

# NUTRITION AND HEALTH

Adrienne Bendich, Ph.D., FASN, FACN, SERIES EDITOR  
Consultants in Consumer Healthcare LLC, Morristown, NJ 07960, USA

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Michael F. Holick • Jeri W. Nieves  
Editors

# Nutrition and Bone Health

Second Edition

 Humana Press

*Editors*

Michael F. Holick  
Department of Medicine, Physiology, and Biophysics  
Boston University Medical Center  
Boston, MA, USA

Jeri W. Nieves  
Helen Hayes Hospital and  
Department of Epidemiology  
Columbia University  
Mailman School of Public Health  
Institute of Human Nutrition  
Columbia University  
New York, NY, USA

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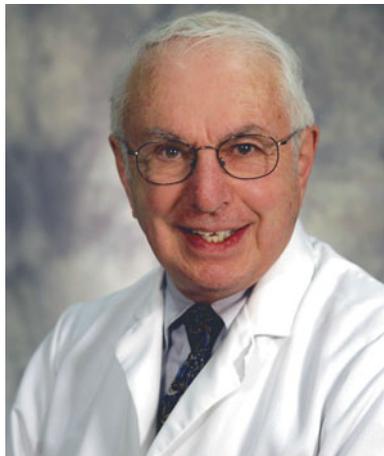
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*The second edition of Nutrition and Bone Health is fondly dedicated to the memory of Dr. Larry Raisz (1925–2010). Larry was one of the most influential and productive physician-scientists the field of bone metabolism has ever seen. He was an outstanding bench scientist, clinician, educator, mentor and advocate for basic and clinical research. Although less well-known than his scientific papers, Larry also wrote poems and, as with everything else he undertook, he was a good poet. Here are his musings on biomedical researchers and the currently sorry state of research funding:*

*The Charge of the White Coat Brigade*

*They come by their hundreds in order to ease  
The suffering of illness, the pain of disease  
They teach us all about healthy behavior  
For in the long run, prevention is saviour.  
But to maintain the progress of this fine brigade  
New knowledge must be sought, new discoveries made  
Government and foundations, which once were there  
Are finding their cupboards ever more bare.  
But if we all work and plan together  
This is a storm we all can weather.  
And make better health our next port of call.  
But this is a gala so let's have a ball.*

Larry Raisz  
April 2010

*Larry led that charge valiantly all his life and his passing has left a void. Older readers of this volume will fondly remember the first person at the microphone after almost every scientific presentation in our field. "Raisz, Connecticut!" would echo around the auditorium by way of introduction and there would then follow a series of insightful and constructive questions, never aggressive or combative, but always seeking and providing enlightenment. Sadly, Larry's voice and pen are stilled now, but he leaves a legacy that will serve as an inspiration for generations of researchers to continue the charge.*

David W. Dempster  
New York, July 2014

# Foreword

A rational approach to understanding the skeleton, its physiology, and pathology requires an integrated approach. Often in textbooks on metabolic bone disease, nutrition is given short shrift. In 41 chapters, *Nutrition and Bone Health* is a comprehensive review of all aspects of nutrition and the skeleton, and the interrelationships between nutrition and skeletal homeostasis. From a teleological perspective, prevention of phosphate deficiency in our saltwater ancestors represented an early environmental adaptation. The move to terrestrial hunter-gatherers changed the requirements, imposing the need to find large quantities of food of low caloric density to satisfy energy requirements. Today's challenges are different. Now a surfeit of high-calorie foods and a corollary obesity has become epidemic. In this environment are we achieving a diet that is adequate enough to allow us to build and maintain a healthy skeleton? To answer this question we need to understand the nutritional requirements of the skeleton, and how these requirements interact with, for example, genetic control of bone growth and remodeling. It is most propitious that this volume, which addresses those very issues, should be published at a time when there is much discussion about the various fad diets that potentially could modify skeletal behavior.

It has become commonplace to think of the skeleton only in terms of calcium nutrition. Indeed, calcium is stressed to be the “building block” of the skeleton and the backbone (so to speak) of all pharmacological interventions. But it is much more complex than that simple view. The skeleton is required to be strong, but flexible. It must support the everyday stresses placed on it, but must also resist sudden traumatic forces. The skeleton is also the depository for potentially harmful metals, and of course it is the major source for ions required in carefully controlled concentrations in serum. That it can achieve these three functions is one of nature's miracles, requiring a carefully controlled remodeling process to maintain its health and vigor, to provide one means for ion storage and release, and to repair stress-related damage. Because we are told that we are what we eat, it is not surprising that the skeleton requires a variety of nutrients for its own health. This remarkable volume tries to place into context the role of nutrition, both good and bad, in the overall health of the skeleton, and consequently of the organism. In putting together a unique group of internationally respected authors, the editors, themselves international experts in vitamin D and calcium homeostasis, have synthesized for the reader the wide variety of impacts that nutrition can have on the skeleton.

The achievement of adequate skeletal mass and strength requires complex interactions among genetics, health, nutrition, and physical stress during growth, and toward the end of growth, a normal transition through puberty. We often forget the many interactions required for this process. From early fetal development, nutrients supplied by the mother provide the basis for bone growth. Maternal nutrition is key here. Recent data suggest that a maternal diet inadequate in protein may result in a deficient stem cell population in the developing fetal skeleton, implying that we may have much more to learn about

the role of maternal nutrition and its interactions with genetics in determining the mass of the skeleton at birth. Why might that be important? It is suggested, but by no means proven, that even early in life, a skeleton that has failed to develop adequately may set the stage for osteoporosis in later life.

The growth of the skeleton in the child is no less important. The interplay between genetics and environment creates an adult skeleton sufficient to withstand the stresses placed on it in everyday life. Big people grow big bones (simplistically put) and, by the tests that we use to measure bones, have “denser” bones as an artifact of the test rather than a biological fact. Nevertheless, in the absence of proper nutrition, clearly the skeleton cannot respond to the variety of endocrine factors stimulating its growth and expansion, nor to the stress of childhood play and sport. Here again, nutrition means much more than assuring optimal calcium intake. It is not commonly recognized that the period of transition through puberty is a period of adaptation by the growing organism to increased needs to sustain the accelerated phase of growth. It is only then that the recognized gender differences in the skeleton become evident. A not infrequent disaster at this point is the appearance of an eating disorder, which can have catastrophic effects on the final maturation of the skeleton. Anorexia, coupled as it often is with failure of the hypothalamic–pituitary–ovarian axis, can lead to significant fracture risk at a young age, as the organism steals from the skeleton the essential nutrients it is failing to get otherwise.

Maintaining an adequate skeleton during adult life is equally complex. Here the effects of poor nutrition more often result in obesity, a highly prevalent feature of our adult society (and increasingly of our pediatric population). Although there is some suggestion that bone density, at least at some sites, may be increased in obese individuals, this by no means offsets the other multiple health problems that besiege the obese. Consequently, efforts at controlling weight abound, largely because of the relative ineffectiveness (usual among individuals not fully committed to the concept, but perhaps not always). Several of these will have detrimental effects on the skeleton. For example, gastric surgery and ketogenic diets will induce nutritional effects that result in excess bone loss. It is transition through menopause that alters the relationship between skeletal homeostasis and nutrition, by rendering the organism less efficient at absorbing and retaining calcium. The consequence is increased bone turnover and loss, with osteoporosis and fractures being the outcome.

At an even later stage in life, the efficiency of calcium absorption across the intestine declines and may be accompanied by vitamin D insufficiency. Secondary hyperparathyroidism ensues, with further loss of bone mass. Nutritional requirements thus change with age, with a need for higher vitamin D intakes, since skin synthesis declines at the same time. Finally, in old age, when hip fractures are common, protein nutrition assumes an important role, and it is clear that recovery from hip fracture, perhaps repair of the bone, and reduction in risk of a second hip fracture can be mediated by improved protein nutrition.

*Nutrition and Bone Health*, crafted by two international experts on calcium and vitamin D, brings together in one place the nutritional aspects of skeletal health and integrates them with other aspects of the control of mineral homeostasis. It begins with teleology, traverses genetics and the control of bone growth and metabolism, and includes discussion of other factors (such as medications) that might alter the nutritional requirements of bone. As the chapters unwind, they interweave the fundamental importance of good nutrition in maintaining the health of the skeleton. The editors have chosen their authors with care and have created a volume that should be read by all interested in bone health and nutrition.

West Haverstraw, NY, USA

Robert Lindsay, M.B.C.H.B., P.H.D., F.R.C.P.

# Preface

The adage “you are what you eat” is certainly true for skeletal health from birth until death. The skeleton is often perceived as an inert structure that simply acts as the scaffolding for the musculature and to house the brain and other essential organs. Thus, the skeleton is taken for granted. However, just as the intricate scaffolding of a suspension bridge requires constant maintenance, so too does the skeleton require nutritional maintenance. It has a voracious appetite for calcium and other macro- and micronutrients in order for it to maximize its size and to maintain its maximum structural strength.

The consequences of not providing the skeleton with its nutritional requirements can be quite severe. Infants and young children who do not get an adequate amount of calcium and vitamin D in their diet suffer from growth retardation and bony deformities of their skull, rib cage, arms, and legs. For adolescents and young adults, inadequate nutrition results in not being able to attain their genetically prescribed maximum peak bone mineral density. For middle-aged and older adults, inadequate calcium, vitamin D, protein, and macro- and micronutrient nutrition leads to a more rapid loss of bone that can precipitate and exacerbate osteoporosis. Twenty-five million Americans and an equal number of Europeans and an untold hundreds of millions of adults worldwide are at risk for osteoporosis and its unfortunate consequences. In the USA, approximately one in two women and up to one in four men age 50 and older will break a bone due to osteoporosis. Osteoporosis is responsible for two million broken bones and \$19 billion in related costs in the USA every year. Approximately 300,000 of these fractures will be of the hip. Twenty-five percent of women and fifteen percent of men will suffer a hip fracture by the age of 80. It is estimated that between \$10–20 billion a year is expended for the acute and chronic care of patients suffering hip fracture. However, the most serious consequences of a hip fracture is that 50 % of patients will never have the quality of life they once had and often become infirm, and 20 % die within the first year after the fracture owing to complications. Therefore, prevention of these devastating fractures becomes very important, and nutrition is a cornerstone of prevention.

The first objective of the second edition of *Nutrition and Bone Health* is to provide practicing health professionals, including physicians, dietitians, nutritionists, dentists, pharmacists, health educators, policymakers, research investigators, graduate students, and medical students with comprehensive, well-balanced reviews of the newest clinical findings as well as up-to-date research discoveries regarding the role of nutrition in maintaining a healthy skeleton. It is a given that adequate calcium and vitamin D are important for skeletal health. However, the skeleton craves other nutrients that are equally essential for bone health.

This second edition of *Nutrition and Bone Health* explores how our earliest ancestors evolved in a relatively calcium-rich environment that served them well in providing a structurally sound skeleton in a hostile environment. Chapters describing the role of genetics, bone physiology, hormones, and biomechanics of bone provide background to the reader as they delve deeper into the role of nutrition

in bone health. The tools used to study nutrition and bone health, including nutritional epidemiology, nutritional assessment and counseling, and dietary patterns, are described and set the stage for the chapters that provide up-to-date reviews of nutritional requirements during pregnancy, for fetal, neonatal, childhood, adolescent, young, middle-aged, and older adult's skeletal health presented in extensively referenced individual chapters. The effects of race and ethnicity on nutrition and bone health are described in detailed chapters.

The second edition of *Nutrition and Bone Health* includes several chapters devoted to examining the effects of specific dietary components on bone health: macronutrients (protein and fat), minerals, and micronutrients. Additionally, dietary components such as food groups, and special diets such as vegetarian diets as well as nutraceuticals are discussed in separate chapters. As examples, the importance of proper acid-based balance and the effect of minerals such as calcium, sodium, potassium, phosphorus, and magnesium, as well as micronutrients including fat-soluble vitamins, zinc, and selenium, are reviewed. The chapter on vitamin K provides an expert perspective on the role of vitamin K and its various forms on bone health and cardiovascular disease. Another goal of the second edition of *Nutrition and Bone Health* is to put into perspective the impact of eating disorders, body weight, exercise, and body weight change on bone health. There are a multitude of diseases and drugs and other environmental and behavioral factors that negatively affect bone health. Among these are cystic fibrosis, celiac disease, HIV/AIDS smoking, and alcohol abuse. The relationship between nutrition, inflammation, and bone health are explored. In addition, the chapter on medications and nutrients provides important information as to the importance of proper nutrition for expensive bone active drugs to have favorable effects on the skeleton.

The role of dietary factors, exercise, and sun exposure on bone cell function and bone mineral density are reviewed in detail to assure that the totality of the evidence presented to the reader provides up-to-date information on these topical, controversial subjects.

As editors, we are very excited about the expanded contents of the second edition of *Nutrition and Bone Health*. Chapters are written by experts who provide not only an overview of the subject, but also specific recommendations for how this information can be effectively utilized for practical application by health care professionals. The volume includes numerous tables and figures to help the reader quickly glean the essentials of each chapter. There is even an app that provides guidance for sensible sun exposure in the chapter on Vitamin D. There is an extensive index that also helps provide a road map to easily cross-reference how particular nutrients, diseases and drugs, environmental factors, race, and age affect bone health.

Metabolic bone diseases, such as rickets and osteomalacia, as well as osteoporosis, are diseases of neglect. Vigilance for satisfying the nutrient requirements of the skeleton is a small price to pay for remaining erect and fracture free throughout life. The second edition of *Nutrition and Bone Health* should serve as a critical resource for health care professionals interested in utilizing nutrition, exercise, and other positive lifestyle factors to enhance the overall health and well-being for skeletal health throughout life, minimizing the need for bone active medications which are expensive and associated with many unwanted side effects.

Boston, MA, USA  
New York, NY, USA

Michael F. Holick  
Jeri W. Nieves

## Series Editor Page

The great success of the Nutrition and Health Series is the result of the consistent overriding mission of providing health professionals with texts that are essential because each includes (1) a synthesis of the state of the science; (2) timely, in-depth reviews by the leading researchers and clinicians in their respective fields; (3) extensive, up-to-date fully annotated reference lists; (4) a detailed index; (5) relevant tables and figures; (6) identification of paradigm shifts and the consequences; (7) virtually no overlap of information between chapters, but targeted, interchapter referrals; (8) suggestions of areas for future research; and (9) balanced, data-driven answers to patient as well as health professionals' questions which are based upon the totality of evidence rather than the findings of any single study.

The series volumes are not the outcome of a symposium. Rather, each editor has the potential to examine a chosen area with a broad perspective, both in subject matter and in the choice of chapter authors. The international perspective, especially with regard to public health initiatives, is emphasized where appropriate. The editors, whose trainings are both research and practice oriented, have the opportunity to develop a primary objective for their book; define the scope and focus; and then invite the leading authorities from around the world to be part of their initiative. The authors are encouraged to provide an overview of the field, discuss their own research, and relate the research findings to potential human health consequences. Because each book is developed *de novo*, the chapters are coordinated so that the resulting volume imparts greater knowledge than the sum of the information contained in the individual chapters.

*Nutrition and Bone Health, 2nd Edition*, edited by Michael F. Holick and Jeri W. Nieves, is a very welcome addition to the Nutrition and Health Series and fully exemplifies the series' goals. The first edition was published a decade ago and it is very timely to have this comprehensive update. The explosion of clinical research over the last decade also warrants the inclusion of five new chapters resulting in this revised 41 chapter volume. The book is designed as a valuable resource for nutritionists and dietitians, internists and endocrinologists who treat patients with potential bone loss, public health scientists, epidemiologists, and health care professionals from various disciplines who interact with clients, patients, and/or family members. The volume is also a unique resource for graduate and medical students who have an interest in how diet affects bone health. This important volume includes objective, relevant information provided in extensive, up-to-date literature reviews, instructive tables and figures, and excellent references on the critical aspects of clinical research on bone health and diseases that are affected by dietary nutrients.

The editors of this volume are experts in their respective fields and represent the medical profession as well as the academic research community. Moreover, Drs. Holick and Nieves have included in-depth chapters by the leading researchers and clinicians in fields including, but not limited to, nutrition, exercise, space travel, infant and childhood growth, molecular biology, endocrinology, genetics,

skeletal health, and osteoporosis. The overall expertise of the editors and chapter authors, who have made significant discoveries as well as serving as outstanding educators, cannot be matched by any other text in the field of nutrition and bone health to date.

Dr. Michael F. Holick, Ph.D., M.D., is Professor of Medicine, Physiology, and Biophysics; Director of the General Clinical Research Unit, Director of the Bone Health Care Clinic; and Director of the Heliotherapy, Light, and Skin Research Center at Boston University Medical Center. Dr. Holick has made numerous contributions to the field of the biochemistry, physiology, metabolism, and photobiology of vitamin D. He was the first to isolate and identify 25-hydroxyvitamin D<sub>3</sub> in human blood and also determined that the active form of vitamin D is 1,25-dihydroxyvitamin D<sub>3</sub>. He participated in the first chemical synthesis of 1,25-dihydroxyvitamin D<sub>3</sub> and its analog 1 $\alpha$ -hydroxyvitamin D<sub>3</sub> that was used to treat vitamin D-dependent rickets and hypoparathyroidism. Dr. Holick is a Diplomat of the American Board of Internal Medicine, a Fellow of the American College of Nutrition, and the recipient of the American College of Nutrition Award, the Robert H. Herman Memorial Award in Clinical Nutrition from the American Society for Clinical Nutrition, the Annual General Clinical Research Centers' Program Award for Excellence in Clinical Research, the Linus Pauling Functional Medicine Award from the Institute for Functional Medicine, Linus Pauling Prize, DSM Innovation In Nutrition Award, American Association of Clinical Chemist's Van Slyke Award, American College of Nutrition's Communication Media Award, the Delbert Fisher Research Scholar, Best Doctors in America 2011–2014, and the American Society of Bone and Mineral Research Louis Avioli Award. Dr. Holick is editor-in-chief for the *Journal for Clinical Laboratories and Laboratories Related to Blood Transfusion* and Associate Editor for *Dermato-Endocrinology*. He has authored more than 500 peer-reviewed publications and written more than 250 review articles as well as numerous book chapters. He has served as editor and/or coeditor on 13 books including *Vitamin D*, both the first and second editions, and the first edition of *Nutrition and Bone Health* which are also part of the Nutrition and Health Series. Dr. Holick was selected by Thompson Reuters as one of the world's most influential scientific minds in the field of clinical medicine in 2014.

Dr. Jeri Wanzor Nieves is a Research Scientist at the Helen Hayes Hospital in New York, where she is investigating various aspects of osteoporosis and serves as the Principal Investigator for the New York State Osteoporosis Prevention and Education Program (NYSOPEP). She also serves on several committees for the National Osteoporosis Foundation. Dr. Nieves is an Associate Professor of Clinical Epidemiology and Nutrition at Columbia University. Dr. Nieves has coauthored over 100 journal articles, reviews, and book chapters on nutrition, epidemiology, and osteoporosis. She is an Associate Editor of *Osteoporosis International*. Dr. Nieves' research has focused on various aspects of bone health and osteoporosis including peak bone mass, stress fractures, vitamin D, anabolic and antiresorptive treatments, and fracture healing. In addition, her research includes aspects of nutritional epidemiology and determining the role of nutrition in various disease states.

*Part 1:* The ten introductory chapters in the first part, entitled "Basics of Nutrition and Bone Biology," provide readers with an introduction to the current understanding of skeletal evolution, genetic factors in bone biology that are affected by diet, a review of the key hormones that control bone growth and health, the current status of bone measurement technologies, and the current mechanisms used to determine dietary intakes. Oral health and nutrition counseling during osteoporosis therapy are each reviewed in separate chapters. The first chapter examines the evolutionary aspects of bone health that are preserved in the fossil record. We learn that developments in genetic analyses have yielded insights into our evolutionary history and breakthroughs have allowed genome sequencing of fossil bones from populations that lived 50,000 years ago. The chapter reviews the evolution of human skeletal adaptation and external factors including diet, which may have affected skeletal health in human ancestors and form the basis for skeletal conditions seen in modern human populations. Chapter 2 describes the gene–nutrient interactions that may affect bone health. The nutritional and genetic factors that interact to influence bone modeling and mineral homeostasis during the years of

peak bone mass acquisition, bone remodeling, and the maintenance of bone mass are described in detail. Candidate gene and genome-wide association studies with bone mineral density and fractures and gene–dietary interaction studies in osteoporosis are also reviewed. The third chapter, coauthored by the late Lawrence Raisz, explores the importance of bone physiology with an emphasis on how bones are formed during growth and how bone tissue continues to be a very active tissue throughout life. The term “modeling” is used to describe bone changes during growth or in response to a change in mechanical loading. Remodeling is defined as bone resorption and formation that occurs essentially at the same site and at the same time. The bone cells, hormones, and nutrients required for successful maintenance of bone density and structure are described in detail and the included figures help the reader to visualize these complex processes.

Chapter 4, authored by Robert Lindsay, who also provides the Foreword critique of this volume, explores the effects of menopause or other causes of estrogen loss on bone remodeling in women. The author reminds us that in all situations of estrogen deprivation there is an increase in skeletal remodeling that in many, but not necessarily all women, results in a loss of bone mass and disruption of skeletal architecture that increases fracture risk significantly. The chapter includes an extensive review of the clinical trials with estrogen treatment and contains discussions of alternatives for preservation of the female skeleton postmenopause. Chapter 5 continues to examine the effects of estrogen loss and also looks at the current tools available to measure the effects of aging on the skeleton of both sexes. The chapter reviews the etiology of age-related fractures from a biomechanics point of view and evaluates the structural failures in aging bone. Whole bone strength is determined by the amount of bone, the spatial distribution of the bone mass, and the intrinsic properties of the materials that make up bone. Factors that influence bone strength, including dietary factors, are examined as potential determinants of bone strength. Chapter 6 explains in detail the benefits and limitations of the current methodologies commonly used to determine bone mineral density (BMD). Bone densitometric techniques can provide quantitative measurement of BMD and are commonly divided into central and peripheral. Central methods measure BMD in the spine and proximal femur and include dual X-ray absorptiometry (DXA) and quantitative computed tomography (QCT). Peripheral methods measure BMD in the phalanges, forearm, tibia, or calcaneus and include peripheral dual X-ray absorptiometry (pDXA) and peripheral quantitative computed tomography (pQCT). Quantitative ultrasound (QUS) does not measure BMD.

The seventh chapter examines the role of nutritional epidemiology and its use of nutrient assessment tools to determine population intakes of nutrients affecting bone health. The 24-h diet recall, diet record, and food frequency questionnaires are compared. Diet–bone linkages have been determined for calcium, phosphorus, and vitamin D. The potential skeletal effects of the two forms of vitamin K, menaquinones (vitamin K<sub>2</sub>) and phyloquinone (vitamin K<sub>1</sub>), phytochemicals, nutrient supplements, protein, vitamin C, certain B vitamins, magnesium, potassium and carotenoids, and other dietary components require randomized controlled trials to test their efficacy. There is a growing awareness that dietary patterns can help us to understand the relationship between certain nutrients and risk of bone fractures. Chapter 8 includes a detailed outline of how to generate dietary patterns with commonly available statistical software and examines the data on the association of dietary patterns and BMD and fractures measured by DEXA and fracture risk in postmenopausal women. Informative tables review the data from survey studies of dietary patterns that are associated with reduced fracture risk. The next chapter looks at the association between dietary patterns and oral health. The chapter includes an extensive review of the literature that indicates that the prevalence of periodontal disease is lower among persons with healthy eating patterns and ideal body weight. There is an in-depth discussion of tooth and jaw structure, inflammatory mediators, and foods associated with decreased risk of tooth loss and diseases, such as diabetes and obesity that are associated with greater risk of tooth loss. The final chapter in this part is of great value to health practitioners as it concentrates on nutrition

counseling for skeletal health. There are evidence-based nutrition recommendations as well as several helpful tables that list the major sources of nutrients associated with bone health.

The second part of the volume examines the effects of life stages and race on the interactions between nutrition and bone health. The seven chapters follow human development and begin with Chapter 11, which concentrates on the major effects of pregnancy and lactation on maternal and fetal bones. The chapter summarizes the literature on the effects of human pregnancy, lactation, and weaning on calcium metabolism and maternal bone health; the role of maternal dietary calcium and vitamin D on maternal calcium metabolism and bone health; the epidemiological evidence relating parity and lactation to maternal osteoporosis and fracture risk later in life; and the role of maternal calcium and vitamin D intake on calcium homeostasis, growth, and bone development of the offspring. The maternal physiological responses to the fetal calcium demands are illustrated in the excellent figures included in the chapter. Chapter 12 follows logically and examines the many factors affecting fetal and neonatal bone growth and development. There is a discussion of “developmental programming” that suggests that metabolic events during critical time periods of antenatal and postnatal development have moderating effects on peak bone mass achieved in late adolescence and osteoporosis risk. This long-term programming of bone growth and bone mass accretion may be influenced by exposures during pregnancy including maternal body composition, diet and lifestyle factors and early infant nutrition, physical activity and growth patterns. The status of the research on the genetic variants responsible for diversity in bone mass between individuals and populations is also reviewed.

The changes in bone growth and development during childhood and adolescence are described in Chapter 13. The chapter includes 17 figures that illustrate that bone accretion during childhood is proportional to the rate of growth. During this age interval height velocity is relatively slow for both boys and girls. Retention of calcium in the body of an average child is lower than the calcium retention in an adolescent. Calcium needs are greater during adolescence (pubertal growth spurt) than in either childhood or adulthood. According to calcium balance studies the threshold intake for adolescents is about 1,500 mg/day. Inadequate calcium intake during growth may increase the risk of childhood fractures and predispose certain individuals to a lower peak bone mass in adulthood and later in life. Dr. Bess Dawson-Hughes, who coedited the first edition of *Nutrition and Bone Health*, reviews the calcium and vitamin D needs of adults for optimal bone health. Chapter 14 includes discussions of studies that span the years between young adulthood and menopause in women and includes an examination of the physiological changes that precede the seventh decade. There is an emphasis on the effects of calcium and vitamin D3 intakes on fracture risk and risk of falls. Chapter 15 explores the relationships between protein, calcium and vitamin D, and fracture risk in the elderly. The anti-fracture efficacy of nutritional intervention in the elderly such as supplementation, fortification, and dietary changes are reviewed, with a particular focus on elderly in institutional care. Future research directions are also examined in an attempt to offset the growing fracture burden due to the rapidly increasing aged population.

Chapters 16 and 17 review the nutritional and skeletal health of non-white racial groups and certain ethnic groups. US blacks have a reduced risk for osteoporosis compared with US whites and others racial groups. The prevalence of osteoporotic fractures and all nonvertebral fractures among US blacks is about half that of US whites. Blacks also have greater BMD compared to age, sex, and BMI-matched whites which is unexpected given that the skin pigmentation in blacks sharply reduces the amount of vitamin D that is produced during sunlight exposure and calcium intakes are significantly lower than matched white populations. Intervention studies with calcium and vitamin D in black postmenopausal women suggest that supplementation may reduce fracture risk; however, the studies have not reached statistical significance. Chapter 17, the last chapter in this part, looks at data from several non-white racial groups in the USA. Adult Asians living in Asia or the USA have lower areal BMD (aBMD) in comparison to whites and other racial/ethnic groups. Most studies indicate that Hispanic Americans have similar or slightly higher aBMD as compared to non-Hispanic whites although there

are inconsistencies between studies. Areal BMD data in American Indian and Native Alaskan women is limited but indicates similar aBMD compared to white women. There are almost no published data in Native Hawaiians/Pacific Islanders in the USA. Hawaiian women tended to have higher aBMD compared to white, Japanese, and Filipino women. Men usually have higher BMD than women of the same race. With regard to fracture risk, Asian and African Americans share a similarly low risk of fractures despite low aBMD. Detailed review of published data concerning specific population groups and potential fracture sites is included in this comprehensive chapter.

Part 3 includes five chapters that examine the effects of dietary macronutrients on bone health. There is an overview of food groups followed by separate chapters on vegetarian diets, protein, fat, and acid-base balance. Chapter 18 looks at the data concerning the effects of food groups and whole foods on bone health. The whole diet and food-based approach has yielded insights into the relationship between nutrition and bone health and suggests that diets that are higher in fruit, vegetables, milk, and cereal are associated with increased bone mass as compared with diets high in processed and snack foods. Chapter 19 provides an insightful review of the possible associations between certain types of vegetarian diets in women and beneficial or negative effects on aspects of bone health. The literature review indicates that following a lacto-ovo-vegetarian diet with adequate calcium, protein, and vitamin D may favorably affect BMD. Long-term adherence to a vegan diet, however, is associated with lower bone density and increased fracture risk. Chapter 20 examines the associations between protein intake levels throughout the life span from bone growth in children to the benefits of adequate protein post-osteoporotic fracture. This comprehensive chapter includes eight informative figures that illustrate the interactions between cellular factors and bone cell responses, production of bone-specific proteins, and other components of bone with an emphasis on the importance of adequate protein intake for synthesis and functioning of the growth factor, IGF1. The next chapter examines the new research on the role of dietary fat and body fat stores on bone size and strength and concentrates on the unexpected effects of obesity on fracture risk. Chapter 21 includes discussions of the increased risk of cardiovascular disease and cancer with increased body mass index and includes a review of the female athlete triad where fat intake is very low, exercise levels are very high, yet BMD is unexpectedly low. Also included is a review of the different effects of saturated versus unsaturated dietary fats on bone. The last chapter examines the strong link between kidney function and bone calcium levels. The chapter contains 18 figures that are of great value in understanding the complex balance that must be maintained to keep bone calcium levels at their optimum. There is an in-depth discussion of the changes in kidney function with aging that results in the potential for increased risk of osteoporosis and fracture.

Part 4 includes three chapters that review the role of key minerals in bone accretion and loss. The first chapter in this part, coauthored by Connie Weaver who coedited the series volume entitled *Calcium and Human Health* with Robert Heaney, the author of Chapter 24, reviews the techniques that enable the accurate calculation of calcium status in bone. Metabolic balance studies using a cross-over design can help to determine the effect of one dietary change on net calcium retention. Balance studies using stable isotopes of calcium are described and the tables and figures included in the chapter illustrate the parameters of calcium metabolism including absorption, endogenous secretion, excretion, bone formation rates, and bone resorption rates. As 99 % of the body's calcium resides in the skeleton, calcium metabolism is directly reflective of bone metabolism. Chapter 24 looks at the dietary sources and metabolism of several minerals that can affect bone health. The chapter reviews the consequences of the variations in intakes of sodium, potassium, phosphorus, and magnesium and their potential effects on the adult and aging skeleton. Chapter 25 describes the effects of trace mineral status on bone health and provides an overview of the importance of adequate copper especially in preterm infants or adults given parenteral nutrition as their only source of nutrients. The author reviews both animal and human studies of zinc deficiency, boron status, strontium supplementation, silica status, and fluoride functions.

The fifth part's four chapters examine the role of the fat-soluble vitamins A, D, and K on skeletal health. Chapter 26 examines the full data set on the role of vitamin A in bone formation and resorption. This chapter includes a review of laboratory animal studies of the vitamin as well as its metabolites that have been used as potent drugs that can also affect bone. The authors conclude that there are insufficient data to determine the high dose of vitamin A that can consistently cause adverse bone effects, and at the same time acknowledge that low vitamin A intakes especially in utero and in children have proven adverse effects. Critical issues involve the age of the subjects as extreme age, either young or old, appear to be more sensitive to high doses of vitamin A; duration of intake; concomitant vitamin D intake; and other lifestyle habits all appear to affect the safety of vitamin A. Relevant studies are tabulated.

Michael Holick, who was also coeditor of the first edition of this volume and editor of the *Vitamin D* volume for the Nutrition and Health Series, has aptly provided the comprehensive review of vitamin D. The chapter, which includes 24 figures and 1 table, examines the formation and metabolism of vitamin D, its role in bone during the lifetime, and the newest research linking vitamin D status with many aspects of health beyond bone. There is an emphasis on the realization of the potential for vitamin D deficiency which was not appreciated until fairly recently. The author indicates that vitamin D deficiency is extremely common and needs to be recognized. Vitamin D deficiency in children and teenagers can result in poor bone health and the inability to attain the genetically predetermined peak bone mass. In young, middle-aged, and older adults, vitamin D deficiency causes osteomalacia and can precipitate and exacerbate osteoporosis. Maintenance of an adequate serum 25(OH) vitamin D level throughout life may help reduce the risk of developing many chronic diseases, including type 1 diabetes, hypertension, multiple sclerosis, infectious diseases, and cancers of the breast, prostate, colon, and ovary. The purpose of the unique and very relevant Chapter 28 is to examine the role of the vitamin D response element binding protein first identified in subhuman primates and other associated intracellular proteins that are involved in the regulation of the expression of vitamin D-controlled genes in nonhuman and human primates. The chapter includes a comprehensive review of the metabolism of vitamin D by New World primates, several of whom have been shown to develop severe rickets when in captivity that is cured by high concentrations of vitamin D and/or significant exposure to sunlight. These primates have helped us to understand the intracellular movements of vitamin D metabolites and this knowledge is of value in understanding the molecular changes in vitamin D in humans.

Vitamin K has been examined closely in the decade since the first edition of this volume was published. Chapter 29 reviews the findings of vitamin K's role in age-related bone loss. The chapter includes an extensive discussion of the different forms of vitamin K and concentrates on the forms found in food and dietary supplements. The non-bone and the bone-related functions of vitamin K are reviewed. Several vitamin K-dependent proteins are present in bone, including osteocalcin, which is one of the most abundant non-collagenous proteins in bone and is the most extensively studied vitamin K-dependent bone protein. The emerging evidence that vitamin K may have roles in skeletal tissue independent of currently accepted functions is also discussed. Of greatest value to the reader, there is a comprehensive review of the vitamin K-related studies in osteoporotic women, mainly from Asia, including survey and intervention studies with several types of vitamin K. At present, the results remain inconsistent.

Part 6 describes the associations between lifestyle factors and use of dietary supplements on bone health parameters. Chapter 30 reviews the effects of cigarette smoking and/or alcohol consumption on bone health in young and older adults. The effects of nicotine and alcohol on bone cells in vitro are reviewed. The author discusses studies that show that smoking adversely affects bone density and increases hip fracture risk in postmenopausal women. In men and younger women the evidence is not conclusive. Recent studies on the role of alcohol on the skeleton suggest a "J"-shaped curve with benefits associated with 1–2 drinks/day and adverse effects seen at higher intakes. Moderate ingestion

of alcohol may be associated with some benefit to the skeleton. Both ethanol and non-ethanol components of alcohol can have effects on skeletal health.

The next two chapters examine the importance of exercise for enhancing peak bone mass and reducing the loss of bone with aging. The first chapter describes the literature on exercise and bone and the second chapter examines the role of diet, especially calcium intake in enhancing the beneficial effects of exercise. Chapter 31 reviews the important role of exercise in maintaining bone health and provides over 200 relevant references for the reader. The author outlines the goals of exercise for fracture prevention that change over the course of the life span. In childhood and adolescence, the emphasis is on achievement of peak bone mass; in middle age, exercise is important for the preservation of bone and muscle strength; and in aging, exercise can be of great help in keeping one's balance and skeletal muscle strength. Intervention studies in young and older population groups of exercisers versus sedentary controls that assessed bone mineral density and fracture risk are tabulated. Clinical studies of aerobic versus resistance training programs are also reviewed. Chapter 32 examines the requirement of adequate calcium to get the full benefits of exercise on bone mineral density. The beneficial effects of weight-bearing exercise during adolescence are stressed and the role of bone-building hormones is reviewed. Each of the important nutritional factors including dietary calcium, vitamin D, protein, total caloric intake, phosphorus, vitamins C and K, copper, zinc, and manganese is discussed. Calcium and phosphorus make up 80–90 % of the mineral content of bone. Many nutrients interact with other nutrients, genetics, and environmental factors. The complexity of these interactions and with physical activity are also examined.

Body weight has a direct effect on bone mineral density and loss of weight can result in loss of bone. Chapter 33 begins with an evaluation of the effects of obesity on bone health. Even though the greater body weight of the obese person should be associated with greater bone strength, there is evidence that obesity and osteoporosis are not mutually exclusive and that obesity does not protect against osteoporosis. Of great interest are the studies that show a higher fracture incidence in obese children and greater fracture risk at certain bone sites in obese versus normal weight, age-matched adults. In contrast, lean older women have an increased annual rate of bone loss compared to heavier women which is linked to the higher rate of bone turnover in leaner women. The chapter also reviews the effects of weight loss, either voluntary or involuntary on bone loss, and also includes a discussion of the effects of bariatric surgery on subsequent bone loss; almost 200 references are included. The last chapter in this part, written by the coeditor of the volume, Jeri W. Nieves, explores the role of nutraceuticals on bone health and includes reviews of both essential and nonessential nutrients as well as certain other dietary substances. The chapter includes discussions of calcium and vitamin D, soy compounds, dehydroepiandrosterone, antioxidants, flavonoids, carotenoids, omega-3-fatty acids, B-vitamins, magnesium, boron, strontium, silicon, phosphorus, red clover, black cohosh, and ipriflavone. The author concludes that there are few consistent beneficial findings for these substances other than for calcium and vitamin D.

The final part of this important volume, Part 7, contains seven chapters of clinical relevance that describe the effects of certain nutrition-related disorders and their effects on bone health. Chapter 35 examines the effects of eating disorders with emphasis on anorexia nervosa as this eating disorder is associated with significant weight loss and low body weight and significant loss of bone mass, density, and structure. The author describes the adverse synergistic effects of this eating disorder that usually occurs in early adolescence at the time when almost 25 % of peak bone mass is being formed in normal weight children. A key factor in the bone loss seen in anorexic girls is low estrogen levels and loss of menses. Bone density correlates inversely with the duration of amenorrhea. There is also an inverse relationship between estrogen levels and markers of bone resorption in adolescent girls with anorexia. The chapter reviews the potential nutritional and pharmacological strategies used in the treatment of anorexia.

Two chapters examine the skeletal effects of genetic diseases. Chapter 36, coauthored by Michael Holick, looks at the multifactorial adverse health effects of cystic fibrosis. We learn that cystic fibrosis

is a recessive genetic disorder that causes abnormal sodium and chloride transport resulting in lung and gastrointestinal complications, lung infections, pancreatic insufficiency, impaired digestion, and malabsorption. The low bone mass seen in cystic fibrosis patients as they age is multifactorial and is influenced by nutritional status, disease severity, glucocorticoid use, hormonal status, inflammation, gastrointestinal function, mechanical loading, and physical activity patterns. The critical issue of calcium and other bone-related nutrient absorption in the face of disease-specific metabolically related issues is reviewed. Chapter 37 reviews the autoimmune disorder, celiac disease that has both genetic and environmental components. It is characterized by innate and adaptive immune responses that are primarily triggered by the ingestion of dietary gluten, resulting in inflammation, small intestinal villous atrophy, and crypt hyperplasia. Genes that code for human leukocyte antigens (HLA) DQ2 and DQ8 are strongly associated with and confer susceptibility for celiac disease. In addition to the characteristic intestinal symptoms, celiac disease is associated with extra-intestinal complications, including those affecting skeletal health. Reduction in bone mineral density and increased risk of bone fracture, caused by malabsorption-related alteration of calcium metabolism and immune-mediated mechanisms, are frequently seen in patients with celiac disease. Reduced bone density and bone derangement are some of the most common extra-intestinal complications found in newly diagnosed celiac disease patients. The chapter summarizes the currently available information regarding the prevalence, pathogenic mechanism, and treatment of celiac disease in the context of bone health.

Chapter 38 examines the effects of both disease and treatment of HIV on the skeleton. We are reminded that HIV is a retrovirus that infects immune cells leading to progressive failure of the immune system. The importance of this unique chapter is due to the increased life expectancy of the HIV-positive population. Most HIV-infected persons in the USA will be 50 years old or older by 2015 and their risk for osteopenia and osteoporosis, and fractures increases as their life expectancy increases. The etiology of osteoporosis in HIV-infected persons is complex and may involve both HIV disease itself and antiretroviral treatment. Traditional risk factors, such as smoking, hypogonadism, and low body weight, also play a role. Bone health screening and nutritional interventions in this population are in the early stages of development.

The last three chapters present early findings and unique perspectives on the potential role of certain nutrients in either maintaining or enhancing bone health. Chapter 39 explores the new clinical findings associated with consistent exposure to low-grade inflammatory responses in populations at risk for osteoporosis. The author indicates that there are data linking dietary benefits in individuals with diseases with known inflammatory pathogenesis such as type 2 diabetes, cardiovascular disease, and cancer. With regard to bone, the limited number of intervention trials that demonstrate that calcium and vitamin D supplementation, high dairy diets, increased dietary protein, vitamin K, and omega-3 fatty acids produce modest reductions in circulating inflammatory biomarkers in people with osteoporosis, sarcopenia, or the presence of other chronic diseases is reviewed. Currently, it is not known if a reduction in inflammatory markers translates into beneficial effects on skeletal health or a reduction in fracture risk. Given the emerging clinical evidence linking low-grade systemic inflammation to osteoporosis, sarcopenia, and fractures in the elderly, the author suggests that further intervention trials are warranted. Chapter 40, co-authored by Jeri W. Nieves, examines the important drug–nutrient interactions in patients with osteoporosis who are given anti-osteoporosis drugs. We are reminded that in virtually all of the intervention trials supporting approval of the marketed anti-osteoporosis drugs, both the drug-placebo and the active cohorts were given supplemental calcium and vitamin D to assure adequate intake of these two nutrients. Although the dosages of calcium and vitamin D may not have been the same in all studies, the data reviewed indicates that no harm was seen in any study and in most, there was a benefit of supplementation. The authors review studies with estrogen, raloxifene, the bisphosphonates, denosumab, and teriparatide. The last unique chapter, which includes almost 200 relevant references and eight helpful figures, summarizes the research on the effects of space flight and long-term exposure to weightlessness in space on bone. The chapter

reviews the deleterious effects of space flight on the human body and the potential for nutritional interventions to reduce these adverse effects on bone. The specific effects of space flight on bone metabolism are enumerated. There is a discussion of the significant loss of bone during space exposure that is normalized over many months following return to Earth. The chapter includes extensive data on effects of individual nutrients as well as a discussion of the technical issues to assure incorporation of the right level of these nutrients into the space food.

The above descriptions of the 41 chapters in *Nutrition and Bone Health, 2nd Edition* attest to the depth of information provided by the well-recognized and respected editors and chapter authors. Each chapter includes complete definitions of terms with the abbreviations fully defined for the reader and consistent use of terms between chapters. Key features of the comprehensive volume includes over 200 detailed tables and informative figures, an extensive, detailed index, and more than 4,000 up-to-date references that provide the reader with excellent sources of worthwhile information. The volume also includes a dedication of the volume to Dr. Lawrence Raisz written by David W. Dempster and an insightful Foreword by Dr. Robert Lindsay.

In conclusion, *Nutrition and Bone Health, 2nd Edition*, edited by Michael F. Holick, M.D., Ph.D. and Jeri W. Nieves, Ph.D., provides health professionals in many areas of research and practice with the most up-to-date, well-referenced volume on the importance of diet and nutritional status throughout life on bone health. The volume places its emphasis on food groups, diets, and key nutrients associated with reduction of the risk of osteoporosis in overall healthy individuals and in patients with certain disease conditions that increase the risk of adverse bone effects. The volume serves the reader as the benchmark in this complex area of interrelationships between dietary intakes of numerous dietary components including calcium, vitamin D, protein, other relevant minerals, essential and nonessential nutrients, exercise, body weight, gender, race, ethnicity, and the dynamic changes in bone tissue that are continuous throughout life. Moreover, the physiological, genetic, and pathological interactions between diet and skeletal integrity are clearly delineated so that students as well as practitioners can better understand the complexities of these interactions. The editors are applauded for their efforts to develop the most authoritative and unique resource in the area of nutrition, bone health, and disease to date and this excellent text is a very welcome addition to the Nutrition and Health Series.

Morristown, NJ, USA

Adrienne Bendich, Ph.D., F.A.C.N., F.A.S.N.  
Series Editor



# About the Series Editor



**Adrienne Bendich, Ph.D., F.A.S.N., F.A.C.N.** has served as the Nutrition and Health Series Editor for over 15 years and has provided leadership and guidance to more than 120 volume editors that have developed the 60+ well respected and highly recommended volumes in the series.

In addition to *Nutrition and Bone Health, Second Edition*, edited by Michael F. Holick Ph.D., M.D., and Jeri W. Nieves, Ph.D., major new editions in 2012–2014 include:

1. *Nutrition and Oral Medicine, Second Edition*, edited by Dr. Riva Touger-Decker, Dr. Connie C. Mobley and Dr. Joel B. Epstein, 2014
2. *Fructose, High Fructose Corn Syrup, Sucrose and Health*, edited by Dr. James M. Rippe, 2014
3. *Nutrition in Kidney Disease, Second Edition*, edited by Dr. Laura D. Byham-Gray, Dr. Jerrilynn D. Burrowes and Dr. Glenn M. Chertow, 2014
4. *Handbook of Food Fortification and Health, volume I* edited by Dr. Victor R. Preedy, Dr. Rajaventhana Srirajaskanthan, Dr. Vinood B. Patel, 2013
5. *Handbook of Food Fortification and Health, volume II* edited by Dr. Victor R. Preedy, Dr. Rajaventhana Srirajaskanthan, Dr. Vinood B. Patel, 2013
6. *Diet Quality: An Evidence-Based Approach, volume I* edited by Dr. Victor R. Preedy, Dr. Lanh-Ahn Hunter and Dr. Vinood B. Patel, 2013
7. *Diet Quality: An Evidence-Based Approach, volume II* edited by Dr. Victor R. Preedy, Dr. Lanh-Ahn Hunter and Dr. Vinood B. Patel, 2013
8. *The Handbook of Clinical Nutrition and Stroke*, edited by Mandy L. Corrigan, M.P.H., R.D., Arlene A. Escuro, M.S., R.D., and Donald F. Kirby, M.D., F.A.C.P., F.A.C.N., F.A.C.G., 2013

9. *Nutrition in Infancy, volume I* edited by Dr. Ronald Ross Watson, Dr. George Grimble, Dr. Victor Preedy and Dr. Sherma Zibadi, 2013
10. *Nutrition in Infancy, volume II* edited by Dr. Ronald Ross Watson, Dr. George Grimble, Dr. Victor Preedy and Dr. Sherma Zibadi, 2013
11. *Carotenoids and Human Health*, edited by Dr. Sherry A. Tanumihardjo, 2013
12. *Bioactive Dietary Factors and Plant Extracts in Dermatology*, edited by Dr. Ronald Ross Watson and Dr. Sherma Zibadi, 2013
13. *Omega 6/3 Fatty Acids*, edited by Dr. Fabien De Meester, Dr. Ronald Ross Watson and Dr. Sherma Zibadi, 2013
14. *Nutrition in Pediatric Pulmonary Disease*, edited by Dr. Robert Dumont and Dr. Youngran Chung, 2013
15. *Magnesium and Health*, edited by Dr. Ronald Ross Watson and Dr. Victor R. Preedy, 2012.
16. *Alcohol, Nutrition and Health Consequences*, edited by Dr. Ronald Ross Watson, Dr. Victor R. Preedy, and Dr. Sherma Zibadi, 2012
17. *Nutritional Health, Strategies for Disease Prevention, Third Edition*, edited by Norman J. Temple, Ted Wilson, and David R. Jacobs, Jr., 2012
18. *Chocolate in Health and Nutrition*, edited by Dr. Ronald Ross Watson, Dr. Victor R. Preedy, and Dr. Sherma Zibadi, 2012
19. *Iron Physiology and Pathophysiology in Humans*, edited by Dr. Gregory J. Anderson and Dr. Gordon D. McLaren, 2012

Earlier books included *Vitamin D, Second Edition*, edited by Dr. Michael Holick; *Dietary Components and Immune Function*, edited by Dr. Ronald Ross Watson, Dr. Sherma Zibadi and Dr. Victor R. Preedy; *Bioactive Compounds and Cancer*, edited by Dr. John A. Milner and Dr. Donato F. Romagnolo; *Modern Dietary Fat Intakes in Disease Promotion*, edited by Dr. Fabien De Meester, Dr. Sherma Zibadi, and Dr. Ronald Ross Watson; *Iron Deficiency and Overload*, edited by Dr. Shlomo Yehuda and Dr. David Mostofsky; *Nutrition Guide for Physicians*, edited by Dr. Edward Wilson, Dr. George A. Bray, Dr. Norman Temple and Dr. Mary Struble; *Nutrition and Metabolism*, edited by Dr. Christos Mantzoros and *Fluid and Electrolytes in Pediatrics*, edited by Leonard Feld and Dr. Frederick Kaskel. Recent volumes include: *Handbook of Drug-Nutrient Interactions*, edited by Dr. Joseph Boullata and Dr. Vincent Armenti; *Probiotics in Pediatric Medicine*, edited by Dr. Sonia Michail and Dr. Philip Sherman; *Handbook of Nutrition and Pregnancy*, edited by Dr. Carol Lammi-Keefe, Dr. Sarah Couch and Dr. Elliot Philipson; *Nutrition and Rheumatic Disease*, edited by Dr. Laura Coleman; *Nutrition and Kidney Disease*, edited by Dr. Laura Byham-Grey, Dr. Jerrilynn Burrowes and Dr. Glenn Chertow; *Nutrition and Health in Developing Countries*, edited by Dr. Richard Semba and Dr. Martin Bloem; *Calcium in Human Health*, edited by Dr. Robert Heaney and Dr. Connie Weaver and *Nutrition and Bone Health*, edited by Dr. Michael Holick and Dr. Bess Dawson-Hughes.

Dr. Bendich is President of Consultants in Consumer Healthcare LLC, and is the editor of ten books including *Preventive Nutrition: The Comprehensive Guide for Health Professionals, Fourth Edition*, co-edited with Dr. Richard Deckelbaum ([www.springer.com/series/7659](http://www.springer.com/series/7659)). Dr. Bendich serves on the *Editorial Boards of the Journal of Nutrition in Gerontology and Geriatrics, and Antioxidants, and has served as Associate Editor for "Nutrition" the International Journal; served on the Editorial Board of the Journal of Women's Health and Gender-based Medicine, and served on the Board of Directors of the American College of Nutrition.*

Dr. Bendich was Director of Medical Affairs at GlaxoSmithKline (GSK) Consumer Healthcare and provided medical leadership for many well-known brands including TUMS and Os-Cal. Dr. Bendich had primary responsibility for GSK's support for the Women's Health Initiative (WHI) intervention study. Prior to joining GSK, Dr. Bendich was at Roche Vitamins Inc. and was involved with the groundbreaking clinical studies showing that folic acid-containing multivitamins significantly reduced major classes of birth defects. Dr. Bendich has co-authored over 100 major clinical research

studies in the area of preventive nutrition. She is recognized as a leading authority on antioxidants, nutrition and immunity and pregnancy outcomes, vitamin safety and the cost-effectiveness of vitamin/mineral supplementation.

Dr. Bendich received the Roche Research Award, is a *Tribute to Women and Industry* Awardee and was a recipient of the Burroughs Wellcome Visiting Professorship in Basic Medical Sciences. Dr. Bendich was given the Council for Responsible Nutrition (CRN) Apple Award in recognition of her many contributions to the scientific understanding of dietary supplements. In 2012, she was recognized for her contributions to the field of clinical nutrition by the American Society for Nutrition and was elected a Fellow of ASN. Dr Bendich is an Adjunct Professor at Rutgers University. She is listed in Who's Who in American Women.



## About the Volume Editors



**Michael F. Holick, Ph.D., M.D.** is Professor of Medicine, Physiology, and Biophysics; Director of the General Clinical Research Unit, and Director of the Bone Health Care Clinic and the Heliotherapy, Light, and Skin Research Center at Boston University Medical Center. After earning a Ph.D. in biochemistry, a medical degree, and completing a research postdoctoral fellowship at the University of Wisconsin, Madison, Dr. Holick completed a residency in medicine at the Massachusetts General Hospital in Boston.

Dr. Holick has made numerous contributions to the field of the biochemistry, physiology, metabolism, and photobiology of vitamin D for human nutrition. As a graduate student at the University of Wisconsin he was the first to isolate and identify 25-hydroxyvitamin D<sub>3</sub> in human blood and the active form of vitamin D as 1,25-dihydroxyvitamin D<sub>3</sub>. He participated in the first chemical synthesis of 1,25-dihydroxyvitamin D<sub>3</sub> and its analog 1 $\alpha$ -hydroxyvitamin D<sub>3</sub> that was used in the first demonstration of their utility in treating vitamin D-dependent rickets type I and hypoparathyroidism. He determined the mechanism for how vitamin D is synthesized in the skin and demonstrated the effects of aging, obesity, latitude, seasonal change, sunscreen use, skin pigmentation, and clothing on this vital cutaneous process. He introduced the concept of using 1,25-dihydroxyvitamin D<sub>3</sub> and active analogs for the treatment of psoriasis. Dr. Holick has established global recommendations advising

sunlight exposure as an integral source of vitamin D with an app [dminder.info](http://dminder.info). He chaired the Endocrine Society's Practice Guidelines Committee on Vitamin D which provided recommendations for the treatment and prevention of vitamin D deficiency for children and adults. He has also helped increase awareness in the pediatric and medical communities regarding vitamin D deficiency pandemic and its role in causing not only metabolic bone disease and osteoporosis in adults but increasing risk of children and adults developing common deadly cancers, autoimmune diseases, including type 1 diabetes and multiple sclerosis as well as heart disease.

Dr. Holick is a Diplomate of the American Board of Internal Medicine, a Fellow of the American College of Nutrition, and a member of numerous organizations, including the American Academy of Dermatology, American Society for Bone and Mineral Research, and the American Association of Physicians. He is the recipient of numerous awards and honors, including the American Skin Association's Psoriasis Research Achievement Award in 2002, the American College of Nutrition Award in 2002, the Robert H. Herman Memorial Award in Clinical Nutrition from the American Society for Clinical Nutrition in 2003, the Annual General Clinical Research Centers' Program Award for Excellence in Clinical Research in 2006, the Linus Pauling Functional Medicine Award from the Institute for Functional Medicine in 2007, Linus Pauling Prize 2009, DSM Innovation In Nutrition Award 2009, American Association of Clinical Chemist's Van Slyke Award 2010, American College of Nutrition's Communication Media Award 2011, the Delbert Fisher Research Scholar 2011, Best Doctors in America 2011–2014, and the American Society of Bone and Mineral Research Louis Avioli Award 2014. His teaching skills were recognized by being chosen to give the Boston University Lecture in 2013 and given the Educator of the Year award in the Masters of Medical Sciences Program in 2014. Dr. Holick serves on a number of national committees, including NIH and NASA and several editorial boards. He has organized and/or co-chaired several international symposia and is editor-in-chief for the *Journal for Clinical Laboratories and Laboratories Related to Blood Transfusion* and Associate editor for *Dermato-Endocrinology*. He has authored more than 500 peer-reviewed publications and written more than 250 review articles as well as numerous book chapters. He has acted as editor and/or co-editor on 13 books.



**Jeri Wanzor Nieves** is a graduate of Columbia University where she received her Ph.D. in Epidemiology, following a Masters Degree in Nutrition from Cornell University. At Helen Hayes Hospital in New York, she is a Research Scientist investigating various aspects of Osteoporosis and serves as the Principal Investigator for the New York State Osteoporosis Prevention and Education

Program (NYSOPEP). She also serves on several committees for the National Osteoporosis Foundation. Dr. Nieves is an Associate Professor of Clinical Epidemiology and Nutrition at Columbia University. Dr. Nieves has co-authored over 100 journal articles, reviews, and book chapters on nutrition, epidemiology, and osteoporosis. She is an Associate Editor of Osteoporosis International. Dr. Nieves' research has focused on various aspects of bone health and osteoporosis including peak bone mass, stress fractures, vitamin D, anabolic and antiresorptive treatments, and fracture healing. In addition, her research includes aspects of nutritional epidemiology and determining the role of nutrition in various disease states.



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Michael F. Holick  
Jeri W. Nieves



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# List of Contributors

**John S. Adams** Orthopaedic Hospital Research Center, University of California Los Angeles, Los Angeles, CA, USA

Molecular Biology Institute, University of California Los Angeles, Los Angeles, CA, USA

**Sabrina C. Agarwal** Department of Anthropology, University of California Berkeley, Berkeley, CA, USA

**Armin Alaedini** Department of Medicine, Columbia University Medical Center, New York, NY, USA

Celiac Disease Center, Columbia University Medical Center, New York, NY, USA

Institute of Human Nutrition, Columbia University Medical Center, New York, NY, USA

**Patrick Amman** Division of Bone Diseases, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland

**John J.B. Anderson** Department of Nutrition, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC, USA

**Stephen M. Arpadi** Department of Epidemiology, Gertrude H. Sergievsky Center and Department of Pediatrics, College of Physicians and Surgeons, Mailman School of Public Health, Columbia University, New York, NY, USA

**Stephanie A. Atkinson** Department of Pediatrics, Faculty of Health Sciences, McMaster University, Hamilton, ON, Canada

**Susan I. Barr** Food, Nutrition & Health, University of British Columbia, Vancouver, BC, Canada

**Jean-Philippe Bonjour** Division of Bone Diseases, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland

**Sarah L. Booth** USDA Human Nutrition Research Center on Aging, Tufts University, Boston, MA, USA

**Mary L. Bouxsein** Center for Advanced Orthopedic Studies, Beth Israel Deaconess Medical Center, Boston, MA, USA

Department of Orthopaedic Surgery, Harvard Medical School, Boston, MA, USA

**Peter Burckhardt** Clinic Hirslanden, Lausanne, Switzerland

**David A. Bushinsky** Department of Medicine, Division of Nephrology, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA

**Hong Chen** Veterans Administration Medical Center and Division of Endocrinology, Metabolism, and Lipids, Department of Medicine, Emory University School of Medicine, Atlanta, GA, USA

**Thierry Chevalley** Division of Bone Diseases, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland

**Rene F. Chun** Orthopaedic Hospital Research Center, University of California Los Angeles, Los Angeles, CA, USA

**Mariana Cifuentes** Institute of Nutrition and Food Technology INTA, Universidad de Chile, Santiago, Chile

**Elaine Cong** New York Presbyterian Hospital, Columbia University Medical Center, New York, NY, USA

**Felicia Cosman** Department of Medicine, Columbia University, New York, NY, USA

Helen Hayes Hospital, West Haverstraw, NY, USA

**Robin M. Daly** Centre for Physical Activity and Nutrition Research, School of Exercise and Nutrition Sciences, Deakin University, Burwood, Melbourne, Australia

**Linda L. Darga** Department of Anthropology, Oakland University, Rochester, MI, USA

**Andrea L. Darling** Faculty of Health and Medical Sciences, Department of Nutritional Sciences, School of Biosciences and Medicine, University of Surrey, Guildford, UK

**Bess Dawson-Hughes** Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, MA, USA

**David W. Dempster** Helen Hayes Hospital, West Haverstraw, NY, USA

Columbia University, New York, NY, USA

**Serge Ferrari** Division of Bone Diseases, Faculty of Medicine, Geneva University Hospital, Geneva, Switzerland

**Alejandro Garcia** Orthopaedic Hospital Research Center, University of California Los Angeles, Los Angeles, CA, USA

**Ian J. Griffin** Department of Pediatrics, UC Davis Children's Hospital, Sacramento, CA, USA

**Susan S. Harris** Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, MA, USA

**Robert P. Heaney** Creighton University, Omaha, NE, USA

**Martina Heer** Department of Nutrition and Food Science, Nutrition Physiology, University of Bonn, Bonn, Germany

**Martin Hewison** Orthopaedic Hospital Research Center, University of California Los Angeles, Los Angeles, CA, USA

Molecular Biology Institute, University of California Los Angeles, Los Angeles, CA, USA

**Michael F. Holick** Department of Medicine and Endocrine/Vitamin D Lab, Boston University School of Medicine, Boston, MA, USA

**Sandra Iuliano** Department of Endocrinology, Heidelberg Repatriation Hospital, Austin Health, University of Melbourne, West Heidelberg, Australia

**David Karasik** Faculty of Medicine in the Galilee, Bar-Ilan University, Safed, Israel

Hebrew SeniorLife, Boston, MA, USA

**Lamya Karim** Center for Advanced Orthopedic Studies, Beth Israel Deaconess Medical Center, Boston, MA, USA

Department of Orthopaedic Surgery, Harvard Medical School, Boston, MA, USA

**Wahida Karmally** Irving Institute for Clinical and Translational Research, Columbia University, New York, NY, USA

**Elizabeth Krall Kaye** Henry M. Goldman School of Dental Medicine, Boston University, Boston, MA, USA

**Douglas P. Kiel** Institute for Aging Research, Hebrew SeniorLife and Beth Israel Deaconess Hospital, Harvard Medical School, Boston, MA, USA

**Anne Klibanski** Neuroendocrine Units, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA

**Nancy S. Krieger** Department of Medicine, Division of Nephrology, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA

**Susan A. Lanham-New** Faculty of Health and Medical Sciences, Department of Nutritional Sciences, School of Biosciences and Medicine, University of Surrey, Guildford, UK

**Leon Lenchik** Department of Radiology, Wake Forest School of Medicine, Winston-Salem, NC, USA

**Robert Lindsay** Department of Medicine, Columbia University College of Physicians and Surgeons, New York, NY, USA

Helen Hayes Hospital, West Haverstraw, NY, USA

**Thomas S. Lisse** Endocrine Unit, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA

**Helen M. Macdonald** Bone and Musculoskeletal Research Programme, University of Aberdeen, Health Sciences Building, Foresterhill, Aberdeen, UK

**Velimir Matkovic** Osteoporosis Prevention and Treatment Center, The Ohio State University, Columbus, OH, USA

Bone and Mineral Metabolism Laboratory, The Ohio State University, Columbus, OH, USA

**Madhusmita Misra** Neuroendocrine Unit, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA

Pediatric Endocrine Unit, Massachusetts General Hospital for Children and Harvard Medical School, Boston, MA, USA

**Fiona L. Morris-Naumann** Head of Exercise & Sports Science, Queensland University of Technology, School of Exercise and Nutrition Sciences, Kelvin Grove, Australia

**Dorothy A. Nelson** Office of Research Administration and Department of Anthropology, Oakland University, Rochester, MI, USA

**Jeri W. Nieves** Department of Epidemiology, Helen Hayes Hospital and Columbia University, West Haverstraw, New York, NY, USA

**Kimberly O. O'Brien** Division of Nutritional Sciences, Cornell University, Ithaca, NY, USA

**Francisco J. A. de Paula** Department of Internal Medicine, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, SP, Brasil

**Thomas C. Register** Department of Pathology, Wake Forest School of Medicine, Winston-Salem, NC, USA

**René Rizzoli** Division of Bone Diseases, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland

**Dilisha Rodrigopulle** Department of Pediatrics, Faculty of Health Sciences, McMaster University, Hamilton, ON, Canada

**Clifford J. Rosen** Center for Clinical and Translational Research, Maine Medical Center Research Institute, Scarborough, ME, USA

**Shivani Sahni** Institute for Aging Research, Hebrew SeniorLife and Beth Israel Deaconess Hospital, Harvard Medical School, Boston, MA, USA

**Kerry J. Schulze** Center for Human Nutrition, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

**Sue A. Shapses** Department of Nutritional Sciences, Rutgers University, New Brunswick, NJ, USA

**M. Kyla Shea** USDA Human Nutrition Research Center on Aging, Tufts University, Boston, MA, USA

**Stephanie Shiau** Department of Epidemiology, Gertrude H. Sergievsky Center, College of Physicians and Surgeons, Mailman School of Public Health, Columbia University, New York, NY, USA

**Maria A. Fiatarone Singh** Exercise, Health and Rehabilitation Faculty Research Group, Faculty of Health Sciences, University of Sydney, NSW, Australia

**Scott M. Smith** Human Health and Performance Directorate, NASA Lyndon B. Johnson Space Center, Houston, TX, USA

**Bonny L. Specker** Ethel Austin Martin Program in Human Nutrition, South Dakota State University, Brookings, SD, USA

**Lisa A. Spence** Innovation & Commercial Development, Tate & Lyle, Hoffman Estates, IL, USA

**Katherine L. Tucker** Department of Clinical Laboratory and Nutritional Sciences, College of Health Sciences, University of Massachusetts Lowell, Lowell, MA, USA

**Diane Visy** GlaxoSmithKline (GSK), Wavre, Belgium

**Marcella Donovan Walker** Columbia University College of Physicians and Surgeons, New York, NY, USA

**John D. Wark** Department of Medicine, Royal Melbourne Hospital, University of Melbourne, Parkville, VIC, Australia

Head, Bone and Mineral Medicine, Royal Melbourne Hospital, Parkville, VIC, Australia

**Meryl Wastney** Metabolic Modeling, West Lafayette, IN, USA

**Connie M. Weaver** Department of Nutrition Science, Purdue University, West Lafayette, IN, USA

**Adrian D. Wood** Bone and Musculoskeletal Research Programme, University of Aberdeen, Health Sciences Building, Foresterhill, Aberdeen, UK

**Scott Wuertzer** Department of Radiology, Wake Forest School of Medicine, Winston-Salem, NC, USA

**Atheer A. Yacoub** Irving Institute for Clinical and Translational Research, Columbia University, New York, NY, USA

**Michael T. Yin** Division of Infectious Diseases, Department of Medicine, College of Physicians and Surgeons, Columbia University, New York, NY, USA

**Sara R. Zwart** Division of Space Life Sciences, Universities Space Research Association, Houston, TX, USA