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Stimulus Frequency Is Essential Information

To the Editor:—The article by Drs. Wymore and Eisele needs further definition of methodology before the authors' results can be interpreted.[1] The authors state that nearly twice as much *d*-tubocurarine was needed to depress ventilatory musculature (as indicated by measurement of inspiratory force) as was required to produce depression of the evoked twitch response in the thumb. The authors also noted that inspiratory force recovered about twice as rapidly as did muscles innervated by the ulnar nerve (thumb twitch). However, the authors have made an important omission in not mentioning the stimulus frequency at which peripheral-nerve stimulation was carried out. It is well known from both animal and human studies[2,*] that the extent of inhibition of indirectly elicited peripheral muscle responses produced by a nondepolarizing relaxant is directly proportional to the frequency of neural stimulation. In other words, faster rates of stimulation result in greater apparent depth of nondepolarizing block as measured by depression of the evoked muscle twitch. We have found that increasing the frequency of ulnar-nerve stimulation from 0.1 to 1 Hz decreased the ED_{95} for the inhibition of thumb twitch by *d*-tubocurarine in patients during nitrous oxide–narcotic–barbiturate anesthesia from 0.5 to 0.16 mg/kg. The time interval for recovery of the twitch from 5 to 25 per cent of control decreased from 30 ± 2 min at 0.1 Hz to 13 ± 2 min at 1 Hz.

Our study emphasizes the importance of defining the stimulus frequency when generating dose–response data for nondepolarizing relaxants. The differential effects of *d*-tubocurarine upon ventilatory and peripheral muscles described by Dr. Wymore and Eisele cannot be precisely defined unless the frequency of peripheral nerve stimulation is stated. In other words, the dose ratio for depression of ventilatory versus peripheral musculature by *d*-tubocurarine could vary by a factor as high as 3 or more, depending on the frequency of ulnar nerve stimulation used by Wymore and Eisele. Clinical studies of neuromuscular function are badly in need of standardization of stimulus patterns!

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In reply:—Doctors Ali and Savarese have correctly pointed out an important omission in our methods of peripheral-nerve stimulation. We are aware of the significance of stimulus frequency and regret that we inadvertently did not indicate that our studies were done at a frequency of 1 Hz. The data of Ali and Savarese show close agreement with our results for depression of thumb adduction with *d*-tubocurarine at 1 Hz. Our ED_{50} was 0.143 (.06 to .198) mg/kg, compared with their ED_{95} of 0.15 (.07 to .32) mg/kg, despite differences in anesthetic technique (halothane/N_2O *vs.* thiopental/N_2O) and rates of *d*-tubocurarine administration.

The differential effects of *d*-tubocurarine between inspiratory and peripheral muscles that we presented are meaningful, since they were done at the same stimulation value. Unpublished data from prior studies performed by direct phrenic-nerve stimulation and gastric balloon recording of the diaphragmatic twitch were done at the same stimulus frequency (1 Hz). The results showed a relationship between hand and diaphragm muscle responses to *d*-tubocurarine similar