

mechanism responsible for the ventricular bigeminy is most likely due to an imbalance between parasympathetic and sympathetic activities with increases in both heart rate and blood pressure.<sup>4</sup>

The dose of thiopental sodium (30 mg/kg) used in this study<sup>1</sup> is relatively higher than the commonly used induction dosage of 15–20 mg/kg, iv prior to maintenance of inhalational anesthesia. Further, in these vagotomized dogs, it is quite possible thiopental sodium caused the observed bigeminy. This, in combination with halothane anesthesia and infusion of epinephrine, may have resulted in an increase in both heart rate and blood pressure in this study, although it was not mentioned.<sup>1</sup>

Thus, while the ventricular bigeminy reported in this study may have in fact originated from the interventricular septum, it is not possible to unequivocally state that in dogs the bigeminy was due to the combination of halothane anesthesia and epinephrine infusion. To rule out the possible effects of thiopental sodium, one must induce and maintain anesthesia with halothane alone.

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*In reply:*—We thank Drs. Seeler and Thurmon for their comment and apologize to them and other readers for not correcting a proofreading error. The dose of thiopental used in our experiments was in fact 20 mg/kg rather than 30 mg/kg. This decreases the probability of the arrhythmia being due to the combination of thiopental–epinephrine alone. We have observed arrhythmias including bigeminy immediately after injection of thiobarbiturates, but these are usually of short duration and were never present at the time halothane administration was begun. Thiobarbiturate-induced arrhythmias first were reported by Gruber.<sup>1</sup> Both blood pressure and hypercapnia were found to be important to their genesis (Gruber *et al.*,<sup>2</sup> Woods *et al.*,<sup>3</sup> and Johnstone<sup>4</sup>).

There is clearly an interaction between thiopental and sensitizing anesthetics. We established this in the case of cyclopropane<sup>5</sup> and have seen recent confirmation and extension for the case of halothane.<sup>6</sup> The doses of epinephrine required to cause various types of arrhythmia are increased in the absence of thiopental, but each type may be demonstrated. Potentiation of very long duration is seen on injection of 5 mg/kg, iv, into cyclopropane-anesthetized dogs, or brief potentiation may be caused by injection of less than 2 mg into the circumflex coronary artery.<sup>5</sup>

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We therefore believe that the arrhythmia we observed was indeed due to thiopental-halothane-epinephrine.

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## Hypothermia and the Electroencephalogram

*To the Editor:*—In their article on hypothermia and thiopental, Quasha *et al.*<sup>1</sup> observed burst-suppression in their control group, and attributed this EEG finding to the hypothermia common to all groups. This is remarkable, because neither our clinical experience nor the published reports of others<sup>2,3</sup> supports the observation that moderate hypothermia (25–30° C) by itself produces prominent burst-suppression. Their study was performed at the start of cardiopulmonary bypass, a period when many physiologic changes are being imposed upon the previously stable cerebral conditions. Included are thermal gradients (not just hypothermia) and acute hemodilution, with associated changes in serum proteins, electrolytes, glucose, osmolarity, and blood viscosity and oxygen-carrying capacity. Halothane was administered during the study period to maintain anesthetic level; however, the anesthetic potency of this agent doubles when the temperature is reduced to 27° C.<sup>4</sup> Thus, an anesthetic steady state may not have been present. The presence of an unusual, and possibly abnormal, control state raises questions about the general applicability of their conclusions. Accordingly, studies under stable hypothermic conditions seem to be in-

dicated before these conclusions (no matter how reasonable) can be accepted.

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*In reply:*—Dr. Warren Levy's letter raises a number of important questions and indirectly suggests likely answers. First, as Dr. Levy indicated, it is known that hypothermia significantly increases the potency of halothane. As noted, this, plus the various transient changes that occur at the start of cardiopulmonary bypass, may well explain why we observed some transient burst suppression in our control group at moderate hypothermia (25–30° C) that by itself may not produce prominent burst suppression. Further, since hypothermia has been demonstrated to potentiate the effect of

halothane, it should not be too surprising that it likely will also potentiate the effects of thiopental, which is the central point of our paper. Nonetheless, we appreciate the possible confounding effect that can be introduced by the various uncontrolled transient changes in numerous variables at the start of cardiopulmonary bypass. Therefore, although we consider our current conclusions as reasonable, we fully recognize them as tentative and in need of further verification based on more controlled studies, including basic animal studies, as well as clinical trials.