from our office address. We publish not only this letter, but also the fact that the series of reports are available nowhere else. Finally, it might help those who still want to acquire accurate information about this enquiry if you were to choose, but does reflect the patient’s expectations of my knowledge and experience. Clinicians must recognize the responsibility that this places upon them and act accordingly.

W. A. CHAMBERS
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Aberdeen

EDITORIAL II—THE NATIONAL CONFIDENTIAL ENQUIRY INTO PERIOPERATIVE DEATHS

Sir,—There are so many errors of fact in your editorial that we consider that it is essential that you be corrected. Your Journal may have limited appeal outside the specialty, but it would be disappointing if the work of the National Enquiry into Perioperative Deaths were to be misunderstood by anaesthetists as a result of this misleading item.

It is true that many departments of anaesthesia do have morbidity and mortality meetings, but by no means all deaths in our study (37%) were considered by such meetings (Table 82 in the Report). Surgeons are better than they used to be and now have more meetings, but not yet have they reached the standard set by anaesthetists. Sadly, combined meetings are still uncommon (36%).

It is difficult to understand how a study of death [1] could as you allege have been prospective; obviously it was not. Beecher and Todd, as anaesthesiologists, studied 10 University hospitals [2] and a sole surgeon was an adviser. There was little if any consideration of surgical factors in that study, and the British efforts are unique in this respect. We did not repeat what was already done before. NICEPOD studied three different Regions in the U.K.—South Western, Northern and North East Thames, the last being the only Metropolitan one. Northern Ireland (not to mention the Channel Islands and the Isle of Man) are included in NICEPOD.

One important epidemiological point that you overlooked was that the sample of deaths in our most recent enquiry was random. During the past 3 yr, 2069 patients (aged 2-88 yr) have been included in the sample. The statement that “The aim of this study was to compare the outcome of deaths associated with propofol and alfentanil relative to deaths associated with tracheal intubation and control of respiration” is not accurate, as the Darex HMEF is “Not currently available”. The trials carried out on the five units they had in their possession were on old American stock supplied circa 1985; also, the trade name Darex was withdrawn more than 4 yr ago. Information was conveyed to the authors of the current position of Dar products in early 1991.

D. FOX
Mediplan-Dar Ltd
Warwick

PROPOFOL AND ALFENTANIL MIXTURE

Sir,—I read with interest the paper by Taylor and colleagues [1]. The authors have shown that propofol and alfentanil may be administered as a mixture with no signs of altered pharmacodynamics. Despite the fact that Kay reported in 1986 [2] that infusions of a mixture of propofol and alfentanil had been undertaken in 21 patients with no signs of adverse outcome, mixing of these two drugs seems to have been avoided for several years. This is probably because of the limited knowledge of the physiochemical, bacteriological, pharmacokinetic and pharmacodynamic properties of such mixtures. However, in addition to the paper by Taylor and colleagues, three papers of relevance to the possibility of using propofol and alfentanil still have to be published this year [3–5], and three of the four previously mentioned theoretical shortcomings have been examined, with encouraging results. However, the pharmacodynamic properties remain to be investigated in patients undergoing mechanically controlled ventilation (i.e. if the use of a fixed dose of propofol and alfentanil causes over-dosing in any respect).

During the past 3 yr, 2069 patients (aged 2-88 yr) have been anesthetized in our department with a mixture of propofol and alfentanil for procedures requiring tracheal intubation and mechanically controlled ventilation (15% abdominal surgery with a concomitant extradural block), and we have found few indications of an unfavourable pharmacodynamic action. This letter is aimed to inform others about our preliminary experience concerning the practical use of this mixture. Naloxone has been used to antagonize the opioid effect in six of these patients, and the elapsed time from end of the infusion to tracheal extubation was a mean of 11.2 min in 612 consecutive patients without extradural block (average duration of surgery 54 (20–60) min). The latest result is very similar to that found by Schütter and colleagues [6], using separate computer-assisted infusions. As our data are retrospective, a controlled, prospective study is being performed currently. Furthermore, four cases of conscious awareness have been identified in the 2069 patients. Thus the incidence of awareness is similar to that found by Liu and colleagues [7]. Two of our cases of conscious awareness were of a technical nature and


clearly resulted from inexperience, while two patients were not sufficiently anaesthetized at the beginning of laparoscopic surgery.

R. Sandin
Länsi-Juhaniat
Kalmar, Sweden


Sir,—Thank you for this opportunity to comment on the letter by Dr Sandin, who reports on his considerable experience of using a mixture of propofol and alfentanil to maintain anaesthesia in patients receiving mechanical ventilation.

We agree that there is no evidence of pharmacodynamic interaction when the two drugs are used in this manner. However, as we have commented, there is a lack of flexibility when a mixture of the drugs is used in patients breathing spontaneously. All the patients in the papers mentioned by Dr Sandin and in his own report, received mechanical ventilation, when there is probably less requirement for close control of the balance between hypnotic and analgesic. When patients breathe spontaneously, it may be necessary to separate these two components of anaesthesia to provide an acceptable balance between hypnotic and analgesic.

We have studied approximately 1400 patients in our hospitals and have identified no cases of conscious awareness when using computerized, target-controlled infusion systems [1]. We estimate that approximately 33% of this total population received neuromuscular blocking drugs and underwent mechanically controlled ventilation.

We recommend that experience be gained in the use of infusion techniques with spontaneously breathing patients so that the skills gained may be more safely applied to patients receiving neuromuscular block.

I. N. Taylor
G. N. C. Kenny
Glasgow Royal Infirmary
Glasgow


DIFFERENT RATES OF INJECTION OF PROPOFOL

Sir,—Peacock and co-workers [1] report that the dose of propofol required per kg body weight for the induction of anaesthesia is greater with a faster infusion. For their older patients, it apparently required twice as much (1.65 mg kg⁻¹) to induce anaesthesia at an infusion rate of 100 mg min⁻¹ as it did at 25 mg min⁻¹ (0.82 mg kg⁻¹). The same effect was seen in their younger patients: 2.39 mg kg⁻¹ at 200 mg min⁻¹ and 1.46 mg kg⁻¹ at 50 mg min⁻¹.

These figures are spurious and in presenting them, Peacock’s group repeat the error made by themselves in their earlier work [2] and in the work they quote of Stokes and Hutton [3]. Peacock writes of these two studies [1]: “In both studies using infusion techniques it was shown that induction of anaesthesia with propofol by slow i.v. infusion reduced the dose requirements.” Peacock defined induction dose as the dose delivered from the syringe at the moment of induction, at loss of verbal contact, which includes the propofol still in transit between the site of injection and the brain. Provided the infusion rate is fast enough to ensure induction, this makes it inevitable that increasing the infusion rate gives an apparently increased induction dose [4].

Peacock’s “smallest effective doses” are overestimates. The true smallest effective dose must be calculated after subtraction of the amount in transit, which both reduces and more or less equalizes the dose, irrespective of infusion rate [4]. Peacock delivered their “smallest effective dose” as a rapid, 5-s injection, which induced anaesthesia in a mean time of 35 s in their younger patients. If we assume 50 s as the transit time, and subtract appropriately from their given doses, induction of anaesthesia occurred with 1.08 mg kg⁻¹ at 200 mg min⁻¹, 1.12 mg kg⁻¹ at 100 mg min⁻¹ and 1.09 mg kg⁻¹ at 50 mg min⁻¹. Induction took 3.5 s longer in the older patients: if we assume a longer transit time of 35 s, induction of anaesthesia occurred with 0.88 mg kg⁻¹ at 100 mg min⁻¹, 0.83 mg kg⁻¹ at 50 mg min⁻¹ and 0.63 mg kg⁻¹ at 25 mg min⁻¹.

These figures, rather than those presented, should be used if comparing induction at different rates of infusion. Peacock repeats the unnecessary and incorrect conclusion of Stokes and Hutton [3] that “a biophase delay” may be the rate limiting factor in onset of induction with propofol and may explain how induction is achieved with smaller doses of propofol at slower infusion rates [4], and then goes on to doubt their conclusion because the same effect was seen in their own preliminary work with thiopentone [5]. The same effect would be seen with any rapidly acting drug the effect and effective dose of which were measured while an infusion of the drug was still running. There is no need to invoke biophase delay. There is no surprise that, despite different doses, induction times were similar in the two groups after rapid injection: both doses were relative overdoses and so induction occurred after one arm–brain circulation time.

Calculating effective dose as delivered dose minus dose-in-transit does not affect Peacock’s discussions of differences between young and old, or of cardiorespiratory effects at induction, but the effects of injection time were predicted by Crawford in 1966 [6], and have been discussed at meetings of the Anaesthetic Research Society; it is disappointing that the misunderstanding continues to appear.

N. W. Goodman
Southmead Hospital
Bristol


Sir,—Thank you for the opportunity to reply to Dr Goodman's letter. Dr Goodman again has recognized the inappropriate use of the word “requirement” when applied to the dose administered for induction of anaesthesia. It is unfortunate that he has identified the use of this term in the introductory paragraph rather than the term “dose administered” which we have used thereafter.

We would agree that, during an infusion technique, the dose administered is an overestimate of the amount of drug “required” as there is always some drug in transit. However, we find it surprising that, after describing the figures presented in our