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*In Reply:*—We appreciate Drs. Fisher's and Shafer's interest in our work.<sup>1</sup> We agree with their view that our model did not optimally fit all data points. There is a large variation in the placebo and 2.0 mg/kg group, and it was difficult to define a model that optimally fits these data points. For higher doses of sugammadex, the model fits the data very well.

We have conducted a Phase 2 clinical trial. Those studies attempt to learn what is a good (if not optimal) drug regimen to achieve useful clinical value (acceptable benefit/risk). In contrast to the confirming phases of drug development, the learning phases entail so-called explanatory analyses; *i.e.*, analyses that estimate the quantitative relationship between inputs and outcomes according to some mechanistic view of the relationship.<sup>2</sup> In a Phase 2 study, a nominal design, including all ostensibly controllable factors affecting the conduct of the trial, is an abstract ideal. In fact, in any real study, deviations from nominal design are inevitable.<sup>2</sup> We decided to apply the model to our data which has been defined *a priori*, and has been used for several data sets on sugammadex which already have been published.<sup>3–5</sup> We did not want to retrospectively change the predefined approach of our statistical efficacy analysis. In future confirmatory studies on sugammadex it will be possible to develop and apply a more sophisticated model. The suggestions of Drs. Fisher and Shafer will be very useful in that context.

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## Conventional Neuromuscular Monitoring versus Acceleromyography: It's Not the Monitor but the Anesthetist

*To the Editor:*—In the September issue of *ANESTHESIOLOGY*, Murphy *et al.*<sup>1</sup> demonstrated that residual neuromuscular blockade may produce adverse respiratory outcomes. We believe that the methodology used in their study is significantly flawed, and that their conclusions comparing qualitative (conventional nerve stimulators) and quantitative (acceleromyography) monitoring are not supported by their results. In our opinion, their study failed to demonstrate that quantitative monitoring is superior to qualitative monitoring in reducing the incidence of adverse respiratory events in the perioperative period.

Naguib *et al.*<sup>2</sup> have written: "(In neuromuscular blockade studies,) nuances in protocol and apparently 'minor' variations in methodology may markedly affect outcome." We find three types of faults with the present methodology. First, they used visual rather than tactile evaluation of train-of-four (TOF) responses. The present study, involving 20 faculty and 50 residents and nurse anesthetists, and similar papers from the same institution<sup>3,4</sup> indicate that they routinely produce a level of blockade which results in two to three visual TOF responses. This practice is based upon an early study comparing electromyogram findings with a single surgeon's subjective evaluation of abdominal relaxation.<sup>3,5</sup> We believe that evaluating visual as compared to tactile TOF responses tends to underestimate the level of blockade and overestimate the amount of recovery. We have observed patients with 4/4 visual and simultaneous 0/4 tactile TOF responses. Others<sup>6,7</sup> have noted that visual TOF tends to overestimate the return of neuromuscular function, as compared with tactile monitoring. Furthermore, we are not aware of any studies that support the use of visual TOF monitoring or maintaining two to three visual TOF responses to attain satisfactory surgical relaxation. There are numerous studies<sup>8–10</sup> that rely upon tactile TOF monitoring, a clinical simplification of the original investigations of TOF using mechanomyography.

Secondly, we do not believe that the present study truly compared one group of patients who were managed with conventional neuro-

muscular monitoring with another group who were managed with quantitative monitoring. Both groups of patients received conventional TOF monitoring to maintain two to three visual TOF responses and guide the administration of additional doses of rocuronium. Acceleromyography was not used in the quantitative group until after administration of the last dose of rocuronium to assure that a TOF ratio of > 0.8 was reached before tracheal extubation. The conventional group underwent tracheal extubation after a conventional nerve stimulator demonstrated the loss of visual TOF fade, an inaccurate indicator of TOF ratio.<sup>7</sup>

Thirdly, the authors did not follow common practices of neuromuscular monitoring and management of extubation when using a conventional monitor. It has been demonstrated that using intermediate neuromuscular blockers and waiting until the appearance of 2 or 3–4 tactile TOF responses before the administration of neostigmine markedly increases the likelihood of adequate (TOF ratio of > 0.8) recovery within 20–30 min, at which time the trachea can be safely extubated.<sup>9,10</sup> It is predictable from the present study design that patients in the quantitative group who are extubated with a TOF ratio of > 0.8 will not have residual blockade in the postanesthesia care unit, while those in the conventional group whose tracheas are extubated on the basis of loss of visual TOF fade will have a deeper level of blockade and more likely demonstrate residual blockade.

While Murphy *et al.* have alerted us to the relationship between residual neuromuscular blockade in the setting and practices described in the article, they have failed to support the editorial opinion that acceleromyography should be available in every operating room where neuromuscular blockers are administered.<sup>11,12</sup> Instead, they have demonstrated that acceleromyography reduces the risk of residual neuromuscular blockade in a setting where evidence based standards for conventional monitoring are not routinely followed. We agree with Naguib *et al.*<sup>2</sup>: "What makes the difference in the incidence of (residual