iment above for an entire cardiac cycle; note that the portion used for analysis of T is between maximum negative dP/dt and mitral valve opening (estimated as LVEDP of the preceding beat). The plot was generated using high fidelity pressure transducers, an analog-to-digital convertor, and special computer software to produce dP/dt from the digitized pressures and time. Since Swanson and Muir did not use an A/D convertor to capture their data, the differentiated pressures might be difficult for them to obtain.

We cannot predict whether the method of analysis herein proposed would change the conclusions of Swanson and Muir. Thompson *et al.*[5] have shown that techniques using equation 1 underestimate T. In fact, however, T may be either overestimated or underestimated, since the P axis intercept (P_{asym}) from equation 4 may be positive or negative (cf figure 3 from reference 6). The error becomes greater as P_{asym} becomes increasingly different from zero. When values of T are compared between interventions that may change P_{asym} (such as halothane or ischemia), both the absolute values and the conclusions may suffer. Most investigators have abandoned the equation 1 model.[4-6]

Finally, it is well to note that the pressure-time asymptote (or the pressure axis intercept in the dP/dt *versus* P plot) is not necessarily identical to the actual physiologic pressure to which the system decays. The issue is really the "apparent" value of P_{asym} that applies over the range of P(t) that is analyzed for T. Over another pressure range, different values of both P_{asym} and T may be obtained. An outstanding feature of the dP/dt *versus* P display is that simple inspection will reveal the extent to which any portion of the relationship does or does not follow the presumed monoexponential fall-off.

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In Reply:—Drs Beattie *et al.* point out a fundamental analytical error in our data describing left ventricular relaxation. We agree with their assessment, and appreciate their critical reading of our manuscript.

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Use Caution when Extrapolating from a Small Sample Size to the General Population

To the Editor:—Sears *et al.* recently reported "that 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."[1] They based this conclusion on the results of a study performed on eight patients. We believe their conclusion is too strong. Because they encountered no dysrhythmias and did not have a statistically significant decrease in heart rate does not imply the true incidence of these undesirable side effects is insignificant.

Whenever the numerator is zero in the incidence of an effect, the true incidence in the population at large represented by the group is:

$$\sqrt[n]{p}$$

where n is the sample size and p is the level of credibility, *i.e.*, if 95% confidence is required, then p = 0.05.[2] 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.[3] 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)."[2] 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,[1] 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.[2]

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.[1–4] 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