TABLE 1. Loading and Maintenance Doses of Pancuronium Bromide for Non-obese and Morbidly Obese Adult Patients

	Pancuronium (mg)	
	For Non-obese Patients (from Miller[3])	For Morbidly Obese Patients (from Tsueda[1])
Loading dose	0.3–1.0	0.8
Maintenance dose		
0–40 min	2.0	3.5
40–80 min	1.0	1.0
80–120 min	0.5	1.0
120–160 min	0.5	1.0

face areas is 2.4 m^2 to 1.7 m^2, which equals 1.4. These differences may not be random, and the lack of statistical significance may have resulted from either their method of data analysis or the small numbers of patients in their study groups.

Even when we accept the importance of the relationship of the pancuronium doses to body surface area, we are still left with a discrepancy in their discussion. Numerous human and animal studies have shown that body surface area is correlated with metabolic rate, cardiac output, and hepatorenal drug excretion. Although allometric correlations with blood volume and extracellular fluid volume also exist, these seem less important for explaining the increased maintenance doses of pancuronium from 30 to 150 min. When the cumulative maintenance doses are expressed as mg/m^2/$min^{1/2}$, the doses from the non-obese group are remarkably similar to my analysis[2] of the pancuronium data from Miller and Eger.[3] The slope of the best-fit line is .19 for the Tsueda *et al.* study, compared with .17 for the Miller and Eger study.

The mean loading and maintenance doses obtained from these two clinical studies conducted during halothane anesthesia may be shown in tabular form (table 1). The doses of pancuronium from the study by Miller and Eger are included in the non-obese column and are converted from mg/m^2 to mg by assuming a mean body surface area of 1.7 m^2. The maintenance doses are calculated for 40-min intervals and are rounded off to the nearest .5 mg. I believe that this table provides useful guidelines for the use of pancuronium during halothane anesthesia in adult patients.

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Is Naloxone a Nonspecific Analeptic?

To the Editor:—Recent publications suggest that naloxone does not antagonize the effects of general anesthesia but that rather, its main activity may be due to the antianalgesic component and a nonspecific analeptic action.[1–5] We would like to describe preliminary observations which support this concept. Utilizing the postanesthesia recovery score (PARS) to assess the rates of recovery in anesthetized patients,[6] we studied 11 ASA class 1 patients who did not receive narcotics for premedication or during their operation. Soon after the patients arrived at the recovery room, a control PARS was taken (average value 4.7). Naloxone, 0.8 mg, was then given intravenously. Five minutes later, scores showed a significant increase of 61 per cent (average 9.2, $P < 0.01$, Mann-Whitney non-parametric test) and peaked at 10 min (average 9.2, $P < 0.01$), remaining stable for the next hour. Spontaneous activity, return to consciousness and incisional pain were suddenly observed in most of the patients within 1 min of the naloxone injection. Three other patients who received doxapram, 40 mg, also showed increases of their PARS 5 (7.7) and 10 (8.7) min after administration. Although consciousness and spontaneous activity also returned promptly, no complaint of incisional pain was reported in this group. Blood pressure and heart rate remained within 20 per cent of preanesthetic levels in all patients. These results are in agreement with the findings in the abovementioned studies. Since naloxone and doxapram had similar effects in patients who had not received narcotic drugs, their actions on the state of consciousness and spontaneous activity may have been due to

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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