stood in Fleming's shadow, even though the Nobel prize for the discovery was awarded jointly to Fleming, Florey, and the chemist member of Fleming's team, E. B. Chain.

Lennard Bickel sets about dispelling the popular idea that Fleming's discovery was the only significant step, after which everything else was inevitable. He contends that Fleming concluded that penicillin could not be purified without destroying its chemical structure and was content to advocate that it be used only for surface infections. The author gives us a picture of Florey as a serious, intense, hard-driving, ambitious scientist whose high standards for obtaining and evaluating scientific data allowed no rest for himself and his colleagues and no compromise with those who had lesser standards. We learn how his personality admirably suited his role of studying carefully the available evidence regarding various substances that seemed to have an antibacterial effect, selecting for his own experiments those that showed the most promise, gathering a team of investigators with the skills needed to fashion these substances into therapeutic agents, and carefully testing them in animals and man, until he had shown that one of them, penicillin, would cure human infections as no other drug had ever done before.

Florey's early life, Bickel shows us, was good preparation for the difficulties that were to follow. Especially it helped Florey push on through many trials and frustrations until Chain found out how to purify penicillin successfully by carrying out the process in the cold and methods could be found to produce enough for the first animal tests and then the large quantities needed to treat patients. Also, a tenacity of purpose, which surfaced during his student days, stood him in good stead when he tried unsuccessfully to interest British pharmaceutical companies in producing penicillin and finally, after much persistence, was able to persuade some American firms to cooperate in large-scale production. But his habitual professional reticence did not allow him to bask in the glow of popular praise.

Bickel makes a good case for his thesis and tells the story well. Unfortunately, he seems to think it necessary to diminish the importance of Fleming's achievement in order to convince us of the significance of Florey's contribution. The reviewer has believed for a long time that Florey was not receiving his due, but he also believes that the Nobel Prize Committee made the proper assessment: Fleming, Florey, and Chain should share equally in the prize, for without any one of the three we probably would not have had penicillin for many years or decades after we did. So great is the significance of penicillin that there is enough glory to go around.

This book is written by an accomplished science writer for the intelligent lay reader, but if the professional reader can overlook the detailed explanations and a certain amount of hyperbole he will find it an interesting account of an important episode in the history of science. Perhaps he will also see in it a reflection of some of his own trials and triumphs as he pursues his less well publicized scientific investigations.

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Insecticides

The Chemistry of Organophosphorus Pesticides. Reactivity, Synthesis, Mode of Action, Toxicology. C. FEST and K.-J. SCHMIDT. Springer-Verlag, New York, 1973. x, 340 pp., illus. $35.20.

Organophosphorus (OP) insecticides are playing an increasingly important role in pest control as the persistent organochlorine compounds are becoming obsolescent both because of the development of resistance on the part of insect pests and because of their pollutant properties. This changing role is emphasized by the rapidly increasing U.S. production of parathion and methyl parathion, which aggregated 19 million pounds in 1960 and reached 56 million pounds in 1970. The greatly increased use of the degradable OP insecticides has had a salutary effect on the quality of the environment. However, most of the OP insecticide used is in the form of highly toxic cholinergic compounds, and these have produced numerous cases of human poisoning and death through misuse, accident, and suicide. Thus the appearance of this authoritative book written by two experienced chemists from the Eberfeld Laboratory of Bayer AG, where Gerhard Schrader, about 1937, began his pioneering work in developing the OP insecticides, is of both historical and current interest.

The book begins with a thoughtful introduction about the role of pesticides in crop production and the challenge of feeding the exploding world population, and recounts the development of the OP compounds. It makes it clear that Schrader's discovery of the nerve gases tabun and sarin took place in 1935–37, antedating both the onset of World War II and the discovery of the first practical OP insecticide, schradan, in 1941, a matter that has often been debated. Parathion and its methyl analog, the most widely used members of the OP group, were not synthesized until 1944. From these beginnings the number of insecticidal OP compounds has certainly exceeded 100,000, and world production is estimated as approaching 200 million pounds.

The authors approach the chemistry of these compounds by emphasizing electronic structure and reactivity, with particular reference to Schrader's formulation in which disubstituted acyl phosphates and phosphorothionates are essential for high activity, and concludes with a condensed section on the confusing subject of OP nomenclature. An excellent chapter of 113 pages on general synthetic methods follows which enumerates the development of the commercial OP insecticides. An amusing item on p. 136 relates the name of malathion to its use in malaria control, when in reality the name was coined from the use of maleic anhydride in the synthesis of the compound, though it has also been ascribed to the compound's mephitic properties.

A chapter on OP biochemistry (105 pages) succinctly summarizes the interactions with cholinesterase, the kinetics of inhibition, structure and activity, insect resistance, metabolism, toxic action, and neurotoxicity. The sections on mechanisms of action are perhaps the least satisfactory of the book, especially with reference to arthropods, where the discussion is simplistic and ignores the considerable amount of histochemical data pointing to acetylcholinesterase of the subesophageal ganglion as the principal target site of OP action. Other disappointing omissions include discussion of desulfuration of phosphorothionates as a critical factor in mode of action and selectivity because of the delay factor, discussion of in vivo lethal synthesis in demeton, phorate, disulfoton, and related systemic insecticides, and the large amount of accurate topical LD_{50} data on insect toxicity of OP compounds, so valuable in structure-activity discussions. Shortcomings such as these are perhaps in-

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. PATERSON. 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" 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