CORRESPONDENCE

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Halothane and Ischemic Injury

To the Editor:—Recent publications[1,2] on anesthesia-related hepatotoxicity suggest that it may be, at least partially, hypoxic in nature. We would like to make two additional suggestions in this regard.

First, if the halothane-induced hepatic damage is hypoxia related, it may not be specific only for the liver. There are a number of publications confirming this. In both canine[3] and primate[4] studies, halothane has been shown to increase the extent of infarction after occlusion of the middle cerebral artery. Halothane also has been demonstrated to have adverse effect on spinal cord ischemic injury caused by temporary occlusion of the aorta in rabbits.[5] It has been shown that halothane increases the size of myocardial infarction induced by coronary artery ligation in rats.[6] In another study, it was reported that myocardial infarct size was significantly larger in halothane anesthetized dogs when compared with fentanyl-anesthetized animals.[7]

Second, since hepatic damage was caused not only by halothane but by other anesthetics as well, it is likely that the "hypoxic" factor contributing to the liver injury is a common factor for many anesthetic agents. Of course, hypoperfusion secondary to a decrease in cardiac output and the resultant hypotension can be one such factor. We would like to point out another effect that is present in the spectrum of actions of general anesthetics—their ability to deteriorate the oxidation-reduction status due to inhibition of the electron transport chain in mitochondria at the level of NADH dehydrogenase.[8,9] This effect may contribute to the development of ischemia and it is probably common for all general anesthetics. In the spectrum of actions of a general anesthetic, there are those that may be detrimental and those with beneficial influence on the outcome of tissue ischemia. The overall result depends on the constellation of various conditions. Inhibition of the electron transport chain is a potentially adverse contribution to the ischemia.

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Mean Airway Pressure and Hemodynamic Effects

To the Editor:—In their recent study,[1] Muneyuki and colleagues concluded that the hemodynamic effects of alternating lung ventilation and synchronous ventilation are the same. We believe it is important to point out that the conclusion is applicable only to the particular circumstances of their experiment, *i.e.*, normovolemic dogs. In healthy animals, cardiac output is determined by venous return to the heart. Institution of positive-pressure ventilation causes an increase in intrathoracic pressure, which tends to impede venous return. Normally, this effect

is offset by an increase in mean systemic pressure, which restores venous return to previous levels.[2] Until intrathoracic pressure rises to a point beyond which compensatory mechanisms fail, there will be no change in cardiac output. A number of other factors (*e.g.*, changes in pulmonary vascular resistance) have been shown to have potential effects on cardiovascular function during positive-pressure breathing. However, changes in intrathoracic pressure consistently have been shown to be the most important in hemodynamic function.

In our experience with similar dog preparations,[3] circulatory hemodynamics during positive-pressure ventilation were unchanged from those measured during spontaneous ventilation, even at tidal volumes and airway pressures higher than those used by Muneyuki *et al.* Although the current study did not have a spontaneously ventilating control group, the reported hemodynamic measurements are similar to those we have observed. If, in fact, the increase in airway pressure with either mode of ventilation in the present study was not great enough to cause a change in hemodynamic status from that found during spontaneous ventilation, then it is not surprising that differences in airway pressures between alternating lung and synchronous ventilation were not associated with differences in hemodynamic status.

This point should be clarified, since it detracts from an obviously well-designed and well-executed study. If *mean* airway pressure during alternating lung ventilation is significantly lower than *mean* airway pressure during synchronous ventilation, there may be a difference in the hemodynamic effects of these two modes of ventilation under circumstances in which increased airway pressure does cause a decrease in cardiac output (*e.g.*, hypovolemia). Perhaps the authors will pursue their studies further and investigate this possibility.

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In reply: In our study, mean airway pressure decreased significantly as well as peak airway pressure when the ventilation mode was changed from synchronous to alternating. Cardiac output, however, did not change significantly. This may be a result of the compensatory mechanisms of the cardiovascular system. It is also conceivable that the advantageous effects of lowered airway pressure during alternating ventilation were offset by unfavorable effects on the cardiovascular system. We agree that it is not surprising that differences in airway pressure between the two ventilation modes used in our study were not associated with significant changes in cardiac output, considering the responses observed by Dr. Otto and his colleagues. Lastly, it deserves emphasis that the purpose of our study was not to clarify the differences in cardiovascular functions between spontaneous and artificial ventilation modes but rather to observe any differences between synchronous and alternating ventilation modes under the conditions of artificial ventilation with complete muscle relaxation.

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