Suxamethonium and auditory evoked potentials

Sir,—I read with interest the article by Brunner and colleagues on the relationship between suxamethonium and cortical auditory evoked potentials [1]. The focus of the article was the hypothesis that suxamethonium may cause arousal of anaesthetized patients, but no plausible explanations were offered by the authors as to the possible mechanism. I suspect that the authors overlooked the effects of neuromuscular blockers on the muscles of the tympanum (tensor tympani and stapedius) which are the most sensitive muscles in the body to the action of blocking drugs. For example, there is considerable literature on the early diagnosis of myasthenia gravis by testing the reflex tensioning of the middle ear ossicles with impedance techniques.

Thus the effect of suxamethonium on the auditory evoked response may not be concerned with arousal. Instead it may merely be the result of abolishing the tensioning reflex mediated by the stapedius, allowing a much larger mechanical signal through to the inner ear and therefore causing a larger stimulus up the auditory nerve. The authors even cited a reference reporting the absence of the “arousal” effect of suxamethonium in the presence of previous non-depolarizing paralysis [ref. [10]] which is what one would expect when the stapedius has been blocked totally, it cannot be blocked further. The results of this article are nevertheless interesting. The discussion section, however, might perhaps have been reduced to a single 10-line paragraph had the authors taken into account the physiology of the stapedius reflex.

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Extradural clonidine for postoperative pain relief

Sir,—With regard to a recent letter by Nishikawa [1] criticizing pain assessment by Lee and Rubin [2], we feel that, as our recent article [3] used similar methodology to theirs, we should reply to the points raised.

First, Nishikawa questions that objective assessment of pain is possible in small children. This is an area of obvious difficulty and is the reason why a previously validated [4] objective pain scoring system was used in both studies [2–3]. This was used by staff [2] or parents [3] to decide when analgesia was necessary. Quite how this makes bias “likely” when observations of randomized groups are being made double-blind is unclear to us.

Nishikawa also states that he “cannot exclude... that intense sedation induced by extradural clonidine (with local anaesthetics) would make estimation of pain intensity impossible”. He cites his own study [5] in support of this. However, this article makes no attempt to assess pain in its methodology. In addition, all patients were adults who were premedicated and sedated during operation. Despite this, and one group receiving a larger mean dose of clonidine (3.3 μg kg⁻¹) than in the paediatric studies (2 μg kg⁻¹), none was “sedated to the degree that she could not respond to verbal commands”. This suggests that ability to communicate was retained.

Lee and Rubin [2] found it difficult to separate analgesia and sedation in their patients receiving extradural clonidine. They also used sedative premedication. In our study [3] no premedication was used and we confirmed that clonidine 2 μg kg⁻¹ provided a longer duration of analgesia than adrenaline 1 : 200 000 when added to caudal 0.25% bupivacaine 1 ml kg⁻¹ (medians: clonidine 5.8 h, adrenaline 3.2 h; P < 0.05). There was no difference in time to spontaneous eye opening after cessation of anaesthesia (medians: clonidine 21 min, adrenaline 20 min) or sedation scores at 4 h (medians: clonidine 0, adrenaline 0). Only three patients in the clonidine group (total 20) required analgesia at 4 h when median sedation score was 0 (eyes open spontaneously). Therefore, it is our contention that sedation does not preclude estimation of pain in children given extradural clonidine 2 μg kg⁻¹ in combination with local anaesthetic, but that the use of other sedative drugs may introduce this difficulty.

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Sir,—I read with interest the article by Cook and colleagues [1] insisting that sedation does not preclude postoperative pain.
Aprotinin during liver transplantation

Sir,—We were interested to read the double-blind, randomized study by Milroy and colleagues [1] on haemodynamic stability after administration of aprotinin during orthotopic liver transplantation (OLT). We wish to make the following observations. Aprotinin reduces transfusion requirements and blood loss in patients undergoing heart surgery [2]. However, this beneficial effect has never been assessed in patients undergoing OLT. In the reference mentioned by the authors [3], as in all articles published previously, comparisons were made with historical controls. Moreover, aprotinin did not significantly reduce oozing during OLT in the only randomized study [4].

In the introduction to the article, the authors wrote “the aim of the present study was to determine if aprotinin influenced blood loss, blood product requirements...”. We were disappointed not to find the answer in the results as they studied 55 patients, a number that is insufficient to provide proper statistical results. Even though Lentschener and Benhamou consider that our study was conducted on a large group of patients, in retrospect we are of the opinion that this study did not have sufficient statistical power to either support or refute the question it was designed to answer, namely does aprotinin reduce blood loss during orthotopic liver transplantation (OLT)? We have realized that patient selection may not have been ideal in helping to answer this important question.

Our original approach for this study was to include all suitable patients undergoing OLT for chronic or acute hepatic failure. This led to the inclusion of a high proportion of “low risk” patients (48 % in the placebo group and 29 % in the aprotinin group) with a preoperative diagnosis of primary biliary cirrhosis and primary sclerosing cholangitis. We now consider these patients to be at low risk of intraoperative fibrinolysis, and no longer administer prophylactic antifibrinolytic therapy.

It was our intention to publish this article merely to highlight the interesting and previously (to our knowledge) unreported finding that administration of aprotinin during OLT can confer statistically significant improvements in haemodynamic stability during the post-reperfusion phase.

We are currently conducting a more powerful randomized, double-blind study in patients we consider to be at high risk of intraoperative fibrinolysis and bleeding during OLT to definitively answer Lentschener and Benhamou’s question.

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Aortic stent surgery

Sir,—We were interested to read the case report by Greiff, Thompson and Langham [1].

To our knowledge there are four centres in the UK, including Liverpool, that are involved in endoluminal repair of abdominal aortic aneurysm. At the 1995 annual scientific meeting of the Vascular Surgical Society, the results of several of the centres were presented, and also recently in Sydney [2]. It is interesting to note that the procedure is not always as straightforward as suggested in the case report by Greiff, Thompson and Langham. Failure to deploy the stent is not uncommon [3]. The need to convert to an open operation may occur in up to 35 % of patients. Although there is a definite learning curve with mortality being reduced the more experienced the team, perioperative mortality is approximately 10 % [4]. Late failure of the graft has also been described.

There are several reasons for these problems. The technique is relatively new and during the early stages of development there is a tendency to use the technique in those patients where open surgery is very likely to result in the death of the patient. For example, the patient may have significant cardiovascular disease and death is a significant risk whatever the operation.

As indicated in the article of Greiff, Thompson and Langham, the main advantage for patients is that when the procedure succeeds smoothly, the postoperative course is usually less complicated than after open surgery. The patient’s trachea can usually be extubated early and the patient may be mobilized early. This improved postoperative course may not, however, outweigh the risk of hypotension that occurs while the balloons are inflated to deploy the stent during the procedure. Studies examining the advantages of this technique compared with open surgery in
different groups of patients are necessary and also studies evaluating the anaesthetic techniques used.

A.P. BARANOWSKI

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Sir,—We are grateful for the comments of Dr Baranowski and Mr Adiseshiah, and appreciate the opportunity to clarify several points.

Numerous centres within the UK have preliminary experience of this technique, although it is probably true to say that only Leicester and Nottingham have a representative experience. It is certain true that there is a definite learning curve to this procedure, but we are unaware of any data to support the assertion that mortality is reduced with increasing experience of the team. It is misleading to describe average mortality for this procedure as many of the patients in the larger series are elderly and unfit for routine conventional surgery [1–3].

It is suggested by Dr Baranowski and Mr Adiseshiah that endovascular aneurysm repair be used in those patients where open surgery is likely to result in patient mortality. It is our view that this is precisely the case in which endovascular surgery should be avoided until the learning curve of the procedure has been overcome and conversion to open operation occurs in a low percentage of patients. It is well documented in the literature that conversion during endovascular aneurysm repair results in a high mortality rate. If a failure to deploy the endograft appropriately is occurring in up to 35% of cases, it may be appropriate to re-think the indications for endovascular repair in this group of patients. At present we feel that a randomized, controlled trial is required to examine procedural morbidity and mortality in patients suitable for both conventional and endovascular aneurysm repair. It must be determined if endovascular aneurysm repair is a safe procedure in “healthy” patients before its use can be advocated routinely in patients unsuitable for conventional transperitoneal surgery.

We were interested to learn that the group at UCL uses significant procedural hypotension during deployment of the aortic stent. During deployment of a balloon expandable stent in our centre, we regard a mean arterial pressure of 70 mm Hg to be adequate.

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**Suxamethonium in children**

Sir,—The importance of recognizing subclinical myopathies in patients undergoing general anaesthesia was demonstrated clearly many years ago [1] and has been stressed recently in the editorial by Hopkins [2].

When the problem of anaesthesia-induced rhabdomyolysis (AIR) is examined retrospectively, a surprising finding is that many clinical reports (including the most recent ones) lack preoperative evaluation of serum creatine kinase (CK) activity. This indicates that our attention to the problem is either poor or frustrated by the knowledge that serum CK activity is not invariably correlated with the presence or absence of myopathic conditions.

The long preclinical phase of many dystrophinopathies, which are frequently involved in AIR [3], may be easily recognized or suspected on the basis of CK activity.

In our experience, a definite decrease in postoperative serum CK activity may be expected in the majority of these patients if they receive general anaesthesia without the use of suxamethonium [4]. In rare circumstances, however, a life-threatening AIR may be observed even though suxamethonium has been avoided [5]. Whether or not these accidents define a particular subpopulation of dystrophinopathic patients or a particular pharmaco-metabolic condition caused by general anaesthesia is unknown.

In our opinion, a poorly investigated problem is the metabolic derangement which might occur when the normal activity of the enzyme carnitine-palmitoyl-transferase is simultaneously stressed by increased lipolysis and by anaesthetic agents [6]. Preoperative fasting, anxiety and restlessness could be important in this regard.

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requires attention to the less frequent but known causes. Adhering to the above guidelines may help.

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Sir,—Fiacchino and colleagues appear to be advocating routine preoperative screening of creatine kinase (CK) activity and yet they observe that the specificity and sensitivity of this investigation for detecting subclinical myopathies is low. Given that the prevalence of myopathies in the population is low, the predictive value of estimating CK activity renders this an unhelpful screening test. If there are clinical features suggestive of myopathy, or there is a family history of such a condition, CK estimation may form part of the investigative process of the underlying condition, but a normal CK result does not exclude a myopathy and will not, therefore, influence short-term anaesthetic management.

I am sympathetic towards Farrell’s views, but before concurring with such rigid and generalized recommendations, it is important to be sure that the necessary alternative techniques are likely to be safer in all situations. I believe that first, we should distinguish between those cases where the diagnosis of a myopathy has been made, or seems likely on the basis of clinical information, and those cases where the likelihood of a myopathy is low (no family history or clinical features).

In the former group, it is generally accepted that the incidence and severity of complications attributable to suxamethonium (myotonia, postoperative ventilatory failure [1] and rhabdomyolysis) is so high as to outweigh the potential advantages of suxamethonium. When we consider the choice of maintenance drugs for general anaesthesia in these patients, the situation is not as clear. Hypermetabolic reactions and sudden massive rhabdomyolysis have been reported in dystrophic patients anesthetized with volatile drugs without suxamethonium, but similar responses can occur in myopathic patients receiving total iv. anaesthesia [2]. However, I believe that volatile anaesthetics do contribute directly to rhabdomyolysis [3, 4]. These disadvantages of volatile drugs need to be weighed against the detrimental cardiovascular effects of iv. agents in patients who may have a severe cardiomyopathy.

Symptoms of heart failure in patients with Duchenne dystrophy are deceivingly uncommon because of the enforced sedentary existence but myocardial dysfunction is common, as is evident from echocardiographic studies [5], which themselves can fail to detect patients with significant ventricular dysfunction [6]. One should also not ignore that there is, albeit anecdotal, great experience of the safe use of halothane in Duchenne patients.

As I hoped was clear from my editorial [7], the overall incidence of cardiac arrest after suxamethonium is low, but by being meticulous in our preoperative assessment of children it is likely that we can further reduce this incidence. What we cannot quantify are the potential advantages of techniques using suxamethonium. There are no published studies that have adequately compared outcome with these and alternative techniques. Again, as argued in the editorial, such studies would need to be extremely large to achieve sufficient power to detect small, but clinically important differences. Neither are there likely to be published case reports of morbidity or mortality associated with failure to rapidly establish a secure airway when suxamethonium was not used.

There will always be a risk with anaesthesia. For some individuals the risk varies according to the technique/drugs used, but there are many factors that can influence relative risk. It is my view, therefore, that rather than rely on rigid dictates, the anaesthetist must tailor the approach to clinical management to the needs of the individual patient if anaesthetic mortality is to be minimized. This requires anaesthetists to be able physicians, trained to a high level of competence in a range of anaesthetic techniques. It also requires anaesthesia to be a strong academic discipline with practitioners motivated to establish the many strands of evidence required for objective clinical decision making, and with the ability to evaluate these in conjunction with other, often conflicting, priorities. In the absence of firm evidence, clinicians can only guess which approach, in their hands, is most likely to provide the best outcome for the patient: this is what we term “clinical judgement”. One aim of my editorial was to highlight that, until we can quantify the complete risk/benefit profile for suxamethonium, its use in children must remain a matter of clinical judgement.

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Isolated forearm technique

Sir,—In reply to our original letter [1], Healy and Pomfrett [2] chastise us on several counts: that nitrous oxide-oxygen anaesthesia “represents a very specific anaesthetic scenario”, that we did not “allay public fears in a public forum” and that the isolated forearm technique (IFT) does not work.

It is true that nitrous oxide and opioid anaesthesia is a little-used, obscure technique, and thus attempts to undermine the significance of the finding that 44 % of patients are sufficiently aware to respond to command. Older readers will not need reminding that up until the late 1980s, nitrous oxide-opioid techniques were the commonest in the UK and an MDU anaesthetic adviser was prompted to discourage their use [3]. However, such techniques are still popular in continental Europe [4] and furthermore, studies using these methods continue to appear in reputable anaesthetic journals [5, 6]. Had the IFT been used more widely in the 1980s, British anaesthetists would have been aware much sooner as to how lightly “anaesthetized” their patients were.

With regard to allaying public fears, the authors were interviewed, both individually and together, for various local, national and international radio and regional television networks. During these interviews it was made clear that in the UK today these anaesthetic techniques are used much less commonly than in the past.

The single case of IFT failure [7] which Healy and Pomfrett make so much of occurred during Russell’s first study of the IFT with some of their textbooks being out of print. This is just one of many hundreds of successful uses of the procedure. This compares well with technical failure rates of common electronic monitoring devices as a result of poor electrode contact–positioning or diasthemia interference.

Healy and Pomfrett suggest that because decerebrate rats show responses to surgical stimuli this invalidates the IFT. Nothing could be further from the truth. The possibility of such subcortical responses in humans is the sine qua non behind the necessity of ascertaining correctly the type of response occurring with the IFT, for example asking the patient to make conditional responses.


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Merely recording that the hand appeared to move is insufficient. Unfortunately, such unverified responses were used in the principal article quoted by Healy and Pomfrett to suggest that the IFT does not work [8]. Bogod and colleagues [8] used the IFT for the first 30 min of surgery and scored their responses as “nothing, non-specific or firm clenching/flexing”. They made no attempt to communicate with the patient. They used a command which asked the patient to open and close their hand if she could hear the message and would rather be more deeply asleep. Bogod and colleagues also classified their patients on the basis of dreams into light and deep groups and assumed that the IFT responses should bear some relationship to this split.

Neither of the two patients reported as being aware [8] showed type-two responses (clenching–flexing responses) but there are major problems in interpreting these data as evidence of intraoperative awareness and failure of the IFT. Patients may not have wished to be more deeply asleep or, as the tape was not personalized with a name, the patients may not have realized the message was intended for them. More importantly, the IFT was used for only 30 min so both experiences (one described as discomfort similar to a previous Caesarean section, the other a suffocating feeling) could easily have occurred after this period, particularly during the waking up and extubation period.

It is true that ketamine is believed to disrupt cognitive function, but unlike thiopentone it also provides analgesia. Although the suggestion of Healy and Pomfrett that patients receiving ketamine do not respond to commands because they are conscious with impaired cognition is a possible explanation, it is much more likely that compared with thiopentone, patients who received ketamine were adequately anaesthetized [9].

Sometimes patients respond to a simple command, but do not respond appropriately to more complex commands. While such simple movements in response to commands might not be a taxing test of cognitive function in the true psychological sense, we do not believe many anaesthetists would be likely to continue surgery without changes to their anaesthetic regimen when they observe a patient squeezing their fingers to a simple command or opening their eyes to command.

In view of the data presented [10, 11], we accept that provided a volatile agent is used appropriately the majority of patients are unconscious during general anaesthesia, but such proof can only be provided by use of the IFT. There is no electronic monitor available which can give real-time quantification of depth of anaesthesia and in its absence we remain firmly of the view that the IFT is the only currently available, real-time, practical method of determining levels of consciousness during general anaesthesia involving neuromuscular block.

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Sir,—Thank you again for allowing us to answer yet another of Dr Wang and Dr Russell’s letters. Our original letter [1] to The Times sought not to chastise these researchers, but rather to temper the conclusions drawn from the original article by a correspondent for The Times during April, 1995 [2], which contained the sensational statement that “half of the patients on every operating list show evidence of wakefulness”. It is unfortunate that, despite their reported attempts to allay public anxiety in the media, Drs Wang and Russell did not also choose to write to The Times. We would then have seen their clarification of the facts, and would not have written any further letters on this subject.

Our statement [3] that opioid anaesthesia “represents a very specific anaesthetic scenario” was not meant to infer that it is a little-used, obscure technique. It was mentioned only because the original article [2] in The Times did not mention the anaesthetic technique used, and its title inferred that half of all patients are awake during all anaesthetic procedures. We are glad to note that Drs Wang and Russell agree with us that this is not the case with appropriate levels of other anaesthetics. It is sad that they chose not to reassure readers of The Times about the outstanding efficacy of anaesthesia.

It is interesting to note that the failures of the IFT reported in the literature, on which we based our statement “the IFT has been proved to be ineffective,” were all, according to Drs Wang and Russell, caused by methodological flaws. Our previous letter [3] discussed the findings of the groups who described the IFT to be ineffective in some detail, and we shall not repeat that discussion here.

If we attempt to attribute something useful to this series of letters, at least we may have put it into proper context. The IFT is, at present, an adjunct to other anaesthetic research. One example of such research [4] used a carefully constructed procedure to define recovery of consciousness in 20 patients after a single dose of thiopentone. The patients were monitored using the IFT and a commercially available EEG monitor (Aspect A-1000). An initial orientating command (“squeeze my fingers”) was repeated every 30 s and followed, after a positive response, with a more complex test of cognition (“squeeze my fingers twice”). Only a response to the second condition was taken as recovery of consciousness. This research suggested that the EEG monitor indicated consciousness at least as effectively as the IFT, but with the addition of a continuous, automatic and objective scale (bispectral index). However, neither the IFT nor the bispectral index answer what the anaesthetist really needs to know, that is what is the absolute depth of anaesthesia and is it sufficient to prevent various stimuli during surgery from causing the patient to awaken? As such a monitor, the IFT is ineffective. After all, it is too late if the patient is already awake. That is failure.

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CSF progesterone concentrations in pregnancy

Sir,—I read with interest the article by Hirabayashi and colleagues [1] in which the authors showed that there was an increase in CSF progesterone concentrations in pregnancy and a greater cephalad spread of anaesthesia as pregnancy progressed. They were unable to demonstrate any correlation between CSF progesterone concentration and maximum cephalad spread of anaesthesia in any of the groups. However, they claimed that the data suggested that “not only a minimum level of progesterone in CSF but also a certain duration of exposure to elevated CSF progesterone concentrations may be necessary for enhancement of spread of spinal anaesthesia...”. Even though they were unable to show a relationship, they seem to want the reader to conclude that progesterone may be related in some way to the higher spread of spinal anaesthesia. They are suggesting causality without any evidence to support it.

All patients had subarachnoid injection of hyperbaric solution which would tend to spread cephalad because of the natural curvature of the spine. One way to avoid the effect of “mechanical factors” on cephalad spread would have been to use an isobaric solution for injection. Spread of isobaric solution is not affected by the position of the patient and other mechanical factors to the same extent as a hyperbaric solution.

The authors have cited several references which support the increased susceptibility of nerve tissue to block by local anaesthetic agents in pregnancy. Mechanisms which have been implicated are the direct effect of progesterone on membrane excitability, indirect actions of neurotransmitters, increased permeability of the neural sheath and potentiation of the analgesic effect of endogenous opioids. These studies can be used to explain an increase in the intensity of subarachnoid block with lignocaine but the references cited cannot explain an increase in cephalad spread of the block.

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Sir,—In our article we demonstrated a time lag between an increase in CSF progesterone concentration and development of enhanced spread of spinal anaesthesia. In addition, enhanced cephalad spread of spinal anaesthesia was found to take place during the middle stage of pregnancy, in spite of its low CSF progesterone concentration. Hence, we concluded that not only a minimum level of progesterone in CSF but also a certain duration of exposure to elevated CSF progesterone concentrations may be necessary for enhanced spread of spinal anaesthesia. Because mechanical factors are insufficient to explain enhanced spread of spinal anaesthesia beginning at the middle stage of pregnancy, an increase in progesterone, as a non-mechanical factor, is expected to play an important role in the enhancement. In addition, our results showed that there was no significant correlation between CSF progesterone concentration and cephalad spread of spinal anaesthesia at any stage of pregnancy, and that cephalad spread did not differ between singleton and twin pregnancies in spite of significantly higher concentrations in CSF progesterone in parturients with twin pregnancies compared with those with singletons. From these data we concluded that the value of CSF progesterone concentration does not correlate directly with the degree of enhancement. This conclusion, however, does not deny involvement of progesterone with pregnancy-induced enhancement of spinal anaesthesia. We presume that a certain duration of exposure to elevated CSF progesterone concentrations causes enhancement of spinal anaesthesia beginning at the middle stage of pregnancy, regardless of the values of CSF progesterone concentration.

We agree with Dr Baliga’s suggestion that to avoid the effect of “mechanical factors” on cephalad spread, isobaric anaesthetic solutions are preferable to hyperbaric. Unfortunately, we do not have our own data on cephalad spread with isobaric solution, particularly with respect to pregnant women [1]. On the other hand, Russell and Holmqvist [2] compared the effects of isobaric with those of hyperbaric bupivacaine in parturients undergoing Caesarean section, and suggested that pregnancy enhances the spread of isobaric more than the spread of hyperbaric bupivacaine. Nonetheless, it remains unclear if pregnancy during the early and middle stages enhances the spread of isobaric anaesthetics.

A hyperbaric solution injected into the mid-lumbar subarachnoid space spreads in both cephalad and caudal directions under the influence of gravity. In a cephalad direction, it pools in the lowest part of the thoracic hollow and then diffuses towards cephalad. The concentration of the anaesthetic agent in CSF at the cephalad part of the hollow should be lower than that at the bottom of the hollow. In this condition, a certain concentration that is devoid of local anaesthetic activity in non-pregnant women may cause conduction block in pregnant women who have an increased susceptibility of nerve tissue, resulting in an increase in cephalad spread of block. Thus increased susceptibility of nerve tissue during pregnancy may explain not only the increase in intensity of subarachnoid block but also the increase in cephalad spread of the block. The references cited in our article support the increased susceptibility of nerve tissue to block by local anaesthetics during pregnancy. The cellular mechanism of this effect, however, is not yet clear.

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Extradural analgesia in the first stage of labour

Sir,—We read with interest the article by Buggy and MacDowell [1] comparing an extradural mixture of clonidine and fentanyl with 0.25 % bupivacaine for the first stage of labour and wish to raise the following points.

(1) While claiming that the power of the study was too low to detect a true difference in sedation scores (30 % power) and the incidence of hypotension (45 % power) between the groups, the authors conveniently omitted details of the study’s power to detect a difference in analgesic efficacy between the two groups, one of the stated aims of their study. The degree of analgesia, as assessed by visual analogue scores, was said to be similar in both groups, but considering there were only 14 patients in each group, we suspect that the study lacked sufficient power to reveal any difference.

(2) Although the design of the study was said to be double-blind, we believe that the anaesthetist performing the assessments in both groups could not have been truly blinded as to which drug regimen was being used. As the data revealed that eight patients in the 0.25 % bupivacaine group, not unexpectedly, developed significant leg weakness, presumably the anaesthetist could not have asked patients in this group to perform a Romberg’s test!

(3) The authors found a median sensory level of T10 in both groups, but stated that all patients in the clonidine–fentanyl group had “preserved pinprick and temperature sensation”. Are both findings compatible? Perhaps other, unspecified, sensory tests were performed.

(4) The authors stated that overall satisfaction with extradural analgesia after delivery was high in both groups: 79 % and 86 % in the clonidine–fentanyl and bupivacaine groups, respectively. The implication is that the clonidine–fentanyl mixture provided...
good analgesia overall. However, the single dose of clonidine–fentanyl used in group 1 provided analgesia only for a mean of 80 min during a much longer labour (median duration 6.4 h). Both groups subsequently received extradural infusions of 0.1 % bupivacaine in addition to further top-ups of 0.25 % bupivacaine if analgesia was inadequate. There is also no mention of the additional amounts of 0.25 % bupivacaine used in both groups. The implied overall satisfaction with the clonidine–fentanyl mixture must therefore be regarded with scepticism.

(5) The authors stated in conclusion that it may be safer for patients receiving clonidine–fentanyl mixtures to walk during labour compared with a group receiving an ambulatory regimen of 0.1 % bupivacaine with fentanyl 2 µg ml⁻¹ because of reduced dorsal column impairment. However, it is unclear how many individual patients had abnormal dorsal column signs in the clonidine–fentanyl group. For example, did the four patients with impaired proprioception also have impaired vibration sense (n = 2) and a positive Romberg’s sign (n = 2)? Otherwise eight different patients (55 %) could have exhibited abnormal dorsal column signs, precluding ambulation.

(6) Finally, neonatal assessment in the study was inadequate. Umbilical cord blood-gas values and possibly neurobehavioural scoring would have provided additional information on neonatal condition.

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SIR,—We thank Drs Fernando and Parry for their interest in our article and respond to their comments sequentially.

(1) Assuming that a reduction of 4 cm on the visual analogue scale (VAS) is a clinically significant reduction in pain intensity, and given a median interquartile range of 2.5 cm on the VAS from all our pain data, the power of our study to detect true differences in VAS scores was 82 %, for an alpha error of 0.05 and n = 14 in each group. The reason for our study’s apparent greater power to detect differences in pain scores compared with its relatively low power to detect differences in the incidences of side effects lies in the nature of the data: much greater power is required to detect differences in proportions between groups than for differences in data on an ordinal scale, especially when, as pointed out in our study, the incidence of these side effects was low.

(2) Our hospital pharmacist ensured that our study was double-blind, using coded, labelled syringes. The table in our article indicated MRC < 3, which may have been misleading. Motor weakness was taken as an MRC grade less than or equal to 3, and sensation of the first finger and little finger was taken in fact MRC grade 3. All eight patients were able to stand and undertake Romberg’s test, although it was deemed abnormal in six.

(3) Sensory level was obtained using a cold ethyl chloride spray, whereas dermatomal sensation was tested with the base of the tuning fork, in addition to pinprick.

(4) All patients received an infusion of 0.1 % bupivacaine after a mean duration of 80 min on the test solutions alone, and although there were no statistically significant differences between the median amounts of bupivacaine infused, there is no doubt that overall patient satisfaction would have been influenced by the analgesia provided by this infusion.

(5) The presence of posterior column signs does not preclude the more likely the patient is to suffer infective complications, in a manner similar to indwelling i.v. catheter-related sepsis. However, this does not seem to be the case from our results or from a study by DuPenn and colleagues [15]. We were, however, surprised by the duration the authors left their catheters in situ, as Bromage [16] recommends that catheters should be changed every 72 h to prevent the occurrence of local tissue reactions. In view of our results, we feel that the use of indwelling extradural catheters in the management of patients who require repeated surgical procedures in the presence of infection cannot be justified as the benefits have not been shown to exceed the risks.

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whatever method of induction with which you are comfortable to allow through LMA intubation \[12\]; (7) use laryngeal mask airway (LMA), a gum elastic bougie and also a 6.0-mm diameter tube to allow through LMA intubation \[12\]; (6) have a cannula in the patient's trachea was intubated successfully. We have not found evidence in theirs or other reports \[3\] that i.v. induction and neuromuscular block in one of their cases, even though the patient's trachea was intubated blindly. The two other cases underwent a tracheotomy; (4) awake fibreoptic intubation in the sitting position is a good technique, but be aware that the airway can deteriorate during the procedure because of (1) above, and (2) reflex glottic activity (coughing, breath-holding and laryngospasm). Obstruction may occur at light levels of induction with halothane and spontaneous ventilation for one patient in our series survived only because muscle paralysis and positive pressure ventilation were commenced \[6\]. Our advice to practitioners treating patients with anterior cervical spine disease. We agree that early intervention is to be encouraged, however, we suggest that it is no more likely to succeed than any other when muscle paralysis is induced, for two reasons: (1) the glottic opening obstructs against the posterior pharyngeal wall as pharyngeal tone decreases \[4, 5\]; and (2) reflex glottic activity (coughing, breath-holding and laryngospasm). Obstruction may occur at light levels of anaesthesia in patients with upper airway pathology whatever method is used, including topical anaesthesia of the glottis [Calder, unpublished observations]. Deep general anaesthesia is required to obtrude glottic reflex activity sufficiently to allow intubation. This can be difficult to obtain with an inhalation technique and may be impossible if the airway is obstructed. Our experience with halothane and spontaneous ventilation for fibreoptic tracheal intubation led us to abandon the technique. At least one patient in our series survived only because muscle paralysis and positive pressure ventilation were commenced \[6\]. In our experience a period of positive pressure ventilation is required to obtain sufficient glottic relaxation when halothane is used. The benefits of positive pressure, or at least CPAP, in the relief of severely obstructed airways have been mentioned by several authors \[7–9\], and positive pressure is the mainstay of treatment in obstructive sleep apnoea \[10\]. We do not seek to dissuade our colleagues from using an inhalation technique, but we suggest that it is no more likely to succeed than any other when severe airway obstruction is present. It is unhelpful to give the impression that the use of airway-friendly i.v. agents such as propofol or neuromuscular blockers may expose practitioners confronted with a desperate emergency to criticism. Our advice to practitioners treating patients with anterior cervical haematoma is: (1) be aware that complete airway obstruction can occur suddenly; (2) inhalation of nebulized adrenaline can improve the airway, but is not a substitute for securing the airway – we have had a fatality in a patient whose airway improved dramatically with adrenaline but obstructed completely some hours later; (3) have a surgeon standing by ready to perform a tracheotomy; (4) awake fibreoptic intubation in the sitting position is a good technique, but be aware that the airway can deteriorate during the procedure because of (1) above, and because lignocaine can provoke laryngospasm when applied to the glottis \[11\]; (5) insufflate oxygen via a nasal catheter; (6) have a laryngeal mask airway (LMA), a gum elastic bougie and also a 6.0-mm diameter tube to allow through LMA intubation \[12\]; (7) use whatever method of induction with which you are comfortable and give neuromuscular blockers if the patient may benefit; and (8) use a small tube (7.0-mm diameter maximum) and do not remove it for at least 24 h. Our aim should be to encourage early intervention by emphasizing that in the early stages any method is likely to be successful, and refraining from criticism if difficulty is encountered, because it is probable that pathology, not technique, is to blame.

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Cervical haematoma and airway obstruction
Sir,—We are grateful to Munro, Makin and Reid \[1\] for their report on cases of airway obstruction after carotid surgery. We have encountered similar problems after anterior cervical spine surgery. We agree with the authors that early intervention is to be encouraged and that deterioration of airway patency is unpredictable and can be rapid; fatalities have occurred in our hospital. The problem is that staff are reluctant to establish a tracheal airway until it is clearly necessary, because they know that the intervention may be difficult and they risk criticism of their management. Professor Eichorn has called anaesthesia a specialty with “zero tolerance for complications” \[2\].

Munro, Makin and Reid apologize for the use of i.v. induction and neuromuscular block in one of their cases, even though the patient’s trachea was intubated successfully. We have not found evidence in theirs or other reports \[3\] that i.v. induction and paralysis are less likely to be successful than inhalation induction. Airway patency nearly always deteriorates when anaesthesia is induced, for two reasons: (1) the glottic opening obstructs against the posterior pharyngeal wall as pharyngeal tone decreases \[4, 5\]; and (2) reflex glottic activity (coughing, breath-holding and laryngospasm). Obstruction may occur at light levels of anaesthesia in patients with upper airway pathology whatever method is used, including topical anaesthesia of the glottis [Calder, unpublished observations]. Deep general anaesthesia is required to obtrude glottic reflex activity sufficiently to allow intubation. This can be difficult to obtain with an inhalation technique and may be impossible if the airway is obstructed. Our experience with halothane and spontaneous ventilation for fibreoptic tracheal intubation led us to abandon the technique. At least one patient in our series survived only because muscle paralysis and positive pressure ventilation were commenced \[6\]. In our experience a period of positive pressure ventilation is required to obtain sufficient glottic relaxation when halothane is used. The benefits of positive pressure, or at least CPAP, in the relief of severely obstructed airways have been mentioned by several authors \[7–9\], and positive pressure is the mainstay of treatment in obstructive sleep apnoea \[10\]. We do not seek to dissuade our colleagues from using an inhalation technique, but we suggest that it is no more likely to succeed than any other when severe airway obstruction is present. It is unhelpful to give the impression that the use of airway-friendly i.v. agents such as propofol or neuromuscular blockers may expose practitioners confronted with a desperate emergency to criticism. Our advice to practitioners treating patients with anterior cervical haematoma is: (1) be aware that complete airway obstruction can occur suddenly; (2) inhalation of nebulized adrenaline can improve the airway, but is not a substitute for securing the airway – we have had a fatality in a patient whose airway improved dramatically with adrenaline but obstructed completely some hours later; (3) have a surgeon standing by ready to perform a tracheotomy; (4) awake fibreoptic intubation in the sitting position is a good technique, but be aware that the airway can deteriorate during the procedure because of (1) above, and because lignocaine can provoke laryngospasm when applied to the glottis \[11\]; (5) insufflate oxygen via a nasal catheter; (6) have a laryngeal mask airway (LMA), a gum elastic bougie and also a 6.0-mm diameter tube to allow through LMA intubation \[12\]; (7) use whatever method of induction with which you are comfortable and give neuromuscular blockers if the patient may benefit; and (8) use a small tube (7.0-mm diameter maximum) and do not remove it for at least 24 h. Our aim should be to encourage early intervention by emphasizing that in the early stages any method is likely to be successful, and refraining from criticism if difficulty is encountered, because it is probable that pathology, not technique, is to blame.

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Sir,—We thank Dr Calder and Dr Koh for their interest in our report. We appreciate that the safest and most appropriate management of a difficult airway is usually that method with which the anaesthetist feels most confident. However, regarding i.v. induction and paralysis we feel that this may not be as successful, as one or our original references indicates \[1\]. In a series of six cases, in the four who were paralysed, the lungs could not be ventilated by hand. Two of these patients became asystolic and two suffered bradycardia of which one was less than 10 beat min \(^{-1}\). Of these one had an emergency tracheotomy and in the other three, the trachea was intubated blindly. The two other cases underwent inhalation induction, one after ensuring the ability to hand ventilate was paralysed, and in both the trachea was intubated with comparative ease. We agree that early intervention is to be encouraged, however, in such cases the degree of airway distortion should never be underestimated, and that a surgical airway may be a safe alternative.

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Management of pre-eclampsia

Sir,—We read with interest the recent review article by Mushambi, Halligan and Williamson [1] on recent developments in the pathophysiology of eclampsia, and wish to draw attention to a recent case who responded dramatically to Centoxin. It raises several interesting questions and possibilities for future research and management of these patients, particularly in respect of liver damage and possible gastrointestinal failure, some aspects of which were not included in this review article.

The case was a 31-yr-old primigravida who was delivered of a live infant under extradural anaesthesia by Ventouse extraction. She had had an uneventful antenatal course with no sign of pregnancy-induced hypertension, although 24-hour protein were recorded in the urine throughout labour. Three hours after delivery she started to complain of headaches and epigastric pains, at this time she was found to be mildly hypertensive (165/95 mm Hg). Simple analgesia and baseline investigations were ordered. Six hours after delivery she convulsed. Further episodes occurred 1 and 2 h later. While observed on the delivery ward she was given phenytoin and diazepam, but additional treatment with Heminvinrin and thiopentone (at low doses) were required to control the convulsions. Unfortunately, there were no intensive care beds available at the time and so management was continued in the delivery suite. Central venous pressure was monitored and urine output (with heavy proteinuria) maintained with careful boluses of human albumin solution. The patient continued to deteriorate, becoming febrile with tachycardia, and a labile arterial pressure, and she showed signs of pulmonary oedema. Serum blood glucose concentration became unstable (reaching as low as 1.2 mmol litre$^{-1}$ at one time) and required supplementary glucose. Biochemical and haematological evidence of worsening multi-organ failure became evident, as her LFT's and blood glucose estimation [2] were abnormal; blood glucose concentration became less erratic. Over the next 24 h and blood glucose concentrations became normal.

Although it could be argued that this eclamptic patient would have stabilized as rapidly without Centoxin, as she had delivered the fetal–placental unit, it does suggest that significant endotoxaemia was occurring. With deranged liver function, especially the reticuloendothelial aspect, it was possible that this was causing significant endotoxaemia. After much discussion with the intensivists it was decided to administer Centoxin (HA-1A) to this patient (she was already receiving cefuroxime and metronidazole). Within 4 h she became demonstrably more stable and less agitated. Sedation was stopped and arterial pressure became normal; blood glucose concentration became less erratic. Over the next 8 h the clinical signs of pulmonary oedema stabilized (she had demonstrable cardiomegaly on the chest x-ray) and her temperature returned to normal. All cultures failed to grow organisms. Despite persisting albuminuria, peripheral oedema stabilized over the next 24 h and blood glucose concentrations became normal.

First, Centoxin was withdrawn from use in 1993. This raises the question of why it was used, unless of course the case described occurred before 1993.

We also wish to question their management of eclampsia using phenytoin, diazepam, chloramethiazole (Heminvinrin) and “low-dose” thiopentone. The use of magnesium sulphate in this patient would have been a preferable choice of drug. Compared with diazepam and phenytoin, magnesium sulphate has been shown to control convulsions, reduce recurrent convulsions and cause fewer side effects [1]. The use of chloramethiazole in the treatment of eclampsia is unacceptable because of the problem of fluid overload and oversedation. Magnesium sulphate is now the drug of choice in patients with eclampsia.

From the clinical signs described and laboratory findings stated, it is most likely that the above patient had HELLP syndrome, and hypoglycaemia is a known complication of this syndrome, as stated in our article [2, 3].

Pulmonary oedema in patients with pre-eclampsia results commonly from fluid overload and less frequently from left ventricular dysfunction. Unfortunately the letter does not indicate the type or amount of fluid their patient received, her urine output or central venous or pulmonary wedge pressures; these data would have been helpful in determining the cause of her pulmonary oedema. Unfortunately, pre-eclampsia is still a disease for which many theoretical and improved aetiologies abound and because it is a multisystem disorder, it has many ways of presenting.

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Sir,—We thank Drs Ward, Caunt and Alderson for their interest in our review article and are grateful for their comments. We were unable to comment on their theory of endotoxaemia or the role of Centoxin, but we wish to make some points.

1. The Eclampsia Trial Collaborative Group. Which anti-

screen and protein–albumin concentrations should also be under-

taken. Perhaps the gastrointestinal tract itself should be en-

compassed in the list of end-organs to fail?

Another form of end-organ damage which may also be part of the pre-eclamptic disease process is that of the heart failure seen in severe eclampsias; perhaps this is part of “cardiomyopathy of pregnancy” and instituted by a similar immunological stimulus. Clearly more studies are required into the specific immuno- logical problems and complex processes that occur in pre-
eclampsia, but perhaps the role of endotoxins could be defined further.

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**ERRATUM**


p. 287. In the legend for figure 2, “……elevated initial $F_{aO_2}$ (0.08)” should read “……elevated initial $F_{aCO_2}$ (0.08)”

We apologize to the authors for this confusion which arose during the editorial process.