
In Reply.—We appreciate the obviously careful reading of our paper by Drs. Brandon and Cook and are grateful to them for drawing our attention to two minor errors. First, in our discussion we stated that Weber et al. used a single twitch mode of nerve stimulation and that Choi et al. 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 Brandon and Cook have made of their dose-response data. The weakness of the original analysis by Weber et al. was that they estimated an ED95 value by extrapolation from values for ED50, ED95, and ED95. 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 Brandon and Cook, 70 µg·kg⁻¹, after their reanalysis of the data of Weber et al. is similar to the value, 67 µg·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 ED95 should be reported. As we noted in our paper,¹ published estimates of ED95 are more uniform than are estimates of ED95.

We would agree with Drs. Brandon 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. Brandon and Cook and others who may be interested, the substrate used in our study to estimate plasma cholinesterase activity was acetylhiocholine.

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

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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 unstimulated state of all these articles is that by whatever route of ad-


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Delayed respiratory depression has also been described after administration of oxymorphone,⁴ and may occur after all opioids. The unstimulated state of all these articles is that by whatever route of ad-
ministration there is risk of respiratory depression associated with the use of potent analgesics and this risk is highest following anesthesia. This is why recovery rooms are important even when a "short-acting narcotic" has been used. "Short-acting" is, of course, a relative term for the elimination half-life of alfentanil and is still measured in hours.

There is little information on the effect of anesthesia and surgery on pharmacokinetics and pharmacodynamics of analgesics. Although changes accounted for by these effects are usually predictable qualitatively, quantitatively they are not. Observation and monitoring of drug effect on vital signs of individual patients are therefore a necessary and important part of postoperative care. It is interesting to note that three of five of these reported cases of delayed respiratory depression following the administration of alfentanil were associated with spinal surgery.

**DR. HARRY OWEN**
**DR. WILLIAM G. BROSE**
Department of Anaesthesia and Intensive Care

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_In Reply—_I am grateful to the authors of this letter for pointing out other cases in the literature of delayed respiratory depression following alfentanil. I also agree with the authors’ emphasis on the need for close monitoring of drug effects in the postoperative period regardless of the opiate chosen.

**MICHAEL E. MAHLA, M.D.**
Assistant Professor of Anesthesiology and Neurosurgery

Department of Anesthesiology
University of Florida, College of Medicine
Box J-254, J. Hillis Miller Health Center
Gainesville, Florida 32610-0234

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**Flinders Medical Centre**
Bedford Park, South Australia 5042

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