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## Clinical Studies in Children

*To the Editor:*—I am writing primarily in support of Drs. Yakaitis, Blitt and Angiulo's recent report.<sup>1</sup> Induction of anesthesia in pediatric patients by inhalation of drugs is not only feasible, but may be as fast as or faster than induction by the intravenous route. Those of us who have observed the change in children's attitudes towards masks since space travel fills the television screens can also attest that such an induction is much less traumatic psychologically than earlier texts would have it.

Precisely because I find the article valuable, I would like to emphasize two points. First, it is highly debatable whether parents or guardians are in a position to give informed consent for their wards' participation in clinical investigations such as that done by Yakaitis *et al.* Canadian committees on human experimentation have taken the stand that informed consent can be given only by the person involved and no one else is entitled to assume any degree of unnecessary risk on someone else's behalf. This attitude might be deplorable from the standpoint of pediatric pharmacology, but it seems to be consistent with the general principles of medical ethics. Second, I would have liked to have seen it emphasized in the article how imprecise it is to derive the  $MAC_{EI}$  from log-probit curves based on 20 observations. The curve is drawn through three points. The first of these, claiming 100 per cent failure rate, is based on five failures out of five tries. The position of this point

might be anywhere between 100 and 85 per cent, because there is little assurance that a sixth attempt at this concentration would have also been unsuccessful. Comparable degrees of uncertainty are associated with the other two points. The rigorous mathematical treatment of data derived from a small number of observations obscures the fact that changing the outcome of a single case in the most populous cell will shift the calculated median value from 3.3 per cent at 700 torr to 2.6 per cent—a 20 per cent difference. Constructing probit curves from 22 observations grouped into three classes in a very different proposition from determining the precise  $MAC_{EI}$  for each of these subjects, ranking the values, and constructing a probit curve through 22 points. If in the present context it turns out that such a determination was not feasible, then the probit or logit analysis of the data is simply not appropriate.

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### REFERENCE

1. Yakaitis RW, Blitt CD, Angiulo JP: End-tidal enflurane concentration for endotracheal intubation. *ANESTHESIOLOGY* 50:59-61, 1979

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*In reply:*—We basically agree with Dr. Keeri-Szanto's comments concerning the numerical precision of  $MAC_{EI}$ . Obviously, his observations can be applied to all MAC values, since statistically, they represent gross estimates based on a relatively limited sample size, and influenced by a variety of clinical conditions. Nevertheless, MAC is the best estimate of anesthetic depth that we have at present.

We derived  $MAC_{EI}$  after the manner in which MAC values had been previously obtained in order to establish and compare additional points on the "potency" curves for halothane and enflurane. Indeed,  $MAC_{EI}$  values for these two agents were cal-

culated to be approximately 30 per cent greater than their respective MACs. Assuming similar confidence intervals for both  $MAC_{EI}$  and MAC, the relationship between these two entities for halothane and for enflurane would hold true regardless of their purely numerical accuracy.

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