4 *Crosby ET.* Epidural catheter migration during labour: a hypothesis for inadequate analgesia. Can J Anaesth 1990; 37: 789–93.
5 *Phillips DC, Macdonald R.* Epidural catheter migration during labour. Anaesthesia 1987; 42: 661–3.

Safety of alfentanil

To the Editor:

Mulroy *et al.*[1] and their publication entitled "Safety and efficacy of alfentanil and halothane in paediatric surgical patients" have declared that alfentanil is a safe anaesthetic, whether combined with nitrous oxide alone or with nitrous oxide and halothane. They have not specified in their methods their measure of safety nor have they identified the threshold used for declaration of safety of an anaesthetic agent.

The acceptability of an anaesthetic relates not only to the severity of minor adverse events associated with its use, but also to the frequency of major adverse events, such as anaphylaxis, late respiratory arrest, and severe metabolic derangement. I would contend that the safety of an anaesthetic agent is more frequently viewed in relation to the incidence of severe adverse events. The number of patients monitored in the aforementioned investigation is insufficient to demonstrate that the frequency of severe adverse events associated with the use of alfentanil is acceptably low.

When used in a scientific publication, the term safety must be defined both in terms of the type of complication studied and the threshold of acceptable frequency for the specified complication. Alfentanil may be a "safe" anaesthetic; safety, however, was neither measured nor demonstrated in the study by Mulroy *et al.*

G.V. Goresky MD FRCPC
Department of Anaesthesia
Alberta Children's Hospital, Calgary

REFERENCE
1 *Mulroy JJ Jr, Davis PJ, Rymer DB, Chaitoff KA.* Safety and efficacy of alfentanil and halothane in paediatric surgical patients. Can J Anaesth 1991; 38: 445–9.

REPLY

Dr. Goresky raises a pertinent and valid point about the use of the term "safe" in evaluating a medical therapy. Defining safety is not a simple task. If the dictionary definition "free from harm" is the criterion applied, perhaps no medical therapy is safe. The definition of safety of any agent or procedure cannot be reduced to a single factor but is based on a multitude of hazards balanced as a risk/benefit judgement by the practitioner.

We would agree that the size of the study that we reported is too small to analyze the incidence of uncommon events such as anaphylaxis and severe metabolic derangements. Therefore, we performed no such analysis. The size of a study needed to examine this aspect of safety and provide a statistically acceptable result for such rare events is dependent on the incidence of the events and on the definition of an acceptable incidence of these complications. For example, we have never observed a case of anaphylaxis, late respiratory depression, or severe metabolic derangement attributable to the use of alfentanil suggesting that it is an infrequent occurrence in our population.

The contention that the safety of an anaesthetic agent can only be measured in relation to the incidence of severe adverse events may be modelled using anaesthetic-related mortality as the ultimate indicator of safety. Tiret reported a 1 in 40,000 incidence of anaesthetic-related mortality in children.[1] One would have to study an enormous number of patients to confirm the null hypothesis that there were no statistically significant differences in mortality among anaesthetic techniques. The relative risk of anaesthetic-related mortality between two different anaesthetic techniques could only be estimated by performing a case control study after both techniques had been used enough to produce mortality.

In order to demonstrate conclusively no statistical difference in the incidence, rare events among different techniques would require patient numbers far in excess of those in our study. Our goals were more modest. We focused on one aspect of the safety question. We attempted only to compare haemodynamic effects (using clinically relevant measures of heart rate and blood pressure) of alfentanil with those observed using halothane, an anaesthetic agent frequently employed in paediatric practice. We found that alfentanil was as safe (free from harm) to the patients as halothane was in the period studied.

The information that alfentanil in the doses studied may be safely administered to paediatric patients without producing haemodynamic depression greater than halothane is a small piece of the mosaic that defines the agent's safety and utility.

John J. Mulroy Jr. MD
University of Washington School of Medicine
Peter J. Davis MD
D. Ryan Cook MD
University of Pittsburgh School of Medicine

REFERENCE
1 *Tiret L, Nivoche Y, Hatton F, Desmonts JM, Vourc'h G.* Complications related to anaesthesia in infants and children. Br J Anaesth 1988; 61: 263–9.

SIADH following minor surgery

To the Editor:

Soroker *et al.* presented a case of the postoperative syndrome of inappropriate antidiuretic hormones (SIADH).[1] We have had a similar case and others have been reported.

Our patient was a 33-yr-old woman with pelvic adhesions secondary to endometriosis. Laparotomy was scheduled and anaesthesia was induced with thiopentone and maintained with O_2:N_2O, and isoflurane. Surgery was uneventful. Estimated blood loss was 150 ml, intravenous