A Hypoxic Tail

Hypoxia is harmful. How and why cerebral hypoxia decreases anesthetic requirements are the major questions asked by the three papers appearing in this issue of the Journal under the common title, "The Effects of Hypoxia and Isovolemic Anemia on the Halothane Requirement (MAC) of Dogs."

In Part I, "The Effect of Hypoxia," Doctors Cullen and Eger find that when $\text {Pa}_2\text {O}_2$ falls below 38 torr, less halothane is required to keep a dog from wiggling (wagging?) when his tail is clamped. Hopefully, this attempt to quantitate the interaction between hypoxia and halothane on MAC is of more academic than clinical importance. Although quantification suffers from the unavoidable absence of a steady state, the authors are able to report correlation of halothane MAC with various measures of oxygenation: arterial and mixed venous oxygen content and oxygen transport (arterial oxygen content $\times$ cardiac output). Correlation of declining MAC with diminishing pH was also observed, though at a constant $\text {Pa}_2\text {O}_2$ of 30 torr MAC decreased much less rapidly in hypocapnic animals than in those maintained at constant, normal $\text {Pa}_2\text {CO}_2$. The explanation offered is that the leftward shift of the hemoglobin dissociation curve with hypocapnic alkalosis permits more oxygen to be carried in arterial blood at a given low $\text {Pa}_2\text {O}_2$.

This explanation is supported by the changes in blood base excess. If we assume a reasonable circulatory status, the arterial base excess provides a measure of anaerobic acid production by the body. The good correlation between halothane MAC and base excess found in this study thus implies a comparable correlation between tissue oxygenation and MAC that is independent of the differences between arterial pH or rate of change of MAC in normocapnic and in hypocapnic dogs. Although measurements of cerebral circulation were not made, we must also conclude that at a $\text {Pa}_2\text {O}_2$ of 30 torr hypocapnia did not result in significant cerebral vasocostriction.

The authors' concluding explanation for the mechanism by which hypoxia reduces MAC is not compatible with the results of most studies of the effect of hypoxia on neuronal function. Measurements of transmembrane potentials in nerve cells indicate, if anything, depolarization rather than hyperpolarization. Eccles et al., as well as others before them, have suggested that presynaptic terminals are much more sensitive to hypoxia than the rest of the neuron and that the depolarization of these terminals might be explained by the effect of hypoxia on the active transport of sodium and potassium ions at these endings.

In Part II, "The Effect of Acute Hypoxia on Halothane Requirement and Cerebral-surface $\text {P}_2\text {O}_2$, $\text {P}_2\text {CO}_2$, pH and HCO$_3$-", Drs. Cullen and Eger were abetted by Drs. Cotev and Severinghaus in an attempt to demonstrate that
cerebral pH is the common denominator for the hypocapnic and normocapnic states in the original study. Because they felt that changes in acid–base status of cisternal cerebrospinal fluid should lag behind changes occurring within the brain, measurements of gas tensions and pH were made using electrodes placed directly on the surface of the brain. The results revealed that the surface electrodes respond rapidly to changes in oxygenation or acid–base state while changes in composition of cisternal cerebrospinal fluid lag far behind. Though the problem of achieving equilibrium between cerebrospinal fluid and extracellular fluid of brain has been recognized by investigators concerned with brain acid–base regulation, this paper represents the first demonstration of the magnitude of dynamic differences. Although the technical expertise involved in this study is impressive, the results only indicate that the best laid plans of men do not always bear fruit. As the authors point out, the scatter in measurements is large, and meaningful conclusions concerning the mechanism of interaction between hypoxia and halothane on MAC cannot be gleaned from this work.

Part III, "The Effects of Acute Isovolemic Anemia," is perhaps of greatest interest to the anesthesiologist. In documenting the absence of an effect of severe anemia (hematocrit = 10 per cent) on halothane requirement, the authors illustrate the fundamental importance to adequate tissue oxygenation of the driving pressure of oxygen in the capillary. In this study oxygen transport was reduced to about 37 per cent of control values compared with a minimum value of 52 per cent for the normocapnic, hypoxemic dogs in the first study. Despite diminished oxygen transport, metabolic acidosis was mild and no significant reduction in halothane MAC was observed. Preservation of cerebral oxygenation in the face of decreased oxygen-carrying capacity resulted from maintenance of a normal \( P_{aO_2} \) in the presence of increased cardiac output. Output increased owing to an increased heart rate and decreased total peripheral resistance, resulting in part from lowered blood viscosity. In addition, the significant decrease in oxygen consumption during anemia presumably provided additional protection. The cause of this decreased oxygen uptake in normothermic anemic animals is not apparent.

The authors conclude this paper by imputing relative safety to replacement of blood loss with crystalloid solutions, on the basis of their observations and those of Rush et al.\(^2\). Undoubtedly, such an approach is safe within limits, but a current concern is—what are the limits? Though tissue oxygenation may be adequate at low hematocrits if volume is maintained, infusion of large volumes of crystalloid solutions has been implicated in the development of respiratory complications.\(^3\) In addition, it should be recognized that man is accustomed to functioning at an optimum hematocrit;\(^4\) deviations from this value demand compensations that might be inadequate during deeper anesthesia and, in any event, may not be every man's cup of salt water.

THOMAS F. HORNBEIN, M.D.
Associate Professor of
Anesthesiology and
Physiology and Biophysics
University of Washington
School of Medicine
Seattle, Washington

References