challenge. This would seem to be a reasonable response. Of course, it is possible that this is not quite as strong a response as compared with other mice, but since the authors seek to use these mice as a model for humans with blunted responses, it might be less suitable than is claimed. We also do not know whether the effect of the three anaesthetics tested is similar in other mice with even more vigorous hypercapnic responses (i.e. there is no control group). The authors have previously reported strain differences for isoflurane with respect to the recovery process, but these observations cannot be extrapolated to other anaesthetic agents without further experiment. If the effects are similar with these other agents, then the anaesthetic effect is a general one, and the initial (baseline) degree of blunting of the hypercapnic response is irrelevant.

J. J. Pandit
Oxford, UK

Editor—Thank you for giving us the opportunity to reply to Dr Pandit’s letter. The most important criticism is that our cited references do not support the effect of arousal on anaesthesia-induced depression of the response to hypercapnia.

However, we cited the references that explicitly write about hypercapnic and hypoxic respiratory responses. Undoubtedly, these references refer to studies on these responses. As Dr Pandit clearly describes, the number of studies looking at hypercapnic responses and the effect on arousal is very small, and we are looking forward to the results of his forthcoming study. Because of the shortage of available data on this topic, we referred in the discussion of our results to these studies as references for central nervous effects on respiratory drive, but we did not differentiate the mode of stimulation. We accept this approach is inaccurate and we apologize for this simplified generalization. Unfortunately, as yet we have not been able to read the article cited as in press by Dr Pandit in Pubmed or other online services.

Second, Dr Pandit comments on the statement that humans preferentially respond with an increase in tidal volume rather than an increase in ventilatory frequency under a hypercapnic challenge and the influence of anaesthesia. Dr Pandit believes that both increase significantly and cites one of his articles to prove this. There is no doubt that tidal volume as well as ventilatory frequency can increase significantly in response to hypercapnia. However, Sollevi and colleagues demonstrated that under the influence of isoflurane, this ‘mixed’ response to hypercapnia at baseline turns into a purely tidal-volume response. Looking at a large number of studies, it was our impression that humans respond more with an increase in ventilatory frequency than an increase in tidal volume.

Overall, this point demonstrates, as described in Dr Pandit’s article from 2002, that the results of studies in humans are affected more with an increase in ventilatory frequency than an increase in tidal volume.

First, we have performed a prospective audit of PONV in 106 consecutive patients undergoing ‘on-pump’ cardiac surgery. Postoperative sedation was with low-dose propofol infusion and nurse-controlled morphine infusion as opposed to bolus midazolam and morphine. Although not all patients were suitable for not Pickwickian mice. They were at the lower end of the ‘normal’ responses from a variety of mice strains. It was one of our main interests to see how individuals with a low but not obviously pathological response behaved. In human terms, these might be the individuals most at risk, in contrast to well monitored patients with a known impairment of their respiratory drive.

We thank Dr Pandit for writing to express his concerns and for pointing out how much is still unclear in this field of research.

H. Groeben
Essen, Germany

5 Temp JA, Henson LC, Ward DS. Effects of subanesthetic minimum alveolar concentration of isoflurane on two tests of the hypoxic ventilatory response. Anesthesiology 1994; 80: 739–50

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Nausea and vomiting after fast-track cardiac anaesthesia

Editor—We read with interest the paper by Kogan and colleagues looking at the incidence and risk factors for postoperative nausea and vomiting (PONV) after fast-track cardiac anaesthesia (FTCA). We would first like to congratulate the authors on producing a study with such high numbers and second to comment on several points. First, we have performed a prospective audit of PONV in 106 consecutive patients undergoing ‘on-pump’ cardiac surgery. Postoperative sedation was with low-dose propofol infusion and nurse-controlled morphine infusion as opposed to bolus midazolam and morphine. Although not all patients were suitable for
FTCA, the mean duration of ventilation was comparable in the two groups (11.0 h after standard cardiac anaesthesia vs 8.1 h in the fast-track patients). Nausea was reported in 11/106 (10.4%) and vomiting occurred in 16/106 patients (15.1%). Whilst our overall incidence of PONV was remarkably similar to Kogan’s (25.5% vs 24%, respectively), a greater percentage of those with postoperative nausea actually vomited in our study. Kogan postulated that this PONV might be caused by the small doses of morphine given after surgery. However, our data show no difference in the incidence of PONV in patients who received more or less than a total dose of morphine 15 mg.

We suspect that a possible explanation may be the routine use of a nasogastric tube by Kogan. This deflects the stomach that may have been distended by gas swallowed by the patient as they wake up, or insufflated during bag and mask ventilation at induction of anaesthesia. Currently, it is not standard practice in our institution to use nasogastric tubes and we will look into this further.

Second, we were surprised by the choice of metoclopramide as a first line antiemetic. Numerous studies have shown it to be inferior to other antiemetics when used in the context of PONV. However, the figures from Kogan’s study suggest that second-line rescue medication (ondansetron) was only needed in 3.1% of cases. This implies metoclopramide is effective at the relatively small dose of 10 mg. We believe that our current practice of using granisetron as a first-line antiemetic is evidence-based. However, as mentioned above, our figures, showing a higher proportion of those with nausea going on to vomit, do not support this. Could this efficacy be attributable to metoclopramide’s gastric prokinetic effects?

Thirdly, we would like to reassure Kogan and colleagues that in our audit (that also looked at chest drain losses), we did not find a relationship between an increased chest drain loss and PONV (763 ml in patients with no PONV vs 773 ml in patients who had PONV).

G. Morton  
M. Lim  
S. Stacey  
London, UK

Editor—In reply to Dr McLeod’s letter, referring to our article in the BJA, I would firstly like to point out the interesting similarity in the results from our department and their own on the prevalence of PONV after fast-track cardiac anaesthesia. The use of opioids in the postoperative period is one of the main risk factors for PONV, and reducing the dose of morphine might decrease its incidence. The routine use of a nasogastric tube may also reduce the occurrence of postoperative vomiting (but not nausea). Metoclopramide has been used for many years as an antiemetic. It is inexpensive and, in the study of Woodward and colleagues, proved to be more effective than ondansetron for PONV prevention after cardiac surgery.

A. Kogan  
Tel Aviv, Israel

4 Gan JG. Postoperative nausea and vomiting—can it be eliminated? JAMA 2002; 287: 1233–6

doi:10.1093/bja/aeh622

Density of spinal anaesthetic solutions

Editor—I read with interest the article by Dr McLeod on the density of spinal anaesthetic solutions. Dr McLeod has done excellent work in measuring the densities of the solutions. We know that density has a major role in the spread of spinal anaesthesia.

I was wondering if there is a printing error in Table 2? According to the table, the density of bupivacaine 7.5 mg ml$^{-1}$ is less than that of ropivacaine 5 mg ml$^{-1}$. Likewise, the density of ropivacaine 10 mg ml$^{-1}$ at 37$^\circ$C is less than that of ropivacaine 7.5 mg ml$^{-1}$. On the other hand, in the text there is mention that ‘increasing the concentration of bupivacaine...significantly increased the density’, which is what one would expect. Which numbers are correct? This is important because Dr McLeod has put major effort into his work and these valuable numbers could be referred to in future studies.

In addition, on page 548, solutions, third line from the bottom: should the dilution of ropivacaine be 10 mg ml$^{-1}$ not 1 mg ml$^{-1}$?

M. Pitkänen  
Helsinki, Finland

Editor—May I thank Dr Pitkänen for taking an interest in my paper and highlighting these points.

With regard to plain solutions, there was a significant increase in the density of bupivacaine 5 mg ml$^{-1}$ and 7.5 mg ml$^{-1}$ compared with bupivacaine 2.5 mg ml$^{-1}$ using one-way ANOVA. There was no difference in density between the 5 mg ml$^{-1}$ and 7.5 mg ml$^{-1}$ solutions of bupivacaine. There was a significant decrease in density between ropivacaine 2 mg ml$^{-1}$ and ropivacaine 10 mg ml$^{-1}$ using one-way ANOVA. In contrast, the density of levobupivacaine significantly increased from concentrations of 2.5 mg ml$^{-1}$ to 7.5 mg ml$^{-1}$. The reason for the discrepancy is to be found in Table 5 of my paper.1

The contribution of electrolyte composition to overall density varies between drugs. With bupivacaine and ropivacaine, there is a reduction in the concentration of sodium as the concentration of local anaesthetic is increased. In contrast, with levobupivacaine, no corresponding reduction in sodium concentration occurs and, hence, osmolarity and density both increase. I hope this clarifies the point.

May I add that all densities should be expressed in g ml$^{-1}$ and not mg ml$^{-1}$ as I have written. I have asked for an erratum notice to be published to acknowledge my mistake.

G. McLeod  
Dundee, UK


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