HEMATIN COMPOUNDS AND BILE PIGMENTS

HEMATIN COMPOUNDS AND BILE PIGMENTS

THEIR CONSTITUTION, METABOLISM, AND FUNCTION

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PREFACE

There is no need to emphasize the importance of a field of science which includes among its subjects hemoglobin, the hematin enzymes, porphyrins, and bile pigments. No monograph or handbook has previously been available in the English language; in German we have the valuable handbook of H. Fischer and H. Orth on the chemistry of pyrrole derivatives, but this has been written entirely from the viewpoint of the organic chemist.

In textbooks of biochemistry and physiology the subject is rarely treated with the care which its importance demands. Perhaps because of the lack of a suitable monograph serious errors are frequent, hypotheses of doubtful value are given as facts, and there is a time lag of many years, sometimes of decades, between the present-day knowledge available and that summarized in the textbooks. A factor which may have contributed to this is that errors, inescapable in the rapid development of this field, have, for reasons of prestige, not always been withdrawn as clearly and frankly as would have been in the interest of science. After completion of the script of this book two valuable reviews were published: "Heme-Linked Groups and Mode of Action of Some Hemoproteins," by H. Theorell, and "Distribution, Structure, and Properties of the Tetrapyrroles," by S. Granick and H. Gilder, both reviews in Volume VII (1947) of *Advances in Enzymology*.

This book is therefore intended to fill two requirements. It is intended to summarize the present state of our knowledge for the student and for workers in other fields, as well as enable the research worker or anyone wishing to acquire special knowledge in this particular field to gather less laboriously than has hitherto been possible the information needed. For the benefit of the latter particularly, but also for that of the general student, the treatment is as critical as possible and every endeavor has been made to avoid dogmatic statements.

The scope of the book had of necessity to be strictly limited. Physicochemist, organic chemist, biochemist, physiologist, bacteriologist, botanist, zoologist, pathologist, and clinician are all interested in various aspects of the subject. Our main emphasis is biochemical, as the title is intended to indicate. Problems of organic structure are dealt with only in so far as they are of importance for an understanding of the functional and metabolic aspects. More emphasis is given to the physicochemical background. The chemistry of hemoglobin and the hematin enzymes is so intimately linked with general problems of protein chemistry that it is impossible to draw a clear line of demarcation. Again, our selection has been guided by consideration as to whether or not a connection could be established between a particular property and aspects of function or metabolism. On the other hand, the functional aspect of the hematin enzymes has been considered from a chemical rather than from a biological angle; the latter is to be found in works on biological oxidation and is beyond the scope of this book. A large number of facts have been discussed which may be of interest for clinicians and pathologists, but it should be realized that they have been selected because they throw light on aspects of normal metabolism, rather than from a general medical viewpoint.

It is obviously impossible to give a complete treatment of this immense subject in a few hundred pages. Hemoglobin alone is probably the most extensively studied biological product; many thousands of research papers deal with it. No special apologies are required for the omission of reference to many publications. The purpose of this book, however, and the need for severe restriction of the extensive bibliography necessitated other, more serious, omissions. We have attempted to give due weight to pioneer work and have treated in detail the latest publications in which our present knowledge is most fully represented, but we have been forced to omit reference to many papers in the intermediate period. At the time of their appearance, these may have contributed greatly to our knowledge. They are quoted, however, in the later publications and may be readily found by a reference to the latter.

We should explain why we elected not to cite in the text all author names and to refer frequently to publications only by a reference number. Again, this was necessitated by the dual purpose of the book: to enable the student not specially interested in this particular problem to read the text without interruption, and to permit the

research scholar to obtain complete information. Every effort has been made to see that names have been mentioned of the workers who have important discoveries to their credit.

Another attempt to solve the problem of the dual purpose of the book is the use of large and small print. *It must be particularly stressed that the parts set in small type are not by any means considered less important or interesting than those set in large type.* On the contrary, they frequently contain the discussion of problems of particular interest for the research scholar, while those set in large type contain the basic facts of primary interest for the student.

A special difficulty has been the lack of a uniform, generally accepted nomenclature. A questionnaire on nomenclature was sent to some authorities working in the field to whom we are indebted for letting us have their opinion. It is evident that this anarchy of nomenclature is felt keenly, but that at present no possibility exists of arriving at a generally accepted agreement. We hope that the suggestions we have made will contribute to the solution of this problem. Those who do not like some of the names we suggest may consider them as shorthand symbols, the meaning of which has been strictly defined in the various chapters.

The period during which the book was written was a propitious choice for the completion of the work, due to the pause in the publication of research papers during the war. The important literature published up to July, 1946, has been included. In some cases, it was difficult to secure copies of papers published during the war years in countries of the European continent. Reprints kindly sent by scholars, and particularly photocopies prepared by the Australian Council for Scientific and Industrial Research and the Bibliofilm Service of the United States Department of Agriculture, Washington, have helped overcome this problem. Not all papers that might have been of importance could, however, be read in full; some had to be quoted from abstracts.

Every effort has been made to bring the book up-to-date by adding short footnotes in which important recent contributions have been cited and shortly discussed. These additions include the period from middle of 1946 to about June, 1948. We wish to thank the publishers for the indulgence they have shown us by permitting these additions at so late a stage of publication of the book.

Our thanks are due to Dr. W. W. Ingram, Director of the Institute, and to the authorities of the Royal North Shore Hospital, for pro-

viding us with all facilities required for our task. The National Health and Medical Research Council of Australia has supported the work of both authors with research grants for a number of years; it has also made a special grant to one of us (J. W. L.) for a period of four months, which allowed him to contribute extensively to several sections of this book, and has provided us with grants for secretarial help. We are indebted to the Trustees of the Estate of the late Sir Henry S. Wellcome for permitting one of us (J. W. L.) to continue his work on this book during his tenure of a Fellowship in England. Mr. J. P. Callaghan, who has been working in this institute as a research worker under a grant from the National Health and Medical Research Council, has contributed Chapter II and has otherwise greatly assisted in writing and checking other chapters.

We are greatly indebted to Prof. D. Keilin and Prof. F. J. W. Roughton, to Drs. P. George, N. E. Goldsworthy, J. Keilin, D. P. Mellor, M. F. Perutz, W. P. Rogers, R. N. Robertson, and to Mr. H. F. Holden for valuable advice; to Prof. A. J. Canny, Dr. E. B. Durie, J. L. Still and Mr. H. F. Holden for reading parts of the script; to Drs. F. Bodansky and B. I. Horecker for sending unpublished material for quotation; to Mr. W. A. Rawlinson for the original diagram on which Figure 1, Chapter VI, is based; to various authors whose work we have quoted *in extenso*, particularly Prof. L. Pauling and Prof. W. M. Clark, and to their publishers for permission to use these quotations; and to several authors who have sent us reprints of their publications.

The work would have been impossible without the loyal support of the members of the staff of the Institute, particularly of my collaborators, Mr. E. C. Foulkes and J. Falk, who, together with Mr. Callaghan, have read and reread the manuscript and proofs.

We shall be indebted to our readers for pointing out errors and obscurities, so that they may be corrected in later editions.

The book will have fulfilled its purpose if it shows to the student and the general reader how much remains to be done in this interesting field of biochemistry, and if it opens new aspects to the research worker and inspires him to attack unsolved problems.

R. LEMBERG

June, 1949 J. W. LEGGE

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