Enzyme Regulation and Metabolic Diseases

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Progress in biochemistry in the last half-century, by focusing the fundamental role of the many, and yet not all known, enzyme activities which play a key role in normal cell metabolism and its pathological alterations, has made available to medical science a large wealth of knowledge, usefully applied to both pathogenetic and clinical problems.

Dr. Francesco Belfiore and his younger co-workers, working in the Institute of Clinical Medicine which I had the honor to lead as Chairman, have been engaged for many years in research concerned with metabolic diseases. Having available the large number of in- and out-patients of this department, Dr. Belfiore has focused his interest primarily on enzyme alterations in diabetes mellitus and obesity, subjects which were investigated with research including etio-pathogenetic, clinical and therapeutic aspects. Original results obtained in this field have already appeared in several published papers, and concern primarily the role of key enzymes of carbohydrate and lipid metabolism in various tissues, especially the hepatic and adipose tissues, both in the normal condition and in pathological states; the relationship between insulin resistance and the pathogenesis of obesity, and the role of lysosomal enzymes in the pathogenesis of vascular complications of diabetes, as these enzymes participate in the catabolism of glycoproteins and mucopolysaccharides, whose accumulation in the capillary basement membrane and in arterial walls characterizes the histopathological picture of the diabetic micro- and macro-angiopathy.

In this book, Dr. Belfiore summarizes the results of his own work on enzyme changes in obesity, diabetes mellitus, hyperlipoproteinemias and atherosclerosis, and integrates them, with meticulous objectivity, to the large body of literature on these subjects. What has come out is an up-to-date and comprehensive review, which will certainly be appreciated by physicians and scientists interested in metabolic diseases or specifically engaged in enzymology, who will draw from this book stimulus to further research, in the interest of scientific progress and possible medical applications.

Saverio Signorelli

Preface

Enzymes certainly represent a major factor in the regulation of metabolic processes, which may often be regarded as epiphenomena of enzymatic events.
This book is devoted to the description of the enzyme alterations that constitute the basis of the metabolic changes characteristic of such diseases as obesity, diabetes mellitus, hyperlipoproteinemia and atherosclerosis, i.e. metabolic diseases that are not due to well-established genetic enzyme defects, but in which a key position is held by alterations in enzyme regulation. The description of the enzyme changes occurring in each of the diseases mentioned above is preceded by a detailed account of the characteristics and metabolic function of the regulatory enzymes involved, followed by a mention of enzyme regulation by factors such as hormones, nutrients, age, development, and environmental factors. This has been judged useful by us as a necessary background to understanding the alterations occurring in diseases, and as basic information which may stimulate further research on pathological conditions.

The subject of this review, as appears from the definition given above, encompassing the characteristics and function of the key enzymes of the main metabolic pathways, their control by regulatory factors, and their changes in metabolic diseases, is exceedingly wide and perhaps beyond practical limits of space and time. Therefore, several limitations have been introduced. First of all, in the various chapters of this book, only those enzymes which are generally thought to play a ‘key’ or ‘regulatory’ role have been considered. However, distinction between regulatory and non-regulatory enzymes is not always simple and perhaps is arbitrary in some instances. Therefore, readers may not always agree with the line followed by us. With only occasional exceptions, our attention has been mainly focused on the behavior of enzymes in the tissues of mammals, with the exclusion of other species which may possess peculiar metabolic characteristics. Furthermore, discussion has been centered on tissues of general metabolic significance, while other tissues, such as bone, skin, mammary gland, spleen and others, have not been considered. In the chapters on regulatory factors, prostaglandins have been excluded, since the rapidly growing literature on these compounds would require an entire volume to be covered. In the chapter on enzyme regulation by nutritional factors, the important metabolic effects of ethanol intake and of vitamin and mineral deficiency or excess have also not been included. Even with these limitations, the vastness of the subject remains so great that a complete review of literature is practically impossible. It has been necessary therefore to be selective. Moreover, of some works dealing with several metabolic aspects of a given subject, only data of mainly enzymatic concern have been cited. In view of these considerations, I apologize in advance to the many who will find that their work has not been mentioned or has not been given the space it certainly deserves.

Preface XXIII

In a work devoted to enzymes, nomenclature is always a troublesome
problem, since one has to choose between trivial names, largely diffused but scientifically often unacceptable, and the systematic names, which are of less immediate understanding and may impair the smoothness of reading. In this book, we followed the ‘recommended names’ recently suggested by the International Union of Pure and Applied Chemistry and the International Union of Biochemistry (1848, 1849), with only few exceptions, and we listed the corresponding E.C. numbers and catalyzed reactions in the appendix. Moreover, in describing changes in enzyme activities, we have often omitted the term ‘activity’ to avoid repetition. However, the described changes must be intended as referring to changes in the measured enzyme activity, since when the cause of the change is known (change in enzyme concentration due to altered synthesis and/or degradation, allosteric effects, covalent modification, etc.) it has been specified.

While licensing this book for printing, I wish to express my gratitude to all those who have taught me during my academic career, and to the younger colleagues, members of our research group, whose names are mentioned in the reference list. My special thanks and deep appreciation are due to my wife Dr. Silvia Iannello, who, with devotion, shared with me the heavy privations imposed by this multi-year work, and who gave me invaluable aid by meticulously preparing the long reference list and by undertaking the many chores incident to publication.

Finally, sincere thanks are due to the Publisher and his staff for their help and assistance.

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