**Blood loss during repair of craniosynostosis**

**Editor**—I write regarding two papers published some time ago, as an issue for clarification or correction. Both papers come from the same group in Paris and both use the same method for estimation of blood loss, detailed in the text and appendix of the two papers, respectively. The method was based on and attributed to the method used by Kearney and colleagues. I believe there is an error in the method used by the Paris group in the calculation of estimated red cell deficit (ERCD). They state that ERCD=estimated red cell volume (ERCV)×packed cell volume (PCV) in Meyer and colleagues’ paper, and ERCD=ERCV×difference in haematocrit in Dahmani and colleagues’ paper. But, ERCD should be calculated as estimated blood volume (EBV; not red cell volume)×difference in haematocrit. This method has been used in a number of other studies that have taken ERCD=EBV×difference in haematocrit.

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**Editor**—We thank Dr Carver for his interest in our contribution. In reply to his comments we would like to point out that in our studies we used a method derived from the method of Kearney and colleagues. In this study, blood loss was calculated on the basis of estimated red cell mass (ERCM), with ERCM=estimated red blood volume (EBV)×haematocrit/100, and ERCD new=ERCM trans-fused−ERCM pre-transfusion. In our two studies, blood loss was calculated on the basis of estimated red cell deficit (ERCD)=estimated red cell volume (ERCV)=EBV×haematocrit×difference in haematocrit (or variation in PCV), with ERCV=EBV×haematocrit pre-transfusion and total blood volume loss as ERCD+ERCV trans-fused.

Therefore, we agree with Dr Carver that there is a difference between the method of Kearney and our method. With our formula we have taken into account the volume of blood transfused during and after surgery: ERCM trans-fused=EBV×0.75, where 0.75 represents the mean haematocrit in packed red cells. From our point of view, this method allows more precise estimation of ERCD. With this mode of calculation we found some negative values indicating overcompensation of blood loss (Table 1). We think that estimating blood loss without taking into account the red cell volume transfused is not appropriate in this kind of haemorrhagic surgery. Dr Carver suggests using another method of calculation of ERCD, with ERCD=EBV×difference in haematocrit, in accordance with other studies. However, using this formula (ERCD=EBV×difference in haematocrit) does not significantly modify the results or their interpretation. To illustrate this point we have performed the statistical analysis again with both the new, and the old formulae, for ERCD, using the data from the study by Dahmani and colleagues (Table 1). As can be seen from this table, there is no significant difference between the results obtained with the two methods of calculation of ERCD. In conclusion, therefore, we think that both methods of calculation of blood loss are useable, but that our method allows more precise estimation of total blood loss.

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**Effect of arousal on hypercapnic ventilatory response needs to be examined**

**Editor**—The observation of Groeben and colleagues that the ventilatory hypercapnic response in their mice was blunted long after anaesthetic exposure is of great interest. However, it is important to consider some potential problems with this paper.

The first and most serious problem is their assertion that arousal of subjects (by visual or auditory stimulation) prevents the depression of the hypercapnic response to anaesthesia. They quote four studies to support this. It is unfortunate that none of the studies quoted examined the interaction of subject arousal and hypercapnic ventilatory response. Indeed, two of these studies did not even measure the hypercapnic ventilatory response. The interaction of arousal and the hypercapnic ventilatory response is an area that still remains to be studied and, so far as we are aware, our recently completed, unpublished study is the first attempt to examine possible interactions.

The authors are confused by the papers reporting possible interactions of arousal with the hypoxic ventilatory response. However, even where the hypoxic response is concerned, there is doubt that arousal has an important influence. For example, we have recently reported that arousal does not reverse the action of halothane on the hypoxic response (an observation which is in contrast to the reported effects of arousal on the effect of isoflurane). The authors claim that humans preferentially increase tidal volume rather than ventilatory frequency in response to hypercapnia. However, data from our previous paper shows that sustained hypercapnia in humans causes a significant increase in both tidal volume and ventilatory frequency. This study also shows that low dose sevoflurane does not affect the ventilatory response to hypercapnia, in contrast to the result of Groeben and colleagues in mice.

The final concern relates to the extent to which the mice used in their study can be properly described as having a ‘blunted hypercapnic response’. The authors’ data suggest that the minute ventilation of the mice quadrupled in response to the carbon dioxide...
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 anesthetics 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 anesthetic agents without further experiment. If the effects are similar with these other agents, then the anesthetic effect is a general one, and the initial (baseline) degree of blunting of the hypercapnic response is irrelevant.

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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 by sometimes only slight differences in study design and more importantly by a wide variation of the individual responses, which can make it difficult to detect small differences. This is also the most likely explanation why Dr Pandit did not find a significant effect of sevoflurane on the hypercapnic response in eight adult volunteers, while we did find significant differences using 11 inbred mice.

Finally, Dr Pandit raises concern about the validity of our mouse model of a blunted respiratory drive. Without doubt, any animal model leaves concerns about how many of the conclusions can be transferred to human physiology and pathophysiology. However, studies on respiratory drive in patients or human volunteers suffer from the wide interindividual differences in hypercapnic and hypoxic responses, discussed in our article. Therefore, we used inbred mice to minimize these individual (genetic) differences. Moreover, as Dr Pandit points out, the mice we used were not without a response to a hypercapnic challenge. They were 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.

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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

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