

- mans during nitrous oxide-fentanyl or nitrous oxide-enflurane anesthesia. *ANESTHESIOLOGY* 70:31-35, 1989
2. Weber S, Brandom BW, Powers DM, Sarner JB, Woelfel SK, Cook DR, Foster VJ, McNulty BF, Weakly JN: Mivacurium chloride (BW B1090U)-induced neuromuscular blockade during nitrous oxide-isoflurane and nitrous oxide-narcotic anesthesia in adult surgical patients. *Anesth Analg* 67:495-499, 1988
3. Savarese JJ: Reply. *ANESTHESIOLOGY* 70:166-167, 1989

4. Sarner JB, Brandom BW, Woelfel SK, Dong ML, Horn MC, Cook DR, McNulty BF, Foster VJ: Clinical pharmacology of mivacurium chloride (BW B1090U) in children during nitrous oxide-halothane and nitrous oxide-narcotic anesthesia. *Anesth Analg*, in press

(Accepted for publication March 21, 1989.)

Anesthesiology
70:1037, 1989

In Reply:—We appreciate the obviously careful reading of our paper by Drs. Brandom and Cook and are grateful to them for drawing our attention to two minor errors.¹ First, in our discussion we stated that Weber *et al.*² used a single twitch mode of nerve stimulation and that Choi *et al.*³ used electromyography to measure neuromuscular response. These authors and their methods were erroneously transposed and, in fact, Weber *et al.* used electromyography and Choi *et al.* used single twitch mode of nerve stimulation. Second, in table 1, the dibucaine number of patient 4 should be 72 and not 84 as printed.

We support the reanalysis which Brandom and Cook have made of their dose-response data. The weakness of the original analysis by Weber *et al.*² was that they estimated an ED₉₅ value by extrapolation from values for ED₂₅, ED₅₀, and ED₇₅. This resulted in an underestimate of the ED₉₅. In our study, we derived the ED₉₅ value from data points covering the entire range of responses from 0% to 100% twitch depression. While it can be argued how best to treat 100% responses, we consider that an accurate determination of ED₉₅ requires data points both above and below 95% response. The revised estimate for ED₉₅ obtained by Brandom and Cook, 70 $\mu\text{g} \cdot \text{kg}^{-1}$, after their reanalysis of the data of Weber *et al.*² is similar to the value, 67 $\mu\text{g} \cdot \text{kg}^{-1}$, which we reported in our paper.¹

The debate concerning the treatment of data points at the extremes of the dose-response curve is too complex to be covered in this forum. Briefly, we would take the position that extrapolation beyond one's data points is undesirable and that to estimate an ED₉₅ will inevitably require the inclusion of some points representing 100% twitch depression. If one has data only within the 20-80% range of response, then only the ED₅₀ should be reported. As we noted in our paper,¹ published estimates of ED₅₀ are more uniform than are estimates of ED₉₅.

We would agree with Drs. Brandom and Cook that the manner by which variations in plasma cholinesterase activity and genotype affect the metabolism of and neuromuscular responses to mivacurium needs to be elucidated. Our data regarding neuromuscular responses in the patients with abnormalities of plasma cholinesterase were purely descriptive and suggested that the pattern of response was inconsistent

and was not the same as might be seen following succinylcholine administration. For the information of Drs. Brandom and Cook and others who may be interested, the substrate used in our study to estimate plasma cholinesterase activity was acetylthiocholine.

JAMES E. CALDWELL, F.F.A.R.C.S.
*Assistant Professor of Anesthesia
Department of Anesthesia*

RONALD D. MILLER, M.D.
*Professor and Chairman
Department of Anesthesia
Professor of Pharmacology*

*University of California
San Francisco, California 94143-0648*

REFERENCES

1. Caldwell JE, Kitts JB, Heier T, Fahey MR, Lynam DP, Miler RD: The dose-response relationship of mivacurium chloride in humans during nitrous oxide-fentanyl or nitrous oxide-enflurane anesthesia. *ANESTHESIOLOGY* 70:31-35, 1989
2. Weber S, Brandom B, Powers DM, Sarner JB, Woelfel SK, Cook DR, Foster VJ, McNulty BF, Weakly JN: Mivacurium chloride (BW B1090U)-induced neuromuscular blockade during nitrous oxide-isoflurane and nitrous oxide-narcotic anesthesia in adult surgical patients. *Anesth Analg* 67:495-499, 1988
3. Choi WW, Mehta MP, Murray D, Forbes R, Sokoli MD, Gergis SD, Krol T, Abou-Donia M, Cotten PJ: Neuromuscular effects of BW B1090U during narcotic nitrous oxide anesthesia (abstract). *ANESTHESIOLOGY* 67:A355, 1987

(Accepted for publication March 21, 1989.)

Anesthesiology
70:1037-1038, 1989

Delayed Respiratory Depression Following Alfentanil

To the Editor:—We were interested to read the report of delayed respiratory depression following administration of alfentanil.¹ However, in contrast to the authors' statement that this phenomenon had not been reported before, we wish to note that delayed respiratory depression following continuous infusion of alfentanil was first described by

Lamarche *et al.* in 1984² and, later that year, two more cases of unexpected respiratory depression were reported after its use.³

Delayed respiratory depression has also been described after administration of oxymorphone,⁴ and may occur after all opioids. The unstated theme of all these articles is that by whatever route of ad-