form of headache was noted in only one versus six patients in the 29-
and 26-G groups, respectively.

The difference between minimal to mild headache (P < 0.05) and
moderate headache (P < 0.01) was statistically significant, but there
was not significant difference between mild and moderate headache
(P < 0.14, exact Fisher test). The technique of spinal anesthesia with
29-G needles is readily learned, requires only little increased time and
no more effort to complete, and is as successful as spinal anesthesia
with larger 26-G needles in the routine practice. We recommend the
use of 29-G needles for use in younger patients at risk for headache.
With the increasing number of patients presenting for ambulatory sur-
gical procedures, these thin needles may prove to be especially beneficial
in precluding headache.

M. DITTMANN, PH.D., M.D.
Head
F. RENKL, M.D.
Consultant

Dose-Response Relationship to Mivacurium in Humans

To the Editor:—We would like to make a correction and comment
regarding the recent paper describing the dose-response relationship
of mivacurium chloride in humans.1 Weber et al.2 did not use a single
 twitch mode of nerve stimulation in their study of the dose-response
relationship of mivacurium. We used a stimulation pattern of 2 Hz for
2 s at 10-s intervals.

Because of recent discussion about the methods of calculation
of the dose-response relationship for mivacurium,3 we would like to offer
reanalysis of our dose-response data for mivacurium. Similar questions
could be asked of Caldwell et al.1 The ED<sub>95</sub> reported by Weber et al.2
was calculated from observations of 26 patients with normal pseudocholi-
esterase activity who each received a single dose of either 30,
40, or 50 μg/kg of mivacurium. If we add an additional nine adult
patients who received 60 μg/kg of mivacurium to the calculation of
the dose-response relationship, then the ED<sub>95</sub> is 45 μg/kg and the ED<sub>90</sub>
is 70 μg/kg.4 This is in contrast to the ED<sub>90</sub> of 41 μg/kg and ED<sub>95</sub>
of 58 μg/kg calculated from the observation of 26 patients.5 Not all
of the nine adults receiving 60 μg/kg developed 100% neuromuscular
blockade. The patients who developed 100% neuromuscular blockade
in this group were assigned a probit of eight. We would expect, as do
others,6 that adding patients with 100% neuromuscular blockade to
the calculation of a dose-response relationship might increase the slope
of the regression line. It is our preference to present dose-response
data based on the responses of patients who have received doses between
the ED<sub>90</sub> and ED<sub>95</sub>, because this is expected to be the linear portion of
the dose-response relationship and linear regression is employed to
estimate the relationship.

These arguments are somewhat specious in that adding nine patients
who received 60 μg/kg of mivacurium to our calculations of the dose-
response relationship produced no statistically significant change in
the slope or intercept of the regression line. Individual patient variability
in response appears to be more important than these small differences
in methods in the determination of the dose-response relationship for
mivacurium.

Variation in pseudocholinesterase activity may contribute to inter-
patient variability in response to mivacurium. We find it interesting
that Caldwell et al.7 noted aberrant response to mivacurium in patients
with slightly abnormal pseudocholinesterase activity. Perhaps the pa-
tient who was sensitive to mivacurium and had pseudocholinesterase
activity at the low end of the normal range and 85% inhibition by
dibucaine is a homozygous normal patient as determined by response
to dibucaine and the substrate used by Smith Kline Bionscience Labo-
ratories, Van Nuys, California. (Could there be a significant difference
between 84 and 86% inhibition?) Undoubtedly, there is a difference
between the effects of pseudocholinesterase on mivacurium and on
the substrate employed to assay pseudocholinesterase in this study. All
patients with "normal pseudocholinesterase activity" may not metab-
olize mivacurium at the same rate. The characterizations of pseudo-
cholinesterase activity that were useful guides for the administration
of succinylcholine may not be as useful in the description of the effects
of mivacurium. To improve our understanding of this area, the sub-
strate used to assess pseudocholinesterase activity should be reported.

In the study of Weber et al.,2 the substrate used was acetylcholine
iodide.

Barbara W. Brandom, M.D.
Associate Professor of Anesthesiology

D. Ryan Cook, M.D.
Professor of Anesthesiology and Pharmacology

Department of Anesthesiology and Critical Care Medicine
University of Pittsburgh
Children's Hospital of Pittsburgh
125 DeSoto Street
Pittsburgh, Pennsylvania 15213

References

dose-response relationship of mivacurium chloride in hu-
CORRESPONDENCE

1037


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. 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 realignment which Brandom and Cook have made of their dose-response data. The weakness of the original analysis by Weber et al. was that they estimated an ED₉₀ value by extrapolation from values for ED₂₀, ED₅₀, and ED₇₀. This resulted in an underestimate of the ED₉₀. In our study, we derived the ED₉₀ 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 ED₉₀ requires data points both above and below 95% response. The revised estimate for ED₉₀ obtained by Brandom and Cook, 70 μg·kg⁻¹, after their realignment of the data of Weber et al. is similar to the value, 67 μg·kg⁻¹, which we reported in our paper.

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 ED₉₀ 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 ED₉₀ should be reported. As we noted in our paper, published estimates of ED₉₀ are more uniform than are estimates of ED₅₀.

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 acetylmethylcholine.

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


(Accepted for publication March 21, 1989.)

Dear Editor—We were interested to read the report of delayed respiratory depression following administration of alfentanil. 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 1984 and, later that year, two more cases of unexpected respiratory depression were reported after its use.

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

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. 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 1984 and, later that year, two more cases of unexpected respiratory depression were reported after its use.

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