THE NUTRITION SOCIETY TEXTBOOK SERIES

Nutrition & Metabolism

Edited by Michael J. Gibney,
Ian A. Macdonald and Helen M. Roche

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Nutrition and Metabolism

Edited on behalf of The Nutrition Society by

Michael J. Gibney, Ian A. Macdonald
and Helen M. Roche

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The Human Nutrition Textbook Series

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Cystic fibrosis
Clinical cases
Water and electrolytes

Series Foreword

The early decades of the twentieth century were a period of intense research on constituents of food essential for normal growth and development and saw the discovery of most of the vitamins, minerals, amino acids and essential fatty acids. In 1941, a group of leading physiologists, biochemists and medical scientists recognized that the emerging discipline of nutrition needed its own learned society and the Nutrition Society was established. Our mission was, and remains, '*to advance the scientific study of nutrition and its application to the maintenance of human and animal health*'. The Nutrition Society is the largest learned society for nutrition in Europe and we have over 2000 members worldwide. You can find out more about the Society and how to become a member by visiting our website at *www.nutsoc.org.uk*

The ongoing revolution in biology initiated by large-scale genome mapping and facilitated by the development of reliable, simple-to-use molecular biological tools makes this a very exciting time to be working in nutrition. We now have the opportunity to get a much better understanding of how specific genes interact with nutritional intake and other lifestyle factors to influence gene expression in individual cells and tissues and, ultimately, effects on health. Knowledge of the polymorphisms in key genes carried by a patient will allow the prescription of more effective, and safe, dietary treatments. At the population level, molecular epidemiology is opening up much more incisive approaches to understanding the role of particular dietary patterns in disease causation. This excitement is reflected in the several scientific meetings which the Nutrition Society, often in collaboration with sister learned societies in Europe, organizes each year. We provide travel grants and other assistance to encourage students and young researchers to attend and to participate in these meetings.

Throughout its history a primary objective of the Society has been to encourage nutrition research and to disseminate the results of such research. Our first journal, *The Proceedings of the Nutrition Society*, recorded, as it still does, the scientific presentations made to the Society. Shortly afterwards, *The British Journal of Nutrition* was established to provide a medium for the publication of primary research on all aspects of human and animal nutrition by scientists from around the world. Recognizing the needs of students and their teachers for authoritative reviews on topical issues in nutrition, the Society began publishing *Nutrition Research Reviews* in 1988. More recently, we launched *Public Health Nutrition*, the first international journal dedicated to this important and growing area. All of these journals are available in electronic as well as in the conventional paper form, and we are exploring new opportunities to exploit the web to make the outcomes of nutritional research more quickly and more readily accessible.

As protection for the public and to enhance the career prospects of nutritionists, the Nutrition Society is committed to ensuring that those who practice as nutritionists are properly trained and qualified. This is recognized by placing the names of suitably qualified individuals on our professional registers and by the award of the qualifications *Registered Public Health Nutritionist (RPHNutr)* and *Registered Nutritionist (RNutr)*. Graduates with appropriate degrees but who do not yet have sufficient postgraduate experience can join our Associate Nutritionist registers. We undertake accreditation of university degree programs in public health nutrition and are developing accreditation processes for other nutrition degree programs.

Just as in research, having the best possible tools is an enormous advantage in teaching and learning. This is the reasoning behind the initiative to launch this series of human nutrition textbooks designed for use worldwide. The Society is deeply indebted to our former President, Professor Mike Gibney for his foresight, and to him and his team of editors for their innovative approaches and hard work, in bringing this major publishing exercise to successful fruition. Read, learn and enjoy.

John Mathers
President of the Nutrition Society

Preface

This is the second of a series of four textbooks which the Nutrition Society is preparing in association with Blackwell Publishing. Whereas the *Introduction to Human Nutrition* textbook was designed to be used not just by nutrition students, but also by students who might take nutrition as a minor option such as in food science, pharmacy, nursing, agriculture, etc., the present textbook is firmly aimed at the student opting to pursue nutrition as a main academic subject. The textbook, as the title implies, has as its focus the physiological and biochemical basis for the role of nutrients in metabolism. The first seven chapters cover some core areas, some traditional such as the integration of metabolic nutrition or those related to stages of growth, and one focussing on molecular nutrition, an area of great growth and one that will undoubtedly greatly shape the next edition of this textbook.

Thereafter, the chapters are organized somewhat differently to the usual format of nutrition textbooks. The editorial committee took the view that the role of individual nutrients needed to be integrated into chapters on 'systems' rather than nutrients. Issues of public health nutrition are by and large avoided, so that the forthcoming textbook of *Public Health Nutrition* can tackle these. However, the *Clinical Nutrition Textbook* will also tackle diet–disease links on a systems-by-systems basis.

As with the introductory textbook, the issue of within- and between-textbook overlap arose. As best we could, we tried to minimize within-textbook overlap and have tried to cross-reference chapters where possible. However, some level of overlap across texts will occur, but from a different perspective. Thus, the present text introduces an analysis of how nutrient influence risk factors for coronary heart disease with a perspective on the metabolic dimension. Much of this will again arise in both the Public Health and the Clinical Nutrition textbooks, from a population and preventive approach and from a patient and therapeutic approach, respectively.

I am, as ever, very grateful to all of the authors who suffered my regular electronic prompts of deadlines and details, and I am especially grateful to several authors who stepped in at the last minute to help out with the project. To the volume editors Helen and Ian, I am very grateful for their diligence, attention to detail and to timetables, and great teamwork. Again, Julie Dowsett was the catalyst that kept the project going and I am very grateful to Julie and her constant bonny humor. Finally, to the officers of the Nutrition Society, thank you for your confidence in supporting this project, which continues to be a labor of love.

Michael J Gibney
Editor-in-Chief

Sadly, we must remember three authors within this series of four textbooks who have passed away: Britt Marie Sandstrom, Peter Reeds and Vichai Tanphaichitr.

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Contents

1
Core Concepts of Nutrition

IA Macdonald and MJ Gibney

Key messages

- The change in body stores of a nutrient is the difference between the intake of that nutrient and the body's utilization of that nutrient. The time-frame necessary to assess the body's balance of a particular nutrient varies from one nutrient to another.
- The concept of turnover can be applied at various levels within the body (molecular, cellular, tissue/organs, whole body).
- The flux of a nutrient through a metabolic pathway is a measure of the rate of activity of the pathway. Flux is not necessarily related to the size of the pool or pathway through which the nutrient or metabolite flows.
- Nutrients and metabolites are present in several pools in the body. The size of these metabolic pools varies substantially for different nutrients/metabolites, and a knowledge of how these pools are interconnected greatly helps us to understand nutrition and metabolism.
- Darwinian theory of evolution implies a capacity to adapt to adverse conditions, including adverse dietary conditions. Many such examples can be cited. Some allow for long-term adaptation and others buy time until better conditions arrive.

1.1 Introduction

This textbook on *Nutrition and Metabolism* covers macronutrient aspects of nutrition in an integrated fashion. Thus, rather than considering the macronutrients separately, this book brings together information on macronutrients and energy in relation to specific states or topics (e.g. undernutrition, overnutrition, cardiovascular disease). Before considering these topics in detail it is necessary to outline the core concepts that underlie nutritional metabolism. The core concepts to be covered in this chapter are nutrient balance, turnover and flux, metabolic pools, and adaptation to altered nutrient supply.

1.2 Balance

As discussed in Chapter 3, nutrient balance must be considered separately from the concepts of metabolic equilibrium or steady state. In this present chapter, the concept of balance is considered in the context of the classical meaning of that term, the long-term sum of all the forces of metabolic equilibrium for a given nutrient.

The concept of nutrient balance essentially restates the law of conservation of mass in terms of nutrient exchange in the body. Thus, the idea of nutrient balance is summarized by the equation:

$$\begin{bmatrix}\text{Nutrient}\\ \text{intake}\end{bmatrix} - \begin{bmatrix}\text{Nutrient}\\ \text{utilization}\end{bmatrix} = \begin{bmatrix}\text{Change in body}\\ \text{nutrient stores}\end{bmatrix}$$

The above equation can have three outcomes:

- **zero balance** (or nutrient balance): intake matches utilization and stores remain constant
- **positive balance** (or positive imbalance): intake exceeds utilization and stores expand
- **negative balance** (or negative imbalance): utilization exceeds intake and stores become depleted.

In relation to macronutrient metabolism, the concept of balance is most often applied to protein (nitrogen) and to energy. However, many research studies now

subdivide energy into the three macronutrients and consider fat, carbohydrate and protein balance separately. This separation of the macronutrients is valuable in conditions of altered dietary composition (e.g. low-carbohydrate diets) where a state of energy balance might exist over a few days but be the result of negative carbohydrate balance (using the body's glycogen store to satisfy the brain's requirement for glucose) matched in energy terms by positive fat balance.

Balance is a function not only of nutrient intake but also of metabolically induced losses. Fat balance is generally driven by periods where energy intake exceeds energy expenditure (positive energy balance) and by periods when intakes are deliberately maintained below energy expenditure such as in dieting (negative energy balance). However, nutrient balance can also be driven by metabolic regulators through hormones or cytokines. For example, the dominance of growth hormone during childhood ensures positive energy and nutrient balance. In pregnancy, a wide range of hormones lead to a positive balance of all nutrients through placental, fetal and maternal stores (Chapter 6). By contrast, severe trauma or illness will dramatically increase energy and protein losses, an event unrelated to eating patterns.

Balance is not something to be thought of in the short term. Following each meal, there is either a storage of absorbed nutrients [triacylglycerol (TAG) in adipose tissue or glucose in glycogen] or a cessation of nutrient losses (breakdown of stored TAG to non-esterified fatty acids or amino acid conversion to glucose via gluconeogenesis). As the period of post-prandial metabolism is extended, the recently stored nutrients are drawn upon and the catabolic state commences again, This is best reflected in the high glucagon to insulin ratio in the fasted state before the meal and the opposite high insulin to glucagon ratio during the meal and immediate post-prandial period. However, when balance is measured over a sufficient period, and that varies from nutrient to nutrient, a stable pattern can be seen: zero, positive or negative (Figure 1.1). It is critically important with respect to obesity that the concept of balance is correctly considered. While at some stage energy balance must have been positive to reach an overweight or obese stage, once attained, most people sustain a stable weight over quite long periods.

In the context of the present chapter, it is worth reflecting on the reasons why the period to assess energy balance correctly varies for different nutrients.

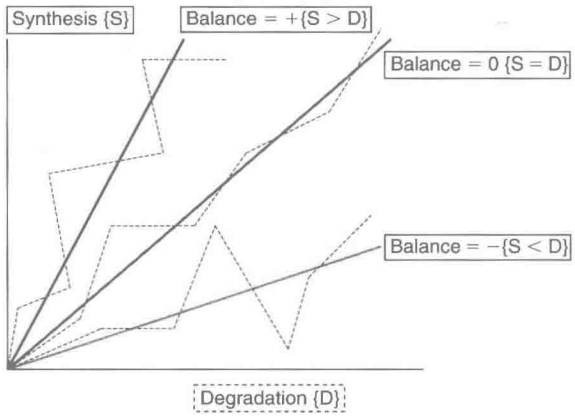

Figure 1.1 Positive, zero and negative nutrient balance over time with fluctuations upwards and downwards within that time.

Fat and adipose tissue (Chapter 5)

- There is a very large capacity to vary the body's pool of adipose tissue. One can double or halve the level of fat stored in the body.
- The capacity to vary the level of TAG in blood *en route* to and from adipose tissue can vary considerably.
- Almost all of the TAG stores in adipose tissue are exchangeable.

Calcium and bone (Chapter 12)

- The human being must maintain a large skeleton as the scaffold on which the musculature and organs are held.
- There is a very strict limit to the level of calcium that can be transported in blood. Excess or insufficient plasma calcium levels influence neural function and muscle function, since calcium is also centrally associated with both.
- Only a small fraction (the miscible pool) of bone is available for movement into plasma.

Because of these differences, calcium balance will require months of equilibrium while fat balance could be equilibrated in days or at most a few weeks.

1.3 Turnover

Although the composition of the body and of the constituents of the blood may appear constant, this does not mean that the component parts are static. In fact, most metabolic substrates are continually being