normal distribution. Therefore the results are described and analysed using nonparametric methods. Thus the amplitudes and latencies are presented as median values with ranges. Within-group differences were analysed using the Friedman two-way analysis of variance. Comparison between groups was undertaken with Wilcoxon's rank sum test (Petrie 1987, Siegal, 1956). Mean arterial pressure between groups was compared using Student's unpaired t-test (Armitage and Berry, 1987).

**FIGURE 3.1**



A trace typical of that obtained. Measurements made are overall amplitude, first, second and third peak amplitude.



**TABLE 3.1****SUMMARY OF STUDIES**

AIM		Number/Sex	Age (yr)
Chapter 4	Effect of epidural lignocaine on the epidural SEP	21F, 3M	18.1 (4.1)
Chapter 5	Effect of epidural diamorphine on the epidural SEP	11F, 5M	20.4 (5.3)
Chapter 6	Effect of epidural etidocaine on the epidural SEP	16F	43.6 (5.6)
Chapter 7	Effect of epidural 0.25%, 0.5% and 0.75% bupivacaine on the epidural SEP	27F, 5M	16.5 (3.2)
COMPLEMENTARY EARLY STUDIES	Effect of halothane on the epidural SEP (Loughnan <i>et al.</i> 1989a)	11F, 1M	17.2 (6.8)
	Effect of halothane on the motor evoked potential (Loughnan <i>et al.</i> 1989b)	10F, 6M	16.9 (2.5)

**CHAPTER IV**  
**EFFECT OF LIGNOCAINE ON THE EPIDURAL SEP**

**4.1 Introduction**

This study assesses the changes in the epidural SEP associated with epidural lignocaine administration. Two control groups were used: one with no epidural injection and a second with an epidural injection of 0.9% sodium chloride. The purpose of the saline control was to establish if any changes observed with lignocaine were due to the local anaesthetic agent itself, or to instillation of fluid into the epidural space.

Lignocaine was chosen for this study because it is an agent in common use and is the local anaesthetic agent with which all others are compared (Arthur, Wildsmith, & Tucker 1987). Although the effect of lignocaine on the SEP could have been assessed either pre- or postoperatively, preoperative experimentation allows standardisation of the anaesthetic and early surgical postoperative assessment.

The onset of action of lignocaine is described by both Reynolds (1984) and Atkinson *et al.* (1987) as 'rapid'. The duration of action of the 1% solution is stated to be one hour (Atkinson *et al.* 1987) and is described by Covino in Nunn, Utting, & Brown (1989) as 'moderate'. In this study I assumed that any effect on the SEP would have worn off after about one hour. If my experiment showed significant attenuation of the SEP after lignocaine, then these changes should have worn off sufficiently to allow the SEP to be used during surgery.

**4.2 Methods**

This study followed the general pattern outlined in the previous chapter. The twenty-four patients studied were all adolescent idiopathic scoliosis patients in whom it was considered essential to insert an electrode for intraoperative monitoring of the epidural SEP. After induction of anaesthesia, tracheal intubation was undertaken and the patient placed prone on a Montreal mattress. After insertion of the epidural recording electrode, the subjects were randomly assigned to receive either lignocaine 2% 10 ml injected into

the L<sub>2-3</sub> epidural space, 0.9% sodium chloride 10 ml in the same epidural space, or no epidural injection. Thus, the study consisted of an experimental lignocaine group and two control groups (one receiving an epidural injection of 0.9% sodium chloride and the other receiving no injection). Anaesthesia was maintained throughout the fifty-minute investigation period with nitrous oxide 67% in oxygen, plus a three-stage propofol infusion.

After completion of the fifty minutes of SEP recordings, patients were taken into theatre and surgery performed. The recording electrode was used for routine intraoperative monitoring of the spinal cord.

Statistical analysis of the data was undertaken as described in Chapter III.

## 4.3 **Results**

### 4.3.1 **Patient Characteristics**

Mean (SD) age and body weight were similar in the three groups: extradural lignocaine 18.5 (4.4) yr and 52.7 (4.0) kg; extradural saline 16.7 (3.2) yr and 51.3 (10.5) kg and control 18.4 (4.2) yr and 54.8 (7.9) kg.

### 4.3.2 **SEP - Within Group Differences**

There were no statistically significant within-group changes in either of the control groups for any of the peak amplitudes, or for the overall amplitude.

A decrease in overall amplitude was found after lignocaine administration. Figure 4.1 shows a typical trace. Although there was a decline in overall amplitude, the most obvious change was seen in the second and third peak amplitudes.

Table 4.1 is a summary of the  $\chi^2$  results obtained for the lignocaine group using the Friedman two-way analysis of variance for the within-group analysis. There was a significant decrease in both overall and third peak amplitude for both legs. There was a significant fall in first and second peak amplitudes, in the left leg only.

First peak latency increased significantly throughout the study in all three groups and for both limbs ( $p < 0.0001$ ).

### 4.3.3 SEP - Between Group Differences

#### 4.3.3.1 Effects of Saline

There was no significant difference between the epidural saline and control group for any of the neurophysiological variables. For the sake of clarity, therefore, data are presented only for the extradural lignocaine and saline groups.

#### 4.3.3.2 Effects of lignocaine

Although overall amplitude decreased after administration of lignocaine, the difference between groups was significant only for the left leg at 50 min ( $p < 0.05$ ) only (Table 4.2). There was no significant difference between the groups in first peak amplitude (Table 4.3).

Epidural lignocaine resulted in a significant decrease in second peak amplitude compared with epidural saline in the left leg only ( $p < 0.01$ ) at 40 and 50 min (Table 4.4).

A similar pattern of change was seen for the third peak amplitude (Table 4.5). There was a significant difference between the groups at 30, 40 and 50 min for the left leg ( $p < 0.01$ ) only.

There was no significant difference in latency between the groups (Table 4.6).

### 4.3.4 Arterial pressure

Mean arterial pressure decreased similarly in all three groups (Table 4.7). During the period of measurement of the SEP, mean arterial pressure was between 76 and 79 mm Hg in the extradural lignocaine group and between 80 and 83 mm Hg in the extradural saline group. There was no significant difference between the groups.

#### 4.4 Discussion

The major finding of this study was that administration of 2% lignocaine 10 ml into the lumbar epidural space resulted in a decrease in the SEP recorded in the cervical extradural space. The L<sub>2-3</sub> site was chosen so that the maximal effect on the posterior tibial nerve could be studied.

Although overall amplitude decreased, the most prominent feature was a decrease in the amplitude of the second and third peaks, with relatively little effect on the first peak amplitude. The first peak of the SEP represents conduction in the anterolateral tracts at 65-80 m s<sup>-1</sup>, while the later two peaks represent slower transmission in the dorsal columns (Jones *et al.* 1982). The results suggest that extradural lignocaine depressed conduction in the dorsal column selectively. This is surprising, as dorsal column transmission is largely asynaptic, whereas the first peak, which was minimally unaffected, involves some synaptic transmission. It is possible that the apparent selectivity of lignocaine for the dorsal column reflected a direct effect of the drug on superficial sites in the spinal cord. It is noteworthy that 2% lignocaine did not completely abolish the SEP in any patient indicating that afferent sensory transmission was preserved, even when sufficient lignocaine was given to achieve good clinical analgesia.

In the present study, we observed a similar increase in latency in all three groups, which was related possibly to the slow cooling of the spinal cord (Nuwer 1986). Saugbjerg *et al.* (1986), in similar experiments, studied the effect of epidural 0.5% bupivacaine on the scalp-recorded SEP to posterior tibial nerve stimulation and found increased latency of the first peak. However, they studied only six patients and did not include a control group. Thus, changes in the latency of the SEP cannot be ascribed to the actions of a local analgesic in the absence of a control group. The latency changes found in the present study were unlikely to be of any pharmacological significance, as they were similar in all groups.

A greater effect of lignocaine on the second and third peak amplitudes was observed after stimulation of the left leg than after stimulation of the right leg (see Tables 4.1, 4.3 and 4.4). This laterality of effect was noted in a previous study examining the action of halothane on the SEP (Loughnan *et al.* 1989a). A similar phenomenon has been

described during monitoring of scoliosis surgery (Shukla *et al.* 1987). It is likely that this finding reflects the surgical model studied, idiopathic adolescent scoliosis, in which the spinal curve is almost invariably concave to the left. The possible occurrence of this laterality in scoliosis patients is missed if only one leg is stimulated or both legs stimulated concurrently (Pathak *et al.* 1984).

The inherent variability of the electrophysiological signal must be considered before any clinical significance is attributed to the change in the SEP during scoliosis surgery. Overall amplitude varies randomly by 10-30% (Jones, Howard, & Shawkat 1988). However, in terms of intraoperative management, a decrease of 50% or more in overall amplitude is considered clinically important. This was observed in the SEP of three patients who received epidural lignocaine.

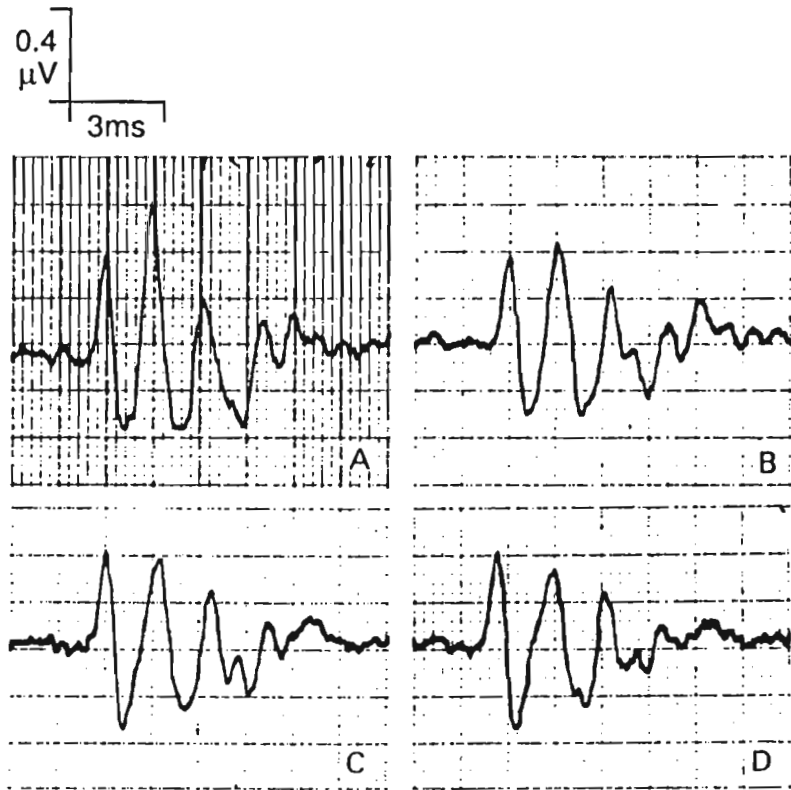
For epidural lignocaine to be used in patients undergoing scoliosis surgery, the technique must not interfere with the intraoperative monitoring of the SEP. The peaks were always present after lignocaine, but in three patients the overall amplitude was decreased by more than 50%. It is probable that this represents the maximal effect of extradural lignocaine 200 mg on the SEP to posterior tibial nerve stimulation, and that lignocaine may have less effect at smaller concentrations and other sites such as the mid-thoracic region.

#### 4.5 Conclusions

- a. Lignocaine 2% 10 ml injected into the L<sub>2-3</sub> epidural space was associated with a significant decrease in overall amplitude and first, second and third peak amplitudes of the SEP.
- b. No significant difference in first peak amplitude was found between patients who received epidural 10 ml 2% lignocaine or 10 ml 0.9% sodium chloride.
- c. There was no effect on the SEP of an epidural injection of sodium chloride 0.9% 10 ml compared with a further control group in whom no epidural solution was injected. Therefore, in future studies, a control with no extradural injection can be used.

- d. Lignocaine 2% 10 ml cannot be recommended for lumbar epidural injection during scoliosis surgery because it caused a decrease in overall amplitude of more than 50% in three out of eight patients.

**FIGURE 4.1**



Effect of 2% lignocaine 10 ml on the SEP recorded in the cervical epidural space

- A baseline;
- B 30 min after lignocaine;
- C 40 min after lignocaine
- D 50 min after lignocaine.



**TABLE 4.1**

	Lignocaine		Saline	
	$\chi^2$	P	$\chi^2$	P
<u>Overall</u>				
Left leg	7.65	0.05	3.35	0.34
Right leg	11.65	0.009	0.75	0.86
<u>Peak 1</u>				
Left leg	8.92	0.03	2.73	0.44
Right leg	1.95	0.58	2.71	0.44
<u>Peak 2</u>				
Left leg	14.50	0.002	1.33	0.72
Right leg	4.98	0.17	2.49	0.48
<u>Peak 3</u>				
Left leg	10.75	0.01	7.10	0.07
Right leg	8.09	0.04	8.72	0.03

Results for within-group analysis of overall amplitude and first, second and third peak amplitudes using Friedman two-way analysis of variance in patients who received lignocaine 2% 10 ml into the L<sub>2-3</sub> epidural space.

**TABLE 4.2**

Time (min)	Left leg		Right leg	
	Lignocaine (n=8)	Saline (n=8)	Lignocaine (n=8)	Saline (n=8)
0	0.86 (0.63-2.37)	0.97 (0.65-3.05)	1.01 (0.67-1.17)	1.57 (0.36-2.00)
30	0.76 (0.57-2.23)	1.13 (0.79-2.88)	0.72 (0.38-0.91)	1.54 (0.36-2.32)
40	0.66 (0.55-2.13)	1.17 (0.81-2.87)	0.74 (0.24-0.94)	1.53 (0.34-2.33)
50	0.67 * (0.52-2.03)	1.12 (0.80-2.68)	0.69 (0.24-0.91)	1.53 (0.35-2.55)

Median (range) overall amplitude of SEP ( $\mu$ V) in patients receiving either extradural 2% lignocaine or extradural saline. Significant difference between the groups: \*  $p < 0.05$ .

**TABLE 4.3**

Time (min)	Left leg		Right leg	
	Lignocaine (n=8)	Saline (n=8)	Lignocaine (n=8)	Saline (n=8)
0	0.96 (0.71-2.07)	0.90 (0.54-2.22)	0.96 (0.47-1.09)	1.03 (0.30-1.98)
30	0.76 (0.55-2.23)	1.12 (0.73-2.25)	0.75 (0.49-1.07)	1.10 (0.30-2.25)
40	0.66 (0.55-2.13)	1.16 (0.73-2.25)	0.73 (0.35-0.94)	1.07 (0.31-2.28)
50	0.67 (0.52-2.03)	1.09 (0.75-2.12)	0.68 (0.24-0.87)	1.08 (0.30-2.13)

Median (range) first peak amplitude of SEP ( $\mu$ V) in patients receiving either extradural 2% lignocaine or extradural saline. No significant difference between the groups.

**TABLE 4.4**

Time (min)	Left leg		Right leg	
	Lignocaine (n=8)	Saline (n=8)	Lignocaine (n=8)	Saline (n=8)
0	0.55 (0.40-2.22)	0.78 (0.61-2.82)	0.84 (0.40-0.85)	0.79 (0.19-1.43)
30	0.41 (0.09-1.48)	0.81 (0.68-2.47)	0.48 (0.10-0.96)	1.00 (0.17-1.30)
40	0.41 ** (0.09-0.83)	0.75 (0.63-2.43)	0.51 (0.12-0.86)	1.15 (0.19-1.19)
50	0.30 ** (0.13-0.93)	0.75 (0.68-2.37)	0.51 (0.12-0.91)	1.10 (0.16-1.20)

Median (range) second peak amplitude of SEP ( $\mu$ V) in patients receiving either extradural 2% lignocaine or extradural saline. Significant difference between the groups: \*\*  $p < 0.01$

**TABLE 4.5**

Time (min)	Left leg		Right leg	
	Lignocaine (n=8)	Saline (n=8)	Lignocaine (n=8)	Saline (n=8)
0	0.63 (0.22-0.98)	0.66 (0.34-1.31)	0.62 (0.29-0.83)	0.93 (0.24-1.67)
30	0.40 ** (0.25-0.53)	0.71 (0.40-1.43)	0.41 (0.21-0.61)	0.89 (0.25-1.67)
40	0.36 ** (0.21-0.52)	0.67 (0.43-1.45)	0.39 (0.23-0.70)	0.89 (0.25-1.34)
50	0.38 ** (0.23-0.48)	0.67 (0.41-1.47)	0.36 (0.11-0.65)	0.79 (0.23-1.37)

Median (range) third peak amplitude of SEP ( $\mu\text{V}$ ) in patients receiving either extradural 2% lignocaine or extradural saline. Significant difference between the groups: \*\* P < 0.01

**TABLE 4.6**

Time (min)	Left leg		Right leg	
	Lignocaine (n=8)	Saline (n=8)	Lignocaine (n=8)	Saline (n=8)
0	14.5 (12.9-15.5)	15.0 (14.0-16.0)	14.5 (13.6-15.2)	15.2 (14.2-16.6)
30	15.2 (13.8-16.4)	15.7 (14.3-16.4)	15.4 (14.2-16.0)	15.6 (14.4-16.8)
40	15.5 (14.4-16.9)	15.7 (14.3-16.4)	15.8 (14.6-16.3)	15.7 (14.5-16.8)
50	15.6 (14.4-17.0)	15.8 (14.4-16.4)	16.1 (14.8-16.7)	15.8 (14.5-16.8)

Median (range) latency (ms) in patients receiving either extradural 2% lignocaine or extradural saline. No significant difference between the groups during the study.

**TABLE 4.7**

Time (min)	Lignocaine (n=8)	Saline (n=8)	Control (n=8)
0	98 (13.5)	96 (13.6)	100 (8.4)
30	78 (8.8)	81 (10.0)	80 (5.1)
40	76 (11.0)	81 (12.2)	80 (5.8)
50	77 (11.0)	81 (13.7)	81 (4.9)

Mean arterial pressure mm Hg. There was no significant difference between the groups.

## CHAPTER V

### EFFECT OF DIAMORPHINE ON THE EPIDURAL SEP

#### 5.1 Introduction

The aim of the next study was to evaluate the effect of a lumbar extradural injection of diamorphine on the extradural SEP. In Chapter 4, it was demonstrated that lignocaine 2% may interfere with the SEP monitoring for scoliosis surgery and caution was advised with regard to the use of this agent.

Alleviation of severe postoperative pain remains an essential component of anaesthesia for scoliosis surgery and this could be provided by extradural opioids. A previous study (Lund *et al.* 1987b) showed that there was a minimal effect of epidural morphine on the scalp-recorded SEP.

I chose diamorphine for this study because it has a rapid onset of action with earlier peak serum levels than other extradural opiates (Morgan 1989). Furthermore, it is considered to be a better analgesic than morphine (Barron & Strong 1981). Although delayed respiratory depression has been observed after epidural diamorphine administration, it is more common after epidural morphine (Morgan 1987). For these reasons, the epidural opiate of choice for scoliosis surgery is probably diamorphine. Therefore, I decided to assess the effects of a lumbar epidural injection of diamorphine  $0.1 \text{ mg kg}^{-1}$  on the SEP recorded from the cervical epidural space.

#### 5.2 Methods

For this study the methodology as outlined in Chapter III was used. All patients suffered from adolescent idiopathic scoliosis and required intraoperative monitoring of their spinal cord conduction by the use of the epidural SEP. After induction of anaesthesia, the trachea was intubated and the patients placed prone on a Montreal mattress. The epidural recording electrode was inserted using a "hanging-drop" technique, after which the subjects were randomly assigned to receive either diamorphine  $0.1 \text{ mg kg}^{-1}$  injected into the L<sub>2-3</sub> epidural space (a solution of  $1 \text{ mg ml}^{-1}$  dissolved in 0.9% sodium chloride) or no epidural injection. Throughout the 50-minute investigation period, anaesthesia was maintained with nitrous oxide 67% in oxygen plus the three-stage propofol infusion



designed to give stable propofol levels between 30 and 50 min after commencement of infusion.

After completion of the 50 min of SEP recordings, patients were taken into theatre and the corrective surgery performed. The recording electrode was used for routine intraoperative monitoring of the spinal cord.

Statistical analysis of the data was undertaken as described in Chapter III.

## 5.3 Results

### 5.3.1 Patient Characteristics

Mean (SD) age and body weight were similar in the two groups: diamorphine 21.2 (1.9) yr and 59.2 (13.1) kg; control 19.8 (1.8) yr and 55.9 (7.3) kg.

### 5.3.2 SEP - Within-Group Analysis

Table 5.1 summarises the analysis undertaken using the Friedman analysis of variance to assess the changes within each group. The  $\chi^2$  and relevant P values are tabulated for overall and individual peak amplitudes. There were no significant within-group differences for any of the amplitude variables except for peak 2 in the right leg ( $p < 0.01$ ) at 40 min.

### 5.3.3 SEP - Between-Group Analysis

The overall amplitude of the epidural SEP for the two groups is shown in Table 5.2. There was no significant difference between the groups in terms of overall amplitude or of first, second or third peak amplitude as shown in Tables 5.3, 5.4, and 5.5.

The first peak latency of the SEP for the two groups is shown in table 5.6. Although latency increased during the study in both groups, there was no significant difference between the groups.

### 5.3.4 Arterial Pressure

Mean arterial pressure decreased from 94 mm Hg to 75 mm Hg in the diamorphine group and from 81 to 75 mm Hg in the control group (see Table

5.7). Mean arterial pressure was significantly lower in the control group than in the diamorphine group at time zero ( $t = 2.20$ ,  $P < 0.05$ ), but there was no significant difference between the two groups at any other time.

#### 5.4 Discussion

I have shown that the administration of diamorphine  $0.1 \text{ mg kg}^{-1}$  does not produce a significant change in the cervical epidural SEP to posterior tibial nerve stimulation. In the only similar study to date, Lund and colleagues (1987b) found that the cortically recorded SEP to electrical stimulation of the  $L_1$  and  $S_1$  dermatomes was unaltered by the lumbar epidural administration of morphine 6 mg. Although this study did not have a control group and utilised stimulation of dermatomes rather than a mixed peripheral nerve (such as the posterior tibial nerve), our findings are similar. The use of an epidural recording electrode in the assessment of afferent neuronal conduction is an improvement on the methodology of Lund *et al.* (1987b). A small increase in latency was observed in Lund's study but, since both control and experimental groups showed a similar increase in this and other studies (Loughnan *et al.* 1989a, Loughnan, Murdoch, Hetreed, Howard & Hall 1990), the latency changes are unlikely to be of pharmacological importance.

The failure of epidural diamorphine to decrease the SEP may be multifactorial. Firstly, the SEP recorded in the cervical epidural space is considered to represent afferent transmission in the anterolateral tracts (first peak) and dorsal columns (second and third peaks) and may not assess completely afferent neuronal activity (Jones *et al.* 1982). Secondly, there may be insufficient diamorphine reaching the opiate receptors in the dorsal horn after passage through the dura. It has been shown in an animal model by Homma, Collins, Kitahata, Matsumoto, & Kawahara (1983) that the direct application to the cord of morphine 0.1 mg is necessary to suppress neuronal activity in the dorsal cord. Thus, the inability to demonstrate an effect of diamorphine on the SEP could be a simple dose-related phenomenon. Thirdly, it is probable that some noxious afferent activity arising after stimulation of the posterior tibial nerve bypasses the opiate receptors in the superficial laminae (1 and 2) of the dorsal horn in the cord (Dickenson 1990). Although C fibres terminate mainly in lamina 2, A- $\delta$  fibres terminate in lamina 1 and 5 so that rostral transmission can still occur in A- $\delta$  fibres after the use of epidural opiates.

A small proportion of C-fibres enter the cord via the ventral horn and also synapse in lamina 5. Fourthly, stimulation of the posterior tibial nerve activates not only the A- $\delta$  and C fibres but also the non-nociceptive fibres. This "contamination" with non-nociceptive afferents is a common problem in all studies in which pain is assessed by evoked potentials (Chudler & Dong 1983), and may contribute to the maintenance of the SEP after diamorphine.

I have shown that diamorphine has a minimal effect on the epidural SEP and may be suitable for scoliosis surgery. However, the possible depressant effects of an epidural opiate on the respiratory system merit consideration. Therefore, diamorphine should only be given when respiratory monitoring can be undertaken and caution should be exercised in any patient with pre-existing ventilatory impairment. In such patients, a low concentration of opiate is prudent, perhaps supplemented with a local analgesic agent.

## 5.5 **Conclusions**

- a. Lumbar epidural diamorphine 0.1 mg kg<sup>-1</sup> administered in the L<sub>2,3</sub> interspace had no significant effect on the cervical epidural SEP evoked in response to posterior tibial nerve stimulation.
- b. Epidural opioids can be recommended for use in scoliosis surgery as they have minimal effects on the intraoperative monitoring of spinal cord function.
- c. The possible depressant effects of epidural diamorphine on respiratory function in ventilatory-impaired patients may be a limiting factor for its use in scoliosis surgery.

**TABLE 5.1**

	Diamorphine		Control	
	$\chi$	P	$\chi^2$	P
<u>Overall</u> Left leg Right leg	4.40 0.66	0.22 0.88	6.72 3.31	0.08 0.35
<u>Peak 1</u> Left leg Right leg	5.15 2.23	0.16 0.53	2.42 3.62	0.49 0.31
<u>Peak 2</u> Left leg Right leg	6.35 12.19 **	0.10 0.01	1.73 0.45	0.63 0.93
<u>Peak 3</u> Left leg Right leg	1.39 1.05	0.71 0.78	3.20 0.45	0.36 0.93

Within group analysis of changes using Friedman two-way analysis of variance.

There were no significant within-group differences for any of the amplitude variables except for peak 2 in the right leg \*\* (p < 0.01)

**TABLE 5.2**

Time (min)	Left Leg		Right Leg	
	Diamorphine n=8	Control n=8	Diamorphine n=8	Control n=8
0	1.32 (0.51-1.95)	1.14 (0.71-2.78)	1.90 (0.95-2.58)	1.48 (0.63-1.81)
30	1.36 (0.64-2.06)	1.18 (0.69-2.65)	1.92 (0.92-2.67)	1.43 (0.66-2.09)
40	1.24 (0.63-2.16)	1.16 (0.68-2.61)	1.81 (0.88-2.75)	1.48 (0.63-2.10)
50	1.24 (0.67-2.09)	1.16 (0.64-2.57)	1.75 (0.89-2.70)	1.44 (0.65-2.09)

Median (range) of overall amplitude of SEP ( $\mu\text{V}$ ) in the epidural diamorphine and control groups. There was no significant difference between the groups in the study.

**TABLE 5.3**

Time (min)	Left Leg		Right Leg	
	Diamorphine n=8	Control n=8	Diamorphine n=8	Control n=8
0	1.19 (0.55-1.85)	0.94 (0.39-2.13)	1.79 (0.97-2.58)	1.11 (0.62-1.65)
30	1.19 (0.64-2.06)	1.01 (0.41-2.47)	1.80 (0.92-2.67)	1.43 (0.62-1.93)
40	1.06 (0.63-2.14)	0.97 (0.36-2.40)	1.72 (0.88-2.75)	1.30 (0.61-1.95)
50	1.14 (0.67-2.09)	1.01 (0.36-1.73)	1.81 (0.89-2.70)	1.25 (0.64-1.91)

Median (range) of first peak amplitude of SEP ( $\mu\text{V}$ ) in the epidural diamorphine and control groups. There was no significant difference between the groups in the study.

**TABLE 5.4**

Time (min)	Left Leg		Right Leg	
	Diamorphine n=8	Control n=8	Diamorphine n=8	Control n=8
0	0.70 (0.27-1.95)	0.77 (0.39-2.37)	1.28 (0.69-2.32)	0.95 (0.35-1.81)
30	0.69 (0.23-1.70)	0.77 (0.38-2.23)	1.37 (0.54-1.93)	0.86 (0.39-2.09)
40	0.66 (0.23-1.53)	0.74 (0.46-1.15)	0.98 (0.52-1.90)	0.88 (0.36-2.10)
50	0.80 (0.24-1.35)	0.71 (0.49-2.17)	1.06 (0.53-2.01)	0.87 (0.35-2.06)

Median (range) of second peak amplitude of SEP ( $\mu\text{V}$ ) in the epidural diamorphine and control groups. There was no significant difference between the groups in the study.

**TABLE 5.5**

Time (min)	Left Leg		Right Leg	
	Diamorphine n=8	Control n=8	Diamorphine n=8	Control n=8
0	0.77 (0.16-1.48)	0.52 (0.34-0.89)	0.79 (0.27-1.51)	0.72 (0.24-1.09)
30	0.62 (0.23-1.37)	0.52 (0.31-0.81)	0.90 (0.22-1.65)	0.62 (0.26-1.38)
40	0.68 (0.23-1.39)	0.51 (0.32-0.76)	1.02 (0.25-1.54)	0.63 (0.24-1.45)
50	0.68 (0.25-1.25)	0.57 (0.28-0.81)	0.77 (0.18-1.57)	0.62 (0.30-1.24)

Median (range) of third peak amplitude of SEP ( $\mu\text{V}$ ) in the epidural diamorphine and control groups. There was no significant difference between the groups in the study.



**TABLE 5.6**

Time (min)	Left Leg		Right Leg	
	Diamorphine n=8	Control n=8	Diamorphine n=8	Control n=8
0	15.4 (15.0-19.9)	16.1 (14.0-16.9)	15.5 (14.4-20.1)	16.1 (14.9-17.8)
30	15.7 (15.1-20.0)	16.3 (14.3-16.9)	15.8 (14.4-20.3)	16.4 (15.1-16.8)
40	15.8 (14.4-20.1)	16.5 (14.5-19.3)	15.9 (13.6-20.3)	16.5 (15.3-19.3)
50	15.8 (14.8-20.0)	16.5 (14.6-19.5)	15.9 (14.1-20.3)	16.5 (16.3-19.4)

Median (range) latency (ms) in the epidural diamorphine and control groups. There was no significant difference between the groups in the study.

**TABLE 5.7**

Time (min)	Diamorphine	Control
0	94 * (11.4)	81 (12.0)
30	79 (9.2)	75 (15.0)
40	75 (7.4)	77 (10.3)
50	75 (6.5)	75 (15.0)

Mean arterial pressure mm Hg (SD). There was a significant difference between the two groups at time zero only. (\* P < 0.05). There was no difference between the groups at any other time point.

**CHAPTER VI**  
**EFFECT OF ETIDOCAINE ON THE EPIDURAL SEP**

**6.1 Introduction**

The previous experiments assessed the effects of lignocaine and diamorphine on the afferent response to posterior tibial nerve stimulation as measured by the somatosensory evoked potential (SEP) recorded from the cervical epidural space. The current study investigated the effect of a lumbar injection of etidocaine 1% on the SEP recorded from the extradural space.

Etidocaine is a local anaesthetic agent which is relatively long acting. Animal work by Cusick *et al.* (1980) suggested that etidocaine may provide a more complete suppression of the SEP than other local analgesics such as bupivacaine or chlorprocaine. The physicochemical properties of this agent are quite different from other local anaesthetic agents. In particular, etidocaine has a very high partition coefficient indicating a high lipid solubility. A study on the effects of etidocaine on spinal cord monitoring will not only delineate the place of this agent in anaesthesia for scoliosis surgery, but will also be of considerable predictive value for determining the likely effect of agents with high lipid solubility.

All the other studies were performed on patients suffering from adolescent idiopathic scoliosis. In the present study, I had the opportunity of studying "normal" patients and so determining whether the laterality of effect observed previously (Loughnan *et al.* 1989a) and Chapter IV, was the result of investigating a particular patient population.

**6.2 Methods and Materials**

Local ethical committee approval and approval of the Committee of Safety of Medicines was obtained for the study, which was performed on sixteen healthy gynaecological patients undergoing total abdominal hysterectomy for menorrhagia. All patients were ASA grades 1 or 2 patients, in whom the insertion of a lumbar epidural catheter for preoperative analgesia was an integral part of the anaesthetic technique. The nature of

the procedure was explained to each patient and informed verbal consent in the presence of a witness (the normal hospital research consent procedure) was gained for the insertion of an epidural electrode to measure the effects of the local analgesic on spinal cord conduction.

After induction of anaesthesia as described in Chapter III, patients were placed in the left lateral position and an epidural catheter inserted 2 cm into the L<sub>2,3</sub> epidural space. A 3 FG bipolar recording electrode (S-Pace Medical) was inserted in the epidural space at the C<sub>7</sub>-T<sub>1</sub> level. Patients were then placed supine, as for surgery, and SEP recordings obtained to alternate stimulation of each posterior tibial nerve, as in the previous experiments.

Baseline responses were obtained after stimulation of each leg. Thereafter, patients were randomly assigned to receive either 10 ml etidocaine 1% plain or 10 ml 0.9% sodium chloride solution via the epidural catheter. Anaesthesia was maintained via a 3-stage propofol infusion regimen. Somatosensory evoked potentials (SEP) to posterior tibial nerve stimulation of each limb were obtained at the same times after epidural injection as in the previous studies (0, 30, 40, and 50 min). Patients were then taken into theatre and surgery performed; the lumbar epidural catheter was "topped up" as deemed appropriate clinically with bupivacaine 0.5% plain. All patients were monitored using an automatic blood pressure recorder pulse oximetry, electrocardiogram, and end-tidal carbon dioxide measure (Capnomac, S & W Vickers). The recording electrode was removed at the end of surgery, just prior to reversal of neuromuscular blockade.

The overall amplitude of the evoked potential and the first, second and third peak amplitudes were measured (Fig. 6.1). If the amplitude had decreased to almost zero on the original scale, the gain was adjusted to maximum sensitivity, but allowance was made for this change in gain when the amplitude of the evoked potential was measured. First peak latency was also measured. The data are presented as median values and ranges and statistical analysis was undertaken as described in Chapter III.

## 6.3 Results

### 6.3.1 Patient Characteristics

Mean (SD) age and body weight were similar in both groups: 39.8 (4.0) yr and 66.7 (12.5) kg for the etidocaine group and 47.3 (6.5) yr and 60.5 (7.8) kg for the control group.

### 6.3.2 SEP - Within-Group Analysis

Figure 6.1 shows a typical trace for the etidocaine group. Overall and first peak amplitudes were unrecordable in two out of eight patients and a very small amplitude ( $< 0.10 \mu\text{V}$ ) was present in a further three patients who received etidocaine. In five of eight etidocaine patients, the second and third peak amplitudes were unmeasurable after fifty minutes. There were no significant changes in the control group patients. In one patient who received etidocaine a minimal effect was seen on the SEP.

Table 6.1 is a summary of the  $\chi^2$  results obtained for the etidocaine group, using the Friedman two-way analysis of variance for the within-group analysis. There was a significant decrease ( $p < 0.001$ ) for overall amplitude and first, second, and third peak amplitudes.

### 6.3.3 SEP - Between-Group Analysis

Tables 6.2 to 6.5 summarise the between-group comparisons for the etidocaine and control groups. There was a significant difference between the etidocaine and control groups for both right and left legs, for all amplitude measurements after 40 and 50 min. For the left leg, there was a significant difference in overall amplitude at 40 and 50 min. ( $p < 0.05$ ), with a significant difference for the right leg at 40 min. ( $p < 0.05$ ) and also at 50 min. ( $p < 0.01$ ).

For the first peak amplitude there was a significant difference between etidocaine and control groups for both legs ( $p < 0.05$ ) at 40 and 50 min. There was a significant difference in second peak amplitude ( $p < 0.05$ ) after 30, 40, and 50 min. for the left leg and a significant difference at 30 and 40 min. ( $p < 0.05$ ) and also at 50 min. ( $p < 0.01$ ) for the right leg, between etidocaine and control

groups. A significant difference was seen for third peak amplitude between the groups at 30 and 50 min. ( $p < 0.05$ ) and at 40 min. ( $p < 0.01$ ) for the left side and at 30, 40 and 50 min. for the right leg ( $p < 0.01$ ).

Although latency increased throughout the investigation period, there was no significant difference between the groups (Table 6.6). In two patients in the etidocaine group the trace was so indistinguishable from background noise that latency could not be determined.

#### 6.3.4 Arterial Pressure

Mean arterial pressure decreased from 94 mm Hg to 75 mm Hg in the etidocaine group and from 81 to 75 mm Hg in the control group (see Table 6.7). There was no significant difference in mean arterial pressure between the two groups at any time.

### 6.4 Discussion

I have shown that 10 ml of etidocaine 1% administered into the lumbar epidural space suppressed spinal cord conduction, as assessed by the SEP to posterior tibial nerve stimulation. This contrasts with lignocaine 2% (Chapter IV), which produced a decrease in overall and second and third peak amplitudes but was sparing of the first peak amplitude. Etidocaine, however, has a more depressant effect on first peak amplitude than lignocaine, inferring a greater effect on the fast conducting fibres in the spinocerebellar tract. This may be because the greater lipid solubility of etidocaine permits it to penetrate further into the spinal cord. This confirms primate work by Cusick *et al.* (1980), who showed that etidocaine profoundly suppressed spinal cord conduction as assessed by the SEP recorded from the thoracic epidural space in response to stimulation of the conus medullaris.

In most cases, suppression of the SEP was such that any remaining response was at the limits of sensitivity of the recording equipment. In one patient who received etidocaine, there was minimal depression of the SEP. However, in this patient there was a fall in arterial pressure with local anaesthetic administration and clinically, in the immediate postoperative period, there was satisfactory analgesia. This suggests that the epidural

catheter was correctly sited in the epidural space. This individual, however, showed a decrease in second and third peak amplitudes, suggesting that these peaks were more sensitive to local anaesthetic action. This minimal suppression of the SEP can only be explained as an individual variation. A similar variability of effect was seen in one patient who received lignocaine (Chapter IV).

Previously I have studied patients suffering from adolescent idiopathic scoliosis undergoing corrective surgery, and any decrease in the SEP has shown a tendency to laterality. It is likely that, in the previous studies, this apparent laterality may have been due, in part, to the group under study. The current study of a "normal" population did not show this laterality, suggesting that adolescent idiopathic scoliosis patients have abnormal patterns of spinal cord conduction, even in the absence of any observable neurological abnormality. Another difference between the current study group and previous patients was the decreased amplitude of the evoked potentials. Again, this may be due to abnormalities in the adolescent scoliosis group when compared with gynaecological patients.

The only similar study was that performed by Lund *et al.* (1991), in which the effects of lumbar epidural administration of etidocaine 1% 20 ml on the cortical SEP to stimulation of the T<sub>10</sub>, L<sub>1</sub> and S<sub>1</sub> dermatomes were compared with that of 1.5% etidocaine 20 ml by the same route. These authors used the scalp-recorded SEP, which is more difficult to interpret than the SEP recorded from the epidural space. Their major finding was that, although comparable analgesia was obtained in both groups, the SEP amplitude was decreased more (in fact, virtually suppressed) by the 1.5% etidocaine. The L<sub>1</sub> dermatomal SEP was obliterated in all ten patients in the 1.5% group and in six out of ten patients in the 1% group. Lund *et al.* (1991) found that etidocaine when injected into the lumbar epidural space caused a greater decrease in the SEP than an equivalent dose of bupivacaine. However, when the thoracic epidural space was injected with etidocaine 1.5% 9ml, Dahl *et al.* (1992) reported minimal suppression of the scalp recorded dermatomal SEP (L<sub>1</sub>, T<sub>10</sub> and T<sub>6</sub> levels). My study supports Lund's finding that, in some patients, the SEP may be abolished by the lumbar epidural injection of etidocaine.

Arterial pressure decreased in both groups in the study but was never below a mean of 70 mm Hg.

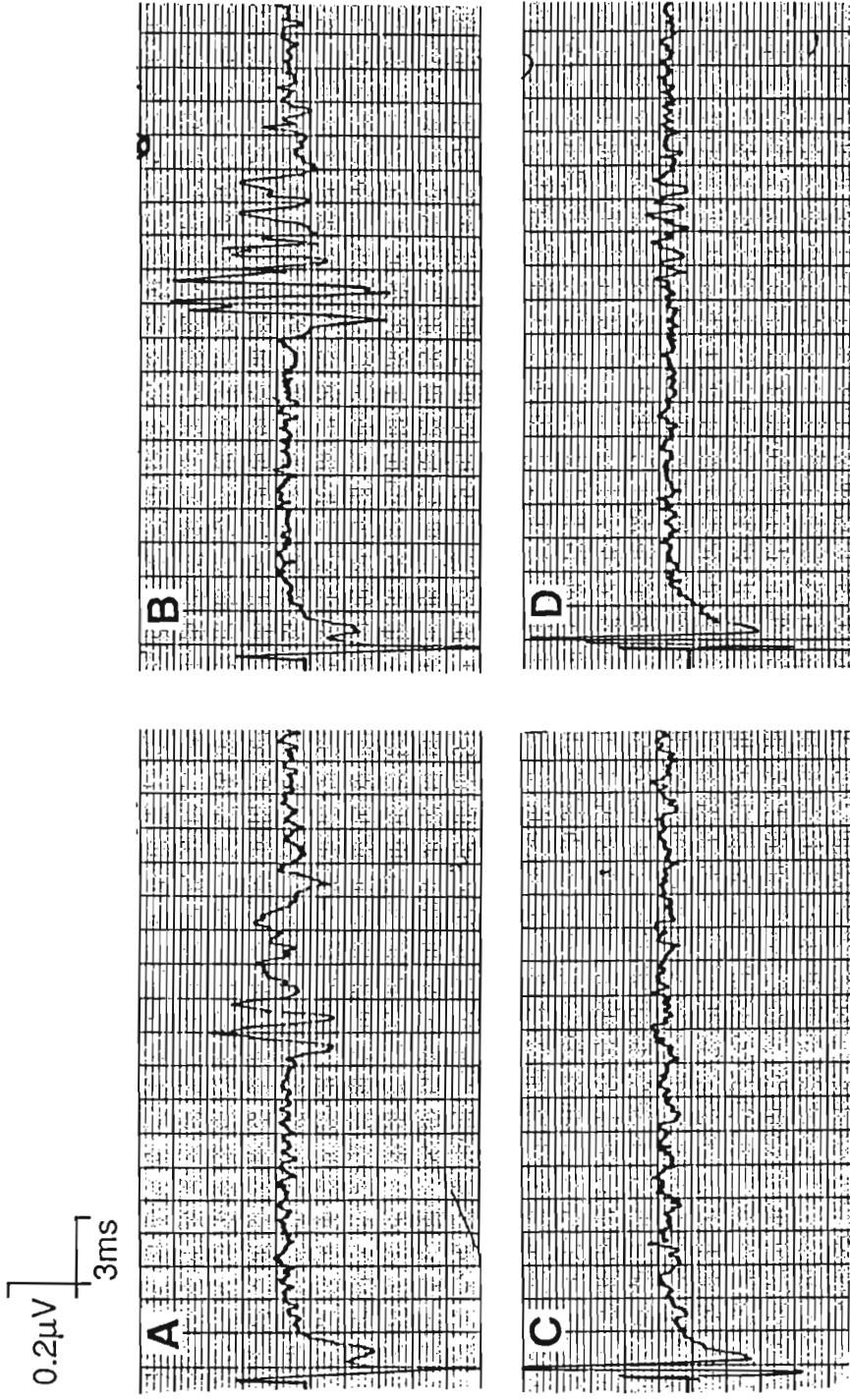
In summary, I have found that etidocaine 1% 10 ml, administered into the lumbar epidural space, is a potent suppressor of spinal cord conduction as assessed by the SEP to posterior tibial nerve stimulation. The suppression of the response was significant for all peaks of the evoked potential at 40 and 50 min. after epidural injection and was similar after stimulation of both legs.

## 6.5 **Conclusions**

- a) Etidocaine 1% 10 ml was associated with a decrease in overall amplitude and the amplitude of all peaks of the epidural SEP.
- b) The amplitude of the epidural SEP was smaller for routine gynaecological patients than for patients suffering from adolescent idiopathic scoliosis and suppression of the SEP was the same for stimulation of the left and right legs.
- c) Etidocaine 1%, and local anaesthetic agents of high lipid solubility, cannot be recommended for lumbar epidural injection during scoliosis surgery.



**FIGURE 6.1**



A typical trace obtained with epidural etidocaine. A and B show baseline SEP after stimulation of left and right legs. C and D show the SEP recorded 50 min. after etidocaine administration.

**TABLE 6.1**

	Etidocaine		Control	
	$\chi^2$	P	$\chi^2$	P
<u>Overall</u>				
Left leg	17.80	0.001	3.51	0.32
Right leg	19.03	0.001	0.38	0.94
<u>Peak 1</u>				
Left leg	18.12	0.001	5.00	0.17
Right leg	18.01	0.001	2.87	0.41
<u>Peak 2</u>				
Left leg	21.87	< 0.001	0.99	0.80
Right leg	25.28	< 0.001	2.81	0.42
<u>Peak 3</u>				
Left leg	19.89	0.001	0.43	0.93
Right leg	23.37	< 0.001	1.68	0.64

Within-group analysis of changes using Friedman two-way analysis of variance.

Significant difference within group receiving etidocaine 1% 10 ml in the L<sub>2-3</sub> epidural space.

**TABLE 6.2**

Time (min)	Left leg		Right leg	
	Etidocaine (n=8)	Control (n=8)	Etidocaine (n=8)	Control (n=8)
0	0.36 (0.17-1.21)	0.44 (0.21-0.61)	0.49 (0.15-0.79)	0.38 (0.19-1.21)
30	0.20 (0.07-0.53)	0.37 (0.16-0.94)	0.21 (0-0.51)	0.38 (0.15-1.67)
40	0.19 * (0-0.53)	0.38 (0.20-1.00)	0.17 * (0-0.50)	0.38 (0.15-1.55)
50	0.15 * (0-0.53)	0.39 (0.31-0.95)	0.09 ** (0-0.46)	0.38 (0.21-1.49)

Median (range) overall amplitude of SEP ( $\mu\text{V}$ ) in patients receiving epidural 1% etidocaine compared with a control group. Significant difference between groups: \*  $p < 0.05$ . \*\*  $p < 0.01$ .

**TABLE 6.3**

Time (min)	Left leg		Right leg	
	Etidocaine (n=8)	Control (n=8)	Etidocaine (n=8)	Control (n=8)
0	0.34 (0.17-1.21)	0.41 (0.19-0.55)	0.43 (0.15-0.79)	0.35 (0.17-1.20)
30	0.22 (0.57-2.23)	0.33 (0.79-2.88)	0.19 (0.38-0.91)	0.34 (0.36-2.32)
40	0.16 * (0-0.53)	0.34 (0.20-0.81)	0.11 * (0-0.50)	0.34 (0.14-1.23)
50	0.13 * (0-0.37)	0.36 (0.21-0.76)	0.10 * (0-0.46)	0.36 (0.14-1.30)

Median (range) first peak amplitude of SEP ( $\mu$ V) in patients receiving epidural 1% etidocaine compared with a control group. Significant difference between groups: \*  $p < 0.05$ .

**TABLE 6.4**

Time (min)	Left leg		Right leg	
	Etidocaine (n=8)	Control (n=8)	Etidocaine (n=8)	Control (n=8)
0	0.25 (0.12-0.63)	0.20 (0.10-0.46)	0.23 (0.13-0.65)	0.31 (0.11-0.65)
30	0.09 * (0-0.41)	0.19 (0.10-0.78)	0.11 * (0-0.17)	0.22 (0.07-1.09)
40	0.07 * (0-0.39)	0.18 (0.10-0.84)	0.08 * (0-0.16)	0.21 (0.06-1.09)
50	0.04 * (0-0.21)	0.16 (0.10-0.79)	0.07 ** (0-0.16)	0.21 (0.08-1.20)

Median (range) second peak amplitude of SEP ( $\mu\text{V}$ ) in patients receiving epidural 1% etidocaine when compared with a control group. Significant difference between groups: \*  $p < 0.05$ .

\*\*  $p < 0.01$ .

**TABLE 6.5**

Time (min)	Left leg		Right leg	
	Etidocaine (n=8)	Control (n=8)	Etidocaine (n=8)	Control (n=8)
0	0.22 (0.07-0.37)	0.19 (0.10-0.45)	0.22 (0.09-0.34)	0.22 (0.08-0.76)
30	0.07 * (0-0.32)	0.21 (0.10-0.69)	0.03 ** (0-0.13)	0.18 (0.07-1.11)
40	0.02 ** (0-0.31)	0.18 (0.08-0.73)	0.07 ** (0-0.13)	0.18 (0.03-1.03)
50	0 * (0-0.53)	0.20 (0.09-0.70)	0 ** (0-0.12)	0.20 (0.09-0.94)

Median (range) third peak amplitude of SEP ( $\mu\text{V}$ ) in patients receiving epidural 1% etidocaine compared with a control group. Significant difference between groups: \*  $p < 0.05$ . \*\*  $p < 0.01$ .

**TABLE 6.6**

Time (min)	Left leg		Right leg	
	Etidocaine (n=8)	Control (n=8)	Etidocaine (n=8)	Control (n=8)
0	16.0 (14.7-17.3)	16.0 (14.8-17.6)	15.9 (14.7-17.9)	15.9 (14.9-17.4)
30	16.4 (16.1-18.6)	16.4 (15.2-17.8)	16.5 (16.3-18.7)	16.1 (15.2-17.6)
40	16.7 (16.3-18.5)	16.4 (15.2-17.8)	16.7 (16.0-18.3)	16.3 (15.1-17.6)
50	16.9 (16.2-20.0)	16.5 (15.2-17.8)	17.0 (16.3-19.5)	16.3 (15.0-17.7)

Median (range) latency of SEP (ms) ( $\mu$ V) in patients receiving epidural 1% etidocaine compared with a control group. There were no significant differences between groups.

**TABLE 6.7**

Time (min)	Etidocaine	Control
0	9.5 (19.7)	97 (13.5)
30	78 (14.8)	72 (8.9)
40	79 (14.7)	75 (8.3)
50	74 (8.0)	78 (16.8)

Mean arterial pressure mm Hg (SD). There was no significant difference between the groups.



**CHAPTER VII**  
**EFFECT OF DIFFERING CONCENTRATIONS OF BUPIVACAINE**  
**ON THE EPIDURAL SEP**

**7.1 Introduction**

Previously, in Chapter IV, I have shown that lignocaine 2% 10 ml injected into the lumbar epidural space resulted in a decrease of 50% or more in the overall amplitude of the SEP in three of the eight patients studied. Therefore, it cannot be recommended for use in scoliosis surgery.

The relative potency of lignocaine:bupivacaine is 1:0.25 and thus the effects of lignocaine 2% and bupivacaine 0.5% should be similar. Because of its relatively long duration of action, bupivacaine is the agent most likely to find a place in scoliosis surgery. Before recommending the use of bupivacaine in scoliosis surgery, it is important to ascertain the effects of differing concentrations of bupivacaine on the SEP.

Using three differing concentrations of the bupivacaine enables a dose/concentration effect of a single agent to be studied, and the concentration most suitable for surgery to be determined. This may have a predictive value when the future use of alternative analgesic agents is considered. The present study, therefore, was undertaken to compare the effects of epidural bupivacaine 0.25%, 0.5%, and 0.75% on the SEP to posterior tibial nerve stimulation.

**7.2 Methods**

Thirty-two patients (twenty-seven female, five male), all suffering from adolescent idiopathic scoliosis were studied. The methodology outlined in Chapter III was used. Most of the patients in this study were undergoing anterior approach procedures, for which the patient was positioned in the left lateral position. Therefore, electrode insertion, lumbar epidural injection and subsequent SEP monitoring, was performed with the patient in the left lateral position.

Once the recording electrode was inserted, the patients were assigned randomly to receive either 0.25%, 0.5% or 0.75% bupivacaine 10 ml into the L<sub>2-3</sub> epidural space, or no epidural injection (control group). The SEP was monitored for a 50 min experimental period after the epidural injection/propofol infusion commencement. Following the investigation period, the patients were taken into theatre and the recording electrode used for routine intraoperative monitoring of the spinal cord.

In addition to the statistical tests outlined in Chapter III, the Kruskal-Wallis test, together with a multiple comparisons test as described by Conover (1980), was used to assess whether the change from baseline differed between concentrations of bupivacaine. The potentials were assessed for the changes in overall and peak amplitudes. The initial amplitude measurement was used as the baseline value, and the change from baseline to the 50 min value was calculated (the 50 min value was chosen to ensure the maximal effect of bupivacaine was seen). One calculation was made for each patient in the analysis; the leg with the greatest decrease was used and the amplitude of each peak and the overall amplitude was analysed.

### 7.3. **Results**

#### 7.3.1 Patient characteristics

Mean age (SD) and body weight were similar in the four groups: 0.75% bupivacaine 15.4 (1.6) yr and 51.6 (5.4) kg; 0.5% bupivacaine 16.8 (4.7) yr and 51.5 (9.0) kg; 0.25% bupivacaine 16.4 (3.5) yr and 53.6 (7.8) kg and control 17.4 (2.5) yr and 52.4 (9.5) kg.

#### 7.3.2 SEP - Within-Group Differences

The effects of 0.75% bupivacaine are shown in Fig. 7.1. The most obvious change is a decrease in overall amplitude together with a decrease in amplitude of the second and third peaks. Similar, but less marked, changes were found with the 0.5% group, while there were minimal changes associated with administration of 0.25% bupivacaine. No patient in either the 0.25% or the control group showed a decrease in amplitude that was clinically significant; however, such changes were seen in three of the eight patients in both the 0.5% and the 0.75% groups.

The within-group changes are summarised in Table 7.1. The relevant  $\chi^2$  and their resultant P values are shown. There was a significant difference for both legs and all neurophysiological variables for the 0.75% bupivacaine group. However, changes reached a higher degree of significance with the right than the left leg.

In the 0.5% bupivacaine group, there were significant decreases in overall amplitude ( $p < 0.01$ ) and peak 1 amplitude ( $p < 0.03$ ) for the right leg and peak 2 amplitude for the left leg ( $p < 0.03$ ). There was no significant change in the 0.25% bupivacaine group.

### 7.3.3 SEP - Description of Changes and Between-Group Differences

The median values together with the range for the overall amplitude, the first, second and third peak amplitude for all the thirty-two patients are shown in Tables 7.2, 7.3, 7.4 and 7.5 respectively. There were no significant differences between the 0.25% group and the control group for any of the neurophysiological variables. There was a significant difference in overall amplitude between 0.5% bupivacaine and control groups at 40 and 50 min and for the right leg only ( $p < 0.05$ ). There was no significant difference between any of the bupivacaine groups and the control group for peak 1 amplitude. For peak 2 amplitude, the only significant difference between the bupivacaine groups and control group was found at 40 and 50 min for 0.5% bupivacaine in the right leg ( $p < 0.05$ ). There was a significant difference between 0.75% group and control group at 40 and 50 min only ( $p < 0.05$ ) and between the 0.5% and control group at 30, 40 ( $p < 0.05$ ), and 50 min ( $p < 0.01$ ) for third peak amplitude. These differences were found for the right leg only. No difference was found between any of the experimental and control groups at any time point for the left leg.

Latency increased throughout the investigation period in all four groups (Table 7.6). There was, however, no difference seen between any of the bupivacaine groups and the control group at any time point.

#### 7.3.4 SEP - Effect of Concentration

There was a significant effect of concentration on overall amplitude and all three-peak amplitudes as indicated by the Kruskal-Wallis test (Table 7.7); the average rank decreased as the concentration increased for all the amplitude variables. The multiple comparisons as described by Conover (1980) is shown in Table 7.8. The average rank for the 0.25% group was not significantly different from the control group. The differences in average rank of the 0.5% and the 0.75% groups were significantly greater than the control group for all amplitudes except for peak 3 of the group receiving 0.5% bupivacaine (Table 7.8).

The changes in peak amplitude with increasing bupivacaine are summarised in diagrammatic form in Fig. 7.2. There was a decrease in amplitude with increasing bupivacaine concentrations and this was noted for all three peaks and for the overall amplitude.

#### 7.3.5 Arterial pressure

Mean arterial pressure decreased from 90 mm Hg to 75 mm Hg in the 0.75% bupivacaine group, from 75 to 647 mm Hg in the 0.5% group and from 77 to 67 mm Hg in the 0.25% bupivacaine group. It fell minimally in the control group (see Table 7.8). There was no significant difference between any of the bupivacaine groups and the control group at any time.

### 7.4 Discussion

I have shown a decrease in SEP amplitude recorded from the cervical epidural space in response to increasing concentrations of bupivacaine. No effect was found with 10 ml bupivacaine 0.25% but 10 ml of bupivacaine 0.5% and 0.75% decreased significantly the SEP.

The concentration comparison showed that, where a decrease occurred (regardless of side), there was a greater fall in SEP amplitude, with increasing concentration of local anaesthetic agent. Thus 0.25% bupivacaine had no effect on any of the amplitudes of the SEP, while 0.5% and 0.75% bupivacaine 10 ml had a progressively greater effect on these peaks. It is likely, therefore, that 10 ml bupivacaine 0.25% may be administered

into the lumbar epidural space without interfering with the SEP monitoring and so is suitable for scoliosis surgery. However, concentrations of 0.5% and greater are not appropriate for scoliosis surgery.

The changes seen with epidural administration of 10 ml bupivacaine 0.5% are similar to those found with 10 ml lignocaine 2% (Chapter IV). The results of the present study suggest that, in terms of their spinal cord action, bupivacaine and lignocaine are similar. Bupivacaine has a slightly more depressant effect on the faster-conducting post-synaptic pathways of the spinocerebellar tract than lignocaine (i.e. peak 1), but has similar effects on peaks 2 and 3, which are thought to represent activity in the dorsolateral tracts (Jones *et al.* 1983).

Saugjberg *et al.* (1986) studied the effects of a lumbar epidural injection of bupivacaine 0.5% 10 ml on the scalp-recorded SEP to posterior tibial nerve stimulation. Although they did not use a control group, they found that there was a decrease in P<sub>1</sub>N<sub>2</sub> amplitude, which is thought to represent dorsal column activity.

Other studies have used the scalp-recorded SEP to stimulation of the T<sub>10</sub>, L<sub>1</sub> and S<sub>1</sub> dermatomes. Criticisms of this mode of stimulation will be discussed in detail in Chapter VIII. However, Lund *et al.* (1987a) found that bupivacaine 0.5% 27 ml injected into the lumbar epidural space was associated with a decrease in the amplitude of all the three dermatomal peaks, but especially the L<sub>1</sub> dermatomal SEP. In a further study comparing the effects of 0.25% with 0.5% bupivacaine on the SEP to stimulation of the same dermatomes, Lund and colleagues (1989) found that, despite similar analgesia to pin-prick in the two groups, bupivacaine 0.25% exerted little effect on the SEP. Other studies by the same group measured the effects of thoracic epidural injection of 10 ml of bupivacaine 0.5% (Lund *et al.* 1987c) and 0.75% (Dahl *et al.* 1990) on the dermatomal scalp-recorded SEP. They found that bupivacaine 0.5% exerted minimal effect on the SEP, with 0.75% causing a significantly consistent effect on the T<sub>10</sub> SEP only, but nevertheless obliterating the T<sub>10</sub> and L<sub>1</sub> dermatomal SEP in some patients. Overall, these studies support the findings of the current study that the 0.75% solution is the most potent and the 0.25% bupivacaine least potent in suppressing the SEP.

Because of the laterality of effect demonstrated in previous studies performed on scoliosis patients (Loughnan *et al.* 1989a, Loughnan *et al.* 1990), in this study I used a statistical analysis which looked at the maximum effect on the SEP regardless of side; nevertheless, laterality was seen. The unusual finding was that the decrease was seen, not in the left leg but in the right leg. Posture has a mild but significant effect on the spread of epidural analgesia (Cousins 1980), with the dependent side having fewer unblocked segments and a more rapid onset of sympathetic blockade. Therefore, on this basis, the left leg should show a greater response to the local anaesthetic administration.

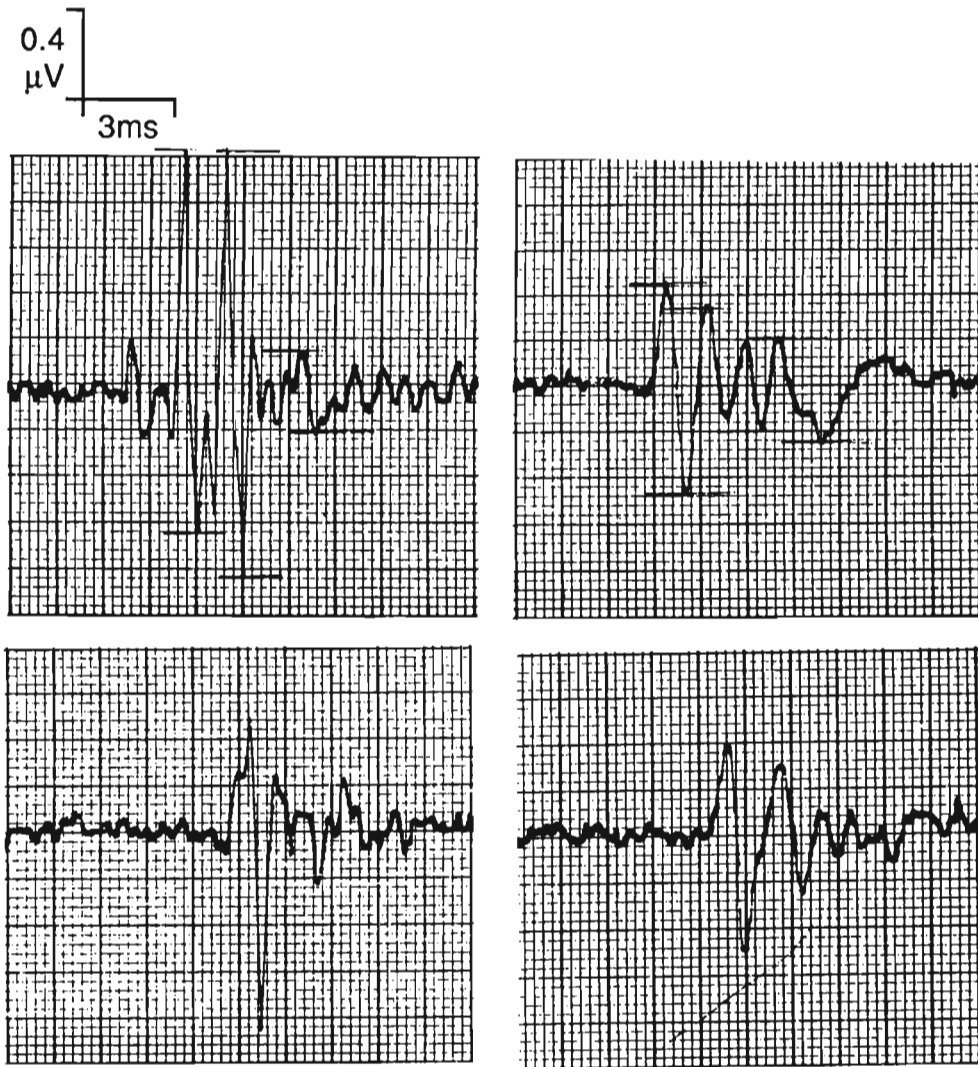
The finding of greater suppression of the right leg is difficult to account for if posture is invoked as a cause. A possible explanation is that the convex (right) side is placed under tension, thereby rendering this side more susceptible to any depressant pharmacological influences. Nevertheless, in the clinical situation, a significant decrease in amplitude is important, regardless of laterality.

In conclusion, because of the minimal effects of bupivacaine 0.25% on spinal cord monitoring, up to 10 ml of the 0.25% solution can be used in the lumbar epidural space as part of the anaesthetic technique for scoliosis surgery. However, both the 0.5% and 0.75% solutions were associated with clinically and statistically significant decreases in the SEP amplitudes and cannot, therefore, be recommended for scoliosis surgery.

## 7.5 Conclusions

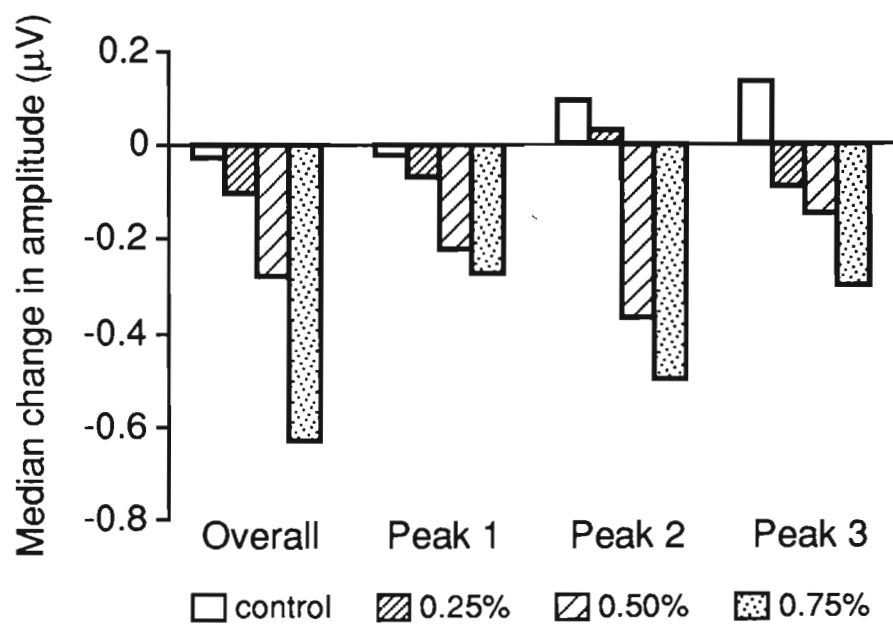
- a) Lumbar epidural bupivacaine 0.25% administered in the L<sub>2,3</sub> interspace has no significant effect on the SEP evoked in response to posterior tibial nerve stimulation measured in the cervical epidural space.
- b) Lumbar epidural bupivacaine 0.75% and 0.5% administered in the L<sub>2,3</sub> interspace were associated with both clinically and statistically significant decreases in SEP amplitude.
- c) Therefore, the 0.25% bupivacaine up to 10 ml can be used in scoliosis surgery, whereas the 0.5% and 0.75% solutions should not be used.

**FIGURE 7.1**



Typical traces obtained for epidural bupivacaine. The upper pair show baseline SEP after stimulation of right and left legs. The lower pair show the SEP recorded 50 min after 0.75% bupivacaine administration.

**FIGURE 7.2**



Median amplitude ( $\mu\text{V}$ ) changes for overall amplitude, peak 1, 2 and 3 amplitudes after the administration of differing concentrations of bupivacaine. The greatest decreases were seen with 0.5% and 0.75% bupivacaine and minimal changes found with administration of 0.25% bupivacaine.



**TABLE 7.1**

	0.75%		0.5%		0.25%		Control	
	$\chi^2$	P	$\chi^2$	P	$\chi^2$	P	$\chi^2$	P
<u>Overall</u>								
Left	10.06	0.02	5.96	0.11	2.70	0.44	4.98	0.17
Right	14.09	0.003	11.54	0.01	0.97	0.81	9.04	0.03
<u>Peak 1</u>								
Left	9.84	0.02	5.25	0.15	1.65	0.65	0.00	1.00
Right	14.39	0.002	9.35	0.03	3.12	0.37	4.19	0.24
<u>Peak 2</u>								
Left	11.12	0.01	9.15	0.03	1.96	0.58	1.42	0.70
Right	11.43	0.01	7.03	0.07	2.09	0.55	14.92	0.001
<u>Peak 3</u>								
Left	11.96	0.01	5.07	0.17	4.67	0.20	1.92	0.59
Right	22.95	<0.001	5.15	0.16	4.14	0.25	3.68	0.30

Results for within-group analysis of overall amplitude and first, second, and third peak amplitudes using Friedman's two-way analysis of variance in patients who received bupivacaine 0.25%, 0.5%, or 0.75% in the L<sub>2,3</sub> epidural space.

**TABLE 7.2**

Time (min)	LEFT SIDE					RIGHT SIDE				
	0.75%	0.5%	0.25%	Control	0.75%	0.5%	0.25%	Control		
0	0.80 (0.65-1.79)	1.51 (0.69-1.74)	0.76 (0.36-1.30)	0.71 (0.33-3.40)	1.13 (0.61-2.04)	0.82 (0.09-0.63)	0.86 (0.57-3.13)	0.86 (0.33-1.27)		
30	0.66 (0.53-1.71)	1.30 (0.34-2.07)	0.77 (0.27-1.30)	0.80 (0.34-3.52)	0.96 (0.40-1.75)	0.58 (0.35-0.89)	0.88 (0.35-3.12)	0.89 (0.37-1.35)		
40	0.65 (0.57-0.65)	1.15 (0.31-2.03)	0.76 (0.25-1.14)	0.78 (0.38-3.40)	0.93 (0.37-1.35)	0.66 * (0.30-0.90)	0.89 (0.38-3.23)	0.92 (0.48-1.34)		
50	0.60 (0.49-1.15)	0.95 (0.26-1.83)	0.74 (0.30-1.13)	0.77 (0.42-2.34)	0.72 (0.35-1.42)	0.59 * (0.27-0.94)	0.84 (0.33-3.38)	0.95 (0.57-1.42)		

Median (range) overall amplitude ( $\mu V$ ) for patients receiving either 0.25%, 0.5% or 0.75% bupivacaine compared with a control group. \*  $p < 0.05$  between bupivacaine group and control.

**TABLE 7.3**

Time (min)	LEFT SIDE				RIGHT SIDE			
	0.75%	0.5%	0.25%	Control	0.75%	0.5%	0.25%	Control
0	0.71 (0.60-1.61)	1.29 (0.63-1.74)	0.62 (0.27-1.30)	0.66 (0.24-3.37)	0.93 (0.30-2.04)	0.70 (0.37-0.88)	0.82 (0.36-2.10)	0.79 (0.21-1.39)
30	0.61 (0.46-1.71)	1.24 (0.34-2.09)	0.64 (0.24-1.02)	0.73 (0.23-3.50)	0.89 (0.30-1.75)	0.70 (0.35-0.81)	0.86 (0.29-2.47)	0.84 (0.21-1.34)
40	0.61 (0.41-1.25)	1.22 (0.31-2.03)	0.66 (0.22-1.00)	0.71 (0.25-3.40)	0.82 (0.35-1.29)	0.64 (0.30-0.83)	0.82 (0.31-2.38)	0.92 (0.43-1.34)
50	0.58 (0.36-1.15)	1.13 (0.26-1.33)	0.67 (0.25-0.78)	0.72 (0.29-3.37)	0.79 (0.29-1.42)	0.59 (0.23-0.77)	0.81 (0.22-2.50)	0.92 (0.39-1.38)

Median (range) first peak amplitude ( $\mu\text{V}$ ) for patients receiving either 0.25%, 0.5% or 0.75% bupivacaine compared with a control group. No significant differences between groups.

**TABLE 7.4**

Time (min)	LEFT SIDE					RIGHT SIDE				
	0.75 %	0.5 %	0.25 %	Control	0.75 %	0.5 %	0.25 %	Control		
0	0.74 (0.45-1.81)	1.16 (0.51-1.52)	0.56 (0.36-0.93)	0.67 (0.22-2.83)	0.88 (0.41-1.69)	0.68 (0.25-1.21)	0.74 (0.51-1.55)	0.81 (0.20-0.93)		
30	0.54 (0.42-1.10)	1.13 (0.17-1.55)	0.58 (0.22-1.03)	0.71 (0.24-2.73)	0.65 (0.40-1.43)	0.52 (0.19-0.89)	0.62 (0.35-2.58)	0.85 (0.23-1.41)		
40	0.61 (0.31-0.92)	1.01 (0.15-1.37)	0.56 (0.22-0.85)	0.70 (0.23-2.62)	0.65 (0.336-1.27)	0.49 * (0.21-0.84)	0.57 (0.32-2.62)	0.85 (0.25-1.09)		
50	0.51 (0.31-0.73)	0.72 (0.09-1.31)	0.53 (0.28-2.86)	0.62 (0.15-2.67)	0.57 (0.33-1.24)	0.43 * (0.16-0.92)	0.58 (0.31-2.70)	0.89 (0.41-1.10)		

Median (range) second peak amplitude ( $\mu V$ ) for patients receiving either 0.25 %, 0.5 % or 0.75 % bupivacaine compared with a control group. \* p < 0.05 between bupivacaine group and control.

**TABLE 7.5**

Time (min)	LEFT SIDE					RIGHT SIDE					
	0.75 %	0.5 %	0.25 %	Control	0.75 %	0.5 %	0.25 %	Control	0.75 %	0.5 %	0.25 %
0	0.41 (0.22-0.77)	0.28 (0.13-1.00)	0.35 (0.23-0.60)	0.29 (0.21-1.22)	0.52 (0.16-1.18)	0.31 (0.09-0.63)	0.41 (0.36-1.22)	0.78 (0.26-0.98)	0.52 (0.16-1.18)	0.31 (0.09-0.63)	0.41 (0.36-1.22)
30	0.30 (0.13-0.65)	0.30 (0.07-0.52)	0.34 (0.20-0.66)	0.33 (0.19-1.45)	0.36 (0.15-1.12)	0.22 * (0.09-0.45)	0.43 (0.28-1.53)	0.57 (0.34-1.13)	0.36 (0.15-1.12)	0.22 * (0.09-0.45)	0.43 (0.28-1.53)
40	0.24 (0.15-0.57)	0.32 (0.06-0.55)	0.30 (0.20-0.65)	0.36 (0.20-1.37)	0.26 * (0.12-0.79)	0.25 * (0.07-0.45)	0.43 (0.25-1.65)	0.53 (0.30-1.05)	0.26 * (0.12-0.79)	0.25 * (0.07-0.45)	0.43 (0.25-1.65)
50	0.28 (0.11-0.49)	0.29 (0.06-0.46)	0.28 (0.19-0.68)	0.38 (0.22-1.87)	0.23 * (0.11-0.77)	0.26 ** (0.07-0.42)	0.38 (0.28-1.68)	0.59 (0.32-1.07)	0.23 * (0.11-0.77)	0.26 ** (0.07-0.42)	0.38 (0.28-1.68)

Median (range) third peak amplitude ( $\mu V$ ) for patients receiving either 0.25%, 0.5% or 0.75% bupivacaine compared with a control group. \* p < 0.05 between bupivacaine and control group. \*\* p < 0.01 between bupivacaine and control group.

**TABLE 7.6**

Time (min)	LEFT SIDE				RIGHT SIDE			
	0.75%	0.5%	0.25%	Control	0.75%	0.5%	0.25%	Control
0	15.4 (13.7-17.1)	15.2 (13.1-16.4)	15.7 (13.9-17.4)	14.5 (13.0-16.1)	15.2 (13.7-16.8)	15.5 (13.1-16.5)	15.7 (14.0-16.7)	14.7 (13.6-15.6)
30	16.2 (13.8-17.6)	15.9 (13.8-16.9)	16.3 (14.0-18.1)	14.7 (12.5-16.1)	15.9 (14.0-17.5)	15.9 (13.6-17.5)	16.2 (14.4-17.2)	14.8 (13.1-16.0)
40	16.2 (14.0-17.7)	16.0 (13.9-17.0)	16.5 (14.0-18.4)	14.8 (12.8-16.1)	16.2 (14.2-17.6)	16.1 (13.6-17.7)	15.3 (14.1-17.4)	14.9 (13.2-16.0)
50	16.6 (14.2-17.4)	16.1 (14.0-17.4)	16.7 (14.1-18.5)	14.9 (12.8-16.2)	16.5 (14.3-18.0)	16.1 (14.0-17.8)	16.4 (14.3-17.5)	14.9 (13.2-16.0)

Median (range) latency (ms) in patients receiving either 0.25%, 0.5% or 0.75% bupivacaine compared with a control. No significant difference between the groups during the study.

**TABLE 7.7**

	H	P
Overall amplitude	17.69	0.0005
Peak 1 amplitude	13.83	0.003
Peak 2 amplitude	12.55	0.006
Peak 3 amplitude	10.19	0.017

Results of the Kruskal Wallis test undertaken for maximum decrease in amplitude (regardless of side) from time 0 to 50 min comparing different concentration levels.

There was a significant effect of concentration seen with each peak and the overall amplitude.

**TABLE 7.8**

Concentration	Difference in average rank from control group	t df = 28	P
<u>Overall amplitude</u>			
0.25%	5.7	1.44	0.160
0.5%	13.6	3.44	0.002
0.75%	18.3	4.61	0.001
<u>Peak 1 amplitude</u>			
0.25%	4.3	1.11	0.280
0.5%	10.1	2.62	0.014
0.75%	15.2	3.95	0.005
<u>Peak 2 amplitude</u>			
0.25%	1.7	0.43	0.670
0.5%	9.8	2.47	0.021
0.75%	13.3	3.36	0.002
<u>Peak 3 amplitude</u>			
0.25%	3.6	0.89	0.380
0.5%	6.1	1.51	0.140
0.75%	14.3	3.53	0.002

Results of a multiple comparison procedure to compare concentration levels of 0.25%, 0.5% and 0.75% with control. The average rank of the 0.25% group was not significantly different from the control group for any variable. The 0.5% group was significantly different from the control group for the overall amplitude, peak 1 and peak 2 but not for peak 3. The 0.75% group was highly significantly different from the control group for all four neurophysiological variables.



**TABLE 7.9**

Time (min)	Bupivacaine 0.75%	Bupivacaine 0.5%	Bupivacaine 0.25%	Control
0	90 (9.8)	75 (6.4)	77 (12.0)	79 (13.8)
30	77 (8.2)	64 (9.3)	70 (9.6)	73 (12.1)
40	75 (8.6)	68 (7.7)	69 (10.0)	74 (14.6)
50	75 (6.4)	67 (11.0)	67 (7.8)	75 (13.9)

Mean arterial pressure mm Hg (SD)

There was no significant difference between the groups.

## CHAPTER VIII

### DISCUSSION

The studies outlined in the preceding chapters show that the administration of an epidural analgesic agent may have profound effects on the cervical epidural SEP to posterior tibial nerve stimulation. The effects of the different agents must be considered in the light of their known pharmacology and physicochemical properties. It is appropriate at this stage to consider the pathways monitored.

#### 8.1 Pathways involved in generation of the SEP

The origin of the SEP recorded from the epidural space is assessed by studies involving published values of sensory conduction velocity in the spinal cord. The data are summarised by Jones *et al.* (1982) and, although much of it is apparently conflicting, a few of the studies are in some measure of agreement. The consensus is that the fastest evoked spinal cord activity, recorded as a triphasic wave and perhaps originating in the lateral tracts, is conducted at 65-80 m s<sup>-1</sup>, while slower potentials, possibly arising in the posterior columns, have conduction velocities ranging from 30-50 ms<sup>-1</sup>.

Jones *et al.* (1982) found that the fastest spinal cord potentials recorded from the epidural space evoked by low intensity stimulation of the posterior tibial nerve at the knee were unobtainable by stimulation at the ankle. He interpreted this as evidence that the peripheral afferent fibres concerned are probably those of groups 1a and 1b, which derive mainly from muscle spindles and tendon organs, and are thus likely to be more numerous at the knee than at the ankle. Some of these fibres may pass directly into the posterior columns, but the majority are likely to synapse in the dorsal horns on cells which give rise to the dorsal spinocerebellar tract. This tract contains large diameter axons which respond to discrete muscle contraction as well as to stimulation of touch and pressure receptors.

In a study by Halonen, Jones, Edgar, & Ransford (1989), multiple level recordings of the epidural SEP were made intraoperatively in scoliosis patients from stimulation of the

tibial nerve in the popliteal fossa and the posterior tibial and sural nerve at the ankle. They concluded that activity was carried in tracts ipsilateral to the site of stimulation with the fastest activity located more laterally. They again found that conduction velocities ranged from 35 - 85 m s<sup>-1</sup>. Because the fastest activity is delayed at the low thoracic level, components may converge at this level and overtake one another further rostrally where the components tend to diverge in latency. As in previous studies by Jones *et al.* 1982, they again found that the most rapidly conducting components had the lowest peripheral stimulation threshold. Again, as in Jones *et al.* (1982), the fastest potential following tibial nerve stimulation in the popliteal fossa was smaller, or absent, when the posterior tibial nerve was stimulated at the ankle.

Therefore my studies assessed spinal cord conduction, but the pathways studied mainly subserve pressure, touch and proprioception. The first peak is thought to represent conduction due to activation of 1a and 1b afferents travelling in the dorsal spinocerebellar tracts. Peaks 2 and 3 are largely cutaneous in origin and conducted mainly via the dorsal columns. The epidural SEP does not assess conduction of pain fibres. However, in the present state of technology, it is the best estimator of afferent conduction that is currently available.

## 8.2 Comparison of epidural with scalp-recorded SEP

The comparability of my studies with previous similar work on the effect of local analgesics on the cortical SEP depends on the extent to which the scalp-recorded SEP indicates spinal cord function. Halliday and Wakefield (1963) studied fourteen patients with dissociated sensory loss and found that the initial positivity only of the scalp-recorded SEP represented spinal cord conduction and depended solely on posterior column activity.

The scalp recorded SEP to posterior tibial nerve stimulation is still used in many centres for monitoring scoliosis surgery (Nuwer 1986). The primary specific complex that appears between 25 and 85 ms is widely used for intraoperative monitoring of spinal cord function (Pathak *et al.* 1984). The primary complex consists of an initial positive spike (P<sub>1</sub>), which is not always recordable, followed by a sharp negative peak N<sub>1</sub>, a slow positive P<sub>2</sub> and negative N<sub>2</sub> peaks. Early P<sub>1</sub> and N<sub>1</sub> are thought to originate subcortically

and therefore may represent an element of spinal cord conduction whereas P<sub>2</sub> and N<sub>2</sub> are thought to originate in the lamacortical and cortical areas of the brainstem respectively (Allison, Goff, Williamson, & VanGilder 1986, Pathak *et al.* 1984).

In only two studies from Kehlet's group are scalp-recorded evoked responses to posterior tibial nerve stimulation measured (Lund *et al.* 1987, Saugbjerg *et al.* 1986). In these studies, they found that the responses after lumbar epidural bupivacaine administration were identical to those obtained after thoracic epidural bupivacaine administration, that is, suppression of the N<sub>1</sub>P<sub>2</sub> scalp-recorded response only. My studies confirm their finding that bupivacaine depresses spinal cord conduction.

### 8.3 Comparison of posterior tibial nerve with dermatomal SEP

Much of the work of Kehlet's group, on the effect of various local analgesic agents on the SEP, utilises the SEP to dermatomal stimulation (Dahl *et al.* 1990, Lund *et al.* 1987a, 1989, 1991). The dermatomal SEP is used in the assessment of lumbar radiculopathies as an adjunct to the selection of patients undergoing lumbar spine surgery (Dvinch *et al.* 1984). Katifi & Sedgwick (1986) have collected normative data to aid future assessment of patients for the presence of radiculopathies. They acknowledged in this paper that there was overlap between zones when the dermatomal SEP was used to assess the various roots.

In a study where the dermatomal SEP was recorded at the scalp after stimulation of the C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, T<sub>2</sub>, T<sub>4</sub>, T<sub>6</sub>, T<sub>8</sub>, T<sub>10</sub>, T<sub>12</sub>, L<sub>2</sub>, L<sub>3</sub>, L<sub>4</sub>, L<sub>5</sub>, and S<sub>1</sub> dermatomes, Slimp and colleagues (1992) found that it was important to standardise the levels of awareness, as sleep significantly obtunded the amplitude of these responses. They also stated that the dermatomal map must be defined by collection of more normative data. They suggested that, to analyse segmentally the spinal cord by use of the SEP to dermatomal stimulation, it is necessary to assess the rostral-caudal pattern of dermatomal responses by level-to-level comparisons (not done in any of the studies of Lund *et al.* 1987, 1989, 1991 or Dahl *et al.* 1990). They also found that dermatomal scalp responses were 25% more variable than the mixed nerve scalp response, with the amplitudes several times more variable than the latencies.

Therefore, the studies using dermatomal responses suffer greater intra-subject variation in amplitude. Also, the anatomical distribution of the dermatomes varies considerably between individuals. Furthermore, in local analgesic studies of the SEP to dermatomal stimulation, level-to-level comparisons were not performed and there was no standardisation of awareness. In the studies of Dvinch *et al.* (1984), Katifi & Sedgwick (1986) and Slimp *et al.* (1992), mention is made each time of the classical "W" configuration, and examples shown. This is not obvious in the studies of Lund *et al.* (1987a, 1987b, 1987c, 1989, 1991) and Dahl *et al.* (1990, 1992).

In a study of dermatomal SEP on 129 patients with cervical and lumbar radiculopathies, Green, Hamm, Benfante, & Green (1988) found that there were more "normal" responses in the upper limbs than in the lower limbs. They inferred that the dermatomal SEP is more specific for the lumbar area and concluded that the dermatomal SEP is a technique of low sensitivity and high specificity. In summary, dermatomal SEPs are of use in assessment of nerve root involvement and not of spinal cord conduction.

The SEP to mixed nerve stimulation, while not necessarily indicating localization, does adequately verify a conduction abnormality. The epidural SEP is known to be stable to end-tidal concentrations of 1.5% halothane (Loughnan *et al.* 1989a). It has a simple configuration, less variability than the dermatomal SEP and assesses spinal cord conduction.

#### 8.4 Scoliosis model and use of normal patients

Chapters IV, V and VII detail studies performed on adolescent idiopathic scoliosis patients undergoing corrective surgery. They all tended to show a laterality of effect. In the preliminary study, investigating the effect of halothane on the SEP, there was only a small effect on the SEP at an end-tidal halothane concentration of 1.5%. This was seen for the left side only.

This laterality of effect was also noted by Shukla *et al.* (1987) in patients undergoing corrective surgery. They found that, where there was a decrease in the SEP in ten of the twelve patients studied, this was on the concave side of the scoliosis curve. Unilateral changes have been reported by Bradshaw, Webb, & Fraser (1984) in a review of the

operative management of forty scoliosis patients. It has also been noted in the experimental setting by Yeoman *et al.* (1989). Previous studies on the SEP in scoliosis patients (Pathak *et al.* 1984, 1987), only studied one limb, so this possible laterality of effect had not been observed.

Furthermore, Shukla and colleagues (1987) found that neither the concurrently recorded cortical, nor the cervical, SEP showed parallel changes in amplitude. This is further confirmation that the epidural SEP has a greater specificity for assessing spinal cord conduction than the cervical or cortical SEP. The cervical SEP is recorded from skin electrodes placed over the vertebrae prominens. Obtaining the cervical SEP to lower limb stimulation is technically more difficult than an extradural recording because of high impedance and greater baseline drift. Several thousand responses need to be averaged and the waveform does not show the triphasic potential found with the epidural SEP (Jones & Small 1978).

Roaf (1966), in a classic paper, presented his evidence that the basic lesion in scoliosis is relative lengthening of the anterior components of the spine, compared with the posterior elements. From this argument it follows that the logical treatment is to reduce this relative lengthening, either by lengthening the posterior elements or shortening the anterior elements. It may be that the basic bony abnormality is associated with a secondary abnormality in spinal cord conducting tracts.

In adolescent idiopathic scoliosis the predominant curve is concave to the left; in congenital scoliosis the reverse is true. The aetiology of these differences is not known. In recent years, it has been proposed that the causative lesion in the development of idiopathic scoliosis is one in the central nervous system (Barrack, Whitecloud, Burke, Cook, & Harding 1984, Ford, Bagnall, Clements, & McFadden 1988, Herman, Mixon, Fisher, Maulucci, & Stuyck 1984, Lidström, Sahlstrand, & Ortengren 1981). Herman and colleagues (1984) postulate that a proprioceptive rearrangement, or recalibration, of the internal representation of the body in space is present and that a non-erect vertebral alignment is erroneously perceived as straight. In a recent study by Keessen, Crowe, & Hearn (1992), assessing the proprioceptive accuracy in idiopathic scoliosis, they found a significant inaccuracy in upper-extremity proprioception when scoliosis and spinal

asymmetry patients were compared with controls. However, Brinker, Willis, Cook, Whitecloud, Bennett, Barrack, & Ellman (1992) found that, when the scalp-recorded SEP to posterior tibial nerve stimulation and median nerve stimulation obtained from scoliosis patients was compared with matched controls, there was no difference between the two groups in terms of latency and conduction velocities. This may be due to the small number of patients studied, or the use of the scalp-recorded SEP which is not as sensitive an indicator of spinal cord conduction as the epidural SEP.

In my studies on the epidural SEP, the median overall amplitude and range was greater for the left side than the right side (Table 8.1). There was a difference in sensitivity to local anaesthetic action; for example, the left side overall amplitude was more depressed than the right side, by the action of epidural lignocaine 2%. The one group of normal patients we studied showed a symmetrical pattern in terms of sensitivity to the depressant effect of the agent (etidocaine) under investigation. Thus, in adolescent idiopathic scoliosis, the difference in spinal cord conduction between sides, if present, is subtle. There is, however, a difference in terms of sensitivity to agents or stimuli (such as distraction) between the sides.

#### 8.5 Difference between local analgesic agents

My study confirms the work of Cusick *et al.* (1980) that etidocaine has a predominantly spinal cord site of action. It was the only local anaesthetic agent in which complete suppression of afferent activity in the spinal cord was seen. Although this was not achieved in all cases, it must be borne in mind that the concentration used in my study was 1.0%. Had 1.5% etidocaine been used (this is currently only available with adrenaline), there might have been complete suppression of the response in more patients.

Mitchell *et al.* (1989) showed that epidural lignocaine 2% had a depressant effect on spinal cord conduction in dogs. My study confirms that this also occurs in humans. Neither my study, nor that of Mitchell *et al.* (1989), gives any information about the relative importance, if any, of the dural root cuff as a site of action for epidural lignocaine. Arthur *et al.* (1987) state that lignocaine and chloroprocaine have low partition coefficients (3 and 1 respectively) relative to bupivacaine and etidocaine (28 and

141); it might, therefore, be expected that lignocaine would have a combined roof cuff and cord site of action. This is not obvious from the data in my study.

My study on bupivacaine showed that in concentrations of 0.5% and higher, there is clinically significant depression of spinal cord conduction. However, this did not occur with 0.25% bupivacaine. This difference in effect of the three concentrations is probably related to the total dose of local anaesthetic agent reaching the spinal cord. Thus bupivacaine 75 mg and 50 mg depressed spinal cord conduction, while there was little effect with 25 mg

All my studies used 10 ml of an analgesic agent injected into the lumbar epidural space at the L<sub>2-3</sub> level. Stimulation of the posterior tibial nerve involves stimulation of the L<sub>4-5</sub> S<sub>1-2-3</sub> nerve roots (Warwick & Williams 1973). Therefore, the studies estimate the maximal effect of lumbar epidural injection of each local analgesic agent. It may be that an epidural injection of local analgesic agent, at for example the thoracic level, has a lesser effect on the epidural SEP. Studies by Lund *et al.* (1987a) and Saugbjerg *et al.* (1986), on the scalp-recorded SEP found that the N<sub>1</sub>P<sub>1</sub> component of the SEP was depressed when bupivacaine was administered in the lumbar epidural space. However Lund *et al.* (1987c) showed that there was a minimal decrease in SEP amplitude when bupivacaine was injected into the thoracic epidural space.

## 8.6 Physical determinants

The epidural SEP is thought to represent conduction in the 1a and 1b fibres subserving touch and proprioception (see above). Because these fibres are surrounded by a myelin sheath, the main determinant of whether conduction is suppressed by a particular agent is its lipid solubility. Etidocaine with a high partition coefficient caused a greater degree of afferent blockade.

Etidocaine was the only agent to suppress all three peaks of the SEP. Both lignocaine and bupivacaine 0.5% and 0.75% were associated with a preferential blockade of the slower conducting tracts, with relative sparing of the faster conducting tracts. Thus the faster (65 - 80 m s<sup>-1</sup>) potentials of the lateral tracts were spared, while the slower potentials (30 - 50 ms<sup>-1</sup>) of the posterior column tracts were more susceptible. In this



respect both bupivacaine and lignocaine have a similar effect on the conducting tracts. This may be related to the fact that the faster conducting fibres are likely to be thicker in diameter. The thicker the fibre, the greater the amount of local anaesthetic required for blockade. The thinner, more slowly conducting fibres, are relatively more sensitive to local anaesthetic action.

Peak 1 amplitude may be less susceptible to suppression by lignocaine and bupivacaine because the tracts responsible for this peak are less superficial than those responsible for the later two peaks. When an agent of high lipid solubility such as etidocaine is used, it rapidly diffuses through into the spinal cord and the differential effects on the tracts are less obvious.

The relative potency of lignocaine : etidocaine : bupivacaine is 1 : 0.5 : 0.25 (Arthur *et al.* 1987). Therefore the effects of lignocaine 2% etidocaine 1% and bupivacaine 0.5% should be broadly similar. In terms of their effect on the SEP, this is true for bupivacaine 0.5% and lignocaine 2.0%. Etidocaine 1%, however, caused marked suppression of the three peak amplitudes in all patients, with complete ablation of the SEP in some subjects. This did not occur with either bupivacaine 0.5% or lignocaine 2.0%. The difference in effect of etidocaine is probably related to its high lipid solubility.

In terms of their effect on the SEP, bupivacaine 0.5% and lignocaine are similar. Because bupivacaine 0.25% had minimal effect on the SEP, lignocaine in concentration of 1.0% or less may be appropriate for use in scoliosis surgery. However, lignocaine has a much shorter duration of action than bupivacaine and shows tachyphylaxis in repeated dosage, which makes its use in scoliosis surgery unlikely.

## 8.7 **Statistics - non-normal distribution**

In total eighty-four patients with adolescent idiopathic scoliosis were studied. The baseline values for these patients were recorded and a frequency distribution plotted.

The frequency distribution of the overall amplitude for the left and right sides had skewness values of 1.33 and 1.12 respectively, indicating that the data were positively skewed. This is confirmed by further analysis which showed that the left leg overall

amplitude had a mean value of 1.27  $\mu\text{V}$ , with a median of 1.07  $\mu\text{V}$ . Corresponding values for the right leg were 1.21  $\mu\text{V}$  and 1.02  $\mu\text{V}$ .

Thus the values for the overall amplitude and the peaks 1, 2 and 3 amplitude are best expressed as median and ranges. Overall amplitude for the left had a median value of 1.07  $\mu\text{V}$  (range of 0.33 to 3.88  $\mu\text{V}$ ) and right side amplitude was 1.02  $\mu\text{V}$  (range of 0.21 to 3.75  $\mu\text{V}$ ). Values for median and range are tabulated for the peak values and latency in Table 8.1

Logarithmic transformation "normalises" the data. The frequency distribution of the transformed data for the overall amplitude had skewness values for the left and right sides of 0.83 and -0.36 respectively. The skewness values of the raw data and the log transformed data for left and right sides are shown in Table 8.2 for the amplitude and latency data. Figure 8.1 shows a histogram of the baseline values for the left leg overall amplitude with, in Fig. 8.2, the corresponding histogram after log transformation. Figures 8.3 and 8.4 show the histogram for the right leg overall amplitude and that of the corresponding log transformation respectively.

The SEP results behave like other biological data such as skinfold thickness and body weight in showing a positively skewed distribution rather than a normal distribution. This suggests a biological "floor" to the variable, but no ceiling (Garn, Sullivan, & Tenhave 1987).

The inherent variability of the signal must be considered before any interpretation is made about changes seen either intraoperatively, or as an apparent result of an experimental intervention. The variability in response to the SEP during scoliosis surgery was assessed by York, Chabot, & Gaines (1987). Although they used the scalp-recorded SEP, they showed that amplitude values varied markedly both within and between individual patients and attributed this to the anaesthetic agents and blood pressure. In modern clinical practice, decreases of 30% (Nuwer 1987) or 50% (Jones *et al.* 1982) in overall amplitude of the SEP merit careful appraisal of the surgical technique.

Little is known about the inherent variability of the epidural SEP. However, according to Jones *et al.* (1988), the overall SEP amplitude varies randomly between 10 and 30% of baseline. This is similar to changes seen in the control groups in each of the local analgesic studies. However, most of the patients receiving epidural lignocaine 2%, or bupivacaine 0.5% and 0.75%, showed a far greater decrement in peak amplitudes.

#### 8.8 **Implications for other methods of monitoring**

The most commonly used form of spinal cord monitoring in the U.K. at the present is the epidural SEP. However, this monitors ascending conduction in the dorsal and lateral columns of the spinal cord only. These are the areas supplied by the posterior spinal arteries of the spinal cord. One of the major precipitating causes of paraplegia is ischaemia, and the areas of the cord most vulnerable are those supplied by the anterior spinal artery. This blood supply is more appropriately monitored using the motor evoked potential (MEP). This form of monitoring is being developed and is not, as yet, in routine practice. It remains to be established what effect, if any, the various local analgesic agents have on the MEP.

Monitoring of spinal cord conduction using the scalp-recorded SEP is still the mainstay of monitoring in the United States. The only study on the effects of an opiate on the scalp-recorded SEP is that by Lund *et al.* (1987b) where epidural morphine was shown to have minimal effect on the SEP in response to dermatomal stimulation. Definitive studies on the effect of the various local analgesic agents on the scalp-recorded SEP to stimulation of a mixed peripheral nerve have not as yet been performed. However, my results show a minimal effect of epidural bupivacaine 0.25% and diamorphine 0.1 mg kg<sup>-1</sup> on the epidural SEP, inferring that these agents are also likely to have a minimal effect on scalp-recorded SEP.

The wake-up test is still used in some centres which do not possess appropriate SEP monitoring. It is occasionally employed in addition to the SEP. The epidural administration of a low concentration of local anaesthetic agent with an opiate results in minimal, if any, motor blockade. Solutions of 0.25% bupivacaine and diamorphine, injected into the epidural space, should have minimal effects on the wake-up test and the early postoperative assessment, and may be an ideal regimen.

Although present monitoring is more sophisticated than that used by Jennings & Delaney (1979), I have essentially confirmed their finding that a weak local anaesthetic agent may be used for scoliosis surgery. However, I have defined limits of safety in terms of concentration and, in addition, assessed the effect of epidural diamorphine on the SEP.

#### 8.9 Effects of Arterial Pressure

The mechanisms of injury during distraction are multifactorial (Taylor 1990). Several animal models suggest that pathological distraction and flexion of the cord may cause physical damage to the tracts (Nuwer 1986), and this mechanism may be more important than ischaemia.

However, blood pressure and perfusion must be considered in the clinical setting because of the synergistic effect of hypotension and mechanical deformation, as first described by Brodkey and colleagues (1972). This has persuaded most anaesthetists to exercise caution when induced hypotension is used as part of the anaesthetic technique in scoliosis surgery. Grundy and colleagues (1981) describe a case where a patient demonstrated scalp-recorded SEP changes reproducibly related to arterial pressure during Harrington rod instrumentation for scoliosis. Although initially the systemic arterial pressure was maintained at 80 to 90 mm Hg by a sodium nitroprusside infusion, the scalp-recorded SEP was only preserved by maintaining the arterial pressure at a level 20% above baseline. Later, in a prospective study, Grundy, Nash, & Brown (1982) evaluated the benefits of induced hypotension in twelve patients undergoing corrective scoliosis surgery and compared them with twelve patients receiving "sham" hypotension. Five patients in the hypotension group had alterations in the scalp-recorded SEP on distraction but, on reversal of the hypotension, the wake-up test was normal and the SEP changes resolved. Grundy recommends, therefore, that hypotension is safe provided the spinal cord function is monitored.

In the original study by Brodkey *et al.* (1972), the mean arterial pressure was decreased to at least one-half the baseline value by occlusion of a Selverstone clamp. The scalp-recorded SEP was measured and the experimental model used was a compressive force where a weight was applied directly to the dorsal surface of the cord. The clinical situation is different in that the force applied in scoliosis surgery is a distractive one, the

hypotension is induced gradually (rather than suddenly by a clamp), and the SEP is recorded from the epidural space. This situation is similar to that described by Yeoman *et al.* (1989), who investigated the combined effects of induced hypotension and spinal distraction on the SEP recorded from the T<sub>11</sub> epidural space. They used a feline model and found that, when hypotension was induced to a mean arterial pressure of 60 mm Hg, there was a significant decrease in mean first peak SEP amplitude after 5mm distraction, when compared with a normotensive control. They concluded that the effects of hypotension and distraction were additive.

Yeoman and colleagues (1989) also found that, in the laboratory animal, changes in SEP at normal arterial pressure may occur with interface distances greater than 1.25 cm, while most SEP changes during hypotension occur with interfacetal distances of 0.75 - 1.00 cm. In scoliosis correction, multisegmental distraction of 2 cm may be required. Thus, at a mean arterial pressure of 60 mm Hg, a smaller amount of distraction will induce changes in the SEP than at normal arterial pressure.

Kobrine, Evans, & Rizzoli (1979b) studied five primates and measured the spinal cord and cerebral blood flow, using the hydrogen clearance method. He showed that electrophysiological activity in the long tracts is relatively resistant to reduced blood flow, but is disturbed when white matter flow decreases to less than 30% of normal. Kobrine, Evans, & Rizzoli (1980) showed that the epidural SEP was more stable to the effect of hypotension and ischaemia than the scalp-recorded SEP. They found that the scalp-recorded SEP disappeared almost immediately after death, but there was a delay of 8 to 18 min before the epidural SEP disappeared in the same animal. They also observed that spinal cord blood flow had to decrease to 30% of normal or less, before any change was seen in the epidural SEP.

Haghighi & Oro (1989) bled twelve anaesthetised cats to a very low mean arterial pressure (< 30 mm Hg) and found that the scalp-recorded SEP and spinal motor evoked potentials disappeared. However, the spinal SEP was more resistant and disappeared at lower levels of hypotension, took longer to do so, and was more rapidly returned after reinfusion of the blood.

In summary, the epidural SEP is relatively resistant to any changes in blood flow, only showing attenuation when spinal cord blood flow is 30% of normal. In the range of mean arterial pressures seen in my studies (systolic maintained above 80 mm Hg), I would not expect to see a change due to alterations in arterial pressure. Evaluation of any intraoperative change in the SEP must consider not only the surgical manoeuvre, but also physiological variables such as arterial pressure and oxygenation. Thus, if epidural local analgesics are used in scoliosis surgery, they should not cause an undue fall in arterial pressure and high total doses must be avoided.

## 8.10 Future Studies

### 8.10.1 **In Scoliosis Patients**

#### 8.10.1.1 Intraoperative Analgesia

The studies outlined in this thesis make recommendations about the concentration of local anaesthetic agent least likely to interfere with intraoperative measurement of the SEP. It is less certain what the effect of increasing the volume of a weak local anaesthetic solution (thereby administering a greater total dose) will have on this potential. Original studies by Bromage (1975) indicated that, for lignocaine in concentrations between 2 and 5%, the dose of drug (volume x concentration) determined the spread of analgesia. He suggested that dose requirements decreased from 30 mg per segment to 20 ml per segment when the lignocaine concentration was increased from 1% to 2%. Erdemir, Soper, & Sweet (1965) showed that 30 ml of 1% lignocaine solution produced a higher sensory level than 10 ml of a 3% solution. Burn, Guyer, & Landon (1973) demonstrated that large volumes of contrast media (40 ml) were more likely to spread into the cervical regions than higher concentrations and smaller volumes.

Cousins (1980) states that increasing dosage results in a linear increase in degree of sensory block and duration of epidural block, while increasing concentration results in a reduction in onset time and increased intensity of motor blockade. However, E.N. Armitage (1987), while agreeing that the extent of sensory blockade produced

by a particular agent depends on the mass of drug, maintains that this principle does not hold true for extremes of concentration and volume. Neither does it hold true for the degree of motor block, as this is very closely related to drug concentration.

Therefore, increasing the total dose administered by increasing the volume of dilute local anaesthetic agent administered, will have a minimal effect on any motor block. However, the effect on the SEP should be studied before routine administration of a larger total dose of local anaesthetic solutions.

The current series of studies assess the effects of local analgesic agents without any vasoconstrictor. Since the major benefit in back surgery has been derived from the use of local anaesthetic with adrenaline (Bromage 1951, Jennings & Delaney 1979, Reynolds *et al.* 1986) future studies should investigate whether the addition of a vasoconstrictor to the epidural solution significantly changes my findings.

#### 8.10.1.2 Postoperative Analgesia

Patients who undergo scoliosis surgery may receive postoperative analgesic agents via an indwelling epidural cannula. For patients undergoing anterior (thoracic) approach surgery, the epidural catheter is most appropriately inserted preoperatively by the anaesthetist. This may be technically difficult, as the curve in scoliosis is usually maximal in the thoracic area. Nevertheless, it is possible, especially if the thoracic spine X-rays are consulted prior to Tuohy needle insertion. However, if performed preoperatively, it is important to leave at least 6 cm of catheter in the epidural space, as any less may result in catheter removal when the spine is rotated by surgery.

The technical problems of preoperative insertion referred to above are avoided in patients undergoing posterior fusions. The epidural cannula

may be inserted toward the end of operation by the surgeon and left in situ.

Although epidural infusions of local anaesthetics can be used postoperatively, caution must be exercised in scoliosis patients. Even when dilute local anaesthetic agents are infused into the epidural space, some lower limb weakness may be seen (E.N. Armitage 1987), thereby confusing any assessments of motor function. Armitage (1986) suggested the use of a high volume/low concentration of local anaesthetic agent and recommended an infusion of 0.1 - 0.125% bupivacaine, at a rate of 16 - 24 ml hr<sup>-1</sup>. Mitchell, Scott, Homquist, & Lamont (1988) found that, in gynaecological patients, a continuous extradural infusion of bupivacaine 15 ml hr<sup>-1</sup> was an effective method of prolonging a block produced by a single dose of bupivacaine 0.5%. However, it was not always adequate as the sole method, and an additional bolus of local anaesthetic or opioid was sometimes needed. Lee, Simpson, Whitfield & Scott (1988), in a double-blind randomized comparison of postoperative epidural infusion regimens after gynaecological surgery, found that a mixture of diamorphine (0.5 mg in 15 ml) with bupivacaine 0.125% and infused at a rate of 15 ml hr<sup>-1</sup> provided significantly superior analgesia than either agent alone. Therefore, epidural infusions of local anaesthetics only may not be sufficient for postoperative analgesia and may produce possible muscle weakness.

Definitive studies should be performed using a lower concentration "loading dose" of bupivacaine. In the meantime, an appropriate regimen would be either a continuous infusion of an epidural opiate or bolus injections of weak local anaesthetic solutions, with or without opiates. If opiates are used postoperatively, it is important that they can produce rapid analgesia following a bolus administration. Furthermore, opiates with high lipid solubility should be used, as they penetrate the cord rapidly and have limited cephalad spread (Cousins



& Mather 1984). Both fentanyl and diamorphine are rapidly acting lipophilic agents suitable for postoperative epidural analgesia (E.N. Armitage 1987). They may be given as a bolus or as a continuous infusion. Welchew & Thornton (1982) found that an extradural infusion of fentanyl  $60 \mu\text{g hr}^{-1}$  provided pain relief superior to that obtained with IM papaveretum. However, it is my experience that a slightly higher infusion rate may be required for scoliosis surgery.

Comparisons between different opioids have been very few (Morgan 1989). Studies in which different postoperative regimens are compared in scoliosis patients would go a long way to improving our knowledge of their analgesic requirements.

#### 8.10.2 In Neurophysiology

The tracts investigated in the studies described in this thesis are those subserving pressure, touch and proprioception. At present, research in pain has been severely limited by the lack of an objective, quantifiable physiological measure which is directly related to noxious stimulation. The scalp-recorded evoked response to noxious stimulation may permit objective assessment of pain.

In measurement of the SEP, as described in this thesis, a mixed peripheral nerve is stimulated via brief stimuli and surface electrodes. The fastest conducting fibres are thereby activated and the SEP represents waves of synchronous activity in the  $A\alpha$  and  $A\beta$  fibres which have a conduction velocity of  $50 \text{ m s}^{-1}$ .

Pain is transmitted via more slowly conducting  $A\delta$  and C fibres, which travel at a velocity of  $0.5 - 30 \text{ m s}^{-1}$ . The late "near-field" cerebral potentials to noxious stimuli and these are the potentials used in pain research. Several papers describe pain-related cerebral potentials in healthy volunteers, using either electrical tooth pulp stimulation (Chatrain, Canfield, Knauss, & Lettich 1975), electrical skin stimuli (Bromm & Meier 1984), or mechanical skin stimuli (Bromm & Scharein 1982, Johnson, Jurgens, Kongehl, & Kornhuber 1975). More recently thermal stimulation, as developed by Mor & Carmon (1975) has

been used. This elicits a sensation considered natural. The amount of energy impinging on the skin can be varied by manipulating the duration of the stimulus. Precautions must be taken to avoid eye and skin injury.

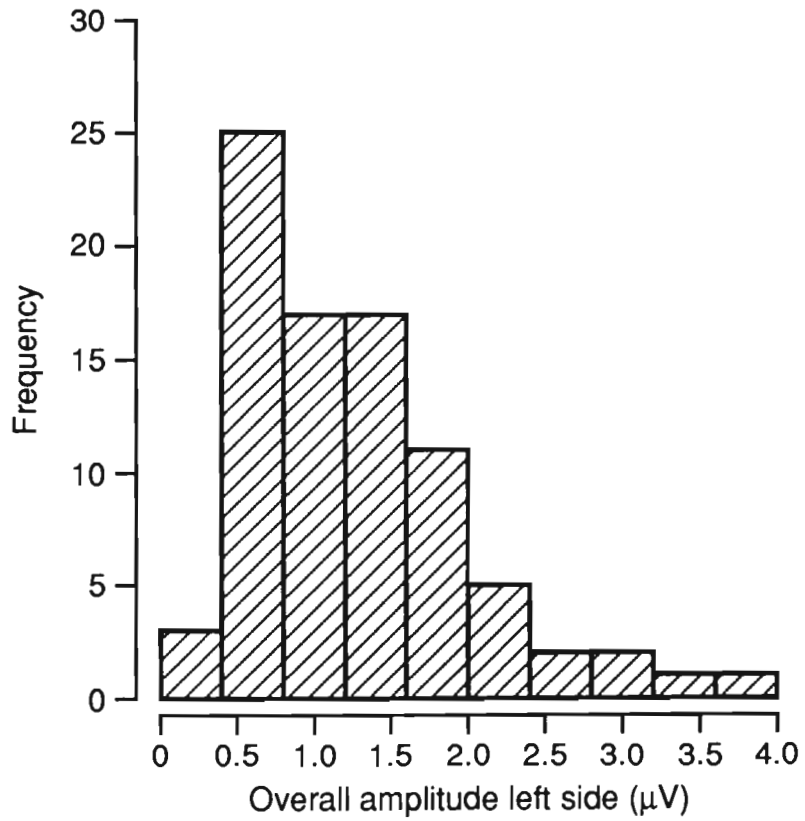
These methods are extensively reviewed by Chudler & Dong (1983), who state that none of these methods of stimulation demonstrably elicit pain sensations without activation of non-nociceptive afferents. At present, thermal methods of stimulation are receiving most attention. Either a CO<sub>2</sub> laser (Bromm & Treede 1991) or an Argon laser (Arendt-Neilson & Bjerring 1988) can be used to stimulate the nociceptive afferents. Tissue damage is a problem, as the CO<sub>2</sub> laser is capable of producing first degree burns (Bromm & Treede 1991). The Argon laser requires the skin to be blackened and much of the radiant energy is reflected at the surface, depending on incident angle and pigmentation. Therefore, the resulting sensory evoked potential amplitudes are more variable. Furthermore, there is evidence to suggest that the amplitude of the evoked response may be related more to the subjective pain perception than to stimulus intensity (Carmon, Friedman, Cogger, & Kenton 1980).

Measurement of pain-related potentials requires apparatus capable of measuring late potentials with conduction velocities as low as 0.5 m s<sup>-1</sup>. At present, these are only measured using scalp-recorded electrodes. In a recent study Arendt-Neilson (1990a, 1990b) outlined optimum recording conditions and quantification techniques for the Argon laser. He also examined variability in amplitude with successive recordings and found some evidence of "learning", that is, less variability with repeated experiments.

Considerable variability of recordings have been noted in the same subjects by Beydoun, Morrow, Shen, & Casey (1993) in a study using the CO<sub>2</sub> laser. They state that at present the clinical study of individual patients is best limited to comparison between sides. Similarly, Purves & Boyd (1993) found substantial variability in latency, amplitude and morphology in individual trials, with absent responses in some instances.

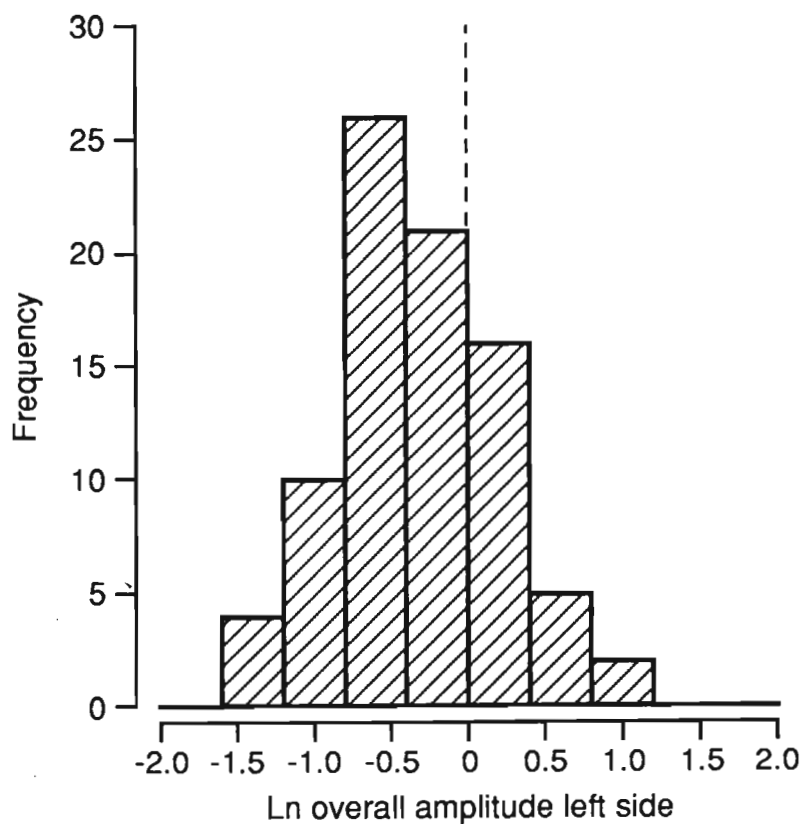
As yet there is no reliable, safe proven method of stimulating pain fibres. The epidural SEP may be a useful measurement of analgesic efficacy, when the technique for recording pain-related potentials has become more refined. These evoked potentials may provide a useful and objective measurement of acute and chronic pain and monitoring therapeutic regimens and interventions.

**FIGURE 8.1**



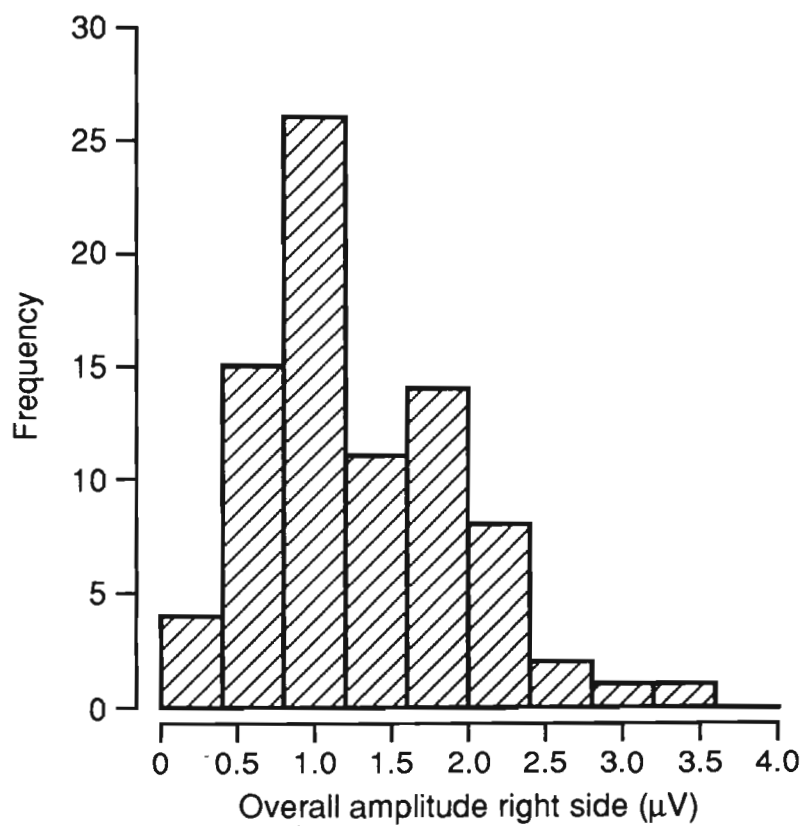
Histogram of overall amplitude of the left side demonstrates that the data has a positive skew.

**FIGURE 8.2**



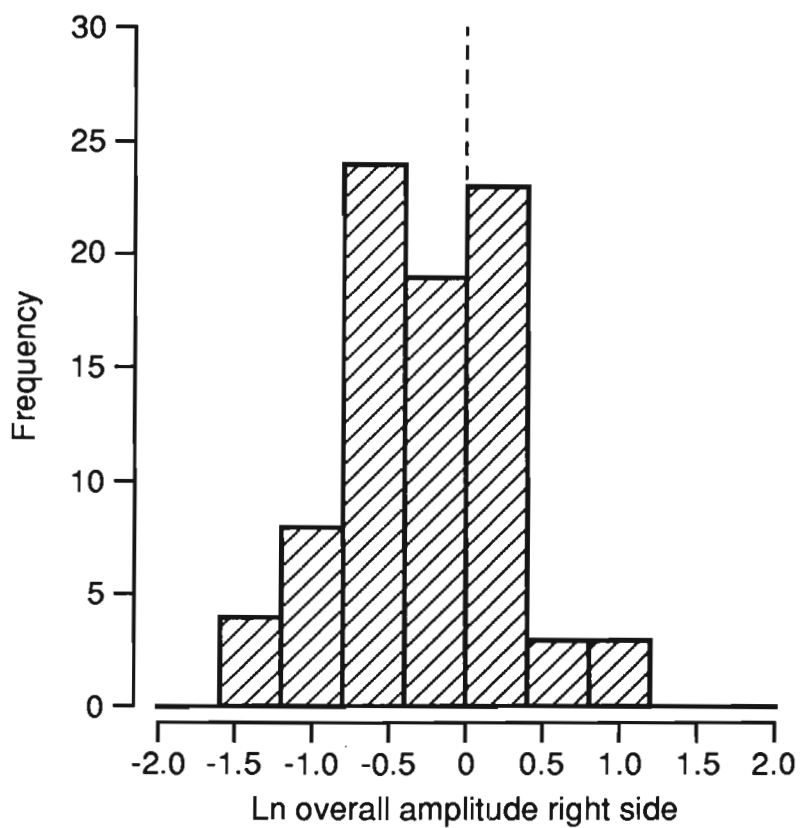
Logarithmic transformation of baseline values overall amplitude left side "normalises" the skewness of the data presented in Figure 8.1.

**FIGURE 8.3**



Baseline values overall amplitude right side demonstrating that the data are positively skewed.

**FIGURE 8.4**



Logarithmic transformation of baseline values overall amplitude left side "normalises" the skewness of the data presented in Figure 8.3.

**TABLE 8.1**

	Left side	Right side
Overall Amplitude $\mu\text{V}$	1.07 (0.33 - 3.55)	1.02 (0.21 - 3.75)
Peak 1 amplitude $\mu\text{V}$	0.94 (0.24 - 3.64)	1.02 (0.21 - 3.75)
Peak 2 amplitude $\mu\text{V}$	0.83 (0.22 - 2.63)	0.87 (0.19 - 3.32)
Peak 3 amplitude $\mu\text{V}$	0.52 (0.13 - 2.03)	0.56 (0.09 - 2.00)
Latency ms	15.36 (12.88 - 19.92)	15.30 (12.92 - 20.08)

Median amplitudes (ranges) for overall amplitude, peak 1, 2 and 3 amplitude for left and right sides.

Also presented are the median values (ranges) for latency after stimulation of left or right side.



**TABLE 8.2**

	Left side		Right side	
	Raw data	Log transformation	Raw data	Log transformation
Overall amplitude	1.33	0.83	1.12	-0.36
Peak 1 amplitude	1.43	-0.03	1.12	-0.36
Peak 2 amplitude	1.07	0.10	1.65	-0.19
Peak 3 amplitude	1.37	0.10	1.01	-0.32
Latency	0.65	0.30	0.70	0.36

Skewness values for the frequency distributions for overall amplitude and peak 1, 2 and 3 amplitude for left and right side, together with values obtained for the frequency distribution of the log transformed data.

The skewness values for the frequency distribution of left and right latency and their log transformation are also presented.

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