

# **New Insights of Anesthesia for Shoulder Surgery**

Alain Borgeat\*

Department of Anaesthesiology, Orthopaedic University Clinic Zurich/Balgrist, Zurich, Switzerland

Early and efficient rehabilitation is a new and widely accepted necessity to improve the success of shoulder surgery. Pain, which is severe to very severe in this condition, is the main factor limiting early rehabilitation. The modified lateral technique is, in our opinion, the safest approach to perform interscalene block. The occurrence of severe complications, such as spinal or epidural anesthesia for example, is reduced as compared to the classic Winnie's approach. Moreover, the insertion of a catheter is more difficult with the latter technique. Performance of the block in an awake or lightly sedated patient with a short-bevelled needle and the aid of a nerve stimulator, will increase the safety of the procedure. After shoulder surgery, regional analgesia provided through an interscalene catheter is a simple, better and safer technique than iv. PCA with morphine. The interscalene catheter seems not to increase the incidence of complications and patients' acceptance and satisfaction are greater than with any other analgesic techniques. Thus, continuous interscalene anesthesia/analgesia should have a place of first choice in the armamentarium of those anesthesiologists involved in the management of shoulder surgery.

Key words: Shoulder surgery, Interscalene block, Modified lateral technique, Postoperative analgesia.

There has been renewed interest in regional anesthesia for the past 10 years, due to the availability of new drugs, new materials and the results of studies demonstrating some major advantages linked with the application of central or peripheral blocks. Indeed, the control of pain is not only necessary for the patient's well-being, but it also has a positive impact on the outcome of surgery, as recently shown by Capdevila et al.<sup>1</sup>, who demonstrated that regional analgesia techniques improve rehabilitation after major knee surgery. The link between anesthetic/analgesic techniques and surgical outcome is a new challenge of major importance for the anesthesiologist.

Postoperative pain is a major concern after orthopedic limb surgery. One of the characteristics of this pain is its dynamic component. Indeed, pain is exacerbated on movement, particularly after shoulder and knee surgery. From moderate at rest, pain becomes most severe during rehabilitation. Pain is a serious problem after shoulder surgery. Up to 70% of patients reported severe pain on movement after open major joint surgery (shoulder and knee), which is more than after hysterectomy (60%), gastrectomy or thoracotomy (60%)<sup>2</sup>. The reason is that

Received: January 25, 2007; Accepted: February 5, 2007 \*Corresponding author: Alain Borgeat, Chief of Staff Anaesthesiology, Orthopaedic University Clinic of Zurich/Balgrist, Forchstrasse 340, CH-8008 Zurich/Switzerland. Tel.:+41-386-11-11; Fax:+41-386-16-09; E-mail: alain. borgeat@balgrist.ch

Communicated by Chen-Hwan Cherng

major joint operations entail massive nociceptive input from the richly innervated joint tissues that produce continuous deep somatic pain and bouts of severe reflex spasm of muscles supplied by the same and adjacent spinal cord segments supplying the site of surgery<sup>2</sup>. Moreover, periarticular structures exhibit not only C afferents but also Aalpha and A-delta afferents<sup>3</sup>, the latter being poorly blocked by opioids<sup>4</sup>. Adequate control of pain is crucial in modern orthopedics since early rehabilitation is necessary for success after major open orthopedic surgery<sup>5,6</sup>. This review will emphasise on the most adequate techniques available to provide the best conditions for the patient in terms of peri- and postoperative pain control and to meet the modern surgical orthopedic requirements in terms of favorable conditions for surgery and early and efficient rehabilitation.

#### **ANATOMY**

Anesthesiologists involved in regional anesthesia have to be familiar with the anatomy of the brachial plexus. Understanding relevant brachial plexus anatomy, ensuring precise needle location within the plexus diffusion space, and injection of appropriate local anesthetic volumes are fundamental in achieving high success rates with brachial plexus anesthesia. The plexus is formed by the ventral rami of the fifth to eighth cervical nerves and the greater part of the ramus of the first thoracic nerve. Additionally, small contributions may be made by the fourth cervical and the second thoracic nerves. The anatomy becomes complex because of the multiple connections to these ventral rami

after they emerge from between the middle and the anterior scalene muscles until they end in the terminal nerves of the upper extremity. However, most of what happens to these roots on their way to becoming peripheral nerves, is not clinically essential information to the anesthesiologist. Some broad concepts as the spatial arrangement of the trunks (superior, middle and inferior) and their implication in the muscular response elicited with the aid of the nerve stimulator, may help clinicians. When performing interscalene block of the brachial plexus, one has to remember some anatomical tricks, such as for example the suprascapular nerve leaving the superior trunk very early and the origin of the supraclavicular nerve (C3-4), these two nerves being important to be successfully blocked for shoulder surgery in awake patients (arthroscopic procedures).

The brachial plexus supplies all the motor and most of the sensory functions of the shoulder except the cephalad cutaneous parts of the shoulder, which are innervated by the supraclavicular nerves, originating from the lower part of the superficial cervical plexus (C3-C4). They supply sensation to the shoulder in that area described by their name, the area above the clavicle in addition to the first two intercostal spaces anteriorly. Further, they supply sensation to the posterior cervical triangle and the upper thorax in this area as well as to the tip of the shoulder<sup>7</sup>.

Only three nerves of the brachial plexus have cutaneous representation in the shoulder. The most proximal of these is the upper lateral brachial cutaneous nerve, a branch of the axillary nerve that innervates the lateral side of the shoulder, and the skin overlying the deltoid muscle. The upper medial side of the arm is innervated by both, the medial brachial cutaneous and the intercostobrachial cutaneous nerves. In the anterior portion of the arm over the biceps muscle, the skin is innervated by the medial antebrachial cutaneous nerve<sup>7</sup>.

Apart from the cutaneous nerve supply to the shoulder the innervation of the joint deserves special consideration. In general the nerves crossing a joint give branches that innervate it. Therefore the nerves supplying the ligaments, capsule, and synovial membrane of the shoulder are fibers from the axillary, suprascapular, subscapular and musculocutaneous nerves<sup>8,9</sup>. The relative contributions of these nerves are not constant and the supply from the musculocutaneus nerve may be very small or completely absent.

Anteriorly the axillary nerve and suprascapular nerve provide most of the nerve supply to the capsule and glenohumeral joint. In some instances, the musculocutaneous nerve may innervate the anterosuperior portion of the joint. In addition, the anterior capsule may be supplied by either the subscapular nerves or the posterior cord of the brachial plexus after piercing the subscapularis muscle. Superiorly, primary contribution is from two branches of the suprascapular nerve, one branch supplying the acromioclavicular joint and proceeding anteriorly as far as the coracoid process and coracoacromial ligament, the other branch reaching the posterior aspect of the joint. Other nerves contributing to this region of the joint are the axillary nerve and musculocutaneous nerve. Posteriorly, the chief nerves are the suprascapular nerve in the upper region and the axillary nerve in the lower region. Inferiorly, the anterior portion is primarily supplied by the axillary nerve, and the posterior portion is supplied by a combination of the axillary nerve and lower ramifications of the suprascapular nerve.

## REGIONAL ANESTHETIC TECHNIQUES

Successful neural blockade of the upper extremity requires extensive anatomic knowledge of the brachial plexus from its origin to its termination in the distal peripheral nerves of the hand. The interscalene approach to the brachial plexus is best suited to surgery of the shoulder<sup>10,11,12</sup> where a block of the lower cervical plexus is also desirable.

Several approaches for interscalene block have been published. Use of a nerve stimulator or elicitation of paraesthesias are possible techniques to place the local anesthetic solution accurately. The techniques of Winnie, Pippa, Meier and finally the modified lateral technique, which is used in our institution, will be described.

## Winnie's Approach

The classical approach of Winnie<sup>13</sup> is performed at the level of the sixth cervical vertebra using originally the paraesthesia technique. The patient is placed in a supine position with the head turned away from the side to be blocked. Then he is asked to elevate the head slightly in order to bring the clavicular head of the sternomastoid muscle into prominence.

A right-handed anesthesiologist should place the index and middle fingers of the left hand immediately behind the lateral edge of the sternomastoid muscle and instruct the patient to relax so that the palpating fingers move medially behind this muscle and finally lie on the belly of the anterior scalene muscle. They are then rolled laterally across the belly of this muscle until the interscalene groove is palpated. With both fingers in the interscalene groove, a 22-gauge, 1 ½ inch short-bevel needle is inserted between them at the level of C6, in a direction that is perpendicular

to the skin in every plane. The needle is advanced slowly until a paraesthesia is elicited or until the transverse process has been encountered. Only a paraesthesia below the level of the shoulder is acceptable, since a paraesthesia to the shoulder could result from stimulation of the suprascapular nerve inside or outside the interscalene space. If bone is contacted without producing a paraesthesia, this is likely the transverse process and the needle should be gently "walked off" anteriorly millimeter, by millimeter, until a paraesthesia is evoked. Once a paraesthesia (below the shoulder) has been obtained, aspiration is carried out to identify blood or cerebrospinal fluid. While the patient is monitored closely for signs of local anesthetic toxicity or inadvertent subarachnoid injection, 20-30 ml of local anesthetics is slowly injected.

Many complications have been reported with Winnie's technique, but the most serious are total spinal anesthesia <sup>14,15</sup>; epidural anesthesia <sup>16</sup> as well as injections into the vertebral artery and the cervical spinal cord<sup>17</sup>, which all can be attributed to the perpendicular direction of the needle towards the cervical spine. Furthermore, another serious, albeit infrequent complication - pneumothorax - has been associated with this technique. This technique is not well suited for the placement of an interscalene catheter.

### The posterior approach of Pippa

The posterior approach of Pippa<sup>18</sup> is performed using the loss of resistance technique and requires the following surface landmarks to be drawn on the skin.

The point of needle insertion lies approximately 3 cm lateral to the interspinous line C6 and C7 and corresponds to the upper edge of the transverse process of the seventh cervical vertebra.

After local infiltration of the skin at the point of needle insertion, a 21-gauge, 9-cm needle is inserted and directed perpendicular to the skin, through the trapezius, splenius cervices and levator scapulae muscles as far as the transverse process of the seventh cervical vertebra. The patient is then asked to turn his head to the contralateral side and the needle (attached to a 5-ml syringe filled with air) is passed over the transverse process and advanced slowly through the posterior and middle scalene muscle into the interscalene space, where a "loss of resistance" can be felt. The patient is then asked to move his head back to the original position. After negative aspiration for blood and cerebrospinal fluid the local anesthetic solution is injected. Apart from transient side-effects, like reduction of pulmonary function, and Horner's syndrome<sup>19,20</sup> serious complications with Pippa's technique have not been described. However, this technique represents a paravertebral approach to the brachial plexus and therefore may be associated with similar complications like Winnie's approach (e. g. total spinal or epidural anesthesia; injections into the vertebral artery or the cervical spinal cord).

# The modified lateral technique by Borgeat

Similar to the technique described by Meier et al.<sup>21</sup> our approach to the interscalene brachial plexus represents also a modification of the classical technique of Winnie. The positioning of the patient's head, the identification of the landmarks and the palpation of the interscalene groove are carried out in a similar way as described by Winnie. The palpation of the interscalene groove is crucial because it provides important information about its shape, depth and course at the lateral neck and helps the anesthesiologist to gain a three dimensional image of the interscalene space. After exact palpation we draw a line on the skin along the interscalene groove. Comparable to Winnie's technique, the point of needle insertion on this line lies on the level of the cricoid cartilage. We use a 5 cm, 22-gauge short bevel needle (Stimuplex A; B. Braun Melsungen AG). The needle is directed caudal and slightly lateral, or medial, according to the plane of the interscalene space. In order to minimise the risks of having some tissue between the tip of the needle and the nerve trunk, we try to place the tip of the needle in close proximity to the posterior - dorsal - part of the superior or middle trunk of the brachial plexus, to obtain preferentially a triceps response (C5, C6, C7 or C8). With the use of a nerve stimulator (Stimuplex-HNS II; B. Braun Melsungen AG, Melsungen, Germany) accurate placement of the needle can be achieved by eliciting twitches in the triceps muscle, occasionally in the deltoid. The position of the needle is considered appropriate if twitches are still present with a current output below 0.4 mA with an impulse duration of 0.1 mA. The use of this technique is associated in our institution with a success rate of more than 97%.

Our approach is suitable for single shot interscalene anesthesia as well as for continuous interscalene anesthesia/analgesia through an interscalene catheter. For the placement of an interscalene catheter we use the "cannula over needle" technique with a 3 or 5 cm, 21-gauge polyure-thane cannula (polymedic, Te me na, Bondy, France, 22 G with stylet) inserted over a 10 cm, 22-gauge short bevel needle (Stimuplex A; B. Braun Melsungen AG). After confirmation of appropriate needle placement into the brachial plexus as described above, the cannula is advanced over the stimulating needle until the tip of the cannula reaches exactly the tip of the stimulating needle, which lies in the interscalene space. After removal of the

needle a 20-gauge catheter with stylet (polymedic, Te me na, Bondy, France, 22 G) is inserted though the cannula 2 to 3 cm further into the interscalene space.

A subcutaneous tunnelling of the interscalene catheter is performed to avoid dislocation<sup>22</sup>. After skin infiltration with 3-4 ml of 1% lidocaine, an 18 gauge iv. cannula is inserted subcutaneously just above the suprasternal notch and then advanced cranially at an angle of 45 degrees to exit 3-4 mm above the primary catheter insertion point. The proximal end of the catheter is then threaded retrogradely through the iv. cannula, before the later is removed, so that the catheter finally is tunnelled 4-5 cm subcutaneously. The catheter is fixed as usual with dressing tapes.

With the use of the lateral modified technique, serious complications as seen with Winnie's technique, can be avoided, because the needle is directed away from the cervical spine towards the interscalene diffusion space. In a prospective study that included 521 patients<sup>23</sup>, one pneumothorax in a Marfan type like patient, and one intravascular injection were recorded as acute complications, but no cases of spinal or epidural injections occurred.

# LOCAL ANESTHETIC SOLUTIONS AND EXPECTED DURATION

The choice of the local anesthetic may depend on different factors including the type and nature of the surgical procedure, the need of early rehabilitation and the patient's wish to have a prolonged pain-free period. Recent studies 1 stressed the importance of early and efficient postoperative rehabilitation and therefore, good and prolonged control of pain is actually becoming mandatory to fulfil the surgical requirements<sup>5,6</sup>.

## **Bolus application**

Interscalene bolus is mainly indicated for arthroscopic procedures. Among the most often used local anesthetics are 1 or 2% mepivacaine, 1.5% lidocaine, 0.5% bupivacaine or 0.5 or 0.75% ropivacaine with or without epinephrine, opioids or clonidine.

The average volume of drug needed varies between 30 and 50 ml and has to be adapted first to the characteristics of the patient (size, weight, athletic profile ...) and second to the anesthetic technique, block alone or combined with general anesthesia. The expected duration of the block varies between 3 to 5 h with 1 or 2% mepivacaine and 1.5% lidocaine<sup>11,24,25</sup> and 8 to 12 h with 0.5% bupivacaine and 0.5 or 0.75% ropivacaine<sup>26,27,28</sup>. The duration of action is also proportional to the volume administered. Clonidine<sup>30</sup>, but not the opioids<sup>31,32</sup>, has a prolonged duration of both

anesthesia and analgesia. The addition of epinephrine may prolong the duration of action of short acting local anesthetics<sup>33</sup>, but the potential of worsening nerve ischemia must be kept in mind<sup>34</sup>. Singelyn et al.<sup>30</sup> demonstrated that a minimal dose of clonidine of 0.5  $\mu$  g/kg was necessary to have a clinically significant positive effect, reduced onset time and improved success rate. Brown et al.11 compared interscalene block to general anesthesia in shoulder arthroscopy. The authors found that interscalene block was safe and effective, providing excellent intraoperative analgesia and muscular relaxation, resulting in fewer postoperative side-effects, hospital admissions, a shorter hospital stay and a very high degree of patient's acceptance. Nowadays, a complete recovery of the motor blockade is no longer a requirement to enable the patient to be discharged from hospital<sup>35</sup>, making the long acting anesthetics more appropriate in this setting, even for day-care surgery. Shoulder surgery remains for most of the cases a very painful procedure. Some arthroscopic procedures like capsulotomy or acromioplasty can profit from an interscalene catheter, not only for pain control, but also for early and efficient rehabilitation. These procedures may well become good indications for patient controlled analgesia at home in the near future, a challenging matter now being investigated <sup>33,36</sup>.

### The interscalene catheter

The interscalene catheter has brought great progress to the management of postoperative pain therapy after major open shoulder surgery. Indeed, studies have shown that a continuous infusion of local anesthetics through an interscalene catheter as compared to traditional PCA with opioids, provides significantly better control of pain, with statistically lower incidence of side-effects and greater patient's satisfaction<sup>37,38,39</sup>. The interscalene catheter is indicated in almost all open shoulder surgeries, the rotator cuff repair being the "gold indication". According to the type of surgery performed, the catheter may be used for 3 to 5 days.

Due to the great amount of periarticular structures rich with nociceptors in the shoulder, postoperative pain is not only severe during movement, but also at rest, making a bolus technique alone inadequate in this context, as shown by Singelyn et al.<sup>39</sup>. The use of a continuous infusion of 0.125% bupivacaine at a rate of 0.125 ml/kg per h was shown to provide efficient pain relief, but at the cost of administrating a large volume of local anesthetics<sup>39</sup>. Moreover, a continuous infusion may not be the best way of administration for this purpose, since it does not comply with the dynamic nature of pain, which is moderate to severe at rest and severe to very severe during movement. The use of a

continuous infusion with supplemental boli seems to be more appropriate.

When compared to the continuous technique<sup>40</sup>, a lower basal infusion of 5 ml/h of 0.125% bupivacaine associated with small PCA boli of 2.5 ml/30 min provides similar pain control, but reduces the consumption of local anesthetics by 37% and lowers the incidence of side-effects, such as Horner's syndrome or clinically apparent phrenic paresis<sup>39</sup>. Borgeat et al. <sup>37,38</sup> have shown that both 0.15% bupivacaine or 0.2% ropivacaine at a rate of 5 ml/h with supplemental boli of 4 ml/20 min were associated with better pain control, lower incidence of nausea, vomiting and pruritus and better patient's satisfaction, as compared to the classical PCA with opioids. In the PCIA (patient controlled interscalene analgesia), all patients were extremely satisfied with the possibility to rapidly reinforce the block shortly before and after a physical therapy session. In our department we have switched from bupivacaine to ropivacaine, since we demonstrated<sup>41</sup> that PCIA with 0.2% ropivacaine compared to PCIA with 0.15% bupivacaine was associated with better preservation of hand strength 24 h and 48 h after the beginning of the infusion as well as 6 h after the infusion was stopped. The incidence of paraesthesias in the fingers 48 h after the start and 6 h after the end of the infusion was also significantly higher in the bupivacaine group.

Actually the application of the PCIA technique with a basal infusion and supplemental boli is the most appropriate technique for analgesia after major open shoulder/elbow surgery. The use of ropivacaine as compared to bupivacaine seems to have some advantages in terms of better sensorimotor dissociation<sup>42,43</sup>. The concentration of 0.2% ropivacaine is adequate for most patients, but has to be increased up to 0.3 or 0.4% in some others, particularly young, athletic patients - unpublished data .

# ADVANTAGES/IMPROVEMENT OF OUTCOME

There is more and more evidence that continuous analgesia through an interscalene catheter is becoming the "gold standard" to provide analgesia after major open shoulder surgery<sup>37,38,39</sup>. Better pain control, lower incidence of side-effects due to non- or decreased-need of opioids and greater patient's acceptance and satisfaction are the obvious known advantages of these techniques. Capdevila et al.<sup>1</sup> have shown that regional analgesic techniques improve early rehabilitation after major knee surgery by effectively controlling pain during continuous passive motion, thereby hastening convalescence. Indeed,

in this study, the authors found that duration of in-patient rehabilitation was significantly shorter in the epidural and femoral catheter groups, 37 and 40 days respectively, as compared to 50 days in the patient-controlled morphine group. A similar study looking at comparable end-points after major shoulder surgery is to date still not available. However, there is little doubt that analgesia provided by the interscalene catheter offers better conditions than any other technique to allow early and efficient rehabilitation, a must in modern orthopedic surgery.

Early and efficient rehabilitation should lead to a decrease of postoperative adhesions, capsule retractions and intra-articular deposits of fibrous tissue. These conditions should lead to better shoulder joint motion and to quicker rehabilitation. Future prospective studies should confirm these clinical impressions, that, as quoted by Todd and Brown, long-term recovery is facilitated by short-term postoperative regional analgesia<sup>44</sup>.

#### REFERENCES

- 1. Capdevila X, Barthelet Y, Biboulet P et al. Effects of perioperative analysesic technique on the surgical outcome and duration of rehabilitation after major knee surgery. Anesthesiology 1999;91:8-15.
- 2. Bonica JJ. Postoperative pain. In Bonica JJ (ed) The Management of Pain. Vol I, 2<sup>nd</sup> edn, pp 461-480, Philadelphia, Lea & Febiger, 1990.
- Bonica JJ. Anatomic and physiologic basis of nociception and pain. In Bonica JJ (ed) The Management of Pain. Vol I, 2<sup>nd</sup> edn, pp 28-94, Philadelphia, Lea & Febiger, 1990.
- Pirec V, Laurito CE, Lu Y & Yeomans DC. The combined effects of N-type calcium channel blockers and morphine on Aδ versus C fiber mediation nocicpetion. Anesth Analg 2001;92:239-243.
- 5. Salter RB, Simmonds DF, Malcolm BW. The biological effect of continuous passive motion on the healing of full-thickness defects in articular cartilage. An experimental investigation in the rabbit. J Bone Joint Surg 1980;62:1232-1251.
- 6. Salter RB. History of rest and motion and the scientific basis for early continuous passive motion. Hand Clinic 1996;12:1-11.
- 7. Hollinshead WH. Anatomy for surgeons, Vol. 3, 3<sup>rd</sup> edn. Philadelphia, Harper & Row, 1982.
- 8. DePalma AF. Surgery of the Shoulder, 3<sup>rd</sup> edn. Philadelphia, JB Lippincrott, 1983.
- 9. Gardner E. The innervation of the shoulder joint. Anat Rec 1948;102:1-18.

- Dekrey JA & Balas GI. Regional anesthesia for surgery on the shoulder: A review of 1500 cases. Der Anaesth 1981;30:46-48.
- 11. Brown AR, Weiss R, Greenberg C. Interscalene block for shoulder arthroscopy: Comparison with general anesthesia. Arthroscopy 1993;9:295-300.
- 12. D'Alessio JG, Rosenblum M, Shea KP & Freitas DG. A retrospective comparison of interscalene block and general anesthesia for ambulatory surgery shoulder arthroscopy. Reg Anesth 1995;20:62-68.
- 13. Winnie AP. Interscalene brachial plexus block. Anesth Analg 1970;49:455-466.
- Dutton RP, Eckhardt WF & Sunder N. Total spinal anesthesia as a compleation of interscalene block of the brachial plexus. Anesthesiology 1994;80:939-941.
- 15. Ross S and Scarborough CD. Total spinal anesthesia following brachial-plexus block. Anesthesiology 1973, 39:458.
- Scammell SJ. Inadvertant epidural anesthesia as a complication of interscalene brachial plexus block. Anaesth Intensive Care 1979;7:56-57.
- Benumof JL. Permanent loss of cervical spinal cord function associated with interscalene block performed under general anesthesia. Anesthesiology 2000;93: 1541-1544.
- 18. Pippa P, Cominelli E, Marinelli C & Aito S. Brachial plexus block using the posterior approach. Eur J Anaesth 1990;7:411-420.
- Dagli G., Güzeldemir EM & Acar HV. The effects and side effects of interscalene brachial plexus block by posterior approach. Reg Anesth Pain Med 1998;23:87-91
- Rucci FS, Pippa P, Barbagli R & Doni L. How many interscalenic blocks are there? A comparison between the lateral and posterior approach. Europen Journal of Anaesthesiology 1993;10:303-307.
- 21. Meier G, Bauereis Ch & Heinrich Ch. Der interscalenäre Plexuskatheter zur Anästhesie und postoperativen Schmerztherapie: Erfahrungen mit einer modifizierten Technik. Der Anaesth 1997;46:715-719.
- 22. Ekatodramis G & Borgeat A. Subcutaneous tunneling of the interscalene catheter. (Letter) Can J Anesth 2000;47:716-717.
- Borgeat A, Ekatodramis G, Kalberer F & Benz C. Acute and nonacute complcations associated with interscalene block and shoulder surgery. Anesthesiology 2001;95:875-880.
- 24. Tetzlaff JE, Yoon HJ, O'Hara J . Alkalinization of mepivacaine accelerates onset of interscalene block for shoulder surgery. Reg Anesth 1990;15:242-244.

- 25. Tackley RM & Coe AJ. Alkalinized bupivacaine and adrenaline for epidural caesarean section. Anaesthesia 1988;43:1019-1021.
- 26. Klein SM, Greengrass RA, Steele SM. A comparison of 0.5% bupivacaine, 0.5% ropivacaine, and 0.75% ropivacaine for interscalene brachial plexus block. Anesth Analg 1998;87:1316-1319.
- 27. Casati A, Fanelli G, Aldegheri G. Interscalene brachial plexus anaesthesia with 0.5%, 0.75% or 1% ropivacaine: a double-blind comparison with 2% mepivacaine. Br J Anaesth 1999;83:872-875.
- 28. Casati A, Fanelli G, Cappelleri G. A clinical comparison of ropivacaine 0.75%, ropivacaine 1% or bupivacaine 0.5% for interscalene brachial plexus anaeshesia. European Journal of Anesthesiology 1999; 16:784-789.
- Bernard JM & Macaire P. Dose-range effects of clonidine added to lidocaine for brachial plexus block. Anesthesiology 1997:87:277-284.
- Singelyn F, Gouverneur JM & Robert A. A minimum dose of clonidine added to mepivacaine prolongs the duration of anesthesia and analgesia after axillary brachial plexus block. Anesth Analg 1996;83:1046-1050.
- 31. Picard P, Tràmer M, McKay H & Moore R. Analgesic efficacy of peripheral opioids (all except intraarticular): a qualitative systematic review of randomised controlled trials. Pain 1997;72:309-318.
- 32. Bouaziz H, Kinirons BP, Macalou D. Sufentanil does not prolong the duration of analgesia in a mepivacaine brachial plexus block: a dose response study. Anesth Analg 2000;90:383-387.
- 33. Tetzlaff JE, Yoon HJ, Brems J & Javorsky T. Alkalinization of mepivacaine improves the quality of motor block associated with interscalene brachial plexus anesthesia for shoulder surgery. Reg Anesth 1995;20: 128-132.
- 34. Selander D, Brattsand R, Lundborg G. Local anesthetics: Importance of mode of application, concentration and adrenaline for the appearance of nerve lesions. An experimental study of axonal degeneration and barrier damage after intrafascicular injection or topical application of bupivacaine (Marcain). Acta Anaesth Scand 1979;23:127-136.
- 35. Klein SM, Grant SA, Greengrass RA. Interscalene brachial plexus block with a continuous catheter insertion system and a disposable infusion pump. Anesth Analg 2000;91:1473-1478.
- 36. Nielson K, Steele S, Klein S, Pietrobon R & Greengrass R. Continuous interscalene brachial plexus block at

- home after major shoulder surgery. Anesthesiology 2000;93:A15 (Abstract).
- 37. Borgeat A, Sch?ppi B, Biasca N & Gerber C. Patient-controlled analgesia after major shoulder surgery. Anesthesiology 1997;87:1343-1347.
- 38. Borgeat A, Tewes E, Biasca N & Gerber C. Patient-controlled interscalene analgesia with ropivacaine after major shoulder surgery: PCIA vs PCA. Br J Anaesth 1998:81:603-605.
- 39. Singelyn F, Seguy S & Gouverneur JM. Interscalene brachial plexus analgesia after open shoulder surgery: continuous versus patient-controlled infusion. Anesth Analg 1999;89:1216-1220.
- 40. Pere P. The effect of continuous interscalene brachial plexus block with 0.125% bupivacaine plus fentanyl on diaphragmatic motility and ventilatory function. Reg Anesth 1993;18:93-97.

- 41. Borgeat A, Kalberer F, Jacob H. Patient-controlled interscalene analgesia with ropivacaine 0.2% versus bupivacaine 0.15% after major open shoulder surgery: the effects on hand motor function. Anesth Analg 2001;92:218-223.
- 42. Rosenberg PH & Heinonen E. Differential sensitivity of A and C nerve fibres to long-acting amide local anaesthetics. Br J Anaesth 1983;55:163-167.
- 43. Wildsmith JA, Brown DT, Paul D & Johnson S. Structure-activity relationships in differential nerve block at high and low frequency stimulation. Br J Anaesth 1989;63:444-452.
- 44. Todd MM & Brown DL. Regional anesthesia and postoperative pain management. Anesthesiology 1999; 91:1-2.