Outline Studies in Biology

A Biochemical Approach to Nutrition

R. A. Freedland and S. Briggs

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OUTLINE STUDIES IN BIOLOGY

Editor's Foreword

The student of biological science in his final years as an undergraduate and his first years as a graduate is expected to gain some familiarity with current research at the frontiers of his discipline. New research work is published in a perplexing diversity of publications and is inevitably concerned with the minutiae of the subject. The sheer number of research journals and papers also causes confusion and difficulties of assimilation. Review articles usually presuppose a background knowledge of the field and are inevitably rather restricted in scope. There is thus a need for short but authoritative introductions to those areas of modern biological research which are either not dealt with in standard introductory textbooks or are not dealt with in sufficient detail to enable the student to go on from them to read scholarly reviews with profit. This series of books is designed to satisfy this need. The authors have been asked to produce a brief outline of their subject assuming that their readers will have read and remembered much of a standard introductory textbook of biology. This outline then sets out to provide by building on this basis, the conceptual framework within which modern research work is progressing and aims to give the reader an indication of the problems, both conceptual and practical, which must be overcome if progress is to be maintained. We hope that students will go on to read the more detailed reviews and articles to which reference is made with a greater insight and understanding of how they fit into the overall scheme of modern research effort and may thus be helped to choose where to make their own contribution to this effort. These books are guidebooks, not textbooks. Modern research pays scant regard for the academic divisions into which biological teaching and introductory textbooks must, to a certain extent, be divided. We have thus concentrated in this series on providing guides to those areas which fall between, or which involve, several different academic disciplines. It is here that the gap between the textbook and the research paper is widest and where the need for guidance is greatest. In so doing we hope to have extended or supplemented but not supplanted main texts, and to have given students assistance in seeing how modern biological research is progressing, while at the same time providing a foundation for self help in the achievement of successful examination results.

J. M. Ashworth, Professor of Biology, University of Essex.

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Preface

Though the major emphasis of this book will be to provide the nutritionist with a biochemical approach to his experimental and practical problems, it is hoped that the book will also be of use to the biochemist and physiologist to demonstrate how dietary nutrition manipulation can be used as a powerful tool in solving problems in both physiology and biochemistry. There will be no attempt to write an all-encompassing treatise on the relationship between biochemistry and nutrition; rather, it is hoped that the suggestions and partial answers offered here will provide the reader with a basis for approaching problems and designing experiments.

Although some foundation material will be presented in discussions, it is assumed that the reader has a basic knowledge of biochemistry and nutrition and some background in physiology. For supplementary information, references to several basic texts are given at the end of the introduction.

To facilitate easy reference, the book has been divided into chapters according to the roles of the basic nutrients in metabolism. Within chapters, discussion will include such topics as the effects of nutrients on metabolism, the fate of nutrients, the roles of various tissues and interaction of tissues in utilizing nutrients, and the biochemical mechanisms involved.

Toward the end of the book, several example problems will be presented, which we hope will provide the reader with the opportunity to form testable hypotheses and design experiments. The problems will be discussed in the final chapter. We wish to emphasize that the answeres presented are not unequivocal and that the solutions proposed by the reader may be more valid than those offered here.

August 1976 R.A.F.

To my wife, Beverly, and my children, Howard, Judith, and Stephen, whose patience and encouragement were an incentive throughout the writing of this book.

R.A.F.

1 Energy and basal metabolism

It seems appropriate to begin our discussion of nutrients with that concept to which all matter is related; namely, energy. Currently there is a controversy as to whether the kilocalorie or the joule is the proper unit of energy measurement in the metric system. Rather than concerning ourselves with units, we shall simply use the generic term 'energy'. Therefore, what you may have heard referred to as the 'caloric content' of a food shall be referred to here as its 'energy content'.

The energy content of a food stuff can be measured by burning it in a bomb calorimeter. The complete oxidation of the food to carbon dioxide and water (and oxides of other elements, such as nitrogen, contained in the food) transforms the chemical energy of the food to heat, the ultimate form of energy, which can be measured.

Not all the energy in a food stuff is available to the body. Some constituents such as cellulose are not digestible, while others may not be absorbed under all circumstances. That part of a food's energy which can be digested and absorbed is referred to as 'digestible energy'. Not all of the digestible energy is fully oxidized by the body and some must be excreted. For instance, mammals do not completely oxidize nitrogen but excrete it as urea, which still contains extractable energy. Also, in conditions of ketosis that lead to ketonuria, partially oxidized carbon is excreted. The energy in food which can be both absorbed and used by the body is known as 'metabolizable energy'.

When food is metabolized by the body, some of the food's energy is converted to heat, some is used for performing work, and some can be stored. When the energy intake exceeds the body's energy expenditure (work + heat), energy is stored and there is weight gain. When the body's energy expenditure exceeds intake, body substance provides the deficit, and there is weight loss.

'Work' is done not only in the physical sense of force through distance, as during muscular movement, but in a chemical way, through altering bonds. The breaking and forming of chemical bonds is not 100% efficient, and some of the energy inherent in those bonds is lost as heat during conversions. It is for this reason that there is a 'basal metabolic rate', or BMR. BMR is defined as the rate of heat production when the body is in a postabsorptive state and at rest, or that amount of energy required to maintain body function when the body is in a postabsorptive state and at rest. (Rest does not denote sleep; energy expenditure is lower during sleep than during rest.)

As the compounds provided by food are converted via the metabolic pathways to compounds of lower energy levels, some of the energy released in the conversion is trapped in particularly high energy compounds. These high-energy compounds, of which adenosine triphosphate (ATP) is the primary one, can later give up their energy to transform other compounds to higher energy levels, allowing biosynthetic processes and work. Other energy currencies include UTP, GTP, CTP, ITP, and their derivatives.

In many cases it is convenient for the biochemist to account for energy yields as potential ATPs that can be formed from a given food constituent. For certain purposes, counting ATPs has an advantage over using a heat unit such as the kilocalorie or joule, since the amount of metabolic work is directly dependent on ATP (or other high-energy compounds) and not on heat. Examples of work performed by energy transfer from ATP include muscle contraction, maintenance of ion balance, protein synthesis, lipid synthesis and glycogen and lipid storage.

1.1 Turnover of body constituents

It would appear at first glance that an adult animal which had achieved its full growth should require only energy and could accept energy in any available form to maintain bodily functions such as ion balance, respiration, blood flow, and nervous system function. However, even adult animals require protein, minerals, vitamins, and certain fatty acids in addition to energy. This is because the body constituents – proteins, lipids, carbohydrates, nucleic acids, cells – are continually undergoing degradation. Renewal of these constituents requires that substrates for synthesis be continually provided. Hormonal and dietary conditions may alter degradation and synthesis rates, but both processes continue even under extreme conditions. As Schoenheimer discovered in his classic experiments, even when an animal is mobilizing fat stores for energy, some lipid synthesis and fat deposition are occurring [1].

References

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2 Regulation of enzyme activity

To live in a changing environment requires the ability to adapt. In its day to day existence an animal encounters variation in environmental stresses, in activity requirements, and in type and amount of food intake. To meet an animal's needs in its current situation, the flow of nutrients through its metabolic pathways must be subject to regulation. One of the primary means of controlling the disposition of nutrients is the regulation of enzyme activities.

Enzymes catalyze chemical reactions. The extent to which an enzyme can increase the rate of a reaction depends on the enzyme's activity, which is a function of the amount of active enzyme available and of the presence of substrates, co-factors, inhibitors, and activators. Consequently, enzyme activity is subject to alteration by three basic mechanisms:

1) synthesis and degradation of enzyme molecules;
2) modification of enzyme to an active or inactive form;
3) changes in concentration of substrates, co-factors, activators, or inhibitors.

Each of these mechanisms will be considered individually.

2.1 Enzyme synthesis and degradation

All enzymes are proteins, and therefore enzyme synthesis requires protein synthesis. It appears that in the *in vivo* animal system, protein synthesis is a zero order reaction [1]. This means that a constant amount of enzyme is synthesized per unit time. In contrast, degradation is a first order process [1]: that is, the number of molecules being degraded at any moment is a certain percentage of the number of enzyme molecules present at that moment.

When the rate of synthesis is equal to the rate of degradation, a 'steady state' is said to exist. A change in either synthesis or degradation rate (or both) results in a new steady state, which manifests itself in a change in enzyme activity.

Effecting a change in enzyme activity by this method requires a considerable length of time, normally ten minutes to several days [2,3]. The time required to manifest a change by this mechanism depends upon the degradation rate of the enzyme [3]. Degradation rate is related to another useful concept, the half-life of the enzyme, by the equation,

$$t_{\frac{1}{2}} = \frac{0{\cdot}693}{d}$$

where $t_{\frac{1}{2}}$ is the half-life (the amount of time required for half the enzyme to disappear when no synthesis is occurring) and d is the degradation rate. The shorter the half-life of the enzyme, the sooner a change in its activity can be manifested following a change in synthesis or degradation rate.

2.2 Conversion to active form

A more rapid mechanism for altering enzyme activity, requiring from a tenth of a second to several minutes, is to convert it from an inact-