Permeability Mechanisms

Blood-Brain Barrier in Physiology and Medicine. STANLEY I. RAPOPORT. Raven, New York, 1976. xii, 316 pp., illus. $25.

The capillary wall in the central nervous system is structurally quite different from capillary walls in other tissues. The differences result in a selective phenomenon known as the blood-brain barrier which governs the exchange of solutes between blood and brain. Although the barrier has been recognized for nearly a century it has not aroused a great deal of interest, perhaps because until the past 10 or 20 years little specific information has been available about its permeability to various solutes. During the past decade, particularly, a great deal has been learned. This book is the first comprehensive monograph on the subject to appear since the structure of the barrier and the molecular criteria governing permeability have been reasonably well defined. So it is timely and fills an obvious gap.

The localization of the blood-brain barrier in capillary endothelial cells is well covered. Penetration of the barrier requires transcellular passage through the plasma membranes of these cells, and membrane penetration is clearly presented. The author's own work defining the temporary opening of the barrier by arterially injected hyperosmotic agents is not overemphasized.

It is well recognized that a wide range of organically abnormal brain states result in a "loss" of the blood-brain barrier, and chapter 5 nicely reviews the literature of this important phenomenon.

The weakest chapter is the sixth, on the entry of drugs into the brain. The accepted theories relating ionic dissociation and lipid-water partition coefficient to rate of diffusion across the barrier are well expounded. But although more than five pages are devoted to the neurotoxicity of hypertonic angiographic contrast agents there is no mention of anesthetics, narcotics, tranquilizers, antipsychotics, antidepressants, or central stimulants. It may be argued that there is much yet to be learned about these classes of drugs, but a great deal is known and the omission is unfortunate because of their clinical and social importance. Figure 6 of this chapter expresses the view, based upon calculation, that more than half of some of the commonly used angiographic contrast agents enter the brain during the first capillary passage following arterial injection. This is unlikely on the evidence both of human angiography and of neurotoxicity. Despite the possible error of this particular prediction, the author's treatment of membrane permeability in relation to angiographic agents and their neurotoxicity seems generally valid.

The remainder of the text is devoted to an excellent review of carrier-mediated permeability of the blood-brain barrier to nonelectrolyte brain metabolic substrates and certain intermediates and to a chapter on the barriers of the eye.

To readers seriously interested in the subject the bibliography alone, which comprises 40 pages, is almost worth the price of the book. The contemporary nature of the material is verified by the fact that virtually all of the references are from the literature of the past decade.

The blood-brain barrier is an important phenomenon. This is a clearly written monograph by an author who has made significant contributions to the field. No one interested in brain function should be dissuaded from buying it because of its omissions. It is the only modern monograph on the subject and will become a classic reference.

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DNA Transcription

Chromosomal Proteins and Their Role in the Regulation of Gene Expression. Proceedings of a colloquium, Gainesville, Fla., Mar. 1975. GARY S. STEIN and LEWIS J. KLEINSMITH, Eds. Academic Press, New York, 1975. xii, 308 pp., illus. $16.

There is growing interest in unraveling the mechanism of gene expression, with good reason: new probes being exploited in laboratories around the world are producing encouraging and highly suggestive results. This book is a welcome account of many current approaches to studying the involvement of proteins in the control of DNA transcription. The "chromosomal proteins" of the title are conveniently classified into two groups for consideration, one being the histones (basic proteins, long known to be associated with nuclear DNA) and the other comprising the rest of the proteins found in the nucleus or chromatin (generally referred to as "nonhistone proteins" or "acidic proteins" of the nucleus). The histones obviously must be considered in any attempt to explain the functioning of chromatin, but their lack of diversity (there are fewer than a dozen kinds) has led to increasing interest in the highly diverse nonhistone proteins as suppliers of the necessary specificity for switching the many genes on and off. Both kinds of proteins must contribute to the process; the authors of the 15 papers in the present volume explore some of the possibilities.

The papers describe experimental procedures and results, with emphasis on the isolation and characterization of the nuclear proteins by a variety of means, among which electrophoresis in gels is basic. Although the series of papers by no means constitutes a laboratory manual, there is an attempt in each case to explain the methods used and to present data for discussion. The types of investigation include chromatin reconstitution, studies on the phosphorylation and methylation of nuclear proteins, digestion of chromatin with nucleases to reveal a DNA-histone subunit structure, identification of certain nonhistone proteins as hormone-binding sites in the nucleus, and the use of DNA-affinity chromatography to separate nonhistone proteins that bind to DNA. The techniques used in these investigations have been almost exclusively biochemical and these are covered well, but the contribution of electron microscopy to the knowledge of the structure of chromatin, for example, is scarcely touched upon, and such useful physical methods as nuclear magnetic resonance and neutron scattering are not represented.

A caveat—some of the conclusions reached have, not unexpectedly, been subject to modification in the light of more recent research. The provocative chromatin reconstitution experiments apparently "work," in that DNA is transcribed, but how they work is poorly understood, with the result that it is difficult to assess the effect in vivo of substituting or withholding different ingredients of the system. In short, in this rapidly advancing area of investigation every breakthrough in understanding also uncovers new areas of obscurity.

The volume is a valuable and concise exposition of important experiments by outstanding practitioners using new, and often imaginative and daring, probes into the mechanism of the control of gene transcription. Most of this material has not yet found its way into books, which makes this one all the more attractive both as an introduction and as a progress report.

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