evitable in view of the complexity of the field and its enormous literature.

The book concludes with a useful glossary of trade and common names. More than 1000 references are cited. The list is especially strong with respect to the European patent literature, but includes only a very few references as late as 1970. The book is attractively printed and remarkably free of errors. It is strongly recommended to the synthetic chemist and the toxicologist interested in research and development in this field.

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Key Process

Nucleotide Metabolism. An Introduction. J. FRANK HENDERSON and A. R. P. PAT-ERSON. Academic Press, New York, 1973. xviii, 304 pp., illus. \$15.

Textbooks of general biochemistry, attempting to cover, as they must, the gamut from chemistry to genetics and physiology, have given progressively less attention to many subjects of crucial importance to biochemistry. One of these is the metabolism of nucleotides. Pathways of energy generation and virtually all aspects of biosynthesis depend on the nucleotides as key catalysts or as essential building blocks. It is not often fully appreciated, for example, that details of the biosynthesis of DNA precursors have a profound influence on overall DNA synthesis by controlling the rate and the characteristics of the product. For these reasons, a separate textbook on nucleotide metabolism is an exceedingly important contribution, filling a need that has not been adequately met by periodic specialized reviews of the subject.

Nucleotide Metabolism is a thorough, comprehensive account. It is clearly written and well supplied with illustrative examples, useful diagrams, and summaries and has an adequate bibliography. All biochemists, especially those with a major interest in nucleotides, will be grateful to the authors that such a treatise can now be had within arm's reach. There are remarkably few omissions or errors that this reviewer could find. However, mention might be made of a few items the treatment of which differs from what I have found useful in lectures to students in a general biochemistry course.

The authors shun the term "salvage" 8 FEBRUARY 1974 now in frequent use to denote the numerous pathways by which cells make use of the free bases and nucleosides produced in the breakdown of nucleic acids and coenzymes. As a result there may be a less clear and dramatic distinction between these pathways and those in which nucleotides are synthesized "de novo" from sugars and amino acids. This lack of focus on the distinction between de novo and salvage pathways becomes apparent in a confusing reversal of order in the sequence of their presentation in the chapter on deoxyribonucleotide synthesis as compared to the sequence in the chapters on purine and pyrimidine ribonucleotide syntheses.

An omission of some importance is the distinction to be made between biosynthetic and degradative pathways of pyrimidine nucleotide synthesis at the step between dihydroorate and orotate. The key intermediate, orotate, is not derived by oxidation of dihydroorotate through the flavoprotein reductase discovered in catabolic studies. Instead, dihydroorotate is converted to orotate by a distinctive biosynthetic oxidase. This example can be used to illustrate the duality of pathways of biosynthesis and degradation and adds to our conviction that, in all cells, biochemical operations of energy production and biosynthesis are sharply separated from one another.

In discussions of salvage mechanisms, no mention is made of intracellular reutilization of nucleotides themselves, perhaps the most important, though least recognizable, salvage operation of all. In this connection the book lacks a critical discussion of an important problem, the evaluation of the precursor role of nucleotides and their components in cellular studies of coenzyme and nucleic acid metabolism. Permeation, compartmentalized pools, and metabolic channeling are crucial considerations often neglected in the numerous studies of nucleotide metabolism in bacterial and animal cells. An interesting example of metabolic channeling observed even in a soluble enzyme system is a complex of enzymes of pyrimidine biosynthesis, in which carbamyl phosphate generated from its precursors is passed on directly to form carbamyl aspartate without dilution by large amounts of carbamyl phosphate added to the solution.

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Immunology

Genetic Control of Immune Responsiveness. Relationship to Disease Susceptibility. Proceedings of a conference, Augusta, Mich., May 1972. HUGH O. McDEVITT and MAURICE LANDY, Eds. Academic Press, New York, 1972. xx, 470 pp., illus. \$19.50. Perspectives in Immunology.

The format of this record of the 1972 Brook Lodge Immunology Conference resembles closely that of the four previous meetings in this distinguished series. Each of 36 investigators who have contributed some of the most interesting experimental evidence and theoretical insight concerning the complex topic under discussion presented a concise description of his research findings and then responded to questions and comments from the floor. By skillfully grouping, ordering, and monitoring the presentations, and by expertly editing (and occasionally clarifying) the transcript, the organizers have prepared a valuable summary of the diverse observations and conjectures concerning the relation of genetics to immune responsiveness.

Throughout the discussion, the immunologists present tended to center their interest upon simplified model systems, most commonly the immune responsiveness of inbred strains of mice to chemically defined antigens. The fascinating hypothesis proposed by Baruj Benacerraf, Hugh McDevitt, and others that the capacity to mount such responses is controlled by a series of autosomal dominant genes (the immune response, or I.R., genes) and that these genes are closely linked to the major histocompatibility locus in mice and other animals was one of the few theoretical points not seriously disputed at the meeting.

Before any mechanistic or theoretical basis for this hypothesis can be agreed upon, however, a consensus would have to be reached on a number of related questions which remain extremely controversial. Among those questions which are discussed in this report are: What is the nature of the antigen receptor on thymus-derived lymphocytes? Do the I.R. genes direct the synthesis of these receptors? Are these genes expressed only in thymus-derived cells? Is the close linkage to the histocompatibility locus causal, evolutionary, or coincidental? What is the relationship among the genes controlling the immune response, the histocompatibility antigens, and the mixed-lymphocyte-culture reaction? Complex arguments and a great deal of sketchily presented experimental

evidence are provided for several possible answers to each of these questions, but it is not evident that any of the participants altered their views on these matters as a consequence of the presentations. Questions concerning the origin of immunoglobulin variability and the nature of the curious two-geneone-polypeptide-chain arrangement presumed to control immunoglobulin biosynthesis are, for the most part, not discussed.

The chapters which follow concerning the multiple genetic loci shown to affect viral infectivity and autoimmunity in mice and concerning the possible associations between histocompatibility antigenic types in man and specific disease entities provide an interesting summary of a vast body of literature. They fail, however, to be illuminated by, or to shed much light on, the basic immunologic questions discussed earlier.

The clear-cut disagreements on several of the most fundamental issues raised suggest that much more thought and experimentation will have to be expended before a hypothetical structure can be constructed to account for all the observations. Those scientists and philosophers interested in the process by which such theoretical paradigms evolve and gain acceptance might well find this volume a useful introduction to a field in which such a process may be approaching a critical stage. They certainly would be interested in the individualistic fashion in which Melvin Cohn in the concluding section of this book constructs the conceptual framework he uses to account for the experimental data by selecting certain phenomena as central (self-nonself discrimination), certain facts as "misleading" (thymus-independent antigens, the linkage between histocompatibility and I.R. genes), and certain hypothetical entities as indispensable (associative antibody, somatic mutations).

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