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ORIGINAL ARTICLES

PERIPHERAL NERVE INJURY CAUSED BY INJECTION NEEDLES USED IN REGIONAL ANAESTHESIA: INFLUENCE OF BEVEL CONFIGURATION, STUDIED IN A RAT MODEL

A. S. C. RICE AND S. B. McMAHON

SUMMARY

We have studied the immediate and long term (up to 28 days) effects of short and long bevelled needle impalement of the rat sciatic nerve. Three techniques were used to assess neural trauma and its consequences: stained longitudinal nerve sections were assessed by light microscopy and scored for injury; the extravasation of Evan's Blue dye, after antidromic electrical nerve stimulation, was used as a test of unmyelinated fibre function; the flexion withdrawal times from a noxious stimulus were measured. The results of all three experiments suggested that, should a nerve fascicle become accidentally impaled during regional anaesthesia, the lesions induced by short bevelled needles are more severe, more frequent and take longer to repair than those induced by long bevelled needles. Nerve injury induced by short bevelled needles was associated with persisting signs of injury 28 days after the injury. These results suggest that the current practice of using short bevelled needles to prevent nerve injury complicating regional anaesthesia be reassessed. (Br. J. Anaesth. 1992; **69**: 433–438).

KEY WORDS

Anaesthetic techniques: regional. Complications: nerve injury. Equipment: short and long bevelled needles.

Nerve injury during regional anaesthesia may result from several factors. One agent is direct trauma from the injection needle; bevel design and needle size are probably important factors.

The effects of bevel configuration upon perineural injury were examined by Selander, Dhuner and Lundborg [1], although others [2] have modified needle design, to reduce the risk of intraneural injection. Using a method of assessing fascicular injury by measuring the permeability of the perineurial sheath, Selander's group found that the frequency of lesions was greater when a long, as opposed to short, bevelled (45°) needle was used. All the nerves were prepared within 2 h of injury, so the effects of intraneural ischaemia and fibre de- and regeneration were not observed. Despite the limitations of that study, the recommendation was made "that a 45° bevelled needle less frequently produces fascicular damage and should therefore be recommended for use in clinical anaesthesia" and current practice reflects this [3].

However, although Selander, Dhuner and Lundborg [1] did not measure severity of injury to intrafascicular structures, the observation was made: "when this needle (short bevelled) pierced the fascicle with the bevel parallel to the fibres, it seemed to produce somewhat more damage than the long bevelled needle of the same orientation". In microneurography experiments, when electrodes are inserted into human nerves, the symptoms of nerve damage are not apparent until 48–72 h after the injury [4–6]. Others [7] have highlighted the late onset of symptoms after nerve trauma during regional anaesthesia. The experiments presented here examined the histological, functional and behavioural effects of impalement of the rat sciatic nerve observed either within 30 min of injury, or at 7 or 28 days after injury. Long and short bevelled needles were used.

MATERIALS AND METHODS

Needles

We examined two types of injection needle commonly used in anaesthetic practice: a 23-gauge (o.d. 0.63 mm) injection needle with a long (12°) double bevelled cutting edge (Becton Dickinson Microlance 000800) (LB) and a 22-gauge (o.d. 0.71 mm) short (27°) bevelled needle of the type used in regional anaesthesia (Becton Dickinson Ref: 008384) (SB). Both needles were studied with the bevel inserted parallel and transverse to the direction of the nerve fibres.

Animals

Wistar rats of both sexes, weight 142–380 g, were anaesthetized for all surgical procedures. For the recovery experiments, pentobarbitone 40 g kg^{-1} i.p. was used and aseptic procedures followed. After surgery, the wound was closed in layers and recovery was uneventful in all cases. For terminal experiments urethane 1.0–1.25 g kg^{-1} i.p. was used as the anaesthetic agent and a lethal dose was administered at the end of the experiment.

The sciatic nerve was exposed bilaterally from the

This article is accompanied by Editorial I.

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dorsal aspect and the needle introduced into the nerve at mid thigh level at an angle of 45° and left undisturbed for 10 min. The insertion site was marked by light application of carbon suspension on the surface of the nerve [8].

Histology

The animals were killed and a length of sciatic nerve was excised, with an adequate clearance each side of the injury site, either immediately after nerve injury or on the 7th or 28th day after operation. The excised nerves were stored under 4% formal saline. They were then embedded and frozen and longitudinal sections of 50 μm thickness were cut. These were passed through serial alcohols and xylene to remove lipids, then stained in neutral red for 12 min and subsequently dehydrated in serial alcohols and xylene. The sections were examined by light microscopy. All sections were assessed by the same observer who was unaware of which type of needle had been inserted into the nerve.

The sections were examined individually for signs of nerve injury, using three different criteria:

Intraneural disruption. This was defined as the degree of disruption to the internal elements of the nerve and included such factors as the reaction at the site of injury, the gliosis. It was scored on a 0–5 scale, 0 representing no intraneural disruption and 5 representing complete loss of identifiable intraneural elements at the site of injury.

Evidence of axonal degeneration distal to the insertion site. This was observed only in sections taken at either 7 or 28 days. It was scored on a present or absent basis (yes/no). This type of lesion implies axonal injury, without necessarily indicating a lesion of severity sufficient to destroy the supporting structure of the nerve.

Evidence of disorganized regeneration of fibres. This was also observed only in sections taken at either 7 or 28 days after injury and was scored also on a present or absent basis. This pattern of nerve fibre regeneration implies that, not only had axonal damage occurred, but the lesion was of a severity sufficient to damage the supporting structure of the nerve. This pattern of regeneration may result in neuroma formation. Indeed, in nerves displaying these features, gross neuromas-in-continuity were often observed during dissection.

Any experiment which relies upon observation of histological preparations has an inherent degree of subjectivity on the part of the observer, therefore we were unwilling to place undue emphasis on any one histologically observable feature of nerve fibre damage. Consequently, we constructed a global assessment of nerve fascicle injury (which had sufficient security to enable statistical analysis to be performed), in the form of summed nerve injury scores. The data from the intraneural disruption, axonal degeneration and disorganized regeneration observations, in addition to observations of epineural disruption (scored in the same manner as intraneural disruption), were used to calculate the summed nerve injury score. For each needle and bevel configuration at each time point (immediately after injury and at 7 or 28 days), a table of high and low score point allocation was constructed. When each nerve was assessed by the blinded observer, one point was allocated to the low score table if the epineural or intraneural disruption score was less than 2.5 or when no evidence of axonal degeneration or disorganized fibre regeneration was observed. The converse applied to point allocation to the high score group.

Comparison was made using the chi-square test with the Yates' correction.

Extravasation test

This test assessed the functional integrity of the unmyelinated afferent nociceptive fibres, which are generally of a size beyond the resolution of light microscopic techniques. When these neurones are activated by peripheral stimulation or by antidromic nerve stimulation, they release agents which cause vasodilatation and oedema in the peripheral tissues, as observed in the triple response of Lewis. It is possible to quantify the degree of neurogenic oedema produced by measuring the extravasation of the dye Evans's Blue, as described fully elsewhere [9, 10].

Needle penetration (once only, per animal) was performed at the sciatico–sural junction. When positioned, the needle was left *in situ* for 10 min, undisturbed, before withdrawal. All animals underwent sham exposure of the contralateral sciatic nerve, as a control.

Immediately, 7 or 28 days later, both sciatic nerves were exposed from the dorsal aspect. The sciatic nerve was crushed proximally, as were all its distal branches, with the exception of the sural nerve. Both test and control sciatic nerves were mounted on bipolar silver hook electrodes, proximal to the site of impalement. Five minutes after an i.a. infusion of Evan's Blue dye 50 mg kg^{-1}, the nerve was stimulated electrically. Square wave impulses of 5 MA amplitude and 500 μs duration were delivered at a frequency of 2 Hz for 10 min. The impulses in the unmyelinated afferents were conducted peripherally, where they caused agents to be released which resulted in oedema and extravasation of Evan's Blue. Division of C fibres obtunds this effect. The amount of extravasated Evan's Blue in the skin innervated by the sural nerve was measured. Five minutes after stimulation was complete, the animals were killed and transcardially perfused with 0.9% saline 100 ml. This perfusion ensured that the Evan's Blue was flushed from the intravascular compartment, but did not remove the extravasated dye. The sural-innervated skin was dissected bilaterally, weighed and stored in 4 ml of a filtered 70:30 extraction mixture of acetone and sodium sulphide 0.5 g $litre^{-1}$ [9, 10]. The concentration of Evan's Blue dye extracted into the solution was measured by spectrophotometry at a wavelength of 620 nm in glass cuvettes [11] and the concentration of dye in sural skin calculated. Baseline values were obtained from eight animals which had no surgery performed on either limb. Results were expressed as ratios of Evan's Blue concentrations in test to control limbs for each animal and compared with baseline ratios using Student's *t* test for unpaired data.

TABLE I. *Histological features of nerve injury caused by long (LB) and short (SB) bevelled needles aligned both parallel (p) and transverse (t) to the direction of nerve fibres. Mean (SEM) intraneural disruption scores immediately after (day 1) and at 7 and 28 days after injury (scored on a scale of 0–5 (see methods)); percentage of nerves which were observed to display features of axonal degeneration at 7 and 28 days after injury; percentage of nerves which were observed to display features of disorganized regeneration at 7 and 28 days after injury*

	Intraneural disruption score	Axonal degeneration (%)	Disorganized regeneration (%)
Day 1			
LB(p)	1 (0.58)	—	—
LB(t)	4 (0.3)	—	—
SB(p)	2.5 (0.42)	—	—
SB(t)	3.75 (0.72)	—	—
Day 7			
LB(p)	1.25 (0.43)	0	50
LB(t)	3.5 (0.37)	50	100
SB(p)	4 (0.25)	100	100
SB(t)	4.25 (0.28)	75	100
Day 28			
LB(p)	0.67 (0.16)	0	0
LB(t)	1.33 (0.16)	100	0
SB(p)	4.25 (0.14)	100	100
SB(t)	3.25 (0.49)	75	75

Limb withdrawal test

The hind limb flexion reflex withdrawal time after foot immersion in water at 49 °C was measured, in order to assess the integrity of both the afferent and efferent limbs of the reflex arc associated with the response to a noxious stimulus and its spinal processing. The left sciatic nerve was used as the test side and the right sciatic nerve was exposed in a sham operation, as a control.

Under anaesthesia, a single needle was inserted into the left sciatic nerve, just proximal to the sciatico-sural junction. The needle was left *in situ*, undisturbed, for 10 min, then withdrawn and the wound closed.

The animals were examined before and at 1, 3, 7, 14, 21 and 28 days after needle insertion. They were observed initially for the presence of any gross motor deficits and behaviourial abnormalities as they moved around their cages. They were inspected for evidence of autotomy, as described by Wall, Scadding and Tomkiewicz [12].

The lateral border of the foot was immersed in hot water (49 °C) and the time for the animal to actively withdraw the limb was measured. The test and control sides were tested alternately. The first readings from each side were ignored and then three subsequent readings for each side were taken; from these values, test and control side means were calculated. The withdrawal times were expressed as a difference between the test and control means. Therefore, a positive score may be taken to represent hypoalgesia of the test side (i.e. a test time of longer duration than observed with the control). Conversely, a negative score may be taken to represent hyperalgesia of the test side. Statistical comparison with baseline values was made using Student's *t* test for paired data.

RESULTS

Histology

Fifty-six animals were studied; 19 were killed immediately after injury, 19 at 7 days and 18 on the 28th day after operation. The limitations of placing excessive emphasis upon one histological feature of nerve fibre injury were outlined in the methods section. However, such data are shown here so that the trends may be observed, before examining the global assessment of nerve fibre injury, which was subjected to statistical analysis.

Table I shows the mean scores for intraneural disruption and the frequency of axonal degeneration and disorganized regeneration. The LB needles, when the bevel was aligned in a parallel fashion, appeared to induce less intraneural damage than the SB needles of either orientation or the LB transverse needle, both immediately after injury and 7 days later. However, by 28 days the injuries caused by the LB needle (both orientations) appeared to be resolving, whereas both orientations of the SB needle displayed evidence of continuing processes. When the frequency of distal axonal degeneration was examined, this feature was observed only in sections taken from animals killed at 7 and 28 days after surgery. This pattern of injury was not observed in nerves impaled by the LB needle when its bevel was aligned parallel to the nerve fibres. Axonal degeneration was apparent in nerves impaled by all other types of needle insertion and there appeared to be no clear difference between the SB and the LB transverse needles. With regard to the frequency of disorganized and random regrowth of axons, as this is a regenerative process it was also observed only in the sections taken at 7 and 28 days after impalement. Although this feature was apparent 7 days after all types of needle injury, the LB parallel needle appeared to induce such changes with the least frequency. By 28 days neither orientation of the LB needles induced these changes. In contrast, most nerves impaled by the SB needles exhibited such changes both at 7 and 28 days.

The summed nerve injury scores are displayed in figure 1. Statistical comparison was made using the chi-square test with Yates' correction. The trend observed in the above data was that the LB parallel needle appeared to induce the least severe nerve

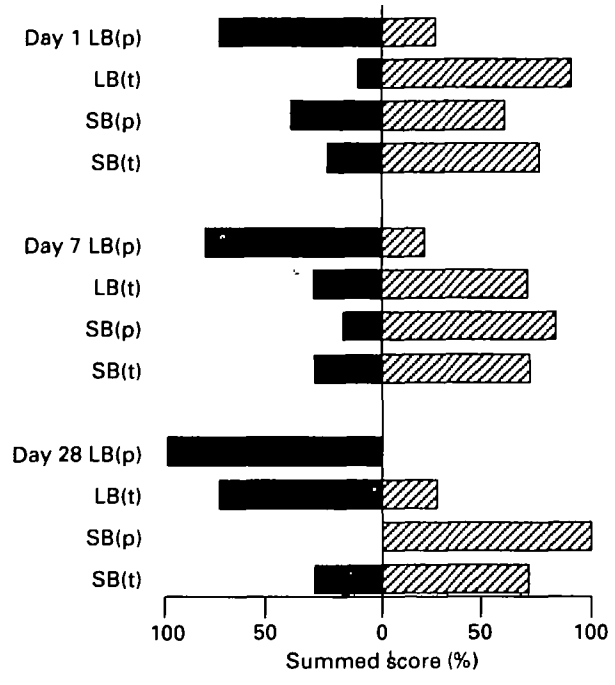

FIG. 1. Summed nerve injury scores obtained from rat sciatic nerves examined immediately after (day 1) and at 7 and 28 days after nerve impalement by long and short bevelled injection needles aligned parallel (p) or transverse (t) to the direction of nerve fibres. The x axis represents the percentage of summed nerve injury scores for each type of needle and each time point. The percentage of high scores (▨) (see methods for greater detail) are shown to the right of the midline and the percentage of low scores (■) to the left.

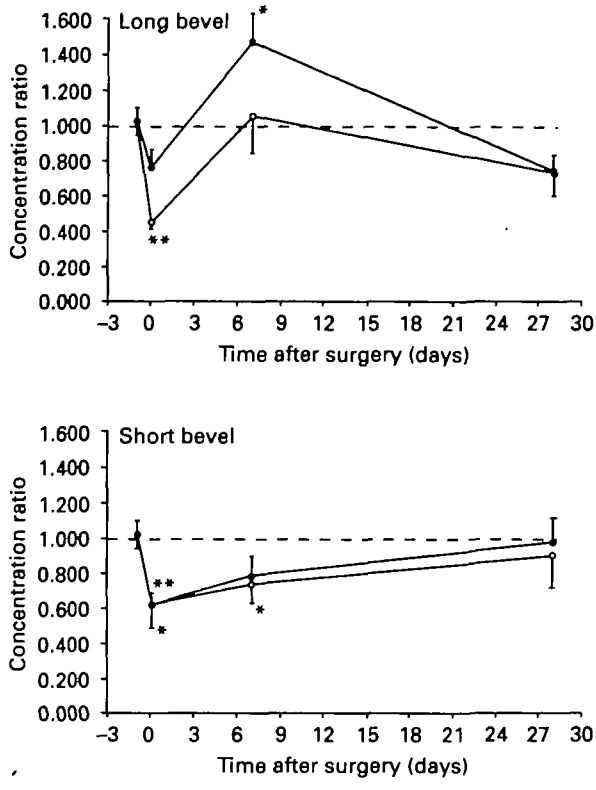

FIG. 2. Concentration of Evan's Blue dye extravasated into the skin innervated by the sural nerve after electrical antidromic stimulation of afferent C fibres. The results are expressed as the mean (SEM) ratio of the concentrations in test and control limbs, plotted against time (days following impalement with injection needles). ● = Transverse orientation of needle; ○ = parallel orientation. *$P < 0.05$; **$P < 0.01$ between groups (unpaired t test).

injury, therefore comparisons were made with the summed nerve injury data from this needle.

Immediately after nerve injury there was little difference between the summed nerve injury scores, although transverse orientation of the LB needle was associated with greater scores than when the same needle was introduced in a parallel manner (LB parallel *vs* LB transverse: $P < 0.05$; LB parallel *vs* SB parallel: $P < 0.5$; LB parallel *vs* SB transverse: $P < 0.5$). However, at 7 days after injury, the LB parallel needle achieved significantly smaller summed nerve injury scores compared with the other needles (*vs* LB transverse: $P < 0.05$; *vs* SB parallel: $P < 0.01$; *vs* SB transverse: $P < 0.05$). By 28 days there was no significant difference between the LB needle summed nerve injury scores, which were significantly less than SB needles scores (*vs* LB transverse: $P < 0.5$; *vs* SB parallel: $P < 0.01$; *vs* SB transverse: $P < 0.01$). Signs of injury after nerve impalement with the SB needle persisted for longer than after the LB needle-induced injury. When bevel orientation was ignored and the summed scores were combined for each type of needle, there was no significant difference ($P > 0.5$) between LB and SB needles immediately after nerve impalement, but the LB needles were associated with significantly smaller scores at 7 ($P < 0.01$) and 28 days ($P < 0.01$).

In summary the LB needle, when introduced with the bevel aligned parallel to the direction of passage of nerve fibres, generally induced injury less frequently and such lesions were less severe and more rapidly repaired injury than lesions caused by the other needles. There was persistence of the structural changes after SB needle-induced nerve injury 28 days after nerve impalement.

Extravasation

Results from 63 animals were included in the analysis. Eight animals were in the control (baseline) group, 20 animals were killed immediately after injury and 17 and 18 on the 7th and 28th days after operation, respectively.

The data were analysed by comparing the concentration of Evan's Blue in the sural skin of the operated limb (test) with that in the contralateral sham operated limb (control) and the result expressed as a ratio (fig. 2). Both orientations of the SB needle and the parallel orientation of the LB needle caused a significant decrease in extravasation of Evan's Blue immediately after nerve injury. There was no significant change with the LB transverse needle. At 7 days after injury, the LB parallel and SB transverse groups showed no significant change from baseline readings, but the SB parallel and LB transverse differed significantly from baseline values. In the case of the LB transverse needle, there was a period of increased extravasation at 7 days. It is not clear why this increase occurred, but it could possibly reflect overproduction of neuropeptides, which mediate this action, as part of the repair process. The results of the flexion withdrawal test also showed

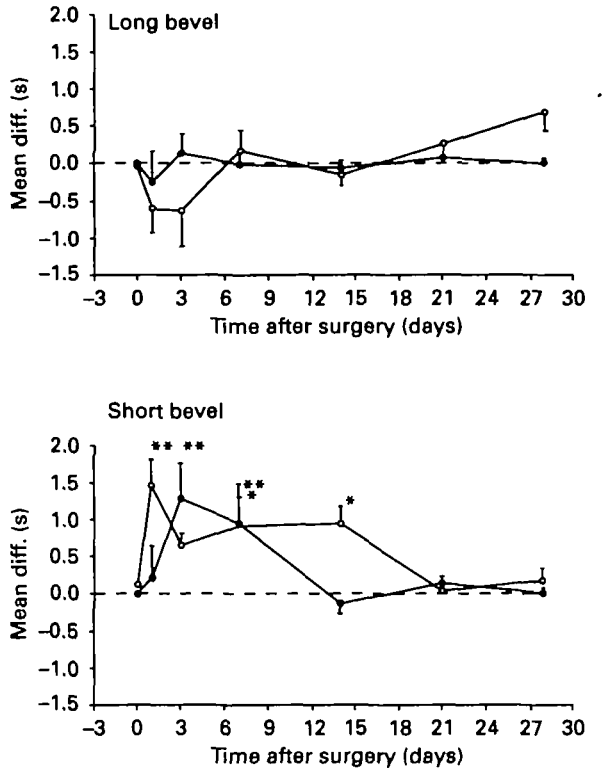

FIG. 3 Mean (SEM) differences between test and control limb flexion withdrawal times up to 28 days after nerve impalement by injection needles. ● = Transverse orientation of needles; ○ = parallel orientation. $*P < 0.05$; $**P < 0.01$ between groups (paired t test).

differential effects. By 28 days none of the needles was associated with a significant change in Evan's Blue extravasation from baseline values, indicating a return of nociceptive neurone function to normal.

Behavioural tests

Results from 40 animals were included in this section, of which 20 were killed after the measurement taken on the 7th day after operation. There was no evidence of autotomy, motor defects or abnormal behaviour in any animal at any time.

The results of the foot withdrawal test are shown in figure 3. There were no significant changes in the flexion withdrawal response at any time after the LB needle was used. In contrast, both orientations of the short bevelled needles produced significant differences in response lasting up to about 2 weeks, but these had also returned to normal by 28 days. The direction of the changes observed with the SB needle suggest that the skin innervated by the impaled nerve became hyposensitive. The changes with the SB needle were therefore significantly more severe and resolved after a longer period than did injuries resulting from nerve impalement by the LB needle.

DISCUSSION

The results of these experiments suggest that when nerve fascicles are impaled by commercially available injection needles (of similar diameter), lesions occur less frequently, are less severe and are repaired more rapidly if they are induced by an LB needle compared with an SB needle. The least traumatic bevel orientation occurred when an LB needle was introduced with its bevel parallel to the course of the nerve fibres. Persistence of signs of injury were apparent 1 month after SB needle impalement and such lesions tended to regenerate in a disorganized fashion.

The results of this study would appear to disagree with the other study [1] which has examined this subject. However, there is a fundamental difference between the two studies, which should be noted when a comparison is made: Selander, Dhuner and Lundborg [1] examined the frequency of injury to the perineural membrane, which surrounds nerve fascicles, after nerve trunk impalement. We have examined the frequency, severity and consequences of injury to fascicular contents after *in vivo* impalement of nerve fascicles.

Selander and his colleagues [1] examined the frequency of lesions in the nerve fascicles of an isolated rabbit sciatic nerve, using 14° and 45° (ground from 14°) bevelled needles inserted both parallel and transverse to the course of nerve fibres. They used a technique of assessing fascicular injury, which estimated the integrity of the perineurium by the transfer of Evan's Blue across this membrane. They also performed a similar experiment with the nerve intact in an *in vivo* model, but the animals were killed only 2 h after nerve injury. Perineural lesions were more frequent with the LB needles but, although severity of injury was not formally assessed, the authors did remark that the SB parallel needle: "seemed to produce somewhat more damage than the LB needle of the same orientation." When the *in vivo* model was examined, there was less fascicular injury with both needles and both bevel orientations, probably because of fascicular sliding, but there was still a greater frequency of perineural injury with LB needles. In the *in vivo* studies, intraneural haemorrhage was observed with both needles, but severity of injury was not discussed.

There are further differences between this and the study by Selander's group [1] which should be considered. Different animal models were used: the rabbit sciatic nerve preparation used in the earlier study is multi-fasciculated and the authors observed sliding of fascicles away from the tip of the needles. They discussed the significance of this and postulated that it may have been a factor in the differing frequency of fascicular injury after the use of SB and LB needles. The rat sciatic nerve used in our study consists of only one fascicle at mid-thigh level and nerve (fascicle) penetration was ensured in all cases. Although there was a direct comparison between the two needle types, there was no control group in Selander's study, to validate the sensitivity of the experimental methods and the effects of surgery; 50% of the preparations were *in vitro* isolated nerves so that the effects of ischaemia, haematomata etc. were not apparent. In the *in vivo* part of the same study, intraneural haematomata were certainly observed and the results of this section of the study may also have been confused by the use of an intraneural injection of 0.05 ml of Evan's Blue. It has been

shown subsequently that the intraneural injection of volumes as small as 100–50 μl may generate intraneural pressures which may exceed capillary perfusion pressure for as long as 10 min and thus cause neural ischaemia [13]. The results were confused further by intrafascicular injection of dye in six cases.

In human microneurography, the symptoms of nerve injury do not generally develop immediately after the injury, but may have their onset several days later [4, 5]. Supporting evidence is given in animal studies [6, 8]. Löfström [7] also observed that there was a delay in the onset of symptoms after accidental nerve injury during regional anaesthesia. For these reasons, we examined the effects of nerve injury for 28 days after impalement. Selander, Dhuner and Lundborg did not extend their study into this period [1].

Selander's study may also have been complicated by the fact that, for the *in vitro* study [1], needles of differing diameters were used and the reader is not informed in which bevel group the larger needles were used. Another study has demonstrated the effect of needle size on the frequency and severity of nerve injury [6]. The present study used a consistent and similar size of needle (commercially available) in each group.

Whilst this study demonstrates some advantages of using LB needles in respect of nerve injury, it has not examined the fact that sharper and therefore longer bevelled needles are more comfortable for the patient [14]. This fact was appreciated by the pioneers of regional anaesthesia [15].

In conclusion, this study provides evidence from several different experiments which show that, should accidental nerve fascicle penetration occur, then the frequency, severity and time course of intrafascicular injury would be greater when SB, as opposed to LB, needles were used. Therefore, we cannot confirm the suggestion of Selander, Dhuner and Lundborg [1] that "a 45° bevelled needle less frequently produces fascicular damage and should therefore be recommended for use in clinical anaesthesia". Indeed, the results of our study suggest that there may be grounds for recommending the use of LB needles, especially if the bevel is aligned parallel to the nerve fibres.

The ability of various types of bevel configuration to impale human nerves and their fascicles in the clinical (percutaneous, as opposed to the *in vitro* or surgically exposed) setting, remains to be ascertained. We were unable to locate any reported human study which demonstrates a lesser incidence of nerve injury symptoms after regional anaesthesia performed with SB compared with LB needles, whether or not paraesthesiae were elicited. Therefore, clinical studies should be performed before any definite recommendations can be made regarding the use of differently configured needles in regional anaesthesia. However, the longer regenerative period and high incidence of disorganized fibre regeneration after injury with SB needles must give particular cause for concern. The optimum bevel configuration of needles used in human regional anaesthesia remains to be ascertained.

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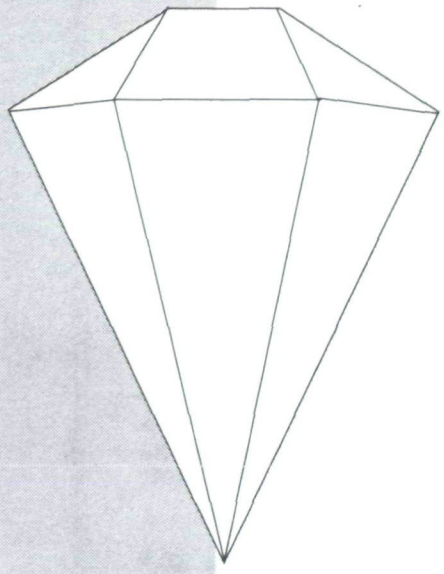

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