

where  $n$  is the sample size and  $p$  is the level of credibility, i.e., if 95% confidence is required, then  $p = 0.05$ .<sup>2</sup> If  $n = 8$  and  $p = 0.05$  as used by Sears, the maximum risk for significant bradydysrhythmias in a very large group of similar patients is actually 31%. Since bradydysrhythmias are undesirable and the true incidence could be as high as 31% based on Sears' study, we believe their conclusion would be more correctly stated that the incidence of bradydysrhythmias with a second dose of succinylcholine after a ketamine induction is (with 95% confidence) no higher than 31%.

When  $n$  is greater than 30, the computation is considerably simplified, and is referred to as the rule of 3.<sup>3</sup> When  $p = 0.05$ , "if none of  $n$  patients shows the event about which we are concerned, we can be 95% confident that the chance of this event is at most 3 in  $n$ , (i.e.,  $3/n$ )."<sup>2</sup> Thus, if Sears *et al.* had observed zero incidence in 50 subjects, they could have predicted the maximum incidence to be no higher than 6% ( $3/50$ ) in a similar but large group.

When negative results are reported, the author should be careful about extrapolating results to the universe of patients as a whole.

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*In Reply:*—We agree with Benefiel *et al.* that our statement "the administration of a second dose of succinylcholine to healthy adult patients after induction with ketamine is safe with respect to cardiac rate and rhythm" may be too strong if only statistical analysis is considered. However, in clinical situations, other factors, such as patient's physical status, the pharmacological properties of the drug, or combination of drugs, must also be considered in the clinical conclusion of a particular study. In our study,<sup>1</sup> although the number is small ( $n = 8$ ), we believe that our conclusion may not be too strong. This conclusion is not only based on the statistical analysis but also on the physical status of the patients (healthy adults) and on the pharmacodynamic property of ketamine as a drug with a sympathomimetic effect.<sup>2</sup>

The practical problem is the number of patients one should study before concluding that a technique is safe or dangerous. Based on our study, we feel it is appropriate to continue to use a second dose of succinylcholine after ketamine where required and continue to observe the patient response. If any serious side effects are encountered, we will of course report them. Thus far we still have not seen any problems with a second dose of succinylcholine in patients who received ketamine.

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## Succinylcholine and Trismus

*To the Editor:*—The recent publication of various articles and letters to the editor about succinylcholine and trismus has resulted in a reevaluation of the use of succinylcholine and a reassessment of our clinical practice when trismus occurs after the administration of succinylcholine.<sup>1-4</sup> The major problem in this whole issue centers around the clinical judgment issue of what constitutes trismus. Unfortunately, Dorland's *Medical Dictionary* does not clarify the issue, nor is it clarified in any of

the papers that have been written. The reason is that it is a clinical judgment call with a broad spectrum of possibilities. At one end of the spectrum, the masseter muscle tone may be so increased that there is a complete inability to open the mouth. At the other end of the spectrum, there may be a mild increase in muscle tone that can be easily overcome. Van Der Spek has certainly thrown an entirely different light on the issue of succinylcholine and "trismus," with the finding

that there is a routine increase of masseter muscle tone in normal patients anesthetized with halothane or enflurane and given succinylcholine at the same time there was complete relaxation of limb muscle clinically, as well as loss of thenar muscle twitch.<sup>1,2</sup> There is certainly good evidence from *in vitro* studies to suggest that partial depolarization (produced by succinylcholine) combined with prior exposure to halothane will result in tension development in normal muscle. This is due to a halothane-induced shift in the voltage dependence of calcium release in the muscle.<sup>5</sup> It now becomes evident why the clinical determination of trismus is so difficult. It is very difficult to determine the difference between an exaggerated normal response to succinylcholine and a pathological response in which the increase in masseter tone may herald malignant hyperthermia susceptibility. Ideally, the use of the word "trismus," or "masseter spasm," should be reserved for the abnormal response of the masseter muscle to succinylcholine, but, practically, this may be very difficult. Fortunately, the incidence of malignant hyperthermia is very rare, occurring anywhere from 1 in 15,000 children up to 1 in 50,000 adults. The incidence of abnormal masseter muscle response (masseter spasm) with a combination of halothane and succinylcholine occurs in 1% of the patients in Boston (1 in 100) and 0.01% of the patients in Charlottesville (1 in 10,000).<sup>6</sup> The reason for the great differences in occurrence is not apparent, although it may represent subtle differences in clinical practice.

The first problem faced by the clinician is what to do if a patient does develop masseter spasm after succinylcholine. The recommendations cover a broad spectrum. Gronert recommends that the anesthesiologist continue the anesthetic with nontriggering agents, while monitoring end-expired CO<sub>2</sub>, venous and/or arterial blood gases, blood pressure, pulse, temperature, and muscle tone.<sup>3</sup> If there is any aberration, then the case is cancelled and treatment begun with dantrolene. On the other hand, if the situation is stable, the anesthetic can proceed with nontriggering agents. We agree with this management. At the other end of the spectrum is the opinion as expressed by Rosenberg with whom we strongly disagree.<sup>4</sup> He would cancel all surgery where there is "trismus" following succinylcholine. We disagree because of the aforementioned variability in the definition of trismus, and because we have monitoring techniques which permit us to detect developing malignant hyperthermia and dantrolene to treat a malignant hyperthermic episode.

A second problem that must be addressed when masseter spasm occurs is whether or not to obtain a muscle biopsy for an MH-susceptibility contracture study. Rosenberg and Gronert recommend it in all patients who develop trismus with succinylcholine.<sup>3,4</sup> If truly 1% of pediatric patients develop trismus with succinylcholine and halothane, then muscle biopsy would be the most frequently performed operation in the United States. Another problem with muscle biopsy is that there are a limited number of centers doing it,<sup>13</sup> and it would require great time and expense for families to travel to these centers.

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*In Reply:* The letter from Drs. Barry and Lynch succinctly raises many questions plaguing clinicians concerning the management of trismus following succinylcholine. Based on the findings that approximately 50% of patients with masseter spasm are truly MH susceptible on contracture testing,<sup>1</sup> and also Van Der Spek's work<sup>2</sup> showing that succinylcholine may increase muscle tone of the masseter muscle in normal patients, it is certainly clear that increased muscle tone after succinylcholine may or may not be related to MH. Whether MH can be differentiated from this hypertonic response found in normals by quantitatively measuring the extent of muscle tone increase has not

yet been explored. Clearly, therefore, there is a subjective element to diagnosing trismus. Again, because of the subjective nature of trismus, the incidence of trismus has been difficult to establish with accuracy. Unfortunately, studies of the incidence of trismus are retrospective. The published studies indicate a range of incidence of 1% in children following halothane and succinylcholine<sup>3</sup> to 1 in 12,000 in the Danish population.<sup>4</sup> I suspect that the much lower incidence of trismus in Charlottesville is in part related to the mode of administration of succinylcholine. I understand the im route of administration of succinylcholine is more

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