



Editorial

Regional anaesthesia – the bride at last?

If you open your browser and search on ‘always the bridesmaid; never the bride’, you will find that one description of the meaning of this English saying is ‘a situation in which someone never achieves the success and recognition they crave and deserve’. For two people who have been calling themselves regional anaesthetists for 20–25 years, we feel that our chosen subspecialty has always been the bridesmaid but never the bride. However, the world may be changing, and there are reasons to believe that the next few years may see regional anaesthesia (RA) achieve some of its ambitions by being chosen by patients and anaesthetists alike, not just as a way of avoiding general anaesthesia (GA) for pregnant women or for elderly patients with multiple comorbidities, but by the majority because of its high success rate, excellent safety and side-effect profile and, perhaps most importantly, positive beneficial effects on outcome. It is perhaps a quirk of fate that although man knew of cocaine long before he synthesised ether, the introduction of GA by Morton predated the discovery of local anaesthesia by Koller by some 38 years. Regional anaesthetists have wasted much time theorising about what the world of anaesthesia would have become had the timing of these two events been reversed. However, as suggested above, the popularity of RA is inevitably related to its success rate, safety profile and effects on outcome, or at very least to anaesthetists’ perception of these.

It is axiomatic that ‘there are no patchy blocks with propofol’, although estimates of the incidence of accidental awareness during GA of 1:500 to 1:1000 seem to indicate otherwise [1]. The success rates of peripheral and neuraxial nerve blocks vary widely, depending upon the approach, the technique used and the experience of

the operator. Most published studies that seek to promote peripheral nerve blocks claim success rates > 90%, with some as high as 100% [2]. Hopes that the use of ultrasound-guided RA would be associated with higher success rates were trumpeted in the bold and declarative titles of studies claiming to support these hopes [3, 4]. However, recent publications comparing success rates with ultrasound guidance and nerve stimulation have produced results that are more equivocal [2], mirroring studies that failed to show a real advantage in terms of success rate of electrical nerve stimulation over the elicitation of paraesthesia [5]. Whatever the claimed success rates in the literature, the success rate of a given individual for a given block will never be 100%. It behoves regional anaesthetists to audit their success rates and communicate these honestly to their patients. There is no shame in having a success rate < 100%; our surgical colleagues spend a lot of their professional lives telling their patients that the success rates of their operations are < 100% and they are not thought inadequate as a result. At least we regional anaesthetists have a ‘Plan B’ for the vast majority of our patients: GA.

The safety of RA is a perennial topic of debate. Some of its complications can be termed ‘anatomical’, that is, they relate to the inadvertent placement of needle or local anaesthetic drug (LA) into a structure located close to the target nerve(s). Although the use of ultrasound guidance may be associated with a decreased incidence of ‘anatomical’ complications, hopes that its use would obviate these have been dashed [6, 7]. Accidental intravascular injection of LA is a constant concern, but genuine hope has been brought by the use of intravenous lipid treatment to treat patients who develop dangerous cardiac arrhythmia as a result [8]. An ongoing major concern to both regional anaesthetists and their ‘generalist’

colleagues is the capacity for RA to cause, or at very least be associated with, permanent nerve damage. Local anaesthetics in themselves are neurotoxic at clinically used concentrations [9], and the direct contact between needle and nerve is well recognised as a cause of damage to the fascicles of human peripheral nerves [10]. Although the incidence of temporary neurological dysfunction may be as high as 16% after upper limb nerve blocks [11], the incidence of permanent nerve damage is thought to be in the order of 1:5000 for most peripheral nerve blocks [12, 13]. Given that the incidence of post-operative neuropathy has been recorded as being 1:2700 after GA [14], the safety of peripheral nerves during RA could be said to compare favourably with that during GA. Debate about whether RA is safer or more dangerous than GA is unlikely to die out soon.

It may well be that we regional anaesthetists can put forward some cogent arguments in favour of RA in terms of success rate and safety. The enthusiastic, the inquisitive and the experimenters may be susceptible to such blandishments. However, to achieve widespread success, we will have to prove that RA has a positive effect on patients’ outcome that goes beyond a short period of excellent analgesia. The road to conclusive proof of improved outcome as manifested by a decreased mortality or major morbidity associated with RA techniques is littered with discarded hopes and inconclusive studies. A meta-analysis published in the *British Medical Journal* in 2000 excited the blocking community by claiming a significant 30% decrease in mortality associated with neuraxial techniques [15]. More, it also claimed that spinal and epidural anaesthesia was associated with decreases in postoperative pulmonary embolism, respiratory depression, myocardial infarction and renal failure. Cries of ‘quod erat demonstrandum’ from

regional anaesthetists were quickly stifled as flaws in the meta-analysis were alleged [16]. Great hopes were pinned on the results of the Australian MASTER study, but were again dashed when this large, prospective, randomised study of high-risk patients failed to show an advantage to the use of epidurals in terms of mortality, adverse cardiovascular events, renal failure or hepatic failure [17]. The publication of the results of the GALA trial, which sought to compare outcome after carotid endarterectomy under GA or RA, brought more disappointment: there was no definite difference in outcome between the two groups [18]. Drawing conclusions from their own systematic assessment of the literature, Liu and Wu opine that there is no current evidence that perineural analgesia has any clinically significant beneficial effect on postoperative complications. They also suggest that those benefits that have been shown to be associated with the use of epidural analgesia, such as faster resolution of postoperative ileus after major abdominal surgery and decreased pulmonary complications, may become irrelevant because of the rapid conversion of major surgery to minimally invasive techniques [19]. However, one point is worth making: in all the studies and meta-analyses that we have read in our many cumulative years of assessing the literature, we have found none that shows that RA is consistently worse than GA in terms of mortality and major morbidity, and some that suggest that it positively beneficial. While this informal assessment of the literature holds no meta-analytical weight, it seems to us suggestive of the benefits of RA.

If all that we can honestly say is that RA is reasonably successful, reasonably safe and might on occasion offer some patients outcome advantages in terms of mortality and major morbidity, have we any hope of drawing a significantly greater proportion of practising anaesthetists into the regional anaesthetic fraternity? There exists a distinct glimmer of hope in a small number of recently published papers. A retrospective analysis of 129 patients undergoing mastectomy for breast cancer under

either GA, or GA combined with intra- and postoperative continuous paravertebral blockade, suggested that those patients receiving regional analgesia experienced a lower incidence of tumour recurrence when followed up for up to 3 years [20]. Another retrospective study of patients undergoing radical prostatectomy under GA, or a combination of GA and epidural analgesia, showed that the latter group had an estimated 57% lower risk of recurrence [21]. Although both these studies are retrospective, and therefore prone to the many flaws commonly associated with such studies, they are both highly suggestive, and the group responsible for them is currently performing a prospective, multicentre study of whether regional analgesia can reduce the risk of recurrence after breast cancer surgery [22]. There has already been written conjecture about why RA may confer this sort of advantage [23], and this can be summarised thus: GA drugs and opioid analgesics impair cell-mediated immunity and may increase angiogenesis. The use of RA techniques, by obviating or reducing the need for GA and opioids, may preserve cell-mediated immunity and angiogenesis, thereby promoting control of the inevitable tumour cell load that is released into the body during cancer surgery. A recently published paper has offered some support to this theory. Serum taken from two groups of patients undergoing breast cancer surgery under GA, or GA with paravertebral analgesia, was added to cultured breast cancer cell lines *in vitro* [24]. The serum from the patients receiving regional analgesia reduced the proliferation of the cancer cells; that from the GA group patients did not. There may be great promise in this line of research.

As we look back at the first 126 years of RA, we are struck by how little has changed in this time: RA as a subspecialty still seems to be a minority interest and an art practised and appreciated by the few rather than by the many. It is, in a sense, still the bridesmaid. However, the longed-for proof of its substantial clinical benefit may not be in the area that we had anticipated, i.e. major postoperative morbidity and mortality.

It may derive from the previously overlooked area of beneficial modification – or rather preservation – of the body's immune processes. It may be that RA will become the standard technique for cancer surgery and that this growth in interest may trigger its increased use for surgery that is not aimed at malignant disease. It may be that when this is achieved, RA will at last truly be the bride. We look forward to that day.

W. Harrop-Griffiths

Consultant Anaesthetist, St Mary's Hospital, Imperial College Healthcare NHS Trust, London, UK
E-mail: harropg@mac.com

M. H. Nathanson

Consultant Anaesthetist, Nottingham University Hospitals NHS Trust, Nottingham, UK

Conflicts of interest

Dr Harrop-Griffiths has been paid for consultancy by AstraZeneca and B Braun and for lecturing by Abbott. Dr Nathanson has received honoraria from AstraZeneca for membership of advisory boards and has received honoraria from Abbott for presentations.

References

- 1 Sebel PS, Bowdle TA, Ghoneim MM, et al. The incidence of awareness during anesthesia: a multicenter United States study. *Anesthesia & Analgesia* 2004; **99**: 833–9.
- 2 Liu SS, Zayas VM, Gordon MA, et al. A prospective, randomized, controlled trial comparing ultrasound versus nerve stimulator guidance for interscalene block for ambulatory shoulder surgery for postoperative symptoms. *Anesthesia & Analgesia* 2009; **109**: 265–71.
- 3 Chan VW, Perlas A, McCartney CJ, Brull R, Xu D, Abbas S. Ultrasound guidance improves success rate of axillary brachial plexus block. *Canadian Journal of Anesthesia* 2007; **54**: 176–82.
- 4 Kapral S, Greher M, Huber G, et al. Ultrasonographic guidance improves the success rate of interscalene brachial plexus blockade. *Regional Anesthesia and Pain Medicine* 2008; **33**: 253–8.

- 5 Liguori GA, Zayas VM, YaDeau JT, et al. Nerve localization techniques for interscalene brachial plexus blockade: a prospective, randomized, comparison of mechanical paresthesia versus electrical stimulation. *Anesthesia & Analgesia* 2006; **103**: 761–7.
- 6 Koscielniak-Nielsen ZJ, Rasmussen H, Hesselbjerg L. Pneumothorax after an ultrasound-guided lateral sagittal infraclavicular block. *Acta Anaesthesiologica Scandinavica* 2008; **52**: 1176–7.
- 7 Zetlaoui PJ, Labbe J-P, Benhamou D. Ultrasound guidance for axillary plexus block does not prevent intravascular injection. *Anesthesiology* 2008; **108**: 761.
- 8 Picard J, Meek T. Lipid emulsion to treat overdose of local anaesthetic: the gift of the glob. *Anaesthesia* 2006; **61**: 107–9.
- 9 Kasaba T, Onizuka S, Takasaki M. Procaine and mepivacaine have less toxicity *in vitro* than other clinically used local anesthetics. *Anesthesia & Analgesia* 2003; **97**: 85–90.
- 10 Sala-Blanch X, Ribalta T, Rivas E, et al. Structural injury to the human sciatic nerve after intraneural needle insertion. *Regional Anesthesia and Pain Medicine* 2009; **34**: 201–5.
- 11 Borgeat A, Ekatodromis G, Kalberer F, Benz C. Acute and nonacute complications associated with interscalene block and shoulder surgery: a prospective study. *Anesthesiology* 2001; **95**: 875–80.
- 12 Auroy Y, Narchi P, Messiah A, Litt L, Rouvier B, Samii K. Serious complications related to regional anesthesia: results of a prospective survey in France. *Anesthesiology* 1997; **87**: 479–86.
- 13 Auroy Y, Benhamou D, Bagues L, et al. Major complications of regional anesthesia in France: the SOS regional anesthesia hotline service. *Anesthesiology* 2002; **97**: 1274–80.
- 14 Warner MA, Warner ME, Martin JT. Ulnar neuropathy: incidence, outcome and risk factors in sedated or anesthetized patients. *Anesthesiology* 1994; **81**: 1332–40.
- 15 Rodgers A, Walker N, Schug S, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. *British Medical Journal* 2000; **321**: 1–12.
- 16 McCulloch TJ, Loadman JA. Reduction of postoperative mortality and morbidity: little information was given on inclusion criteria. *British Medical Journal* 2001; **322**: 1182.
- 17 Rigg JRA, Jamrozik K, Myles PS, et al. Epidural anaesthesia and analgesia and outcome of major surgery: a randomised trial. *Lancet* 2002; **359**: 1276–82.
- 18 GALA Trial Collaborative Group. General anaesthesia versus local anaesthesia for carotid surgery (GALA): a multicentre, randomised controlled trial. *Lancet* 2008; **372**: 2132–42.
- 19 Liu SS, Wu CL. Effect of postoperative analgesia in major postoperative complications: a systematic update of the evidence. *Anesthesia & Analgesia* 2007; **104**: 689–702.
- 20 Exadaktylos AK, Buggy DJ, Moriarty DC, Mascha E, Sessler DI. Can anaesthetic technique for primary breast cancer surgery affect recurrence or metastasis? *Anesthesiology* 2006; **105**: 660–4.
- 21 Biki B, Mascha E, Moriarty DC, Fitzpatrick JM, Sessler DI, Buggy DJ. Anaesthetic technique for radical prostatectomy surgery affects cancer recurrence. *Anesthesiology* 2008; **109**: 180–7.
- 22 Sessler DI, Ben-Eliyahu S, Mascha EJ, Parat M-O, Buggy DJ. Can regional analgesia reduce the risk of recurrence after breast cancer? Methodology of a multicenter randomized trial. *Contemporary Clinical Trials* 2008; **29**: 517–26.
- 23 Sessler DI. Does regional analgesia reduce the risk of cancer recurrence? A hypothesis. *European Journal of Cancer Prevention* 2008; **17**: 269–72.
- 24 Deegan CA, Murray D, Doran P, Ecimovic P, Moriarty DC, Buggy DJ. Effect of anaesthetic technique on oestrogen-negative breast cancer cell function *in vitro*. *British Journal of Anaesthesia* 2009; **103**: 685–90.