NUTRITION

An Integrated Approach

RUTH L. PIKE   MYRTLE L. BROWN

THIRD EDITION

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preface to the third edition

The enormous task of bringing so large and so broad a volume up to date before it, too, becomes dated led us to seek the assistance of others. We asked some of the contributors to revise chapters and some to revise sections of chapters. We retained complete editorial responsibility, which in a number of instances, entailed rewriting contributions to conform to the style, purpose, and spirit of the book.

The format remains essentially the same as the second edition, and we still subscribe to one of our original and expressed purposes: to show how present knowledge evolved from previous findings through a step-by-step procedure over long years of study. To further the appreciation of this concept, we have stressed historical development of the science of nutrition throughout this volume as in the two editions that have preceded it. We believe that it is necessary to know where one has been in order to understand where one is going. In examining the past, ideas often arise that have remained buried in the literature waiting to be rediscovered and reinterpreted in the context of current scientific knowledge.

We are grateful to all our contributors and especially acknowledge the outstanding contribution of Dr. Carol V. Gay who provided an excellent revision of eight chapters in the style and spirit established by the authors.

We wish to thank Dr. Howerde E. Sauberlich for his careful review of the material sent to him, and Dr. J. Elizabeth Miles for her helpful suggestions.

For the preparation of the index, we extend thanks to Sylvia MacKinnon Carson.

For this edition, as for the previous two, we are indebted to Dr. Helen G. Oldham for her counsel and help in the writing and preparation of the manuscript and for her assistance in the tedious work of proofreading the entire book.

Ruth L. Pike
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preface to the second edition

What started out to be a revision has become almost a completely rewritten book. In addition to bringing the subject matter in this rapidly changing field up to date, we have reorganized it and presented it in a more logical fashion.

The book is now divided into five parts. Part I, "The Nutrients," is essentially the same as it was in the previous edition but it has been expanded. Part II, "Physiological Aspects of Nutrition," includes a new chapter on digestion and an enlarged section on absorption. Another new chapter is devoted to exchange and transport as well as mechanisms of homeostatic control. Since the nutrients must go through the intestinal mucosa and be transported to the cells to participate in metabolism, it seemed logical to place this material before the section on the cell. Part III, "The Cell," presents the basic biochemical cytology that is important to the nutritionist. As in the first edition, the nutrients are brought to the organelles within the cell, the locus of physiological and biochemical action. Where possible, basic reactions in cellular metabolism are discussed in terms of the complex multicellular organism. Each of these chapters has been rewritten and expanded. Two new chapters have been added: an introductory one on the methods used in studying cellular structure and mechanisms, and a chapter on the Golgi apparatus. Part IV, "Specialized Cells," is a new section that replaces the single chapter in the previous edition. The cells discussed are the ones that we think are of special interest to the nutritionist. Parts III and IV may contain more detail than some nutritionists believe is essential; others, however, will agree that the nutritionist must understand cell structure to understand how the nutrients participate as part of the dynamic complex of the cell. Part V, "The Complex Organism," includes a new chapter presenting the fundamental concepts underlying growth and development. Two chapters in the previous edition have been omitted. "Nutrients in Foods" was primarily a discussion of methodology; this material now has been incorporated into other parts of the book. Instead of the chapter on "Interrelationships of Nutrients," we have shown the interrelationships throughout the book because, indeed, they are interrelated on metabolism.

Our purpose is the same: to integrate the contributions of related scientific disciplines with the study of nutrition; to foster a questioning attitude; and to emphasize the depth and limitations of present knowledge.

We thank Dr. Helen G. Oldham for counsel and help in the preparation of the manuscript; Dr. Marian E. Swendseid for carefully reading the manuscript and making suggestions; and Dr. Lawrence M. Marshall for critically reading portions of the material.

Again we are indebted to Dr. Harald Schraer, who prepared many of the electron micrographs for our use.

If there are errors in the text, we assume full responsibility for them.

Ruth L. Pike
Myrtle L. Brown

preface to the first edition

"He that publishes a book runs a very great hazard, since nothing can be more impossible than to compose one that may secure the approbation of every reader."

Don Quixote, Book III

Advanced study in nutrition presupposes basic knowledge of biochemistry, physiology and, of course, nutrition. This previously acquired knowledge too often tends to be separated in time and in the students' thinking, whereas, in fact, the biochemical, physiological, and nutritional aspects of living matter are inseparable. The disciplines that we have thought of as nutrition, physiology, biochemistry, and genetics have converged at the cellular level and, because the approach of each has been from a different perspective, the convergence has been to mutual advantage.

The nutritionist who understands how the coordination of structure and function is related to the metabolic needs of the cell and its response to its environment has at his disposal the fundamental knowledge for evaluating the nutrient needs of the whole man. The plan of this book and the philosophy that we hope pervades it are based upon this premise.

The book is divided into three parts. Part I briefly presents the historical development of nutritional science and basic information on the nutrients. This section is not intended as a substitute for fundamental biochemistry but includes relevant material applying specifically to mammalian metabolism, which will be drawn upon in later chapters. Part II presents basic biochemical cytology from the viewpoint of the nutritionist, bringing the nutrients to their locus of physiological and biochemical action and indicating, where possible, how basic reactions in cellular metabolism become meaningful in terms of the complex multicellular organism. Part III presents fundamental concepts underlying applied human nutrition. We have concentrated upon the development of these concepts in the belief that *how* and *why* are ultimately of greatest value to the student.

The purpose of this book has been to integrate, as far as possible, the contributions of related scientific disciplines to the study of nutrition. We have tried throughout to foster a questioning attitude and a recognition of both the depth and the limitations of present knowledge. The book is not all-inclusive nor was it intended to be, and we take seriously Don Quixote's warning. We are fully aware that our directions, interests, prejudices, and concerns show and, indeed, we believe that they should. Any nutrition text, to be a complete treatise and to cover the broad areas of concern to all nutritionists in today's world, would have to delve in depth not only into those disciplines we have included but also into public health, sociology, psychology, economics, and perhaps still other areas. Choices therefore are inevitable. It is our belief that a nutritionist must understand the biological aspects of the subject before venturing into the sociological or psychological arenas and, whereas we are convinced of their importance, these are areas that are outside our province. If we have been able to impart an enthusiasm and insight into the study of nutrition, we will have accomplished what we set out to do.

We wish to express our gratitude to Dr. Helen G. Oldham for her counsel in the preparation of the manuscript and for her active participation in the chores associated with the checking of galleys and preparation of the index.

We are sincerely grateful for the helpful suggestions and criticisms we received from Dr. Rosemary Schraer, Dr. Max Kleiber, Dr. Terence A. Rogers, Dr. Lawrence M. Marshall, and Dr. Augustus C. Jennings. However, we assume full responsibility for any errors that may appear in the text.

We are greatly indebted to Dr. Harald Schraer for the preparation of the majority of electron micrographs that appear in the text.

Thanks are due to Dr. Janet M. Wardlaw and to Mrs. Helen A. Guthrie for testing our approach in the teaching of courses in advanced nutrition; and to our own students who were, in fact, most helpful in the development of this manuscript.

We also wish to thank Mrs. Lois Smith and Mrs. Elizabeth Isenberg for their help in the preparation of the manuscript; and Mrs. Carol Winkler for her help in reading proof.

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contents

part one

the nutrients

The material in the following four chapters should be familiar to the student, but since it is fundamental to the integrated study that follows and since memories sometimes falter, it is included either for surreptitious reading or careful study, whatever the need may be.

Nutrition is the science that interprets the relationship of food to the functioning of the living organism. It includes the intake of food, liberation of energy, elimination of wastes, and all the syntheses that are essential for maintenance, growth, and reproduction. These fundamental activities are characteristic of all living organisms from the simplest to the most complex plants and animals.

Nutrition is a relatively new science that evolved from chemistry and physiology just as biophysics has more recently evolved from biology and physics. Recognition of nutrition as an independent field of study came only after the beginning of this century following a developmental period that stemmed from the experiments of Antoine Lavoisier almost 200 years earlier. Lavoisier's work formed the basis for the studies on respiratory exchange and calorimetry, the beginnings of scientific nutrition. Almost 100 years elapsed before carbohydrates, fats, and proteins were identified as the sources of energy for the animal body. By the end of the nineteenth century the significance of protein as a source of nitrogen and the necessity for certain minerals in the diet were established. During the early part of this century conclusive evidence was obtained indicating that proteins varied in their ability to support growth and maintenance. Furthermore it was established that purified diets containing only the major foodstuffs (including suitable protein sources) and minerals were inadequate to maintain life. It was therefore obvious that foods carried other substances yet to be identified.

Investigations with laboratory animals led to the crude separation of fat-soluble and water-soluble fractions from foods that contained the essential factors, but it was not until the 1930s that the majority of the vitamins were identified, isolated from foods, and synthesized in the laboratory. The development of methods for synthesizing the vitamins was a crucial step in the future of nutritional research. It then became possible to develop a completely synthetic diet that could support the life of laboratory animals, and research could be directed toward elucidating the functional roles of individual nutrients.

However crude the early work appears from the vantage point of current methodology and instrumentation, much of it was sophisticated, elegant in design, and carefully executed; this work provided the basic information that is the core of the science of nutrition.

chapter 1

historical perspective

"What little we know, what little power we possess, we owe to the accumulated endeavors of our ancestors. Mere gratefulness would already oblige us to study the history of the endeavors, our most precious heirlooms. But we are not to remain idle spectators. It is not enough to appreciate and admire what our ancestors did, we must take up their best traditions, and that implies expert knowledge and craftsmanship, science and practice."

George Sarton, The History of Science and the New Humanism, 1956

Ancient and Medieval Ideas

Before the eighteenth century little of a truly scientific nature was accomplished in the development of nutrition or, in fact, of any science. The ancient Greek philosophers apparently were interested in science, but logical reasoning, rather than experimentation, was the Greek way.

Hippocrates (460–364 B.C.) wrote the following passage that is accurate in essence although somewhat imprecise in detail.

> *Growing bodies have the most innate heat; they therefore require the most food, for otherwise their bodies are wasted. In old persons, the heat is feeble and therefore they require little fuel as it were to the flame, for it would be extinguished by much . . .*

For nearly 1500 years after Hippocrates' time, little was accomplished in the development of science. The alchemists of the Middle Ages were devoted to the task of transforming common metals into gold, and medical knowledge had advanced little beyond the knowledge possessed by the ancient civilizations. It was not until the sixteenth century that the intellectual climate again became conducive to scientific development; interest revived in the relation of man to his environment and particularly to the air surrounding him. It was in the seventeenth century that van Helmont (1577–1644), a Belgian nobleman, discovered the lethal effect of carbon dioxide. In the same period, Sanctorius (1561–1636) published the results of experiments on himself clearly indicating that a major pathway of excretion from the human body was the "insensible perspiration," a loss of body weight not accountable by measurements of urine and feces and thus presumed to be expelled into the surrounding air. The sketch of Sanctorius sitting in his chair-scale has escaped few students of nutrition.

The Phlogiston Theory of Combustion

A major contribution to scientific thought at the beginning of the eighteenth century, unfortunately, was a misconception, the phlogiston theory of combustion that was promoted by Stahl (1660–1734), a German chemist. Although the theory was accepted by a majority of scientists of the period, it was based apparently on no more than a lively flight of imagination. Stahl maintained that all combustible materials contained phlogiston, which passed from them into the atmosphere when the substances were burned. The phlogiston theory, along with the generally held misconception that air was an elemental substance, profoundly influenced scientific thinking and interpretation of new discoveries for almost a century. Consequently, Black (1728–1799) termed carbon dioxide "fixed air"; Cavendish (1731–1810) called hydrogen "inflammable air" and believed it to be phlogiston. Rutherford's (1749–1810) "residual air" was what we now know as nitrogen. Two independent discoverers of oxygen, Priestley (1733–1804) and Scheele (1742–1786), used the terms "dephlogisticated air" and "fire air."

It was in a scientific climate dominated by misconception that Lavoisier began his experiments on combustion that led to studies on animal respiration and paved the way for the development of modern calorimetry.

Studies of Respiration: Development of Calorimetry

The truly great scientist not only observes phenomena (which anyone can do) but has the genius to interpret his findings and the strength to bear the consequences of possible failure. As Szent-Györgyi (1957) stated:

There is but one safe way to avoid mistakes; to do nothing, or, at least, to avoid doing something new . . . The unknown lends an insecure foothold and venturing out into it, one can hope for no more than that the possible failure will be a honorable one.

Antoine Lavoisier (1743–1794) was one of the first to repudiate Stahl's theory of phlogiston.[1] By repeating experiments previously performed by some of his contemporaries of the late eighteenth century, for example, heating mercury oxide with carbon, Lavoisier concluded that "fixed air" (carbon dioxide) was formed by the combination of carbon and "air eminently respirable" (oxygen). In his *Reflections upon Phlogiston* he stated, "All the phenomena of combustion and calcination are much more readily explained without phlogiston than with phlogiston." (See Lusk, 1928.)

Thus without the impediment of the phlogiston theory, Lavoisier went on to apply his theory of combustion to the problem of the origin of animal heat. Experimenting with guinea pigs and later with his assistant, Seguin, as subjects, Lavoisier measured body heat loss, oxygen consumed, and carbon dioxide expired and concluded that respiration is a combustion process similar to what happens when substances are burned outside the body. Furthermore, he was able to show that heat production in the animal body is directly related to oxygen consumption.

Respiration is only a slow combustion of carbon and hydrogen which is entirely similar to that which obtains in a lamp or lighted candle and from this point of view, animals which respire are truly combustible bodies which burn and consume themselves. In respiration as in combustion it is the air which furnishes the heat—if animals do not repair constantly the losses of respiration, the lamp soon lacks oil, and the animal dies, as a lamp goes out when it lacks food. (See Lusk, 1928.)

Measurements taken in the fasting and resting state, as initially performed by Lavoisier, represent essentially the basal metabolism. In another series of experiments in which Seguin was the subject, Lavoisier showed that oxygen consumption and therefore heat production was increased above the basal state by a decrease in environmental temperature, ingestion of food, and by physical exercise. The following table indicates the relative increases in oxygen consumption under the conditions of his experiment.

There were some technical inaccuracies in Lavoisier's work and in his interpretation of the data. His figures for oxygen consumption were too high, and he erroneously believed that carbon dioxide and water were formed in the lungs. However, in spite of these errors, refinements in instrumentation and in scientific thought have added little to the general concepts derived from his experiments. The increase in oxygen consumption following ingestion of food was later described by Rubner (1854–1932) as the *specific dynamic effect* of food (Rubner, 1902). The effects of temperature and exercise on oxygen consumption and body

[1]As the result of a long series of experiments, Lavoisier established the law of the conservation of mass, a concept later refined by Einstein. For this reason Lavoisier is known as the father of modern chemistry as well as the father of nutrition.

Condition	Environmental Temperature	Liters Oxygen Absorbed per Hour
Without food	26	24
Without food	12	27
With food		38
Work (9.195 foot pounds—without food)		65
Work (9.195 foot pounds—with food)		91

Source: From G. Lusk, *The Elements of the Science of Nutrition*, 4th ed., W. B. Saunders Co., Philadelphia, 1928, p. 19.

heat production have been confirmed repeatedly and are basic tenets of modern calorimetry.

Lavoisier, however, did not recognize the nature of the foodstuffs and believed that elemental carbon and hydrogen were oxidized in the body. François Magendie (1783–1855), an early nineteenth century physiologist, was the first to distinguish between the different kinds of foodstuffs (carbohydrate, fat, and protein). Even so, this information was not applied to studies of respiratory exchange for many years. Regnault (1810–1878), however, showed that the ratio of carbon dioxide to oxygen consumed varied with kind of food (Regnault and Reiset, 1849). This ratio is now called the *respiratory quotient* (RQ).

Later Calorimetric Studies

Liebig (1803–1873), of the nineteenth century German school, apparently recognized that proteins, carbohydrates, and fats were oxidized in the body, and he then calculated energy values for some foodstuffs. He proposed that since only proteins contain nitrogen, the nitrogen of the urine must arise from protein in the body (Liebig, 1842). He erroneously believed that muscular work caused the metabolism of protein and that oxygen caused the destruction of carbohydrate and fat.

The first report of a balance-type experiment is credited to Boussingault (1802–1887), a Frenchman and contemporary of Liebig. He measured carbon, hydrogen, oxygen, nitrogen, and salts of a cow's food and excreta. During the same period in Germany, Bidder (1810–1894) and Schmidt (1822–1894) performed a similar experiment but also related their balance data to the animal's respiratory exchange, a closer approximation to modern calorimetric method (Bidder and Schmidt, 1852). In their writings, they described a *typical minimum* of necessary metabolism which is apparent in experiments when no food is given. This typical minimum is now referred to as the *resting metabolism*.

Voit (1831–1908) was a particularly gifted student of Liebig and was distinguished not only by his own work but also by that of his students: Rubner (1854–1932), Atwater (1844–1907), Lusk (1866–1932), and many others. In the late nineteenth century the laboratory at Munich was the center for calorimetric stud-