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## Pancuronium Requirements of the Morbidly Obese

*To the Editor:*—Tsueda *et al.* have measured increased cumulative requirements of pancuronium bromide in morbidly obese as compared with non-obese patients.<sup>1</sup> Their attempt to explain their data in terms of a three-compartment pharmacokinetic model distracts from their otherwise nice clinical study. A three-compartment model requires the measurement or estimation of at least six parameters. A difference of one or more of these parameters could cause the differences in doses of pancuronium in their patients. Their discussion focuses on the parameters of the first two compartments, which have half-lives of 5 and 10 min. This is contrary to their published data, which begin at 30 min and end at 150 min. Only by fitting their data to their compartmental model can they estimate and compare these parameters.

I suggest an alternative method for analyzing the data of Tsueda *et al.* by use of the previously described relationship between the cumulative doses of pancuronium and the square root of elapsed minutes.<sup>2</sup> The least-squares best-fit lines are drawn through the data points and extrapolated with dashes to time zero (fig. 1). The equations for the lines, the real time in min, and the correlation coefficients ( $r = .99$ ) are also

shown. The cumulative doses of pancuronium in both groups are clearly proportional to the square root of elapsed min.

In contrast to the three-compartment model referred to by Tsueda *et al.*, the square-root-of-time model requires only two parameters, the slope and the y-intercept, to describe the experimental data. Furthermore, the translation of these pharmacokinetic data into the clinical quantities of loading and maintenance doses becomes a simple calculation. For example, the figure shows that the loading doses (y-intercepts) for the obese and non-obese patients are quite similar. This finding is contrary to the experimental protocol of Tsueda *et al.*, which required the administration of loading doses calculated from body surface area ( $1 \text{ mg/m}^2$ ).

The authors state that "when the amounts of pancuronium were corrected for body surface area . . . there was no difference between the groups." However, four of the five mean doses of pancuronium/ $\text{m}^2$  (shown in their figure 1) were greater in the obese group. This also appears in my analysis of their data. The ratio of the slopes of the best-fit lines is .52 to .33, which equals 1.6. The ratio of the mean body sur-

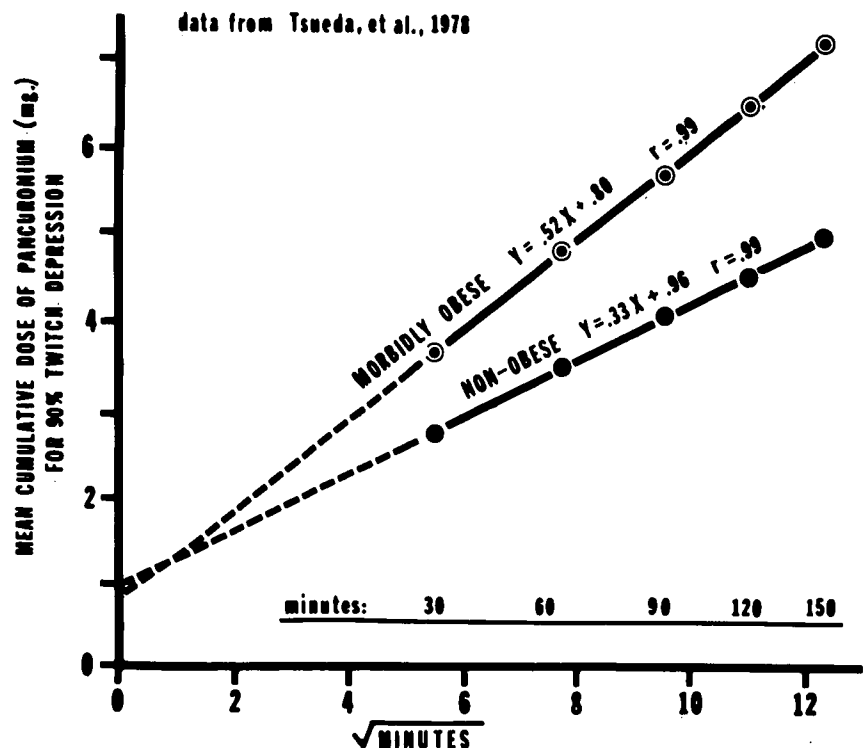


FIG. 1. Cumulative doses of pancuronium for 90 per cent twitch depression in morbidly obese and non-obese patients.

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 <sup>3</sup> )	For Morbidly Obese Patients (from Tsueda <sup>1</sup> )
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<sup>2</sup> to 1.7 m<sup>2</sup>, 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<sup>2</sup>/min<sup>1/2</sup>, the doses from the non-obese group are remarkably similar to my analysis<sup>2</sup> of the

pancuronium data from Miller and Eger.<sup>3</sup> 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<sup>2</sup> to mg by assuming a mean body surface area of 1.7 m<sup>2</sup>. 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.<sup>1-5</sup> 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,<sup>6</sup> 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 above-mentioned 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