analeptic effect. However, the fact that those who received doxapram did not complain of incisional pain suggests that an antianalgesic effect is lacking. Use of naloxone for reversal of inhalational anesthesia deserves further investigation.

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Equal Liquid Volumes Not Valid for Comparing Volatile Anesthetics

To the Editor:—The recent article by Stacey *et al.*[1] suggests that since hepatocytic function is adversely altered by liquid volumes of chloroform and methoxyflurane to a greater extent than by the same liquid volumes of halothane and enflurane, that some meaningful index of relative hepatotoxicity is demonstrated. On an equal-volume basis the above conclusion may be correct. However, utilizing identical liquid volumes for comparing anesthetic drug effects is completely misleading and inappropriate, for it ignores other more conventional and certainly more clinically relevant methods for comparing anesthetic effects. The question is: what should the "dose" coordinate of the dose–response tests in this study be labeled? I contend that the least appropriate label is "volume," for it fails to take into account differences in specific gravity, molecular weight, and anesthetic solubility, all of which establish the system partial pressure, which in turn determines anesthetic activity. Much more appropriate labels of dose for anesthetics might be molar fraction, critical volume, or MAC multiple. The attractiveness of the latter is that it has become a standard understood by anesthesiologists–clinicians and research investigators alike and, in a way, normalizes the doses for the various agents' physical characteristics.

I have restated the doses used in the study by Stacey *et al.* in terms of MAC multiples (table 1). It is obvious that any given dose represents a sixfold greater MAC multiple of methoxyflurane than of enflurane, with halothane and chloroform intermediate between the two. Thus, when methoxyflurane, 10 μl, results in potassium leakage from the hepatocyte, whereas enflurane, 10 μl, does not, rather than concluding methoxyflurane is more toxic to hepatocytes than enflurane, one should conclude that the dose of methoxyflurane is roughly 27 MAC while the dose of enflurane is only 4.5 MAC. In fact, when the data are replotted for potassium loss and alanine aminotransferase activity using MAC equivalence as the dose, below 10 MAC, halothane, methoxyflurane and enflurane have equally minimal effects and chloroform only a slight effect. One must then ask the value of any inferences about clinical hepatotoxicity from the subsequent increased doses wherein as much as 55 times the clinically useful dose is used as the provocateur.

TABLE 1. MAC Multiple of Anesthetic Doses Used in Study*

Dose (μl)	Enflurane	Halothane	Chloroform	Methoxyflurane
2.5	1.13	2.7	3	6.87
5	2.25	5.4	6	13.75
10	4.5	10.8	12	27.5
15	6.75	16.2	18	41.0
20	9.0	21.6	24	55.0

* MAC multiple determined by calculating the partial pressure present in the system at 37 C and assuming solvent solubility to approximate blood solubility. In fact, if solvent solubility were less than blood solubility, the MAC multiple values would all be greater than those in table 1.

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