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Correspondence

Neostigmine Antagonism of Neuromuscular Block

To the Editor:—In their recent article, "Antagonism of *d*-Tubocurarine-, Gallamine-, and Pancuronium-induced Neuromuscular Blockades by Neostigmine" (ANESTHESIOLOGY 37: 503–509, 1972), Miller, Larson, and Way state that comparison of the durations of action of two muscle relaxants requires knowledge of equipotency but that determination of the latter is impossible, since the dose–response curves are not parallel. We did determine the dose–response curves for *d*-tubocurarine and gallamine in humans and found them to be parallel (Ghoneim, M.M., *et al.*, Can Anaesth Soc J 19:66–74, 1972). *d*-Tubocurarine in a dose of 2.5 mg/m² produced 27.47 ±6.4 per cent blockade with a mean recovery time (80 per cent twitch height recovery) of 13.9 ± 2.7 minutes. Gallamine in a dose of 15 mg/m² produced 28.18 ± 4.3 per cent blockade with a mean recovery time of 14.8 ± 2.9 minutes. At a higher dose level *d*-tubocurarine produced a 62.6 ± 5.4 per cent blockade with a mean recovery time of 42.4 ± 1.3 minutes, while gallamine produced a 77.88 ± 3.6 per cent blockade with a 54.4 ± 3.6 minute recovery time. Our results support their contention that there is no justification for the belief that gallamine is a shorter-acting muscle relaxant than *d*-tubocurarine.

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To the Editor:—We are pleased to receive support for our observation that the duration of action of gallamine is not shorter than that of *d*-tubocurarine. Our conclusions that dose–response curves for relaxants are not parallel was based on the work of Lund and Stovner,[1] who observed steeper dose–response curves for alcuronium and pancuronium than for *d*-tubocurarine; they did not study gallamine. Although the studies of Ghoneim *et al.*[2] suggest that the dose–response curves of *d*-tubocurarine and gallamine may be parallel, we have had some reservations concerning their methods. Ghoneim *et al.* studied only two doses of each drug. It is nearly impossible to prove either linearity or parallelism of dose–response curves obtained from only two doses. For example, the slope of their two-point dose-response curve of *d*-tubocurarine might have been radically altered had a third dose been studied (fig. 1). Apart from this simple mathematical consideration, Ghoneim *et al.* administered the larger dose of relaxant one hour after the smaller dose to the same patient.[2] The depression of twitch height from the second, larger, dose of relaxant may represent a cumulative effect of the two doses. If this were true, dose–response curves would be steeper than they would be if only one dose of relaxant had been given to each patient. Ghoneim *et al.* observed mean times from relaxant administration to return of 80 per cent of control twitch height of 14.8 and 54.4 minutes for gallamine 15 mg/m² and 20 mg/m², respec-

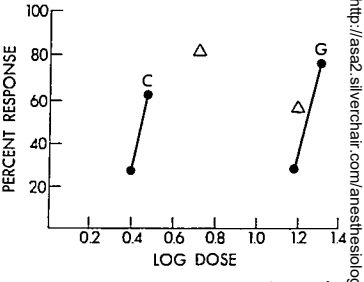

FIG. 1. Dose–response regression lines taken from Ghoneim *et al.*[2] The triangles represent fictitious data inserted by this author, *C* represents *d*-tubocurarine, and *G* represents gallamine. Had a third dose been given with results as depicted, the slope of the *d*-tubocurarine curve would be flatter than that of the gallamine curve.

TABLE 1. Doses of Gallamine and *d*-Tubocurarine (*d*Tc) Necessary for 20, 50, and 80 Per Cent Depression of Twitch Height

	Gallamine (mg/m²)	*d*Tc (mg/m²)	Gallamine (mg/m²)/ *d*Tc (mg/m²) Ratio
20 per cent	16	3.7	4.3
50 per cent	22.5	4.9	4.6
80 per cent	29	6.1	4.8

* Data of Miller *et al.*[4]

tively. At this point in recovery, more than 80 per cent of the receptors are still occupied by gallamine.[3] Does it take longer than an hour for all the receptors to be free of gallamine?

Stimulated by Doctor Ghoneim's letter, we replotted data from studies previously reported.[4] These data indicate that the dose–response curves of *d*-tubocurarine and gallamine do not deviate from parallelism during 1.25 MAC halothane anesthesia (table 1). These limited findings support the conclusions of Ghoneim *et al.*,[2] despite our reservations concerning their protocol. We conclude that the dose–response curves of pancuronium and *d*-tubocurarine are not parallel, while the curves of *d*-tubocurarine and gallamine are parallel, at least during halothane anesthesia.

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Metabolism

INAPPROPRIATE CALCIUM HOMEOSTASIS The authors have attempted to define the origin of the abnormally high plasma calcium levels in children with severe hypercalcemic syndrome, a condition associated with supravalvular aortic stenosis, mental retardation, and "elfin facies." An intravenous infusion of calcium (10 mg/kg) was given over a period of one hour to each of eight children with severe idiopathic hypercalcemia, 4 to 15 years old, as well as to controls. The average half-time for the postinfusion decrease in total calcium was 1.7 times longer in the patients than in the controls, suggesting an inability to handle acute calcium loads.

The authors postulate that the prolonged half-time found in the hypercalcemic subjects is caused by inadequate decline of bone resorption in response to an induced hypercalcemia. The most likely explanation for the phenomenon appears to be a deficiency of thyrocalcitonin.

The postinfusion decrease of total calcium in the control group varied directly with age, with the older children demonstrating the slowest declines. This appeared in keeping with the effect of age on the rate of radiocalcium redistribution following injection in experimental animals. (*Forbes, G. B., and others: Impaired Calcium Homeostasis in the Infantile Hypercalcemic Syndrome, Acta Pediatr. Scand. 61: 305–309, 1972.*)