

peripheral nerve stimulator applied to the patient prior to induction of anesthesia (stimulation can be begun after induction of anesthesia).

We do not believe the previous report from Sosis *et al.*⁵ seriously proves the priming principle to be nonefficacious. Our interpretation of their results is that they simply chose an inferior combination of priming dose, priming interval, and intubating dose to test the technique.

Despite the priming principle, succinylcholine still has the most rapid onset of neuromuscular blockade. We were careful to point out that use of the priming principle "may be the method of choice when succinylcholine is contraindicated or undesirable."¹ In these instances, the use of the priming principle will shorten the onset of complete neuromuscular blockade by more than a minute in most patients compared with the use of a single, large dose of nondepolarizing muscle relaxant. We feel that this fact makes the use of the priming principle an important clinical tool.

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Concentration versus Partial Pressure: Which Is Important?

To the Editor:—I wish to call attention to a possible misinterpretation of the recent article by Nakagawara *et al.*¹ This article presents interesting findings for enflurane, halothane, and isoflurane that have potential relevance to immune defenses against infection and cancer.² However, the relevance of the findings may be limited because the anesthetic partial pressures used in this study exceed those applied in clinical practice. The three anesthetics were equilibrated with a modified Hanks' solution "by bubbling each vaporized anesthetic with a carrier gas of air (4 l/min) at 4° C on a shaking plate." The solution temperature then was increased to 37° C.

This increase in temperature decreased the solubility of the anesthetic and thereby increased the partial pressure of anesthetic. The increase can be calculated from the data supplied in figure 1 of the paper. That figure indicates that 1% enflurane, halothane, and isoflurane (the

lowest concentrations used) produced 0.43, 0.45, and 0.37 mg of anesthetic per liter of electrolyte solution, respectively. Each concentration can be converted to a partial pressure (given as a percentage of one atmosphere) at 37° C by the following calculations: divide by the molecular weight to give the moles; multiply by 22,400 ml/mole to give the ml of anesthetic at standard conditions; multiply by 310/273 to give the ml at 37° C; divide by the electrolyte/gas partition coefficient³ to give the equivalent ml of anesthetic vapor per liter of air; and divide by 10 to give the percentage of one atmosphere composed by the anesthetic. These calculations indicate that at 37° C the "1%" concentrations actually were 8.0% enflurane, 7.7% halothane, and 9.3% isoflurane. Such lethal concentrations had no effect on the generation of superoxide. An effect on intracellular free calcium was produced by these concentrations of halothane and en-

flurane (but not isoflurane). Interpolation to lower, clinically relevant concentrations suggests that enflurane and halothane only minimally affect intracellular free calcium.

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In reply:—It has been known that oxygen radicals produced by phagocytes play a crucial role in the host-defense mechanism. The inhibitory effects of volatile anesthetics on the oxidative metabolism in human neutrophils were reported by Welch *et al.*^{1,2} They have shown that the anesthetics inhibited oxidative metabolism of human neutrophils reversibly at clinically relevant concentrations.

Our intent was to study the mechanism of the inhibitory effects of the anesthetics on the superoxide-releasing activity of human neutrophils.³ We used the relatively high concentrations of the anesthetics to obtain distinct evidence of the inhibitory effects of the anesthetics on the superoxide release and Ca^{2+} mobilization. The concentrations we used were not lethal to the neutrophils as shown by the trypan blue exclusion test, wherein more than 90% of the cells were viable and that functional recovery of 65–85% was observed after removal of the anesthetics. This may be due to a short anesthetic exposure time of only 10 min. In clinical usage, the volatile anesthetics might not so strongly affect oxidative metabolism and the mobilization of Ca^{2+} , but we believe that the same mechanism may work with a longer exposure time even at lower anesthetic concentrations. Further study by using a more sensitive method for determination of intracellular free Ca^{2+} concentration, such as aequorin,⁴ would be necessary.

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In reply:—Dr. Eger suggests that the findings of Nakagawara *et al.* are interesting, but may have limited clinical relevance because of the very high partial pressures of anesthetics required to achieve the reported effects. I have always found “anesthetic concentrations” *in vitro* to be a

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controversial topic, perhaps due to the ambiguity of what constitutes a clinically relevant anesthetic concentration in an *in vitro* system.

The partition coefficient of Hanks' buffer at 37° C for halothane is $\sim 0.8^2$ and for whole blood at 37° C, 2.4. If