it very appropriately: every dose should be a test dose in labouring women.

A test dose should rapidly and reliably indicate if the needle or the catheter through which it is injected has entered a blood vessel or the subarachnoid space. An intravenous injection should produce mild and transient systemic effects. Although epinephrine containing test doses are neither specific nor sensitive, they cause very little harm. Here, we agree with Chestnut et al.[6] that the adverse consequences to the mother and fetus of unrecognized intravenous injection of a therapeutic dose of local anaesthetic are likely to be more severe, and there is no published report of an adverse neonatal outcome after an intravascular injection of an epinephrine containing test dose.

There is, however, a concern regarding the haemodynamic response to intravascular injection of epinephrine in hypertensive and pre-eclamptic parturients. We do not use epinephrine containing test doses in such patients.

The study reported by Hood et al.[7] describes the decreases in uterine blood flow following iv epinephrine test doses. These decreases were transient, were not accompanied by any changes in fetal heart rates or blood pressures and none actually developed fetal distress. Transient decreases in uterine perfusion undoubtedly occur during normal uterine contractions.

In the excellent study reported by Leighton et al.[8] on the maternal haemodynamic response to 15 μg iv epinephrine (versus placebo), epinephrine proved to be neither a specific nor sensitive indicator of an intravenous injection based on their base-to-peak criteria, but both the sensitivity and specificity increased by using the peak-to-peak criteria. Even more interesting, however, is that their data collecting investigator, who observed maternal symptoms and heart rate and blood pressure changes, correctly guessed the treatment group of all patients. Two out of ten patients in the epinephrine group developed fetal distress, but both were subsequently delivered vaginally with good Apgar scores.

Dr. Lucy mentions the use of air test dose. We have no personal experience with this technique. Addition of epinephrine to the lidocaine test dose, in our opinion, is safe and increases the probability of detecting an intravenous catheter placement or migration and the benefits outweigh the risks, even in the obstetric population.

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Esmolol

To the Editor:

I read with interest the recent editorial and original paper on the cardioselective beta blocker, esmolol.[1,2] Chung's conclusion that esmolol 2 $mg \cdot kg^{-1}$ is effective in obtunding the haemodynamic response to laryngoscopy and intubation concurs with our findings in another stressful situation, electroconvulsive therapy.[3] As Chung's study involved the use of a rapid-sequence induction technique with high dosages of succinylcholine (1.5 $mg \cdot kg^{-1}$), it is important to consider the possible theoretical drug interaction. Both esmolol and succinylcholine are metabolized by esterases and their combined administration may be associated with prolonged duration of action.[4]

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REPLY (1)

We appreciate the concern raised by Dr. O'Flaherty, as it calls attention to the potential for unplanned pharmacologic interactions when a new drug is introduced in the clinical setting. As noted by Dr. O'Flaherty, esmolol has the theoretical potential to affect neuromuscular as well as haemodynamic events.

Initial concern about the impact of esmolol on succinylcholine was based upon the fact that, like succinylcholine, esmolol is metabolized by an esterase.[1] However, in contrast to rats and guinea pigs, the esterase responsible for esmolol metabolism in humans resides primarily in the cytosol of red blood cells and not in the plasma. Investigators have reported varied effects of esmolol on succinylcholine-induced block[1-3] ranging from no effect to as much as 50% prolongation. Barabas et al. identified no change in the ability to hydrolyze benzoylcholine in plasma obtained after subjects received an infusion of up to 1400 $\mu g \cdot kg^{-1}$.[1] Murthy et al. reported delay of 50% recovery of twitch height to 8.3 min in patients who received 1 $mg \cdot kg^{-1}$ of succinylcholine in the presence of 4400 $\mu g \cdot kg^{-1}$ of esmolol (vs 5.6 min in non-esmolol treated patients).[2]

It should be noted that, unless there is a marked decline in pseudocholinesterase activity, succinylcholine-induced-block typically is not prolonged in subjects with genotypically normal enzyme.[3] We believe that it is more likely that any prolongation would be a consequence of the esmolol-induced decrease of cardiac output. This delays succinylcholine redistribution, a vital feature of the rapid recovery from this relaxant.[4,5] In addition, the use of a beta antagonist may impact on catecholamine-induced changes in acetylcholine release and/or membrane reactivity.[6]

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REPLY (2)

Dr. O'Flaherty raises the possibility of an interaction between esmolol and succinylcholine leading to a prolonged duration of action when the drugs are co-administered since both drugs are metabolized by esterases. Succinylcholine is metabolized by plasma pseudocholinesterase[1] but this enzyme is devoid of activity against esmolol.[2] Esmolol is metabolized by an arylesterase found in red blood cell cytosol.[2] It is therefore unlikely that prolongation of effect for either agent could be ascribed to a competitive interaction for metabolic enzymes. Should prolongation of effect occur when these drugs are co-administered, it is likely that this is related not to a drug interaction but to a relative deficiency or abnormality of the corresponding agent-specific esterase.

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Breathlessness

To the Editor:

From antiquity, breathlessness has been considered a very serious complaint, representing a threat to life and an indication of the severity of any disorder associated with it.

In 1966, Dr. E.J. Moran Campbell and Dr. Jack B.L. Howell were able to bring together experts from many disciplines to discuss breathlessness. Their subsequently published book based upon the Manchester Breathlessness Symposium was a landmark in the evolution of our understanding of breathlessness and provided a stimulus for research in the succeeding years. The text and conference were funded by Boehringer Ingelheim of the United Kingdom. A new text is now available to assess how far this evolution has progressed.

This text entitled "Breathlessness: The Campbell Symposium" based upon a Continuing Medical Education programme held in Hamilton, Ontario, Canada from May 16 to May 19, 1991 is now available free of charge. The text is edited by Norman L. Jones, MD, FRCPC (London), FRCP(C) and Kieran J. Killian, MBBS, FRCP(I), FRCPC. Both physicians are associated with the Faculty of Health Sciences, McMaster University, Hamilton, Ontario, Canada. The text was published by Decker Periodicals Inc. of Hamilton, Ontario, Canada.

Funding for the meeting and the publication was provided by Boehringer Ingelheim (Canada) Ltd., a pharmaceutical company which is dedicated to Respiratory Therapy. The three-day conference which was organized by McMaster University, Faculty of Health Sciences, Hamilton, Ontario, Canada was held to mark the retirement of Dr. E.J. Moran Campbell and the 25th anniversary