by performing the two experiments simultaneously using the two isolated forearms of volunteers [2]. Thus, at the time of the second administration of the drugs, the background minimal plasma concentration was the same in both arms.

A further argument against this phenomenon being caused by acetylcholine receptor occupancy is our observation that, at the point of 100% recovery of T1 and presumably about 80% residual receptor occupancy, no effect of the conditioning drug upon the second drug was observed. As a result of this and other observations, we concluded that the effect described was the result of biophase binding in the effect compartment and was not directly dependent upon pharmacokinetic events [3].

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2. Feldman SA, Fauvel NJ, Hood JR. Recovery from pancuronium and vecuronium administered simultaneously in the isolated forearm and the effect on recovery following administration after cross-over of drugs. Anesthesia and Analgesia 1993; 76: 92-95.

Sir,—We thank Professor Feldman and Dr Hood for drawing our attention to their recent work, which had not been published when our manuscript was submitted to British Journal of Anaesthesia. They have confirmed our clinical finding [1] that neuromuscular blockers administered during partial block have their duration of action modified by the residual drug [2]. We agree that this interaction is not a result of residual plasma concentrations, and did not intend to suggest such a mechanism in our article.

We referred to the ACh receptor in rather loose terms, but concede that the authors are more correct to suggest that this phenomenon takes place in the "biophase". However, there is no proof of the exact anatomical location at which the biophase interaction occurs.

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EFFECT OF NITROUS OXIDE ON CEREBRAL BLOOD FLOW

Sir,—We were interested to read the paper by Field and colleagues [1] on the effect of nitrous oxide on cerebral blood flow (CBF) in humans. They interpreted the data to suggest a cerebral concentration of nitrous oxide, they also breathed a smaller concentration of oxygen. This can be avoided only by introducing an inert third gas.

Moreover, we argue that it would be more relevant to clinical practice to maintain the inhaled oxygen concentration constant: the practical choice is really between (say) 30% oxygen and 70% of either nitrous oxide or nitrogen.

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Sir,—Drs Dirnhuber and Davies have suggested that our data may be interpreted as confirmation of the well-established cerebral vasocostructor properties of oxygen.

We thank them for the opportunity to challenge the view that inhalation of 100% oxygen typically reduces cerebral blood flow (CBF) by 10-15%. The studies by Kety and Schmidt [1] and Lambertson and colleagues [2] on which this assumption is based were flawed in that the volunteers taking part hyperventilated whilst inhaling 100% oxygen. A small decrease in mean arterial carbon dioxide tension of 0.13 kPa in the former study and a greater change of 0.26 kPa in the latter, whilst not statistically significant, could account for 4% and 8% reductions in CBF, respectively [3]. Lambertson and colleagues pointed out that a 0.67 kPa reduction in arterial carbon dioxide tension does not result in a reduction in CBF greater than that produced by a 0.67-kPa reduction in carbon dioxide tension alone [1]. Furthermore, he concluded that "a physiologically important specific vasoconstrictor action of oxygen probably does not exist in the intact human brain" and that reduced CBF during oxygen inhalation may be explained by a primary hyperperfusion and reduction in arterial carbon dioxide tension.

Our volunteers did not hyperventilate as confirmed by a stable end-tidal carbon dioxide concentration throughout the study. We believe that further information is required on the influence of moderate hyperoxia (for instance that produced by inhalation of 40-100% oxygen) on cerebral haemodynamics before the findings of Kety and Lambertson can be validated.

Our purpose was to mimic as closely as possible the clinical situation in which nitrous oxide is administered in varying concentrations with oxygen. The introduction of a third gas in the equation does not conform with current anaesthetic practice. We do not wish to criticize the use of nitrous oxide in neuroanaesthesia, merely to shed some light on the conflicting evidence surrounding its effects on cerebral haemodynamics: we believe, for the reasons explained above, that our data reflect the effect of nitrous oxide on CBF.

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