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Book Reviews

Immunologic Aspects of Anesthetic and Surgical Practice. EDITED BY ALIX MATHIEU AND BARRY D. KAHAN. New York, Grune and Stratton, Inc., 1975. Pages: 400. Price: $29.00.

Drs. Mathieu and Kahan are to be congratulated for publishing the first text relating the fields of anesthesiology and immunology. Although articles describing the effects of anesthesia on immune phenomena were published as early as 1904, only in the past ten years has this subject received serious consideration. It is now apparent that surgery and anesthesia are not innocuous from an immunologic standpoint and that the anesthesiologist must have an increased awareness of the patient's immunologic responses to infection, cancer, drugs, blood transfusion, and transplanted organs.

The book contains 17 chapters primarily written by young American investigators in anesthesia, surgery, and internal medicine. It is divided into two parts. The first is an introduction to immunology covering cell-mediated immunity, lymphocyte transformation, humoral immunity, and the effects of surgery and anesthesia on general immunity. The second is a discussion of specific clinical subjects, such as viral hepatitis, postanesthetic hepatitis, drug allergy, asthma, blood transfusion, and organ transplantation. In the preface, the editors state a desire to "present fundamental immunologic concepts and to illustrate their implication for clinical practice in a readily understandable fashion." Part II of the book fulfills that objective. It is easy to read, understandable and clinically relevant for the anesthesiologist. The same cannot be said about Part I. From reading Part I, it is unclear to what audience the book is directed. Ostensibly, the book is designed as a primer in immunology for anesthesiologists. However, the first few chapters are complex and overly detailed. This is exemplified on page 4 of Chapter 1 where, without prior definition, the reader is presented with immunologic jargon such as "alloantigens," "HL-A phenotypes," and "haplotypes." The early chapters are well written, and they contain a wealth of information, but they do not present a clear overview of the immune response that can be readily understood by the non-immunologist. A clearer understanding of the immune response could have been accomplished by a more careful definition of terms and by more extensive use of diagrams such as those in a similar text by Alexander and Good, *Immunobiology for Surgeons* (W. B. Saunders Co., 1970).

As frequently occurs when many authors are involved, the book tends to be a collection of independent papers rather than a cohesive unit. Many subjects are discussed in more than one chapter; there are major differences in writing style, excessive emphasis is placed on a few topics (for example, hepatitis) and too little emphasis is placed on others (for example, anesthetic effects on the immune response). When writing a book, there is an unavoidable delay between preparation of the initial manuscript and final publication. As a result, some of the material is outdated and a moderate amount of new information is omitted. This is particularly evident in those chapters dealing with the effects of anesthesia and surgery on general immunity and infection. The references following each chapter are basically good; however, there is great variation in the quantities (220 in Chapter 4, 18 in Chapter 9), and "unpublished observations" are frequently included.

Overall, this book is a worthy undertaking that has three major attributes. First, it is educational; it contains recent information about immunology that will make the anesthesiologist a more knowledgeable general physician. Second, the book emphasizes the need for anesthesiologists to consider the influence of anesthesia on immune function. This is true whether one is concerned with the effects of anesthetic drugs on the patient's immune defenses, or whether he is caring for a patient who has an immunologic disorder. Third, the book demonstrates that our understanding of the interaction between anesthesia and the immune response is relatively limited and that many questions remain to be answered. Hopefully, this book will stimulate increased interest in the subject.

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Progress in Anesthesiology. Volume 1. Molecular Mechanisms of Anesthesia. EDITED BY B. RAYMOND FINK. New York, Raven Press, 1975. Pages: 652. Price: $35.00.

This volume records the proceedings of a three-day multidisciplinary international symposium sponsored by the Department of Anesthesiology, University of Washington. Recent advances in elucidating mechanisms of anesthetic actions on a variety of biological systems are documented here as reviews or as research papers. The scope is rather wide, including not only the current concepts and theories of how anesthetics might act to induce unconsciousness (at molecular levels); actions of local anesthetics; effects of general anesthetics on metabolism, enzymes, cyclic AMP system, putative neurotransmitters, and finally, on myocardial contractility are also considered. This book is therefore different from that edited by M. J. Halsey *et al.*, bearing a similar title, published in England in 1974.

This reviewer has been treated to a wealth of information. Experimental models varied from lipid membranes, mitochondria, reconstituted myofibrils,

slime molds, and cell cultures, to synapses, and even whole animals. At first it may be mind-boggling. Closer scrutiny reveals the serious attempts of many physiochemists, physiologists, pharmacologists and anesthesiologists to answer the yet unsolved problem central to our daily work —how *indeed* do anesthetics act?

It seems that no one is now working on or even discussing the possibility that anesthetics react with water to induce an unconscious state. The clathrate theory proposed barely 14 years ago remains a theory with little experimental support. Instead, all evidence points to anesthetic-induced changes in cell membranes, be they expansions to a "critical volume," conformational changes of protein molecules, or increases in fluidity. Experimental results in support of each have been obtained using exquisitely sophisticated instruments of measurement. There are, of course, disagreements, and for that matter the true picture of the "elephant" has yet to be painted.

The number of anesthetic molecules residing within the lipid membrane to produce anesthesia is estimated to be 10,000 per μm^2, or one anesthetic molecule per 100 lipid molecules. The membrane itself expands to an extent of about 0.5 per cent, not explainable by the presence of anesthetic molecules but by conformational changes in membrane proteins. To arrive at these estimates the reader is treated to heavy doses of mathematical equations, perhaps not easily comprehended by non-physicochemists.

In support of the concept of membrane expansion, the phenomenon of pressure reversal suggests that high pressure using helium from 80 to 200 atmospheres would "compress" the expanded membrane, resulting in antagonism of narcosis, or increase in anesthetic requirement. Pressure reversal has been observed with firefly luminescence, nerve conduction, tadpole mobility, and righting reflexes of newts and mice. The theme seems to run something like this: interaction of anesthetics with the cell membrane or its components, by virtue of various anesthetic-induced changes, would impede ionic permeability, thus interfering with impulse transmission at the synapse, essential for cerebral function. In spite of this simplistic interpretation of massive evidence, it is clear that much more remains to be done. For instance, pressure does not reverse anesthetic-induced depression of synaptic transmission.

The reader may find many more useful and some esoteric bits of information. Local anesthetics, in ionized form, block conduction by occupying strategic points *inside* the membrane. Local anesthetics inhibit axonal transport of subcellular substances from cell bodies toward nerve terminals in a dose-dependent fashion, a possible neurotoxic action of these drugs if applied in excessive concentrations. Anesthetics, including halothane, morphine and ketamine, increase brain concentrations of cyclic AMP and glucose, but not other intermediate metabolites. Free radicals of intermediary metabolites are the likely culprit in producing hepatotoxicity with chloroform; but the same could not be demonstrated with halothane. Protection of the brain from ischemia could perhaps be achieved by massive doses of thiopental or pentobarbital, but probably not by deep halothane anesthesia. Halothane decreases the synthesis of acetylcholine in synaptosomal preparations from rat brain slices, probably owing to synaptic inhibition, which in turn is the result of accumulation of γ-aminobutyric acid.

The papers have appropriate references and are grouped for continuity. Brief relevant discussions by participants add to the feeling of some degree of uncertainty. For serious students and scientists who consider mechanisms of anesthetic action a challenge, this volume serves as the latest summary of progress. For others, the challenge is to understand.

Dr. Fink is to be congratulated, first for having put together a conference with so many distinguished participants, and then for being able to publish the proceedings within a year.

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