luded to here and in the article by Bellville and Hara indicate areas in need of incorporation. Electrical principles, analog computer fundamentals such as those so well presented by them, and speaking even more generally and fundamentally, mathematics and physical science are the prerequisites for understanding developments along these lines that are sure to come.

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Functional Importance of the Hepatic Circulatory Changes Induced by Anesthesia

IN this issue of ANESTHESIOLOGY, Price and his co-authors, from the University of Pennsylvania and Columbia University, report their observations of the effects of halothane and cyclopropane on some aspects of the liver's metabolic activity. This work is important. For the first time, direct insight is provided into the possible significance of hepatic circulatory changes induced by general anesthetic agents.

It is well known that anesthesia may be accompanied by changes in hepatic perfusion.[1,2,3] The best evidence in man is that thiopental–nitrous oxide anesthesia by itself produces no change in the liver blood flow, while cyclopropane, halothane, and thiopental–nitrous oxide anesthesia complicated by carbon dioxide retention all reduce it. On the other hand, during halothane anesthesia, hypercapnia increases total perfusion, apparently because of the direct vasodilator effects of CO_2 together with the tendency of halothane to block sympathetic responses generally.

The present work now makes clear that these apparently similar (although differently mediated) effects on total hepatic perfusion are accompanied by differing metabolic actions with respect to the lactate-pyruvate system, which is important in the main chain of the conversion of glucose to energy. Cyclopropane produced a significant increase in "excess lactate"; halothane did not have this effect despite similar changes in blood flow. Furthermore, maneuvers which increase hepatic blood flow while maintaining anesthesia do not necessarily affect the metabolic changes seen in lactate and pyruvate metabolism. Nor was there evidence that changes in blood flow had any important effect on splanchnic oxygen utilization.

In the light of this study, and the preceding ones upon which it is based,[2,3] it now appears doubtful that hepatic circulatory changes of the magnitude described in normal subjects are responsible for significant effects on the integrity of hepatic function following uncomplicated anesthesia and operation, although they doubtless are of importance in determining the total circulatory adjustment to anesthesia. Furthermore, it is worth noting that hepatic dysfunction following anesthesia may be exaggerated by drugs or events which offset the hepatic circulatory effects, *e.g.*, hypercapnia during halothane anesthesia.[4]

One must recognize that hepatic blood flow may theoretically change in ways not completely reflected in measurements of total flow, and that such changes might well be of func-

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tional significance. For example, changes in the relative contribution of portal venous and hepatic arterial inflow as well as of the intrahepatic distribution of flow may occur. Methods for the study of such changes in man are, unfortunately, lacking.

Finally, it should be recognized that the indices of functional alteration selected by Price and his co-workers represent only a few of a complex variety of hepatic functions. It is conceivable that under other circumstances or in other ways, circulatory changes may play a more important role in influencing the functional behavior of the liver.

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SUCCINYLCHOLINE Actions of succinylcholine on the cat motor nerve terminal has been investigated by means of single motor axone recordings and single motor unit recordings. Succinylcholine which is usually assumed to act exclusively on the postjunctional structures of the neuromuscular junction, profoundly affects the motor nerve terminal. It attenuates post-tetanic neural repetitive activity, causes the neural response to a single stimulus to become repetitive, and initiates in the motor nerve, action potentials which are independent of an external stimulus. These effects are produced by a wide range of succinylcholine doses, including those well below threshold for blockade of neuromuscular transmission. Provided the dose is kept below the transmission blocking dose, these neural effects are fully reflected in muscle electrical and mechanical activity. The fact that succinylcholine affects the motor nerve terminal in much smaller and much larger doses than those which affect neuromuscular transmission and that some of these effects are capable of causing transmission block suggests that the motor nerve terminal is the primary site of succinylcholine action. (*Standaert, F. G., and Adams, J. E.: Actions of Succinylcholine on the Mammalian Motor Nerve Terminal, J. Pharmacol. Exp. Ther. 149: 113 (July) 1965.*)

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