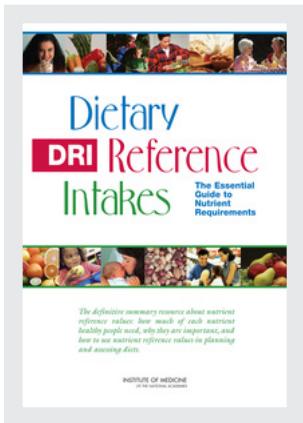


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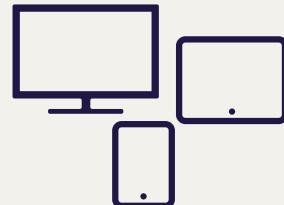
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# Dietary **DRI** Reference Intakes



# Dietary **DRI** Reference Intakes

**The Essential  
Guide to  
Nutrient  
Requirements**



Jennifer J. Otten, Jennifer Pitzi Hellwig, Linda D. Meyers,  
*Editors*

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The serpent has been a symbol of long life, healing, and knowledge among almost all cultures and religions since the beginning of recorded history. The serpent adopted as a logotype by the Institute of Medicine is a relief carving from ancient Greece, now held by the Staatliche Museen in Berlin.

*“Knowing is not enough; we must apply.  
Willing is not enough; we must do.”*  
—Goethe



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# PREFACE

This book is a selective summary of the series of publications on *Dietary Reference Intakes* (DRIs). Its goal is to serve as a practical, hands-on reference to help guide health professionals in the United States and Canada in their day-to-day task of assessing and planning for the nutrient needs of individuals and groups of people. The book also provides educators with a tool for guiding students in the understanding of the DRI concept and use of the reference values. It is derived from work authored by the Food and Nutrition Board (FNB) of the Institute of Medicine (IOM).

This book is not meant to replace the original DRI series of nutrient reference values published between 1997 and 2005 nor is it intended to be a thorough representation of the series. Based on material from the original DRI series, this book stays true to the findings and recommendations from the original reports. Without introducing new data or conclusions, this document recasts essential ideas from the original reports in an accessible and more compact form.

The DRI values and paradigm replace the former Recommended Dietary Allowances (RDAs) for the United States and Recommended Nutrient Intakes (RNIs) for Canada. In the past, RDAs and RNIs were the primary values available to U.S. and Canadian health professionals for planning and assessing the diets of individuals and groups. The DRIs represent a more complete set of values. They were developed in recognition of the growing and diverse uses of quantitative reference values and the availability of more sophisticated approaches for dietary planning and assessment purposes.

Although all reference values in this book are based on data, available data were often sparse or drawn from studies with significant limitations in addressing various questions confronted by the original DRI panel and subcommittees. Thus, although governed by scientific rationale, informed judgments were often required in setting reference values. Where data were available, criteria of nutritional adequacy were carefully identified; these criteria are listed in tables in each nutrient chapter.

Readers are urged to recognize that the DRI process is iterative in character. We expect that the DRI conceptual framework will continue to evolve and be improved as new information becomes available and is applied to an expanding list of nutrients and other food components. Thus, because the DRI activity is ongoing, comments were solicited widely and received on the originally published reports of this series. With more experience, the proposed models for

establishing reference intakes of nutrients and other food components that play significant roles in promoting and sustaining health and optimal functioning will be refined. Also, as new information or new methods of analysis are adopted, these reference values undoubtedly will be reassessed. This book will be updated in the future as the original series is revised.

This book has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Research Council's Report Review Committee. The purpose of this independent review is to provide candid, confidential, and critical comments that will assist the institution in making its published book as sound as possible and to ensure that the book meets institutional standards. We wish to thank the following individuals for their review of this report: Lawrence Appel, Johns Hopkins Medical Institutions; Stephanie A. Atkinson, McMaster University; Susan I. Barr, University of British Columbia; Ann M. Coulston, Ely Lilly and Co.; John W. Erdman, University of Illinois at Urbana-Champaign; Norman I. Krinsky, Tufts University; Joanne R. Lupton, Texas A&M University; Suzanne Murphy, University of Hawaii; Roy M. Pitkin, University of California, Los Angeles; Robert M. Russell, Tufts University.

Although these reviewers provided many constructive comments and suggestions, they were not asked to endorse nor did they see the final draft of the book before its release and publication. The review of this report was overseen by Clyde J. Behney, who was responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered.

The Institute of Medicine gratefully acknowledges Health Canada's support and participation in this initiative. This close collaboration represents a pioneering step in the harmonization of nutrient reference intakes in North America. In particular, the Food and Nutrition Board wishes to extend special thanks to our Health Canada partners who helped refine drafts and provided invaluable comments that vastly improved the project: Mary Bush, Danielle Brulé, Margaret Cheney, Krista Esslinger, Linda Greene-Finstone, and Sylvie St-Pierre. We also express our gratitude and thanks to Health Canada for permitting incorporation of materials on the Dietary Reference Intakes extracted from *The Canadian Community Health Survey 2.2, Nutrition Focus: A Guide to Accessing and Interpreting the Data*, published by Health Canada in 2006.

The consultants for this project—Johanna T. Dwyer, Rachel K. Johnson, Rena Mendelson, Esther F. Myers, Sharon M. Nickols-Richardson, Linda G. Snetselaar, Huguette Turgeon-O'Brien, and Susan Whiting—ably performed their work under severe time pressures (see Appendix B for biographical sketches). All gave their time and effort willingly and without financial reward; the public and the science and practice of nutrition are among the major beneficiaries of

their dedication. This project would not have been undertaken and completed without the dedicated work of the project staff, in particular, Jennifer Otten who co-wrote and managed the project and its many iterations, Jennifer Pitzi Hellwig who co-wrote and copyedited parts of the book, Mary Kalamaras who guided initial plans and copyedited a very complex and complicated manuscript, and Linda D. Meyers who oversaw the project and never hesitated to assist when help was needed. The intellectual and managerial contributions made by these individuals to the project were critical. Sincere thanks also go to other IOM and National Academies staff, including Ricky Washington, Gerri Kennedo, Ann Merchant, Virginia Bryant, Barbara Kline Pope, Estelle Miller, Will Mason, Lara Andersen, Sally Stanfield, Charles Baum, Sally Groom, Dorothy Lewis, Stephen Mautner, Marc Gold, Linda Kilroy, Anton Bandy, Gary Walker, Vivian Tillman, Bronwyn Schrecker Jamrok, Tyjen Tsai, and Sandra Amamoo-Kakra.

I also want to extend my personal gratitude to the many volunteers who served the Institute of Medicine and the nation as members of the Food and Nutrition Board, members of the committees who prepared the DRI series and reviewers of the draft reports in that series. Their dedication and expertise in reviewing, interpreting, and translating scientific evidence into nutrient reference values is a substantial contribution to the public's health.

Harvey V. Fineberg, M.D., Ph.D.  
*President, Institute of Medicine*



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\*Full references, which also appear in the parent report series, the *Dietary Reference Intakes*, are not printed in this book but are provided online at <http://www.nap.edu/catalog/11537.html>.



# INTRODUCTION

For more than half a century, the Recommended Dietary Allowances (RDAs) of the United States and the Dietary Standards/Recommended Nutrient Intakes (RNIs) of Canada have served as the chief components for nutrition policy in their respective countries, playing dominant roles in the task of meeting the known nutritional needs of healthy people in North America.

Revised and updated many times throughout their history, the RDAs and RNIs generally reflected changes resulting from the broader evolution taking place in the field of nutrition science. However, by the 1990s, a number of important developments had occurred that dramatically altered the nutrition research landscape and ultimately challenged the RDA and RNI status quo. Among them were the significant gains made in scientific knowledge regarding the link between diet, health, and chronic disease, and the emergence of advanced technologies that could measure small changes in individual adaptations to various nutrient intakes. Additionally, the use of fortified or enriched foods and the increased consumption of nutrients in pure form, either singly or in combination with others outside of the context of food, prompted the closer examination of the potential effects of excess nutrient intake.

In 1994, in response to these and other important considerations, the Food and Nutrition Board of the National Academies' Institute of Medicine, with support from the U.S. and Canadian governments and others, embarked on an initiative to develop a new, broader set of dietary reference values, known as the Dietary Reference Intakes (DRIs). The DRIs expand upon and replace the RDAs and RNIs with four categories of values intended to help individuals optimize their health, prevent disease, and avoid consuming too much of a nutrient. These dietary reference values were subsequently published in a series of reports released between 1997 and 2005, titled the *Dietary Reference Intakes*.

Recognizing the groundbreaking nature of the series and its impact on the nutrition community, the Food and Nutrition Board and Health Canada came together again in 2005 in an effort to extend the reach of the original reports to a wider audience. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements* is the result of their collaboration. Based on the key concepts and recommendations set forth in the original DRI series, this book serves as a practical, hands-on reference to help guide health professionals in the United States and Canada in their day-to-day task of assessing and planning for the nutrient needs of individuals and groups of people. This book also provides educators

with a tool for guiding students in the understanding of the DRI concept and use of the reference values.

The book is divided into four parts: Part I provides a foundation for understanding how and why the DRIs were developed, definitions of the DRI categories, and specific guidance on their appropriate uses. Part II presents discussions on reference values for dietary carbohydrate, fiber, total fat, fatty acids, cholesterol, protein, amino acids, and water. Major new approaches and findings included in this section are formulas for estimating energy requirements; recommended physical activity levels; the definition of dietary fiber; and Acceptable Macronutrient Distribution Ranges (AMDRs), which have been introduced as a percentage of energy intake for fat, carbohydrate, protein, and linoleic and  $\alpha$ -linolenic acids. Also included is information on the relationship between macronutrients and chronic disease.

Part III profiles 35 individual nutrients. In addition to providing reference values, each profile reviews the function of a given nutrient in the human body; summarizes the known effects of deficiencies and excessive intakes; describes how a nutrient may be related to chronic disease or developmental abnormalities; and provides the indicator of adequacy for determining the nutrient requirements.

A comprehensive set of appendixes, including a glossary and summary tables of DRI values appear in Part IV. Full references, which also appear in the parent report series, the *Dietary Reference Intakes*, are provided online at <http://www.nap.edu/catalog/11537.html>.

# PART I

## DEVELOPMENT AND APPLICATION

The Dietary Reference Intakes (DRIs) represent a radical new approach toward nutrition assessment and dietary planning, and therefore necessitate a thorough understanding of their origin, purpose, and intended applications. Part I of this book first addresses these areas, then follows with practical guidance on the correct application of the DRI values to the task of assessing and planning the diets of individuals and groups.

“Introduction to the Dietary Reference Intakes” provides a history of the creation of the DRIs, along with an introduction to the four categories they comprise: the Estimated Average Requirement (EAR), the Recommended Dietary Allowance (RDA), the Adequate Intake (AI), the Tolerable Upper Intake Level (UL), as well as the new Acceptable Macronutrient Distribution Ranges (AMDRs). The values are defined and their appropriate uses are discussed in detail, as are the parameters that were used to develop them, such as life stage groups and applicable populations. Also discussed are how the values differ from each other, as well as from the previous Recommended Dietary Allowances (RDAs) and Canada’s Recommended Nutrient Intakes (RNIs).

“Applying the Dietary Reference Intakes” provides guidance on how to use and interpret the DRI values when assessing and planning the nutrient intakes of both individuals and groups. It summarizes pertinent information taken from two DRI reports published by the Food and Nutrition Board of the National Academies’ Institute of Medicine. They are *Dietary Reference Intakes: Applications in Dietary Assessment* (2000) and *Dietary Reference Intakes: Applications in Dietary Planning* (2003). The chapter is divided into two main sections, “Working with Individuals” and “Working with Groups,” which are each subdivided into assessment and planning sections. The sections on assessment also include explanations of the methods and equations that are used to determine whether individuals and groups are consuming adequate levels of nutrients. In addition, the chapter summary includes a quick-reference table on the appropriate uses of DRI values for specific aspects of nutrition assessment and planning.



# INTRODUCTION TO THE DIETARY REFERENCE INTAKES

In 1941, the National Research Council issued its first set of Recommended Dietary Allowances (RDAs) for vitamins, minerals, protein, and energy. Developed initially by the forerunner of the Food and Nutrition Board of the Institute of Medicine, the recommendations were intended to serve as a guide for good nutrition and as a “yardstick” by which to measure progress toward that goal. Since then, RDAs have served as the basis for almost all federal and state food and nutrition programs and policies. By 1989, they had been revised nine times and expanded from a coverage of 8 original nutrients to 27 nutrients.

In 1938, the Canadian Council on Nutrition prepared the first dietary standard designed specifically for use in Canada. The *Dietary Standard for Canada* was revised in 1950, 1963, 1975, and 1983 and published by Health Canada and its predecessors. The 1983 revision was renamed *Recommended Nutrient Intakes (RNIs) for Canadians*. In the late 1980s, it was decided to incorporate considerations of the prevention of chronic diseases as well as nutritional deficiencies into the revision of the RNIs. In 1990, *Nutrition Recommendations: The Report of the Scientific Review Committee* was published. The report contained updated RNIs and recommendations on the selection of a dietary pattern that would supply all essential nutrients, while reducing risk of chronic diseases.

Both RDA and RNI values have been widely used for planning diets, assessing the adequacy of diets in individuals and populations, providing nutrition education and guidance, and as a standard for nutrition labeling and fortification. However, the former RDAs and RNIs were not always well suited for these applications and the need for new values was recognized. Also of note, the RNIs and RDAs differed from each other in their definition, revision and publication dates, and how their data have been interpreted by both U.S. and Canadian scientific committees.

Beginning in 1994, the Food and Nutrition Board, with support from the U.S. and Canadian governments and others, set out to develop and implement a new paradigm to establish recommended nutrient intakes that replaced and

expanded upon the RDAs and RNIs. Reflecting updated scientific and statistical understandings, this decade-long review resulted in the development of the family of reference values collectively known as the Dietary Reference Intakes (DRIs). In contrast to the creation of the RDAs and RNIs, which involved establishing single values for each nutrient, adjusted for age, sex, and physiological condition, the DRIs feature four reference values, only one of which, the RDA, is familiar to the broad nutrition community (although the method by which it is derived has changed). The DRIs are a common set of reference values for Canada and the United States and are based on scientifically grounded relationships between nutrient intakes and indicators of adequacy, as well as the prevention of chronic diseases, in apparently healthy populations.

The development of the DRIs publication series (see Box 1 for a list of publications in the series) was undertaken by the standing Committee on the Scientific Evaluation of Dietary Reference Intakes, two standing subcommittees (the Subcommittee on Upper Reference Levels of Nutrients and the Subcommittee on Uses and Interpretation of Dietary Reference Intakes), and a series of expert panels. Each of the panels was responsible for reviewing the requirements for a specific group of nutrients.

Totaling nearly 5,000 pages, these reports summarize what is known about how nutrients function in the human body; the selection of indicators of adequacy on which to determine nutrient requirements; the factors that may affect how nutrients are utilized and therefore affect requirements; and how nutrients may be related to the prevention of chronic disease across all age groups. They also provide specific guidance on how to use the appropriate values to assess and plan the diets of groups and individuals.

## **A NEW APPROACH TO NUTRIENT REFERENCE VALUES**

Collectively referred to as the Dietary Reference Intakes, the DRIs include four nutrient-based reference values that are used to assess and plan the diets of healthy people. The reference values include the Estimated Average Requirement (EAR), the Recommended Dietary Allowance (RDA), the Adequate Intake (AI), and the Tolerable Upper Intake Level (UL). (Brief definitions of the DRI categories are provided in Box 2.) Developed for vitamins, minerals, macronutrients, and energy, these reference values replace and expand upon the previous nutrient reference values for the United States and Canada. New to the nutrition world, the DRIs represent a significant paradigm shift in the way dietary reference values are established and used by practitioners, educators, and researchers. Unlike the RDAs and RNIs (prior to 1990), which focused primarily on reducing the incidence of diseases of deficiency, the DRI values are also

**PART I: INTRODUCTION TO THE DIETARY REFERENCE INTAKES****BOX 1 The DRI Publications**

Nutrient-specific reports:

- *DRIs for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride* (1997)
- *DRIs for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline* (1998)
- *DRIs for Vitamin C, Vitamin E, Selenium, and Carotenoids* (2000)
- *DRIs for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc* (2001)
- *DRIs for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* (2002/2005)
- *DRIs for Water, Potassium, Sodium, Chloride, and Sulfate* (2005)

Reports that explain appropriate uses:

- *DRIs: Applications in Dietary Assessment* (2000)
- *DRIs: Applications in Dietary Planning* (2003)

Related or derivative reports:

- *DRIs: Proposed Definition and Plan for Review of Dietary Antioxidants and Related Compounds* (1998)
- *DRIs: A Risk Assessment Model for Establishing Upper Intake Levels for Nutrients* (1998)
- *DRIs: Proposed Definition of Dietary Fiber* (2001)
- *DRIs: Guiding Principles for Nutrition Labeling and Fortification* (2003), prepared as a separate activity

<http://www.nap.edu/catalog/dri>

intended to help individuals optimize their health, prevent disease, and avoid consuming too much of a nutrient. Specifically, the DRIs differ from the former RDAs and RNIs in several key ways:

- When available, data on a nutrient's safety and role in health are considered in the formulation of a recommendation, taking into account the potential reduction in the risk of chronic degenerative disease or developmental abnormality, rather than just the absence of signs of deficiency.

**BOX 2 DRI Definitions**

**Estimated Average Requirement (EAR):** The average daily nutrient intake level that is estimated to meet the requirements of half of the healthy individuals in a particular life stage and gender group.<sup>a</sup>

**Recommended Dietary Allowance (RDA):** The average daily dietary nutrient intake level that is sufficient to meet the nutrient requirements of nearly all (97–98 percent) healthy individuals in a particular life stage and gender group.

**Adequate Intake (AI):** The recommended average daily intake level based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people that are assumed to be adequate; used when an RDA cannot be determined.

**Tolerable Upper Intake Level (UL):** The highest average daily nutrient intake level that is likely to pose no risk of adverse health effects to almost all individuals in the general population. As intake increases above the UL, the potential risk of adverse effects may increase.

<sup>a</sup> In the case of energy, an Estimated Energy Requirement (EER) is provided. The EER is the average dietary energy intake that is predicted to maintain energy balance in a healthy adult of a defined age, gender, weight, height, and level of physical activity consistent with good health. In children and pregnant and lactating women, the EER is taken to include the needs associated with the deposition of tissues or the secretion of milk at rates consistent with good health.

- The concepts of probability and risk explicitly underpin the determination of the DRIs and inform their application in assessment and planning.
- Greater emphasis is placed on the distribution of nutrient requirements within a population, rather than on a single value (like the former RDAs and RNIs).
- Where data exist, upper levels of intake have been established regarding the risk of adverse health effects.
- Compounds found naturally in foods that may not meet the traditional concept of a nutrient, but have a potential risk or possible benefit to health, are reviewed and, if sufficient data exist, reference intakes are established.

## PART I: INTRODUCTION TO THE DIETARY REFERENCE INTAKES

As discussed earlier, the previous RDAs and RNIs were originally only intended to plan nutritional adequacy for groups. But because previous RDAs and RNIs were the only values available to health professionals, they were also used to assess and plan the diets of individuals and to make judgments about excess intakes for both individuals and groups. However, they were not ideally suited for these purposes. To prevent further misapplication, the expansion to the DRI framework included methodologies for appropriate uses of the nutrient values with individuals and groups.

The four primary uses of the DRIs are to assess the intakes of individuals, assess the intakes of population groups, plan diets for individuals, and plan diets for groups. Some of the dietary planning activities that are most relevant to DRI use include dietary guidance, institutional food planning, military food and nutrition planning, planning for food-assistance programs, food labeling, food fortification, developing new or modified food products, and food-safety assurance.

### THE DRI CATEGORIES

Most nutrients have a set of DRIs. Often, a nutrient has an Estimated Average Requirement (EAR) from which the Recommended Dietary Allowance (RDA) is mathematically derived. When an EAR for a nutrient cannot be determined (thus precluding the setting of an RDA), then an Adequate Intake (AI) is often developed. Many nutrients also have a Tolerable Upper Intake Level (UL).

The values for the EAR and AI are defined by using specific criteria for nutrient adequacy and answer the question “adequate for what?”. For example, values for vitamin C were set based on the amount of vitamin C that would nearly saturate leukocytes without leading to excessive urinary loss, rather than the level necessary to prevent scurvy. The UL is defined by using a specific indicator of excess, if one is available. Where data were available, the chosen criteria have been identified in each nutrient chapter.

In some cases, various intake levels can produce a range of benefits. For example, one criterion, or indicator, of adequacy may be the most appropriate one to use when determining an individual’s risk of becoming deficient in the nutrient, while another criterion of adequacy may be more applicable to reducing one’s risk of chronic diseases or conditions, such as certain neurodegenerative diseases, cardiovascular disease, cancer, diabetes mellitus, or age-related macular degeneration.

It is also important to note that each reference value refers to average daily nutrient intake. Some deviation around this average value is expected over a number of days. In fact, it is the average mean intake over this time frame that

serves as the nutritionally important reference value. In most cases, the amounts derived from day-to-day intake may vary substantially without ill effect.

### Estimated Average Requirement

The Estimated Average Requirement (EAR) is the average daily nutrient intake level that is estimated to meet the nutrient needs of half of the healthy individuals in a life stage or gender group. Although the term “average” is used, the EAR actually represents an estimated median requirement. As such, the EAR exceeds the needs of half of the group and falls short of the needs of the other half.

The EAR is the primary reference point for assessing the adequacy of estimated nutrient intakes of groups and is a tool for planning intakes for groups. It is also the basis for calculating the RDA. Although it can also be used to examine the probability that usual intake is inadequate for individuals (in conjunction with information on the variability of requirements), it is not meant to be used as a goal for daily intake by individuals. In the case of energy, an estimated energy requirement called the Estimated Energy Requirement (EER) is provided.

### Recommended Dietary Allowance

The Recommended Dietary Allowance (RDA) is an estimate of the daily average dietary intake that meets the nutrient needs of nearly all (97–98 percent) healthy members of a particular life stage and gender group. The RDA thus exceeds the requirements of nearly all members of the group. It can be used as a guide for daily intake by individuals, and because it falls above the requirements of most people, intakes below the RDA cannot be assessed as being inadequate. Usual intake at the RDA should have a low probability of inadequacy.

If an EAR cannot be set due to data limitations, no RDA will be calculated. For nutrients that have a statistically normal requirement distribution, the RDA is set by adding two standard deviations (SD) to the EAR. Thus,

$$\text{RDA} = \text{EAR} + 2\text{SD}$$

For nutrients with skewed requirement distributions (most notably, iron in menstruating women) the RDA is set between the 97th and 98th percentile of the requirement distribution. (See Part I, “Applying the Dietary Reference Intakes” for more information on calculating RDAs when nutrient requirements are skewed.)

### Adequate Intake

If sufficient or adequate scientific evidence is not available to establish an EAR and thus an RDA, an AI is usually derived for the nutrient instead. An AI is

## PART I: INTRODUCTION TO THE DIETARY REFERENCE INTAKES

### Acceptable Macronutrient Distribution Ranges (AMDR)

A growing body of evidence indicates that an imbalance in macronutrients (e.g., low or high percent of energy), particularly with certain fatty acids and relative amounts of fat and carbohydrates, can increase risk of several chronic diseases. Based on this evidence, Acceptable Macronutrient Distribution Ranges (AMDRs) have been estimated for individuals. An AMDR is the range of intakes of an energy source that is associated with a reduced risk of chronic disease, yet can provide adequate amounts of essential nutrients.

The AMDR is expressed as a percentage of total energy intake. A key feature of each AMDR is that it has a lower and upper boundary. For example, the AMDR for carbohydrates ranges from 45 to 65 percent of total energy intake. Intakes that fall below or above this range increase the potential for an elevated risk of chronic diseases. Intakes outside of the range also raise the risk of inadequate consumption of essential nutrients. The AMDRs are discussed in more detail in Part II, “Macronutrients, Healthful Diets, and Physical Activity.”

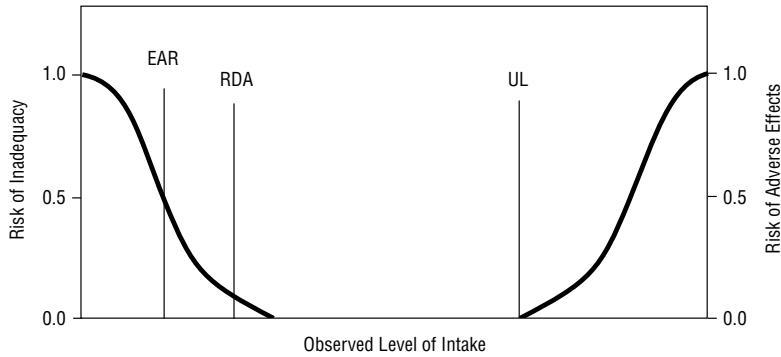
based on fewer data and incorporates more judgment than is used in establishing an EAR and subsequently the RDA. The setting of an AI usually indicates that more research is needed to determine, with some degree of confidence, the mean and distribution of requirements for that specific nutrient.

The AI is a recommended average daily nutrient intake level based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people who are assumed to be maintaining an adequate nutritional state. Examples of adequate nutritional states include normal growth, maintenance of normal levels of nutrients in plasma, and other aspects of nutritional well-being or general health.

The AI is expected to meet or exceed the needs of most individuals in a specific life stage and gender group. When an RDA is not available for a nutrient (because an EAR could not be developed), the AI can be used as the guide for an individual's intake. However, the AI has very limited uses in assessments of any type.

### Tolerable Upper Intake Level

The Tolerable Upper Intake Level (UL) is the highest average daily nutrient intake level likely to pose no risk of adverse health effects for nearly all people



**FIGURE 1** Relationship between Dietary Reference Intakes. This figure shows that the Estimated Average Requirement (EAR) is the intake at which the risk of inadequacy is 0.5 (50 percent) to an individual. The Recommended Dietary Allowance (RDA) is the intake at which the risk of inadequacy is very small—only 0.02 to 0.03 (2 to 3 percent). The Adequate Intake (AI) does not bear a consistent relationship to the EAR or the RDA because it is set without the estimate of the requirement. At intakes between the RDA and the Tolerable Upper Intake Level (UL), the risks of inadequacy and of excess are both close to zero. At intakes above the UL, the risk of adverse effects may increase.

in a particular group. As intake increases above the UL, the potential risk for adverse effects increases. The need for setting a UL grew out of two major trends: increased fortification of foods with nutrients and the use of dietary supplements by more people and in larger doses.

The UL is not a recommended level of intake, but rather the highest intake level that can be tolerated without the possibility of causing ill effects. The value applies to chronic daily use and is usually based on the total intake of a nutrient from food, water, and supplements if adverse effects have been associated with total intake. However, if adverse effects have been associated with intake from supplements or food fortificants alone, the UL is based on the nutrient intake from one or both of these sources only, rather than on total intake.

For some nutrients, not enough data were available to set a UL. However, this does not mean that consuming excess amounts poses no risks. Instead, it indicates a need for caution in consuming large amounts. See Figure 1 for a visual relationship between the DRIs.

## PARAMETERS USED IN DEVELOPING DRIS

The DRIs presented in this publication apply to the healthy general population. In addition, DRI values are assigned to life stage groups that correspond to

various periods of the human lifespan. Reference heights and weights for life stage and gender groups were used for extrapolations performed on the basis of body weight or size. They also indicate the extent to which intake adjustments might be made for individuals or population groups that significantly deviate from typical heights and weights.

## **Applicable Populations**

An important principle underlying the DRIs is that they are standards for apparently healthy people and are not meant to be applied to those with acute or chronic disease or for the repletion of nutrient levels in previously deficient individuals. Meeting the recommended intakes for the nutrients would not necessarily provide enough for individuals who are already malnourished, nor would they be adequate for certain disease states marked by increased nutrient requirements. Although the RDA or AI may serve as the basis for specialized guidance, qualified medical and nutrition personnel should make the needed adjustments for individuals with specific needs.

## **Life Stage Groups**

Where data were available, DRIs were divided into 12 life stage groups and also by gender. The life stage groups were chosen by considering variations in the requirements of all of the nutrients under review. If data were too limited to distinguish different nutrient requirements by life stage or gender groups, the analysis was then presented for a larger grouping.

### **INFANCY**

Infancy covers the first 12 months of life and is divided into two 6-month intervals. The first 6-month interval was not subdivided because intake is relatively constant during this time. That is, as infants grow, they ingest more food; however, on a body-weight basis their intake remains the same. During the second 6 months of life, growth rate slows. As a result, total daily nutrient needs on a body-weight basis may be less than those during the first 6 months of life.

The average intake by full-term infants born to healthy, well-nourished mothers and exclusively fed human milk has been adopted as the primary basis for deriving the AI for most nutrients during the first 6 months of life. The only exception to this criterion is vitamin D, which occurs in low concentrations in human milk.

In general, special consideration was not given to possible variations in physiological need during the first month after birth or to the intake variations that result from differences in milk volume and nutrient concentration during

early lactation. Specific recommended intakes to meet the needs of formula-fed infants have not been set.

- First 6 months (Ages 0 through 6 months): The AI for a nutrient for infants in this age group was calculated using two measures, the average concentration of the nutrient from 2 through 6 months of lactation and an estimated average volume of human milk intake of 0.78 L/day. The AI represents the product of these two measures. Infants are expected to consume increasing volumes of human milk as they grow.
- Second 6 months (Ages 7 through 12 months): During this time, infants experience slowed growth and gradual weaning to a mixed diet of human milk and solid foods. There is no evidence for markedly different nutrient needs, except for some nutrients such as iron and zinc, which have relatively high requirements. An EAR and RDA for iron and zinc have been derived for this age group. The AIs (again, with the exception of vitamin D) are based on the sum of the average amount of the nutrient provided by 0.6 L/day of human milk and the average amount of the nutrient provided by the usual intakes of complementary weaning foods consumed by infants at this age.

### **TODDLERS: AGES 1 THROUGH 3 YEARS**

Toddlers experience greater velocity of growth in height compared to 4- and 5-year-olds, and this distinction provides the biological basis for establishing separate recommended intakes for this age group. Data on which to base DRIs for toddlers are sparse, and in many cases, DRIs were derived by extrapolating data taken from the studies of infants or adults (see Appendix C).

### **EARLY CHILDHOOD: AGES 4 THROUGH 8 YEARS**

Children aged 4 through 8 or 9 years (the latter depending on puberty onset in each gender) undergo major changes in velocity of growth and endocrine status. For many nutrients, a reasonable amount of data was available on nutrient intake and various criteria for adequacy to serve as the basis for the EARs/RDAs and AIs for this group. For nutrients that lack data on the requirements of children, EARs and RDAs for children are based on extrapolations from adult values.

### **PUBERTY/ADOLESCENCE: AGES 9 THROUGH 13 YEARS, AND 14 THROUGH 18 YEARS**

The adolescent years were divided into two categories because growth occurs in some children as late as age 20 years. For some nutrients, different EARs/

## PART I: INTRODUCTION TO THE DIETARY REFERENCE INTAKES

RDAs and AIs were derived for girls and boys. Several indicators support the biological appropriateness of creating two adolescent age groups and gender groups:

- Age 10 years as the mean age of onset of breast development for white females in the United States; this is a physical marker for the beginning of increased estrogen secretion (in African American girls, onset is about a year earlier, for unknown reasons).
- The female growth spurt begins before the onset of breast development, thereby supporting the grouping of 9 through 13 years.
- The mean age of onset of testicular development in males is 10.5 through 11 years.
- The male growth spurt begins 2 years after the start of testicular development, thereby supporting the grouping of 14 through 18 years.

### **YOUNG ADULTHOOD AND MIDDLE AGE: AGES 19 THROUGH 30 YEARS, AND 31 THROUGH 50 YEARS**

Adulthood was divided into two age groups to account for the possible value of achieving optimal genetic potential for peak bone mass with the consumption of higher nutrient intakes during early adulthood rather than later in life. Moreover, mean energy expenditure decreases from ages 19 through 50 years, and nutrient needs related to energy metabolism may also decrease.

### **ADULTHOOD AND OLDER ADULTS: AGES 51 THROUGH 70 YEARS, AND OVER 70 YEARS**

The age period of 51 through 70 years spans active work years for most adults. After age 70, people of the same age increasingly display different levels of physiological functioning and physical activity. Age-related declines in nutrient absorption and kidney function also may occur.

### **PREGNANCY AND LACTATION**

Nutrient recommendations are set for these life stages because of the many unique changes in physiology and nutrition needs that occur during pregnancy and lactation.

In setting EARs/RDAs and AIs, consideration was given to the following factors:

- The needs of the fetus during pregnancy and the production of milk during lactation

- Adaptations to increased nutrient demand, such as increased absorption and greater conservation of many nutrients
- Net loss of nutrients due to physiological mechanisms, regardless of intake, such as seen with calcium in lactation

Due to the last two factors, for some nutrients there may not be a basis for setting EAR/RDA or AI values for pregnant or lactating women that differ from the values set for other women of comparable age.

## Reference Heights and Weights

Reference heights and weights for life stage and gender groups are useful when more specificity about body size and nutrient requirements is needed than that provided by life stage categories. For example, while an EAR may be developed for 4- to 8-year-olds, it could be assumed that a 4-year-old girl small for her age might require less than the EAR for her age group. Conversely, an 8-year-old boy who is big for his age might require more than the EAR for his age group. However, based on the model for establishing RDAs, the RDA (and AI) should meet the needs of both.

There are other reasons for using reference heights and weights in determining requirements. Data regarding nutrient requirements that are reported on a body-weight basis (such as with protein) necessitate the use of reference heights and weights to transform the data for comparison purposes. Or, frequently, the only available data are those regarding adult requirements. In these situations, extrapolating the data on the basis of body weight or size is a possible option to arrive at values for other age groups. Thus, when data are not available, the EARs or ULs for children or pregnant women may be established by extrapolating from adult values on the basis of body weight or, depending on the nutrient, on the basis of relative energy expenditure.

The reference heights and weights used in the more recent DRI reports are shown in Table 1. Earlier reports used slightly different reference heights and weights. (For more information on previous reference heights and weights see Appendix B of the report titled *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids, 2002/2005*.) The new charts include reference heights and weights that are more representative of U.S. and Canadian populations.

**TABLE 1 Reference Heights and Weights for Children and Adults**

Gender	Age	Median Body Mass Index <sup>a</sup> (kg/m <sup>2</sup> )	Median Reference Height, <sup>a</sup> cm (in)	Reference Weight, <sup>b</sup> kg (lb)
Males/females	2–6 mo	—	62 (24)	6 (13)
	7–12 mo	—	71 (28)	9 (20)
	1–3 y	—	86 (34)	12 (27)
	4–8 y	15.3	115 (45)	20 (44)
Males	9–13 y	17.2	144 (57)	36 (79)
	14–18 y	20.5	174 (68)	61 (134)
	19–30 y <sup>c</sup>	22.5	177 (70)	70 (154)
Females	9–13 y	17.4	144 (57)	37 (81)
	14–18 y	20.4	163 (64)	54 (119)
	19–30 y <sup>c</sup>	21.5	163 (64)	57 (126)

<sup>a</sup>Taken from data on male and female median body mass index and height-for-age data from the Centers for Disease Control and Prevention (CDC)/National Center for Health Statistics (NCHS) Growth Charts.

<sup>b</sup>Calculated from CDC/NCHS Growth Charts; median body mass index and median height for ages 4 through 19 years.

<sup>c</sup>Since there is no evidence that weight should change as adults age, if activity is maintained, the reference weights for adults aged 19 through 30 years are applied to all adult age groups.

## SUMMARY

The Dietary Reference Intakes (DRIs) replace and expand upon the previous revisions of the RDAs and RNIs and represent a new approach to setting nutrient values by greatly extending the scope and application of previous nutrient standards.

DRIs are a family of quantitative estimates of nutrient intakes intended for use in assessing and planning diets for healthy people. The DRI concept goes beyond the goal of former RDAs and RNIs of ensuring healthy diets, quantifying the relationship between a nutrient and the risk of disease, including chronic disease that results from either inadequate or excess intake.

The next chapter, “Applying the Dietary Reference Intakes,” provides helpful guidelines and methods on how to accurately apply the DRI values when assessing and planning the diets of both individuals and groups.



# APPLYING THE DIETARY REFERENCE INTAKES

The goal of dietary assessment is to determine if the nutrient intakes of an individual or group are meeting the needs of that individual or group.

The goal of dietary planning is to recommend a diet that provides adequate, but not excessive, levels of nutrients. It is important to note that when planning for individuals, the goal is to achieve recommended and adequate nutrient intakes using food-based guides. However, for group planning, this chapter presents a new approach, one based on considering the entire distribution of usual nutrient intakes, rather than focusing on the mean intake of a group.

While reading this chapter, keep in mind the following important points: First, the Dietary Reference Intakes (DRIs) apply to healthy people and do not pertain to those who are sick or malnourished or whose special circumstances may alter their nutrient needs. Second, an individual's exact requirement for a specific nutrient is generally unknown. The DRIs are intended to help practitioners arrive at a reasonable estimate of the nutrient level required to provide adequacy and prevent adverse effects of excess intake. Third, using the DRIs for assessment and planning is most effective when conducted as a cyclical activity that comprises assessment, planning, implementation, and reassessment.

When assessing and planning diets, it is important to be mindful of the limitations in the data that underpin the DRIs and their application, which include the following:

- The Estimated Average Requirements (EARs) may be based on data from a limited number of individuals.
- For most nutrients, the precise variation in requirements is not known but is approximated.
- In the absence of evidence to the contrary, variation in individual requirements is assumed to follow a normal distribution.
- The EAR is often extrapolated from one population group to another.
- The degree of uncertainty associated with the EAR has not been specified.

The appropriate application of the DRIs represents a significant departure from

**BOX 1 Definitions Associated with Assessing and Planning Nutrient Intakes**

**Distribution of requirements:** The distribution that reflects the individual-to-individual variability in requirements. Variability exists because not all individuals in a group have the same requirements for a nutrient, even if the individuals belong to the same life stage and gender group.

**Probability of inadequacy:** The outcome of a calculation that compares an individual's usual (long-term) intake to the distribution of requirements for people of the same life stage and gender group; used to determine the probability that the individual's intake does not meet his or her requirement.

**Probability of adequacy:** 100 percent minus the probability of inadequacy.

**Prevalence of inadequacy:** The percentage of a group with intakes that fall below requirements.

how nutrition assessment and planning were carried out using the former Recommended Dietary Allowances (RDAs) and Recommended Nutrient Intakes (RNIs). Although many practitioners may have regarded the use of RDAs and RNIs as a way to determine “exact” assessments of intake, this presumed level of accuracy was actually misleading. Dietary assessment is not an exact science. In fact, it generally has always involved a process that included a “best estimate” of an individual or group’s intake. The new DRIs, however, afford an opportunity to substantially improve the accuracy of dietary assessment because they allow practitioners to calculate the probability of inadequacy for an individual and the prevalence of inadequacy within a group and to plan for a low probability of inadequacy while minimizing potential risk of excess (see Box 1). These concepts are explained in greater detail later in this chapter, beginning with a short review of the statistical foundation underlying the concept of a distribution.

**PART I: APPLYING THE DIETARY REFERENCE INTAKES****STATISTICAL FOUNDATION**

The DRIs and their applications are based on the statistical concept of a distribution. A distribution is an arrangement of data values showing their frequency of occurrence throughout the range of the various possible values. One of the most common distributions is a “normal” distribution, which is a symmetrical bell-shaped curve that has most of the values clustered in the center of the distribution and a few values falling out in the tails (see Figure 1).

Important measures that describe a distribution are the mean, median, and standard deviation.

- The mean is the average of the data values. It is calculated by adding all the data values and then dividing by the number of data values.
- The median is the data value that occurs right in the middle of the distribution. It is the point at which half the data values are below and half the data values are above. The median is also referred to as the 50th percentile. In a symmetrical/normal distribution, the mean and median occur in the same place.
- The standard deviation (SD) is a measure of how much, on average, each individual data value differs from the mean. The smaller the SD, the less each data value varies from the mean. The larger the spread of data values, the larger SD becomes.
- The variance is another measure of how much individual data values differ from the mean. It is equivalent to the square of the standard deviation ( $SD^2$ ).

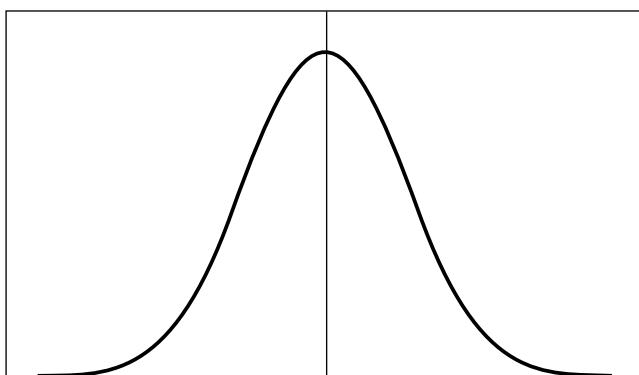
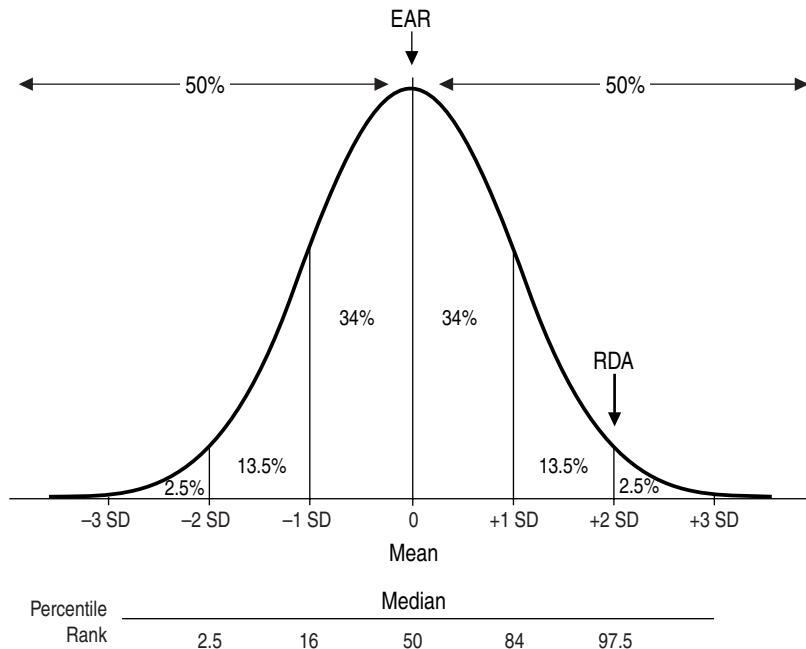


FIGURE 1 Schematic of a normal distribution.



*FIGURE 2 Normal requirement distribution of hypothetical nutrient showing percentile rank and placement of EAR and RDA on the distribution.*

One important use of the normal distribution is the way it can be used to convert scores into percentile ranks, or probabilities. The “z-score” is a standard score that changes values into SD units (i.e., the score is now so many SDs above or below the mean). This score can be related directly to the normal distribution and the associated percentage probability of nutrient adequacy or inadequacy, as seen in Figure 2.

By making use of this property of the normal distribution, the probability (or prevalence) of adequacy or inadequacy can be estimated. For example, a z-score of +1.50 is associated with a probability of adequacy of 93 percent. A z-score of -1.00 is associated with a probability of adequacy of 15 percent. Table 1 lists a selection of z-scores and their associated probabilities. It should be noted that not all data will form a normal distribution. For example, a “skewed” distribution is one where the curve has one tail longer than the other end. If the data do not form a normal distribution, then the properties of the normal distribution do not apply.

**TABLE 1 Probability of Adequacy for Selected Z-Scores**

z-score	Probability of Adequacy
2.00	0.98
1.65	0.95
1.50	0.93
1.25	0.90
1.00	0.85
0.86	0.80
0.68	0.75
0.50	0.70
0.00	0.50
-0.50	0.30
-0.85	0.20
-1.00	0.15

## Applying the DRIs Makes Use of Two Distributions

In applying the DRIs, two distributions are used simultaneously. The first is the distribution of requirements. The second is the distribution of intakes.

### REQUIREMENT DISTRIBUTION

The distribution of requirements is the distribution upon which the DRIs (specifically the EAR and RDA) are based. This distribution reflects the variability in requirements between individuals. Variability exists because not all individuals have the same requirement for a nutrient. For nutrients where requirements are normally distributed, the EAR is located at the mean/median of the distribution. The RDA is located at 2 standard deviations above the mean, the level at which 97.5 percent of requirements should be met.

### INTAKE DISTRIBUTION

The distribution of intakes is obtained from observed or reported nutrient intakes gathered through dietary assessment methods such as 24-hour recalls. A 24-hour recall is a detailed description of all foods and beverages consumed in the previous 24-hour period. Nutrient intake from supplements should also be collected. When more than one 24-hour recall is collected, intake data can reflect the day-to-day variability within an individual that occurs because different foods are eaten on different days.

When working with individuals, this variability is taken into account in the formulas used for assessment. When working with groups, statistical procedures should be used to adjust the distribution of observed intakes by partially removing the day-to-day variability in individual intakes so that the adjusted distribution more closely reflects a usual intake distribution.

Usual intake is an important concept in application of the DRIs. Usual intake is the average intake over a long period of time. It is seldom possible to accurately measure long-term usual intake due to day-to-day variation in intakes as well as measurement errors. Therefore, mean observed intakes (over at least two non-consecutive days or three consecutive days) are used to estimate usual intake.

## **Overlap of the Requirement Distribution and the Intake Distribution**

The requirement and intake distributions can overlap to varying degrees. In some cases, the two distributions will barely intersect, if at all (see Figure 3, Panel A), and in others there may be a lot of overlap between intakes and requirements (see Figure 3, Panel B).

In applying the DRIs to assessment, the distribution of intakes is compared to the distribution of requirements and inferences are made about the degree of adequacy. In dietary planning, efforts are made to ensure that the distribution of intakes is adequate relative to the distribution of requirements.

## **WORKING WITH INDIVIDUALS**

### **How to Assess the Nutrient Intakes of an Individual**

The goal of assessing an individual's nutrient intake is to determine if that intake is meeting the person's nutrient requirements. Assessment of dietary adequacy for an individual is difficult because of the imprecision involved in estimating an individual's usual intake and the lack of knowledge of an individual's actual nutrient requirements. Interpreting nutrient intake data in relation to the DRIs can enhance the assessment of an individual's diet; however, the information obtained must be interpreted cautiously because an individual's true usual intake and true requirements must be estimated, and assessment of dietary adequacy is only one component of a nutritional status assessment. Ideally, intake data are combined with clinical, biochemical, or anthropometric information to provide a valid assessment of nutritional status.

Recognizing the inherent limitations and variability in dietary intakes and requirements is a major step forward in nutrition. The reports on using the DRIs for assessment and planning have provided a method with which one can

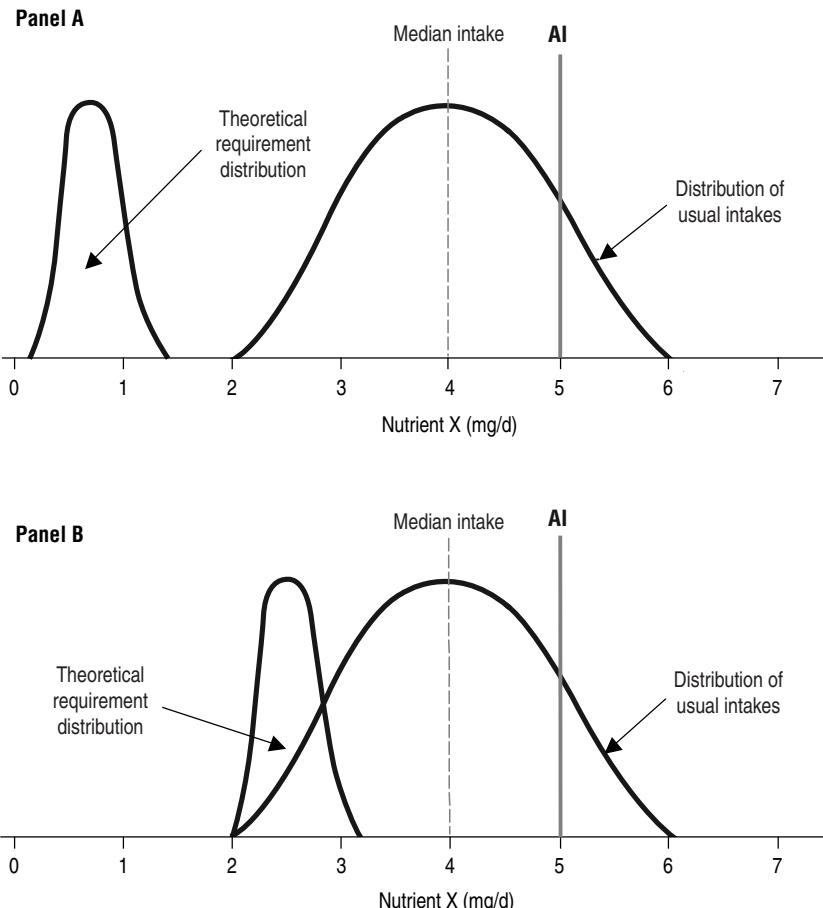
**PART I: APPLYING THE DIETARY REFERENCE INTAKES**

FIGURE 3 *Overlap of requirement and intake distributions varies.*

estimate the degree of confidence that an individual's intake meets his or her requirement. There are also equations that have been developed to estimate the degree of confidence that an individual's intake is above the AI, and below the Tolerable Upper Intake Level (UL).

It is important to keep in mind that the DRIs are estimates based on available data, and that even when an EAR, RDA, and UL for a nutrient are provided for a life stage and gender group, there is considerable uncertainty about these values. Because information on both dietary intakes and requirements are estimated, it is very difficult to exactly determine whether an individual's diet meets his or her individual requirement, even with the statistical approaches described

in this chapter. Thus, assessment of dietary intakes should be used as only one part of a nutritional assessment, and the results must be kept in context. Nutrient intake data should always be considered in combination with other information, such as anthropometric measurements, biochemical indices, diagnoses, clinical status, and other factors. Dietary adequacy should be assessed and diet plans formulated based on the totality of evidence, and not on dietary intake data alone.

### **ESTIMATING AN INDIVIDUAL'S USUAL INTAKE AND REQUIREMENT**

To conduct a dietary assessment, information is needed on both dietary intakes and dietary requirements. Information on dietary intake of individuals is usually gathered through food records or dietary recalls, and the requirement estimate is provided through the DRI process. In all cases the individual's usual intake and true requirement can only be approximated.

#### *Estimation of Usual Intake*

Obtaining accurate information on dietary intakes is challenging for a number of reasons, including the accuracy of dietary assessment techniques, as well as the challenges related to variability in intakes. The strongest methods for dietary assessment of nutrient adequacy are 24-hour recalls, diet records, or quantitative diet histories. Even so, the literature indicates that a sizeable proportion of individuals systematically misreport their dietary intakes, with the tendency toward underreporting (particularly for energy and percentage of energy from fat). It is unclear how this affects the accuracy of self-reported intakes of nutrients. Well-accepted, validated methods to statistically correct for the effects of underreporting are presently lacking.

There is also large day-to-day variation within a given individual's intake due to factors such as variation in appetite, food choices, day of the week, and season. The result is that the calculation of dietary intake from one or even several days of intake may give an inaccurate estimate of that individual's usual nutrient intake, especially if food choices vary greatly from one day to the next. Thus, observed dietary intake is probably not the same as the long-term usual intake of an individual. However, the observed mean intake is still the best available estimate of dietary intake, and can still be used providing that it is recognized there is an amount of variability associated with that best estimate.

#### *Estimation of Requirement*

It is nearly impossible to determine what an individual's exact requirement for a nutrient is, unless that individual has participated in a requirement study.

Therefore, the fall-back assumption is that the individual's requirement will be close to the average, in which case the EAR is the best estimate for an individual's unobservable requirement. It is important to note that there is variation in nutrient requirements between different individuals, and this needs to be taken into account when conducting an assessment.

## **Using a Qualitative Approach to Assess an Individual's Nutrient Intake**

Many users of the DRIs may find a qualitative assessment of an individual's nutrient intakes to be useful. When conducting this type of descriptive assessment, it is important to keep in mind the limitations associated with the estimation of both intakes and requirements.

For nutrients with an EAR and RDA:

- Observed mean intake below the EAR very likely needs to be improved (because the probability of adequacy is 50 percent or less).
- Observed mean intake between the EAR and the RDA probably needs to be improved (because the probability of adequacy is more than 50 percent but less than 97.5 percent).
- Intakes below the RDA cannot be assumed to be inadequate because the RDA by definition exceeds the actual requirements of all but 2–3 percent of the population; many with intakes below the RDA may be meeting their individual requirements.
- The likelihood of nutrient inadequacy increases as usual intake falls further below the RDA.
- Only if intakes have been observed for a large number of days and are at or above the RDA should one have a high level of confidence that the intake is adequate.

For nutrients with an Adequate Intake (AI):

- If observed mean intake equals or exceeds the AI, it can be concluded that the diet is almost certainly adequate.
- If, however, observed mean intake falls below the AI, no estimate can be made about the probability of nutrient inadequacy.
- Professional judgment, based on additional types of information about the individual, should be exercised when interpreting intakes below the AI.

For nutrients with a UL:

- Observed mean intake less than the UL is likely to be safe.
- Observed mean intake equal to or greater than the UL may indicate a potential risk of adverse effects. The higher the intake in comparison to the UL, the greater the potential risk.

For nutrients with an Acceptable Macronutrient Distribution Range (AMDR):

- Observed mean intake between the lower and upper bound of the AMDR is within the acceptable range.
- Observed mean intake below the lower bound or above the upper bound of the AMDR may heighten concern for possible adverse consequences.

For energy:

- Body mass index (BMI) should be used to assess the adequacy of energy intake, rather than a comparison to the Estimated Energy Requirement (EER).

## **Using a Quantitative Approach to Assess an Individual's Nutrient Intake**

An approach has been developed that statistically estimates the level of confidence that an individual's usual intake is above an individual's requirement, or below the UL. The equations developed for the assessment of individuals are based on the principles of hypothesis testing and levels of confidence based on a normal distribution curve.

The equations proposed here are not applicable to all nutrients because they assume a normal distribution of daily intakes and requirements. For nutrients for which a distribution is skewed (such as iron requirements of menstruating women, or dietary intakes of vitamin A, vitamin B<sub>12</sub>, vitamin C, and vitamin E), a different methodology needs to be developed. For these nutrients, individual assessment should continue to place emphasis on other types of information available.

### **NUTRIENTS WITH AN EAR**

For nutrients with an EAR, a z-score is calculated using the following equation:

$$z\text{-score} = \frac{\text{mean observed intake} - \text{EAR}}{\sqrt{[(\text{SD of requirement})^2 + (\text{within-person SD})^2 / \text{number of days of intake records}]}}$$

The use of this equation requires the following information:

- Mean observed intake: The mean nutrient intake of an individual is the best estimate of an individual's usual intake.
- EAR: The EAR is the best estimate of an individual's requirement for a nutrient.
- SD (standard deviation) of requirement: This is the variation in requirements between individuals. It is calculated as the coefficient of variation (CV) times the EAR (see Appendix H).
- Within-person SD of intake: The variation in day-to-day nutrient intake within the individual is an indicator of how much observed intake may deviate from usual intake. (This has been estimated in the original DRI reports by using CSFII data; see Appendix I.)
- The number of days of intake records or recalls.

As illustrated in Box 2, the equation solves for a z-score on the normal distribution curve. Some z-scores and their associated probabilities are listed in Table 1. The larger the z-score, the larger the probability associated with that value. The numerator of the equation is the difference between the estimated intake and the estimated requirement. It can intuitively be seen that the higher an intake is compared to the requirement, the larger the numerator will be. The denominator of the equation is the term that incorporates all the variability. Thus, as the variability gets smaller, the z-score will get larger. Note that an increase in the number of days of records will lead to a decrease in the amount of variability.

### **NUTRIENTS WITH AN AI**

For nutrients with an AI it is not possible to estimate the requirement of individuals. The AI represents an intake (not a requirement) that is likely to exceed the actual requirements of almost all individuals in a life stage and gender group. In fact, the AI may even be higher than an RDA (if it was possible to calculate one).

When trying to compare an individual's intake to his or her requirement, the AI is not very useful because it is in excess of the median requirement, perhaps by a very large margin. Therefore, when intakes are compared to the AI, all that can be concluded is whether the intake is above the AI or not. It is possible to determine the confidence with which one can conclude that usual intake exceeds the AI using the following equation:

**BOX 2 Example: Using the Quantitative Approach for Individual Assessment for a Nutrient with an EAR**

Suppose a 40-year-old woman had a magnesium intake of 320 mg/day, based on 3 days of dietary records. The question is whether this observed mean intake of 320 mg/day indicates that her usual magnesium intake is adequate.

To determine the probability that her usual intake meets her requirement, the following data are used:

- The mean observed intake for this woman is 320 mg/day.
- The EAR for magnesium for women 31–50 years is 265 mg/day
- The SD of the requirement distribution for magnesium is 10 percent of the EAR (Appendix H), therefore 26.5 mg/day.
- The within-person SD (day-to-day variability) in magnesium intake for women this age is estimated to be 86 mg/day (Appendix I).
- There are 3 days of dietary records.

Solving for the z-score yields:

$$z\text{-score} = \frac{320 - 265}{\sqrt{(26.5)^2 + (86)^2 / 3}} = \frac{55}{56} = 0.98 \approx 1.0$$

Table 1 lists a selection of and their associated probabilities. Looking up a z-score of 1.0, it can be seen that 85% probability of correctly concluding that this intake is adequate for a woman in this age category.

$$z\text{-score} = \frac{\text{mean observed intake} - \text{AI}}{\text{within-person SD} / \sqrt{\text{number of days of intake records}}}$$

The use of this equation requires the following information:

- Mean Observed Intake: The individual's mean observed intake
- AI: The AI for a similar life stage and gender group

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- Within-person SD of intake: The variation in day-to-day nutrient intake within the individual is an indicator of how much observed intake may deviate from usual intake (see Appendix I)
- The number of days of intake records or recalls

Solving for the equation gives the confidence with which one can conclude that usual intake is greater than the AI. If an individual's intake equals or exceeds the AI, it can be concluded that the diet is almost certainly adequate. However, if the calculation does not result in the conclusion that there is a high probability that the usual intake is larger than the AI, it cannot be inferred that intake is inadequate. Professional judgment, based on additional types of information about the individual, should be exercised when interpreting intakes below the AI.

### NUTRIENTS WITH A UL

The UL can be used to assess the likelihood that an individual may be at risk of adverse effects from high intakes of that nutrient. An equation has been determined to assess the probability that usual intake is below the UL given the mean observed intake. This equation is useful because even when mean observed intake is less than the UL, it cannot always be concluded with the desired amount of accuracy that usual intake is also below the UL (due to the variability associated with observed intake). This is particularly the case when the observed mean intake is a value close to that of the UL (as could be the case when considering intake from food plus supplements).

When using a UL to assess a person's nutrient intake, it is important to know whether the UL applies to intake from all sources or just from specific sources, such as supplements, fortified foods, or pharmacological preparations. The equation is as follows:

$$z\text{-score} = \frac{\text{mean observed intake} - \text{UL}}{\text{within-person SD} / \sqrt{\text{number of days of intake records}}}$$

The use of this equation requires the following information:

- Mean Observed Intake: The individual's mean observed intake (from applicable sources)
- UL: The UL for a similar life stage and gender group
- The within-person SD of intake: The variation in day-to-day nutrient intake within the individual is an indicator of how much observed intake may deviate from usual intake (see Appendix I)
- The number of days of intake records or recalls

Solving for the equation yields the confidence with which one can conclude that usual intake is less than the UL. Intakes less than the UL are likely to be safe; and intakes equal to or greater than the UL may indicate a potential risk of adverse effects. The higher the intake in comparison to the UL, the greater the potential risk.

The consequences associated with nutrient excess vary for different nutrients. It should also be noted that the UL does not apply to individuals who are consuming high intakes of nutrient on the advice of a physician who is monitoring the nutritional status of the individual.

### **NUTRIENTS WITH AN AMDR**

The AMDRs represent intakes of macronutrients that minimize the potential for chronic disease over the long term, permit essential nutrients to be consumed at adequate levels, and are associated with adequate energy intake and physical activity to maintain energy balance. To estimate the degree of confidence that an individual's diet falls within the AMDR, the equations developed for the AI and the UL can be used. The equation for the AI can be used to determine the degree of confidence that intake is above the lower bound of the AMDR, and the equation for the UL can be used to determine the degree of confidence that intake is below the upper bound of the AMDR.

Practically, observed mean intake between the lower and upper bounds of the AMDR is within the acceptable range. Observed mean intake below the lower bound or above the upper bound of the AMDR may heighten concern for possible adverse consequences.

### **ENERGY**

Theoretically, the usual energy intake of an individual could be compared with his or her requirement to maintain current weight with a certain level of physical activity, as estimated using the EER equations. However, by definition, the EER provides an estimate that is the midpoint of the range within which the energy expenditure of an individual could vary, and the individual's actual expenditure could be considerably above or below this estimated midpoint. Accordingly, comparing an individual's intake with the calculated average expenditure is essentially meaningless because of the difficulty in interpreting the result.

In contrast, BMI provides a useful indicator of the adequacy of usual energy intake in relation to usual energy expenditure. A BMI within the normal range of 18.5 up to 25 kg/m<sup>2</sup> (for adults) indicates that energy intake is adequate relative to expenditure. A BMI below the normal range indicates inadequate energy intake, whereas a BMI above the normal range is indicative of excessive energy intake.

**PART I: APPLYING THE DIETARY REFERENCE INTAKES**

## Quantitative vs. Qualitative Approaches to Dietary Assessment of Individuals

Box 2 provides a brief example of a quantitative assessment for a nutrient (magnesium) with an EAR. A qualitative assessment could be done using the same mean intake of 320 mg/day. This value is higher than the EAR (265 mg/day) and equal to the RDA (320 mg/day). Thus, it would be assumed that the woman's intake was almost certainly adequate, when in fact there is only 85 percent confidence that this intake is adequate.

The shortcoming of the qualitative method is that it does not incorporate any variability at all. If the variability in magnesium intake was even larger than 86 mg/day, the probability that an intake of 320 mg is adequate for this woman would be even lower than 85 percent, but the result of the qualitative assessment would not change at all.

For this reason it is strongly encouraged that the statistical method be the method of choice when assessing nutrient adequacy, because even an intake that looks as though it is at the upper end of the distribution (e.g., at or above the RDA) may have an unacceptably low probability of being adequate depending on the amount of variability associated with the estimated intake.

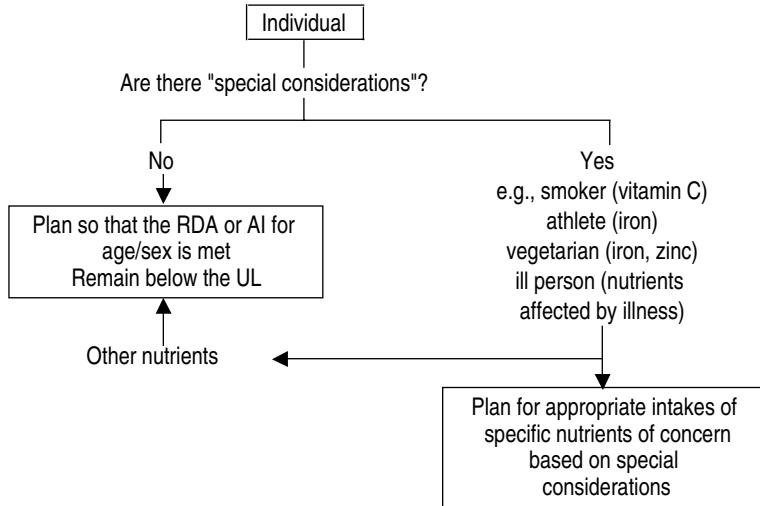
## Using the DRIs to Plan an Individual's Diet

The goal for individual planning is to ensure that the diet, as eaten, has an acceptably low risk of nutrient inadequacy while simultaneously minimizing the risk of nutrient excess. More simply put, the goal is to plan an individual's intake that will result in a low risk of that person not meeting his or her requirements.

For nutrients that have an RDA, this value should be used as a guide for planning. For nutrients with an AI, the AI should be used. The EAR should not be used for planning an individual's nutrient intake because, by definition, a diet that provides the EAR of a nutrient has a 50 percent likelihood of not meeting an individual's requirement.

Planning diets for individuals involves two steps: First, appropriate nutrient intake goals must be set, taking into account the various factors that may affect a person's nutrient needs. For example, a person who smokes may have greater needs for vitamin C. Second, the diet developed should be one that the individual can afford and will want to consume. Food-based education tools such as the United States Department of Agriculture's (USDA's) Food Guide Pyramid and Canada's Food Guide are commonly used by practitioners to teach individuals how to plan healthful diets that are adequate in nutrients.

Dietary planning involves using the DRIs to set goals for what intakes should be. When planning for nutrients such as vitamins, minerals, and protein, a low



*FIGURE 4 Decision tree for planning diets of individuals.*

risk of inadequacy is planned for by meeting the RDA or AI, and a low risk of excess is planned by remaining below the UL.

In some cases it may be appropriate to use a target other than the RDA for individuals since the DRIs apply only to the apparently healthy population. Special guidance should be provided for those with greatly increased or decreased needs. Although the RDA or AI may serve as the basis for such guidance, qualified health care personnel should make the necessary adaptations for specific situations. Figure 4 is a flow chart that describes decisions that need to be made during the planning process.

### PLANNING NUTRIENT INTAKES FOR AN INDIVIDUAL USING THE RDA

The RDA may be used for planning nutrient intakes that result in an acceptably low probability of inadequacy for an individual. The RDA is intended to encompass the normal biological variation in the nutrient requirements of individuals. It is set at a level that meets or exceeds the actual nutrient requirements of 97–98 percent of individuals in a given life stage and gender group. This level of intake, at which there is a 2–3 percent probability of an individual not meeting his or her requirement, has traditionally been adopted as the appropriate reference for planning intakes for individuals.

There are neither adverse effects nor documented benefits associated with exceeding the RDA, provided that intake remains below the UL. When coun-

**PART I: APPLYING THE DIETARY REFERENCE INTAKES**

seling an individual, a practitioner must consider whether there is any recognizable benefit to increasing an individual's current intake level. The likelihood of the benefit must be weighed against the cost, monetary and otherwise, likely to be incurred by increasing the intake level.

If intake levels other than the RDA are chosen, they should be explicitly justified. For example, for women between the ages of 19 and 30 years, the RDA for iron is 18 mg/day, which was set to cover the needs of women with the highest menstrual blood losses. A particular woman might feel that her menstrual losses are light and, accordingly, she may be willing to accept a 10 percent risk of not meeting her requirement and thus would have an intake goal of only 13 mg/day (see Part III, "Iron"; Part IV, "Appendix G").

The EAR is not recommended for planning nutrient intakes of individuals. Despite the fact that the EAR is the best estimate of an individual's requirement, by definition, half the individuals in a group have requirements that are higher than the EAR. Accordingly, an intake at the level of the EAR is associated with a probability of inadequacy of 50 percent and is not suitable as a goal for planning. As intake increases above the EAR, the probability of inadequacy decreases and reaches 2–3 percent with intakes at the RDA.

**PLANNING NUTRIENT INTAKES FOR AN INDIVIDUAL USING THE AI**

When scientific evidence is not sufficient to set an EAR and thus calculate an RDA for a particular nutrient, an AI is usually developed. Under these circumstances, the AI is the recommended target for planning the nutrient intakes of individuals. Although greater uncertainty exists in determining the probability of inadequacy for a nutrient that has an AI instead of an RDA, the AI provides a useful basis for planning. Intake at the level of the AI is likely to meet or exceed an individual's requirement, although the possibility still exists that it could fail to meet the requirements of some individuals. The probability of inadequacy associated with a failure to achieve the AI is unknown.

**PLANNING NUTRIENT INTAKES FOR AN INDIVIDUAL USING THE UL**

The UL can be used to plan intakes that have a low probability of adverse effects resulting from excessive consumption. The UL is not a recommended level of intake, but rather an amount that can be biologically tolerated with no apparent risk of adverse effects by almost all healthy people. Thus, the goal for planning an individual's diet is to not exceed the UL. It is important to note that for many nutrients the UL applies to intake from all sources, whereas for some it may only apply to intake from certain sources, such as supplements, fortificants, and pharmacological preparations. (The profiles of individual nutrients found in Part III provide this information.)

For most nutrients, intakes at or above the UL would rarely be attained from unfortified food alone.

### **PLANNING NUTRIENT INTAKES FOR AN INDIVIDUAL USING THE AMDR**

In addition to meeting the RDA or AI, and remaining below the UL, an individual's intake of macronutrients should be planned so that carbohydrate, fat, and protein are within their respective acceptable ranges.

### **PLANNING ENERGY INTAKES FOR AN INDIVIDUAL**

The underlying objective of planning for energy is similar to planning for other nutrients: to attain an acceptably low risk of inadequacy and of excess. However, the approach to planning for energy differs substantially from planning for other nutrients. When planning for individuals for nutrients such as vitamins and minerals, there are no adverse effects to consuming an intake above an individual requirement, provided intake remains below the UL. The situation for energy is quite different because for individuals who consume energy above their requirements and needs over long periods of time, weight gain will occur. This difference is reflected in the fact that there is no RDA for energy, as it would be inappropriate to recommend an intake that exceeded the requirement for a large number of individuals. Thus, the requirement for energy is expressed as an EER.

As explained in Part II, an EER is based on energy expenditure and is defined as the average dietary energy intake required to maintain current body weight and activity level (and to allow for growth or milk production, as appropriate) in healthy, normal-weight individuals of specified age, sex, height, weight, and physical activity level (PAL) that is consistent with good health.

The best way to plan for energy intake of individuals is to consider their body weight or BMI. When body weight is stable in normal-weight individuals (BMI of 18.5 kg/m<sup>2</sup> up to 25 kg/m<sup>2</sup>), the energy requirement is equal to total energy expenditure and is also the usual intake.

The prediction equations to calculate an EER can be used as a starting point for planning (see Part II, "Energy"). They are only a starting point because energy expenditures vary from one individual to another even though their characteristics may be similar. The EER is the midpoint of a range of energy requirements. By definition, the EER would be expected to underestimate the true energy expenditure 50 percent of the time and to overestimate it 50 percent of the time. These errors in estimation would eventually lead to a gain or loss in body weight, which would be undesirable when the goal is to maintain a healthy weight. Body weight should be monitored and the amount of energy in the diet adjusted up or down from the EER as required to maintain an appro-

priate body weight. Additionally, self-reported energy intake should not be relied on to determine a person's energy needs, since underreporting of intakes is a serious and pervasive problem.

## **Developing Dietary Plans for an Individual**

Once appropriate nutrient intake goals have been identified for the individual, these must be translated into a dietary plan that is acceptable to the individual. This is most frequently accomplished using nutrient-based food guidance systems such as national food guides.

## **Special Considerations**

Factors such as nutrient bioavailability and physiological, lifestyle, and health characteristics may alter nutrient requirements and lead to the need for adjustments in DRI values when planning dietary intakes. Table 2 summarizes some common special considerations.

**TABLE 2 Common Reasons for Adjustment in DRI Values When Planning Dietary Intake**

Consideration	Nutrient	Adjustment
Recommended consumption from synthetic sources	Folic acid for women of childbearing age	It is recommended that all women capable of becoming pregnant take 400 µg folic acid every day from fortified foods, supplements, or both, in addition to the amount of food folate found in a healthful diet.
	Vitamin B <sub>12</sub> for those older than 50 years of age	It is advisable for those older than 50 years to meet the RDA mainly by consuming foods fortified with vitamin B <sub>12</sub> or a supplement containing vitamin B <sub>12</sub> .
Smoking	Vitamin C	The requirement for smokers is increased by 35 mg/day.
Bioavailability in vegetarian diets	Iron	The requirement for iron is 1.8 times higher for vegetarians due to the lower bioavailability of iron from a vegetarian diet.
	Zinc	The requirement for zinc may be as much as 50 percent greater for vegetarians, particularly for strict vegetarians whose major food staples are grains and legumes.
Age of menstruation	Iron (it is assumed that girls younger than 14 years do not menstruate and that girls 14 years and older do menstruate)	If menstruation occurs prior to age 14, an additional amount (about 2.5 mg/day) would be needed to cover menstrual blood losses. Conversely, girls ages 14 and above who are not yet menstruating can subtract 2.5 mg from the RDA for this age group.
Athletes engaged in regular intense exercise	Iron	Average requirements for iron may range from 30 to 70 percent above those for normally active individuals.
Recommendation set according to reference weight	Protein	Recommendation is set in g/kg/day. RDA for adults is 0.80 g/kg/day.
Recommendation set per 1,000 kcal	Fiber	Recommendation is 14 g/1,000 kcal.

**PART I: APPLYING THE DIETARY REFERENCE INTAKES****KEY POINTS FOR WORKING WITH INDIVIDUALS****ASSESSING NUTRIENT INTAKES**

- ✓ The goal of assessing an individual's nutrient intake is to determine if that intake is meeting his or her nutrient requirements.
- ✓ Assessment requires using the individual's observed or reported mean intake as an estimate of usual intake and using the EAR of the appropriate life stage and gender group as an estimate of the individual's requirement.
- ✓ For nutrients with an EAR, a statistical equation can be applied to assess the likelihood of adequacy. This equation yields a z-score that allows a practitioner to determine a probability value that reflects the degree of confidence that the person's usual intake meets his or her requirement.
- ✓ For nutrients with an AI, a statistical equation can be applied to determine whether usual intake is at or above the AI, in which case intake is deemed adequate. Intakes below the AI cannot be assessed.
- ✓ For nutrients with a UL, a statistical equation can be applied to determine whether usual intake falls below the UL, in which case the person is assessed as having a low risk of adverse effects related to excessive intake.
- ✓ The RDA should not be used for assessing an individual's intake.
- ✓ In all cases, individual assessments should be cautiously interpreted, preferably in combination with other information on factors that can affect nutritional status, such as anthropometric data, biochemical measurements, dietary patterns, lifestyle habits, and the presence of disease.

**PLANNING NUTRIENT INTAKES**

- ✓ The goal of planning nutrient intakes for individuals is to achieve a low probability of inadequacy while not exceeding the UL for each nutrient.
- ✓ Planning diets for individuals involves two steps: First, appropriate nutrient goals must be set, taking into account the various factors that may affect a person's nutrient needs. Second, the diet developed should be one that the individual can afford and will want to consume.

- ✓ For nutrients with an EAR and an RDA, the probability of inadequacy is 50 percent at the EAR and 2–3 percent at the RDA. Thus, the RDA is often used as a guide for planning for individuals. If an RDA is not available, the AI should be used as a guide for planning nutrient intake.
- ✓ For nutrients with a UL, this value should be used as the level not to exceed.
- ✓ An individual's intake of macronutrients should be planned so that carbohydrate, fat, and protein are within their respective AMDRs.
- ✓ The best way to plan for energy intake of individuals is to consider the healthfulness of their body weight or BMI.

## WORKING WITH GROUPS

Although some nutrition professionals primarily work with individuals, others need to be able to assess and plan the nutrient intakes of groups. Examples of such groups include nursing home residents, research study participants, and children attending residential schools. This section describes ways to assess and plan nutrient intakes of groups.

### How to Assess the Nutrient Intakes of a Group

The goal of assessing the nutrient intakes of groups is to determine the prevalence of inadequate (or excessive) nutrient intakes within a particular group of individuals (see Box 1 for definitions). Within any given group, even a homogeneous group such as individuals in the same life stage and gender group, variability will exist among the different individuals' nutrient needs and nutrient intakes. To accurately determine the proportion of a group that has a usual intake of a nutrient that is less than their requirement, information on both the distribution of usual intakes and the distribution of requirements in the group is needed.

Several characteristics of dietary intake data make estimating the distribution of usual intakes for a group challenging. When single 24-hour recalls or diet records are obtained from members of a group, the variability of the nutrient intakes will reflect both differences between individuals as well as differences within individuals (i.e., on any given day, a particular individual could eat much more or much less of a nutrient than usual).

To obtain a distribution of usual intakes for a group, the distribution of observed intakes (i.e., the intake obtained from a single 24-hour recall) must

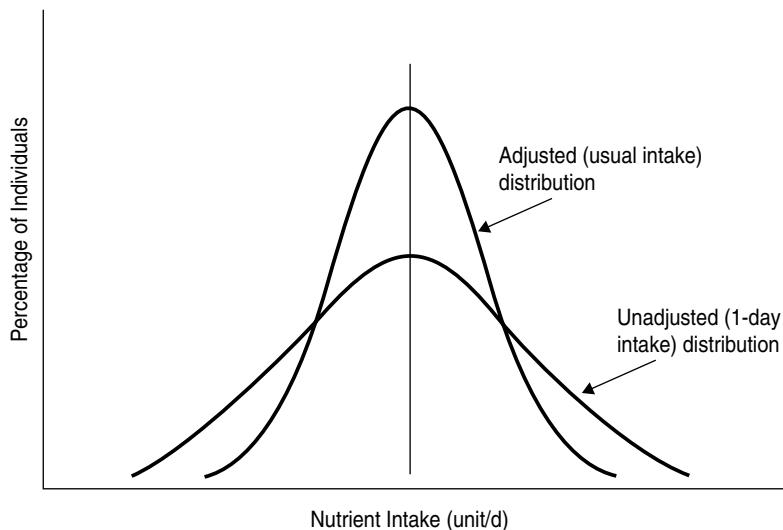
**PART I: APPLYING THE DIETARY REFERENCE INTAKES**

FIGURE 5 Comparison of 1-day and usual intakes.

be statistically adjusted to remove the effects of within-person variability, so that the distribution reflects only between-person variability. To do this, at least two 24-hour recalls or diet records obtained on nonconsecutive days (or at least three days of data from consecutive days) are needed from a representative subsample of the group. When this adjustment is performed, the intake distribution narrows (i.e., the tails of the distribution draw closer to the center). If intake distributions are not properly adjusted, the prevalence of nutrient inadequacy will be incorrectly estimated and is usually overestimated (see Figure 5).

Several methods to obtain usual intake distributions are available. The National Research Council (NRC) and Iowa State University have both developed software programs for adjusting intake distributions. Further information is available at <http://cssm.iastate.edu/software/side.html>. Although these methods will adjust for variability in day-to-day intakes, they do not make up for inaccuracies in reported or observed intakes.

The summary below explains how the DRIs are appropriately used in the assessment of a group's nutrient intakes. Further explanation of the approach and the methods used are provided in the sections that follow:

- For nutrients with an EAR, the EAR can be used to estimate the prevalence of inadequate intakes using the probability approach or a shortcut derived from the probability approach called the EAR cut-point method.
- The RDA is inappropriate for assessing nutrient intakes of groups because the RDA is the intake level that exceeds the requirements of a large proportion of individuals in a group. Consequently, estimating the prevalence of nutrient inadequacy in a group by determining the proportion of individuals with intakes below the RDA leads to an overestimation of the true prevalence of inadequacy.
- For nutrients without an EAR, the AI is instead used. Groups with mean or median intakes at or above the AI can generally be assumed to have a low prevalence of inadequate intakes.
- For nutrients with a UL, this value can be used to estimate the proportion of a group at potential risk of adverse effects from excessive nutrient intake.
- For nutrients with an AMDR, the proportion of the group that falls below, within, and above the AMDR can be used to assess population adherence to the recommendations and to determine the proportion of the population that is outside the range. If significant proportions of the population fall outside the range, concern could be heightened for possible adverse consequences.
- For energy, the distribution of BMI within a group can be assessed, and the proportions of the group with BMIs below, within, and above the desirable range would reflect the proportions with inadequate, adequate, and excessive energy intakes.

### **USING THE PROBABILITY APPROACH TO ASSESS PREVALENCE OF NUTRIENT INADEQUACY IN A GROUP**

The probability approach is a statistical method that involves determining the probability of inadequacy of the usual intake level for each person in the group and then averaging these individual probabilities across the group to obtain an estimate of the group's prevalence of inadequacy. This method depends on two key assumptions: that intakes and requirements are independent and thus no correlation exists between usual intakes and requirements (this is thought to be true for most nutrients, although it is not known to be true for energy) and that the distribution of requirements for the nutrient in question is known. This method then uses statistical equations to estimate the prevalence of inadequacy.

Case studies one and two at the end of the chapter illustrate the use of the probability approach. Practically, this approach will most likely be used only when the EAR cut-point method cannot be used.

## USING THE EAR CUT-POINT METHOD TO ASSESS PREVALENCE OF NUTRIENT INADEQUACY IN A GROUP

The EAR cut-point method is a shortcut derived from the probability approach. When certain conditions are satisfied, the proportion of the group with intakes below the EAR will be similar to the proportion that does not meet their requirement. The conditions (assumptions) that must be satisfied to use the EAR cut-point method are:

- *Intakes and requirements must not be correlated:* This is thought to be true for most nutrients, but is known *not* to be true for energy, as individuals with higher energy requirements have higher energy intakes.
- *The distribution of requirements must be symmetrical:* This is thought to be true for most nutrients, but is known not to be true for iron for menstruating women. Blood (and therefore iron) losses during menstrual flow greatly vary among women, and some women have unusually high losses. As a result, the distribution of iron requirements for this life stage and gender group is skewed rather than symmetrical, and the EAR cut-point method cannot be used to assess the prevalence of inadequacy. Instead, the probability approach should be used, as shown in case study two.
- *The distribution of intakes must be more variable than the distribution of requirements:* Stated another way, the SD of the intake distribution is greater than the SD of the requirement distribution. This is thought to be true among groups of free-living individuals. Note, however, that the assumption that intakes are more variable than requirements might not hold for groups of similar individuals who were fed similar diets (e.g., prison inmates). If the assumption is not met, the probability method can be used instead of the EAR cut-point method.

The reasons that the EAR cut-point method can approximate the prevalence of inadequacy in a group as determined by the full probability method are explained below and illustrated in the third case study at the end of the chapter.

1. Although the probability of inadequacy exceeds 50 percent when usual intakes are below the EAR, not everyone with an intake below the EAR fails to meet his or her own requirement: Some individuals with lower-than-average requirements will have adequate intakes (their usual intake, although below the EAR, exceeds their own requirement).
2. Similarly, although the probability of inadequacy is less than 50 percent when usual intakes are above the EAR, not everyone with intakes above the EAR meets their own requirement. Some individuals with higher-than-average

requirements will have inadequate intakes (their usual intake, although above the EAR, is below their own requirement).

3. When the requirement distribution is symmetrical, when intakes are more variable than requirements, and when intakes and requirements are independent, the proportion of the group described in item 1 cancels out the proportion described in item 2. The prevalence of inadequacy in the group can thus be approximated by the proportion with usual intakes below the EAR. See Box 3 for an example.

### **THE RDA IS INAPPROPRIATE FOR ASSESSING GROUP NUTRIENT INTAKES**

It is not appropriate to use the RDA to assess nutrient intakes of groups. In the past, the RDA, or the RNI in Canada, has been used incorrectly to make inferences about nutrient inadequacy in groups by using the RDA as a cut-point or comparing mean or median intakes with the RDA.

The RDA should not be used as a cut-point because it overestimates the requirements of 97.5 percent of the population. The mean or median intake of a group should not be compared with the RDA to assess nutrient adequacy in a group because the prevalence of inadequacy depends on the distribution of usual intakes, and this is not taken into account when only the mean or median is used. For example, as shown in Box 3, women 51 to 70 years of age had a median dietary vitamin B<sub>6</sub> intake of 1.51 mg/day in the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994). Comparing this median intake with the RDA for this group, 1.5 mg/day, might lead one to believe that inadequate vitamin B<sub>6</sub> intake is not a problem. However, appropriate analysis of the data relative to the EAR reveals that the prevalence of inadequacy in this group is actually greater than 25 percent.

### **USING THE AI TO ASSESS A GROUP'S NUTRIENT INTAKES**

The AI has limited uses in assessing the nutrient intakes of groups. When an AI is set for a nutrient, it means that there was insufficient evidence to establish the distribution of requirements and thereby determine an EAR. For this reason, it is simply not possible to determine the proportion of a group with intakes below requirements. Accordingly, only limited inferences can be made about the adequacy of group intakes. If the median or mean intake of a group is at or above the AI, it can be assumed that the prevalence of inadequate intakes in the group is low.

If group median or mean intake is below the AI, nothing can be concluded about the prevalence of inadequacy. Again, this occurs because we do not know the requirement distribution, and whether its upper end (if it could be deter-

**BOX 3 Assessing Group Nutrient Intakes—The RDA Is Inappropriate**

The EAR for vitamin B<sub>6</sub> for women aged 51–70 years is 1.3 mg /day and the RDA is 1.5 mg/day. Shown below is a distribution of dietary vitamin B<sub>6</sub> intakes for a group of women 51–70 years of age. The distribution has been adjusted for individual variability using the method developed by the National Research Council. The data are from NHANES III.

**Selected Percentiles of Dietary Vitamin B<sub>6</sub> Intake, Women 51–70 Years of Age,  
NHANES III**

Percentile	5th	10th	15th	25th	50th	75th	85th	90th	95th
Vitamin B <sub>6</sub> intake (mg/day)									
	0.92	1.02	1.11	1.24	1.51	1.90	2.13	2.31	2.65

Comparing the median intake of 1.51 mg/day to the RDA of 1.5 mg/day for this group might lead one to believe that inadequate vitamin B<sub>6</sub> intake is not a problem. However, comparison of the distribution of usual intakes to the EAR cut-point shows that the EAR value of 1.3 mg/day falls somewhere between the 25th percentile and the 50th percentile of usual intakes. Thus, it can be concluded that greater than 25 percent of usual intakes are below the EAR cut-point and the prevalence of inadequacy in this group is estimated to be greater than 25 percent (but less than 50 percent).

mined) is relatively close to the AI or falls well below it. It follows from the above discussion that individuals with intakes below the AI cannot be assessed as having inadequate intakes. Although the proportion of a group with usual intakes below the AI could be determined, great care should be taken to avoid implying that this proportion does not meet their requirements (i.e., the AI should not be used as a cut-point in the way that the EAR may be).

**USING THE UL TO ASSESS A GROUP'S NUTRIENT INTAKES**

The UL can be used to estimate the proportion of a group with intakes above the UL and, therefore, at potential risk of adverse health effects from excess nutrient intake. The method for applying the UL is similar to the EAR cut-

point method in that the proportion of the group with intakes above the UL is determined.

Because ULs for nutrients are based on different sources of intake, the appropriate usual intake distribution must be used in the assessment. For some nutrients, such as fluoride, phosphorus, and vitamin C, the distribution of usual intakes would need to include intake from all sources. For others, such as magnesium, folate, niacin, and vitamin E, only the distribution of usual intakes from synthetic sources added to foods and from supplements (and in the case of magnesium, medications) would be needed.

Another issue to consider when interpreting the proportion of a group with intakes above the UL is that there is considerable uncertainty with regard to some of the ULs for children. In many cases, these ULs were established based on extrapolation from the ULs for adults or infants, and thus for some nutrients, this resulted in very small margins or an overlap between the adult RDA and the UL for young children. Surveys in the United States have revealed that young children have a high prevalence of intakes above the UL for nutrients such as vitamin A and zinc; however, few studies have been conducted in children to assess the effects of such intakes.

### **USING THE AMDR TO ASSESS A GROUP'S NUTRIENT INTAKE**

By determining the proportion of the group that falls below, within, and above the AMDR, it is possible to assess population adherence to the recommendations and to determine the proportion of the population that is outside the range. If significant proportions of the population fall outside the range, concern could be heightened for possible adverse consequences.

### **ASSESSING THE ENERGY ADEQUACY OF A GROUP'S DIET**

The probability approach and the EAR cut-point method do not work for assessing energy adequacy. This is because empirical evidence indicates a strong correlation between energy intake and energy requirement. This correlation most likely reflects either the regulation of energy intake to meet needs or the adjustment of energy expenditure to be consistent with intakes. Therefore, the use of BMI as a biological indicator is preferable. The distribution of BMI within a population group can be assessed, and the proportions of the group with BMIs below, within, and above the desirable range would reflect the proportions with inadequate, adequate, and excessive energy intakes.

### **How to Plan for the Nutrient Intakes of a Group**

The goal of planning nutrient intakes for groups is to achieve usual intakes in the group that meet the requirements of most individuals, but that are not

excessive. This can be challenging because the amount and selection of foods that group individuals eat will vary, even if the same meal is offered. Situations where group planning occurs include residential schools, prisons, military garrisons, hospitals, nursing homes, child nutrition programs, and food assistance programs.

When planning for groups, a practitioner should aim for a low prevalence of inadequate intakes. In the past, this may have involved considering the average intake of the group and comparing it with the RDA, which was inappropriate because even if a group's average intake meets the RDA, the prevalence of inadequacy is likely to be unacceptably high. This is because the variability in nutrient intakes among group members usually exceeds the variability in the requirements of group members, and it is the variability in requirements that is used to set the RDA.

Instead, the new DRIs present an approach to planning that involves consideration of the entire distribution of usual nutrient intakes within a group, rather than just the average intake of the group. The goal is that the distribution of usual nutrient intakes that results from the plan will have a low prevalence of inadequate or excessive intake, as defined by the proportion of individuals in the group with usual intakes less than the EAR or greater than the UL. An important caveat: By focusing explicitly on the distribution of nutrient intakes of a group as the goal of group planning, the framework presented here is, in many respects, a new paradigm, and it should be tested before being implemented in large-scale group-feeding situations.

To apply the framework presented here, an acceptable prevalence of inadequacy must be defined (a critical step on the part of the planner) and the distribution of usual intakes in the group must be estimated. As previously stated, this is accomplished by determining the distribution of reported or observed intakes, and performing a statistical adjustment to estimate the distribution of usual intakes. A target (desired) usual intake distribution can then be determined by positioning the distribution of usual intakes relative to the EAR to achieve the desired prevalence of inadequacy.

Because the goal of planning is to achieve a target distribution of usual intakes, assessment must occur (see “Probability Approach” and “EAR Cut-Point Method” earlier in the chapter). In most cases, planning group intakes is an ongoing process, in which planners set goals for usual intake, implement the plan, assess whether the goals have been achieved, and then accordingly modify their planning procedures.

Before describing how the different DRI values are appropriately used to plan intakes for groups, the next section explains the importance of a target usual intake distribution and how to estimate this distribution for nutrients with normal distributions and for nutrients with skewed distributions.

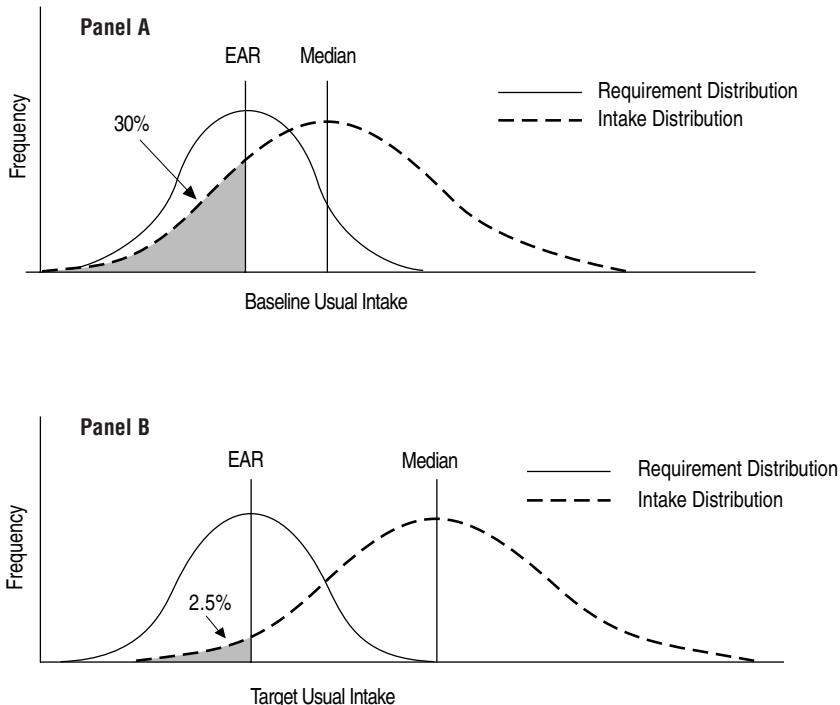
## What Is a Target Usual Nutrient Intake Distribution?

Suppose a practitioner is interested in planning a group diet with a high probability of nutrient adequacy (e.g., such that the prevalence of inadequacy in the group is no more than 2–3 percent). Given this target, and assuming that the EAR cut-point method can be used in the assessment, the usual intake distribution of the group should be positioned so that only 2–3 percent of the individuals in the group have usual intakes less than the EAR.

To achieve this goal of a low prevalence of nutrient inadequacy, it may be necessary to modify the baseline usual nutrient intake distribution. The change may be as simple as a shift (up or down) of the entire baseline distribution or it may include changes in both the location and the shape of the distribution. In either case, the appropriate changes to the baseline usual nutrient intake distribution are intended to result in the desired distribution of usual intakes. This desired distribution is referred to as the target usual nutrient intake distribution.

The simplest approach to determining the target usual nutrient intake distribution is to shift the baseline distribution, with the assumption that there will be no change in its shape. This is illustrated for a hypothetical nutrient in Figure 6. Panel A shows the baseline usual intake distribution, in which the prevalence of inadequate intakes (the percentage of the group below the EAR) is about 30 percent. If the planning goal were to attain a prevalence of inadequacy of no more than 2–3 percent, the target usual nutrient intake distribution could be achieved by simply shifting the baseline usual intake distribution up, as shown in Panel B.

The appropriate shift (up or down) can be calculated as the additional (or decreased) amount of the nutrient that must be consumed to achieve the prevalence of usual intakes below the EAR that is the planning goal. For example, the EAR for zinc for girls aged 9 to 13 years is 7 mg/day. Current data from the National Health and Nutrition Examination Survey (NHANES III, 1988–1994) show that about 10 percent of the girls have usual intakes below the EAR. If the goal were to plan intakes so that only 2–3 percent fell below the EAR, intakes would have to be increased. When the intervention is designed to increase everyone's usual zinc intake, then the amount of the increase can be calculated as the difference between the current intake at the second to third percentile, which is 6.2 mg/day, and the desired intake at the second to third percentile, which is the EAR of 7 mg/day. This difference is 0.8 mg/day, which means that the distribution of usual intakes needs to shift up by 0.8 mg/day in order to have only 2–3 percent of the girls with intakes below the EAR.

**PART I: APPLYING THE DIETARY REFERENCE INTAKES**

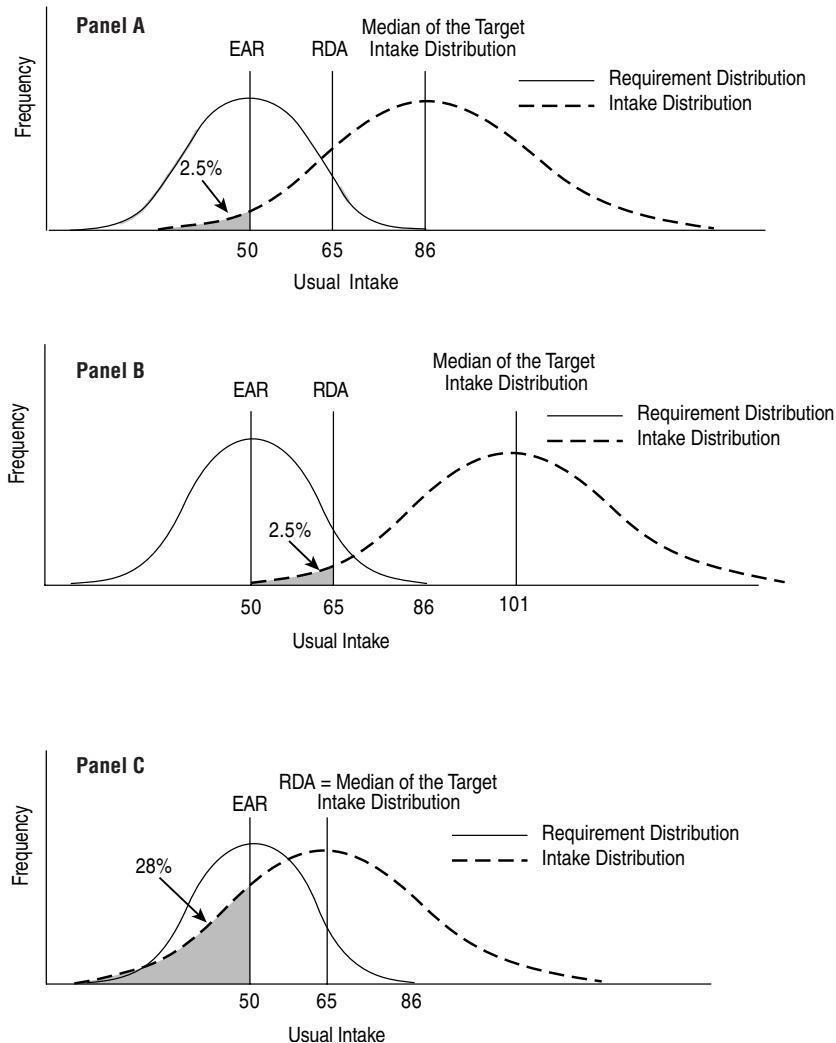
*FIGURE 6 Concept of a target usual intake distribution. Panel A shows the baseline usual nutrient intake distribution with 30 percent prevalence of inadequate intakes. Panel B shows the effect of shifting the baseline distribution to attain the target usual nutrient intake distribution of 2–3 percent inadequate intakes.*

#### HOW TO ESTIMATE THE TARGET INTAKE DISTRIBUTION FOR GROUPS WITH NORMAL INTAKE DISTRIBUTIONS

To set a target usual nutrient intake distribution with a selected prevalence of inadequacy for a specific group, it is useful to examine a simple example depicting a normal distribution of usual intake.

When it is known that the usual intake distribution of the group being assessed approximates normality, as depicted in all panels of Figure 7, the position of the target usual nutrient intake distribution can be estimated very simply with a table of selected areas under the normal distribution. The median (midpoint) of the target usual intake distribution can be determined using the following equation:

$$\text{EAR} + (Z \times \text{SD}_{\text{usual intake}})$$



**FIGURE 7** Target usual intake distributions. Panel A: Low group prevalence of inadequacy: 2.5 percent of the population has usual intake below the estimated average requirement. Panel B: Low individual risk of inadequacy: 2.5 percent of the population has usual intake below the RDA. Panel C: Higher group and individual risk of inadequacy: target median intake equals the RDA.

**PART I: APPLYING THE DIETARY REFERENCE INTAKES**

where Z comes from a table of areas under the curve of a normal distribution and  $SD_{usual\ intake}$  is the standard deviation of the intake distribution. Table 3 reproduces part of a table of z-scores.

For example, as shown in Panel of A of Figure 7, when the EAR is 50 units and the  $SD_{usual\ intake}$  is 18 units, a 2.5 percent prevalence of inadequacy ( $Z = 1.96$  at 2.5 percent) would be expected when the median intake was 86 units ( $86 = 50 + [1.96 \times 18]$ ). On the other hand, if a 5 percent prevalence of inadequacy were chosen, the calculated median intake would be 80 ( $80 = 50 + [1.65 \times 18]$ ), a lower value since more of the group would have intakes below the EAR.

### **HOW TO ESTIMATE THE TARGET INTAKE DISTRIBUTION FOR GROUPS WITH SKEWED INTAKE DISTRIBUTIONS**

The previous section described how to estimate a target distribution assuming a normal distribution of usual intakes within the group. However, in most cases, the usual intakes within a group are not normally distributed. Therefore, the  $SD_{usual\ intake}$  cannot be used to identify the position of the target usual nutrient intake distribution. Instead, the necessary approach is similar in principle to the one in the previous section, although it does not depend on the SD of usual intake and a z-score. A practitioner would first specify the acceptable prevalence of inadequate intake, and then position the usual intake distribution so

**TABLE 3 Setting the Target Median Intake<sup>a</sup> for Nutrients with Intake Distributions Approximating Normality: Selecting Z-Scores**

Acceptable Group Risk of Inadequate Intakes (%)	Z-Score: Multiplier for the Standard Deviation of Intake
0.05	3.27
0.5	2.57
1.0	2.33
1.5	2.17
<b>2.0</b>	<b>2.05</b>
<b>2.5</b>	<b>1.96</b>
<b>3.0</b>	<b>1.88</b>
5.0	1.65
10.0	1.28
15.0	1.03
25.0	0.68
50.0	0.00

<sup>a</sup> Target median intake = EAR + Z × SD<sub>usual intake</sub> where EAR = Estimated Average Requirement, Z = statistical tool to determine areas under the normal distribution, SD = standard deviation of intake.

that the percentile of usual intake associated with this specified prevalence of inadequate intake equals the EAR.

## **Using the DRIs to Plan a Group's Nutrient Intakes**

The summary below explains how DRIs are appropriately used in planning a group's nutrient intakes. Further details are provided in the sections that follow and in the case studies at the end of the chapter.

- For nutrients with an EAR and RDA, the EAR is used in conjunction with the usual nutrient intake distribution to plan for an acceptably low prevalence of inadequate intakes within the group. For most nutrients, the planning goal is to minimize the prevalence of intakes below the EAR. The RDA is not recommended for use in planning the nutrient intakes of groups.
- For nutrients without an EAR, the AI is used instead. The AI is used as the target for the mean, or median, intake of the group. The goal is to increase the group's mean or median intake to the level of the AI.
- For nutrients with a UL, this value is used to plan for an acceptably low prevalence of intakes at risk of being excessive.
- For nutrients with an AMDR, an additional goal of planning is to achieve a macronutrient distribution in which the intakes of most of the group fall within the AMDRs.
- For energy, the goal is for the group's mean intake to equal the EER. For energy, the estimated energy requirement of a reference individual or an average of estimated maintenance energy needs for the group members can be used in planning energy intake of groups.

### **USING THE EAR TO PLAN A GROUP'S NUTRIENT INTAKES**

For nutrients that have an EAR, this value is used in conjunction with the usual nutrient intake distribution to plan for an acceptably low prevalence of inadequate intakes within the group. For most nutrients, the planning goal is to minimize the prevalence of intakes below the EAR.

### **USING THE AI TO PLAN A GROUP'S NUTRIENT INTAKES**

Due to limitations in available data, the AIs for various nutrients are set using different criteria. For some nutrients, the AI is based on the observed mean or median intakes by groups that are maintaining health and nutritional status consistent with meeting requirements. In these cases, the AI is conceptually similar to the median of a target usual nutrient intake distribution. For other nutrients, the AI is the level of intake at which subjects in an experimental

**PART I: APPLYING THE DIETARY REFERENCE INTAKES****TABLE 4 Method Used to Estimate Adequate Intake (AI) for Groups of Healthy Adults**

Estimation Method	Nutrient
Experimental derivation	Biotin Calcium Choline Vitamin D Fiber, total Fluoride Potassium Sodium and chloride
Mean intake	Chromium
Median intake	Vitamin K Manganese Pantothenic acid <i>n</i> -6 Polyunsaturated fatty acids <i>n</i> -3 Polyunsaturated fatty acids Water, total

study met the criterion of adequacy. In these cases, the AI is not directly comparable to a target median intake.

Because of these differences in how the AI is set for different nutrients, the appropriate use of the AI in planning group intakes also varies. The AI can be used if the variability in the usual intake of the population being planned for is similar to the variability in intake of the healthy population that was used to set the AI. In this case, the appropriate use of the AI would be as the target median intake of the group.

However, if the AI is not based on a group mean or median intake of a healthy population, practitioners must recognize that there is a reduced level of confidence that achieving a mean or median intake at the AI will result in a low prevalence of inadequacy. In addition, the AI cannot be used to estimate the proportion of a group with inadequate intakes. Thus, regardless of how the AI has been estimated, it is not possible to use the AI to plan a target distribution of usual intakes with a known prevalence of inadequacy. Table 4 presents a summary of the nutrients for which AIs have been estimated and notes the cases in which these estimates reflect experimental derivation and observed

mean and median intake of healthy groups. Practitioners who want to compare their target groups to the groups used to set the AIs can obtain this information in each of the individual nutrient profiles found in Part III.

### **USING THE UL TO PLAN A GROUP'S NUTRIENT INTAKES**

For nutrients that have a UL, the planning goal is to achieve an acceptably low prevalence of intakes above the UL.

### **USING THE EER TO PLAN A GROUP'S DIET**

As is true for individuals, the underlying objective in planning the energy intake of a group is similar to planning intakes for other nutrients: to attain an acceptably low prevalence of inadequacy and potential excess. When planning the energy intakes of groups, the goal is for the group's mean intake to equal the EER. Because energy intake is related to energy requirement, it is assumed that people in the group with energy requirements above the EER will choose energy intakes that are above the EER, and those with requirements below the EER will choose intakes below the EER, so that the average intake will equal the EER.

The EAR cut-point approach should not be used for planning energy intakes, because it is expected, and desirable, for half of the group to have intakes below the EER.

There are two possible approaches to estimate energy intakes of groups. One can estimate energy requirements for the reference person or obtain an average of estimated maintenance energy needs for the group members. For example, to plan for a large group of men aged 19 through 30 years, one can estimate the EER for the reference male with a weight of 70 kg (154 lbs) and a height of 1.76 m (~ 5 ft 8 in) and who is considered low active, and use this number (~ 2,700 kcal) as the target for the group. This approach would require the assumption that all members of the group were similar to the reference person or that the reference person accurately represented the group's average values for age, height, weight, and activity level, and that these variables were symmetrically distributed.

The preferred approach would be to plan for an intake equal to the average energy expenditure for the group. For example, assuming that there is access to data on height, weight, age, and activity level, the energy expenditure for each individual in the group could be estimated. The average of these values would then be used as the planning goal for the maintenance of the group's current weight and activity level. As with other planning applications, assessing the plan for a group's energy intake, following its implementation, would lead to further refinements. In the case of energy, however, assessment would be based on monitoring body weight rather than on reported energy intake.

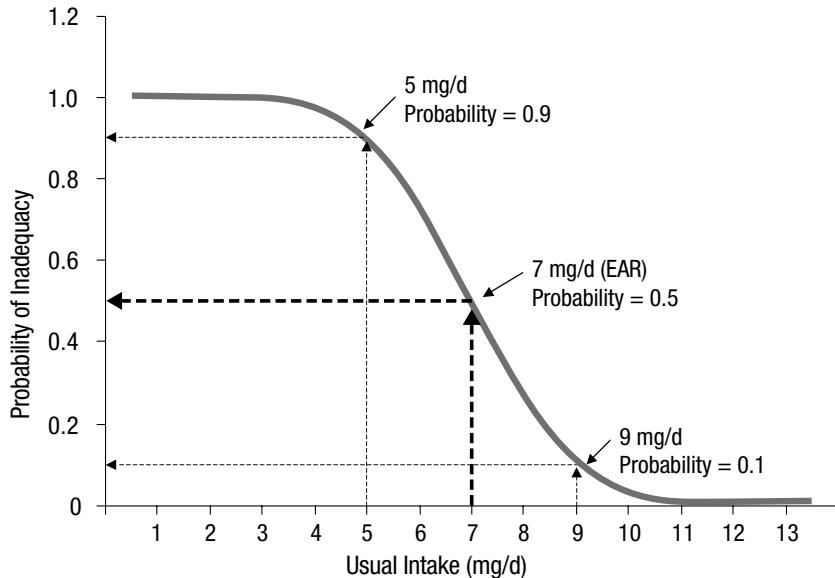
## CASE STUDIES

### Case Study One: Using the Probability Approach to Assess Intakes in a Group

Using a group of 650 adult men aged 19 to 30 years and a hypothetical nutrient with an EAR of 7 mg/day for this age and gender group illustrates the probability approach. Individuals in this group, even though they are similar in age and gender, differ in both their requirements for the nutrient and their usual intakes of the nutrient. At a conceptual level, determining the prevalence of inadequate nutrient intakes in the group would simply involve comparing each individual's usual nutrient intake with his individual requirement, and totaling the number of men with usual intakes below their individual requirements. For example, a man with a usual nutrient intake of 9 mg/day and a requirement of 10 mg/day would not meet his requirement and would be classified as inadequate, whereas another man with a usual nutrient intake of 9 mg/day and a requirement of 5 mg/day would exceed his requirement. In practice, however, we almost never know individuals' nutrient requirements. Instead, we may have information on the distribution of requirements for a small group of individuals who are similar in age and gender, and who took part in studies to determine nutrient requirements. From that information, we can determine the probability, or risk, that a given intake will be adequate or inadequate.

Knowledge of the distribution of requirements allows one to construct a risk curve that defines the probability that any given intake is inadequate, whether the requirement distribution is statistically normal or not. Figure 8 shows a risk curve for the example nutrient with an EAR of 7 mg/day. The requirement distribution for this nutrient is statistically normal, and the SD is ~ 1.5 mg/day. As described earlier, for nutrients with normal requirement distributions, 95 percent of individuals have requirements within  $\pm 2$  SD of the EAR. In this example, 95 percent of men aged 19 to 30 years would have requirements between 4 mg/day (7 mg/day minus twice the SD of 1.5 mg/day) and 10 mg/day (7 mg/day plus twice the SD of 1.5 mg/day). The probability of inadequacy associated with any intake can be determined by assessing where the intake level intersects the risk curve.

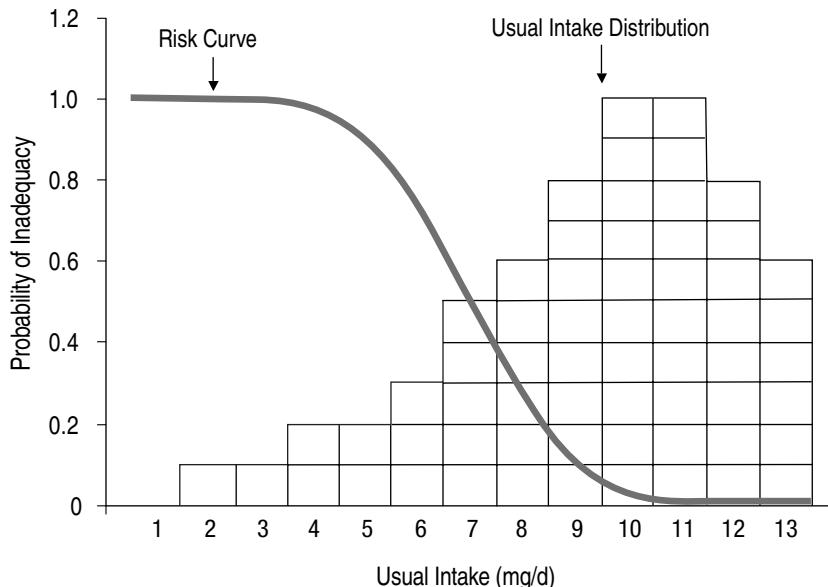
As illustrated in Figure 8, the probability of inadequacy at a usual intake at or below about 3 mg/day is associated with a probability of inadequacy of 1.0 (100 percent), meaning that virtually everyone with a usual intake in this range does not meet their own requirement. When usual intakes are at or above about 11 mg/day, the probability of inadequacy is zero, meaning that virtually everyone with a usual intake in this range would meet their own requirement. When usual intake is between 4 mg/day and 10 mg/day, the probability of inadequacy varies, and can be estimated by determining where the usual intake level intersects the risk curve:



*FIGURE 8* Risk curve. This risk curve is from a normal requirement distribution with a mean of 7 mg/day and a SD of 1.5 mg/day.

- It is relatively high at intakes that are just above the lower end of the distribution of requirements (about 0.9 or 90 percent at a usual intake of 5 mg/day in this example).
- By definition, the probability of inadequacy at the EAR is 0.5 or 50 percent (7 mg/day in this example).
- It is relatively low at intakes that are closer to the upper end of the distribution of requirements (about 0.1 or 10 percent at a usual intake of 9 mg/day in this example).

The information on the probability of inadequacy of different usual intake levels is used to estimate the prevalence of inadequate intakes in the group. This is done by determining the probability of inadequacy for each usual intake level in the group, and then computing the average for the group as a whole. Figure 9 and Table 5 illustrate this approach. Figure 9 shows the risk curve from Figure 8, as well as a usual intake distribution for the group of 650 men in the example (each “box” in the figure represents 10 men and there are 65 boxes). Table 5 shows the usual intake levels from the distribution shown in Figure 9, the associated probability of inadequacy, and the number of men at that intake level.

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*FIGURE 9 Comparison of the risk curve to a usual intake distribution. In this simplified usual intake distribution, each “box” represents 10 men aged 19 to 30 years. The prevalence of inadequate intakes in the group is estimated by determining the probability of inadequacy associated with each individual usual intake level, and then calculating the average probability.*

To illustrate how Figure 9 and Table 5 work to determine the prevalence of inadequacy, consider men with intakes of 5 mg/day and 9 mg/day. Twenty men have usual intakes of 5 mg/day, and an intake of 5 mg/day intersects the risk curve at a probability of inadequacy of 0.90. Because each individual with a usual intake of 5 mg/day has a 90 percent (0.9) probability of being inadequate, one would expect 18 of 20 men (90 percent) to be inadequate. In contrast, 80 men have usual intakes of 9 mg/day, and an intake of 9 mg/day intersects the risk curve at a probability of inadequacy of 10 percent.

One would thus expect 8 men (10 percent of the 80 men with usual intakes of 9 mg/day) to be inadequate. The average probability of inadequacy is calculated by totaling the number of individuals likely to have inadequate intakes, and then dividing by the total number of men. (This is mathematically identical to adding up all the individual probabilities of inadequacy [i.e., 1.0 + 1.0 + 1.0 + . . . + 0 + 0 + 0] and dividing by the total number of men.) In this example, the group prevalence of inadequacy is approximately 20 percent.

**TABLE 5 Using the Probability Approach to Estimate Group Prevalence of Inadequacy in a Group of 650 Adult Men Ages 19 to 30 Years for a Nutrient with an EAR of 7 mg/day**

Usual Intake Level (mg/day)	Probability of Inadequacy	Number of People	Probability × Number <sup>a</sup>
2	1.0	10	10
3	1.0	10	10
4	0.97	20	19.4
5	0.90	20	18.0
6	0.73	30	21.9
7	0.50	50	25.0
8	0.27	60	16.2
9	0.10	80	8.0
10	0.03	100	3.0
11	0	100	0
12	0	80	0
13	0	60	0
14	0	30	0
<b>Total</b>		<b>650</b>	<b>131.5</b>
<b>Average probability</b>	$= \text{probability} \times \text{number/total}$ $= 131.5/650 = 0.20$ (20 percent)		

<sup>a</sup> This represents the number of men expected to have inadequate intakes at each intake level.

### **Case Study Two: Using the Probability Approach to Assess Iron Intakes in a Group of Menstruating Women**

The probability approach involves first determining the risk of inadequacy for each individual in the population, and then averaging the individual probabilities across the group. For iron, Appendix Tables G-5, G-6, and G-7 give the probability of inadequacy at various intakes. These tables may be used to calculate the risk of inadequacy for each individual, and then the estimated prevalence of inadequacy for a population. In addition, Appendix C of the original report titled, *Dietary Reference Intakes: Applications in Dietary Assessment* (2000), demonstrates how to carry out the necessary calculations to obtain a prevalence estimate for a group.

This case study presents a simplified estimate that could also be determined manually. The estimate is illustrated in Table 6 for a hypothetical group of 1,000 menstruating women not taking oral contraceptives and consuming a

**PART I: APPLYING THE DIETARY REFERENCE INTAKES**

typical omnivorous diet. The first and second columns of this table are based on information in Appendix Tables G-4 and G-7. Intakes below 4.42 mg/day are assumed to have a 100 percent probability of inadequacy (risk = 1.0). Individuals with intakes above 18.23 mg/day are assumed to have a zero risk of inadequacy. For intakes between these two extremes, the risk of inadequacy is calculated as 100 minus the midpoint of the percentile of requirement. For example, intakes between 4.42 and 4.88 fall between the 2.5 and 5th percentile of requirement. The midpoint is 3.75, and the probability of inadequacy is  $100 - 3.75 \approx 96.3$  percent, or a risk of 0.96. The appropriate risk of inadequacy is then multiplied by the number of women with intakes in that range. In this case study, only one woman had an intake between 4.42 and 4.87 mg/day, so the number of women with inadequate intake is 0.96 ( $1 \times 0.96$ ). In the next range (4.88 mg/day to 5.46 mg/day, or between the 5th and 10th percentiles) there were three women, with an associated number of women with inadequate intake of 2.79 ( $3 \times 0.93$ ). If this is done for each intake range, the total number of women with inadequate intakes can be determined. In this example, 165 of the 1,000 women have inadequate intakes, for an estimated prevalence of inad-

**TABLE 6 Illustration of the Full Probability Approach to Estimate the Prevalence of Dietary Iron Inadequacy in a Group of 1,000 Menstruating Women (Not Using Oral Contraceptives and Following an Omnivorous Diet)**

Percentiles of Requirement Distribution	Range of Usual Intake Associated with Requirement Percentiles (mg/day)	Probability of Inadequacy	Number of Women with Intake in Range	Number of Women with Inadequate Intake
< 2.5	< 4.42	1.0	1	1
2.5–5.0	4.42–4.88	0.96	1	0.96
5–10	4.89–5.45	0.93	3	2.79
10–20	5.46–6.22	0.85	10	8.5
20–30	6.23–6.87	0.75	15	11.25
30–40	6.88–7.46	0.65	20	13
40–50	7.47–8.07	0.55	23	12.65
50–60	8.08–8.76	0.45	27	12.15
60–70	8.77–9.63	0.35	50	17.5
70–80	9.64–10.82	0.25	150	37.5
80–90	10.83–13.05	0.15	200	30.0
90–95	13.06–15.49	0.08	175	14
95–97.5	15.50–18.23	0.04	125	5
> 97.5	> 18.23	0.0	200	0
Total			1,000	165

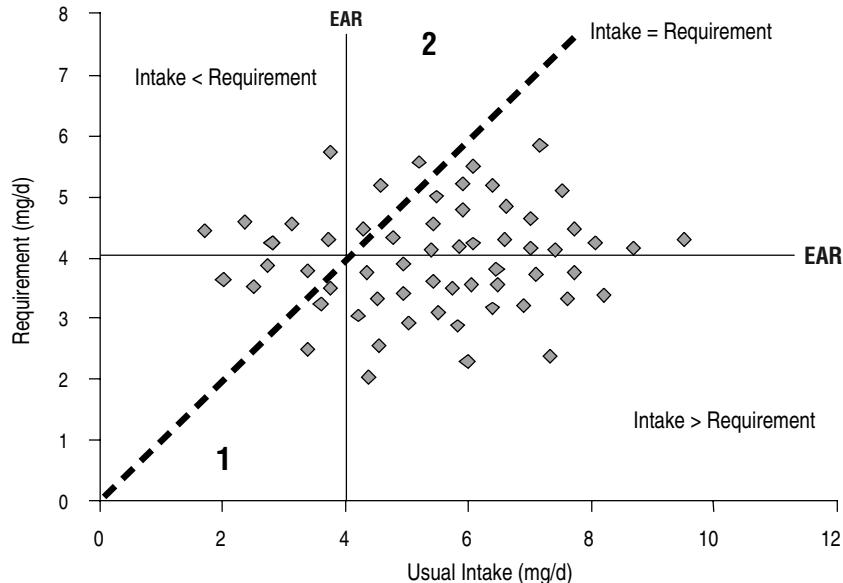
equacy of 16.5 percent. It is important to remember that this approach does not identify the specific women with inadequate intakes, but is rather a statistical calculation of the prevalence of inadequate intakes. Thus, it cannot be used to screen individuals at risk of inadequacy.

Note that the prevalence of nutrient inadequacy that is estimated by the full probability approach differs considerably from that estimated by the cut-point method (the proportion with intakes below the EAR). In this example, the EAR (median requirement) is 8.07 mg/day, and only 73 women have intakes below this amount. Thus, the cut-point method would lead to an estimated prevalence of inadequacy of 7.3 percent, which differs considerably from the estimate of 16.5 percent obtained by using the full probability approach. The reason for the discrepancy is that one of the conditions needed for the cut-point approach (a symmetrical requirement distribution) is not true for iron requirements of menstruating women.

### Case Study Three: Using the EAR Cut-Point Method

The EAR cut-point method is illustrated in Figure 10, which shows a hypothetical joint distribution of usual intakes and individual requirements for a group of 60 individuals. This example is hypothetical because in practice we almost never have access to accurate data on either usual intakes of individuals or their individual requirements. Figure 10 includes a 45° dashed line labeled “Intake = Requirement.” Individuals who fall to the right of and below this line have usual intakes that exceed their individual requirements (i.e., they have adequate intakes), whereas individuals who fall to the left of and above the line have usual intakes that do not meet their requirements (i.e., they have inadequate intakes). Determining the prevalence of inadequacy in this hypothetical situation is easy: one simply counts the number of individuals with usual intakes below their individual requirements. In this example, 13 individuals have intakes to the left of and above the “Intake = Requirement” line, so the group prevalence of inadequacy is 13/60, or 21.7 percent.

Figure 10 also shows the EAR (in this example, it is 4 mg/day) on both the requirement axis (the Y axis) and the usual intake axis (X axis). Focusing on the X axis, note that most individuals with usual intakes below the EAR have inadequate intakes (they are to the left of and above the “Intake = Requirement” line), but that some (who appear in the triangle labeled 1) have usual intakes that exceed their individual requirements. Similarly, although most individuals with usual intakes above the EAR meet their requirements (they are to the right of and below the “Intake = Requirement” line), some (who appear in the triangle labeled 2) do not.

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**FIGURE 10** Joint distribution of requirements and usual intakes. Individuals with usual intakes below their individual requirements are found to the left of and above the dashed 45° line labeled Intake = Requirement. When assumptions for the EAR cut-point method are satisfied, this proportion of the group is mathematically similar to the proportion to the left of the vertical EAR line.

The assumptions required for use of the EAR cut-point method are satisfied in this example, as described below:

1. Requirement distribution is approximately symmetrical. In Figure 10, it can be seen that similar proportions of the group have requirements above and below the EAR of 4 mg/day (the number of individuals above the horizontal EAR line is similar to the number of individuals below).
2. Intakes and requirements are independent. Figure 10 shows that individuals with low requirements are just as likely as individuals with high requirements to have high (or low) usual intakes.
3. The usual intake distribution is more variable than the requirement distribution. In Figure 10, it can be seen that there is more variability in the intake distribution (it ranges from less than 2 mg/day to almost 10 mg/day) than in the requirement distribution (which ranges from about 2 mg/day to about 6 mg/day).

When the above conditions are met, the individuals in triangle 1 (with intakes below the EAR but above their own requirements) are similar in number to the individuals in triangle 2 (with intakes above the EAR and below their own requirements). These two triangles cancel one another out, and the number of individuals that do not meet their requirements (those found to the left of the 45° “Intake = Requirement” line) is thus mathematically similar to the number with usual intakes below the EAR.

The EAR cut-point method can also be applied to the example of 650 men described in the first case study, as the requirement distribution is symmetrical, intakes and requirements are independent, and the usual intake distribution is more variable than the requirement distribution. In this case, one would simply determine the number of men with intakes at or below the EAR of 7 mg/day. From Table 5, this would be 10 (2 mg/day) + 10 (3 mg/day) + 20 (4 mg/day) + 20 (5 mg/day) + 30 (6 mg/day) + 50 (7 mg/day), for a total of 140 men. Dividing this by the total group size of 650 yields the estimated prevalence of inadequacy of 21.5 percent, which is very similar to the estimate of 20 percent obtained using the full probability method.

In summary, the full probability method and a shortcut, known as the EAR cut-point method, can be used to estimate the prevalence of nutrient inadequacy in a group. Both methods require knowledge of the distribution of usual intakes for the group, and that intakes and requirements are independent. The EAR cut-point method has two additional requirements; namely, that the requirement distribution is symmetrical, and that the distribution of usual intakes is more variable than the distribution of requirements. If either of these two additional requirements is not met, the full probability method can be used instead, provided the requirement distribution is known.

### Case Study Four: Planning Diets in an Assisted-Living Facility for Senior Citizens

An example of planning diets for institutionalized groups is menu planning for senior citizens who reside in an assisted-living facility. Menus planned for these institutions usually assume that the residents have no other sources of foods or nutrients, and thus the menus are designed to meet all nutrient needs of the residents. The goal of menu planning is to provide meals that provide adequate nutrients for a high proportion of the residents, or conversely, the prevalence of inadequate intakes is acceptably low among the residents.

The planner is developing a menu for an assisted living facility in which the residents are retired nuns aged 70 years and above. For this age group, the EAR for vitamin B<sub>6</sub> is 1.3 mg/day. Assume that no data can be located on the distribution of usual intakes of this group or a similar group, and that resources are not available to conduct a dietary survey in the institution. How could the

**PART I: APPLYING THE DIETARY REFERENCE INTAKES**

planner proceed to determine the target intake distribution of vitamin B<sub>6</sub> needed to attain an acceptable prevalence of inadequacy?

**STEP 1. DETERMINE AN ACCEPTABLY LOW PREVALENCE OF INADEQUACY**

For vitamin B<sub>6</sub>, the EAR was set at a level adequate to maintain plasma pyridoxal phosphate levels at 20 nmol/L. This plasma level is not accompanied by observable health risks, and thus allows a moderate safety margin to protect against the development of signs or symptoms of deficiency. This cut-off level was selected recognizing that its use may overestimate the B<sub>6</sub> requirement for health maintenance of more than half the group. For this reason, assume that the planner has determined that a 10 percent prevalence of inadequacy (i.e., 10 percent with intakes below the EAR) would be an acceptable planning goal.

**STEP 2. DETERMINE THE TARGET USUAL NUTRIENT INTAKE DISTRIBUTION**

Next, the planner needs to position the intake distribution so the nutrient intake goals are met. In this example, the planner decides that the prevalence of inadequacy in the group will be set at 10 percent, and as a result the usual intake distribution of the group should be positioned such that only 10 percent of the group has usual intakes less than the EAR.

Because data on the usual nutrient intake distributions of the residents are not available, other sources must be used to estimate the target usual nutrient intake distribution. Data on the distribution of usual dietary intakes of vitamin B<sub>6</sub> are available from several national surveys and thus are used. The adjusted percentiles for women are summarized in Table 7.

Assuming there are no changes in the shape of the distribution, the amount of the shift can be calculated as the additional amount of the nutrient that must be consumed to reduce the proportion of the group that is below the EAR. This is accomplished by determining the difference between the EAR and the intake at the acceptable prevalence of inadequacy (in this case, the 10th percentile of the usual intake distribution).

**TABLE 7 Selected Percentiles of the Distributions of Usual Intake of Vitamin B<sub>6</sub> from Foods in Older Women**

Study	n	Percentile of Usual Intake Distribution of Vitamin B <sub>6</sub> (mg/day)						
		5th	10th	25th	50th	75th	90th	95th
Survey A	1,368	0.92	1.04	1.24	1.53	1.93	2.43	2.76
Survey B	221	0.76	0.88	1.11	1.41	1.76	2.12	2.35
Survey C	281	0.5	0.6	0.7	1.0	1.3	1.6	1.8

**TABLE 8 Identification of the Target Median Intake<sup>a</sup> of Vitamin B<sub>6</sub> to Obtain a 10 Percent Prevalence of Inadequacy in Older Women**

Study	EAR (mg/day)	Intake at 10th Percentile (mg/day)	Difference (EAR – intake at 10th percentile) (mg/day)	Median Intake (mg/day)	Target Median Intake (mg/day)
Survey A	1.3	1.04	0.26	1.53	1.79
Survey B	1.3	0.88	0.42	1.41	1.83
Survey C	1.3	0.6	0.7	1.0	1.70

<sup>a</sup> The target median intake is estimated by adding the difference between the Estimated Average Requirement (EAR) and the intake at the acceptable prevalence of inadequacy (in this case, 10 percent) to the observed median intake.

Examination of the data from the three surveys shows that estimated usual intakes of vitamin B<sub>6</sub> vary by as much as 30 percent among the surveys. As a result, the difference between the EAR of 1.3 mg and the intake at the 10th percentile varies, depending on which data are used. Table 8 shows that for Survey A the difference is 0.26 mg (1.3 mg – 1.04 mg = 0.26 mg); for Survey B, the difference is 0.42 mg (1.3 mg – 0.88 mg = 0.42 mg); and for Survey C, the difference is 0.7 mg (1.3 mg – 0.6 mg = 0.7 mg). In this example, the planner may have no reason to choose data from one particular survey as “more applicable” to the group than another, so he may estimate target usual nutrient intake distributions using all three data sets. Accordingly, the target intake distributions shift up by 0.26 mg, by 0.42 mg, and by 0.7 mg, using Survey A, B, or C. In each case the target usual nutrient intake distribution would lead to the accepted prevalence of inadequacy. Rather than choosing one set of survey data over another, the planner could simply average the summary measures described in the next section.

### STEP 3. SELECT A SUMMARY MEASURE OF THE TARGET USUAL NUTRIENT INTAKE DISTRIBUTION TO USE IN PLANNING

After the planner has estimated a target usual intake distribution, then this information needs to be operationalized into a menu. In order to do this, the planner will first have to select a summary measure of the target usual nutrient intake distribution to use as a tool in planning the menu. The median of the target intake distribution is the most useful; it can be calculated as the median of the current intake distribution, plus (or minus) the amount that the distribution needs to shift to make it the target usual intake distribution.

In the current example, although the baseline intakes at the 10th percentile and the median differ among the three surveys, the estimates of the medians

of the target usual intake distributions are quite similar, as shown in Table 8. Assuming that a 10 percent prevalence of intakes below the EAR was considered acceptable, a median intake for vitamin B<sub>6</sub> of 1.7 to 1.8 mg/day would be the planning goal. Accordingly, the menu would need to be planned so that vitamin B<sub>6</sub> intakes would be at this level.

Estimates of target nutrient intakes must be converted to estimates of foods to purchase, offer, and serve that will result in the usual intake distributions meeting the intake goals. This is not an easy task. Meals with an average nutrient content equal to the median of the target usual nutrient intake distribution may not meet the planning goals, as individuals in a group tend to consume less than what is offered and served to them. Thus, the planner might aim for a menu that offers a choice of meals with a nutrient content range that includes, or even exceeds, the median of the target usual nutrient intake distribution.

#### **STEP 4. ASSESS IMPLEMENTATION OF THE PLAN**

Ideally, after the menu had been planned and implemented, a survey would be conducted to assess intakes and determine whether the planning goal had been attained. This would then be used as the basis for further planning.

### **KEY POINTS FOR WORKING WITH GROUPS**

#### **ASSESSING NUTRIENT INTAKES**

- ✓ The goal of assessing nutrient intakes of groups is to determine the prevalence of inadequate (or excessive) nutrient intakes within a particular group of individuals.
- ✓ Assessment of groups should always be performed using intakes that have been adjusted to represent a usual intake distribution.
- ✓ The probability approach and the EAR cut-point method are two statistical methods of determining the prevalence of inadequacy in a group. The EAR cut-point method is a simpler method derived from the probability approach.
- ✓ For nutrients in which it is appropriate to do so, the EAR can be used as part of the EAR cut-point method to determine the prevalence of nutrient inadequacy within a group. Otherwise, the probability approach can be used.
- ✓ The AI has limited application in assessing a group's nutrient intakes. For nutrients with an appropriately estimated AI, groups with mean or median intakes at or above the AI can generally be assumed to have a low prevalence of inadequate intakes.

- ✓ The UL can be used to estimate the proportion of a group at potential risk of adverse effects from excessive nutrient intakes.
- ✓ The RDA should not be used in the assessment of a group's nutrient intakes. Comparing mean or median intake with the RDA is inappropriate.
- ✓ To assess the energy adequacy of an individual or group diet, information other than self-reported intakes should be used because underreporting of energy intake is a serious and pervasive problem. Body weight for height, BMI, or other anthropometric measures are suitable for use in assessing long-term energy intake.

### ***PLANNING NUTRIENT INTAKES***

- ✓ The goal of planning nutrient intakes for groups is to achieve usual intakes that meet the requirements of most individuals, but that are not excessive.
- ✓ The DRIs present an approach to planning that involves consideration of the entire distribution of usual nutrient intakes within a group.
- ✓ The basic steps in planning for groups are as follows: First the practitioner decides on an acceptable prevalence of inadequacy. The distribution of usual intakes in the group must then be estimated using the distribution of reported or observed intakes. Finally, a target usual intake distribution is determined by positioning the distribution of usual intakes relative to the EAR to achieve the desired prevalence of inadequacy.
- ✓ For nutrients with an EAR, the planning goal is to aim for an acceptably low prevalence of intakes below the EAR.
- ✓ The RDA is not recommended for use when planning nutrient intakes of groups.
- ✓ For nutrients with an AI, this value is used as the target for the mean or median intake when planning for groups.
- ✓ For nutrients with a UL, the planning goal is to achieve an acceptably low prevalence of intakes above the UL.
- ✓ When planning a group's energy intake, the goal is for the group's mean intake to equal the EER.

## **SUMMARY**

The DRI values can be used by nutrition professionals to assess and plan the nutrient intakes of individuals and of groups. Table 9 summarizes the chapter discussions on the appropriate uses of each of the DRI values to achieve these goals.

**TABLE 9 Using the DRIs to Assess and Plan the Nutrient Intakes of Individuals and Groups**

	EAR	RDA	AI	UL
<b>When Assessing Diets</b>				
For individuals:	Usual intake below the EAR likely needs to be improved. The probability of adequacy is 50 percent or less.	Not recommended for use when assessing nutrient intakes of individuals.	Usual intake at or above the AI has a low probability of inadequacy.	Usual intake above the UL may place an individual at risk of adverse effects.
For groups:	Used as part of the EAR cut-point method to determine the prevalence of nutrient inadequacy within a group.	Not used when assessing nutrient intakes of groups.	Limited application. Groups with mean or median intakes at or above the AI can generally be assumed to have a low prevalence of inadequate intakes.	Used to estimate the proportion of a group at potential risk of adverse effects from excessive nutrient intake.
<b>When Planning Diets</b>				
For individuals:	Intake at EAR has 50 percent probability of not meeting requirement.	Low probability of inadequate intake at RDA. Therefore, often used as a guide.	Intakes at AI will likely meet or exceed an individual's requirement.	Low probability of adverse effects from excessive consumption so average intake should not exceed the UL.
For groups:	Aim for an acceptably low prevalence of intakes below the EAR.	Not used when planning the nutrient intakes of groups.	Use as a target for the mean or median intake.	Aim for an acceptably low prevalence of intakes above the UL.

# PART II

## ENERGY, MACRONUTRIENTS, WATER, AND PHYSICAL ACTIVITY

Part II of this publication takes information from the DRI reports titled *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* (2002/2005) and *Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate* (2005) and presents nutrient reference values for carbohydrates, fiber, fatty acids, protein, amino acids, and water, as well as recommendations for energy, fat, cholesterol, and physical activity.

“Macronutrients, Healthful Diets, and Physical Activity” begins with a review of the available data regarding the relationships of carbohydrates, fiber, fat, fatty acids, cholesterol, protein, and amino acids, collectively known as macronutrients, and physical activity and energy to major chronic diseases. It will introduce the term Acceptable Macronutrient Distribution Range (AMDR), which is a range of intake for a particular energy source that is associated with reduced risk of chronic disease. AMDRs are set for fat, carbohydrate, protein, and n-6 and n-3 polyunsaturated fatty acids.

“Energy” introduces the term Estimated Energy Requirement (EER), which is defined as the average dietary energy intake that is predicted to maintain energy balance in a healthy individual of a defined age, gender, height, weight, and level of physical activity consistent with good health. “Physical Activity” provides recommendations for levels of physical activity associated with a normal body mass index and reduced risk of chronic disease. The remaining chapters discuss data on carbohydrates (sugars and starches), fiber, fats and fatty acids, cholesterol, protein and amino acids, and water. In these chapters, AIs are provided for *Total Fiber*, linoleic acid and  $\alpha$ -linolenic acid, and water, and EARs and RDAs are provided for carbohydrate, and protein. No ULs were set for any of the macronutrients or for water.

**TABLE 1 Acceptable Macronutrient Distribution Ranges**

Macronutrient	AMDR (as percent of energy) <sup>a</sup>		
	Children 1–3 y	Children 4–18 y	Adults
Fat	30–40	25–35	20–35
<i>n</i> -6 polyunsaturated fatty acids <sup>b</sup> (linoleic acid)	5–10	5–10	5–10
<i>n</i> -3 polyunsaturated fatty acids <sup>b</sup> ( $\alpha$ -linolenic acid)	0.6–1.2	0.6–1.2	0.6–1.2
Carbohydrate	45–65	45–65	45–65
Protein	5–20	10–30	10–35

**Additional Macronutrient Recommendations**

Macronutrient	Recommendation
Dietary cholesterol	As low as possible while consuming a nutritionally adequate diet
<i>Trans</i> fatty acids	As low as possible while consuming a nutritionally adequate diet
Saturated fatty acids	As low as possible while consuming a nutritionally adequate diet
Added sugars	Limit to a maximal intake of no more than 25 percent total energy <sup>c</sup>

<sup>a</sup>AMDR = Acceptable Macronutrient Distribution Range. This is the percent of energy intake that is associated with reduced risk of chronic disease, yet provides adequate amounts of essential nutrients.

<sup>b</sup>Approximately 10 percent of the total can come from longer-chain *n*-3 or *n*-6 fatty acids.

<sup>c</sup>Not a recommended intake. A daily intake of added sugars that individuals should aim for to achieve a healthful diet was not set.

# MACRONUTRIENTS, HEALTHFUL DIETS, AND PHYSICAL ACTIVITY

Unlike vitamins and minerals, fats, carbohydrates, and proteins can substitute for one another to some extent in order to meet the body's energy needs. Thus, for a certain level of energy intake, increasing the proportion of one macronutrient necessitates decreasing the proportion of one or both of the other macronutrients. Acceptable ranges of intake for each of these energy sources were set based on a growing body of evidence that has shown that macronutrients play a role in the risk of chronic disease.

These ranges, termed Acceptable Macronutrient Distribution Ranges (AMDRs), are defined as a range of intake for a particular energy source that is associated with reduced risk of chronic diseases (e.g., coronary heart disease [CHD], obesity, diabetes, and/or cancer) while providing adequate intakes of essential nutrients. These ranges are also based on adequate energy intake and physical activity to maintain energy balance. The AMDR of a macronutrient is expressed as a percentage of total energy intake because its requirement, in a classical sense, is not independent of other energy fuel sources or of the total energy requirement of the individual. Each must be expressed in terms relative to the other. A key feature of each AMDR is that it has a lower and upper boundary. If an individual consumes below or above this range, there is a potential for increasing risk of chronic diseases shown to affect long-term health, as well as increasing the risk of insufficient intakes of essential nutrients.

For example, with regard to carbohydrate and fat, studies have shown a connection between low-fat and, therefore, high-carbohydrate diets and decreased high density lipoprotein (HDL) cholesterol in the bloodstream, an indicator associated with increased risk of CHD. Conversely, diets too high in fat may result in increased energy and saturated fat intake, and therefore lead to increased risk of obesity and its complications, such as CHD.

In this chapter, AMDRs for carbohydrate, fat, fatty acids (*n*-6 and *n*-3 polyunsaturated), and protein are discussed. Recommendations for cholesterol, *trans* fatty acids, saturated fatty acids, and added sugars are also provided (see Table 1).

Finally, the chapter reviews the available data regarding the relationships between major chronic diseases that have been linked with consumption of dietary macronutrients (carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids) and physical activity.

## ACCEPTABLE MACRONUTRIENT DISTRIBUTION RANGES (AMDRs)

Many causal relationships among over- or underconsumption of macronutrients, physical inactivity, and chronic disease have been proposed. When the diet is modified for one energy-yielding nutrient, it invariably changes the intake of other nutrients, which makes it extremely difficult to have adequate substantiating evidence for providing clear and specific nutritional guidance.

However, based on the evidence to suggest a role in chronic disease, as well as information to ensure sufficient intakes of other essential nutrients, Acceptable Macronutrient Distribution Ranges (AMDRs) have been established. An AMDR is defined as a range of intakes for a particular energy source that is associated with reduced risk of chronic disease while providing adequate intakes of essential nutrients. The AMDR of a macronutrient is expressed as a percentage of total energy intake because its requirement is not independent of other energy fuel sources or of the total energy requirement of the individual.

A key feature of each AMDR is that it has a lower and upper boundary. Intakes that fall above or below this range appear to increase the risk of chronic disease and may result in the inadequate consumption of essential nutrients. AMDRs have been set for carbohydrate, protein, fat, and *n*-6 and *n*-3 polyunsaturated fatty acids based on evidence from intervention trials, with support of epidemiological evidence. Recommendations have been made for limiting cholesterol, *trans* fatty acids, saturated fatty acids, and added sugars (see Table 1).

An AMDR was not set for fiber or monounsaturated fatty acids. An AMDR was not set for fiber because it is an insignificant contributor to total energy intake; no known adverse effects associated with its consumption were available. Monounsaturated fatty acids are not essential in the diet, and the evidence relating low and high intakes of monounsaturated fatty acids to chronic disease is limited. Practical limits on intakes of monounsaturated fatty acids will be imposed by AMDRs for total fat and other types of fatty acids.

### Total Fat and Carbohydrate

#### BASIS FOR ADULT AMDRs FOR TOTAL FAT AND CARBOHYDRATE

These AMDRs were estimated based on evidence indicating a risk for coronary heart disease (CHD) with diets high in carbohydrate and low in fat and on

## MACRONUTRIENTS, HEALTHFUL DIETS, AND PHYSICAL ACTIVITY

evidence for increased risk for obesity and its complications (including CHD) at high intakes of fat.

Intakes of low-fat, high-carbohydrate diets, compared with higher fat intakes, can induce a lipoprotein pattern called the atherogenic lipoprotein phenotype (characterized by high triglycerides, low HDL cholesterol, and small low density lipoprotein [LDL] cholesterol particles), which is associated with high risk of CHD, particularly in sedentary people who tend to be overweight. On the other hand, when fat intake is high, many individuals consume additional energy, and therefore gain additional weight. Weight gain on high-fat diets can be detrimental to individuals already susceptible to obesity and can worsen the metabolic consequences of obesity, particularly the risk of CHD. Moreover, high-fat diets are usually accompanied by increased intakes of saturated fatty acids, which can raise LDL cholesterol levels, further increasing risk of CHD. Diets containing energy from fat and carbohydrate in the recommended ranges minimize the risks of diabetes, obesity, and CHD. In addition, these ranges allow adequate consumption of essential nutrients and moderate saturated fat intake. Diets containing less than the minimum AMDR for carbohydrate are highly unlikely to meet the AI for fiber.

### BASIS FOR AMDRs FOR CHILDREN FOR TOTAL FAT AND CARBOHYDRATE

The AMDR for carbohydrate for children is the same as for adults. Children have a higher fat oxidation rate than adults, and low-fat diets can lead to reduced intake of certain micronutrients, including fat-soluble vitamins. Conversely, high-fat intakes during childhood may set the stage for CHD and obesity, although the evidence for this is tenuous.

Because the evidence is less clear on whether low- or high-fat intakes during childhood can lead to increased risk of chronic diseases later in life, the estimated AMDRs for children are primarily based on a transition from high-fat intakes during infancy to the lower adult AMDR. During childhood, the amount of saturated fat in the diet should be as low as possible without compromising nutritional adequacy.

## Protein

### BASIS FOR AMDR FOR CHILDREN AND ADULTS

There is no evidence suggesting that the AMDR for protein should be at levels below the adult Recommended Dietary Allowance (RDA) for protein (see Part II, “Protein”), which is about 10 percent of energy for adults. In addition, there were insufficient data to suggest a UL for protein (see Part II, “Protein”) and insufficient data to suggest an upper range or boundary for an AMDR for pro-

tein. All of the AMDRs were set, in part, to complement the AMDRs for fat and carbohydrate.

## ***n*-6 Polyunsaturated Fatty Acids**

### **BASIS FOR AMDR FOR CHILDREN AND ADULTS**

Based on usual median intakes of energy reported in the U.S. Continuing Survey of Food Intakes by Individuals (CSFII 1994–1996, 1998), it is estimated that a lower boundary level of 5 percent of energy from linoleic acid would be needed to meet the Adequate Intake (AI) (see Part II, “Dietary Fat: Total Fat and Fatty Acids”). The upper boundary for linoleic acid of 10 percent of energy intake is based on the following information:

- In North America, individual dietary intakes rarely exceed 10 percent of energy from linoleic acid.
- Epidemiological evidence for the safety of intakes greater than 10 percent of energy are generally lacking.
- High intakes of linoleic acid create a pro-oxidant state that may predispose to several chronic diseases, such as CHD and cancer. Human studies demonstrate that enrichment of lipoproteins and cell membranes with *n*-6 polyunsaturated fatty acids contributes to a pro-oxidant state.

## ***n*-3 Polyunsaturated Fatty Acids**

### **BASIS FOR AMDR FOR CHILDREN AND ADULTS**

Based on usual median intakes of energy report in CSFII (1994–1996, 1998), it is estimated that a lower boundary level of 0.6 percent of energy from  $\alpha$ -linolenic acid would be needed to meet the AI (see Part II, “Dietary Fat: Total Fat and Fatty Acids”). The upper boundary corresponds to the highest  $\alpha$ -linolenic acid intakes from foods consumed by individuals in the United States and Canada. Data supporting the benefit of even higher intakes of  $\alpha$ -linolenic acid were not considered strong enough to warrant an upper boundary greater than 1.2 percent of energy.

A growing body of evidence suggests that higher intakes of  $\alpha$ -linolenic acid, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) may afford some degree of protection against CHD. However, it is impossible to estimate an AMDR for all *n*-3 fatty acids because the physiological potency of EPA and DHA is much greater than that of  $\alpha$ -linolenic acid. Up to 10 percent of the AMDR for *n*-3 fatty acids can be consumed as EPA and/or DHA.

## MACRONUTRIENTS, HEALTHFUL DIETS, AND PHYSICAL ACTIVITY

### ADDITIONAL MACRONUTRIENT RECOMMENDATIONS

#### Saturated Fatty Acids, *Trans* Fatty Acids, and Cholesterol

##### BASIS FOR RECOMMENDATIONS

There are no known risks of chronic disease associated with consuming diets very low in saturated fatty acids, *trans* fatty acids, or cholesterol. Since certain micronutrients are found mainly in animal foods (which are typically high in saturated fats and cholesterol), it is possible that diets low in saturated fat and cholesterol may contain low levels of micronutrients, such as iron and zinc. Furthermore, analysis of nutritionally adequate menus indicates that there is a minimum amount of saturated fat that can be consumed so that adequate levels of linoleic and  $\alpha$ -linolenic acids are provided.

A substantial body of evidence suggests that saturated fatty acids, *trans* fatty acids, and cholesterol raise blood total and LDL cholesterol levels, which in turn increases risk of CHD. Because there is a positive linear trend between intake of each of these fats and risk of CHD, even very low intakes of each may increase risk. It is thus recommended that intakes of saturated fatty acids, *trans* fatty acids, and cholesterol remain as low as possible while a nutritionally adequate diet is consumed.

#### Added Sugars

##### BASIS FOR RECOMMENDATIONS

It has been shown the increasing intakes of added sugars can result in decreased intakes of certain micronutrients in United States subpopulations. This can occur because of the abundance of added sugars in energy-dense, nutrient-poor foods in a diet. As such, it is suggested that adults and children consume no more than 25 percent of energy from added sugars to ensure sufficient consumption of essential micronutrients. Note that a daily intake of added sugars that individuals should aim for to achieve a healthy diet was not set. Foods containing added sugars and few micronutrients include soft drinks, fruit drinks, cakes, cookies, and candies.

The impact of total sugar intake on the intake of micronutrients does not appear to be as great as for added sugars. Total sugars include both the added sugars and the naturally occurring sugars found in fruits, milk, and dairy products.

**TABLE 2 Relationship of Macronutrients and Physical Activity to Chronic Disease**

	Energy	Fat	Protein
<b>Cancer</b>	<ul style="list-style-type: none"> <li>Animal studies suggest that energy restriction may inhibit cell proliferation and tumor growth.</li> <li>Increased childhood energy intakes have been associated with increased cancer mortality.</li> <li>Excess energy contributes to obesity, which may increase risk of certain cancers.</li> </ul>	<ul style="list-style-type: none"> <li>High fat intakes have been implicated in development of certain cancers, although evidence is mixed.</li> <li>Epidemiological studies have shown an inverse relationship between fish consumption and risk of breast and colorectal cancer, possibly due to protective effects of <i>n</i>-3 fatty acids.</li> </ul>	<ul style="list-style-type: none"> <li>No clear role for total protein has yet emerged.</li> </ul>
<b>Heart Disease</b>	<ul style="list-style-type: none"> <li>Excess energy contributes to obesity, which increases risk of heart disease.</li> </ul>	<ul style="list-style-type: none"> <li>Increased saturated fat intake can increase total and LDL blood cholesterol levels.</li> <li>Increasing intakes of <i>trans</i> fatty acids and cholesterol increase total and LDL blood cholesterol levels, although there is wide interindividual variation in serum cholesterol response to dietary cholesterol.</li> <li>Monounsaturated and polyunsaturated fatty acids decrease total and LDL blood cholesterol levels.</li> <li>High intakes of <i>n</i>-6 and <i>n</i>-3 polyunsaturated fats are associated with decreased risk of heart disease.</li> </ul>	<ul style="list-style-type: none"> <li>Independent effects of protein on heart disease mortality have not been shown.</li> <li>Soy-based protein may reduce blood cholesterol, but the evidence is mixed.</li> </ul>

**MACRONUTRIENTS, HEALTHFUL DIETS, AND PHYSICAL ACTIVITY**

Carbohydrate	Fiber	Physical Activity
<ul style="list-style-type: none"> <li>Several case-control studies have shown increased risk of colorectal cancer in people with high intakes of sugar-rich foods.</li> <li>High vegetable and fruit intake and avoidance of foods with highly refined sugars have been negatively correlated to risk of colon cancer.</li> </ul>	<ul style="list-style-type: none"> <li>High fiber diets may protect against colorectal cancer, though the evidence is conflicting.</li> <li>Fiber may protect against hormone-related cancers including prostate, endometrial, and ovarian cancer.</li> <li>Certain cereal foods may protect against some types and stages of breast cancer.</li> </ul>	<ul style="list-style-type: none"> <li>Regular exercise has been negatively correlated with risk of colon cancer.</li> <li>Numerous epidemiological studies suggest that regular physical activity decreases risk of breast cancer.</li> <li>Exercise may help compensate for potential cancer-promoting effects of excess energy intake.</li> <li>Exercise may bolster the immune system.</li> </ul>
<ul style="list-style-type: none"> <li>High carbohydrate (low fat) intakes tend to increase plasma triacylglycerol and decrease plasma HDL cholesterol levels. These effects are more extreme if the source is monosaccharides, especially fructose.</li> </ul>	<ul style="list-style-type: none"> <li>Dietary fiber, particularly naturally occurring viscous fiber, reduces total and LDL cholesterol levels.</li> <li>Reduced rates of heart disease have been observed in individuals consuming high fiber diets.</li> <li>Dietary fiber intake has been shown to be negatively associated with hypertension in men.</li> </ul>	<ul style="list-style-type: none"> <li>Numerous studies have shown an inverse relationship between exercise and heart disease mortality.</li> <li>Regular exercise increases HDL cholesterol; decreases triacylglycerol, blood pressure, and risk of cardiac arrhythmias; enhances fibrinolysis, glucose effectiveness, and insulin sensitivity; and lessens platelet adherence.</li> </ul>

*continued*

**TABLE 2 Continued**

	Energy	Fat	Protein
<b>Dental Caries</b>			
<b>Type II Diabetes Mellitus</b>	<ul style="list-style-type: none"> <li>Excess energy contributes to obesity, which may increase risk of Type II diabetes.</li> <li>Obesity, particularly abdominal obesity, is a risk factor for Type II diabetes.</li> </ul>	<ul style="list-style-type: none"> <li>Some studies show a correlation between high fat intakes and insulin resistance, but it is not clear whether the association is due to fat or to obesity.</li> </ul>	
<b>Obesity</b>	<ul style="list-style-type: none"> <li>Excess energy intake causes obesity.</li> </ul>	<ul style="list-style-type: none"> <li>Available data on whether diets high in total fat increase the risk for obesity are conflicting; this may be partly due to underreporting of food intake, notably fat intake.</li> </ul>	<ul style="list-style-type: none"> <li>Available data on whether diets high in protein are associated with obesity are mixed: some have shown a positive association with protein intake and body fatness, others have demonstrated weight loss.</li> </ul>
<b>Bone Health</b>			
		<ul style="list-style-type: none"> <li>The relationship between protein intake and bone health is very controversial with some studies showing bone loss and osteoporosis in relationship to high intakes and others showing no association in the presence of adequate calcium intakes.</li> </ul>	

**MACRONUTRIENTS, HEALTHFUL DIETS, AND PHYSICAL ACTIVITY**

Carbohydrate	Fiber	Physical Activity
<ul style="list-style-type: none"> <li>Sugars play a role in development of dental caries (as do fluoride, oral hygiene and frequency of food intake).</li> <li>While there is little evidence that total carbohydrate is associated with Type II diabetes, there may be increased risk when the glycemic index of a meal, rather than total carbohydrate, is considered.</li> <li>Published reports have produced conflicting results about the existence of a direct link between high sugar intakes and obesity; this may be partly due to underreporting of food intake.</li> </ul>	<ul style="list-style-type: none"> <li>Viscous soluble fibers may attenuate the insulin response and thus protect against Type II diabetes.</li> <li>Intervention studies suggest that high fiber diets may assist in weight loss, although evidence overall is mixed.</li> </ul>	<ul style="list-style-type: none"> <li>Increased physical activity levels improve insulin sensitivity in people with Type II diabetes.</li> <li>Physical activity can reduce risk of Type II diabetes and can reduce total and abdominal obesity, which are risk factors for Type II diabetes.</li> <li>Physical inactivity is a major risk factor for development of obesity.</li> <li>Physical activity increases bone mass in children and adolescents and maintains bone mass in adults.</li> <li>Physical activity enhances muscle strength, coordination, and flexibility, which may prevent falls and fractures in elderly adults.</li> </ul>

## **RELATIONSHIP TO CHRONIC DISEASE**

During the past 40 years, a growing body of evidence has accumulated regarding the risk of chronic disease and consumption of energy and the macronutrients, specifically dietary fats, carbohydrate, protein, and fiber. Because most diets are composed of a variety of foods that provide varying amounts of macronutrients, research to determine causal relationships is somewhat limited. Research linking chronic diseases with dietary macronutrients and physical activity is summarized in Table 2.

**MACRONUTRIENTS, HEALTHFUL DIETS, AND PHYSICAL ACTIVITY****KEY POINTS FOR MACRONUTRIENTS,  
HEALTHFUL DIETS, AND PHYSICAL  
ACTIVITY**

- ✓ Fats, carbohydrates, and proteins can substitute for one another to some extent to meet the body's energy needs.
- ✓ Acceptable Macronutrient Distribution Ranges (AMDRs) were set for some macronutrients based on evidence that consumption above or below these ranges may be associated with nutrient inadequacy and increased risk of developing chronic diseases, including coronary heart disease, obesity, diabetes, and/or cancer.
- ✓ An AMDR is defined as a range of intakes for a particular energy source that is associated with reduced risk of chronic disease while providing adequate intakes of essential nutrients.
- ✓ The AMDR for a macronutrient is expressed as a percentage of total energy intake because its requirement is not independent of other energy fuel sources or of the total energy requirement of the individual.
- ✓ To meet the body's daily nutritional needs while minimizing risk for chronic disease, adults should consume 45–65 percent of their total calories from carbohydrates, 20–35 percent from fat, and 10–35 percent from protein. The acceptable ranges for children are similar to those for adults, except that infants and younger children need a somewhat higher proportion of fat in their diets.
- ✓ These ranges may be more useful and flexible for dietary planning than single values recommended in the past.
- ✓ AMDRs were not set for fiber or monounsaturated fatty acids.
- ✓ Over- and underconsumption of macronutrients as well as physical inactivity and energy imbalance have been linked to major chronic diseases such as cancer, obesity, coronary heart disease, dental caries, and Type II diabetes, and to skeletal health.

**TABLE 1 Equations to Estimate Energy Requirement****Infants and Young Children**

Estimated Energy Requirement (kcal/day) = Total Energy Expenditure + Energy Deposition

0–3 months	$EER^a = (89 \times \text{weight [kg]} - 100) + 175$
4–6 months	$EER = (89 \times \text{weight [kg]} - 100) + 56$
7–12 months	$EER = (89 \times \text{weight [kg]} - 100) + 22$
13–35 months	$EER = (89 \times \text{weight [kg]} - 100) + 20$

**Children and Adolescents 3–18 years**

Estimated Energy Requirement (kcal/day) = Total Energy Expenditure + Energy Deposition

**Boys**

3–8 years	$EER = 88.5 - (61.9 \times \text{age [y]}) + PA^b \times [(26.7 \times \text{weight [kg]}) + (903 \times \text{height [m]})] + 20$
9–18 years	$EER = 88.5 - (61.9 \times \text{age [y]}) + PA \times [(26.7 \times \text{weight [kg]}) + (903 \times \text{height [m]})] + 25$

**Girls**

3–8 years	$EER = 135.3 - (30.8 \times \text{age [y]}) + PA \times [(10.0 \times \text{weight [kg]}) + (934 \times \text{height [m]})] + 20$
9–18 years	$EER = 135.3 - (30.8 \times \text{age [y]}) + PA \times [(10.0 \times \text{weight [kg]}) + (934 \times \text{height [m]})] + 25$

**Adults 19 years and older**

Estimated Energy Requirement (kcal/day) = Total Energy Expenditure

<b>Men</b>	$EER = 662 - (9.53 \times \text{age [y]}) + PA \times [(15.91 \times \text{weight [kg]}) + (539.6 \times \text{height [m]})]$
<b>Women</b>	$EER = 354 - (6.91 \times \text{age [y]}) + PA \times [(9.36 \times \text{weight [kg]}) + (726 \times \text{height [m]})]$

**Pregnancy**

Estimated Energy Requirement (kcal/day) = Nonpregnant EER + Pregnancy Energy Deposition

1st trimester	$EER = \text{Nonpregnant EER} + 0$
2nd trimester	$EER = \text{Nonpregnant EER} + 340$
3rd trimester	$EER = \text{Nonpregnant EER} + 452$

**Lactation**

Estimated Energy Requirement (kcal/day) = Nonpregnant EER + Milk Energy Output – Weight Loss

0–6 months postpartum	$EER = \text{Nonpregnant EER} + 500 - 170$
7–12 months postpartum	$EER = \text{Nonpregnant EER} + 400 - 0$

NOTE: These equations provide an estimate of energy requirement. Relative body weight (i.e., loss, stable, gain) is the preferred indicator of energy adequacy.

<sup>a</sup> **EER** = Estimated Energy Requirement.

<sup>b</sup> **PA** = Physical Activity Coefficient (see Table 2).

# ENERGY

**E**nergy is required to sustain the body's various functions, including respiration, circulation, physical work, metabolism, and protein synthesis. This energy is supplied by carbohydrates, proteins, fats, and alcohol in the diet. A person's energy balance depends on his or her dietary energy intake and energy expenditure. Numerous factors affect energy expenditure and requirements, including age, body composition, gender, and physical activity level. An imbalance between energy intake and expenditure results in the gain or loss of body components, mainly in the form of fat, and determines changes in body weight.

The Estimated Energy Requirement (EER) is defined as the average dietary energy intake that is predicted to maintain energy balance in a healthy adult of a defined age, gender, weight, height, and a level of physical activity that is consistent with good health. A person's body weight is a readily monitored indicator of the adequacy or inadequacy of habitual energy intake.

To calculate the EER, prediction equations for normal-weight individuals (body mass index [BMI] of 18.5 kg/m<sup>2</sup> up to 25 kg/m<sup>2</sup>) were developed using data on total daily energy expenditure as measured by the doubly labeled water (DLW) technique. Equations can be found in Table 1. In children and in pregnant and lactating women, the EER accounts for the needs associated with growth, deposition of tissues, and the secretion of milk at rates that are consistent with good health. The EER does not represent the exact dietary energy intake needed to maintain energy balance for a specific individual; instead it reflects the average needs for those with specified characteristics.

Although EERs can be estimated for four levels of activity from the equations provided in Table 2, the active Physical Activity Level (PAL) is recommended to maintain health. Thus, energy requirements are defined as the amounts of energy that need to be consumed by an individual to sustain a stable body weight in the range desired for good health (BMI of 18.5 kg/m<sup>2</sup> up to 25 kg/m<sup>2</sup>), while maintaining a lifestyle that includes adequate levels of physical activity.

There is no Recommended Dietary Allowance (RDA) for energy because energy intakes above the EER would be expected to result in weight gain. Similarly, the Tolerable Upper Intake Level (UL) concept does not apply to energy because any intake above a person's energy requirement would lead to weight gain and likely increased risk of morbidity.

**TABLE 2 Physical Activity Coefficients (PA Values) for Use in EER Equations**

	Sedentary (PAL <sup>a</sup> 1.0–1.39)	Low Active (PAL 1.4–1.59)	Active (PAL 1.6–1.89)	Very Active (PAL 1.9–2.5)
				Typical daily living activities PLUS at least 60 minutes of daily moderate activity
		Typical daily living activities PLUS 30–60 minutes of daily moderate activity	Typical daily living activities PLUS at least 60 minutes of daily moderate activity	PLUS an additional 60 minutes of vigorous activity or 120 minutes of moderate activity
Typical daily living activities (e.g., household tasks, walking to the bus)	1.00	1.13	1.26	1.42
Boys 3–18 y	1.00	1.16	1.31	1.56
Girls 3–18 y	1.00	1.11	1.25	1.48
Men 19 y +	1.00	1.12	1.27	1.45
Women 19 y +				

<sup>a</sup> PAL = Physical Activity Level.

When energy intake is lower than energy needs, the body adapts by reducing voluntary physical activity, reducing growth rates (in children), and mobilizing energy reserves, primarily adipose tissue, which in turn leads to weight loss. In adults, an abnormally low BMI is associated with decreased work capacity and limited voluntary physical activity.

When energy intake is higher than energy needs, weight gain occurs and consequently chronic disease risk increases, including risk of Type II diabetes, hypertension, coronary heart disease (CHD), stroke, gallbladder disease, osteoarthritis, and some types of cancer.

## ENERGY AND THE BODY

### Function

Energy is required to sustain the body's various functions, including respiration, circulation, metabolism, physical work, and protein synthesis.

## Background Information

Energy in foods is released in the body through the oxidation of various organic substances, primarily carbohydrates, fats, and amino acids, yielding the chemical energy required to sustain metabolism, nerve transmission, respiration, circulation, physical work, and other bodily functions. The heat produced during oxidation is used to maintain body temperature.

Carbohydrate, fat, protein, and alcohol provide all of the energy supplied by foods and are generally referred to as macronutrients (in contrast to vitamins and elements, which are referred to as micronutrients). The amount of energy released by the oxidation of macronutrients is shown in Table 3.

### ENERGY VERSUS NUTRIENTS

For many nutrients, a Recommended Dietary Allowance (RDA) is calculated by adding two standard deviations (SD) to the median amounts that are sufficient to meet a specific criterion of adequacy in order to meet the needs of nearly all healthy individuals (see Part I, “Introduction to the Dietary Reference Intakes”). However, this is not the case with energy because excess energy cannot be eliminated and is eventually deposited in the form of body fat. This reserve provides a means to maintain metabolism during periods of limited food intake, but it can also result in obesity. Therefore, it seems logical to base estimated energy intake on the amounts of energy that need to be consumed to maintain energy balance in adults who maintain desirable body weights, also taking into account the increments in energy expenditure elicited by their habitual level of activity.

There is another fundamental difference between the requirements for energy and those for nutrients. A person’s body weight is a readily monitored indicator of the adequacy or inadequacy of habitual energy intake. A compara-

**TABLE 3 Energy Provided by Macronutrients**

Macronutrient	Kcal/g <sup>a</sup>
Carbohydrate	4
Fat	9
Protein	4
Alcohol <sup>b</sup>	7

<sup>a</sup> These values for carbohydrate, fat, protein, and alcohol are known as Atwater Factors. Atwater, a pioneer in the study of nutrients and metabolism, proposed the use of these values. They are often used in nutrient labeling and diet formulation.

<sup>b</sup> The alcohol (ethanol) content of beverages is usually described in terms of percent by volume. One mL of alcohol weighs 0.789 g and provides 5.6 kcal/mL.

bly obvious and individualized indicator of inadequate or excessive intake is not usually evident for other nutrients.

### BODY MASS INDEX

Body mass index, or BMI, is defined as weight in kilograms divided by the square of height in meters. A growing body of literature supports the use of BMI as a predictor of the impact of body weight on morbidity and mortality risks. The National Institutes of Health (NIH) and the World Health Organization (WHO) have defined BMI cutoffs for adults over 19 years of age, regardless of age and gender: underweight is defined as a BMI of less than 18.5 kg/m<sup>2</sup>, overweight as a BMI from 25 up to 30 kg/m<sup>2</sup>, and obese as a BMI of 30 kg/m<sup>2</sup> or higher. A healthy or desirable BMI is considered to be from 18.5 kg/m<sup>2</sup> up to 25 kg/m<sup>2</sup>. This range of BMI is used in deriving the equations for estimating the energy requirement.

### Components of Energy Expenditure

**Basal and resting metabolism:** The basal metabolic rate (BMR) reflects the energy needed to sustain the metabolic activities of cells and tissues, plus the energy needed to maintain blood circulation, respiration, and gastrointestinal and renal function while awake, in a fasting state, and resting comfortably (i.e., the basal cost of living). BMR includes the energy expenditure associated with remaining awake, reflecting the fact that the sleeping metabolic rate (SMR) during the morning is some 5–10 percent lower than BMR during the morning hours.

BMR is commonly extrapolated to 24 hours and is then called basal energy expenditure (BEE), expressed as kcal per 24 hours. Resting metabolic rate (RMR) reflects energy expenditure under resting conditions and tends to be somewhat higher (10–20 percent) than under basal conditions, due to the increases in energy expenditure caused by recent food intake (i.e., by the thermic effect of food) or by the delayed effect of recently completed physical activity.

Basal, resting, and sleeping energy expenditures are related to body size, being most closely correlated with the size of fat-free mass (FFM), which is the weight of the body less the weight of its fat mass. The size of the FFM generally explains 70–80 percent of the variance in RMR among individuals. However, RMR is also affected by age, gender, nutritional state, inherited variations, and differences in the endocrine state.

**Thermic effect of food:** The thermic effect of food (TEF) refers to the increased energy expenditure caused by food consumption, including its digestion, transport, metabolization, and storage. The intensity and duration of meal-induced

TEF are primarily determined by the amount and composition of the foods consumed, mainly due to the metabolic costs of handling and storing ingested nutrients. The increments in energy expenditure during digestion above baseline rates, divided by the energy content of the food consumed, vary from 5 to 10 percent for carbohydrate, 0 to 5 percent for fat, and 20 to 30 percent for protein. The high TEF for protein reflects the relatively high metabolic cost involved in processing the amino acids. The TEF for a mixed diet is 10 percent of the food's energy content.

**Thermoregulation:** This is the process by which mammals regulate their body temperature within narrow limits. Because most people can adjust their clothing and environment to maintain comfort, the additional energy cost of thermoregulation rarely has an appreciable effect on total energy expenditure.

**Physical activity:** The energy expended for physical activity varies greatly among individuals and from day to day. In sedentary people, about two-thirds of total energy expenditure (TEE) goes to sustain basal metabolism over 24 hours (the BEE), while one-third is used for physical activity. In very active people, 24-hour TEE can rise to twice as much as BEE, while even higher total expenditures can occur among heavy laborers and some athletes.

In addition to the immediate energy cost of individual activities, exercise induces a small increase in energy expenditure that persists for some time after an activity has been completed. The body's excess post-exercise oxygen consumption (EPOC) depends on exercise intensity and duration and has been estimated at some 15 percent of the increment in expenditure that occurs during the activity.

**Physical activity level:** The ratio of total to basal daily energy expenditure (TEE:BEE) is known as the Physical Activity Level (PAL). PAL categories are defined as sedentary ( $\text{PAL} \geq 1.0 < 1.4$ ), low active ( $\text{PAL} \geq 1.4 < 1.6$ ), active ( $\text{PAL} \geq 1.6 < 1.9$ ), and very active ( $\text{PAL} \geq 1.9 < 2.5$ ). In this publication, PAL is used to describe and account for physical activity habits (see Part II, "Physical Activity").

**Total energy expenditure:** Total energy expenditure (TEE) is the sum of the basal energy expenditure, the thermic effect of food, physical activity, thermoregulation, and the energy expended in depositing new tissues and in producing milk. With the emergence of information on TEE by the doubly labeled water method, it has become possible to determine the energy expenditure of infants, children, and adults in free-living conditions. It refers to energy expended during the oxidation of energy-yielding nutrients to water and carbon dioxide.

## DETERMINING DRIS

### Estimated Energy Requirement

The Estimated Energy Requirement (EER) is defined as the average dietary energy intake that is predicted to maintain energy balance in a healthy adult of a defined age, gender, weight, height, and a level of physical activity that is consistent with good health. There is no RDA for energy because energy intakes above the EER would be expected to result in weight gain.

To calculate the EER for adults, prediction equations for normal-weight individuals (BMI of 18.5–25 kg/m<sup>2</sup>) were developed using data on total daily energy expenditure as measured by the DLW technique (see Table 1). In children and in pregnant or lactating women, the prediction equations for the EER account for the additional needs associated with the deposition of tissues or the secretion of milk at rates that are consistent with good health.

### Criteria for Determining Energy Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Energy expenditure plus energy deposition
7 through 12 mo	Energy expenditure plus energy deposition
1 through 18 y	Energy expenditure plus energy deposition
> 18 y	Energy expenditure

<i>Pregnancy</i>	
14 through 18 y	Adolescent female EER plus change in TEE plus pregnancy energy deposition
19 through 50 y	Adult female EER plus change in TEE plus pregnancy energy deposition

<i>Lactation</i>	
14 through 18 y	Adolescent female EER plus milk energy output minus weight loss
19 through 50 y	Adult female EER plus milk energy output minus weight loss

### Factors That Affect Energy Expenditure and Requirements

**Body composition and body size:** Although body size and weight exert apparent effects on energy expenditure, it is disputed whether differences in body composition quantitatively affect energy expenditure. It is unlikely that body

composition markedly affects energy expenditure at rest or the energy costs of physical activity in adults with BMIs of 18.5–25 kg/m<sup>2</sup>. In adults with higher percentages of body fat, mechanical hindrances can increase the energy expenditure associated with certain activities.

The proportion of fat-free mass (FFM) is the major parameter in determining the rate of energy expenditure under fasting basal metabolic rate (BMR) and resting metabolic rate (RMR) conditions. RMR/kg of weight or RMR/kg of FFM falls as mass increases because the contributions made by the most metabolically active tissues (the brain, liver, and heart) decline as body size increases.

Findings from different studies suggest that low energy expenditure is a risk factor for weight gain in a subgroup of people susceptible to excess weight gain, but not in all susceptible people and not in those with a normal level of risk. These data are consistent with the general view that obesity is a multi-factorial problem.

**Physical activity:** The increased energy expenditure that occurs during physical activity accounts for the largest part of the effect of activity on overall energy expenditure. Physical activity also affects energy expenditure in the post-exercise period, depending on exercise intensity and duration, environmental temperatures, one's state of hydration, and the degree of trauma to the body. This effect lasts for as many as 24 hours following exercise.

Spontaneous non-exercise activity reportedly accounts for 100–700 kcal/day. Sitting without fidgeting or sitting with fidgeting raises energy expenditure by 4 or 54 percent, respectively, compared with lying down. Standing while motionless or standing while fidgeting raises energy expenditure by 13 or 94 percent, respectively.

**Gender:** There are substantial data on the effects of gender on energy expenditure throughout the lifespan. Gender differences in BMR are due to the greater level of body fat in women and to differences in the relationship between RMR and FFM.

**Growth:** Energy requirements in infants and children include the energy associated with the deposition of tissues at rates consistent with good health. The energy cost of growth as a percentage of total energy requirements decreases from around 35 percent at age 1 month to 3 percent at age 12 months. It remains low until the adolescent growth spurt, when it then increases to about 4 percent. The timing of the adolescent growth spurt, which typically lasts 2 to 3 years, is also very variable, with the onset typically occurring between ages 10 and 13 years in the majority of children.

**Older age:** All three major components of energy expenditure (RMR, TEF, and energy expenditure of physical activity [EEPA]), decrease with aging. There is an average 1–2 percent decline per decade in men who maintain constant weight. The suggested breakpoint for a more rapid decline appears to occur at approximately age 40 years in men and age 50 years in women. For women, this may be due to an accelerated loss of FFM during menopause. PAL has been shown to progressively decrease with age and is lower in elderly adults compared to young adults.

**Genetics:** Individual energy requirements substantially vary due to combinations of differences in body size and composition; differences in RMR independent of body composition; differences in TEF; and differences in physical activity and EEPA. All of these determinants of energy requirement are potentially influenced by genetics, with cultural factors also contributing to variability.

**Ethnicity:** Data from studies of adults and children indicate that the BMR is usually lower in African Americans than Caucasians. Currently, insufficient data exist to create accurate prediction equations of BMRs for African American adults. In this publication, the general prediction equations in Table 1 are used for all races, recognizing their potential to overestimate BMR in some groups such as African Americans.

**Environment:** There is a modest 2–5 percent increase in sedentary TEE at low-normal environmental temperatures (20–28°C, or 68–82°F) compared with high-normal temperatures (28–30°C, or 82–86°F). However, in setting energy requirements, no specific allowance was made for environmental temperatures. The TEE values used to predict energy requirements can be considered values that have been averaged for the environmental temperatures of different seasons. High altitude also increases BMR and TEE due to the hypobaric hypoxia. However, it is unclear at which heights the effect becomes prominent.

**Adaptation and accommodation:** Adaptation implies the maintenance of essentially unchanged functional capacity in spite of some alteration in a steady-state condition, and it involves changes in body composition that occur over an extended period of time. The term adaptation describes the normal physiological responses of humans to different environmental conditions. An example of adaptation is the increase in hemoglobin concentration that occurs when individuals live at high altitudes.

Accommodation refers to relatively short-term adjustments that are made to maintain adequate functional capacity under altered steady-state conditions. The term accommodation characterizes an adaptive response that allows sur-

vival but results in some consequences on health or physiological function. The most common example of accommodation is a decrease in growth velocity in children. By reducing growth rate, children's bodies are able to save energy and may subsist for prolonged periods of time on marginal energy intakes, although this could be at the cost of eventually becoming stunted. The estimation of energy requirements from energy expenditure implicitly assumes that the efficiency of energy use is more or less uniform across all individuals, an assumption that is supported by experimental data.

## The UL

The Tolerable Upper Intake Level (UL) is the highest daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. The UL concept does not apply to energy because intake above an individual's energy requirements would lead to weight gain and likely increased risk of morbidity.

## EFFECTS OF UNDERNUTRITION

Undernutrition is still a common health concern in many parts of the world, particularly in children. When energy intake does not match energy needs due to insufficient dietary intake, excessive intestinal losses, or a combination thereof, several mechanisms of adaptation come into play. A reduction in voluntary physical activity is a rapid means to reduce energy output. In children, a reduction in growth rate is another mechanism to reduce energy needs. However, if this condition persists in children, low growth weight results in short stature and low weight-for-age, a condition known as stunting. A chronic energy deficit elicits the mobilization of energy reserves, primarily adipose tissue, which leads to changes in body weight and body composition over time.

In children, the effects of chronic undernutrition include decreased school performance, delayed bone age, and an increased susceptibility to infections. In adults, an abnormally low BMI is associated with decreased work capacity and limited voluntary physical activity.

## ADVERSE EFFECTS OF OVERCONSUMPTION

Two major adverse effects result from the overconsumption of energy:

- *Adaptation to high levels of energy intake:* When people are given a diet providing a fixed, but limited, amount of excess energy, they initially gain weight. However, over a period of several weeks, their energy expenditure will increase, mostly because of their increased body size. As such, their body weight will eventually stabilize at a higher weight level.

Reducing energy intake will produce the opposite effect. For most individuals, it is likely that the main mechanism for maintaining body weight is controlling food intake rather than adjusting physical activity.

- *Increased risk of chronic disease:* A BMI of  $\geq 25 \text{ kg/m}^2$  is associated with an increased risk of premature mortality. In addition, as BMI increases beyond  $25 \text{ kg/m}^2$ , morbidity risk increases for Type II diabetes, hypertension, coronary heart disease (CHD), stroke, gallbladder disease, osteoarthritis, and some types of cancer. Because some studies suggest that disease risk begins to rise at lower BMI levels, some investigators have recommended aiming for a BMI of  $22 \text{ kg/m}^2$  at the end of adolescence. This level would allow for some weight gain in mid-life without surpassing the  $25 \text{ kg/m}^2$  threshold.

For the above reasons, energy intakes associated with adverse risks are defined as those that cause weight gain in individuals with body weights that fall within the healthy range (BMI of  $18.5\text{--}25 \text{ kg/m}^2$ ) and overweight individuals (BMI of  $25\text{--}30 \text{ kg/m}^2$ ). In the case of obese individuals who need to lose weight to improve their health, energy intakes that cause adverse risks are those that are higher than intakes needed to lose weight without causing negative health consequences.

## KEY POINTS FOR ENERGY

- ✓ Energy is required to sustain the body's various functions, including respiration, circulation, metabolism, physical work, and protein synthesis.
- ✓ A person's energy balance depends on his or her dietary energy intake and total energy expenditure, which includes the basal energy expenditure, the thermic effect of food, physical activity, thermoregulation, and the energy expended in depositing new tissues and in producing milk.
- ✓ Imbalances between energy intake and expenditure result in the gain or loss of body components, mainly in the form of fat. These gains or losses determine changes in body weight.
- ✓ The EER is the average dietary energy intake that is predicted to maintain energy balance in a healthy adult of a defined age, gender, weight, height, and a level of physical activity that is consistent with good health.
- ✓ In children and in pregnant and lactating women, the EER accounts for the needs associated with growth, deposition of tissues, and the secretion of milk at rates that are consistent with good health.

- ✓ A person's body weight is a readily monitored indicator of the adequacy or inadequacy of habitual energy intake.
- ✓ Numerous factors affect energy expenditure and requirements, including age, body composition, gender, and ethnicity.
- ✓ There is no RDA for energy because energy intakes above the EER would be expected to result in weight gain.
- ✓ The UL concept does not apply to energy because any intake above a person's energy requirements would lead to undesirable weight gain.
- ✓ When energy intake is less than energy needs, the body adapts by mobilizing energy reserves, primarily adipose tissue.
- ✓ In adults, an abnormally low BMI is associated with decreased work capacity and limited voluntary physical activity.
- ✓ The overconsumption of energy leads to the adaptation to high levels of energy intake with weight gain and an increased risk of chronic diseases, including Type II diabetes, hypertension, CHD, stroke, gallbladder disease, osteoarthritis, and some types of cancer.

**TABLE 1 Physical Activity Recommendations**

**ADULT**

An average of 60 minutes per day of moderately intense physical activity (e.g., brisk walking or jogging at 3–4 mph) or shorter periods of more vigorous exertion (e.g., jogging for 30 minutes at 5.5 mph), in addition to activities identified with a sedentary lifestyle, was associated with a normal BMI range and is the amount of physical activity recommended for normal-weight adults.

**CHILDREN**

An average of 60 minutes of moderately intense daily activity is also recommended for children.

# PHYSICAL ACTIVITY

Physical activity promotes health and vigor, and the lack of it is now a recognized risk factor for several chronic diseases. Observational and experimental studies of humans and animals have provided biologically plausible insights into the benefits of regular physical activity on the delayed progression of several chronic diseases, including cancer, cardiovascular disease, Type II diabetes, obesity, and skeletal conditions. In addition, acute or chronic aerobic exercise may be related to favorable changes in anxiety, depression, stress reactivity, mood, self-esteem, and cognitive functioning.

Cross-sectional data from a doubly labeled water (DLW) database were used to define a recommended level of physical activity based on the physical activity level (PAL) that is associated with a normal body mass index (BMI) of 18.5–25 kg/m<sup>2</sup>. An average of 60 minutes per day of moderately intense physical activity (e.g., brisk walking or jogging at 3–4 mph) or shorter periods of more vigorous exertion (e.g., jogging for 30 minutes at 5.5 mph), in addition to activities identified with a sedentary lifestyle, is the amount of physical activity recommended for normal-weight adults. An average of 60 minutes of moderately intense daily activity is also recommended for children. This amount of physical activity leads to an “active” lifestyle. Because the Dietary Reference Intakes are for the general healthy population, recommended levels of physical activity for weight loss of obese individuals are not provided.

Historically, most individuals have unconsciously balanced their dietary energy intake and total energy expenditure due to occupation-related energy expenditure. However, occupational physical activity has significantly declined over the years. According to the 1996 *Surgeon General’s Report* on physical activity and health, more than 60 percent of American adults were not regularly physically active and 25 percent were not active at all. This trend in decreased activity by adults is similar to trends seen in children who are less active both in and out of school. Physical activity and fitness objectives of the U.S. government’s Healthy People 2010 seek to increase the proportion of Americans who engage in daily physical activity to improve health, fitness, and quality of life. Similar recommendations to increase physical activity have been proposed in Canada.

Excessive physical activity can lead to overuse injuries, dehydration and hyperthermia, hypothermia, cardiac events, and female athlete triad (loss of menses, osteopenia, and premature osteoporosis). To prevent adverse effects,

previously sedentary people are advised to use caution when beginning a new activity routine.

## DETERMINING RECOMMENDATIONS

Cross-sectional data from a DLW database were used to define a recommended level of physical activity for adults and children, based on the PAL associated with a normal BMI in the healthy range of 18.5 kg/m<sup>2</sup> up to 25 kg/m<sup>2</sup>. PAL is the ratio of total energy expenditure (TEE) to basal energy expenditure (BEE). The data PAL categories were defined as sedentary (PAL ≥ 1.0 < 1.4), low active (PAL ≥ 1.4 < 1.6), active (PAL ≥ 1.6 < 1.9), and very active (PAL ≥ 1.9 < 2.5).

Because an average of 60 minutes per day of moderate-intensity physical activities (or shorter periods of more vigorous exertion) provides a PAL that is associated with a normal BMI range, this is the amount of activity that is recommended for normal-weight individuals. For children, the physical activity recommendation is also an average of 60 minutes of moderate-intensity daily activity. In terms of making a realistic physical activity recommendation for busy individuals to maintain their weight, it is important to recognize that exercise and activity recommendations consider “accumulated” physical activity.

Box 1 provides examples of various physical activities at different intensities. Additional examples of activity, along with instructions for keeping a weekly activity log, can be found in *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* (2002/2005).

## Special Considerations

**Pregnant women:** For women who have been previously physically active, continuing physical activities during pregnancy and postpartum can be advantageous. However, excessive or improper activity can be injurious to the woman and fetus.

Appropriate physical fitness during pregnancy improves glucose tolerance and insulin action, improves emotional well-being, and helps prevent excessive weight gain. Fitness promotes a faster delivery, and the resumption of physical activity after pregnancy is important for restoring normal body weight. A full description of the benefits and hazards of exercise for the pregnant woman and fetus is beyond the scope of this publication. Women should consult with their physicians on how to safely exercise during pregnancy.

## Physical Activity Level and Energy Balance

Increasing or maintaining an active lifestyle provides an important means for individuals to balance their energy intake with their total energy expenditure.

**BOX 1 Examples of Various Physical Activities****Mild ( $\Delta$ PAL/hr: 0.05–0.10)<sup>a</sup>**

Billiards  
Canoeing (Leisurely)  
Dancing (Ballroom)  
Golf (with Cart)  
Horseback Riding (Walking)  
Loading/Unloading Car  
Playing  
Taking out Trash  
Walking (2 mph)  
Walking the Dog  
Watering Plants

**Moderate ( $\Delta$ PAL/hr: 0.13–0.22)**

Calisthenics (No Weight)  
Cycling (Leisurely)  
Gardening (No Lifting)  
Golf (without Cart)  
Household Tasks, Moderate Effort  
Mopping  
Mowing Lawn (Power Mower)  
Raking Lawn  
Swimming (Slow)  
Vacuuming  
Walking (3–4 mph)

**Vigorous ( $\Delta$ PAL/hr: 0.23–0.63)**

Chopping Wood  
Climbing Hills (No Load up to 5-kg Load)  
Cycling (Moderately)  
Dancing (Aerobic, Ballet, Ballroom, Fast)  
Jogging (10-Minute Miles)  
Rope Skipping  
Surfing  
Swimming  
Tennis

<sup>a</sup>  $\Delta$ PAL/hr is the increase in PAL caused by the activity.

Changing one's usual activity level can have a major impact on total energy expenditure and energy balance. The ultimate indicator of this energy balance is body weight, as seen through its maintenance or change.

Energy intake and the energy expenditure of physical activity are controllable variables that impact energy balance, in contrast to other uncontrollable variables that include age, height, and gender. During exercise, energy expenditure can increase far beyond resting rates, and the increased energy expenditure induced by a workout can persist for hours, if not a day or longer. Furthermore, exercise does not necessarily boost appetite or intake in direct proportion to activity-related changes in energy expenditure.

## **HEALTHFUL EFFECTS OF PHYSICAL ACTIVITY**

Observational and experimental studies of humans and animals provide biologically plausible insights into the benefits of regular physical activity on the delayed progression of several chronic diseases, including cancer, cardiovascular disease, Type II diabetes, obesity, and skeletal conditions. In addition, acute or chronic aerobic exercise may be related to favorable changes in anxiety, depression, stress reactivity, mood, self-esteem, and cognitive functioning.

It is difficult to determine a quantifiable recommendation for physical activity based on reduced risk of chronic disease. However, meeting the physical activity recommendation of 60 minutes per day offers additional benefits in reducing the risk of chronic disease; for example, by favorably altering blood lipid profiles, changing body composition by decreasing body fat, and increasing muscle mass, or both.

### **Endurance (Aerobic) Exercise**

Traditionally, the types of activities recommended for cardiovascular fitness are those of a prolonged endurance nature, such as bicycling, hiking, jogging, and swimming. Because of the energy demands associated with these prolonged mild to moderate intensity endurance activities, they have the potential to decrease body fat mass and preserve fat-free mass, thus changing body composition.

### **Resistance Exercise and General Physical Fitness**

Although resistance training exercises have not yet been shown to have the same effects as endurance activities on the risks of chronic disease, their effects on muscle strength are an indication to include them in exercise prescriptions, in addition to activities that promote cardiovascular fitness and flexibility. Exer-

cises that strengthen the muscles, bones, and joints stimulate muscular and skeletal development in children, as well as assist in balance and locomotion in the elderly, thereby minimizing the incidence of falls and associated complications of trauma and bed rest.

## **EXCESSIVE PHYSICAL ACTIVITY**

Excessive physical activity can lead to the following adverse effects:

- *Overuse injuries:* Too much or improper physical exercise can cause overuse injuries to muscles, bones, and joints, as well as injuries caused by accidents. In addition, pre-existing conditions can be aggravated by the initiation of a physical activity program. Activity-related injuries are often avoidable but do occur and need to be resolved in the interest of long-term general health and short-term physical fitness.
- *Dehydration and hyperthermia:* Exercise may cause dehydration, which can be aggravated by environmental conditions that increase fluid losses, such as heat, humidity, and lack of wind. People should consume water before, during (if possible), and after exercise.
- *Hypothermia:* Hypothermia can result from water exposure and heat loss during winter sports. Poor choice of clothing during skiing, accidental water immersion due to a capsized boat, weather changes, or physical exhaustion may lead to the inability to generate adequate body heat to maintain core body temperature, which can lead to death, even when temperatures are above freezing.
- *Cardiac events:* Although regular physical activity promotes cardiovascular fitness, heavy physical exertion can trigger the development of arrhythmias or myocardial infarctions or, in some instances, can lead to sudden death.
- *Female athlete triad:* Athletic women who undereat or overtrain can develop a condition, or cluster of conditions, called the “female athlete triad.” In this triad, disordered eating and chronic energy deficits can lead to loss of menses, osteopenia, and premature osteoporosis, increasing the risk of hip, spine, and forearm fractures.

## **Prevention of Adverse Effects**

Previously sedentary people are advised to begin a new activity routine with caution. The following people should seek medical evaluation, as well as clinical exercise testing, clearance, and advice prior to starting an exercise program: men over age 40 years, women over age 50 years, people with pre-existing

medical conditions, and people with known or suspected risk factors or symptoms of cardiovascular and other chronic diseases (physical inactivity being a risk factor). For those with cardiovascular risk or orthopedic problems, physical activity should be undertaken with professional supervision. For all individuals, easy exercise should be performed regularly before more vigorous activities are conducted.

## KEY POINTS FOR PHYSICAL ACTIVITY

- ✓ Lack of physical activity and obesity are now recognized risk factors for several chronic diseases.
- ✓ Observational and experimental studies of humans and animals provide biologically plausible insights into the benefits of regular physical activity on the delayed progression of several chronic diseases, including cancer, cardiovascular disease, Type II diabetes, obesity, and skeletal conditions.
- ✓ Acute or chronic aerobic exercise may be related to favorable changes in anxiety, depression, stress reactivity, mood, self-esteem, and cognitive functioning.
- ✓ Changing one's usual activity level can have a major impact on total energy expenditure and energy balance.
- ✓ In addition to activities that characterize a sedentary lifestyle, an average of 60 minutes per day of moderate-intensity physical activities (e.g., brisk walking or jogging at 3–4 mph) or shorter periods of more vigorous exertion (e.g., jogging for 30 minutes at 5.5 mph) is the amount of physical activity recommended for normal-weight adults. For children, the physical activity recommendation is also an average of 60 minutes of moderate-intensity daily activity.
- ✓ More than 60 percent of American adults are not regularly physically active and 25 percent are not active at all. Similar trends are seen in children.
- ✓ Excessive physical activity can lead to overuse injuries, dehydration and hyperthermia, hypothermia, cardiac events, and female athlete triad (loss of menses, osteopenia, and premature osteoporosis).
- ✓ Previously sedentary people are advised to begin a new activity routine with caution to prevent adverse effects.

**TABLE 1 Dietary Reference Intakes for Dietary Carbohydrates: Sugars and Starches by Life Stage Group**

	DRI values (g/day)		
	EAR <sup>a</sup>	RDA <sup>b</sup>	AI <sup>c</sup>
<b>Life stage group<sup>d</sup></b>			
0 through 6 mo			60
7 though 12 mo			95
1 through 3 y	100	130	
4 through 8 y	100	130	
9 through 13 y	100	130	
14 through 18 y	100	130	
19 through 30 y	100	130	
31 through 50 y	100	130	
51 through 70 y	100	130	
> 70 y	100	130	
<b>Pregnancy</b>			
All ages	135	175	
<b>Lactation</b>			
All ages	160	210	

<sup>a</sup> **EAR** = Estimated Average Requirement. An EAR is the average daily nutrient intake level estimated to meet the requirements of half of the healthy individuals in a group.

<sup>b</sup> **RDA** = Recommended Dietary Allowance. An RDA is the average daily dietary intake level sufficient to meet the nutrient requirements of nearly all (97–98 percent) healthy individuals in a group.

<sup>c</sup> **AI** = Adequate Intake. If sufficient scientific evidence is not available to establish an EAR, and thus calculate an RDA, an AI is usually developed. For healthy breast-fed infants, the AI is the mean intake. The AI for other life stage and gender groups is believed to cover the needs of all healthy individuals in the group, but a lack of data or uncertainty in the data prevents being able to specify with confidence the percentage of individuals covered by this intake.

<sup>d</sup> All groups except Pregnancy and Lactation represent males and females.

# DIETARY CARBOHYDRATES: SUGARS AND STARCHES

The primary role of carbohydrates (i.e., sugars and starches) is to provide energy to all of the cells in the body. Carbohydrates are divided into several categories: monosaccharides, disaccharides, oligosaccharides, polysaccharides, and sugar alcohols.

The requirements for carbohydrates are based on the average minimum amount of glucose that is utilized by the brain. Evidence was insufficient to set a Tolerable Upper Intake Level (UL) for carbohydrates. However, a maximal intake level of 25 percent or less of total calories from added sugars is suggested. This suggestion is based on trends indicating that people with diets at or above this level of added sugars are more likely to have poorer intakes of important essential nutrients. DRI values are listed by life stage group in Table 1.

Nondiet soft drinks are the leading source of added sugars in U.S. diets, followed by sugars and sweets, sweetened grains, fruit ades, sweetened dairy products, and breakfast cereals and other grains.

Most carbohydrates occur as starches in food. Grains and certain vegetables are major contributors. Other sources include corn, tapioca, flour, cereals, popcorn, pasta, rice, potatoes, and crackers. Fruits and darkly colored vegetables contain little or no starch.

The amount of dietary carbohydrate that confers optimal health in humans is unknown. A significant body of data suggests that more slowly absorbed starchy foods that are less processed, or have been processed in traditional ways, may have health advantages over those that are rapidly digested and absorbed.

## CARBOHYDRATE AND THE BODY

### Function

The primary role of carbohydrates (i.e., sugars and starches) is to provide energy to the cells in the body. The only cells that have an absolute requirement for glucose are those in the central nervous system (i.e., the brain) and those cells that depend upon anaerobic glycolysis, such as red blood cells. Normally, the brain uses glucose almost exclusively for its energy needs.

## Classification of Dietary Carbohydrates

Carbohydrates are classified by their number of sugar units: monosaccharides, such as glucose or fructose, consist of one sugar unit; disaccharides, such as sucrose, lactose, and maltose, consist of two sugar units; oligosaccharides, such as raffinose and stachyose, contain 3 to 10 sugar units and may be produced by the breakdown of polysaccharides; and polysaccharides, such as starch and glycogen, contain more than 10 sugar units and are the storage forms of carbohydrates in plants and animals, respectively. Sugar alcohols, such as sorbitol and mannitol, are alcohol forms of glucose and fructose, respectively.

### SUGARS AND ADDED SUGARS

The term “sugars” is traditionally used to describe the monosaccharides and disaccharides. Monosaccharides include glucose, galactose, and fructose. Disaccharides include sucrose, lactose, maltose, and trehalose. Sugars are used to sweeten or preserve foods and to give them certain functional attributes, such as viscosity, texture, body, and browning capacity.

“Added sugars” are defined as sugars and syrups that are added to foods during processing or preparation. They do not include naturally occurring sugars, such as lactose in milk or fructose in fruits. Major food sources of added sugars include soft drinks, cakes, cookies, pies, fruit ades, fruit punch, dairy desserts, and candy. Specifically, added sugars include white sugar, brown sugar, raw sugar, corn syrup, corn-syrup solids, high-fructose corn syrup, malt syrup, maple syrup, pancake syrup, fructose sweetener, liquid fructose, honey, molasses, anhydrous dextrose, and crystal dextrose.

Although added sugars are not chemically different from naturally occurring sugars, many foods and beverages that are major sources of added sugars have lower micronutrient densities compared with foods and beverages that are major sources of naturally occurring sugars.

### STARCHES

Starch is a carbohydrate polymer found in grains, legumes, and tubers. It is a polysaccharide composed of less than 1,000 to many thousands of  $\alpha$ -linked glucose units and its two forms are amylose and amylopectin. Amylose is the linear form of starch, while amylopectin consists of linear and branched glucose polymers. In general, amylose starches are compact, have low solubility, and are less rapidly digested. Amylopectin starches are more rapidly digested, presumably because of their more open-branched structure.

## Absorption, Metabolism, and Storage

The breakdown of starch begins in the mouth, where enzymes act on the linkages of amylase and amylopectin. The digestion of these linkages continues in the intestine, where more enzymes are released, breaking amylase and amylopectin into shorter glucose chains of varying lengths. Specific enzymes that are bound to the intestinal brush border membrane hydrolyze the glucose chains into monosaccharides, which are then absorbed into the bloodstream via active transport or facilitated diffusion mechanisms. Other sugars are also hydrolyzed to monosaccharide units before absorption.

Once absorbed, sugars (glucose, galactose, and fructose) are transported throughout the body to cells as a source of energy. Glucose is the major fuel used by most of the body's cells. Blood glucose concentration is highly regulated by the release of insulin, and the uptake of glucose by adipocytes and muscle cells is dependent on the binding of insulin to a membrane-bound insulin receptor.

Galactose and fructose are taken up by the liver (when blood circulates past it) where they are metabolized. Galactose is mostly converted to glycogen for storage. Fructose is transformed into intermediary metabolites or converted to a precursor for glycogen synthesis. When blood glucose is high and cellular energy demand is low, glucose can be converted to glycogen for storage (in skeletal muscle and liver), a process called glycogenesis. Glycogenesis is activated in the skeletal muscle by a rise in insulin concentration that occurs after the consumption of carbohydrate. It is activated in the liver by an increase in circulating monosaccharide or insulin concentrations.

Glycogen is present in the muscle for storage and utilization and in the liver for storage, export, and the maintenance of blood glucose concentrations. When blood glucose levels become too low, glycogenolysis occurs, which is the release of glucose from glycogen stores in the liver. Following glycogenolysis, the body can export glucose from the liver to maintain normal blood glucose concentrations and be used by other tissues. Muscle glycogen is mainly used in the muscle.

Gluconeogenesis, the production of glucose from a noncarbohydrate source (amino acids or glycerol), can occur during fasting (or in the absence of dietary carbohydrate), thus allowing the liver to continue to release glucose to maintain adequate blood glucose concentrations.

## Glycemic Index

A significant body of data suggests that more slowly absorbed starchy foods that are less processed, or have been processed in traditional ways, may have health advantages over those that are rapidly digested and absorbed. The former have been classified as having a low glycemic index (GI) and reduce the diet's

glycemic load. GI is a measure of the increase in blood glucose in the two hours after eating a given amount (e.g., 50 g) of a carbohydrate relative to its response to a reference carbohydrate (white bread or glucose). The glycemic load is an indicator of the glucose response or insulin demand that is induced by total carbohydrate intake. Dietary GI and glycemic load have relatively predictable effects on circulating glucose, hemoglobin A<sub>1c</sub>, insulin, triacylglycerol, high density lipoprotein (HDL) cholesterol, and urinary C-peptide concentrations. As such, it is theoretically plausible to expect a low GI diet to reduce risk of Type II diabetes and cardiovascular disease. However, the sufficient evidence needed to recommend substantial dietary changes based on GI is not available.

## DETERMINING DRIS

### Determining Requirements

The requirements for carbohydrates are based on the average minimum amount of glucose that is utilized by the brain. Because brain size remains fairly constant after 1 year of age and approximates adult size, the EAR and RDA are identical for all age and gender groups after age 12 months, except pregnant and lactating women. The recommended amount also prevents ketosis, which is a rise in keto acid production in the liver to provide the brain with an alternative fuel in times of low glucose availability.

### Criteria for Determining Carbohydrate Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Average content of human milk
7 through 12 mo	Average intake from human milk + complementary foods
1 through 18 y	Extrapolation from adult data
> 18 y	Brain glucose utilization
<i>Pregnancy</i>	
14 through 18 y	Adolescent female EAR plus fetal brain glucose utilization
19 through 50 y	Adult female EAR plus fetal brain glucose utilization
<i>Lactation</i>	
14 through 18 y	Adolescent female EAR plus average human milk content of carbohydrate
19 through 50 y	Adult female EAR plus average human milk content of carbohydrate

## The AMDR

The AMDR for carbohydrates for both adults and children is 45–65 percent of total calories (see Part II, “Macronutrients, Healthful Diets, and Physical Activity”).

## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Evidence was insufficient to set a UL for carbohydrates. However, a maximal intake level of 25 percent or less of total energy from added sugars is suggested, based on trends indicating that people with diets at or above this level of added sugars are more likely to have poorer intakes of important essential nutrients.

## DIETARY SOURCES

### Foods

According to U.S. Department of Agriculture food consumption survey data from 1994 to 1996, nondiet soft drinks were the leading source of added sugars in U.S. diets, accounting for one-third of added sugar intake. This was followed by sugars and sweets (16 percent), sweetened grains (13 percent), fruit ades and drinks (10 percent), sweetened dairy products (9 percent), and breakfast cereals and other grains (10 percent). Together, they account for 90 percent of the added sugars that are consumed in the United States.

Most carbohydrates occur as starches in food. Grains and certain vegetables are major contributors. Grain sources include corn, tapioca, flour, cereals, popcorn, pasta, rice, potatoes, and crackers. Fruits and darkly colored vegetables contain little or no starch.

## INADEQUATE INTAKE AND DEFICIENCY

The amount of dietary carbohydrate that confers optimal health in humans is unknown. The ability of humans to endure weeks of starvation after endogenous glycogen supplies are exhausted is indicative of the body's ability to survive without an exogenous supply of glucose. However, adapting to a fat and protein fuel requires considerable metabolic adjustments.

In Western urban societies, one particular concern is the long-term effect of a diet so low in carbohydrate that it induces a chronically increased production of keto acids. Such a diet may lead to bone mineral loss, hypercholesterolemia, increased risk of urolithiasis, and impaired development and function of the central nervous system. It also may adversely affect a person's sense of

well-being and fail to provide adequate glycogen stores. The latter is required for hypoglycemic emergencies and for maximal short-term power production by muscles.

## **ADVERSE EFFECTS OF OVERCONSUMPTION**

Data are mixed on potential adverse effects of overconsuming carbohydrate (i.e., sugars and starches), which include dental caries, behavioral changes, cancer, risk of obesity, and risk of hyperlipidemia. For more information on the association between carbohydrates and chronic disease, see Part II, “Macronutrients, Healthful Diets, and Physical Activity.”

## **KEY POINTS FOR DIETARY CARBOHYDRATES: SUGARS AND STARCHES**

- ✓ Carbohydrates (sugars and starches) provide energy to the cells in the body.
- ✓ The requirements for carbohydrate are based on the average minimum amount of glucose that is utilized by the brain.
- ✓ Evidence was insufficient to set a UL for carbohydrates.
- ✓ A maximal intake level of 25 percent or less of total energy from added sugars is suggested, based on trends indicating that people with diets at or above this level of added sugars are more likely to have poorer intakes of important essential nutrients.
- ✓ Nondiet soft drinks are the leading source of added sugars in U.S. diets, followed by sugars and sweets, sweetened grains, fruit ades, sweetened dairy products, and breakfast cereals and other grains.
- ✓ Most carbohydrates occur as starches in food. Grains and certain vegetables are major contributors. Grain sources include corn, tapioca, flour, cereals, popcorn, pasta, rice, potatoes, and crackers.
- ✓ The amount of dietary carbohydrate that confers optimal health in humans is unknown.
- ✓ Of particular concern is the long-term effect of a diet so low in carbohydrate that it induces a chronically increased production of keto acids. Such a diet may lead to bone mineral loss, hypercholesterolemia, increased risk of urolithiasis, and impaired development and function of the central nervous system.
- ✓ Data are mixed on potential adverse effects of overconsuming carbohydrate.

**TABLE 1 Dietary Reference Intakes for *Total Fiber*<sup>a</sup> by Life Stage Group**

	DRI values (g/1,000 kcal) [g/day] <sup>b</sup>	
	males	females
<b>Life stage group</b>		
0 through 6 mo	ND <sup>d</sup>	ND
7 through 12 mo	ND	ND
1 through 3 y	14 [19]	14 [19]
4 through 8 y	14 [25]	14 [25]
9 through 13 y	14 [31]	14 [26]
14 through 18 y	14 [38]	14 [26]
19 through 30 y	14 [38]	14 [25]
31 through 50 y	14 [38]	14 [25]
51 through 70 y	14 [30]	14 [21]
> 70 y	14 [30]	14 [21]
<b>Pregnancy</b>		
< 18 y		14 [28]
19 through 50 y		14 [28]
<b>Lactation</b>		
< 18 y		14 [29]
19 through 50 y		14 [29]

<sup>a</sup>*Total Fiber* is the combination of *Dietary Fiber*, the edible, nondigestible carbohydrate and lignin components as they exist naturally in plant foods, and *Functional Fiber*, which refers to isolated, extracted, or synthetic fiber that has proven health benefits.

<sup>b</sup> Values in parentheses are example of the total g/day of total fiber calculated from g/1,000 kcal multiplied by the median energy intake (kcal/1,000 kcal/day) from the Continuing Survey of Food Intakes by Individuals (CSFII 1994–1996, 1998).

<sup>c</sup> AI = Adequate Intake. If sufficient scientific evidence is not available to establish an Estimated Average Requirement (EAR), and thus calculate a Recommended Dietary Allowance (RDA), an AI is usually developed. For healthy breast-fed infants, the AI is the mean intake. The AI for other life stage and gender groups is believed to cover the needs of all healthy individuals in the group, but a lack of data or uncertainty in the data prevents being able to specify with confidence the percentage of individuals covered by this intake.

<sup>d</sup> ND = Not determined.

# FIBER

The term *Dietary Fiber* describes the carbohydrates and lignin that are intrinsic and intact in plants and that are not digested and absorbed in the small intestine. *Functional Fiber* consists of isolated or purified carbohydrates that are not digested and absorbed in the small intestine and that confer beneficial physiological effects in humans. *Total Fiber* is the sum of *Dietary Fiber* and *Functional Fiber*. Fibers have different properties that result in different physiological effects, including laxation, attenuation of blood glucose levels, and normalization of serum cholesterol levels.

Since data were inadequate to determine an Estimated Average Requirement (EAR) and thus calculate a Recommended Dietary Allowance (RDA) for *Total Fiber*, an Adequate Intake (AI) was instead developed. The AIs for *Total Fiber* are based on the intake levels that have been observed to protect against coronary heart disease (CHD). The relationship of fiber intake to colon cancer is the subject of ongoing investigation and is currently unresolved. A Tolerable Upper Intake Level (UL) was not set for fiber. DRI values are listed by life stage group in Table 1.

*Dietary Fiber* is found in most fruits, vegetables, legumes, and grains. *Dietary* and *Functional Fibers* are not essential nutrients; therefore, inadequate intakes do not result in biochemical or clinical symptoms of a deficiency. As part of an overall healthy diet, a high intake of *Dietary Fiber* will not cause adverse effects in healthy people.

## DEFINITIONS OF FIBER

### Dietary Fiber, Functional Fiber, and Total Fiber

This publication defines *Total Fiber* as the combination of *Dietary Fiber*, the edible, nondigestible carbohydrate and lignin components as they exist naturally in plant foods, and *Functional Fiber*, which refers to isolated, extracted, or synthetic fiber that has proven health benefits. Nondigestible means that the material is not digested and absorbed in the human small intestine (see Box 1 for definitions). Fiber includes viscous forms that may lower serum cholesterol concentrations (e.g., oat bran, beans) and the bulking agents that improve laxation (e.g., wheat bran).

*Dietary Fiber* in foods is usually a mixture of the polysaccharides that are integral components of plant cell walls or intracellular structures. *Dietary Fiber*

**BOX 1 Definitions of Fiber<sup>a</sup>**

- *Dietary Fiber* consists of nondigestible carbohydrates and lignin that are intrinsic and intact in plants.
- *Functional Fiber* consists of isolated nondigestible carbohydrates that have beneficial physiological effects in humans.
- *Total Fiber* is the sum of *Dietary Fiber* and *Functional Fiber*.

<sup>a</sup> In the United States, dietary fiber is defined for regulatory purposes by a number of analytical methods that are accepted by the Association of Official Analytical Chemists International (AOAC). In Canada, a distinction is made between dietary fiber (defined as the endogenous components of plant material in the diet that are resistant to digestion by enzymes produced by man) and novel fibers, whose definition is similar to *functional fiber*. Novel fibers must be demonstrated to have beneficial effects to be considered as fiber for the purposes of labeling and claims.

sources contain other macronutrients (e.g., digestible carbohydrate and protein) normally found in foods. For example, cereal brans, which are obtained by grinding, are anatomical layers of the grain consisting of intact cells and substantial amounts of starch and protein. Other examples include plant nonstarch polysaccharides (e.g., cellulose, pectin, gums, and fibers in oat and wheat bran), plant carbohydrates (e.g., inulin, fructans), lignin, and some resistant starch.

*Functional Fiber* may be isolated or extracted using chemical, enzymatic, or aqueous steps, such as synthetically manufactured or naturally occurring isolated oligosaccharides and manufactured resistant starch. In order to be classified as a *Functional Fiber*, a substance must demonstrate a beneficial physiological effect. Potential *Functional Fibers* include isolated nondigestible plant (e.g., pectin and gums), animal (e.g., chitin and chitosan), or commercially produced (e.g., resistant starch, polydextrose) carbohydrates.

## FIBER AND THE BODY

### Function

Different fibers have different properties and thus varying functions. They aid in laxation and promote satiety, which may help reduce energy intake and therefore the risk of obesity. They can also attenuate blood glucose levels, normalize serum cholesterol levels, and reduce the risk of CHD. For example, viscous

fibers can interfere with the absorption of dietary fat and cholesterol, as well as the enterohepatic recirculation of cholesterol and bile acids, which may result in reduced blood cholesterol concentrations and a reduced risk of CHD.

## Absorption, Metabolism, and Excretion

Once consumed, *Dietary Fiber* and *Functional Fiber* pass relatively intact into the large intestine. Along the gastrointestinal tract, the properties of different fibers result in varying physiological effects:

**Gastric emptying and satiety:** Viscous fiber delays gastric emptying, thereby slowing the process of absorption in the small intestine. This can cause a feeling of fullness, as well as delayed digestion and absorption of nutrients, including energy. Delayed gastric emptying may also reduce postprandial blood glucose concentrations and potentially have a beneficial effect on insulin sensitivity.

**Fermentation:** Microflora in the colon can ferment fibers to carbon dioxide, methane, hydrogen, and short-chain fatty acids. Foods rich in hemicellulose and pectin, such as fruits and vegetables, contain *Dietary Fiber* that is more completely fermented than foods rich in celluloses, such as cereals. The consumption of *Dietary* and certain *Functional Fibers*, particularly those that are poorly fermented, is known to improve fecal bulk and laxation and ameliorate constipation.

**Contribution of fiber to energy:** When fiber is anaerobically fermented by micro-flora of the colon, the short-chain fatty acids that are produced are absorbed as an energy source. Although the exact yield of energy from fiber in humans remains unclear, current data indicate that the yield is between 1.5 and 2.5 kcal/g.

**Physiological effects of isolated and synthetic fibers:** Table 2 summarizes the beneficial physiological effects of certain isolated and synthetic fibers. Note that the discussion of these potential benefits should not be construed as endorsements of the fibers. For each fiber source listed, evidence relating to one of the three most commonly accepted benefits of fibers is presented: laxation, normalization of blood lipid levels, and attenuation of blood glucose responses.

## DETERMINING DRIS

### Determining Requirements

There is no biochemical assay that can be used to measure *Dietary Fiber* or *Functional Fiber* nutritional status. Blood fiber levels cannot be measured be-

**TABLE 2 The Physiological Effects of Isolated and Synthetic Fibers**

		Potential Effect on			
		Normalization of Blood Lipid Levels	Attenuation of Blood Glucose Responses	Other Physiological Effects	
Laxation					
<b>Cellulose</b>	Increases stool weight; may decrease transit time.	No effect on blood lipid levels or a slight increase in them.	Did not decrease postprandial glucose response.	—	
<b>Chitin and Chitosan</b>	There was no evidence for a laxative effect in humans.	Numerous animal studies suggested that chitin and chitosan may decrease lipid absorption. However, this has not always been observed in controlled human studies. More research is needed.	No known reports in humans.	Some animal studies have shown that chitosan reduces fat absorption and may promote weight loss. However, human studies have found no effect of chitosan supplementation on weight.	
<b>Guar Gum</b>	Little effect on fecal bulk or laxation.	Numerous studies have shown an 11–16 percent reduction in blood cholesterol levels with guar gum supplementation. In addition, guar gum has been shown to decrease triacylglycerol concentrations and blood pressure.	Viscous fibers, including guar gum, produced significant reductions in glycemic response in 33 of 50 studies.	—	

**TABLE 2 Continued**

Potential Effect on				
	Laxation	Normalization of Blood Lipid Levels	Attenuation of Blood Glucose Responses	Other Physiological Effects
<b>Inulin, Oligofructose, and Fructooligosaccharides</b>	A few studies have shown a small increase in fecal bulk and stool frequency with ingestion of inulin or oligofructose.	Studies with inulin or oligofructose have provided mixed results.	Some, but not all, studies suggest that inulin and fructooligosaccharides reduce fasting insulin concentrations or fasting blood glucose.	Numerous human studies show that the ingestion of fructooligosaccharides increases fecal <i>Bifidobacteria</i> . This bacteria strain has been shown to have beneficial health effects in animals, but the potential benefits to humans are not well understood.
<b>Oat Products and β-Glucans</b>	Extracted β-glucans have minimal effects on fecal bulk. Oat bran increases stool weight by supplying rapidly fermented viscous fiber to the colon for bacterial growth.	In a large study of adults with multiple risk factors for heart disease, including high LDL cholesterol levels, oat cereal consumption was linked to a dose-dependent reduction in LDL cholesterol. Other research also suggests that oat products help lower LDL cholesterol.	Some research suggests that oat bran reduces postprandial rises in blood glucose levels.	—

*continued*

**TABLE 2 Continued**

		Potential Effect on			
		Normalization of Blood Lipid Levels	Attenuation of Blood Glucose Responses	Other Physiological Effects	
	Laxation				
<b>Pectin</b>	A meta-analysis of about 100 studies showed that pectin is not an important fecal-bulking agent.	Pectin has been shown to lower cholesterol to varying degrees. There was some evidence that this effect was due to increased excretion of bile acids and cholesterol.	Viscous fibers, including pectin, have significantly reduced glycemic response in 33 of 50 studies.	—	—
<b>Polydextrose</b>	Polydextrose was shown to increase fecal mass and sometimes stool frequency. Findings on the effect of polydextrose on fecal bacterial production are mixed.	In one study, polydextrose lowered HDL (high density lipoprotein) cholesterol levels.	—	—	—
<b>Psyllium</b>	There is extensive literature on the laxative effect of psyllium, which is the active ingredient in some over the counter laxatives.	A number of studies have shown that psyllium lowers total and LDL cholesterol levels via the stimulation of bile acid production.	When added to a meal, psyllium has been shown to decrease the rise of postprandial glucose levels and to reduce the glycemic index of foods.	—	—

**TABLE 2 Continued**

Potential Effect on				
	Laxation	Normalization of Blood Lipid Levels	Attenuation of Blood Glucose Responses	Other Physiological Effects
<b>Resistant Dextrins</b>	No evidence to support a laxative effect.	One study showed that resistant maltodextrin helps reduce blood cholesterol and triacylglycerol levels.	One animal study and two human studies suggest that resistant maltodextrins reduce fasting and postprandial blood glucose levels.	—
<b>Resistant Starch</b>	Increased fecal bulk due to increased starch intake has been reported. Because resistant starch is partly fermented in the colon, intake may lead to an increased production of short-chain fatty acids.	Several animal studies have shown that resistant starch lowers blood cholesterol and triacylglycerol levels. In humans, resistant starch does not appear to provide the cholesterol-lowering effects of viscous fiber, but rather acts more like nonviscous fiber.	In one study, adding resistant starch to bread at various levels was shown to reduce the glycemic index in a dose-dependent manner.	—

cause fiber is not absorbed. Therefore, the potential health benefits of fiber consumption have been considered in determining DRIs.

Since information was insufficient to determine an EAR and thus calculate an RDA, an AI was instead developed. The AIs for *Total Fiber* are based on the intake level observed to protect against CHD based on epidemiological, clinical, and mechanistic data. The reduction of risk of diabetes can be used as a secondary endpoint to support the recommended intake level. The relationship of fiber intake to colon cancer is the subject of ongoing investigation and is currently unresolved. Recommended intakes of *Total Fiber* may also help ameliorate constipation and diverticular disease, provide fuel for colonic cells, reduce blood glucose and lipid levels, and provide a source of nutrient-rich, low energy-dense foods that could contribute to satiety, although these benefits were not used as the basis for the AI.

There is no AI for fiber for healthy infants aged 0 to 6 months who are fed human milk because human milk does not contain *Dietary Fiber*. During the 7- to 12-month age period, solid food intake becomes more significant, and so *Dietary Fiber* intake may increase. However, there are no data on *Dietary Fiber* intake in this age group and no theoretical reason to establish an AI. There is also no information to indicate that fiber intake as a function of energy intake differs during the life cycle.

### **Criteria for Determining Fiber Requirements, by Life Stage Group**

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	ND <sup>a</sup>
7 through 12 mo	ND
1 through 70 y	Intake level shown to provide the greatest protection against coronary heart disease (14 g/1,000 kcal) × median energy intake level from CSFII (1994–1996, 1998) (kcal/1,000 kcal/day)
<i>Pregnancy and Lactation</i>	Intake level shown to provide the greatest protection against coronary heart disease (14 g/1,000 kcal) × median energy intake level from CSFII (1994–1996, 1998) (kcal/1,000 kcal/day)

<sup>a</sup> Not determined.

## The UL

The Tolerable Upper Intake Level (UL) is the highest daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Although occasional adverse gastrointestinal symptoms are observed when consuming some of the isolated or synthetic fibers, serious chronic adverse effects have not been observed. A UL was not set for *Dietary Fiber* or *Functional Fiber*. Due to the bulky nature of fibers, excess consumption is likely to be self-limited.

## DIETARY SOURCES

*Dietary Fiber* is found in most fruits, vegetables, legumes, and grains. Nuts, legumes, and high-fiber grains typically contain fiber concentrations of more than 3 percent *Dietary Fiber*, or greater than 3 g/100 g of fresh weight. *Dietary Fiber* is present in the majority of fruits, vegetables, refined grains, and miscellaneous foods such as ketchup, olives, and soups, at concentrations of 1 to 3 percent or 1 g/100 g to 3 g/100 g of fresh weight.

## Dietary Supplements

This information was not provided at the time the DRI values for fiber were set.

## Bioavailability

Fiber is not absorbed by the body.

## Dietary Interactions

Foods or diets that are rich in fiber may alter mineral metabolism, especially when phytate is present. Most studies that assess the effect of fiber intake on mineral status have looked at calcium, magnesium, iron, or zinc (see Table 3).

## INADEQUATE INTAKE AND DEFICIENCY

*Dietary* and *Functional Fibers* are not essential nutrients, so inadequate intakes do not result in biochemical or clinical symptoms of a deficiency. A lack of these fibers in the diet, however, can cause inadequate fecal bulk and may detract from optimal health in a variety of ways depending on other factors, such as the rest of the diet and the stage of the life cycle.

**TABLE 3 Potential Interactions of Dietary Fiber with Other Dietary Substances**

Substance	Potential Interaction	Notes
<b>FIBER AFFECTING OTHER SUBSTANCES</b>		
<b>Calcium</b>	Decreased calcium absorption when ingested with <i>Dietary Fiber</i>	Some types of fiber have been shown to significantly increase fecal excretion of calcium. However, most human studies have reported no effect.
<b>Magnesium</b>	Decreased magnesium absorption when ingested with <i>Dietary Fiber</i>	Studies report no effect on magnesium balance or absorption.
<b>Iron</b>	Reduced iron absorption when ingested with <i>Dietary Fiber</i>	In one study, the addition of 12 g/day of bran to a meal decreased iron absorption by 51–74 percent, which was not explained by the presence of phytate. Other studies suggest that the effect of bran on iron absorption is due to phytate content rather than fiber.
<b>Zinc</b>	Reduced zinc absorption when ingested with <i>Dietary Fiber</i>	Most studies also include levels of phytate that are high enough to affect zinc absorption. Metabolic balance studies in adult males consuming 4 oat bran muffins daily show no changes in zinc balance.

## ADVERSE EFFECTS OF CONSUMPTION

Although occasional adverse gastrointestinal symptoms were observed with the consumption of *Dietary* and *Functional Fibers*, serious chronic adverse effects have not been observed. The most potentially deleterious effects may arise from the interaction of fiber with other nutrients in the gastrointestinal tract. Additionally, the composition of *Dietary Fiber* varies, making it difficult to link a specific fiber with a particular adverse effect, especially when phytate is also present. It has been concluded that as part of an overall healthy diet, a high intake of *Dietary Fiber* will not cause adverse effects in healthy people. In addition, the bulky nature of fiber tends to make excess consumption self-limiting.

## KEY POINTS FOR FIBER

- ✓ A new set of definitions for fiber has been developed for *Dietary Fiber*, *Functional Fiber*, and *Total Fiber*. The term *Dietary Fiber* describes the nondigestible carbohydrates and lignin that are intrinsic and intact in plants. *Functional Fiber* consists of the isolated nondigestible carbohydrates that have beneficial physiological effects in humans. *Total Fiber* is the sum of *Dietary Fiber* and *Functional Fiber*. Nondigestible means not digested and absorbed in the human small intestine.
- ✓ There is no biochemical assay that reflects *Dietary Fiber* or *Functional Fiber* nutritional status. Blood fiber levels cannot be measured because fiber is not absorbed.
- ✓ Since data were inadequate to determine an EAR and thus calculate an RDA for *Total Fiber*, an AI was instead developed.
- ✓ The AI for fiber is based on the median fiber intake level observed to achieve the lowest risk of CHD.
- ✓ A UL was not set for *Dietary Fiber* or *Functional Fiber*.
- ✓ *Dietary Fiber* is found in most fruits, vegetables, legumes, and grains.
- ✓ *Dietary* and *Functional Fibers* are not essential nutrients, therefore inadequate intakes do not result in biochemical or clinical symptoms of a deficiency.
- ✓ As part of an overall healthy diet, a high intake of *Dietary Fiber* will not cause adverse effects in healthy people.

**TABLE 1 Dietary Reference Intakes for Dietary Fat: Total Fat and Fatty Acids by Life Stage Group**

Life stage group	DRI Values (g/day)		
	Total Fat/AI <sup>a</sup>	Linoleic Acid/AI	α-Linolenic Acid/AI
<i>Males and Female</i>			
0 through 6 mo	31	4.4	0.5
7 through 12 mo	30	4.6	0.5
1 through 3 y	ND <sup>b</sup>	7	0.7
4 through 8 y	ND	10	0.9
<i>Males</i>			
9 through 13 y	ND	12	1.2
14 through 18 y	ND	16	1.6
19 through 30 y	ND	17	1.6
31 through 50 y	ND	17	1.6
51 through 70 y	ND	14	1.6
> 70 y	ND	14	1.6
<i>Females</i>			
9 through 13 y	ND	10	1.0
14 through 18 y	ND	11	1.1
19 through 30 y	ND	12	1.1
31 through 50 y	ND	12	1.1
51 through 70 y	ND	11	1.1
> 70 y	ND	11	1.1
<i>Pregnancy</i>			
All ages	ND	13	1.4
<i>Lactation</i>			
All ages	ND	13	1.3

<sup>a</sup> AI = Adequate Intake. If sufficient scientific evidence is not available to establish an EAR, and thus calculate an RDA, an AI is usually developed. For healthy breast-fed infants, the AI is the mean intake. The AI for other life stage and gender groups is believed to cover the needs of all healthy individuals in the group, but a lack of data or uncertainty in the data prevents being able to specify with confidence the percentage of individuals covered by this intake.

<sup>b</sup> ND = Not determined.

# DIETARY FAT: TOTAL FAT AND FATTY ACIDS

A major source of energy for the body, fat also aids in the absorption of fat-soluble vitamins A, D, E, K, and other food components, such as carotenoids. Dietary fat consists mainly (98 percent) of triacylglycerol (which is made up of one glycerol molecule esterified with three fatty acid molecules) and small amounts of phospholipids and sterols. In this publication, total fat refers to all forms of triacylglycerol, regardless of fatty acid composition.

Neither an Estimated Average Requirement (EAR), and thus a Recommended Dietary Allowance (RDA), nor an Adequate Intake (AI) was set for total fat for individuals aged 1 year and older because data were insufficient to determine a defined intake level at which risk of inadequacy or prevention of chronic disease occurs. However, AIs were set for infants aged 0 through 12 months based on observed mean fat intake of infants who were principally fed human milk. Since there is no defined intake level of fat at which an adverse effect occurs, a Tolerable Upper Intake Level (UL) was not set for total fat. An Acceptable宏-nutrient Distribution Range (AMDR) has been estimated for total fat at 20–35 percent of energy for adults and children ages 4 and older and 30–40 percent for children ages 1 through 3. Main food sources of total fat are butter, margarine, vegetable oils, visible fat on meat and poultry products, whole milk, egg yolk, nuts, and baked goods, such as cookies, doughnuts, pastries and cakes and various fried foods.

Fatty acids are the major constituents of triglycerides and fall into the following categories: saturated fatty acids, *cis* monounsaturated fatty acids, *cis* polyunsaturated fatty acids (*n*-6 fatty acids and *n*-3 fatty acids), and *trans* fatty acids.

Saturated fatty acids can be synthesized by the body, where they perform structural and metabolic functions. Neither an EAR (and thus an RDA) nor an AI was set for saturated fatty acids because they are not essential (meaning that they can be synthesized by the body) and have no known role in preventing chronic disease.

There is a positive linear trend between saturated fatty acid intake and total and low density lipoprotein (LDL) cholesterol levels and an increased risk of coronary heart disease (CHD). However, a UL was not set for saturated fatty

acids because any incremental increase in intake increases the risk of CHD. It is recommended that individuals maintain their saturated fatty acid consumption as low as possible, while consuming a nutritionally adequate diet. Food sources of saturated fatty acids tend to be animal-based foods, including whole milk, cream, butter, cheese, and fatty meats. Coconut oil, palm oil, and palm kernel oil are also high in saturated fatty acids.

Monounsaturated fatty acids (*n*-9) can be synthesized by the body and confer no known independent health benefits. Neither an EAR (and thus an RDA) nor an AI was set. Evidence was insufficient to set a UL for *cis* monounsaturated fatty acids. Foods high in monounsaturated fatty acids include canola oil, olive oil, high-oleic sunflower oil, high-oleic safflower oil, and animal products, primarily meat fat. Animal products provide about 50 percent of dietary monounsaturated fatty acids.

*Cis* polyunsaturated acids include the *n*-6 fatty acids and *n*-3 fatty acids. The parent acid of the *n*-6 fatty acid series is linoleic acid, the only *n*-6 fatty acid that is an essential fatty acid (EFA), meaning that it cannot be made by the body and must be obtained through the diet. Linoleic acid acts as a precursor for arachidonic acid, which in turn serves as the precursor for eicosanoids (e.g., prostaglandins, thromboxanes, and leukotrienes). Alpha-linolenic ( $\alpha$ -linolenic) acid, the parent acid of the *n*-3 fatty acid series is the only *n*-3 fatty acid that is an essential fatty acid meaning that it cannot be made by the body and must be obtained through the diet. The *n*-3 fatty acids play an important role as a structural membrane lipid, particularly in the nerve tissue and retina. The *n*-3 fatty acids also compete with the *n*-6 fatty acids for enzymes responsible for the production of the long-chain *n*-3 fatty acids and thereby influence the balance of *n*-3 and *n*-6 fatty acid-derived eicosanoids.

The AIs for linoleic acid are based on the median intake of linoleic acid by different life stage and gender groups in the United States, where the presence of *n*-6 polyunsaturated fatty acid deficiency is nonexistent in healthy individuals. Evidence was insufficient to set a UL for this and other *n*-6 polyunsaturated fatty acids. Foods rich in *n*-6 polyunsaturated fatty acids include nuts, seeds, and vegetable oils, such as sunflower, safflower, corn, and soybean oils.

The AIs for  $\alpha$ -linolenic acid are based on the median intakes of  $\alpha$ -linolenic acid in the United States, where the presence of *n*-3 polyunsaturated fatty acid deficiency is basically nonexistent in healthy individuals. Evidence was insufficient to set a UL for this and other *n*-3 fatty acids. Major food sources include certain vegetable oils and fish. Flaxseed, canola, and soybean oils contain high amounts of  $\alpha$ -linolenic acid. Fatty fish, fish oils, and products fortified with fish oils contain longer chain *n*-3 fatty acids.

*Trans* fatty acids are not essential and confer no known health benefits. Therefore, no EAR (and thus an RDA) or AI was set. As with saturated fatty

acids, there is a positive linear trend between *trans* fatty acid intake and LDL cholesterol concentration and therefore an increased risk of coronary heart diseases. It is recommended that individuals maintain their *trans* fatty acid consumption as low as possible without compromising the nutritional adequacy of their diet. Foods that contain *trans* fatty acids include traditional stick margarine and vegetable shortenings subjected to partial hydrogenation and various bakery products and fried foods prepared using partially hydrogenated oils. Milk, butter, and meats also contain *trans* fatty acids but at lower levels.

A lack of either of the two essential fatty acids (EFAs), linoleic or  $\alpha$ -linolenic acid, will result in symptoms of deficiency that include scaly skin, dermatitis, and reduced growth. Such deficiency is very rare in healthy populations in the United States and Canada. Certain types of fatty acids, such as *trans* and saturated, have been shown to heighten the risk of heart disease in some people by boosting the level of LDL cholesterol in the bloodstream. DRI values are listed by life stage group in Table 1.

## FAT, FATTY ACIDS, AND THE BODY

### Background Information

Dietary fat consists mainly of triacylglycerol (98 percent) and small amounts of phospholipids and sterols. Triacylglycerols are made up of one glycerol molecule esterified with three fatty acid molecules. In this publication, total fat refers all to forms of triacylglycerol, regardless of fatty acid composition.

Fatty acids are hydrocarbon chains that contain a methyl ( $\text{CH}_3-$ ) and a carboxyl ( $-\text{COOH}$ ) end. Table 2 shows the major fatty acids found in the diet. Fatty acids vary in their carbon chain length and degree of unsaturation (the number of double bonds in the carbon chain) and can be classified as follows:

- saturated fatty acids
- *cis* monounsaturated fatty acids
- *cis* polyunsaturated fatty acids
  - *n*-6 fatty acids
  - *n*-3 fatty acids
- *trans* fatty acids

A very small amount of dietary fat occurs as phospholipids, a form of fat that contains one glycerol molecule that is esterified with two fatty acids and either inositol, choline, serine, or ethanolamine. In the body, phospholipids are mainly located in the cell membranes and the globule membranes of milk.

**TABLE 2 Major Dietary Fatty Acids**

Category of Fatty Acid	Specific Fatty Acids Found in the Diet
<b>Saturated fatty acids</b>	<ul style="list-style-type: none"> <li>• caprylic acid, 8:0<sup>a</sup></li> <li>• caproic acid, 10:0</li> <li>• lauric acid, 12:0</li> <li>• myristic acid, 14:0</li> <li>• palmitic acid, 16:0</li> <li>• stearic acid, 18:0</li> </ul>
<b>Cis monounsaturated fatty acids</b>	<ul style="list-style-type: none"> <li>• myristoleic acid, 14:1 <i>n</i>-7</li> <li>• palmitoleic acid, 16:1 <i>n</i>-7</li> <li>• oleic acid, 18:1 <i>n</i>-9 (account for 92% of monounsaturated dietary fatty acids)</li> <li>• <i>cis</i>-vaccenic acid, 18:1 <i>n</i>-7</li> <li>• eicosenoic acid, 20:1 <i>n</i>-9</li> <li>• erucic acid, 22:1 <i>n</i>-9</li> </ul>
<b>Cis polyunsaturated fatty acids</b>	
<i>n</i> -6 polyunsaturated fatty acid	<ul style="list-style-type: none"> <li>• linoleic acid,<sup>b</sup> 18:2</li> <li>• <math>\gamma</math>-linoleic acid, 18:3</li> <li>• dihomo-<math>\gamma</math>-linolenic acid, 20:3</li> <li>• arachidonic acid, 20:4</li> <li>• adrenic acid, 22:4</li> <li>• docosapentaenoic acid, 22:5</li> </ul>
<i>n</i> -3 polyunsaturated fatty acid	<ul style="list-style-type: none"> <li>• <math>\alpha</math>-linolenic acid,<sup>b</sup> 18:3</li> <li>• eicosapentaenoic acid, 20:5</li> <li>• docosapentaenoic acid, 22:5</li> <li>• docosahexaenoic acid, 22:6</li> </ul>
<b>Trans fatty acid</b>	<ul style="list-style-type: none"> <li>• 9-trans, 18:1; 9-trans, 16:1; 9-cis,11-trans, 18:2; 9-trans,12-cis, 18:2; 9-cis,12-trans, 18:2</li> </ul>

<sup>a</sup> The first value refers to chain length or number of carbon atoms and the second value refers to the number of double bonds.

<sup>b</sup> Linoleic acid and  $\alpha$ -linolenic acid cannot be synthesized in the body and are therefore essential in the diet.

## Function

A major source of energy for the body, fat aids in the absorption of fat-soluble vitamins A, D, E, K, and other food components, such as carotenoids. Fatty acids function in cell signaling and alter the expression of specific genes in-

**TABLE 3 The Functions of Fat and Fatty Acids**

Fat and Fatty Acids	Function
<b>Total fat<sup>a</sup></b>	<ul style="list-style-type: none"> <li>• Major source of energy</li> <li>• Aids in absorption of the fat-soluble vitamins and carotenoids</li> </ul>
<b>Saturated fatty acids</b>	<ul style="list-style-type: none"> <li>• Sources of energy</li> <li>• Structural components of cell membranes</li> <li>• Enable normal function of proteins</li> </ul>
<b>Cis monounsaturated fatty acids</b>	<ul style="list-style-type: none"> <li>• Key components of membrane structural lipids, particularly nervous tissue myelin</li> </ul>
<b>Cis polyunsaturated fatty acids</b>	
<i>n</i> -6 polyunsaturated fatty acids	<ul style="list-style-type: none"> <li>• Substrates for eicosanoid production, including prostaglandins</li> <li>• Precursors of arachidonic acid</li> <li>• Components of membrane structural lipids</li> <li>• Important in cell signaling pathways</li> <li>• Vital for normal epithelial cell function</li> <li>• Involved in the regulation of genes for proteins that regulate fatty acid synthesis</li> </ul>
<i>n</i> -3 polyunsaturated fatty acids	<ul style="list-style-type: none"> <li>• Precursors for synthesis of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). EPA is the precursor for <i>n</i>-3 eicosanoids</li> </ul>
<b>Phospholipids</b>	<ul style="list-style-type: none"> <li>• Major constituents of cell membranes</li> </ul>

<sup>a</sup> Total fat refers to all forms of triacylglycerol, regardless of fatty acid composition.

volved in lipid and carbohydrate metabolism. Fatty acids, the major constituents of triglycerides, may also serve as precursors or ligands for receptors that are important regulators of adipogenesis, inflammation, insulin action, and neurological function. Table 3 summarizes the functions of fat and fatty acids.

## Absorption, Metabolism, Storage, and Excretion

### TOTAL FAT

In the intestine, dietary fat is emulsified with bile salts and phospholipids (secreted into the intestine by the liver), hydrolyzed by pancreatic enzymes, and

almost completely absorbed. Following absorption, the fats are reassembled together with cholesterol, phospholipids, and apoproteins into chylomicrons, which enter the circulation through the thoracic duct. Chylomicrons come into contact with the enzyme lipoprotein lipase (LPL) (located on the surface of capillaries of muscle and adipose tissue) and LPL hydrolyzes the chylomicron triacylglycerol fatty acids. Most of the fatty acids released in this process are taken up by adipose tissue and re-esterified into triacylglycerol for storage.

When fat is needed for fuel, free fatty acids from the liver and muscle are released into the circulation to be taken up by various tissues, where they are oxidized to provide energy. Muscle, which is the main site of fatty acid oxidation, uses both fatty acids and glucose for energy. Fatty acids released from fat tissue can also be oxidized by the liver.

As fatty acids are broken down through oxidation, carbon dioxide and water are released. Small amounts of ketone bodies are also produced and excreted in the urine. The cells of the skin and intestine also contain fatty acids. Thus, small quantities are lost when these cells are sloughed.

### SATURATED FATTY ACIDS

When absorbed along with fats containing appreciable amounts of unsaturated fatty acids, saturated fatty acids are absorbed almost completely by the small intestine. In general, the longer the chain length of the fatty acid, the lower the efficiency of absorption. Following absorption, long-chain saturated fatty acids are re-esterified along with other fatty acids into triacylglycerols and released in chylomicrons. Medium-chain saturated fatty acids are absorbed, bound to albumin, transported as free fatty acids in the portal circulation, and cleared by the liver. Oxidation of saturated fatty acids is similar to oxidation of other types of fatty acids (see “Total Fat” above).

A unique feature of saturated fatty acids is that they suppress expression of LDL receptors, thus raising blood LDL cholesterol levels. Like other fatty acids, saturated fatty acids tend to be completely oxidized to carbon dioxide and water. Saturated fatty acids also increase HDL cholesterol.

### C<sub>is</sub> MONOUNSATURATED FATTY ACIDS

Absorption of *cis* monounsaturated fatty acids is in excess of 90 percent (based on oleic acid data) in adults and infants, and the pathways of digestion, absorption, metabolism, and excretion are similar to those of other fatty acids (see “Total Fat” above).

### Cis-POLYUNSATURATED FATTY ACIDS

- n-6 polyunsaturated fatty acids: Digestion and absorption of n-6 fatty acids is efficient and occurs via the same pathways as those of other long-chain fatty acids (see “Total Fat” above). The parent fatty acid of the n-6 fatty acids series is linoleic acid. Humans can desaturate and elongate linoleic acid to form arachidonic acid. Arachidonic acid is the precursor to a number of eicosanoids (e.g., prostaglandins, thromboxanes, and leukotrienes) that are involved in platelet aggregation, hemodynamics, and coronary vascular tone. The n-6 fatty acids are almost completely absorbed and are either incorporated into tissue lipids, used in eicosanoid synthesis, or oxidized to carbon dioxide and water. Small amounts are lost via the sloughing of skin and other epithelial cells.
- n-3 polyunsaturated fatty acids: Digestion and absorption is similar to that of other long-chain fatty acids (see “Total Fat” above). The body cannot synthesize α-linolenic acid, the parent fatty acid of the n-3 series, and thus requires a dietary source of it. α-Linolenic acid is not known to have any specific functions other than to serve as a precursor for synthesis of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The n-3 fatty acids are almost completely absorbed and are either incorporated into tissue lipids, used in eicosanoid synthesis, or oxidized to carbon dioxide and water. Small amounts are lost via sloughing of skin and other epithelial cells.

### TRANS FATTY ACIDS

As with other fatty acids, absorption is about 95 percent. *Trans* fatty acids are transported similarly to other dietary fatty acids and are distributed within the cholesteryl ester, triacylglycerol, and phospholipid fractions of lipoprotein. Available animal and human data indicate that the *trans* fatty acid content of tissues (except the brain) reflects diet content and that selective accumulation does not occur. *Trans* fatty acids are completely catabolized to carbon dioxide and water.

## DETERMINING DRIS

### Determining Requirements

#### TOTAL FAT

Neither an EAR (and thus an RDA) nor an AI was set for total fat for individuals aged 1 year and older because data were insufficient to determine an intake level at which risk of inadequacy or prevention of chronic disease occurs. How-

ever, because of the importance of fat to provide the energy needed for growth, AIs were set for infants aged 0 through 12 months. These AIs were based on the observed mean fat intake of infants who were principally fed human milk (0–6 months) and human milk and complementary foods (7–12 months).

### SATURATED FATTY ACIDS

Neither an EAR (and thus an RDA) nor an RDA was set for saturated fatty acids because they are not essential and have no known role in preventing chronic disease.

### CIS MONOUNSATURATED FATTY ACIDS

Cis monounsaturated fatty acids (*n*-9) confer no known independent health benefits. Since these fatty acids are not required in the diet, neither an EAR (and thus an RDA) nor an AI was set.

### CIS POLYUNSATURATED FATTY ACIDS

- *n*-6 polyunsaturated fatty acids: In the absence of adequate information on the amount of linoleic acid required to correct the symptoms of an *n*-6 polyunsaturated fatty acid deficiency, an EAR (and hence an RDA) could not be established. The AIs for linoleic acid are based on the median intake of linoleic acid by different life stage and gender groups in the United States, where the presence of *n*-6 polyunsaturated fatty acid deficiency is basically nonexistent in healthy individuals.
- *n*-3 polyunsaturated fatty acids: Because of the lack of evidence for determining a requirement in healthy individuals, an EAR (and thus an RDA) could not be established. The AIs for  $\alpha$ -linolenic acid are based on the median intakes of  $\alpha$ -linolenic acid in the United States where the presence of *n*-3 polyunsaturated fatty acid deficiency is basically nonexistent in healthy individuals.

### TRANS FATTY ACIDS

Trans fatty acids confer no known health benefits. They are chemically classified as unsaturated fatty acids, but behave more like saturated fatty acids in the body. Therefore, no EAR (and thus RDA) or AI was set.

### CONJUGATED LINOLEIC ACID

There are no known requirements for conjugated linoleic acid (CLA) in the body. Therefore, no EAR (and thus RDA) or AI was set.

## Criteria for Determining Fat Requirements, by Life Stage Group

### *TOTAL FAT*

<i>Life stage group<sup>a</sup></i>	<i>Criterion</i>
0 through 6 mo	Average consumption of total fat from human milk
7 through 12 mo	Average consumption of total fat from human milk and complementary foods

### *LINOLEIC ACID*

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Average consumption of total n-6 fatty acids from human milk
7 through 12 mo	Average consumption of total n-6 fatty acids from human milk and complementary foods
1 through 18 y	Median intake from CSFII <sup>b</sup>
19 through 50 y	Median intake from CSFII for 19 to 30 y group
51 y and through 70 y	Median intake from CSFII
> 70 y	Median intake from CSFII for 51 through 70 y group
<i>Pregnancy</i>	Median intake from CSFII for all pregnant women
<i>Lactation</i>	Median intake from CSFII for all lactating women

### *ALPHA-LINOLENIC ACID*

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Average consumption of total n-3 fatty acids from human milk
7 through 12 mo	Average consumption of total n-3 fatty acids from human milk and complementary foods
1 through 18 y	Median intake from CSFII <sup>b</sup>
19 y and older	Median intake from CSFII for all adult age groups
<i>Pregnancy</i>	Median intake from CSFII for all pregnant women
<i>Lactation</i>	Median intake from CSFII for all lactating women

<sup>a</sup> A DRI value for total fat was not set for any life stage group other than infants.

<sup>b</sup> Continuing Survey of Food Intake by Individuals (1994–1996, 1998).

## The AMDR

An AMDR has been estimated for total fat at 20–35 percent of energy for adults and children aged 4 and older and 30–40 percent for children ages 1 through 3. The AMDRs for *n*-6 polyunsaturated fatty acids (linoleic acid) and *n*-3 polyunsaturated fatty acids ( $\alpha$ -linolenic acid) are 5–10 percent and 0.6–1.2 percent, respectively (see Part II, “Macronutrients, Healthful Diets, and Physical Activity”).

## The UL

### TOTAL FAT

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Since there is no defined intake level of total fat at which an adverse effect occurs, a UL was not set for total fat.

### SATURATED FATTY ACIDS AND *TRANS* FATTY ACIDS

There is a positive linear trend between saturated fatty acid intake and total and LDL cholesterol levels and a positive linear trend between *trans* fatty acid and LDL cholesterol concentration. Any incremental increases in saturated and *trans* fatty acid intakes increase CHD risk, therefore a UL was not set for saturated or *trans* fatty acids. It is neither possible nor advisable to achieve zero percent of energy from saturated fatty acids or *trans* fatty acids in typical diets, since this would require extraordinary dietary changes that may lead to inadequate protein and micronutrient intake, as well as other undesirable effects. It is recommended that individuals maintain their saturated and *trans* fatty acid consumption as low as possible while following a nutritionally adequate diet.

### *Cis* MONOUNSATURATED AND *Cis* POLYUNSATURATED FATTY ACIDS

Evidence was insufficient to set a UL for *cis* monounsaturated fatty acids, and *cis* polyunsaturated (*n*-6 and *n*-3) fatty acids.

## DIETARY SOURCES

### Foods

Dietary fat intake is primarily (98 percent) in the form of triacylglycerols and is derived from both animal- and plant-based products. The principal foods that contribute to fat intake are butter, margarine, vegetable oils, visible fat on meat

and poultry products, whole milk, egg yolk, nuts, and baked goods, such as cookies, doughnuts, and cakes.

In general, animal fats have higher melting points and are solid at room temperature, which is a reflection of their high content of saturated fatty acids. Plant fats (oils) tend to have lower melting points and are liquid at room temperature because of their high content of unsaturated fatty acids. Exceptions to this rule are some tropical oils (e.g., coconut oil and palm kernel oil), which are high in saturated fat and solid at room temperature.

*Trans* fatty acids have physical properties that generally resemble saturated fatty acids, and their presence tends to harden fats. Food sources for the various fatty acids that are typically consumed in North American diets are listed in Table 4.

## Dietary Supplements

This information was not provided at the time the DRI values for total fat and fatty acids were set.

# INADEQUATE INTAKE AND DEFICIENCY

## Total Fat

Inadequate intake of dietary fat may result in impaired growth and an increased risk of chronic disease. If fat intake, along with carbohydrate and protein intake, is too low to meet energy needs, an individual will be in negative energy balance. Depending on the severity and duration of the deficit, this may lead to malnutrition or starvation.

If the diet contains adequate energy, carbohydrate can replace fat as an energy source. However, fat restriction is of particular concern during infancy, childhood, and pregnancy, during which there are relatively high energy requirements for both energy expenditure and fetal development.

Imbalanced intake can also be of concern. Compared with higher fat diets, low-fat and high-carbohydrate diets may alter metabolism in a way that increases the risk of chronic diseases, such as coronary heart disease and diabetes. These changes include a reduction in high density lipoprotein (HDL) cholesterol concentration, an increase in serum triacylglycerol concentration, and higher responses in glucose and insulin concentrations following food consumption. This metabolic pattern has been associated with an increased risk of CHD and Type II diabetes, although strong evidence does not exist that low-fat diets actually predispose an individual to either CHD or diabetes.

Some populations that consume low-fat diets, and in which habitual energy intake is relatively high, have a low prevalence of these chronic diseases.

**TABLE 4 Commonly Consumed Food Sources of Fatty Acids**

Fatty Acid	Food Sources
Saturated fatty acids	Sources tend to be animal-based foods, including whole milk, cream, butter, cheese, and fatty meats such as pork and beef. Coconut, palm, and palm kernel oils also contain relatively high amounts of saturated fatty acids. Saturated fatty acids provide approximately 20–25 percent of energy in human milk.
<i>Cis</i> monounsaturated fatty acids	Animal products, primarily meat fat, provide about 50 percent of monounsaturated fatty acids in a typical North American diet. Oils that contain monounsaturated fatty acids include canola and olive oil. Monounsaturated fatty acids provide approximately 20 percent of energy in human milk.
<i>Cis</i> polyunsaturated fatty acids:	
<i>n</i> -6 polyunsaturated fatty acids	Nuts, seeds, and vegetable oils such as sunflower, safflower, corn, and soybean oils. $\gamma$ -Linolenic acid is found in black currant seed oil and evening primrose oil. Arachidonic acid is found in small amounts in meat, poultry, and eggs.
<i>n</i> -3 polyunsaturated fatty acids	Major sources include certain vegetable oils and fish. Flaxseed, canola, and soybean contain high amounts of $\alpha$ -linolenic acid. Fatty fish are major dietary sources of EPA and DHA.
<i>Trans</i> fatty acids	Traditional stick margarine and vegetable shortenings subjected to partial hydrogenation, milk, butter, and meats. Pastries, fried foods, doughnuts, and french fries are also contributors of <i>trans</i> fatty acid intake. Human milk contains approximately 1–5 percent of total energy as <i>trans</i> fatty acids and, similarly, infant formulas contain approximately 1–3 percent.

Similarly, populations that consume high-fat diets (i.e.,  $\geq 40$  percent of energy) and experience a low prevalence of chronic diseases often include people who engage in heavy physical labor, are lean, and have a low family history of chronic diseases.

Conversely, in sedentary populations, such as those in the United States and Canada where overweight and obesity are common, high-carbohydrate, low-fat diets induce changes in lipoprotein and glucose/insulin metabolism in ways that could raise the risk for chronic diseases. Available prospective studies have not concluded whether high-carbohydrate, low-fat diets present a health risk in the North American population.

### ***n*-6 Polyunsaturated Fatty Acids**

Because adipose tissue lipids in free-living healthy adults contain about 10 percent of total fatty acids as linoleic acid, the biochemical and clinical signs of essential fatty acid deficiency do not appear during dietary fat restriction or malabsorption when they are accompanied by an energy deficit. In this situation, the release of linoleic acid and small amounts of arachidonic acid from adipose tissue reserves may prevent the development of essential fatty acid deficiency. However, during total parenteral nutrition (TPN) with dextrose solutions, insulin concentrations are high and mobilization of adipose tissue is prevented. This results in the characteristic signs of essential fatty acid deficiency.

When *n*-6 fatty acid intake is inadequate or absorption is impaired, tissue concentrations of arachidonic acid decrease, inhibition of the desaturation of oleic acid is reduced, and synthesis of eicosatrienoic acid from oleic acid increases. A lack of dietary *n*-6 polyunsaturated fatty acids is characterized by rough scaly skin, dermatitis, and an elevated eicosatrienoic acid:arachidonic acid (triene:tetraene) ratio.

### ***n*-3 Polyunsaturated Fatty Acids**

A lack of  $\alpha$ -linolenic acid in the diet can result in clinical symptoms of a deficiency (e.g., scaly dermatitis). Unlike essential fatty acid deficiency (of both *n*-6 and *n*-3 fatty acids), plasma eicosatrienoic acid (20:3 *n*-9) remains within normal ranges, and skin atrophy and scaly dermatitis are absent when the diet is only deficient in *n*-3 fatty acids.

Because of their function, growing evidence suggests that dietary *n*-3 polyunsaturated fatty acids (EPA and DHA) may reduce the risk of many chronic diseases including CHD, stroke, and diabetes. For example, *n*-3 fatty acids may reduce CHD risk through a variety of mechanisms, such as by preventing arrhythmias, reducing atherosclerosis, decreasing platelet aggregation and plasma

triacylglycerol concentration, slightly increasing HDL concentration, modulating endothelial function, and decreasing proinflammatory eicosanoids.

## ADVERSE EFFECTS OF OVERCONSUMPTION

As mentioned earlier, there is no defined level of fat intake at which an adverse effect, such as obesity, can occur. An AMDR for fat intake, however, has been estimated based on potential adverse effects occurring from consuming low-fat and high-fat diets (see Part II, “Macronutrients, Healthful Diets, and Physical Activity”). High-fat diets in excess of energy needs can cause obesity. Several studies have shown associations between high-fat intakes and an increased risk of CHD, cancer, and insulin resistance. However, the type of fatty acid consumed is very important in defining these associations. The potential adverse effects of overconsuming fatty acids are summarized in Table 5.

## Special Considerations

**Individuals sensitive to n-3 polyunsaturated fatty acids:** People who take hypoglycemic medications should consume n-3 fatty acids with caution. Because n-3 fatty acids may excessively prolong bleeding time, DHA and EPA supplements should be taken with caution by people who take anticoagulants, including aspirin and warfarin.

**Exercise:** High-fat diets may result in a positive energy balance and therefore in weight gain under sedentary conditions. Active people can probably consume relatively high-fat diets while maintaining their body weight. Athletes may not be able to train as effectively on short-term (fewer than 6 days) high-fat diets as they could on high-carbohydrate diets. It is important to note that physical activity may account for a greater percentage of the variance in weight gain than does dietary fat.

**Genetic factors:** Some data indicate that genes may affect the relationship between diet and obesity. Some people with relatively high metabolic rates appear to be able to eat high-fat diets (44 percent of energy from fat) without becoming obese. Intervention studies have shown that people susceptible to weight gain and obesity appear to have an impaired ability to oxidize more fat after eating high-fat meals.

**Alcohol:** Significant alcohol intake (23 percent of energy) can depress fatty acid oxidation. If the energy derived from alcohol is not used, the excess is stored as fat.

**TABLE 5 Potential Adverse Effects of Fatty Acid Overconsumption**

Fatty Acid	Potential Adverse Effects of Overconsumption
Saturated fatty acids	In general, the higher the saturated fatty acid intake, the higher the serum total and LDL cholesterol concentrations. There is a positive linear relationship between serum total and LDL cholesterol concentrations and the risk of CHD or mortality from CHD.
<i>Cis</i> monounsaturated fatty acids	Overconsumption of energy related to a high-fat, high-monounsaturated fatty acid diet is one risk associated with excess monounsaturated fatty acid intake. High intakes can also cause an increased intake of saturated fatty acids, since many animal fats that contain one have the other.
<i>Cis</i> polyunsaturated fatty acids:	
<i>n</i> -6 polyunsaturated fatty acids	An AMDR was estimated based on the adverse effects from consuming a diet too high or low in <i>n</i> -6 polyunsaturated fatty acids (see Part II, “Macronutrients, Healthful Diets, and Physical Activity”).
<i>n</i> -3 polyunsaturated fatty acids	Data on the effects of EPA and DHA intakes on bleeding times are mixed. Until more information is available, supplemental forms of EPA and DHA should be taken with caution. An AMDR was estimated based on the adverse effects from consuming a diet too high or low in <i>n</i> -3 polyunsaturated fatty acids (see Part II, “Macronutrients, Healthful Diets, and Physical Activity”).
<i>Trans</i> fatty acids	There is a positive linear trend between <i>trans</i> fatty acid intake and LDL concentration, and therefore an increased risk of CHD. Recent data have shown a dose-dependent relationship between <i>trans</i> fatty acid intake and the LDL:HDL ratio. The combined results of numerous studies have indicated that the magnitude of this effect is greater for <i>trans</i> fatty acids, compared with saturated fatty acids.

**Interaction of n-6 and n-3 fatty acid metabolism:** Many studies, primarily in animals, have suggested that the balance between linoleic and  $\alpha$ -linolenic acids is important in determining the amounts of arachidonic acid, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) in tissue lipids. An inappropriate ratio may involve too high an intake of either linoleic acid or  $\alpha$ -linolenic acid, too little of one fatty acid, or a combination leading to an imbalance between the two. The ratio between the two is likely to be of most importance in diets that are low in or devoid of arachidonic acid, EPA, and DHA. The importance of this ratio is unknown in diets that are high in these three fatty acids.

**n-6:n-3 polyunsaturated fatty acid ratio:** The ratio of linoleic acid to  $\alpha$ -linolenic acid in the diet is important because the two fatty acids compete for the same desaturase enzymes. Thus, a high ratio of linoleic acid to  $\alpha$ -linolenic acid can inhibit the conversion of  $\alpha$ -linolenic acid to DHA, while a low ratio will inhibit the desaturation of linoleic acid to arachidonic acid.

Although limited, the available data suggest that linoleic to  $\alpha$ -linolenic acid ratios below 5:1 may be associated with impaired growth in infants. Based on limited studies, the linoleic to  $\alpha$ -linolenic acid or total n-3 to n-6 fatty acid ratios of 5:1–10:1, 5:1–15:1, and 6:1–16:1 have been recommended for infant formulas. Based on limited studies, a reasonable linoleic to  $\alpha$ -linolenic acid ratio of 5:1–10:1 has been recommended for adults.

## KEY POINTS FOR FAT AND FATTY ACIDS

- ✓ A major source of energy for the body, fat aids in tissue development and the absorption of the fat-soluble vitamins A, D, E, K, and other food components, such as carotenoids.
- ✓ Dietary fat contains fatty acids that fall into the following categories: saturated fatty acids, cis monounsaturated fatty acids, cis polyunsaturated fatty acids (n-6 fatty acids and n-3 fatty acids), trans fatty acids, and conjugated linoleic acid.
- ✓ Neither an EAR (and thus RDA) nor an AI was set for total fat for individuals aged 1 year and older because data were insufficient to determine an intake level at which risk of inadequacy or prevention of chronic disease occurs. A UL was not set for total fat. Als for total fat were set for infants aged 0 through 12 months based on observed mean fat intake of infants who were principally fed human milk.
- ✓ An AMDR has been estimated for total fat at 20–35 percent of energy for adults and children aged 4 and older and 30–40 percent for children ages 1 through 3.

- ✓ The main food sources of total fat are butter, margarine, vegetable oils, visible fat on meat and poultry products, whole milk, egg yolk, nuts, and baked goods.
- ✓ Neither an EAR (and thus RDA) nor an AI was set for *trans* or saturated fatty acids because they are not essential and have no known role in preventing chronic disease.
- ✓ There is a positive linear trend between both *trans* and saturated fatty acid intake and LDL cholesterol levels, and thus increased risk of CHD. A UL was not set for *trans* or saturated fatty acids because any incremental increase in intake increases the risk of CHD.
- ✓ It is recommended that individuals maintain their *trans* and saturated fatty acid intakes as low as possible while consuming a nutritionally adequate diet.
- ✓ Food sources of saturated fatty acids tend to be meats, bakery items, and full-fat dairy products. Foods that contain *trans* fatty acids include traditional stick margarine and vegetable shortenings that have been partially hydrogenated, with lower levels in meats and dairy products.
- ✓ *Cis* monounsaturated fatty acids can be synthesized by the body and confer no known health benefits. Since they are not required in the diet, neither an AI nor an RDA was set. There was insufficient evidence to set a UL.
- ✓ Animal products, primarily meat fat, provide about 50 percent of dietary *cis* monounsaturated fatty acids intake.
- ✓ Linoleic and  $\alpha$ -linolenic fatty acids are essential, and therefore must be obtained from foods. AIs were set based on intake of healthy individuals. There was insufficient evidence to set a UL for *cis* polyunsaturated (*n*-6 and *n*-3) fatty acids.
- ✓ Foods rich in *n*-6 polyunsaturated fatty acids include nuts, seeds, certain vegetables, and vegetable oils, such as sunflower, safflower, corn, and soybean oils. Major food sources of *n*-3 polyunsaturated fatty acids include certain vegetable oils (flaxseed, canola, and soybean oils) and fatty fish.
- ✓ High-fat diets in excess of energy needs can cause obesity. Several studies have shown associations between high-fat intakes and an increased risk of CHD, cancer, and insulin resistance. However, the type of fatty acid consumed is very important in defining these associations.

# CHOLESTEROL

**C**holesterol plays an important role in steroid hormone and bile acid biosynthesis. It also serves as an integral component of cell membranes. Most people absorb between 40 and 60 percent of ingested cholesterol. Such variability, which is probably due in part to genes, may contribute to the individual differences that occur in plasma cholesterol response to dietary cholesterol.

All tissues are capable of synthesizing enough cholesterol to meet their metabolic and structural needs. Consequently, there is no evidence for a biological requirement for dietary cholesterol. Neither an Estimated Average Requirement (EAR), and thus a Recommended Dietary Allowance (RDA), nor an Adequate Intake (AI) was set for cholesterol.

Much evidence indicates a positive linear trend between cholesterol intake and low density lipoprotein (LDL) cholesterol concentration, and therefore an increased risk of coronary heart disease (CHD). A Tolerable Upper Intake Level (UL) was not set for cholesterol because any incremental increase in cholesterol intake increases CHD risk. It is recommended that people maintain their dietary cholesterol intake as low as possible, while consuming a diet that is nutritionally adequate in all required nutrients.

High amounts of cholesterol are found in liver and egg yolk. The main adverse effect of dietary cholesterol is increased LDL cholesterol concentration, which could result in an increased risk for CHD.

## CHOLESTEROL AND THE BODY

### Function

Cholesterol is a sterol that is present in all animal tissues. Tissue cholesterol occurs primarily as free (unesterified) cholesterol, but is also bound covalently (via chemical bonds) to fatty acids as cholesterol esters and to certain proteins. Cholesterol is an integral component of cell membranes and serves as a precursor for hormones such as estrogen, testosterone, and aldosterone, as well as bile acids.

### Absorption, Metabolism, Storage, and Excretion

Cholesterol in the body comes from two sources: endogenous and dietary. All cells can synthesize sufficient amounts of cholesterol for their metabolic and

structural needs. Dietary cholesterol comes from foods of animal origin, such as eggs, meat, poultry, fish, and dairy products.

Dietary and endogenous cholesterol are absorbed in the proximal jejunum, primarily by passive diffusion. Cholesterol balance studies show a wide variation in the efficiency of intestinal cholesterol absorption (from 20 to 80 percent), with most people absorbing between 40 and 60 percent of ingested cholesterol. Such variability, which is probably due in part to genetic factors, may contribute to the differences seen among individuals in plasma cholesterol response to dietary cholesterol. In addition, cholesterol absorption may be reduced by decreased intestinal transit time.

In the body, cholesterol can be stored in the liver; secreted into the plasma in lipoproteins, primarily very low density lipoproteins (VLDL); oxidized and secreted as bile acids; or directly secreted into the bile. Free and esterified cholesterols circulate principally in LDL in the blood. The body tightly regulates cholesterol homeostasis by balancing intestinal absorption and endogenous synthesis with hepatic excretion and bile acids derived from hepatic cholesterol oxidation. Increased hepatic cholesterol delivery from the diet and other sources results in a complex mixture of metabolic effects that are generally directed at maintaining tissue and plasma cholesterol homeostasis. Observational studies have shown that increased dietary cholesterol intake leads to a net increase in plasma LDL cholesterol concentrations.

## **DETERMINING DRIS**

### **Determining Requirements**

All tissues are capable of synthesizing enough cholesterol to meet their metabolic and structural needs. Consequently, there is no evidence for a biological requirement for dietary cholesterol. Neither an Estimated Average Requirement (EAR), and thus a Recommended Dietary Allowance (RDA), nor an Adequate Intake (AI) was set for cholesterol. However, it is recommended that people maintain their dietary cholesterol intake as low as possible, while consuming a diet nutritionally adequate in all required nutrients.

### **The UL**

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Much evidence indicates a positive linear trend between cholesterol intake and LDL cholesterol concentration, and therefore an increased risk of CHD.

A UL was not set for cholesterol because any incremental increase in cholesterol intake increases CHD risk. Because cholesterol is unavoidable in ordi-

nary non-vegan diets, eliminating cholesterol in the diet would require significant dietary changes. These changes require careful planning to ensure adequate intakes of proteins and certain micronutrients. Still, it is possible to eat a low-cholesterol, yet nutritionally adequate, diet.

## DIETARY SOURCES

### Foods

Foods of animal origin contain cholesterol. High amounts are found in liver and egg yolk. Moderate amounts are found in meats, some types of seafood, including shrimp, lobster, certain fish (such as salmon and sardines), and full-fat dairy products.

## ADVERSE EFFECTS OF CONSUMPTION

The main adverse effect of dietary cholesterol is increased LDL cholesterol concentration, which could result in an increased risk for CHD. Serum HDL concentration also increases, although to a lesser extent, but the impact of such a diet-induced change in CHD risk is uncertain. Studies have shown that serum cholesterol concentrations increase with increased dietary cholesterol and that the relationship of blood cholesterol to the risk of CHD progressively increases. On average, an increase of 100 mg/day of dietary cholesterol is predicted to result in a 0.05–0.1 mmol/L increase in total serum cholesterol, of which approximately 80 percent is in the LDL fraction.

There is also increasing evidence that genetic factors underlie a substantial portion of the variation among individuals in response to dietary cholesterol. Although mixed, there is evidence that increases in serum cholesterol concentration due to dietary cholesterol are blunted by diets low in saturated fat, high in polyunsaturated fat, or both.

No consistent significant associations have been established between dietary cholesterol intake and cancer, including lung, breast, colon, and prostate cancers.

## KEY POINTS FOR CHOLESTEROL

- ✓ Cholesterol plays an important role in steroid hormone and bile acid biosynthesis and serves as an integral component of cell membranes.
- ✓ Because all tissues are capable of synthesizing enough cholesterol to meet their metabolic and structural needs, there is no evidence for a biological requirement for dietary cholesterol.
- ✓ Neither an EAR, RDA, nor AI was set for cholesterol.
- ✓ Much evidence indicates a positive linear trend between cholesterol intake and LDL cholesterol concentration, and therefore increased risk of CHD.
- ✓ It is recommended that people maintain their dietary cholesterol intake as low as possible, while consuming a diet nutritionally adequate in all required nutrients.
- ✓ A UL was not set for cholesterol because any incremental increase in cholesterol intake increases CHD risk.
- ✓ High amounts of cholesterol are found in liver and egg yolk. Meats, some types of seafood, including shrimp, lobster, and certain fish, as well as full-fat dairy products contain moderate amounts of cholesterol.
- ✓ The main adverse effect of dietary cholesterol is increased LDL cholesterol concentration, which could result in an increased risk of CHD.

**TABLE 1 Dietary Reference Intakes for Total Protein by Life Stage Group<sup>a</sup>**

Life stage group	DRI values (g/kg/day)			
	EAR <sup>b</sup>		RDA <sup>c</sup>	
	males	females	males	females
0 through 6 mo				1.52 (9.1)
7 through 12 mo	1.0	1.0	1.2 (11) <sup>e</sup>	1.2 (11)
1 through 3 y	0.87	0.87	1.05 (13)	1.05 (13)
4 through 8 y	0.76	0.76	0.95 (19)	0.95 (19)
9 through 13 y	0.76	0.76	0.95 (34)	0.95 (34)
14 through 18 y	0.73	0.71	0.85 (52)	0.85 (46)
19 through 30 y	0.66	0.66	0.80 (56)	0.80 (46)
31 through 50 y	0.66	0.66	0.80 (56)	0.80 (46)
51 through 70 y	0.66	0.66	0.80 (56)	0.80 (46)
> 70 y	0.66	0.66	0.80 (56)	0.80 (46)
<b>Pregnancy</b>		0.88 <sup>f</sup>		1.1 (71) <sup>f</sup>
<b>Lactation</b>		1.05		1.3 (71)

<sup>a</sup> Dietary Reference Intakes for individual amino acids are shown in Appendix E.<sup>b</sup> **EAR** = Estimated Average Requirement. An EAR is the average daily nutrient intake level estimated to meet the requirements of half of the healthy individuals in a group.<sup>c</sup> **RDA** = Recommended Dietary Allowance. An RDA is the average daily dietary intake level sufficient to meet the nutrient requirements of nearly all (97–98 percent) healthy individuals in a group.<sup>d</sup> **AI** = Adequate Intake. If sufficient scientific evidence is not available to establish an EAR, and thus calculate an RDA, an AI is usually developed. For healthy breast-fed infants, the AI is the mean intake. The AI for other life stage and gender groups is believed to cover the needs of all healthy individuals in the group, but a lack of data or uncertainty in the data prevents being able to specify with confidence the percentage of individuals covered by this intake.<sup>e</sup> Values in parentheses ( ) are examples of the total g/day of protein calculated from g/kg/day times the reference weights in Part I, “Introduction to the Dietary Reference Intakes,” Table 1.<sup>f</sup> The EAR and RDA for pregnancy are only for the second half of pregnancy. For the first half of pregnancy, the protein requirements are the same as those of nonpregnant women.

# PROTEIN AND AMINO ACIDS

Proteins form the major structural components of all the cells of the body. Proteins also function as enzymes, in membranes, as transport carriers, and as hormones. Amino acids are constituents of protein and act as precursors for nucleic acids, hormones, vitamins, and other important molecules. Thus, an adequate supply of dietary protein is essential to maintain cellular integrity and function, and for health and reproduction.

The requirements for protein are based on careful analyses of available nitrogen balance studies. Data were insufficient to set a Tolerable Upper Intake Level (UL). DRI values are listed by life stage group in Table 1. The Acceptable Macronutrient Distribution Range (AMDR) for protein is 5–20 percent of total calories for children 1 through 3 years of age, 10–30 percent of total calories for children 4 to 18 years of age, and 10–35 percent of total calories for adults older than 18 years of age.

For amino acids, isotopic tracer methods and linear regression analysis were used whenever possible to determine requirements. The estimated average requirements (EARs) for amino acids were used to develop amino acid scoring patterns for various age groups based on the recommended intake of dietary protein. Data were insufficient to set a Tolerable Upper Intake Level (UL) for any of the amino acids. However, the absence of a UL means that caution is warranted in using any single amino acid at levels significantly above those normally found in food.

Proteins found in animal sources such as meat, poultry, fish, eggs, milk, cheese, and yogurt provide all nine indispensable amino acids and are referred to as “complete proteins.” Proteins found in plants, legumes, grains, nuts, seeds, and vegetables tend to be deficient in one or more of the indispensable amino acids and are called “incomplete proteins.”

Both protein and nonprotein energy (from carbohydrates and fats) must be available to prevent protein-energy malnutrition (PEM). Similarly, if amino acids are not present in the right balance, the body’s ability to use protein will be affected. Protein deficiency has been shown to affect all organs and many systems. The risk of adverse effects from excess protein intake from food appears to be very low. The data are conflicting on the potential for high-protein diets to produce gastrointestinal effects, changes in nitrogen balance, or chronic disease, such as osteoporosis or renal stones.

## PROTEIN AND THE BODY

### Function

Protein is the major functional and structural component of every cell in the body. All enzymes, membrane carriers, blood transport molecules, the intracellular matrices, hair, fingernails, serum albumin, keratin, and collagen are proteins, as are many hormones and a large part of membranes. Amino acids are constituents of protein and act as precursors for many coenzymes, hormones, nucleic acids, and other important molecules.

The most important aspect and defining characteristic of protein from a nutritional point of view is its amino acid composition (amino [or imino] nitrogen group). Amino nitrogen accounts for approximately 16 percent of protein weight, and so nitrogen metabolism is often considered to be synonymous with protein metabolism. Amino acids are required for the synthesis of body protein and other important nitrogen-containing compounds as mentioned above. The amino acids that are incorporated into protein are  $\alpha$ -amino acids, with the exception of proline, which is an  $\alpha$ -imino acid.

### NUTRITIONAL AND METABOLIC CLASSIFICATION OF AMINO ACIDS

Different sources of protein widely vary in chemical composition and nutritional value. Although amino acids have been traditionally classified as indispensable (essential) and dispensable (nonessential), accumulating evidence on the metabolic and nutritional characteristics of dispensable amino acids has blurred their definition, forming a third classification called conditionally indispensable. The term conditionally indispensable recognizes that under most normal conditions, the body can synthesize these amino acids.

The nine indispensable amino acids are those that cannot be synthesized to meet the body's needs, and therefore must be obtained from the diet. The five dispensable amino acids can be synthesized in the body. Six other amino acids are conditionally indispensable because their synthesis can be limited under special pathophysiological conditions, such as prematurity in the young infant or individuals in severe catabolic stress. Table 2 lists the classification of amino acids in the human diet.

### Protein Quality

The quality of a source of dietary protein depends on its ability to provide the nitrogen and amino acid requirements that are necessary for the body's growth, maintenance, and repair. This ability is determined by two factors: digestibility and amino acid composition. Digestibility affects the number and type of amino acids made available to the body. If the content of a single indispensable

**TABLE 2 Indispensable, Dispensable, and Conditionally Indispensable Amino Acids in the Human Diet**

Indispensable	Dispensable	Conditionally Indispensable <sup>a</sup>	Precursors of Conditionally Indispensable
Histidine <sup>b</sup>	Alanine	Arginine	Glutamine/glutamate, aspartate
Isoleucine	Aspartic acid	Cysteine	Methionine, serine
Leucine	Asparagine	Glutamine	Glutamic acid/ammonia
Lysine	Glutamic acid	Glycine	Serine, choline
Methionine	Serine	Proline	Glutamate
Phenylalanine		Tyrosine	Phenylalanine
Threonine			
Tryptophan			
Valine			

<sup>a</sup> Conditionally indispensable is defined as requiring a dietary source when endogenous synthesis cannot meet metabolic need.

<sup>b</sup> Although histidine is considered indispensable, unlike the other eight indispensable amino acids, it does not fulfill the criteria of reducing protein deposition and inducing negative nitrogen balance promptly upon removal from the diet.

amino acid in the diet is less than the individual's requirement, then this deficiency will limit the utilization of other amino acids and thus prevent normal rates of protein synthesis, even when the total nitrogen intake level is adequate. As a result, the "limiting amino acid" will determine the nutritional value of the diet's total nitrogen or protein content.

The concept of the "limiting amino acid" has led to the practice of amino acid (or chemical) scoring, whereby the indispensable amino acid composition of a given protein source is compared with that of a reference amino acid composition profile to evaluate the quality of food proteins or their capacity to efficiently meet both nitrogen and indispensable amino acid requirements.

## Absorption, Metabolism, Storage, and Excretion

Amino acids are present in the body as free amino acids or as part of protein. They are available through two major pathways: dietary intake in the form of proteins or de novo synthesis by the body.

When proteins are ingested from food, they are denatured by stomach acid. In the stomach, they are also cleaved into smaller peptides by the enzyme pepsin, which is activated in response to a meal. The proteins and peptides then enter the small intestine, where a variety of enzymes hydrolyze the peptide bonds. The resulting mix of free amino acids and peptides is transported into the mucosal cells. The amino acids are then either secreted into the blood or further metabolized within the cells. Absorbed amino acids pass into the liver, where some are taken up and used and others are circulated to and used by the peripheral tissues.

About 43 percent of the total protein content of the body is present as skeletal muscle, while other structural tissues, such as skin and blood, each contain approximately 15 percent of the body's total protein. The metabolically active visceral tissues (e.g., liver and kidney tissue) contain comparatively small amounts of protein (together about 10 percent of the total). Other organs such as the brain, heart, lung, and bone contribute the remainder. Almost half of the total protein content of the body is represented by only four proteins (myosin, actin, collagen, and hemoglobin).

Amino acids are lost in the body by oxidation, excretion, or conversion to other metabolites. Metabolic products of amino acids, such as urea, creatinine, and uric acid, are excreted in the urine; fecal nitrogen losses may account for 25 percent of the obligatory loss of nitrogen. Other routes of loss of intact amino acids are through the sweat and other body secretions and through the skin, nails, and loss of hair.

### PROTEIN TURNOVER

The process by which all body proteins are being continuously broken down and resynthesized is known as protein turnover. From a nutritional and metabolic point of view, it is important to recognize that protein synthesis is a continuing process that takes place within most of the body's cells. In a steady state, when neither net growth nor protein loss is occurring, protein synthesis is balanced by an equal amount of protein degradation.

The major consequence of inadequate protein intake, or of consuming diets that are low or lacking in specific indispensable amino acids, is a shift in this balance. Rates of synthesis of some body proteins decrease while protein degradation continues in order to provide an endogenous source of the amino acids most in need. The mechanism of intracellular protein degradation by which protein is hydrolyzed to free amino acids is more complex and not as well characterized at the mechanistic level as that of protein synthesis.

The daily amount of protein turned over is greater in infants and less in the elderly when compared with young adults on a body-weight basis; and some

body tissues are more active than others with regard to it. Despite their rather small contribution to the total protein content of the body, the liver and the intestine together are believed to contribute as much as 50 percent of whole body protein turnover. Conversely, although skeletal muscle is the largest single component of body protein mass (43 percent), it contributes only about 25 percent to total body protein turnover.

## DETERMINING DRIS

### Determining Requirements

#### PROTEIN

The requirements for protein were based on careful analyses of available nitrogen balance studies.

#### AMINO ACIDS

Age-based recommendations were set for all nine of the indispensable amino acids found in dietary proteins (see Appendix E). These requirements are based on isotopic tracer methods and linear regression analysis, which were used whenever possible.

The requirements for amino acids and for total protein were used to develop a new FNB/IOM Protein Scoring Pattern for use in children aged 1 year and older and in all other age groups. The recommended amino acid scoring pattern for proteins for individuals aged 1 year and older and all other age groups is as follows (in mg/g of protein): isoleucine, 25; leucine, 55; lysine, 51; methionine + cysteine (SAA), 25; phenylalanine + tyrosine, 47; threonine, 27; tryptophan, 7; valine, 32; and histidine, 18. This pattern allows comparison of the relative nutritional quality of different protein sources by calculating a protein digestibility corrected amino acid score (PDCAAS). The calculation compares the amino acid in a test protein with the amount of that amino acid in the FNB/IOM scoring pattern multiplied by the true digestibility. Illustration of the calculation involved is detailed in *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* (2005).

### Special Considerations

**Multiparous pregnancies:** Multiparous pregnancies are associated with a marked increase in low birth weight and perinatal mortality. Thus, it is logical to assume that women supporting the growth of more than one fetus have higher protein

needs, and some evidence supports this assumption. Thus, it is prudent that women carrying twins should increase their protein intake by an additional 50 g/day beginning in the second trimester, as well as ensure for themselves a sufficient energy intake to utilize the protein as efficiently as possible.

**Physically active individuals:** It is commonly believed that athletes should consume a higher-than-normal protein intake to maintain optimum physical performance. However, since compelling evidence of additional need is lacking, no additional dietary protein is suggested for healthy adults who undertake resistance or endurance exercise.

**Vegetarian diets:** Individuals who restrict their diet to plant-based foods may be at risk of deficiencies in certain indispensable amino acids because the concentration of lysine, sulfur amino acids, and threonine are sometimes lower in plant proteins than in animal proteins. However, vegetarian diets that include complementary mixtures of plant proteins can provide the same quality of protein as that from animal proteins. Available evidence does not support recommending a separate protein requirement for individuals who consume complementary mixtures of plant proteins.

## Criteria for Determining Protein Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Average consumption of protein from human milk
6 through 12 mo	Nitrogen equilibrium plus protein deposition
1 through 18 y	Nitrogen equilibrium plus protein deposition
> 18y	Nitrogen equilibrium

<i>Pregnancy</i>	Age-specific requirement plus protein deposition
<i>Lactation</i>	Age-specific requirement plus milk nitrogen

## The AMDR

The Acceptable Macronutrient Distribution Range (AMDR) for protein is 5–20 percent of total calories for children 1 through 3 years of age, 10–30 percent of total calories for children 4 to 18 years of age, and 10–35 percent of total calories for adults older than 18 years of age (see Part II, “Macronutrients, Healthful Diets, and Physical Activity”).

## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Data were insufficient to establish a UL for total protein or for any of the amino acids. However, the absence of a UL warrants caution in using any single amino acid at levels significantly above those normally found in food.

## PROTEIN SOURCES

### Foods

Proteins from animal sources such as meat, poultry, fish, eggs, milk, cheese, and yogurt provide all nine indispensable amino acids and are referred to as “complete proteins.” Proteins from plants, legumes, grains, nuts, seeds, and vegetables tend to be deficient in one or more of the indispensable amino acids and are called “incomplete proteins.”

### Dietary Supplements

With the exception of discussion of amino acids from all sources, this information was not provided at the time the DRI values for protein and amino acids were set. Given limited data, caution is warranted in using any single amino acid at a level significantly above that normally found in food.

### Bioavailability

(See “Protein Quality.”)

### Dietary Interactions

This information was not provided at the time the DRI values for protein and amino acids were set.

## INADEQUATE INTAKE AND DEFICIENCY

Both protein and nonprotein energy (from carbohydrates and fats) must be available to prevent protein-energy malnutrition (PEM). Similarly, if amino acids are not present in the right balance, the body's ability to use protein will be affected.

Worldwide, PEM is fairly common in both children and adults and is associated with the deaths of about 6 million children each year. In the industrial-

ized world, PEM is predominately seen in hospitals, is associated with disease, or is often found in the elderly.

Protein deficiency has been shown to affect all of the body's organs and many of its systems, including the brain and brain function of infants and young children; the immune system, thus elevating risk of infection; gut mucosal function and permeability, which affects absorption and vulnerability to systemic disease; and kidney function.

The physical signs of protein deficiency include edema, failure to thrive in infants and children, poor musculature, dull skin, and thin and fragile hair. Biochemical changes reflecting protein deficiency include low serum albumin and low serum transferrin.

## EXCESS INTAKE

### Protein

The risk of adverse effects from excess protein intake from foods appears to be very low. The data are conflicting on the potential for high-protein diets to produce gastrointestinal effects, changes in nitrogen balance, or chronic disease, such as osteoporosis or renal stones. Further research is needed in these areas.

### Amino Acids

There is no evidence that amino acids derived from usual or even high intakes of protein from food present any risk. Data were limited on the adverse effects of high levels of amino acid intakes from dietary supplements and therefore caution is warranted in using any single amino acid at a level significantly above that normally found in food.

### Special Considerations

**Maple syrup urine disease (MSUD):** MSUD is the most common disorder associated with genetic anomalies in the metabolism of branched-chain amino acids (BCAAs), such as leucine, isoleucine, and valine. The condition stems from inadequate function of a multienzyme system called branched-chain ketoacid dehydrogenase and is characterized by elevated plasma levels of BCAAs, especially leucine. Although MSUD can be diagnosed in infancy, there are six other forms of the condition that begin later in life. People with MSUD must severely restrict their consumption of BCAAs. Without proper treatment and medical management, mental retardation and death may occur.

***Phenylketonuria (PKU):*** PKU is a genetic disorder that impairs activity of the enzyme phenylalanine hydroxylase (PAH). This allows phenylalanine or by-products of its breakdown to build up in the plasma during critical periods of brain development. Chronically elevated plasma phenylalanine levels before and during infancy and childhood can cause irreversible brain damage, growth retardation, and skin abnormalities. To prevent these problems, dietary phenylalanine must be restricted within one month of birth and this restriction continued at least through childhood and adolescence. In the United States, approximately 1 of every 15,000 infants is born with PKU.

## KEY POINTS FOR PROTEIN AND AMINO ACIDS

- ✓ Protein is the major functional and structural component of every cell in the body. All enzymes, membrane carriers, blood transport molecules, the intracellular matrices, hair, fingernails, serum albumin, keratin, and collagen are proteins, as are many hormones and a large part of membranes.
- ✓ The amino acids that make up proteins act as precursors for nucleic acids, hormones, vitamins, and other important molecules.
- ✓ The most important aspect and defining characteristic of protein from a nutritional point of view is its amino acid composition (amino [or imino] nitrogen group).
- ✓ Although amino acids have traditionally been classified as indispensable (essential) and dispensable (nonessential), accumulating evidence on the metabolic and nutritional characteristics of dispensable amino acids has blurred their definition, forming a third classification called conditionally indispensable.
- ✓ The quality of a source of dietary protein depends on its ability to provide the nitrogen and amino acid requirements that are necessary for the body's growth, maintenance, and repair.
- ✓ The adult requirements for protein are based primarily on nitrogen balance studies.
- ✓ The Acceptable Macronutrient Distribution Range (AMDR) for protein is 5–20 percent of total calories for children 1 through 3 years of age, 10–30 percent of total calories for children 4 to 18 years of age, and 10–35 percent of total calories for adults older than 18 years of age.
- ✓ Data were insufficient to establish a UL for total protein or amino acids.
- ✓ Proteins from animal sources such as meat, poultry, fish, eggs, milk, cheese, and yogurt provide all nine indispensable amino acids and are referred to as “complete proteins.”
- ✓ Proteins from plants, legumes, grains, nuts, seeds, and vegetables tend to be deficient in one or more of the indispensable amino acids and are called “incomplete proteins.”
- ✓ Both protein and nonprotein energy (from carbohydrates and fats) must be available to prevent protein-energy malnutrition (PEM).

- ✓ Protein deficiency has been shown to affect all of the body's organs and many systems.
- ✓ The data are conflicting on the potential for high-protein diets to produce gastrointestinal effects, changes in nitrogen balance, or chronic disease, such as osteoporosis or renal stones.
- ✓ There is no evidence that amino acids derived from usual or even high intakes of protein from food present any risk. Data were limited on the adverse effects of high levels of amino acid intakes from dietary supplements and therefore caution is warranted in using any single amino acid at a level significantly above that normally found in food.

**TABLE 1 Dietary Reference Intakes for Water by Life Stage Group**

Life stage group <sup>c</sup>	DRI values (L/day) <sup>a</sup>
	AI <sup>b</sup>
0 through 6 mo	0.7, assumed to be from human milk
7 through 12 mo	0.8 of <i>total</i> <sup>d</sup> water, assumed to be from human milk, complementary foods and beverages. This includes approximately 0.6 L (about 3 cups) as total fluid, including formula or human milk, juices, and drinking water.
1 through 3 y	1.3 of <i>total</i> water. This includes approximately 0.9 L (about 4 cups) as total beverages, including drinking water.
4 through 8 y	1.7 of <i>total</i> water. This includes approximately 1.2 L (about 5 cups) as total beverages, including drinking water.
9 through 13 y	
males	2.4 of <i>total</i> water. This includes approximately 1.8 L (about 8 cups) as total beverages, including drinking water.
females	2.1 of <i>total</i> water. This includes approximately 1.6 L (about 7 cups) as total beverages, including drinking water.
14 through 18 y	
males	3.3 of <i>total</i> water. This includes approximately 2.6 L (about 11 cups) as total beverages, including drinking water.
females	2.3 of <i>total</i> water. This includes approximately 1.8 L (about 8 cups) as total beverages, including drinking water.
19 through > 70y	
males	3.7 of <i>total</i> water. This includes approximately 3.0 L (about 13 cups) as total beverages, including drinking water.
females	2.7 of <i>total</i> water. This includes approximately 2.2 L (about 9 cups) as total beverages, including drinking water.

**TABLE 1 Continued**

DRI values (L/day) <sup>a</sup>	
AI <sup>b</sup>	
<b>Pregnancy</b>	
14 through 50 y	3.0 of <i>total</i> water. This includes approximately 2.3 L (about 10 cups) as total beverages, including drinking water.
<b>Lactation</b>	
14 through 50 y	3.8 of <i>total</i> water. This includes approximately 3.1 L (about 13 cups) as total beverages, including drinking water.

<sup>a</sup> Conversion factors: 1 L = 33.8 fluid oz; 1 L = 1.06 qt; 1 cup = 8 fluid oz.

<sup>b</sup> AI = Adequate Intake. If sufficient scientific evidence is not available to establish an Estimated Average Requirement (EAR), and thus calculate a Recommended Dietary Allowance (RDA), an AI is usually developed. For healthy breast-fed infants, the AI is the mean intake. The AI for other life stage and gender groups is believed to cover the needs of all healthy individuals in the group, but a lack of data or uncertainty in the data prevents being able to specify with confidence the percentage of individuals covered by this intake.

<sup>c</sup> Life stage groups through 8 years of age represent males and females.

<sup>d</sup> Total water (as italicized) includes all water contained in food, beverages, and drinking water. For infants, 7 through 12 months, *total* water assumed to be from human milk, complementary foods and beverages.

# WATER

Water, vital for life, is the largest single constituent of the human body, averaging approximately 60 percent of body weight. It is essential for cellular homeostasis and for maintaining vascular volume. It also serves as the medium for transport within the body by supplying nutrients and removing waste.

Since data were insufficient to establish an Estimated Average Requirement (EAR) and thus calculate a Recommended Dietary Allowance (RDA) for water, an Average Intake (AI) was instead developed. The AIs for water are based on the median *total* water intake from U.S. survey data. (*Total* water intake includes drinking water, water in beverages and formula, and water that is contained in food.) These reference values represent the *total* water intake that is considered likely to prevent deleterious, primarily acute, effects of dehydration, including metabolic and functional abnormalities. Although a low intake of *total* water has been associated with some chronic diseases, this evidence is insufficient to establish water intake recommendations as a means to reduce the risk of chronic diseases.

Higher intakes of *total* water will be required for those who are physically active or exposed to hot environments. Because healthy individuals have a considerable ability to excrete excess water and thereby maintain water balance, a Tolerable Upper Intake Level (UL) was not set for water. DRI values for water are listed by life stage group in Table 1.

Over the course of a few hours, body water deficits can occur due to reduced intake or increased water loss from physical activity and environmental (heat) exposure. However, on a day-to-day basis, fluid intake, usually driven by the combination of thirst and mealtime beverage consumption, helps maintain hydration status and total body water (TBW) at normal levels.

Sources of water include beverages, food, and drinking water. Inadequate water intake leads to dehydration. Excessive water intake can lead to hyponatremia, an extremely rare condition marked by a low concentration of sodium in the blood.

## WATER AND THE BODY

### Function

Water is the solvent for biochemical reactions and represents the largest single constituent of the human body, averaging approximately 60 percent of body weight. Water absorbs the body heat from metabolic processes, maintains vascular volume, and serves as the medium for transport within the body by supplying nutrients and removing waste. It is also essential for cellular homeostasis. Cell hydration has been suggested to be an important signal in the regulation of cell metabolism and gene expression.

Daily water intake must be balanced with water loss in order to maintain total body water (TBW). TBW is comprised of both the intracellular (ICF) and the extracellular (ECF) fluids and varies by individual due to differences in body composition.

### Absorption, Metabolism, Storage, and Excretion

Water that is consumed via liquid and food is digested and absorbed within the gastrointestinal tract. Body water is distributed between the ICF and the ECF, which contain 65 and 35 percent of TBW, respectively. Body water balance depends on the net difference between water gain and water loss. Perturbations such as exercise, heat exposure, fever, diarrhea, trauma, and burns will greatly affect the net volumes and water turnover rates between these fluid compartments.

TBW gain occurs from consumption and as a by-product of the metabolism of energy-yielding nutrients from foods. Production of metabolic water is proportional to daily energy expenditure for people eating a mixed diet. TBW loss results from respiratory, skin, renal, and gastrointestinal tract water losses, which are described as follows:

**Respiratory:** Physical activity generally has a greater effect on water loss through evaporation within the lungs than do environmental factors, such as ambient air temperature and humidity. Daily loss averages about 200–350 mL/day for sedentary people and can increase to 500–600 mL/day for active people who live in temperate climates at sea level.

**Urinary and gastrointestinal:** Renal output can vary depending on specific macronutrient, salt, and water loads. Urine output inversely varies with body hydration status (usually averaging 1–2 L/day) and also generally increases in healthy older individuals because they are unable to concentrate urine as well as younger individuals. Exercise and heat reduce urine output, while cold and

hypoxia increase output. Fecal water loss in healthy adults is approximately 100–200 mL/day.

**Skin:** Water loss through skin occurs by insensible diffusion and secreted sweat. For the average adult, loss of water by insensible diffusion is approximately 450 mL/day. In hot weather, sweat evaporation is the primary avenue of heat loss to defend the body's core temperature. Daily sweat loss considerably varies due to differences in metabolic rate and environment (e.g., clothing worn, ambient temperatures, air motion, and solar load).

## DETERMINING DRIS

### Determining Requirements

Since data were insufficient to establish an EAR and thus calculate an RDA for water, an AI was instead developed. The AIs for water are based on median *total* water intakes using survey data from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994). These reference values represent *total* water intakes that are considered likely to prevent deleterious, primarily acute, effects of dehydration, including metabolic and functional abnormalities. Although a low intake of *total* water has been associated with some chronic diseases, the evidence is insufficient to establish water intake recommendations as a means to reduce the risk of chronic diseases.

As with AIs for other nutrients, for a healthy person, daily consumption below the AI may not confer additional risk because a wide range of intakes is compatible with normal hydration. In this setting, the AI should not be interpreted as a specific requirement. Higher intakes of *total* water will be required for those who are physically active or exposed to hot environments.

Over the course of a few hours, body water deficits can occur due to reduced intake or increased water loss from physical activity and environmental (heat) exposure. However, on a day-to-day basis, fluid intake, usually driven by the combination of thirst and mealtime beverage consumption, helps maintain hydration status and TBW at normal levels.

### Special Considerations

Generally, groups that are more active will have a greater total water intake:

- **Active adults:** Physical activity, particularly when performed in hot weather, increases daily fluid needs. Daily water requirements for adults can double in hot weather (86°F or 30°C) and triple in very hot weather (104°F or 40°C) to make up for water lost via sweating.

- *Active children:* Children who are active produce considerably less sweat than active adults, even when exercising in hot environments. This difference in sweat production prevails until midpuberty and should be considered when determining the water requirements of active children and adolescents.
- *Elderly:* Hydration status continues to be normal in elderly individuals over a wide range of intakes. However, a deficit in thirst and fluid intake regulation, age-related impairments in renal-concentrating and sodium-conserving ability, prior history of stroke, or evidence of hypothalamic or pituitary dysfunction may contribute to increased incidence of dehydration and hypernatremia.

## Factors Affecting Water Requirements

**Physical activity and heat strain:** Physical activity and heat strain can substantially increase water loss through sweating. The daily water requirement increases that arise from activity and ambient temperature are the result of increased sweating to meet evaporative cooling requirements. A person's sweating rate depends on climatic conditions, the clothing worn, and exercise intensity and duration. Physical fitness level has a modest effect on sweat loss, unless accompanied by heat acclimation. Studies have shown broad ranges in fluid requirements based on these influences. Examples include:

- People in very hot (e.g., desert) climates, who often have sweating rates of 0.3–1.2 L/hour while performing occupational activities
- People wearing protective clothing, who often have sweating rates of 1–2 L/hour while performing light-intensity exercise in hot weather
- Male competitive runners, who can have sweating rates of 1 to > 2 L/hour while training or racing in the heat
- Female competitive runners may increase their sweat losses from approximately 0.7 L/hour in temperate weather to approximately 1.1 L/hour in warm weather when performing the same event

**Altitude and cold temperature:** Altitude exposure increases respiratory water loss and hypoxia-induced diuresis. There may also be reduced fluid consumption and, for persons traversing rugged mountain terrains, elevated sweating due to high metabolic rates. The net effect can lead to dehydration. Body fluid loss in cold climates can be as high as loss in hot climates due to high rates of energy expenditure and the use of highly insulated heavy clothing. Fluid loss during cold exposure is thought to result from cold-induced diuresis and increased respiratory loss.

**Diabetes mellitus:** Dehydration is clearly associated with the worsening control of diabetes. In addition, uncontrolled diabetes dramatically contributes to development of severe dehydration and volume depletion due to osmotic diuresis. In people with poorly controlled diabetes, reduced water intake can also lead to dehydration owing to infection or hypotension, which can lead to delirium and an impaired ability to seek water.

**Cystic fibrosis:** People with cystic fibrosis have high concentrations of sodium chloride in their sweat. They may lose excessive amounts of sodium and chloride when their sweating rates are high and, unlike healthy people, their body fluid osmolality does not increase due to the high concentrations of sodium chloride in their sweat. Without elevated serum osmolality, a major trigger for thirst, cystic fibrosis patients can quickly become dehydrated during physical activity, particularly in the heat.

**Diuretics and other medications:** There are no medications that directly stimulate water intake. When decreased fluid intake has occurred due to illness, medications that improve metabolic and cognitive function should indirectly help people increase their fluid intake. Examples include antibiotics for infections, insulin for unstable diabetics, and analgesics for delirium-inducing pain. However, some drugs, such as diuretics, cause excess water loss. Diuretics are commonly used medications that are prescribed for the treatment of conditions such as hypertension, heart failure, and chronic kidney disease. Dehydration may occur in people who do not modify their use of diuretics in hot weather or in other situations where excess water loss occurs. Other medications, such as lithium, may interfere with the kidneys' regulatory systems, leading to excessive water loss.

## Criteria for Determining **Total Water Requirements, by Life Stage Group**

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 months	Average consumption from human milk content
7 through 12 months	Average consumption from human milk + complementary foods and other beverages
1 through > 70 y	Median <i>total</i> water intake using data from NHANES III
<i>Pregnancy</i>	Same as age-specific values for nonpregnant women
<i>Lactation</i>	Same as age-specific values for nonpregnant women

## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Because healthy individuals have considerable ability to excrete excess water and thereby maintain water balance, a UL was not set for water. However, acute water toxicity has been reported from the rapid consumption of large quantities of fluids that greatly exceeded the kidneys' maximal excretion rate of approximately 0.7–1.0 L/hour.

According to NHANES III (1988–1994), the highest total water intake (99th percentile) reported was 8.1 L/day. No adverse intakes have been reported with chronic high intakes of water in health people consuming a normal diet, as long as fluid intake is approximately proportional to losses.

## DIETARY SOURCES

Sources of water include beverages, food, and drinking water. Fruits and vegetables contain a high percentage of water. According to data from NHANES III, adults in the United States obtained *total* water from the following sources:

- 35–54 percent from drinking water
- 49–63 percent from other beverages (with juice, carbonated drinks, coffee, and milk being the major sources)
- 19–25 percent from foods (such as fruits, vegetables, soups, ice cream, and meats)

## Dietary Interactions

There is evidence that water may interact with certain nutrients and dietary substances (see Table 2).

## INADEQUATE INTAKE

Inadequate water intake leads to dehydration, the effects of which include the following:

- Impaired mental function and motor control
- Diminished aerobic and endurance exercise performance
- Enhanced fever response (fever is a regulated rise in body temperature)
- Increased core temperature during exercise
- Reduced tolerance to the stress of exercise and heat
- Increased resting heart rate when standing or lying down

**TABLE 2 Potential Substances That Affect Water Requirements**

Substance	Potential Interaction	Notes
<b>SUBSTANCES THAT AFFECT WATER REQUIREMENTS</b>		
Caffeine	Due to its diuretic effect, caffeine in high amounts may lead to a total body water (TBW) deficit.	Available data were inconsistent. Unless future research proves otherwise, caffeinated beverages appear to contribute to total water intake to the same degree as noncaffeinated fluids do.
Alcohol	Alcohol intake appears to increase water excretion.	Based on limited data, ethanol ingestion did not appear to result in appreciable fluid loss over a 24-hour period. An increased excretion of water due to ethanol ingestion was transient.
Sodium	Increased sodium intake may increase urine volume.	Based on limited data, it was not possible to determine the extent to which sodium intake influences water intake.
Protein	Increased protein consumption may increase water needs. Urea, a major end product of the metabolism of dietary proteins and amino acids, requires water for excretion by the kidneys.	Studies showed that increased protein intake did not affect water intake or urine volume in the setting of <i>ad libitum</i> water consumption.
Fiber	Fecal water loss is increased with increased dietary fiber.	Limited studies showed significant increases in fecal water loss with high-fiber diets.
Carbohydrate	The presence of dietary carbohydrates may affect	On average, 100 g/day of carbohydrates (the amount needed to prevent ketosis) has been shown to decrease body water deficit by decreasing the quantity of body solutes (ketone bodies) that need to be excreted. This response is similar when ketosis occurs with the consumption of very low carbohydrate diets.

- Impaired ability to maintain blood pressure when presented with vascular challenges
- Fainting (in susceptible people)
- Reduced cardiac output during exercise and heat stress
- Apparent increased risk of life-threatening heat stroke

## **EXCESS INTAKE**

No adverse effects have been reported with chronic high intakes of water by healthy people who consume a normal diet, as long as fluid intake is approximately proportional to fluid loss. Excessive water intake can lead to hyponatremia, which is a low concentration of sodium in the blood (defined as serum sodium concentration of less than 135 mmol/L). The lowering of the extracellular fluid sodium concentration causes fluid to move into the intracellular fluid space, resulting in central nervous system edema, lung congestion, and muscle weakness. Hyponatremia can also occur from excessive fluid intake, the under-replacement of sodium, or both, during or after prolonged endurance athletic events. In severe cases, hyponatremia can be life-threatening.

Hyponatremia is rare in healthy persons who consume an average North American diet. The condition is most often seen in infants, psychiatric patients with psychogenic polydipsia (chronic excessive thirst and fluid intake), patients on psychotropic drugs, women who have undergone surgery using a uterine distension medium, and participants in prolonged endurance events, such as military recruits.

A series of case studies has suggested that gross overconsumption of fluids (for example, more than 20 L/day) is associated with irreversible bladder lesions and possibly thinner bladder muscles, delayed bladder sensation, and flow rate impairment.

## KEY POINTS FOR WATER

- ✓ Water, vital for life, is essential for cellular homeostasis and for maintaining vascular volume. It also serves as the medium for transport within the body by supplying nutrients and removing waste.
- ✓ Since data were insufficient to establish an EAR and thus calculate an RDA for water, an AI was instead developed.
- ✓ The AIs for water are based on the median *total* water intake from U.S. survey data. These reference values represent *total* water intakes that are considered likely to prevent deleterious, primarily acute, effects of dehydration, including metabolic and functional abnormalities.
- ✓ Although a low intake of *total* water has been associated with some chronic diseases, this evidence is insufficient to establish water intake recommendations as a means to reduce the risk of chronic diseases.
- ✓ Over the course of a few hours, body water deficits can occur due to reduced intake or increased water loss from physical activity and environmental (heat) exposure. However, on a day-to-day basis, fluid intake, driven by the combination of thirst and mealtime beverage consumption, helps maintain hydration status and total body water at normal levels.
- ✓ Because healthy individuals have a considerable ability to excrete excess water and thereby maintain water balance, a UL was not set for water.
- ✓ Acute water toxicity has been reported from the rapid consumption of large quantities of fluids that greatly exceeded the kidneys' maximal excretion rate of approximately 0.7–1.0 L/hour.
- ✓ Sources of water include drinking water, beverages, and food.
- ✓ Inadequate water intake leads to dehydration, which can impair mental function, exercise performance, exercise and heat stress tolerance, and blood pressure regulation.
- ✓ Excessive water intake can lead to hyponatremia, which is a low concentration of sodium in the blood. This condition leads to central nervous system edema, lung congestion, and muscle weakness.

## PART III

# VITAMINS AND MINERALS

Part Three of this publication summarizes information from the DRI reports titled *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids* (2000); *Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate* (2005); *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride* (1997); *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline* (1998); and *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc* (2001). This section is divided into chapters that are organized by nutrient for 35 individual vitamins and minerals. Each chapter provides a table of known nutrient reference values; reviews the function of a given nutrient in the human body; summarizes the known effects of deficiencies and excessive intakes; describes how a nutrient may be related to chronic disease or developmental abnormalities, where data were available; and provides the indicator of adequacy for determining the nutrient requirements.

Vitamins covered in Part Three include vitamin A, vitamin B<sub>6</sub>, vitamin B<sub>12</sub>, biotin, vitamin C, carotenoids, choline, vitamin D, vitamin E, folate, vitamin K, niacin, pantothenic acid, riboflavin, and thiamin. Minerals covered in Part Three include calcium, chromium, copper, fluoride, iodine, iron, magnesium, manganese, molybdenum, phosphorus, potassium, selenium, sodium chloride, sulfate, and zinc; there is also a chapter on other substances including arsenic, boron, nickel, silicon, and vanadium.



## **DEFINITIONS USED IN TABLES IN PART III**

**EAR** = Estimated Average Requirement. An EAR is the average daily nutrient intake level estimated to meet the requirements of half of the healthy individuals in a group.

**RDA** = Recommended Dietary Allowance. An RDA is the average daily dietary intake level sufficient to meet the nutrient requirements of nearly all (97–98 percent) healthy individuals in a group.

**AI** = Adequate Intake. If sufficient scientific evidence is not available to establish an EAR, and thus calculate an RDA, an AI is usually developed. For healthy breast-fed infants, the AI is the mean intake. The AI for other life stage and gender groups is believed to cover the needs of all healthy individuals in the group, but a lack of data or uncertainty in the data prevents being able to specify with confidence the percentage of individuals covered by this intake.

**UL** = Tolerable Upper Intake Level. The UL is the highest level of daily nutrient intake that is likely to pose no risk of adverse health effects to almost all individuals in the general population. Unless otherwise specified, the UL represents total intake from food, water, and supplements. In the absence of a UL, extra caution may be warranted in consuming levels above the recommended intake. Members of the general population should be advised not to routinely exceed the UL. The UL is not meant to apply to individuals who are treated with the nutrient under medical supervision or to individuals with predisposing conditions that modify their sensitivity to the nutrient.

**TABLE 1 Dietary Reference Intakes for Vitamin A by Life Stage Group**

Life stage group	DRI values ( $\mu\text{g RAE}^a/\text{day}$ )				
	EAR <sup>b</sup>		RDA <sup>c</sup>		AI <sup>d</sup>
	males	females	males	females	UL <sup>e,f</sup>
0 through 6 mo					400 600
7 through 12 mo					500 600
1 through 3 y	210	210	300	300	600
4 through 8 y	275	275	400	400	900
9 through 13 y	445	420	600	600	1,700
14 through 18 y	630	485	900	700	2,800
19 through 30 y	625	500	900	700	3,000
31 through 50 y	625	500	900	700	3,000
51 through 70 y	625	500	900	700	3,000
> 70 y	625	500	900	700	3,000
<b>Pregnancy</b>					
≤ 18 y		530		750	2,800
19 through 50 y		550		770	3,000
<b>Lactation</b>					
≤ 18 y		885		1,200	2,800
19 through 50 y		900		1,300	3,000

<sup>a</sup> RAE = Retinol activity equivalent. 1  $\mu\text{g RAE} = 1 \mu\text{g retinol, } 12 \mu\text{g } \beta\text{-carotene, and } 24 \mu\text{g } \alpha\text{-carotene or } \beta\text{-cryptoxanthin. The RAE for dietary provitamin A carotenoids in foods is twofold greater than retinol equivalents (RE), whereas the RAE for preformed vitamin A in foods is the same as RE.}$

<sup>b</sup> EAR = Estimated Average Requirement.

<sup>c</sup> RDA = Recommended Dietary Allowance.

<sup>d</sup> AI = Adequate Intake.

<sup>e</sup> UL = Tolerable Upper Intake Level.

<sup>f</sup> The UL for vitamin A applies only to preformed vitamin A (e.g., retinol, the form of vitamin A found in animal foods, most fortified foods, and supplements). It does not apply to vitamin A derived from carotenoids.

# VITAMIN A

**V**itamin A is a fat-soluble nutrient that is important for vision, gene expression, reproduction, embryonic development, growth, and immune function. Forms of vitamin A include retinol (preformed vitamin A), retinal, retinoic acid, and retinyl esters. The term vitamin A also includes provitamin A carotenoids that are dietary precursors of retinol. The term retinoids refers to retinol and its metabolites, and any synthetic analogues that have a similar structure.

The requirements for vitamin A are now denoted in retinol activity equivalents (RAEs), such that  $1\text{ }\mu\text{g RAE} = 1\text{ }\mu\text{g all}-trans\text{-retinol}$ ,  $12\text{ }\mu\text{g } \beta\text{-carotene}$ , and  $24\text{ }\mu\text{g } \alpha\text{-carotene or } \beta\text{-cryptoxanthin}$ . This recognizes that 50 percent less bioconversion of carotenoids to vitamin A occurs than was previously thought when vitamin A was expressed in retinol equivalents (REs). The change means that twice the amount of provitamin A-rich carotenoids contained in leafy green vegetables and certain fruits is required to provide a given amount of vitamin A activity.

The requirements for vitamin A are based on the assurance of adequate liver stores of vitamin A. The Tolerable Upper Intake Level (UL) is based on liver abnormalities as the critical endpoint. For women of childbearing age, the UL is based on teratogenicity as the critical adverse effect. DRI values are listed by life stage group in Table 1.

Preformed vitamin A (retinol) is naturally found in animal-based foods, whereas dietary carotenoids (provitamin A carotenoids), which are converted to vitamin A in the body, are present in oils, fruits, and vegetables. Common dietary sources of preformed vitamin A in the United States and Canada include liver, dairy products, and fish. Foods fortified with vitamin A are margarine and low-fat and nonfat (skim and partly skimmed) milk. Provitamin A carotenoids are found in carrots, broccoli, squash, peas, spinach, and cantaloupe.

The most specific clinical effect of vitamin A deficiency is xerophthalmia and its various stages, including night blindness, conjunctival xerosis, Bitot's spots, corneal xerosis, corneal ulceration, and scarring. Preformed vitamin A toxicity (hypervitaminosis A) due to high vitamin A intakes may be acute or chronic.

## VITAMIN A AND THE BODY

### Function

Vitamin A is a fat-soluble vitamin that is important for normal vision, gene expression, reproduction, embryonic development, growth, and immune function. Forms of vitamin A include retinol (preformed vitamin A), retinal, retinoic acid, and retinyl esters. Some examples of vitamin A functions include retinal, which is required by the eye to transduce light into the neural signals necessary for vision; retinoic acid, which is required to maintain normal differentiation of the cornea and conjunctival membranes, thus preventing xerophthalmia; and retinoic acid, which is required to regulate the expression of various genes that encode for structural proteins (e.g., skin keratins), enzymes (e.g., alcohol dehydrogenase), extracellular matrix proteins (e.g., laminin), and retinol binding proteins and receptors.

The term vitamin A also includes provitamin A carotenoids that are the dietary precursors of retinol. The term retinoids refers to retinol and its metabolites, and any synthetic analogues that have a similar structure to retinol. Of the more than 600 forms of carotenoids found in nature, several have provitamin A nutritional activity, but food composition data are available for only three ( $\alpha$ -carotene,  $\beta$ -carotene, and  $\beta$ -cryptoxanthin). The proposed functions of provitamin A carotenoids are described in Part III, "Carotenoids."

### Absorption, Metabolism, Storage, and Excretion

Preformed vitamin A (retinol) is absorbed in the small intestine. The efficiency of absorption of preformed vitamin A is generally high, ranging from 70 to 90 percent. Absorption is carrier-mediated and saturable, but becomes nonsaturable at high pharmacological doses. As the amount of ingested preformed vitamin A increases, its absorbability remains high.

Carotenoids are absorbed into the small intestine by passive diffusion. Efficiency of absorption has been estimated at 9–22 percent, although this decreases as the amount ingested increases. Some carotenoids ( $\beta$ -carotene,  $\alpha$ -carotene, and  $\beta$ -cryptoxanthin) are converted to vitamin A in the body.

Along with exogenous lipids, retinal esters (newly formed in the intestine) and nonhydrolyzed carotenoids are transported from the intestine to the liver in chylomicrons and chylomicron remnants. Retinoic acid, another form of vitamin A, is absorbed via the portal system bound to albumin. Liver, lung, adipose, and other tissues possess carotene enzyme activity, and so it is presumed that carotenes may be converted to vitamin A as they are delivered to tissues.

When vitamin A intake is adequate, more than 90 percent of total body vitamin A is located in the liver, which releases the nutrient into the circulation

in a process that depends on the availability of retinol binding protein (RBP). That which is not released remains stored in the liver. The majority of vitamin A metabolites are excreted in the urine; some vitamin A is also excreted in the bile. Amounts excreted via the bile increase as the liver vitamin A exceeds a critical concentration. This serves as a protective mechanism for reducing the risk of excess storage.

## DETERMINING DRIS

### Determining Requirements

The requirements for vitamin A are based on the assurance of adequate liver stores of vitamin A. Although a large body of observational epidemiological evidence suggests that higher blood concentrations of β-carotenes and other carotenoids obtained from foods are associated with a lower risk of several chronic diseases, there is currently insufficient evidence to support a recommendation that requires a certain percentage of dietary vitamin A to come from provitamin A carotenoids in meeting the vitamin A requirement. However, existing recommendations for the increased consumption of carotenoid-rich fruits and vegetables for their health-promoting benefits are strongly supported (see Part III, “Carotenoids”). For example, consuming the recommended 5 servings of fruits and vegetables per day could provide 5.2–6 mg/day of provitamin A carotenoids, which would constitute approximately 50–65 percent of the adult male RDA for vitamin A.

### Special Considerations

**Vegetarian diets:** Preformed vitamin A (retinol) is found only in animal-based foods. People who do not consume such foods must meet their requirements with foods that contain sufficient provitamin A carotenoids, such as deeply colored fruits and vegetables, or with fortified foods, such as margarine, some plant-based beverages, and cereals.

**Parasites and infection:** Malabsorption of vitamin A can occur with diarrhea and intestinal infections, such as those observed in developing countries. With infection and fever, the requirement for vitamin A may be greater than the requirements listed in this chapter, which are based on generally healthy individuals.

## Retinol Activity Equivalents (RAEs)

Based on data demonstrating that the efficiency of absorption of  $\beta$ -carotene is less than what has been traditionally thought, retinol activity equivalents (RAEs) were developed to address the new findings about reduced absorption of  $\beta$ -carotene. The requirements for vitamin A are now denoted in RAEs rather than retinol equivalents (REs). Using  $\mu\text{g}$  RAEs, the vitamin A activity of provitamin A carotenoids is half of the vitamin A activity that is assumed when using  $\mu\text{g}$  REs. This change in equivalency values is based on data demonstrating that the vitamin A activity of purified  $\beta$ -carotene in oil is half of the activity of vitamin A. It is also based on recent data demonstrating that the vitamin A activity of dietary  $\beta$ -carotene is one-sixth, rather than one-third, of the vitamin activity of purified  $\beta$ -carotene in oil. This change in bioconversion means that a larger amount of provitamin A carotenoids, and therefore darkly colored, carotene-rich fruits and vegetables, is needed to meet the vitamin A requirement. It also means that, in the past, vitamin A intake has been overestimated. The RAEs for dietary  $\beta$ -carotene,  $\alpha$ -carotene, and  $\beta$ -cryptoxanthin are 12, 24, and 24  $\mu\text{g}$ , respectively, compared to the corresponding REs of 6, 12, and 12  $\mu\text{g}$  reported by the National Research Council in 1989 (see Figure 1).

Nutrient databases will need to be revised to provide total vitamin A activity in  $\mu\text{g}$  RAE. In the meantime, it is possible to estimate total vitamin A activity in  $\mu\text{g}$  RAE from existing tables that list  $\mu\text{g}$  RE. For foods, such as liver, that

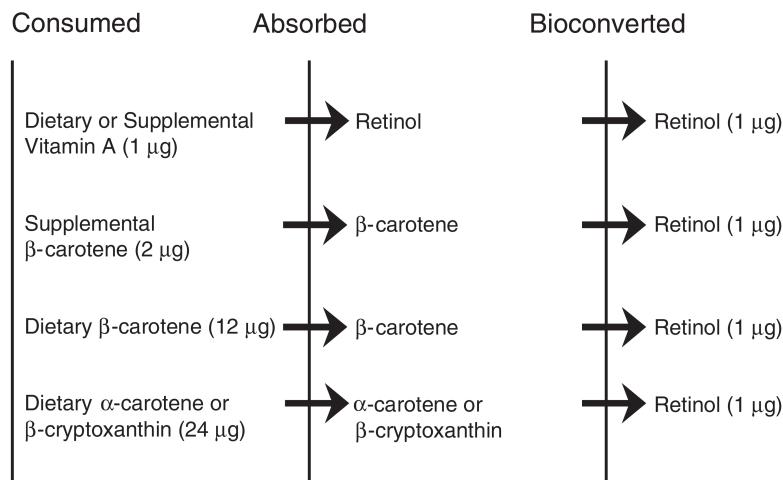


FIGURE 1 Absorption and bioconversion of ingested provitamin A carotenoids to retinol based on new equivalency factors (retinol equivalency ratio).

contain only vitamin A activity from preformed vitamin A (retinol), no adjustment is necessary. Vitamin A values for foods that contain only plant sources (provitamin A carotenoids) of vitamin A can be adjusted by dividing the µg RE by two. For foods that contain both plant and animal sources of vitamin A (e.g., a casserole containing meat and vegetables), the adjustment process is more complex. (See Appendix F for more information on determining the vitamin A content of foods.)

Supplemental β-carotene has a higher bioconversion to vitamin A than does dietary β-carotene. With low doses, the conversion is as high as 2:1; developers of composition information for dietary supplements should use this higher conversion factor. Little is known about the bioconversion of the forms of β-carotene that are added to foods, so fortification of forms of β-carotene should be assumed to have the same bioconversion as food forms, 12:1.

Food and supplement labels usually state vitamin A levels in International Units (IUs). One IU of retinol is equivalent to 0.3 µg of retinol, or 0.3 µg RAE. One IU of β-carotene in supplements is equivalent to 0.5 IU of retinol, or 0.15 µg RAE ( $0.3 \times 0.5$ ). One IU of dietary β-carotene is equivalent to 0.165 IU retinol, or 0.05 µg RAE ( $0.3 \times 0.165$ ). One IU of other dietary provitamin A carotenoids is equivalent to 0.025 µg RAE.

***Equivalency examples:***

- Example 1. A diet contains 500 µg retinol, 1,800 µg β-carotene and 2,400 µg β-carotene:  $500 + (1,800 \div 12) + (2,400 \div 24) = 750$  µg RAE
- Example 2. A diet contains 1,666 IU of retinol and 3,000 IU of β-carotene:  $(1,666 \times 0.3) + (3,000 \times 0.05) = 650$  µg RAE
- Example 3. A supplement contains 5,000 IU of vitamin A:  $5,000 \times 0.3 = 1,500$  µg RAE

For more information on vitamin A conversions, please see Appendix F.

## **Criteria for Determining Vitamin A Requirements, by Life Stage Group**

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Average vitamin A intake from human milk
7 through 12 mo	Extrapolation from 0 through 6 mo AI
1 through 18 y	Extrapolation from adult EAR
19 through > 70 y	Adequate liver vitamin A stores

<i>Pregnancy</i>	
≤18 y	Age-specific requirement + estimated daily accumulation by fetus
19 through 50 y	Age-specific requirement + estimated daily accumulation by fetus
<i>Lactation</i>	
≤18 y	Age-specific requirement + average amount of vitamin A secreted in human milk
19 through 50 y	Age-specific requirement + average amount of vitamin A secreted in human milk

## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Members of the general population should not routinely exceed the UL, which for vitamin A applies to the chronic intake of preformed vitamin A from foods, fortified foods, and some supplements. The UL for adults is based on liver abnormalities as the critical adverse effect; for women of childbearing age, the UL is based on teratogenicity as the critical adverse effect. High β-carotene intakes have not been shown to cause hypervitaminosis A.

Based on data from the Third National Health and Nutrition Examination Survey (NHANES III, 1994–1996), the highest median intake of preformed vitamin A for any gender and life stage group was 895 µg/day for lactating women. The highest reported intake at the 95th percentile was 1,503 µg/day for lactating women. For U.S. adults who took supplements containing vitamin A, intakes at the 95th percentile ranged from approximately 1,500 to 3,000 µg/day. Fewer than 5 percent of pregnant women had dietary and supplemental intake levels that exceeded the UL. The risk of exceeding the UL for vitamin A appears to be small based on the intakes cited above.

## Special Considerations

**Individuals susceptible to adverse effects:** People with high alcohol intake, pre-existing liver disease, hyperlipidemia, or severe protein malnutrition may be distinctly susceptible to the adverse effects of excess preformed vitamin A intake. These individuals may not be protected by the UL for vitamin A for the general population. The UL is not meant to apply to communities of malnourished individuals prophylactically receiving vitamin A, either periodically or through fortification, as a means to prevent vitamin A deficiency, or for individuals being treated with vitamin A for diseases such as retinitis pigmentosa.

## DIETARY SOURCES

### Foods

Preformed vitamin A (retinol) is found naturally in animal-based foods, whereas dietary carotenoids, which are converted to vitamin A in the body, are present in oils, fruits, and vegetables. Common dietary sources of preformed vitamin A in the United States and Canada include liver, dairy products, and fish. However, according to data from the Continuing Survey of Food Intakes by Individuals (CSFII, 1994–1996), in the United States the major contributors of vitamin A from foods were grains (fortified with vitamin A) and vegetables (which contain provitamin A carotenoids) at approximately 55 percent, followed by dairy and meat products at approximately 30 percent.

Foods fortified with vitamin A are margarine and low-fat and non-fat (skim and partly skimmed) milk. Major contributors as provitamin A carotenoids to dietary intake include:  $\beta$ -carotene found in carrots, broccoli, squash, peas, spinach, and cantaloupe; carrots as  $\alpha$ -carotene; and fruits as the sole contributors of  $\beta$ -cryptoxanthin.

### Dietary Supplements

According to NHANES III data, the median intake of vitamin A from supplements was approximately 1,430  $\mu\text{g}$  RAE/day for men and women. According to U.S. data from the 1986 National Health Interview Survey (NHIS), approximately 26 percent of adults in the United States took supplements that contained vitamin A.

### Bioavailability

Factors such as dietary fat intake, intestinal infections, the food matrix, and food processing can affect the absorption of vitamin A by the body. Dietary fat appears to enhance absorption, whereas absorption is diminished in individuals with diarrhea, intestinal infections, and infestations. The matrix of foods affects the ability of carotenoids to be released from food. For example, serum  $\beta$ -carotene concentration was significantly lower when individuals consumed  $\beta$ -carotene from carrots than from  $\beta$ -carotene supplements. Food processing affects the absorption of carotenoids. For example, absorption is greater from cooked compared to raw carrots and spinach.

### Dietary Interactions

There is evidence that vitamin A may interact with certain nutrients and dietary substances (see Table 2).

**TABLE 2 Potential Interactions with Other Dietary Substances**

<i>Substance</i>	<i>Potential Interaction</i>	<i>Notes</i>
<b>SUBSTANCES THAT AFFECT VITAMIN A</b>		
Dietary fat	Dietary fat may enhance the absorption of vitamin A and provitamin A carotenoids.	Research results in this area are mixed.
Iron	Iron deficiency may negatively affect vitamin A status.	It was reported that iron deficiency alters the distribution of vitamin A concentration between the plasma and liver.
Zinc	Zinc deficiency may negatively affect vitamin A status.	Zinc deficiency influences the mobilization of vitamin A from the liver and its transport into the circulation. However, human studies have not established a consistent relationship between zinc and vitamin A status. It has been suggested that zinc intake may positively affect vitamin A status only in individuals with moderate to severe protein-energy malnutrition.
Alcohol	Alcohol consumption may negatively affect vitamin A status.	Because both retinol and ethanol are alcohols, there is potential for overlap in the metabolic pathways of these two compounds. Ethanol consumption results in a depletion of liver vitamin A stores in humans. Although the effect on vitamin A is due, in part, to liver damage associated with chronic alcohol intake and to malnutrition, the reduction in liver stores of vitamin A is also a direct effect of alcohol consumption.
<b>VITAMIN A AFFECTING OTHER SUBSTANCES</b>		
Iron	Vitamin A deficiency may negatively affect iron status.	Studies suggest that vitamin A deficiency impairs iron mobilization from stores and that, therefore, vitamin A supplementation improves hemoglobin concentrations.

## INADEQUATE INTAKE AND DEFICIENCY

The most specific clinical effect of inadequate vitamin A intake is xerophthalmia, which is estimated to affect 3 million to 10 million children (mostly in developing countries) annually. Of those affected, 250,000 to 300,000 go blind every year. Xerophthalmia is an irreversible drying of the conjunctiva and cornea. Various stages of the disease include night blindness (impaired dark adaptation due to the slowed regeneration of rhodopsin), conjunctival xerosis, Bitot's spots, corneal xerosis, corneal ulceration, and scarring, all related to vitamin A deficiency. Night blindness is the first ocular symptom to be observed with vitamin A deficiency; however, it does respond rapidly to treatment with vitamin A.

Other adverse effects associated with vitamin A deficiency include decreased immune function and an increased risk of infectious morbidity and mortality, such as respiratory infection and diarrhea. Although vitamin A supplementation has been shown to reduce the severity of diarrhea, it has had little effect on the risk or severity of respiratory infections, except when associated with measles. The World Health Organization (WHO) recommends treating children who suffer from xerophthalmia, measles, prolonged diarrhea, wasting malnutrition, and other acute infections with vitamin A. Furthermore, the American Academy of Pediatrics recommends vitamin A supplementation for children in the United States who are hospitalized with measles.

## EXCESS INTAKE

Preformed vitamin A toxicity (hypervitaminosis A) due to high vitamin A intakes may be acute or chronic. (High β-carotene intake has not been shown to produce vitamin A toxicity.) Acute toxicity usually produces transient effects resulting from single or short-term large doses of retinol  $\geq 150,000 \mu\text{g}$  in adults and proportionately less in children and is characterized by the following:

- Nausea
- Vomiting
- Headache
- Increased cerebrospinal fluid pressure
- Vertigo
- Blurred vision
- Muscular incoordination
- Bulging fontanel (in infants)

Chronic toxicity is usually associated with the ingestion of large doses of retinol  $\geq 30,000 \mu\text{g}/\text{day}$  for months or years. Chronic toxicity generally produces less specific and more varied symptoms, such as birth defects, liver ab-

normalities, reduced bone mineral density, and disorders of the central nervous system. More research is needed to clarify whether chronic vitamin A intake may lead to loss in bone mineral density and a consequent increased risk of hip fracture in certain population groups, particularly among premenopausal and postmenopausal women.

Human and animal data show a strong causal association between excess vitamin A intake and liver abnormalities because the liver is the main storage site and target organ for vitamin A toxicity. These abnormalities range from reversibly elevated liver enzymes to widespread fibrosis, cirrhosis, and sometimes death.

## Special Considerations

**Teratogenicity:** Concern for the possible teratogenicity of high vitamin A intake in humans is based on the unequivocal demonstration of human teratogenicity following high-dose supplementation of vitamin A. The critical period for susceptibility appears to be during the first trimester of pregnancy. The primary birth defects associated with excess vitamin A intake are those derived from cranial neural crest cells, such as craniofacial malformations and abnormalities of the central nervous system (except neural tube defects), thymus, and heart. Most of the human data on teratogenicity of vitamin A involve doses  $\geq 7,800 \mu\text{g}/\text{day}$ .

**Adverse effects in infants and children:** There are several case reports of toxic effects of vitamin A in infants, toddlers, and children who have ingested excess vitamin A for a period of months to years. Of particular concern are intracranial (bulging fontanel) and skeletal abnormalities that can result in infants who are given vitamin A doses of 5,500–6,750  $\mu\text{g}/\text{day}$ . Other effects of toxicity in infants and children include bone tenderness and pain, increased intracranial pressure, desquamation, brittle nails, mouth fissures, alopecia, fever, headache, lethargy, irritability, weight loss, vomiting, and hepatomegaly.

## KEY POINTS FOR VITAMIN A

- ✓ Vitamin A is a fat-soluble vitamin that is important for normal vision, gene expression, reproduction, embryonic development, growth, and immune function.
- ✓ The requirements for vitamin A are now denoted in retinol activity equivalents (RAEs), such that 1 RAE = 1 µg all-*trans*-retinol, 12 µg β-carotene, and 24 µg α-carotene or β-cryptoxanthin.
- ✓ The requirements for vitamin A are based on the assurance of adequate liver stores of vitamin A. The UL is based on liver abnormalities as the critical endpoint; for women of childbearing age, the UL is based on teratogenicity as the critical adverse effect.
- ✓ People with high alcohol intake, preexisting liver disease, hyperlipidemia, or severe protein malnutrition may not be protected by the UL set for the general population.
- ✓ Food and supplement labels usually state vitamin A levels in International Units, or IUs. One IU of retinol is equivalent to 0.3 µg of retinol, or 0.3 µg RAE.
- ✓ There is currently insufficient evidence to support a recommendation that requires a certain percentage of dietary vitamin A to come from provitamin A carotenoids in meeting the vitamin A requirement. However, existing recommendations for the increased consumption of carotenoid-rich fruits and vegetables for their health-promoting benefits are strongly supported.
- ✓ Preformed Vitamin A (retinol) is found naturally only in animal-based foods.
- ✓ Good sources of provitamin A carotenoids are fruits and vegetables, including carrots, broccoli, squash, peas, spinach, and cantaloupe.
- ✓ The most specific clinical effect of inadequate vitamin A intake and deficiency is xerophthalmia, an irreversible drying of the conjunctiva and cornea.
- ✓ Vitamin A toxicity (hypervitaminosis A) may be acute or chronic. (High β-carotene intake has not been shown to produce vitamin A toxicity.) The adverse effects of excess vitamin A are from excessive intake of preformed vitamin A, or retinol.

**TABLE 1 Dietary Reference Intakes for Vitamin B<sub>6</sub> by Life Stage Group**

Life stage group	DRI values (mg/day)				
	EAR <sup>a</sup>		RDA <sup>b</sup>		AI <sup>c</sup>
	males	females	males	females	UL <sup>d</sup>
0 through 6 mo					0.1 ND <sup>e</sup>
7 through 12 mo					0.3 ND
1 through 3 y	0.4	0.4	0.5	0.5	30
4 through 8 y	0.5	0.5	0.6	0.6	40
9 through 13 y	0.8	0.8	1.0	1.0	60
14 through 18 y	1.1	1.0	1.3	1.2	80
19 through 30 y	1.1	1.1	1.3	1.3	100
31 through 50 y	1.1	1.1	1.3	1.3	100
51 through 70 y	1.4	1.3	1.7	1.5	100
> 70 y	1.4	1.3	1.7	1.5	100
<b>Pregnancy</b>					
≤ 18 y		1.6		1.9	80
19 through 50 y		1.6		1.9	100
<b>Lactation</b>					
≤ 18 y		1.7		2.0	80
19 through 50 y		1.7		2.0	100

<sup>a</sup> EAR = Estimated Average Requirement.<sup>b</sup> RDA = Recommended Dietary Allowance.<sup>c</sup> AI = Adequate Intake.<sup>d</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.<sup>e</sup> ND = Not determinable. This value is not determinable due to the lack of data of adverse effects in this age group and concern regarding the lack of ability to handle excess amounts. Source of intake should only be from food to prevent high levels of intake.

# VITAMIN B<sub>6</sub>

**V**itamin B<sub>6</sub> (pyridoxine and related compounds) functions as a coenzyme in the metabolism of amino acids, glycogen, and sphingoid bases. Vitamin B<sub>6</sub> comprises a group of six related compounds: pyridoxal (PL), pyridoxine (PN), pyridoxamine (PM), and their respective 5'-phosphates (PLP, PNP, and PMP). The major forms found in animal tissue are PLP and PMP; plant-derived foods primarily contain PN and PNP, sometimes in the form of a glucoside.

The primary criterion used to estimate the requirements for vitamin B<sub>6</sub> is a plasma pyridoxal 5'-phosphate value of at least 20 nmol/L. The Tolerable Upper Intake Level (UL) is based on sensory neuropathy as the critical adverse effect. DRI values are listed by life stage group in Table 1.

Rich food sources of vitamin B<sub>6</sub> include highly fortified cereals, beef liver and other organ meats, and highly fortified, soy-based meat substitutes. The clinical signs and symptoms of vitamin B<sub>6</sub> deficiency have only been observed during depletion with very low levels of the vitamin and have never been seen at intakes of 0.5 mg/day or more. No adverse effects have been associated with high intakes of the vitamin from food sources. Very large oral doses (2,000 mg/day or more on a chronic basis) of supplemental pyridoxine have been associated with the development of sensory neuropathy and dermatological lesions.

## VITAMIN B<sub>6</sub> AND THE BODY

### Function

Vitamin B<sub>6</sub> functions as a coenzyme in the metabolism of amino acids, glycogen, and sphingoid bases. Vitamin B<sub>6</sub> comprises a group of six related compounds: pyridoxal (PL), pyridoxine (PN), pyridoxamine (PM), and their respective 5'-phosphates (PLP, PNP, and PMP). The major forms found in animal tissue are PLP and PMP; plant-derived foods primarily contain PN and PNP, sometimes in the form of a glucoside.

### Absorption, Metabolism, Storage, and Excretion

Absorption of vitamin B<sub>6</sub> in the gut occurs via phosphatase-mediated hydrolysis followed by the transport of the nonphosphorylated form into the mucosal

cell. Transport occurs by nonsaturable passive diffusion. Even large doses of the nutrient are well absorbed.

Most of the absorbed nonphosphorylated vitamin B<sub>6</sub> goes to the liver, and certain forms of the vitamin (pyridoxal, pyridoxine, and pyridoxamine) are converted to their respective 5'-phosphates by pyridoxal kinase. Vitamin B<sub>6</sub> can be bound to proteins in tissues, which limits accumulation at very high intakes. When this capacity is exceeded, nonphosphorylated forms of vitamin B<sub>6</sub> are released by the liver and other tissues into the circulation. At pharmacological doses of vitamin B<sub>6</sub>, high amounts accumulate in the muscle, plasma, and erythrocytes when other tissues are saturated.

Most of the body's vitamin B<sub>6</sub> is found in the muscle; the muscle pool of the vitamin appears to very slowly turn over. Vitamin B<sub>6</sub> is oxidized in the liver and then released and primarily excreted in the urine.

## DETERMINING DRIS

### Determining Requirements

The primary criterion used to estimate the requirements for vitamin B<sub>6</sub> is a plasma 5'-pyridoxal phosphate value of at least 20 nmol/L.

### Criteria for Determining Vitamin B<sub>6</sub> Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Human milk content
7 through 12 mo	Mean of extrapolation from younger infants and from adults
1 through 18 y	Extrapolation from adults
19 through > 70 y	Plasma pyridoxal 5'-phosphate level

<i>Pregnancy</i>	
≤ 18 y through 50 y	Plasma pyridoxal 5'-phosphate level

<i>Lactation</i>	
≤ 18 y through 50 y	Amount of vitamin B <sub>6</sub> secreted in milk

### The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Members of the general population should not routinely consume more than the UL. For adults, the UL for Vitamin B<sub>6</sub> represents total intake from food,

water, and supplements and is based on sensory neuropathy as the critical adverse effect. The UL is not meant to apply to individuals who are receiving vitamin B<sub>6</sub> under medical supervision.

Based on data from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994), 9 mg/day was the highest mean intake of vitamin B<sub>6</sub> from food and supplements reported for any life stage and gender group. The highest reported intake at the 95th percentile was 21 mg/day in pregnant females aged 14 through 55 years, most of which was pyridoxine from supplements. The risk of adverse effects resulting from excess intake of vitamin B<sub>6</sub> from food and supplements appears to be very low at these intake levels.

## **DIETARY SOURCES**

### **Foods**

Data from the Continuing Survey of Food Intakes by Individuals (CSFII, 1994–1996) indicated that the greatest contribution to the vitamin B<sub>6</sub> intake of the U.S. adult population came from fortified, ready-to-eat cereals; mixed foods (including sandwiches) with meat, fish, or poultry as the main ingredient; white potatoes and other starchy vegetables; and noncitrus fruits. Especially rich sources of vitamin B<sub>6</sub> include highly fortified cereals; beef liver and other organ meats; and highly fortified, soy-based meat substitutes.

### **Dietary Supplements**

Approximately 26 percent of all adults reported taking a supplement containing vitamin B<sub>6</sub>, according to the 1986 National Health Interview Survey (NHIS) in the United States. For adults over age 60 years who took supplements and participated in the Boston Nutritional Status Survey (1981–1984), the median supplemental vitamin B<sub>6</sub> intake was 2.2 mg/day for both men and women.

### **Bioavailability**

The bioavailability of vitamin B<sub>6</sub> from a mixed diet is approximately 75 percent.

### **Dietary Interactions**

This information was not provided at the time the DRI values for this nutrient were set.

## INADEQUATE INTAKE AND DEFICIENCY

In controlled studies, clinical signs and symptoms of vitamin B<sub>6</sub> deficiency have only been observed during depletion with very low levels of the vitamin and have never been seen at intakes of 0.5 mg/day or more. The signs and symptoms of vitamin B<sub>6</sub> deficiency include the following:

- Seborrheic dermatitis
- Microcytic anemia (from decreased hemoglobin synthesis)
- Epileptiform convulsions
- Depression and confusion

## Special Considerations

**Medications:** Drugs that can react with carbonyl groups have the potential to interact with a form of vitamin B<sub>6</sub>. For example, isoniazid, which is used in the treatment of tuberculosis, and L-DOPA, which is metabolized to dopamine, have been reported to reduce plasma concentrations of vitamin B<sub>6</sub>.

**Oral contraceptives:** Studies have shown decreased vitamin B<sub>6</sub> status in women who receive high-dose oral contraceptives. Plasma concentrations of the nutrient are lowered, but the decrease is quite small. (It should be noted that these studies were conducted when the level of estrogen in oral contraceptives was three to five times higher than current levels.)

**Alcohol:** Chronic alcoholics tend to have low vitamin B<sub>6</sub> status, which is distinct from deficiency caused by liver disease or by poor diet. The extent to which this causes an increased vitamin B<sub>6</sub> requirement is not known.

**Preeclampsia:** Lowered vitamin B<sub>6</sub> status is observed in preeclampsia and eclampsia, suggesting a potentially increased requirement for the vitamin in preeclampsia.

## EXCESS INTAKE

No adverse effects have been associated with high intakes of vitamin B<sub>6</sub> from food sources. Very large oral doses (2,000 mg/day or more) of supplemental pyridoxine, which are used to treat many conditions, including carpal tunnel syndrome, painful neuropathies, seizures, premenstrual syndrome, asthma, and sickle cell disease, have been associated with the development of sensory neuropathy and dermatological lesions.

## KEY POINTS FOR VITAMIN B<sub>6</sub>

- ✓ Vitamin B<sub>6</sub> (pyridoxine and related compounds) functions as a coenzyme in the metabolism of amino acids, glycogen, and sphingoid bases.
- ✓ The requirements for vitamin B<sub>6</sub> are based on a plasma pyridoxal 5'-phosphate value of at least 20 nmol/L. The UL is based on sensory neuropathy as the critical adverse effect.
- ✓ Rich food sources of vitamin B<sub>6</sub> include highly fortified cereals, beef liver and other organ meats, and highly fortified, soy-based meat substitutes. Other contributors to vitamin B<sub>6</sub> intake include mixed foods with meat, fish, or poultry as the main ingredient; white potatoes and other starchy vegetables; and noncitrus fruits.
- ✓ Clinical signs and symptoms of vitamin B<sub>6</sub> deficiency have only been observed during depletion with very low levels of the vitamin and have never been seen at intakes of 0.5 mg/day or more.
- ✓ The signs and symptoms of vitamin B<sub>6</sub> deficiency are seborrheic dermatitis, microcytic anemia, epileptiform convulsions, and depression and confusion.
- ✓ No adverse effects have been associated with high intakes of vitamin B<sub>6</sub> from food sources.
- ✓ Very large oral doses (2,000 mg/day or more) of supplemental pyridoxine have been associated with the development of sensory neuropathy and dermatological lesions.

**TABLE 1 Dietary Reference Intakes for Vitamin B<sub>12</sub> by Life Stage Group**

Life stage group	DRI values (μg/day)			
	EAR <sup>a</sup>		RDA <sup>b</sup>	
	males	females	males	females
0 through 6 mo				0.4
7 through 12 mo				0.5
1 through 3 y	0.7	0.7	0.9	0.9
4 through 8 y	1.0	1.0	1.2	1.2
9 through 13 y	1.5	1.5	1.8	1.8
14 through 18 y	2.0	2.0	2.4	2.4
19 through 30 y	2.0	2.0	2.4	2.4
31 through 50 y	2.0	2.0	2.4	2.4
51 through 70 y	2.0	2.0	2.4 <sup>e</sup>	2.4 <sup>e</sup>
> 70 y	2.0	2.0	2.4 <sup>e</sup>	2.4 <sup>e</sup>
<b>Pregnancy</b>				
≤ 18 y		2.2		2.6
19 through 50 y		2.2		2.6
<b>Lactation</b>				
≤ 18 y		2.4		2.8
19 through 50 y		2.4		2.8

<sup>a</sup> EAR = Estimated Average Requirement.<sup>b</sup> RDA = Recommended Dietary Allowance.<sup>c</sup> AI = Adequate Intake.<sup>d</sup> UL = Tolerable Upper Intake Level. Data were insufficient to set a UL. In the absence of a UL, extra caution may be warranted in consuming levels above the recommended intake.<sup>e</sup> Because 10 to 30 percent of older people may malabsorb food-bound vitamin B<sub>12</sub>, for adults over 50 years old it is advisable for most of this amount to be obtained by consuming foods fortified with vitamin B<sub>12</sub> or a vitamin B<sub>12</sub>-containing supplement.

# VITAMIN B<sub>12</sub>

**V**itamin B<sub>12</sub> (cobalamin) functions as a coenzyme for a critical reaction that converts homocysteine to methionine and in the metabolism of fatty acids of odd chain length. An adequate supply of vitamin B<sub>12</sub> is essential for normal blood formation and neurological function.

The requirements for vitamin B<sub>12</sub> are based on the amount needed to maintain hematological status and normal serum vitamin B<sub>12</sub> values. An assumed absorption of 50 percent is included in determining the Estimated Average Requirement (EAR). Data were insufficient to set a Tolerable Upper Intake Level (UL). DRI values are listed by life stage group in Table 1.

Because 10–30 percent of older people may be unable to absorb naturally occurring vitamin B<sub>12</sub>, most likely due to atrophic gastritis, it is advisable for those older than 50 years to meet their needs mainly by consuming foods fortified with vitamin B<sub>12</sub> or by taking a supplement that contains it. Individuals with vitamin B<sub>12</sub> deficiency caused by a lack of intrinsic factor require medical treatment.

Naturally occurring vitamin B<sub>12</sub> is found primarily in foods of animal origin. Many plant-based foods are fortified with the vitamin. The major cause of vitamin B<sub>12</sub> deficiency is pernicious anemia, a condition in which the stomach does not produce intrinsic factor. The hematological effects that occur with this deficiency are identical to those that accompany folate deficiency. No adverse effects have been associated with excess vitamin B<sub>12</sub> intake from food or supplements in healthy individuals. The apparent low toxicity of the vitamin may be because, when high doses are given orally, only a small percentage of it can be absorbed from the gastrointestinal tract.

## VITAMIN B<sub>12</sub> AND THE BODY

### Function

Vitamin B<sub>12</sub> (cobalamin) functions as a coenzyme for a critical reaction that converts homocysteine to methionine and for a separate reaction in the metabolism of fatty acids and amino acids. An adequate supply of vitamin B<sub>12</sub> is essential for normal blood formation and neurological function. Although the preferred scientific use of the term vitamin B<sub>12</sub> is usually restricted to cyanocobalamin, in this publication vitamin B<sub>12</sub> refers to all potentially biologically active cobalamins.

## Absorption, Metabolism, Storage, and Excretion

Small amounts of vitamin B<sub>12</sub> are absorbed by an active process that requires an intact stomach, intrinsic factor (a glycoprotein that the parietal cells of the stomach secrete after being stimulated by food), pancreatic sufficiency, and a normally functioning terminal ileum. Vitamin B<sub>12</sub> is processed in the stomach and the small intestine before being released into the circulation. The liver takes up approximately 50 percent of circulating nutrient; the remainder is transported to other tissues.

There is a lack of data on the absorption of vitamin B<sub>12</sub> from many foods. Therefore, for this publication, a conservative adjustment for the bioavailability of naturally occurring vitamin B<sub>12</sub> was used. In particular, it is assumed that 50 percent of dietary vitamin B<sub>12</sub> is absorbed by healthy adults with normal gastric function.

If there is a lack of intrinsic factor (as in the case of pernicious anemia), malabsorption of the vitamin results. If untreated, this may lead to potentially irreversible neurological damage and possibly life-threatening anemia. Malabsorption also results from atrophic gastritis with low stomach acid secretion, a condition estimated to occur in 10–30 percent of people older than 50 years.

Vitamin B<sub>12</sub> is continually secreted in the bile. In healthy individuals, most of it is reabsorbed and available for metabolic functions. However, in the absence of intrinsic factor, essentially all the vitamin B<sub>12</sub> from the bile is excreted in the stool rather than recirculated. Thus, deficiency develops more rapidly in individuals who have no intrinsic factor or who malabsorb vitamin B<sub>12</sub> for other reasons than it does in those who do not ingest it (such as those with complete vegetarian diets). The excretion of vitamin B<sub>12</sub> is proportional to body stores; it is excreted mainly in the stool but also in the urine and through the skin.

## DETERMINING DRIS

### Determining Requirements

The requirements for vitamin B<sub>12</sub> are based on the amount needed to maintain hematological status and normal serum vitamin B<sub>12</sub> values. An assumed absorption of 50 percent is included in determining the EAR.

### Special Considerations

**Aging and atrophic gastritis:** Vitamin B<sub>12</sub> status tends to decline with age, perhaps due to a decrease in gastric acidity and the presence of atrophic gastritis and of bacterial overgrowth accompanied by malabsorption of food-bound vitamin B<sub>12</sub>. It is estimated that approximately 10–30 percent of elderly people

have atrophic gastritis, although the condition may often go undiagnosed. Thus, it is advisable for those older than 50 years to meet their needs mainly by consuming foods fortified with vitamin B<sub>12</sub> or by taking a supplement that contains it.

**Infants of vegan mothers:** Infants of vegan mothers should be supplemented with vitamin B<sub>12</sub> at the level of the AI from birth because their stores at that time are low and their mothers' milk may supply very small amounts of the vitamin.

**Individuals with increased needs:** A person with any malabsorption syndrome will likely require increased amounts of vitamin B<sub>12</sub>. Patients with pernicious anemia or Crohn's disease involving the terminal ileum and patients who have had a gastrectomy, gastric bypass surgery, or ileal resection will require the nutrient under a physician's direction. People who are HIV-positive with chronic diarrhea may also require either increased oral or parenteral vitamin B<sub>12</sub>. Patients with atrophic gastritis, pancreatic insufficiency, or prolonged omeprazole treatment will have decreased bioavailability of food-bound vitamin B<sub>12</sub> and will require normal amounts of crystalline vitamin B<sub>12</sub> (either in fortified foods or in a supplement).

## Criteria for Determining Vitamin B<sub>12</sub> Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Human milk content
7 through 12 mo	Extrapolation from younger infants
1 through 18 y	Extrapolation from adults
19 through > 70 y	Amount needed to maintain hematological status and normal serum vitamin B <sub>12</sub> values

### *Pregnancy*

≤ 18 y through 50 y	Age-specific requirement + fetal deposition of the vitamin B <sub>12</sub>
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### *Lactation*

≤ 18 y through 50 y	Age-specific requirement + amount of vitamin B <sub>12</sub> secreted in human milk
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## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Due to inadequate data on adverse effects of excess vitamin B<sub>12</sub> consumption, a UL for the vitamin could not be determined.

Based on data from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994), the highest median intake of B<sub>12</sub> from diet and supplements for any life stage and gender group was 17 µg/day; the highest reported intake at the 95th percentile was 37 µg/day. Furthermore, there appear to be no risks associated with intakes from supplemental B<sub>12</sub> that are more than two orders of magnitude higher than the 95th percentile intake. However, this does not mean that there is no potential for adverse effects to occur with high intakes.

## DIETARY SOURCES

### Foods

Vitamin B<sub>12</sub> is naturally found in foods of animal origin. It is also found in plant-based foods that have been fortified, such as ready-to-eat cereals and meal replacement formulas. Particularly rich sources of natural vitamin B<sub>12</sub> such as shellfish, organ meats such as liver, some game meats (such as venison and rabbit), and some fish (such as herring, sardines, and trout) are not a regular part of many people's diets. According to the Continuing Survey of Food Intakes by Individuals (CSFII, 1994–1996), the greatest contributors to vitamin B<sub>12</sub> intake in U.S. adults were mixed foods (including sandwiches) with meat, fish, or poultry as the main ingredient. For women, the second highest contributor to intake was milk and milk beverages; for men it was beef. Fortified ready-to-eat cereals contributed a greater proportion of dietary vitamin B<sub>12</sub> for women than for men.

Although milk is a good source of vitamin B<sub>12</sub>, cooking it may greatly reduce its vitamin content. For example, boiling milk for 10 minutes reduces vitamin B<sub>12</sub> content by about 50 percent.

### Dietary Supplements

In the United States, cyanocobalamin is the only commercially available vitamin B<sub>12</sub> preparation used in supplements and pharmaceuticals. It is also the principal form used in Canada. Approximately 26 percent of all adults reported taking a supplement that contained vitamin B<sub>12</sub>, according to the 1986 National Health Interview Survey (NHIS). For adults over age 60 years who took supplements and participated in the Boston Nutritional Status Survey, median supplemental vitamin B<sub>12</sub> intakes were 5.0 µg/day for men and 6.0 µg/day for women.

## Bioavailability

Data on the bioavailability of vitamin B<sub>12</sub> are few. Studies have found the absorption of the nutrient in healthy adults to be 65 percent from mutton, 11 percent from liver, 24–36 percent from eggs, 60 percent from chicken, and 25–47 percent from trout. Because of a lack of data on dairy foods and most forms of red meat and fish, a conservative adjustment for the bioavailability of naturally occurring vitamin B<sub>12</sub> was used for this publication. In particular, it is assumed that 50 percent of dietary vitamin B<sub>12</sub> is absorbed by healthy adults with normal gastric function.

## Dietary Interactions

There is evidence that vitamin B<sub>12</sub> may interact with certain nutrients (see Table 2).

**TABLE 2 Potential Interactions with Other Nutrients**

Substance	Potential Interaction	Notes
<b>NUTRIENTS THAT AFFECT VITAMIN B<sub>12</sub></b>		
Folate	Adequate or high folate intake may mitigate the effects of a vitamin B <sub>12</sub> deficiency on normal blood formation.	There is no evidence that folate intake or status changes the requirement for vitamin B <sub>12</sub> .

## INADEQUATE INTAKE AND DEFICIENCY

The clinical effects of vitamin B<sub>12</sub> deficiency are hematological, neurological, and gastrointestinal:

- *Hematological effects:* The major cause of vitamin B<sub>12</sub> deficiency is pernicious anemia, a condition in which the gastric mucosa of the stomach does not produce intrinsic factor. The hematological effects of vitamin B<sub>12</sub> deficiency include weakness, fatigue, shortness of breath, and palpitations. These effects are identical to those observed in folate deficiency. As in folate deficiency, the underlying mechanism of anemia is an interference with normal deoxyribonucleic acid (DNA) synthesis. This results in megaloblastic change, which causes the production of larger-than-normal erythrocytes (macrocytosis). By the time anemia is established, there is usually also some degree of neutropenia and thrombocytopenia because the megaloblastic process affects all rapidly divid-

ing bone-marrow elements. The hematological complications are completely reversed by treatment with vitamin B<sub>12</sub>.

- *Neurological effects:* Neurological complications are present in 75–90 percent of individuals with clinically observable vitamin B<sub>12</sub> deficiency and may, in about 25 percent of cases, be the only clinical manifestation of deficiency. Evidence is mounting that the occurrence of neurological complications is inversely correlated with the degree of anemia; that is, patients who are less anemic show more prominent neurological complications, and vice versa. Neurological manifestations include tingling and numbness in the extremities (worse in the lower limbs), gait disturbances, and cognitive changes such as loss of concentration, memory loss, disorientation, and dementia, with or without mood changes. Visual disturbances, insomnia, impotency, and impaired bowel and bladder control.
- *Gastrointestinal effects:* Vitamin B<sub>12</sub> deficiency is also frequently associated with various gastrointestinal complaints, including sore tongue, loss of appetite, flatulence, and constipation. Some of these gastrointestinal effects may be related to the underlying gastric disorder in pernicious anemia.

## EXCESS INTAKE

No adverse effects have been associated with excess vitamin B<sub>12</sub> intake from food or supplements in healthy individuals. The apparent low toxicity of the vitamin may be because, when high doses are orally given, only a small percentage of it can be absorbed from the gastrointestinal tract. Although there are extensive data showing no adverse effects associated with high intakes of supplemental vitamin B<sub>12</sub>, the studies in which such intakes were reported were not designed to assess adverse effects.

## KEY POINTS FOR VITAMIN B<sub>12</sub>

- ✓ Vitamin B<sub>12</sub> (cobalamin) functions as a coenzyme for a reaction that converts homocysteine to methionine and for a separate reaction in the metabolism of certain fatty acids and amino acids.
- ✓ Although the preferred scientific use of the term vitamin B<sub>12</sub> is usually restricted to cyanocobalamin, in this publication vitamin B<sub>12</sub> refers to all potentially biologically active cobalamins.
- ✓ The requirements for vitamin B<sub>12</sub> are based on the amount needed to maintain hematological status and normal serum vitamin B<sub>12</sub> values.
- ✓ Data were insufficient to set a UL.
- ✓ Because 10–30 percent of older people may be unable to absorb naturally occurring vitamin B<sub>12</sub>, it is advisable for those older than 50 years to meet their needs mainly by consuming foods fortified with vitamin B<sub>12</sub> or by taking a supplement that contains vitamin B<sub>12</sub>.
- ✓ A person with any malabsorption syndrome will likely require increased amounts of vitamin B<sub>12</sub>.
- ✓ Individuals with vitamin B<sub>12</sub> deficiency caused by a lack of intrinsic factor require medical treatment.
- ✓ Vitamin B<sub>12</sub> is naturally found in foods of animal origin. It is also found in plant-based foods that have been fortified, such as ready-to-eat cereals and meal replacement formulas. Although milk is a good source, cooking it may greatly reduce its vitamin B<sub>12</sub> content.
- ✓ The major cause of vitamin B<sub>12</sub> deficiency is pernicious anemia, a condition in which the gastric mucosa of the stomach does not produce intrinsic factor. The hematological effects that occur with this deficiency are identical to those observed in folate deficiency.
- ✓ No adverse effects have been associated with excess vitamin B<sub>12</sub> intake from food or supplements in healthy individuals. The apparent low toxicity of the vitamin may be because, when high doses are orally given, only a small percentage of it can be absorbed from the gastrointestinal tract.

**TABLE 1 Dietary Reference Intakes for Biotin by Life Stage Group**

<b>Life stage group<sup>c</sup></b>	DRI values (μg/day)	
	AI <sup>a</sup>	UL <sup>b</sup>
<b>0 through 6 mo</b>	5	
<b>7 through 12 mo</b>	6	
<b>1 through 3 y</b>	8	
<b>4 through 8 y</b>	12	
<b>9 through 13 y</b>	20	
<b>14 through 18 y</b>	25	
<b>19 through 30 y</b>	30	
<b>31 through 50 y</b>	30	
<b>51 through 70 y</b>	30	
<b>&gt; 70 y</b>	30	
<b>Pregnancy</b>		
<b>≤ 18 y</b>	30	
<b>19 through 50 y</b>	30	
<b>Lactation</b>		
<b>≤ 18 y</b>	35	
<b>19 through 50 y</b>	35	

<sup>a</sup> AI = Adequate Intake.<sup>b</sup> UL = Tolerable Upper Intake Level. Data were insufficient to set a UL. In the absence of a UL, extra caution may be warranted in consuming levels above the recommended intake.<sup>c</sup> All groups except Pregnancy and Lactation represent males and females.

# BIOTIN

**B**iotin functions as a coenzyme in bicarbonate-dependent carboxylation reactions. It exists both as free biotin and in protein-bound forms in foods. Little is known about how protein-bound biotin is digested.

Since data were insufficient to set an Estimated Average Requirement (EAR) and thus calculate a Recommended Dietary Allowance (RDA) for biotin, an Adequate Intake (AI) was instead developed. The AIs for biotin are based on data extrapolation from the amount of biotin in human milk. Data were insufficient to set a Tolerable Upper Intake Level (UL). DRI values are listed by life stage group in Table 1.

The biotin content of foods is generally not documented. It is widely distributed in natural foods, but its concentration varies. Signs of biotin deficiency have been conclusively demonstrated in individuals consuming raw egg whites over long periods and in patients receiving total parenteral nutrition (TPN) solutions that do not contain biotin. No adverse effects have been documented for biotin at any intake tested.

## BIOTIN AND THE BODY

### Function

Biotin functions as a coenzyme in bicarbonate-dependent carboxylation reactions.

### Absorption, Metabolism, Storage, and Excretion

Biotin exists both as free biotin and in protein-bound forms in foods. Little is known about how protein-bound biotin is digested. It appears to be absorbed in both the small intestine and the colon. The mechanism of biotin transport to the liver and other tissues after absorption has not been well established. Avi-din, a protein found in raw egg white, has been shown to bind to biotin in the small intestine and prevent its absorption. The mechanism of biotin transport to the liver and other tissues after absorption has not been well established. Biotin is excreted in the urine.

## DETERMINING DRIS

### Determining Requirements

Since data were insufficient to establish an EAR and thus calculate an RDA, an AI was instead developed. The AIs for biotin are based on extrapolation from the amount of biotin in human milk. Most major nutrition surveys do not report biotin intake.

### Special Considerations

*Individuals with increased needs:* People who receive hemodialysis or peritoneal dialysis may have an increased requirement for biotin, as do those with genetic biotinidase deficiency.

### Criteria for Determining Biotin Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Human milk content
7 through 12 mo	Extrapolation from infants
1 through > 70 y	Extrapolation from infants
<i>Pregnancy</i>	
≤ 18 through 50 y	Extrapolation from infants
<i>Lactation</i>	
≤ 18 through 50 y	To cover the amount of biotin secreted in milk, the AI is increased by 5 µg/day

### The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Due to insufficient data on the adverse effects of excess biotin consumption, a UL for biotin could not be determined.

## DIETARY SOURCES

### Foods

Biotin content has been documented for relatively few foods, and so it is generally not included in food composition tables. Thus, intake tends to be underes-

timated in diets. Although biotin is widely distributed in natural foods, its concentration significantly varies. For example, liver contains biotin at about 100 µg/100 g, whereas fruits and most meats contain only about 1 µg/100 g.

## **Dietary Supplements**

According to the 1986 National Health Interview Survey (NHIS), approximately 17 percent of U.S. adults reported taking a supplement that contained biotin. Specific data on intake from supplements were not available.

## **Bioavailability**

This information was not provided at the time the DRI values for this nutrient were set.

## **Dietary Interactions**

This information was not provided at the time the DRI values for this nutrient were set.

## **INADEQUATE INTAKE AND DEFICIENCY**

Signs of biotin deficiency have been conclusively demonstrated in individuals consuming raw egg whites over long periods and in patients receiving total parenteral nutrition (TPN) solutions that do not contain biotin. The effects of biotin deficiency include the following:

- Dermatitis (often appearing as a red scaly rash around the eyes, nose, and mouth)
- Conjunctivitis
- Alopecia
- Central nervous system abnormalities, such as depression, lethargy, hallucinations, and paresthesia of the extremities

Symptoms of deficiency in infants on biotin-free TPN appear much earlier after the initiation of the TPN regimen than in adults. In biotin-deficient infants, hypotonia, lethargy, and developmental delays, along with a peculiar withdrawn behavior, are all characteristic of a neurological disorder resulting from a lack of biotin.

## **EXCESS INTAKE**

There have been no reported adverse effects of biotin in humans or animals. Toxicity has not been reported in patients given daily doses of biotin up to 200 mg orally and up to 20 mg intravenously to treat biotin-responsive inborn errors of metabolism and acquired biotin deficiency.

## KEY POINTS FOR BIOTIN

- ✓ Biotin functions as a coenzyme in bicarbonate-dependent carboxylation reactions.
- ✓ Since data were insufficient to establish an EAR and thus calculate an RDA, an AI was instead developed.
- ✓ The AIs for biotin are based on extrapolation from the amount of biotin in human milk.
- ✓ People who receive hemodialysis or peritoneal dialysis may have an increased requirement for biotin, as may those with genetic biotinidase deficiency.
- ✓ Data were insufficient to set a UL.
- ✓ The biotin content of foods is generally not documented. It is widely distributed in natural foods, but its concentration varies.
- ✓ Signs of biotin deficiency have been conclusively demonstrated in individuals consuming raw egg whites over long periods and in patients receiving total parenteral nutrition (TPN) solutions that do not contain biotin.
- ✓ The effects of biotin deficiency include dermatitis, alopecia, conjunctivitis, and abnormalities of the central nervous system.
- ✓ No adverse effects have been associated with high intakes of biotin.

**TABLE 1 Dietary Reference Intakes for Vitamin C by Life Stage Group**

Life stage group	DRI values (mg/day)				
	EAR <sup>a</sup>		RDA <sup>b</sup>		AI <sup>c</sup>
	males	females	males	females	UL <sup>d</sup>
0 through 6 mo					40
7 through 12 mo					50
1 through 3 y	13	13	15	15	400
4 through 8 y	22	22	25	25	650
9 through 13 y	39	39	45	45	1,200
14 through 18 y	63	56	75	65	1,800
19 through 30 y	75	60	90	75	2,000
31 through 50 y	75	60	90	75	2,000
51 through 70 y	75	60	90	75	2,000
≥ 70 y	75	60	90	75	2,000
<b>Pregnancy</b>					
≤ 18 y		66		80	1,800
19 through 50 y		70		85	2,000
<b>Lactation</b>					
≤ 18 y		96		115	1,800
19 through 50 y		100		120	2,000

<sup>a</sup> EAR = Estimated Average Requirement.<sup>b</sup> RDA = Recommended Dietary Allowance.<sup>c</sup> AI = Adequate Intake.<sup>d</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.

<sup>e</sup> ND = Not determinable. This value is not determinable due to the lack of data of adverse effects in this age group and concern regarding the lack of ability to handle excess amounts. Source of intake should only be from food to prevent high levels of intake.

# VITAMIN C

**V**itamin C (ascorbic acid) is a water-soluble nutrient that acts as an antioxidant and a cofactor in enzymatic and hormonal processes. It also plays a role in the biosynthesis of carnitine, neurotransmitters, collagen, and other components of connective tissue, and modulates the absorption, transport, and storage of iron.

The adult requirements for vitamin C are based on estimates of body pool or tissue vitamin C levels that are deemed adequate to provide antioxidant protection. Smokers have an increased requirement. The adverse effects upon which the Tolerable Upper Intake Level (UL) is based are osmotic diarrhea and gastrointestinal disturbances. DRI values are listed by life stage group in Table 1. Foods rich in vitamin C include fruits and vegetables, including citrus fruits, tomatoes, potatoes, strawberries, spinach, and cruciferous vegetables. Vitamin C deficiency is by and large not a problem in the United States and Canada, and the risk of adverse effects of excess intake appears to be very low at the highest usual Vitamin C intakes.

## **VITAMIN C AND THE BODY**

### **Function**

Vitamin C (ascorbic acid) is a water-soluble nutrient that acts as an antioxidant by virtue of its high reducing power. It has a number of functions: as a scavenger of free radicals; as a cofactor for several enzymes involved in the biosynthesis of carnitine, collagen, neurotransmitters, and in vitro processes; and as a reducing agent. Evidence for in vivo antioxidant functions of ascorbate include the scavenging of reactive oxidants in activated leukocytes, lung, and gastric mucosa, and diminished lipid peroxidation as measured by urinary isoprostane excretion.

### **Absorption, Metabolism, Storage, and Excretion**

Vitamin C is absorbed in the intestine via a sodium-dependent active transport process that is saturable and dose-dependent. As intake increases, absorption decreases. At low intestinal concentrations of vitamin C, active transport is the primary mode of absorption. When intestinal concentrations of vitamin C are high, passive diffusion becomes the main form of absorption.

Besides dose-dependent absorption, body vitamin C content is also regulated by the kidneys, which conserve or excrete unmetabolized vitamin C. Renal excretion of vitamin C increases proportionately with higher intakes of the vitamin. These processes allow the body to conserve vitamin C during periods of low intake and to limit plasma levels of vitamin C at high intakes.

The amount of vitamin C stored in different body tissues widely varies. High levels are found in the pituitary and adrenal glands, leukocytes, eye tissues and humors, and the brain, while low levels are found in plasma and saliva. A total body pool of less than 300 mg is associated with symptoms of scurvy, a disease of severe vitamin C deficiency; maximum body pools (in adults) are limited to about 2,000 mg.

With high intakes, unabsorbed vitamin C degrades in the intestine, which may account for the diarrhea and gastrointestinal upset sometimes reported by people taking large doses. At very low ascorbate intakes, essentially no ascorbate is excreted unchanged and a minimal loss occurs.

## DETERMINING DRIS

### Determining Requirements

The requirements for vitamin C are based on estimates of body pool or tissue vitamin C levels that are deemed adequate to provide antioxidant protection with minimal urinary loss. Although some studies have reported a possible protective effect of vitamin C against diseases such as cardiovascular disease, cancer, lung disease, cataracts, and even the common cold, others have failed to do so. Additionally, the majority of evidence accumulated thus far has been largely observational and epidemiological and thus does not prove cause and effect.

### Special Considerations

**Gender:** Women tend to have higher blood levels of vitamin C than men of the same age, even when intake levels are the same, making the requirements for women lower than for men. The difference in vitamin C requirements of men and women is assumed based on mean differences in body size, total body water, and lean body mass.

**Age:** No consistent differences in the absorption or metabolism of vitamin C due to aging have been demonstrated at median vitamin C intakes. This suggests that reports of low blood concentrations of vitamin C in elderly populations may be due to poor dietary intakes, chronic disease or debilitation, or other factors, rather than solely an effect of aging. Therefore, the requirements of older adults do not differ from those of younger adults.

**Smoking:** Studies have shown that smokers have decreased plasma and leukocyte levels of vitamin C compared to nonsmokers, even after adjusting for vitamin C intake from foods. Metabolic turnover of the vitamins has been shown to be about 35 mg/day greater in smokers. This means that smokers need 35 mg/day more to maintain the same body pool as nonsmokers. The mechanism by which smoking compromises vitamin C status has not been well established.

**Exposure to environmental tobacco smoke:** Increased oxidative stress and vitamin C turnover have been observed in nonsmokers who are regularly exposed to tobacco smoke. Although the available data were insufficient to estimate a special requirement, these nonsmokers are urged to ensure that they meet the RDA for vitamin C.

**Certain pregnant subpopulations:** Pregnant women who smoke, abuse drugs or alcohol, or regularly take aspirin may have increased requirements for vitamin C.

**Individuals susceptible to adverse effects:** People with hemochromatosis, glucose-6-phosphate dehydrogenase deficiency, and renal disorders may be particularly susceptible to the adverse effects of excess vitamin C intake and therefore should be cautious about ingesting vitamin C at levels greater than the RDA. Vitamin C may enhance iron absorption and exacerbate iron-induced tissue damage in individuals with hemochromatosis, while those with renal disorders may have increased risk of oxalate kidney stone formation from excess vitamin C intake.

### Criteria for Determining Vitamin C Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Human milk content
7 through 12 mo	Human milk + solid food
1 through 18 y	Extrapolation from adult
19 through 30 y	Near-maximal neutrophil concentration
31 through > 70 y	Extrapolation of near-maximal neutrophil concentration from 19 through 30 y

#### *Pregnancy*

≤ 18 y through 50 y	Age-specific requirement + transfer to the fetus
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#### *Lactation*

≤ 18 y through 50 y	Age-specific requirement + vitamin C secreted in human milk
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## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Members of the general population should not routinely exceed the UL, which for vitamin C applies to intake from both food and supplements. Osmotic diarrhea and gastrointestinal disturbances are the critical endpoints upon which the UL for vitamin C is based.

Based on data from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994), the highest mean intake of vitamin C from diet and supplements for any gender and lifestage group was estimated to be about 200 mg/day (for males aged 51 through 70 years and females aged 51 years and older). The highest reported intake at the 99th percentile was greater than 1,200 mg/day in males aged 31 through 70 years and in females aged 51 through 70 years. The risk of adverse effects resulting from excess intake of vitamin C from food and supplements appears to be very low.

## DIETARY SOURCES

### Foods

Almost 90 percent of vitamin C found in the typical diet comes from fruits and vegetables, with citrus fruits and juices, tomatoes and tomato juice, and potatoes being major contributors. Other sources include brussels sprouts, cauliflower, broccoli, strawberries, cabbage, and spinach. Some foods are also fortified with vitamin C. The vitamin C content of foods can vary depending on growing conditions and location, the season of the year, the stage of maturity, cooking practices, and the storage time prior to consumption.

### Dietary Supplements

Data from the Boston Nutritional Status Survey (1981–1984) estimated that 35 percent of men and 44 percent of women took some form of vitamin C supplements; of them, 19 percent of men and 15 percent of women had intakes greater than 1,000 mg/day.

### Bioavailability

There does not appear to be much variability in the bioavailability of vitamin C between different foods and dietary supplements. Approximately 70–90 percent of usual dietary intakes of vitamin C (30–180 mg/day) is absorbed by the body. However, absorption falls to 50 percent or less as intake increases to doses of 1,000 mg/day or more.

**TABLE 2 Potential Interactions with Other Dietary Substances**

<i>Substance</i>	<i>Potential Interaction</i>	<i>Notes</i>
<b>VITAMIN C AFFECTING OTHER SUBSTANCES</b>		
Iron	Vitamin C may enhance the absorption of nonheme iron.	Vitamin C added to meals facilitates the intestinal absorption of nonheme iron, possibly due to lowering of gastrointestinal iron to the more absorbable ferrous state or to countering the effect of substances that inhibit iron absorption. However, studies in which the vitamin was added to meals over long periods have not shown significant improvement of body iron status, indicating that ascorbic acid has a lesser effect on iron bioavailability than has been predicted from tests involving single meals.
Copper	Vitamin C may reduce copper absorption.	Excess vitamin C may reduce copper absorption, but the significance of this potential effect in humans is questionable because the data have been mixed.
Vitamin B <sub>12</sub>	Large doses of vitamin C may reduce vitamin B <sub>12</sub> levels.	Low serum B <sub>12</sub> values reported in people receiving megadoses of vitamin C are likely to be artifacts of the effect of vitamin C on the radiotope assay for B <sub>12</sub> , and thus not a true nutrient–nutrient interaction.

## Dietary Interactions

There is evidence that vitamin C may interact with certain nutrients and dietary substances (see Table 2).

## INADEQUATE INTAKE AND DEFICIENCY

Severe vitamin C deficiency is rare in industrialized countries, but it is occasionally seen in people whose diets lack fruits and vegetables or in those who abuse alcohol or drugs. In the United States, low blood levels of vitamin C are more common in men, particularly elderly men, than in women, and in populations of lower socioeconomic status.

The classic disease of severe vitamin C deficiency is scurvy, which is characterized by the symptoms related to connective tissue defects. Scurvy usually occurs at a plasma concentration of less than 11 µmol/L (0.2 mg/dL). The signs and symptoms of scurvy include the following:

- Follicular hyperkeratosis
- Petechiae

- Ecchymoses
- Coiled hairs
- Inflamed and bleeding gums
- Perifollicular hemorrhages
- Joint effusions
- Arthralgia
- Impaired wound healing

Other signs and symptoms include dyspnea, edema, Sjögren's syndrome (dry eyes and mouth), weakness, fatigue, and depression. In experimental subjects who were made vitamin C deficient but not frankly scorbutic, gingival inflammation and fatigue were among the most sensitive markers of deficiency.

Vitamin C deficiency in infants, known as infantile scurvy, may result in bone abnormalities, hemorrhagic symptoms, and anemia. Infantile scurvy is rarely seen because human milk provides an adequate supply of vitamin C and infant formulas are fortified with the vitamin.

## EXCESS INTAKE

Adverse effects from vitamin C intake have been associated primarily with large doses ( $> 3,000$  mg/day) and may include diarrhea and other gastrointestinal disturbances. There is no evidence suggesting that vitamin C is carcinogenic or teratogenic or that it causes adverse reproductive effects.

## Special Considerations

**Blood and urine tests:** Vitamin C intakes of 250 mg/day or higher have been associated with false-negative results for detecting stool and gastric occult blood. Therefore, high-dose vitamin C supplements should be discontinued at least 2 weeks before physical exams to avoid interference with blood and urine tests.

## KEY POINTS FOR VITAMIN C

- ✓ Vitamin C (ascorbic acid) is a water-soluble nutrient that acts as an antioxidant and a cofactor in enzymatic and hormonal processes. It also plays a role in the biosynthesis of carnitine, neurotransmitters, collagen, and other components of connective tissue, and modulates the absorption, transport, and storage of iron.
- ✓ Vitamin C requirements for adults are based on estimates of body pool or tissue vitamin C levels that are deemed adequate to provide antioxidant protection. The adverse effects upon which the UL is based are osmotic diarrhea and gastrointestinal disturbances.
- ✓ Although some studies have reported a possible protective effect of vitamin C against diseases such as cardiovascular disease, cancer, lung disease, cataracts, and even the common cold, others have failed to do so.
- ✓ Because smokers suffer increased oxidative stress and metabolic turnover of vitamin C, the requirements are raised by 35 mg/day.
- ✓ Increased oxidative stress and vitamin C turnover have been observed in nonsmokers who are regularly exposed to tobacco smoke, and thus nonsmokers are urged to ensure that they meet the RDA for vitamin C.
- ✓ The risk of adverse effects resulting from excess vitamin C intake appears to be very low.
- ✓ Almost 90 percent of vitamin C found in the typical diet comes from fruits and vegetables, with citrus fruits and juices, tomatoes and tomato juice, and potatoes being major contributors. Other sources include brussels sprouts, cauliflower, broccoli, strawberries, cabbage, and spinach.
- ✓ Low blood concentrations of vitamin C in elderly populations may be due to poor dietary intakes, chronic disease or debilitation, or other factors, rather than solely an effect of aging.
- ✓ The classic disease of severe vitamin C deficiency is scurvy, the signs and symptoms of which include follicular hyperkeratosis, petechiae, ecchymoses, coiled hairs, inflamed and bleeding gums, perifollicular hemorrhages, joint effusions, arthralgia, and impaired wound healing.

- ✓ Severe vitamin C deficiency is rare in industrialized countries, but it is occasionally seen in people whose diets lack fruits and vegetables or in those who abuse alcohol or drugs.
- ✓ Adverse effects have been associated primarily with large doses ( $> 3,000$  mg/day) and may include diarrhea and other gastrointestinal disturbances.

## CAROTENOIDS

**C**arotenoids are natural pigments found in plants, and are abundant in deeply colored fruits and vegetables. The most prevalent carotenoids in North American diets are  $\alpha$ -carotene,  $\beta$ -carotene, lycopene, lutein, zeaxanthin, and  $\beta$ -cryptoxanthin. Of these,  $\alpha$ -carotene,  $\beta$ -carotene, and  $\beta$ -cryptoxanthin can be converted into retinol (vitamin A) in the body and are called provitamin A carotenoids. Lycopene, lutein, and zeaxanthin have no vitamin A activity and are called nonprovitamin A carotenoids. The only known function of carotenoids in humans is to act as a source of vitamin A in the diet (provitamin A carotenoids only).

There are no DRIs specifically for carotenoids (see Part III, “Vitamin A” for vitamin A DRIs and the contribution of carotenoids to vitamin A intake). Although epidemiological evidence suggests that higher blood concentrations of  $\beta$ -carotene and other carotenoids obtained from foods are associated with a lower risk of several chronic diseases, other evidence suggests possible harm arising from very large doses in population subgroups, such as smokers and asbestos workers. Currently, there is insufficient evidence to recommend that a certain percentage of dietary vitamin A should come from provitamin A carotenoids. However, existing recommendations calling for the increased consumption of carotenoid-rich fruits and vegetables for their health-promoting benefits are strongly supported.

Based on evidence that  $\beta$ -carotene supplements have not been shown to aid in the prevention or cure of major chronic diseases, and may cause harm in certain population subgroups,  $\beta$ -carotene supplements are not advisable other than as a provitamin A source and for the prevention and control of vitamin A deficiency in at-risk populations.

Foods rich in carotenoids include deep yellow-, red-, and orange-colored fruits and vegetables and green leafy vegetables. Carotenoids found in ripe fruits and cooked yellow tubers are more efficiently converted into vitamin A than are carotenoids from equal amounts of dark green, leafy vegetables. If adequate retinol (vitamin A) is provided in the diet, there are no known clinical effects of consuming diets low in carotenes over the short term; carotenodermia or lycopenodermia (skin discoloration) are the only proven adverse effects associated with excess consumption of carotenoids.

## CAROTENOIDS AND THE BODY

### Function

In plants, carotenoids function as pigments. In humans, the only known function of carotenoids is their provitamin A activity. Carotenoids may have additional functions, such as enhancing immune function and decreasing the risk of macular degeneration, cataracts, some cardiovascular events, and some types of cancer (particularly lung, oral cavity, pharyngeal, and cervical cancers), but the evidence is inconclusive. The risks for some diseases appear to be increased in certain population subgroups when large doses of β-carotene are taken.

### Absorption, Metabolism, Storage, and Excretion

Dietary carotenoids are fat-soluble and are absorbed in the intestine via bile acid micelles. The uptake of β-carotene by intestinal mucosal cells is believed to occur by passive diffusion. Once inside the mucosal cells, carotenoids or their metabolic products (e.g., vitamin A) are incorporated into chylomicrons and released into the lymphatic system. Carotenoids are either absorbed intact or, in the case of provitamin A carotenoids, cleaved to form vitamin A prior to secretion into the lymph.

Carotenoids are transported in the blood by lipoproteins and stored in various body tissues, including the adipose tissue, liver, kidneys, and adrenal glands. (The adipose tissue and liver appear to be the main storage sites.) Excretion occurs via the bile and urine.

## DETERMINING DRIS

### Determining Requirements

Data were inadequate to estimate the requirements for β-carotene and other carotenoids. Although epidemiological evidence suggests that higher blood concentrations of β-carotene and other carotenoids obtained from foods are associated with a lower risk of several chronic diseases, this evidence could not be used to establish a requirement for β-carotene or other carotenoid intake because the observed effects may be due to other substances found in carotenoid-rich food, or other behavioral correlates of increased fruit and vegetable consumption. Other evidence suggests possible harm arising from very large doses in population subgroups, such as smokers and asbestos workers.

Currently, there is insufficient evidence to recommend that a certain percentage of dietary vitamin A should come from provitamin A carotenoids. Although no DRI values are proposed for carotenoids, existing recommendations calling for the increased consumption of carotenoid-rich fruits and vegetables

for their health-promoting benefits are strongly supported. The existing recommendation to consume 5 or more servings of fruits and vegetables per day would provide 3–6 mg/day of β-carotene.

(For vitamin A DRIIs, the contribution of carotenoids to vitamin A intake, and conversion factors of the various carotenoids to retinol activity equivalents [RAEs], see Part III, “Vitamin A,” and Appendix F.)

## The UL

There were insufficient data available on the potential adverse effects of excess carotenoid intake to derive a Tolerable Upper Intake Level (UL). However, in light of research indicating an association between high-dose β-carotene supplements and lung cancer in smokers (see “Excess Intake”), β-carotene supplements are not advisable for the general population. No adverse effects other than carotenodermia (skin discoloration) have been reported from the consumption of carotenoids in food.

## DIETARY SOURCES

### Foods

Foods rich in carotenoids include deep yellow-, red-, and orange-colored fruits and vegetables and green leafy vegetables. Major contributors of β-carotene to the diets of U.S. women of childbearing age include carrots (the major contributor), cantaloupe, broccoli, vegetable-beef or chicken soup, spinach, and collard greens. Major contributors of α-carotene, β-cryptoxanthin, lycopene, and lutein and zeaxanthin, respectively, are carrots, orange juice and orange juice blends, tomatoes and tomato products, and spinach and collard greens.

Carotenoids are not added to most infant formulas (milk- or soy-based), and the carotenoid content of human milk highly varies depending on the carotenoid content of the mother’s diet.

### Dietary Supplements

β-Carotene, α-carotene, β-cryptoxanthin, lutein and zeaxanthin, and lycopene are available as dietary supplements. However, there are no reliable estimates of the amount being consumed by people in the United States or Canada.

### Bioavailability

The extent of conversion of a highly bioavailable source of dietary β-carotene to vitamin A in humans has been shown to be between 60 and 75 percent, with an

additional 15 percent of the  $\beta$ -carotene absorbed intact. However, absorption of most carotenoids from foods is considerably lower and can be as low as 2 percent. Several other factors affect the bioavailability and absorption of carotenoids, including:

**Food matrix:** The food matrix in which ingested carotenoids are found affects bioavailability the most. For example, the absorption of  $\beta$ -carotene supplements that are solubilized with emulsifiers and protected by antioxidants can be 70 percent or more; absorption from fruits exceeds tubers, and the absorption from raw carrots can be as low as 5 percent.

**Cooking techniques:** Cooking appears to improve the bioavailability of some carotenoids. For example, the bioavailability of lycopene from tomatoes is vastly improved when tomatoes are cooked with oil. Steaming also improves carotenoid bioavailability in carrots and spinach. However, prolonged exposure to high temperatures, through boiling, for example, may reduce the bioavailability of carotenoids from vegetables.

**Dietary fat:** Studies have shown that to optimize carotenoid absorption, dietary fat must be consumed during the same meal as the carotenoid.

**Other factors:** Lipid-lowering drugs, olestra, plant sterol-enriched margarines, and dietary pectin supplements have all been shown to reduce carotenoid absorption.

## Dietary Interactions

Different carotenoids may compete with each other for absorption. This is more likely to occur in people who take supplements of a particular carotenoid than in people who consume a variety of carotenoid rich fruits and vegetables. For example,  $\beta$ -carotene supplements reduce lutein absorption from food; and when carotene and lutein are given as supplements,  $\beta$ -carotene absorption increases.

## INADEQUATE INTAKE AND DEFICIENCY

If adequate retinol (vitamin A) is provided in the diet, there are no known clinical effects of consuming diets low in carotenes over the short term.

## Special Considerations

**Smoking:** Smokers tend to have lower plasma concentrations of carotenoids compared to nonsmokers. It is unknown whether this is attributable solely to

poor intake or if tobacco smoke somehow reduces the circulating levels of carotenoids. The greater the intensity of smoking (the number of cigarettes per day), the greater the decrease in serum carotenoid concentrations. Although smoking may result in a need for higher intakes of dietary carotenoids to achieve optimal plasma concentrations, caution is warranted because studies have shown an increased risk of lung cancer in smokers who took  $\beta$ -carotene supplements (see “Excess Intake”). Recommendations made to smokers to increase carotenoid intake should emphasize foods, not supplements, as the source.

**Alcohol consumption:** As with tobacco, alcohol intake is inversely associated with serum carotenoid concentrations. Those who chronically consume large quantities of alcohol are often deficient in many nutrients, but it is unknown whether the deficiency is the result of poor diet or of the metabolic consequences of chronic alcoholism or the synergistic effect of both.

## EXCESS INTAKE

Harmless skin discoloration in the form of carotenodermia (yellow discoloration) or lycopenodermia (orange discoloration) is the only proven adverse effect associated with the excess consumption of carotenoids from food and supplements. This condition has been reported in adults who took supplements containing 30 mg/day or more of  $\beta$ -carotene for long periods of time or who consumed high levels of carotenoid-rich foods, such as carrots. Skin discoloration is also the primary effect of excess carotenoid intake noted in infants, toddlers, and young children. The condition is reversible when carotene ingestion is discontinued.

## Special Considerations

**Increased risk of lung cancer in smokers:** In the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Trial, an increase in lung cancer was associated with supplemental  $\beta$ -carotene in doses of 20 mg/day or greater (for 5 to 8 years) in current smokers. Another multicenter lung cancer prevention trial, the Carotene and Retinol Efficacy Trial (CARET), which involved smokers and asbestos-exposed workers, reported more lung cancer cases in a group supplemented with a nutrient combination that contained both  $\beta$ -carotene and retinol than in a group that received placebos. In contrast, the Physicians’ Health Study, conducted in the United States, reported no significant effect of 12 years of supplementation with  $\beta$ -carotene (50 mg every other day) on cancer or total mortality, even among smokers who took the supplements for up to 12 years.

Supplemental forms of  $\beta$ -carotene have markedly greater bioavailability than  $\beta$ -carotene from foods, and the concentrations associated with possible adverse

effects are well beyond the concentrations achieved through foods. So, although 20 mg/day of supplemental β-carotene is enough to raise blood concentrations to a range associated with increased lung cancer risk, the same amount of β-carotene in foods is not.

***Individuals with increased needs:*** Supplemental β-carotene can be used as a provitamin A source or for the prevention of vitamin A deficiency in populations with inadequate vitamin A nutriture. Long-term supplementation with β-carotene in people with adequate vitamin A status does not increase the concentration of serum retinol. For vitamin A-deficient individuals and for people suffering from erythropoietic protoporphyrina (a photosensitivity disorder), treatment using higher doses may be called for, but only under a physician's direction.

## KEY POINTS FOR CAROTENOIDS

- ✓ Carotenoids are natural pigments found in plants, and are abundant in deeply colored fruits and vegetables. Certain carotenoids function as a source of vitamin A in humans.
- ✓ There are no DRIs specifically for carotenoids.
- ✓ Currently, there is insufficient evidence to recommend that a certain percentage of dietary vitamin A should come from provitamin A carotenoids.
- ✓ Carotenoids may enhance immune function and decrease the risk of macular degeneration, cataracts, some vascular events, and some types of cancer. But carotenoids have also been linked to an increased incidence of cancer in certain population subgroups, such as smokers and asbestos workers.
- ✓ Foods rich in carotenoids include deep yellow-, red-, and orange-colored fruits and vegetables and green leafy vegetables. Carotenoids found in ripe fruits and cooked yellow tubers are more efficiently converted into vitamin A than are carotenoids from equal amounts of dark green, leafy vegetables.
- ✓ Several factors influence the bioavailability and absorption of carotenoids, including the food matrix, cooking techniques, the presence of dietary fat, and lipid-lowering drugs and dietary constituents.
- ✓ If adequate retinol (vitamin A) is provided in the diet, there are no known clinical effects of consuming diets low in carotenes over the short term.
- ✓ Harmless skin discoloration can result from excess consumption of carotenoids from food or supplements.
- ✓ Based on evidence that β-carotene supplements have not been shown to aid in the prevention of major chronic diseases, and may cause harm in certain population subgroups, β-carotene supplements are not advisable other than as a provitamin A source and for the prevention and control of vitamin A deficiency in at-risk populations.

**TABLE 1 Dietary Reference Intakes for Choline by Life Stage Group**

Life stage group	DRI values (mg/day)		
	AI <sup>a,b</sup>		UL <sup>c</sup>
	males	females	
0 through 6 mo	125	125	ND <sup>d</sup>
7 through 12 mo	150	150	ND
1 through 3 y	200	200	1,000
4 through 8 y	250	250	1,000
9 through 13 y	375	375	2,000
14 through 18 y	550	400	3,000
19 through 30 y	550	425	3,500
31 through 50 y	550	425	3,500
51 through 70 y	550	425	3,500
> 70 y	550	425	3,500
<b>Pregnancy</b>			
≤ 18 y		450	3,000
19 through 50 y		450	3,500
<b>Lactation</b>			
≤ 18 y		550	3,000
19 through 50 y		550	3,500

<sup>a</sup> AI = Adequate Intake.<sup>b</sup> Although AIs have been set for choline, there are few data to assess whether a dietary supply of choline is needed at all stages of the life cycle. It may be that the choline requirement can be met by endogenous synthesis at some of these stages.<sup>c</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.<sup>d</sup> ND = Not determinable. This value is not determinable due to the lack of data of adverse effects in this age group and concern regarding the lack of ability to handle excess amounts. Source of intake should only be from food to prevent high levels of intake.

# CHOLINE

**C**holine is required for the structural integrity of cell membranes. It is also involved in methyl metabolism, cholinergic neurotransmission, transmembrane signaling, and lipid and cholesterol transport and metabolism. Choline in the diet is available as free choline or is bound as esters such as phosphocholine, glycerophosphocholine, sphingomyelin, or phosphatidylcholine.

Since data were insufficient to set an Estimated Average Requirement (EAR) and thus calculate a Recommended Dietary Allowance (RDA) for choline, an Adequate Intake (AI) was instead developed. The AIs for choline are based on the intake required to maintain liver function, as assessed by measuring serum alanine aminotransferase levels. The Tolerable Upper Intake Level (UL) is based on hypotension as the critical effect, with fishy body odor as the secondary consideration.

Although AIs have been set for choline, there are few data to assess whether a dietary supply of choline is needed at all stages of the life cycle. It may be that the choline requirement can be met by endogenous synthesis at some of these stages. DRI values are listed by life stage group in Table 1.

Foods rich in choline include milk, liver, eggs, and peanuts. Lecithin, a food additive used as an emulsifying agent, also adds choline to the diet. Although choline is clearly essential to life, few data exist on the effects of inadequate dietary intake in healthy people. The signs and symptoms associated with excess choline intake are fishy body odor, sweating, vomiting, salivation, hypotension, gastrointestinal effects, and liver toxicity.

## CHOLINE AND THE BODY

### Function

Choline is required for the structural integrity of cell membranes. It is also involved in methyl metabolism, cholinergic neurotransmission, transmembrane signaling, and lipid and cholesterol transport and metabolism. For example, choline accelerates the synthesis and release of acetylcholine, an important neurotransmitter involved in memory and muscle control. It is also a precursor for the synthesis of phospholipids, including phosphatidylcholine (a membrane constituent important for the structure and function of membranes), for intracellular signaling and hepatic export of very low density lipoproteins. Lecithin, a substance commonly added to foods as an emulsifying agent, is

rich in phosphatidylcholine. The term lecithin is often interchangeably used with phosphatidylcholine.

## Absorption, Metabolism, Storage, and Excretion

Dietary choline is absorbed in the small intestine. Before it can be absorbed from the gut, some is metabolized by bacteria to form betaine, which may be absorbed and used as a methyl donor, and methylamines, which are not methyl donors.

Choline is found in foods as free choline and as esterified forms such as phosphocholine, glycerophosphocholine, sphingomyelin, and phosphatidylcholine. Pancreatic enzymes can liberate choline from some of the latter to form free choline. Free choline enters the portal circulation of the liver, whereas phosphatidylcholine may enter the lymph in chylomicrons. All tissues, including the brain, liver, and kidneys, accumulate choline by diffusion and mediated transport. Some choline is excreted in the urine unchanged but most is oxidized in the kidneys to form betaine.

## DETERMINING DRIS

### Determining Requirements

Since data were not sufficient for deriving an EAR, and thus calculating an RDA, an Adequate Intake (AI) was instead developed. The AIs for choline are based on the prevention of liver damage, as assessed by measuring serum alanine aminotransferase levels. The estimate is uncertain because it is based on a single published study and may need revision when data are available. This amount is influenced by the availability of methionine and folate in the diet (see “Dietary Interactions”). It may also be influenced by gender, pregnancy, lactation, and stage of development. Although AIs are set for choline, it may be that the requirement can be met by endogenous synthesis at some of these life stages.

Most major nutrition surveys in the United States and Canada do not report choline intake. The choline content of foods is also not included in major nutrient databases.

### Criteria for Determining Choline Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Human milk content
7 through 12 mo	Extrapolation from infants or from adults
1 through 3 y	Extrapolation from adults
4 through >70 y	Serum alanine aminotransferase levels

*Pregnancy*

≤ 18 y through 50 y      Age-specific + fetal and placental accumulation of choline

*Lactation*

≤ 18 y through 50 y      Age-specific + choline secreted in human milk

**The UL**

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Members of the general population should not routinely consume more than the UL. The UL for choline represents total intake from food, water, and supplements. Hypotension was selected as the critical effect in deriving a UL for choline, with fishy body odor selected as the secondary consideration.

Because there is no information from national surveys on choline intakes or on supplement usage, the risk of adverse effects within the United States or Canada cannot be characterized.

**Special Considerations**

**Individuals susceptible to adverse effects:** People with fish odor syndrome (trimethylaminuria), renal disease, liver disease, depression, and Parkinson's disease may have an increased susceptibility to the adverse effects of choline intakes at the UL.

**DIETARY SOURCES****Foods**

Most choline in foods is in the form of phosphatidylcholine in membranes. Foods that are especially rich in choline include milk, liver, eggs, and peanuts. It is possible for usual dietary intakes to provide as much as 1,000 mg/day of choline. Lecithin added during food processing may increase the average daily per capita consumption of phosphatidylcholine by 1.5 mg/kg of body weight for adults.

**Dietary Supplements**

Choline is available as a dietary supplement as choline chloride or choline bitartrate and as lecithin, which usually contains approximately 25 percent phosphatidylcholine or 3–4 percent choline by weight. There are no reliable estimates of the frequency of use or the amount of these supplements consumed by individuals in the United States and Canada.

## Bioavailability

This information was not provided at the time the DRI values for this nutrient were set.

## Dietary Interactions

Choline, methionine, and folate metabolism interact at the point that homocysteine is converted into methionine. Disturbing the metabolism of one of these methyl donors can affect the metabolism of the others.

## INADEQUATE INTAKE AND DEFICIENCY

Although choline is clearly essential to life, few data exist on the effects of inadequate dietary intake in healthy people. Based on one study examining the effects of artificially induced choline deficiency in healthy men who consumed an otherwise adequate diet, liver damage occurred, resulting in elevated levels of alanine aminotransferase in the blood. Fatty infiltration of the liver has also been shown to occur in individuals fed with total parenteral nutrition (TPN) solutions devoid of choline.

## EXCESS INTAKE

Choline doses that are in orders of magnitude greater than estimated intake from food have been associated with fishy body odor (trimethylaminuria), sweating, salivation, hypotension, and hepatotoxicity in humans. There are no indications in the literature that excess choline intake produces any additional adverse effects in humans. Fishy body odor results from the excretion of excessive amounts of trimethylamine, a choline metabolite, as the result of bacterial action. Lecithin does not present a risk of fishy body odor.

## KEY POINTS FOR CHOLINE

- ✓ Choline is required for the structural integrity of cell membranes. It is also involved in methyl metabolism, cholinergic neurotransmission, transmembrane signaling, and lipid and cholesterol transport and metabolism.
- ✓ Since data were insufficient to set an EAR and thus calculate an RDA for choline, an AI was instead developed.
- ✓ The AIs for choline are based on the prevention of liver damage, as assessed by measuring serum alanine aminotransferase levels.
- ✓ Although AIs have been set for choline, there are few data to assess whether a dietary supply of choline is needed at all stages of the life cycle. It may be that the requirement can be met by endogenous synthesis at some of these stages.
- ✓ The UL is based on hypotension as the critical effect, with fishy body odor as the secondary consideration.
- ✓ People with fish odor syndrome (trimethylaminuria), renal disease, liver disease, depression, and Parkinson's disease may have an increased susceptibility to the adverse effects of choline intakes at the UL.
- ✓ Foods rich in choline include milk, liver, eggs, and peanuts. Lecithin, a food additive used as an emulsifying agent, also adds choline to the diet.
- ✓ Although choline is clearly essential to life, few data exist on the effects of inadequate dietary intake in healthy people. Based on one study examining the effects of induced inadequate dietary intake in healthy men who consumed an otherwise adequate diet, liver damage occurred.
- ✓ Choline doses that are in orders of magnitude greater than estimated intake from food have been associated with fishy body odor (trimethylaminuria), sweating, salivation, hypotension, and hepatotoxicity in humans. There are no indications in the literature that excess choline intake produces any additional adverse effects in humans.

**TABLE 1 Dietary Reference Intakes for Vitamin D by Life Stage Group**

Life stage group <sup>e</sup>	DRI values (μg/day)	
	AI <sup>a,b,c</sup>	UL <sup>d</sup>
0 through 6 mo	5	25
7 through 12 mo	5	25
1 through 3 y	5	50
4 through 8 y	5	50
9 through 13 y	5	50
14 through 18 y	5	50
19 through 30 y	5	50
31 through 50 y	5	50
51 through 70 y	10	50
> 70 y	15	50
<b>Pregnancy</b>		
≤ 18 y	5	50
19 through 50 y	5	50
<b>Lactation</b>		
≤ 18 y	5	50
19 through 50 y	5	50

<sup>a</sup> AI = Adequate Intake.<sup>b</sup> As cholecalciferol. 1 μg cholecalciferol = 40 IU vitamin D.<sup>c</sup> In the absence of adequate exposure to sunlight.<sup>d</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.<sup>e</sup> All groups except Pregnancy and Lactation represent males and females.

# VITAMIN D

**V**itamin D (calciferol) is involved in bone health and is naturally found in very few foods. Synthesized in the skin through exposure to ultraviolet B rays in sunlight, its major biological function is to aid in the absorption of calcium and phosphorus, thereby helping maintain normal serum levels of these minerals. Vitamin D also functions as an antiproliferation and prodifferentiation hormone, but the exact role it plays is not yet known.

The AIs for vitamin D are based on serum 25-hydroxyvitamin D [25(OH)D], which is the form that represents vitamin D storage. The Tolerable Upper Intake Level (UL) was derived using studies of the effect of vitamin D intake on serum calcium concentrations (to prevent hypercalcemia) in humans. Since data were inadequate to determine an Estimated Average Requirement (EAR) and thus calculate a Recommended Dietary Allowance (RDA) for vitamin D, an Adequate Intake (AI) was instead developed. DRI values are listed by life stage group in Table 1.

Foods naturally rich in vitamin D include the flesh of fatty fish, some fish-liver oils, and eggs from hens fed vitamin D. Fortified milk products and breakfast cereals are also good sources of vitamin D. Vitamin D deficiency can impair normal bone metabolism, which may lead to rickets in children or osteomalacia (undermineralized bone) or osteoporosis (porous bones) in adults. In contrast, excess vitamin D intake can cause high blood calcium, high urinary calcium, and the calcification of soft tissues, such as blood vessels and certain organs.

## VITAMIN D AND THE BODY

### Function

The primary function of vitamin D in the body is to aid in the intestinal absorption of calcium and phosphorus, thereby helping maintain normal serum levels of these minerals in the body. Other roles in cellular metabolism involve antiproliferation and prodifferentiation actions.

Vitamin D is fat-soluble and occurs in many forms, but the two dietary forms are vitamin D<sub>2</sub> (ergocalciferol) and vitamin D<sub>3</sub> (cholecalciferol). Vitamin D<sub>2</sub> originates from the yeast and plant sterol, ergosterol; vitamin D<sub>3</sub> originates from 7-dehydrocholesterol, a precursor of cholesterol, when synthesized in the skin. Vitamin D<sub>2</sub> and vitamin D<sub>3</sub> are similarly metabolized. Vitamin D without a

subscript represents either vitamins D<sub>2</sub> or D<sub>3</sub>, or both, and is biologically inert. The biologically active hormone form of vitamin D is 1,25-dihydroxyvitamin D [1,25(OH)<sub>2</sub>D].

### Absorption, Metabolism, Storage, and Excretion

Vitamin D is either synthesized in the skin through exposure to ultraviolet B rays in sunlight or ingested as dietary vitamin D. After absorption of dietary fat-soluble vitamin D in the small intestine, it is incorporated into the chylomicron fraction and absorbed through the lymphatic system.

Whether from the skin or from the lymphatic system, vitamin D accumulates in the liver, where it is hydroxylated to 25-hydroxyvitamin D [25(OH)D] and then enters the circulation. The circulating 25(OH)D concentration is a good indicator of vitamin D status. In order to have biological activity at physiological concentrations, 25(OH)D must be hydroxylated to 1,25(OH)<sub>2</sub>D. This conversion occurs in the kidneys and is tightly regulated by parathyroid hormone in response to serum calcium and phosphorus levels. Vitamin D is absorbed in the small intestine and is principally excreted in the bile after metabolites are inactivated. A variety of vitamin D metabolites are excreted by the kidney into the urine.

## DETERMINING DRIS

### Determining Requirements

Because sufficient data were not available to establish an EAR and thus calculate an RDA, an AI was instead developed. The AIs for vitamin D are based on serum 25(OH)D concentrations; they assume that no vitamin D is available from sun-mediated cutaneous synthesis. The AI is the intake value that appears to be needed to maintain (in a defined group of healthy individuals with limited but uncertain sun exposure and stores) serum 25-hydroxyvitamin D concentrations above a defined amount. The latter is that concentration below which vitamin D deficiency rickets or osteomalacia occurs. When consumed by an individual, the AI is sufficient to minimize the risk of low serum 25(OH)D.

Because human milk contains very little vitamin D, breast-fed infants who are not exposed to sunlight are unlikely to obtain adequate amounts of vitamin D from mother's milk to satisfy their needs beyond early infancy. Therefore, the AI for infants aged 0 through 12 months does not assume vitamin D synthesis from sunlight exposure and is based on the lowest dietary intake associated with adequate serum 25(OH)D concentrations.

Accurate estimates of vitamin D intakes in the United States are lacking, in part because the vitamin D composition of fortified foods highly varies and also because many surveys do not include estimates of vitamin D intake.

## **Special Considerations**

**Older adults:** Older adults, especially those who live in northern industrialized cities of the world, are more prone to developing vitamin D deficiency.

**Infants:** Whether fed human milk or formula, infants have the same requirements for dietary vitamin D if they have not been exposed to sunlight. Most standard infant formulas contain enough vitamin D to meet needs, but because human milk has very little vitamin D, breast-fed infants who are not exposed to sunlight are unlikely to obtain adequate amounts of vitamin D from mother's milk to satisfy their needs beyond early infancy.

For infants who live in far-northern latitudes or whose sunlight exposure is restricted, a minimal intake of 2.5 µg (100 IU)/day of vitamin D will likely prevent rickets. However, at this intake and in the absence of sunlight, many infants will have serum 25(OH)D concentrations within the range that is often observed in cases of rickets. For this reason, and assuming that infants are not obtaining any vitamin D from sunlight, an AI of at least 5 µg (200 IU)/day is recommended.

## **Criteria for Determining Vitamin D Requirements, by Life Stage Group**

<i>Life stage group</i>	<i>Criterion</i>
For all life stage groups	Serum 25(OH)D

## **The UL**

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Members of the general population should not routinely exceed the UL. The DRI for vitamin D was derived using studies of the effect of vitamin D intake on serum calcium concentrations (to prevent hypercalcemia) in humans and represents total intake from food, water, and supplements.

Because milk is fortified to contain 10 µg (400 IU)/quart of vitamin D in the United States and 8.8 µg (352 IU)/liter of vitamin D in Canada, people with high milk intakes also may have relatively high vitamin D intakes. The 1986 National Health Interview Survey (NHIS) estimated that the 95th percentile of

intake by users of vitamin D supplements was 20 µg (800 IU)/day for men and 17.2 µg(686) IU/day for women. For most people, vitamin D intake from food and supplements is unlikely to exceed the UL. However, people who are at the upper end of the ranges for both sources of intake, particularly those who use many supplements and those with high intakes of fish or fortified milk, may be at risk for vitamin D toxicity.

## Special Considerations

**Granulomatous diseases:** The UL for vitamin D only applies to healthy individuals and does not apply to people with granulomatous diseases (such as sarcoidosis, tuberculosis, and histoplasmosis). Granulomatous diseases are characterized by hypercalcemia or hypercalciuria, or both, in individuals with normal or less-than-normal vitamin D intakes or with exposure to sunlight (see “Inadequate Intake and Deficiency”).

## SOURCES OF VITAMIN D

### Sunlight

Exposure to ultraviolet B rays through sunlight is a primary way by which humans obtain vitamin D. However, several factors can limit the skin's synthesis of vitamin D, including the use of sunscreen, increased levels of skin melanin, the distance one is from the Equator, the time of day, and the season of the year. Above and below latitudes of approximately 40 degrees N and 40 degrees S, vitamin D<sub>3</sub> in the skin is absent during most of the 3–4 winter months. The far-northern and southern latitudes extend this period for up to 6 months.

### Foods

Vitamin D naturally occurs in very few foods, mainly in the flesh of fatty fish, some fish-liver oils, and eggs from hens fed vitamin D. Most people's dietary intake of vitamin D comes from foods fortified with vitamin D. In Canada, all milks and margarines must be fortified. In the United States, milk products, breakfast cereals, and some fruit juices are fortified.

### Dietary Supplements

In the 1986 NHIS, the use of vitamin D supplements was reported in more than one-third of children 2 to 6 years of age, more than one-fourth of women, and almost one-fifth of men. The median supplement dose was the same for all users: 10 µg (400 IU).

## Bioavailability

This information was not provided at the time the DRI values for this nutrient were set.

## Dietary interactions

There is evidence that vitamin D may interact with certain other nutrients and dietary substances (see Table 2).

**TABLE 2 Potential Interactions with Other Dietary Substances**

Substance	Potential Interaction	Notes
<b>SUBSTANCES THAT AFFECT VITAMIN D</b>		
Magnesium	Magnesium deficiency may affect the body's response to pharmacological vitamin D.	Individuals with hypocalcemia and magnesium deficiency are resistant to pharmacological doses of vitamin D, 1,α-hydroxyvitamin D, and 1,25-dihydroxyvitamin D.

## INADEQUATE INTAKE AND DEFICIENCY

Vitamin D deficiency results in the inadequate bone mineralization or demineralization of the skeleton. The potential effects of vitamin D deficiency include the following:

- Rickets (in children)
- Osteomalacia (in adults)
- Elevated serum parathyroid hormone
- Decreased serum phosphorus
- Elevated serum alkaline phosphatase
- Osteoporosis (porous bones)

Epidemiological studies have found an association between vitamin D deficiency and an increased risk of colon, breast, and prostate cancer in people who live at higher latitudes. However, additional studies are needed to further explore this association.

## Special Considerations

**Older adults:** As adults age, their ability to synthesize vitamin D in the skin significantly decreases. Adults over the age of 65 years produce four times less vitamin D in the skin compared with adults aged 20 to 30 years.

**Sunlight and skin pigmentation:** The major source of vitamin D for humans is the exposure of the skin to sunlight, which initiates the conversion of 7-dehydrocholesterol to previtamin D<sub>3</sub> in the skin. An increase in skin melanin pigmentation or the topical use of sunscreen reduces the production of vitamin D<sub>3</sub> in the skin.

**Malabsorption disorders:** Conditions that cause fat malabsorption, such as severe liver failure, Crohn's disease, Whipple's disease, and celiac sprue, are associated with vitamin D deficiency because people with these conditions are unable to absorb vitamin D.

**Medications:** Glucocorticoids inhibit vitamin D-dependent intestinal calcium absorption and therefore can cause osteopenia. Individuals on glucocorticoid therapy may require supplemental vitamin D to maintain normal serum levels of 25(OH)D. Medications used to control seizures, such as phenobarbital and dilantin, can alter the metabolism and circulating half-life of vitamin D. People taking these medications (particularly those without exposure to sunlight) may require supplemental vitamin D.

## EXCESS INTAKE

Excess intake of vitamin D can cause hypervitaminosis D, which is characterized by a considerable increase in the serum levels of 25(OH)D (to 400–1,250 nmol/L). The adverse effects of hypervitaminosis D are probably largely mediated via hypercalcemia. The potential effects of the hypercalcemia associated with hypervitaminosis D include the following:

- Polyuria
- Polydipsia
- Hypercalciuria
- Calcification of soft tissues (including the kidneys, blood vessels, heart, and lungs)
- Anorexia
- Nausea
- Vomiting
- Reduced renal function

There is no evidence that vitamin D obtained through sun exposure can contribute to vitamin D toxicity because there is a limit to the amount of vitamin D<sub>3</sub> formed. Once this amount is reached, the previtamin and vitamin D<sub>3</sub> remaining in the skin are destroyed with continued sunlight exposure.

## KEY POINTS FOR VITAMIN D

- ✓ Vitamin D (calciferol) is involved in bone health. It aids in the absorption of calcium and phosphorus, thereby helping maintain normal serum levels of these minerals.
- ✓ Vitamin D is either synthesized in the skin through exposure to ultraviolet B rays in sunlight or ingested as dietary vitamin D. As adults age, their ability to synthesize vitamin D in the skin significantly decreases.
- ✓ Since data were inadequate to determine an EAR and thus calculate an RDA for vitamin D, an AI was instead developed.
- ✓ The AIs for vitamin D are based on serum 25(OH)D, which is the form that represents vitamin D storage.
- ✓ The UL was derived using studies of the effect of vitamin D intake on serum calcium concentrations (to prevent hypercalcemia) in humans.
- ✓ For most people, dietary vitamin D intake is unlikely to exceed the UL.
- ✓ Most standard infant formulas contain enough vitamin D to meet needs, but because human milk has very little vitamin D, breast-fed infants who are not exposed to sunlight are unlikely to obtain adequate amounts of vitamin D from mother's milk to satisfy their needs beyond early infancy.
- ✓ Exposure to ultraviolet B rays through sunlight is a primary way by which humans obtain vitamin D. However, several factors can limit the skin's synthesis of vitamin D, including the use of sunscreen, increased levels of skin melanin, the distance one is from the Equator, the time of day, and the season of the year.
- ✓ Vitamin D naturally occurs in very few foods, mainly in the flesh of fatty fish, some fish-liver oils, and eggs from hens fed vitamin D. In Canada, all milks and margarines must be fortified. In the United States, milk products, breakfast cereals, and some fruit juices are fortified.
- ✓ Vitamin D deficiency can impair normal bone metabolism, which may lead to rickets in children and osteomalacia in adults. It is also implicated in osteoporosis in adults.

- ✓ Older adults, especially those who live in northern industrialized cities of the world, are more prone to developing vitamin D deficiency.
- ✓ There is no evidence that vitamin D obtained through sun exposure can contribute to vitamin D toxicity.
- ✓ Excess intake of vitamin D can cause hypervitaminosis D, the effects of which include hypercalcemia, hypercalciuria, and calcification of soft tissues, such as blood vessels and certain organs.

**TABLE 1 Dietary Reference Intakes for Vitamin E  
( $\alpha$ -Tocopherol<sup>a</sup>) by Life Stage Group**

Life stage group <sup>g</sup>	DRI values (mg <sup>a</sup> /day)			
	EAR <sup>b</sup>	RDA <sup>c</sup>	AI <sup>d</sup>	UL <sup>e,f</sup>
0 through 6 mo			4	ND <sup>h</sup>
7 through 12 mo			5	ND
1 through 3 y	5	6		200
4 through 8 y	6	7		300
9 through 13 y	9	11		600
14 through 18 y	12	15		800
19 through 30 y	12	15		1,000
31 through 50 y	12	15		1,000
51 through 70 y	12	15		1,000
> 70 y	12	15		1,000
<b>Pregnancy</b>				
≤ 18 y	12	15		800
19 through 50 y	12	15		1,000
<b>Lactation</b>				
≤ 18 y	16	19		800
19 through 50 y	16	19		1,000

<sup>a</sup> For the EAR, RDA, and AI:  $\alpha$ -Tocopherol includes *RRR*- $\alpha$ -tocopherol, the only form of  $\alpha$ -tocopherol that occurs naturally in foods, and the *2R*-stereoisomeric forms of  $\alpha$ -tocopherol (*RRR*-, *RSR*-, *RPS*-, and *RSS*- $\alpha$ -tocopherol) that occur in fortified foods and supplements. This does not include the *2S*-stereoisomeric forms of  $\alpha$ -tocopherol (*SRR*-, *SSR*-, *SRS*-, and *SSS*- $\alpha$ -tocopherol), also found in fortified foods and supplements. The *2S*-stereoisomers are not stored in the body.

<sup>b</sup> EAR = Estimated Average Requirement.

<sup>c</sup> RDA = Recommended Dietary Allowance.

<sup>d</sup> AI = Adequate Intake.

<sup>e</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.

<sup>f</sup> As  $\alpha$ -tocopherol; applies to any form of supplemental  $\alpha$ -tocopherol since all are absorbed and can potentially contribute to vitamin E toxicity. The UL applies to synthetic forms obtained from supplements, fortified foods, or a combination of the two. Little information exists on the adverse effects that might result from ingestion of other forms.

<sup>g</sup> All groups except Pregnancy and Lactation represent males and females.

<sup>h</sup> ND = Not determinable. This value is not determinable due to the lack of data of adverse effects in this age group and concern regarding the lack of ability to handle excess amounts. Source of intake should only be from food to prevent high levels of intake.

# VITAMIN E

**V**itamin E is a fat-soluble nutrient that functions as a chain-breaking antioxidant in the body by preventing the spread of free-radical reactions. Of the eight naturally occurring forms of vitamin E only the  $\alpha$ -tocopherol form of the vitamin is maintained in the plasma.

The requirements for vitamin E are based on the prevention of hydrogen peroxide-induced hemolysis. The Estimated Average Requirement (EAR), Recommended Dietary Allowance (RDA), and Adequate Intake (AI) values for vitamin E only apply to intake of the 2*R*-stereoisomeric forms of  $\alpha$ -tocopherol from food, fortified foods, and supplements. Other naturally occurring forms of vitamin E do not meet the vitamin E requirement because they are not converted to  $\alpha$ -tocopherol in humans and are poorly recognized by the  $\alpha$ -tocopherol transfer protein in the liver.

The Tolerable Upper Intake Level (UL) is based on the adverse effect of increased tendency to hemorrhage. The UL for vitamin E applies to any forms of supplemental  $\alpha$ -tocopherol because all are absorbed; these forms of synthetic vitamin E are almost exclusively used in supplements, food fortification, and pharmacological agents. Little information exists on the adverse effects that might result from the ingestion of other forms of vitamin E. DRI values are listed by life stage group in Table 1.

Food sources of vitamin E include vegetable oils and spreads, unprocessed cereal grains, nuts, fruits, vegetables, and meats (especially the fatty portion). Overt deficiency of vitamin E in the United States and Canada is rare and is generally only seen in people who are unable to absorb the vitamin or who have inherited conditions that prevent the maintenance of normal blood concentrations. There is no evidence of adverse effects from the consumption of vitamin E naturally occurring from foods. The possible chronic effects of lifetime exposures to high supplemental levels of  $\alpha$ -tocopherol remain uncertain.

## VITAMIN E AND THE BODY

### Function

Unlike most nutrients, vitamin E does not appear to play a specific role in certain metabolic pathways. Its major function seems to be as a nonspecific chain-breaking antioxidant that prevents the spread of free-radical reactions. It scavenges peroxy radical and protects polyunsaturated fatty acids within membrane phospholipids and in plasma lipoproteins.

On the molecular level, vitamin E ( $\alpha$ -tocopherol form) inhibits protein kinase C activity (involved in cell proliferation and differentiation) in smooth muscle cells, platelets, and monocytes. It may also improve vasodilation and inhibit platelet aggregation by enhancing the release of prostacyclin.

### Absorption, Metabolism, Storage, and Excretion

Vitamin E is absorbed in the intestine, although the precise rate of absorption is not known. All of the forms of vitamin E appear to have similar low absorption efficiency. Absorbed vitamin E in the form of chylomicron remnants is taken up by the liver, and then only one form of vitamin E,  $\alpha$ -tocopherol, is preferentially secreted in very low density lipoproteins. Thus, it is the liver, not the intestine, that discriminates between tocopherols. Tissues take up vitamin E from the plasma. Vitamin E rapidly transfers between various lipoproteins and also between lipoproteins and membranes, which may enrich membranes with vitamin E. Vitamin E is excreted in both the urine and feces, with fecal elimination being the major mode of excretion.

### DETERMINING DRIS

There are eight naturally occurring forms, or isomers, of vitamin E: four tocopherols ( $\alpha$ -,  $\beta$ -,  $\gamma$ -, and  $\delta$ -tocopherols) and four tocotrienols ( $\alpha$ -,  $\beta$ -,  $\gamma$ -, and  $\delta$ -tocotrienols). These various forms of vitamin E are not interconvertible in humans, and thus do not behave the same metabolically. Of the eight, only  $\alpha$ -tocopherol is maintained in the plasma.

The isomer  $\alpha$ -tocopherol has eight possible stereoisomers: four in the 2R-stereoisomeric form (RRR-, RSR-, RRS-, and RSS- $\alpha$ -tocopherol) and four in the 2S-stereoisomeric form (SRR-, SSR-, SRS-, and SSS- $\alpha$ -tocopherol). Of these, only one—the RRR form—naturally occurs in foods. All eight stereoisomers are represented by synthetic forms (together called *all-rac-* $\alpha$ -tocopherol) and are present in fortified foods and in vitamin supplements.

Of the eight stereoisomers of  $\alpha$ -tocopherol, the only forms that are maintained in the plasma are naturally occurring RRR- $\alpha$ -tocopherol and the 2R-stereoisomeric forms present in synthetic forms. Since the 2S-stereoisomers are not maintained in the plasma or tissues, they are not included in the definition of active components for vitamin E activity in humans.

For the purpose of establishing the requirements, vitamin E activity is defined here as being limited to the 2R-stereoisomeric forms of  $\alpha$ -tocopherol. However, all eight stereoisomeric forms of supplemental  $\alpha$ -tocopherol are used as the basis for establishing the UL for vitamin E. This is because all eight forms are absorbed. These recommended intakes and ULs vary from past definitions and recommendations for vitamin E.

## Determining Requirements

The adult requirements for vitamin E are based largely on induced vitamin E deficiency in humans and the intake that correlated with *in vitro* hydrogen peroxide-induced red blood cell hemolysis and plasma  $\alpha$ -tocopherol concentrations. Although some studies have reported a possible protective effect of vitamin E on conditions such as cardiovascular and neurological diseases, cancer, cataracts, and diseases of the immune system, the data are inadequate to support population-wide dietary recommendations that are specifically based on preventing these diseases.

The EAR, RDA, and AI values for vitamin E apply only to intake of the 2*R*-stereoisomeric forms of  $\alpha$ -tocopherol from food, fortified foods, and supplements. The other naturally occurring isomers of vitamin E ( $\beta$ -,  $\gamma$ -, and  $\delta$ -tocopherols and  $\alpha$ -,  $\beta$ -,  $\gamma$ -, and  $\delta$ -tocotrienols) do not contribute to meeting the vitamin E requirement because they are not converted to  $\alpha$ -tocopherol in humans; these forms of synthetic vitamin E are almost exclusively used in supplements, food fortification, and pharmacological agents. Little information exists on the adverse effects that might result from ingestion of excess amounts of other isomeric forms (such as  $\gamma$ - and  $\beta$ -tocopherol).

Currently, most nutrient databases, as well as nutrition labels, do not distinguish among all the different forms of vitamin E found in food. These databases often present the data as  $\alpha$ -tocopherol equivalents ( $\alpha$ -TE), and thus include the contributions of all eight naturally occurring forms of vitamin E, after adjustment for bioavailability using previously determined equivalencies. It is recommended that the use of  $\alpha$ -TE be abandoned due to the lack of evidence of bioavailability via transport in the plasma or tissues. Because these other forms of vitamin E occur in foods, the intake of  $\alpha$ -TE is greater than the intake of  $\alpha$ -tocopherol alone. The values above were converted from  $\alpha$ -TE to  $\alpha$ -tocopherol using a factor of 0.8 as described later in this chapter (see “Dietary Sources”).

## Criteria for Determining Vitamin E Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Human milk content
7 through 12 mo	Extrapolation from 0 to 5.9 mo
1 through 18 y	Extrapolation from adult
19 through 30 y	Prevention of hydrogen peroxide-induced hemolysis
31 through > 70 y	Extrapolation of hydrogen peroxide-induced hemolysis from 19 through 30 y

*Pregnancy*

≤ 18 y through 50 y      Age-specific requirement + plasma concentration

*Lactation*

≤ 18 y through 50 y      Age-specific requirement + vitamin E secreted in milk

## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Members of the general population should not routinely consume more than the UL. The UL for vitamin E is based on the adverse effect of increased tendency to hemorrhage. The UL applies to all supplemental  $\alpha$ -tocopherol forms of vitamin E (*RRR*- $\alpha$ -tocopherol and *all-rac*- $\alpha$ -tocopherol), since all are absorbed and can thus potentially contribute to vitamin E toxicity.

Sources of vitamin E available as supplements are usually labeled as international units (IUs) of natural vitamin E and its esters or as synthetic vitamin E and its esters. Table 2 shows the IUs of various sources of supplemental vitamin E that are equivalent to the UL for adults of 1,000 mg/day of any form of supplemental  $\alpha$ -tocopherol.

Based on the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994) data, the highest mean reported intake of vitamin E from food and supplements for all life stage and gender groups was approximately 45 mg/day of  $\alpha$ -tocopherol equivalents (reported by women aged 51 to 70 years). This group also had the highest reported intake at the 99th percentile, at 508 mg/day of  $\alpha$ -tocopherol equivalents, which is well below the UL of 1,000 mg/day for any form of  $\alpha$ -tocopherol. Vitamin E supplement use is high in the U.S. population. In the 1986 National Health Interview Survey (NHIS), supplements containing vitamin E were used by 23 percent of men, 29 percent of women, and 37 percent of young children in the United States. The risk of adverse effects resulting from excess intake of  $\alpha$ -tocopherol from food and supplements appears to be very low based on this information.

## Special Considerations

**Vitamin K deficiency or anticoagulant therapy:** The UL for vitamin E pertains to individuals in the general population with adequate vitamin K intake. Individuals who are deficient in vitamin K or who are on anticoagulant therapy are at increased risk of coagulation defects and should be monitored when taking vitamin E supplements.

**TABLE 2 Amounts in International Units (IU) of Any Forms of  $\alpha$ -Tocopherol<sup>a</sup> Contained in Vitamin E<sup>b</sup> Supplements Equivalent to the UL for Adults<sup>c</sup>**

Sources of Vitamin E Available as Supplements	UL for Adults Total $\alpha$ -Tocopherol (mg/day)	IU from Source Providing Adult UL
<b>Synthetic Vitamin E and Esters</b>		
<i>dl</i> - $\alpha$ -Tocopheryl acetate	1,000	1,100
<i>dl</i> - $\alpha$ -Tocopheryl succinate	1,000	1,100
<i>dl</i> - $\alpha$ -Tocopherol	1,000	1,100
<b>Natural Vitamin E and Esters</b>		
<i>d</i> - $\alpha$ -Tocopheryl acetate	1,000	1,500
<i>d</i> - $\alpha$ -Tocopheryl succinate	1,000	1,500
<i>d</i> - $\alpha$ -Tocopherol	1,000	1,500

<sup>a</sup> All forms of supplemental  $\alpha$ -tocopherol include all eight stereoisomers of  $\alpha$ -tocopherol. The UL is based on animal studies feeding either *all racemic*- or *RRR*- $\alpha$ -tocopherol, both of which resulted in equivalent adverse effects.

<sup>b</sup> Vitamin E supplements have been historically, although incorrectly, labeled *d*- or *dl*- $\alpha$ -tocopherol. Sources of vitamin E include the *all racemic*- (*dl*- $\alpha$ -tocopherol [*RRR*-, *RRS*-, *RSR*-, *RSS*-, *SSS*-, *SRS*-, *SSR*-, and *SRR*-]) or synthetic form and its esters. All of these forms of vitamin E may be present in supplements.

<sup>c</sup> The conversion factors used in this table are based on 2S-forms contributing to the adverse effects

## DIETARY SOURCES

### Foods

The main dietary sources of vitamin E are vegetable oils, such as wheat-germ oil, sunflower oil, cottonseed oil, safflower oil, canola oil, olive oil, palm oil, and rice-bran oil. Fats and oils in the form of spreads often contribute to vitamin E intake. Other sources of vitamin E include unprocessed cereal grains, nuts, fruits, vegetables, and meats (especially the fatty portion). As previously stated, only the natural form of  $\alpha$ -tocopherol (*RRR*- $\alpha$ -tocopherol) found in these unfortified foods counts toward meeting the RDA. Other non- $\alpha$ -tocopherol forms of vitamin E present in food do not.

It is important to note that because vitamin E is generally found in fat-containing foods and is more easily absorbed from fat-containing meals, intakes of vitamin E by people who consume low-fat diets may be less than optimal unless food choices are carefully made to enhance vitamin E intake.

**Estimating  $\alpha$ -tocopherol content of foods and diets:** As discussed, many databases of nutrient content and many food-intake surveys list vitamin E in the form of  $\alpha$ -tocopherol equivalents ( $\alpha$ -TE) rather than  $\alpha$ -tocopherol. To estimate  $\alpha$ -tocopherol content, multiply the number of  $\alpha$ -tocopherol equivalents by a factor of 0.8:

$$\text{mg of } \alpha\text{-tocopherol in a meal} = \text{mg of } \alpha\text{-TEs in a meal} \times 0.8$$

## Dietary Supplements

Vitamin E supplement use appears to be high in the U.S. population. Data from the Boston Nutritional Status Survey (1981–1984) on adults aged 60 years and older found that 38 percent of men took dietary supplements and, of them, 68 percent took a vitamin E supplement. Of the women surveyed, 49 percent used supplements, and 73 percent of them took a vitamin E supplement. In the 1986 NHIS, 26 percent of all adults reported using supplements that contained vitamin E.

**Converting IUs to mg of  $\alpha$ -tocopherol:** To determine the milligrams of  $\alpha$ -tocopherol in a dietary supplement labeled in international units (IUs), one of two conversion factors may be used:

- If the form of the supplemental vitamin E is naturally occurring or *RRR*- $\alpha$ -tocopherol (which has been historically and incorrectly labeled as *d*- $\alpha$ -tocopherol), the correct factor is 0.67 mg/IU. Thus, 30 IUs of *RRR*- $\alpha$ -tocopherol (labeled as *d*- $\alpha$ -tocopherol) in a multivitamin supplement would equate to 20 mg of  $\alpha$ -tocopherol ( $30 \times 0.67$ ). The same factor is used for 30 IUs of either *RRR*- $\alpha$ -tocopherol acetate or *RRR*- $\alpha$ -tocopherol succinate because the amount in grams of these forms in a capsule has been adjusted based on their molecular weight.

$$\text{Mg of } \alpha\text{-tocopherol in food, fortified food, or multivitamin} = \text{IU of the } RRR\text{-}\alpha\text{-tocopherol compound} \times 0.67$$

- If the form of the supplement is *all-rac*- $\alpha$ -tocopherol (historically and incorrectly labeled as *dl*- $\alpha$ -tocopherol), the appropriate factor is 0.45 mg/IU. (This reflects the inactivity of the 2S-stereoisomers.) Thus, 30 IU of *all-rac*- $\alpha$ -tocopherol (labeled as *dl*- $\alpha$ -tocopherol) in a multivitamin supplement would equate to 13.5 mg of  $\alpha$ -tocopherol ( $30 \times 0.45$ ). The same factor is used for the *all-rac*- $\alpha$ -tocopherol acetate and succinate forms.

$$\text{Mg of } \alpha\text{-tocopherol in food, fortified food, or multivitamin} = \text{IU of the } all\text{-}rac\text{-}\alpha\text{-tocopherol compound} \times 0.45$$

See Appendix F on conversion factors on converting IUs of vitamin E to  $\alpha$ -tocopherol.

## Bioavailability

Because vitamin E is a fat-soluble nutrient, its absorption is enhanced when it is consumed in a meal that contains fat; however, the optimal amount of fat to enhance absorption has not been reported. This is probably more of a consideration for people who take vitamin E in supplement form, rather than for those who consume it from foods, since most dietary vitamin E is found in foods that contain fat.

## Dietary Interactions

There is evidence that vitamin E may interact with certain dietary substances (see Table 3).

**TABLE 3 Potential Interactions with Other Dietary Substances**

Substance	Potential Interaction	Notes
<b>SUBSTANCES THAT AFFECT VITAMIN E</b>		
Polyunsaturated fatty acids (PUFAs)	Vitamin E requirements may increase when intakes of PUFAs are increased.	High PUFA intakes should be accompanied by increased vitamin E intakes.

## INADEQUATE INTAKE AND DEFICIENCY

Vitamin E deficiency is very rare; overt symptoms of deficiency in healthy individuals consuming diets low in vitamin E have never been described. Vitamin E deficiency occurs only as a result of genetic abnormalities of vitamin E metabolism, fat malabsorption syndromes, or protein-energy malnutrition. The signs and symptoms of deficiency include the following:

- Peripheral neuropathy (primary symptom)
- Spinocerebellar ataxia
- Skeletal myopathy
- Pigmented retinopathy
- Increased erythrocyte fragility
- Increased ethane and pentane production

## EXCESS INTAKE

There is no evidence of adverse effects from the excess consumption of vitamin E naturally occurring in foods. With regard to supplemental vitamin E intake in the form of synthetic  $\alpha$ -tocopherol (as a supplement, food fortificant, or pharmacological agent), most studies in humans showing the safety of vitamin E were conducted in small groups of individuals who received supplemental amounts of 3,200 mg/day or less (usually less than 2,000 mg/day) of  $\alpha$ -tocopherol for periods of a few weeks to a few months. Thus, the possible chronic effects of longer exposure to high supplemental levels of  $\alpha$ -tocopherol remain uncertain and some caution must be exercised in judgments regarding the safety of supplemental doses of  $\alpha$ -tocopherol over multiyear periods. The potential adverse effects of excess vitamin E intake include hemorrhagic toxicity and diminished blood coagulation in individuals who are deficient in vitamin K or on anticoagulant therapy.

## Special Considerations

**Premature infants:** Hemolytic anemia due to vitamin E deficiency is of frequent concern in premature infants. However, its management via vitamin E supplementation must be carefully controlled because small premature infants are particularly vulnerable to the toxic effects of  $\alpha$ -tocopherol.

## KEY POINTS FOR VITAMIN E

- ✓ Vitamin E ( $\alpha$ -tocopherol) is a fat-soluble nutrient that functions as a chain-breaking antioxidant in the body by preventing the spread of free-radical reactions.
- ✓ The adult requirements for vitamin E are based on prevention of hydrogen peroxide-induced hemolysis. The UL is based on the adverse effect of increased tendency to hemorrhage.
- ✓ The EAR, RDA, and AI values for vitamin E apply only to intake of the 2*R*-stereoisomeric forms of  $\alpha$ -tocopherol from food, fortified foods, and supplements. The UL applies to any form of supplemental  $\alpha$ -tocopherol because all are absorbed; these forms of synthetic vitamin E are almost exclusively used in supplements, food fortification, and pharmacological agents.
- ✓ Food sources of vitamin E include vegetable oils and spreads, unprocessed cereal grains, nuts, fruits, vegetables, and meats (especially the fatty portion).
- ✓ Vitamin E deficiency is very rare in the United States and Canada, generally occurring only as the result of genetic abnormalities of vitamin E metabolism, fat malabsorption syndromes, or protein-energy malnutrition. The primary effect of vitamin E deficiency is peripheral neuropathy.
- ✓ There is no evidence of adverse effects from the consumption of vitamin E naturally occurring in foods.
- ✓ The primary known adverse effect resulting from excessive supplemental vitamin E intake is hemorrhagic toxicity.

**TABLE 1 Dietary Reference Intakes for Folate by Life Stage Group**

Life stage group	DRI values ( $\mu\text{g}/\text{day}$ )				
	EAR <sup>b</sup>		RDA <sup>c</sup>		
	males	females	males	females	
0 through 6 mo				65	ND <sup>g</sup>
7 through 12 mo				80	ND
1 through 3 y	120	120	150	150	300
4 through 8 y	160	160	200	200	400
9 through 13 y	250	250	300	300	600
14 through 18 y	330	330	400	400 <sup>h</sup>	800
19 through 30 y	320	320	400	400 <sup>h</sup>	1,000
31 through 50 y	320	320	400	400 <sup>h</sup>	1,000
51 through 70 y	320	320	400	400	1,000
> 70 y	320	320	400	400	1,000
<b>Pregnancy</b>					
≤ 18 y		520		600 <sup>i</sup>	800
19 through 50 y		520		600 <sup>i</sup>	1,000
<b>Lactation</b>					
≤ 18 y		450		500	800
19 through 50 y		450		500	1,000

<sup>a</sup> As dietary folate equivalents (DFEs). 1 DFE = 1  $\mu\text{g}$  food folate = 0.6  $\mu\text{g}$  of folic acid from fortified food or as a supplement consumed with food = 0.5  $\mu\text{g}$  of folic acid from a supplement taken on an empty stomach.

<sup>b</sup> EAR = Estimated Average Requirement.

<sup>c</sup> RDA = Recommended Dietary Allowance.

<sup>d</sup> AI = Adequate Intake.

<sup>e</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.

<sup>f</sup> The UL for folate applies to synthetic forms obtained from supplements, fortified foods, or a combination of the two.

<sup>g</sup> ND = Not determinable. This value is not determinable due to the lack of data of adverse effects in this age group and concern regarding the lack of ability to handle excess amounts. Source of intake should only be from food to prevent high levels of intake.

<sup>h</sup> To reduce risk of neural tube defects, women capable of becoming pregnant should take 400  $\mu\text{g}$  of folic acid daily from fortified foods, supplements, or both, in addition to consuming food folate from a varied diet.

<sup>i</sup> It is assumed that women will continue consuming 400  $\mu\text{g}$  from supplements or fortified food until their pregnancy is confirmed and they enter prenatal care, which ordinarily occurs after the end of the periconceptional period—the critical time for formation of the neural tube.

# FOLATE

**F**olate is a B vitamin that functions as a coenzyme in the metabolism of nucleic and amino acids. Folate is a generic term that includes both the naturally occurring form of the vitamin (food folate or pteroyl-polyglutamates) and the monoglutamate form (folic acid or pteroylmonoglutamic acid), which is used in fortified foods and dietary supplements.

The requirements for folate are based on the amount of dietary folate equivalents (DFEs, with values adjusted for differences in the absorption of food folate and folic acid) needed to maintain erythrocyte folate. DFEs adjust for the nearly 50 percent lower bioavailability of food folate compared to that of folic acid. The Tolerable Upper Intake Level (UL) is based on the precipitation or exacerbation of neuropathy in vitamin  $B_{12}$ -deficient individuals as the critical endpoint and represents total intake from fortified food or dietary supplements. The UL does not include naturally occurring food folate. Although epidemiological evidence suggests that folate may protect against vascular disease, cancer, and mental disorders, the evidence was not sufficient to use risk reduction of these conditions as a basis for setting folate requirements. DRI values are listed by life stage group in Table 1.

Rich food sources of folate include fortified grain products, dark green vegetables, and beans and legumes. Chronic inadequate folate intake results in macrocytic anemia. The adverse effect of consuming excess supplemental folate is the onset or progression of neurological complications in people with vitamin  $B_{12}$  deficiency. Excess folate can obscure or mask and thus potentially delay the diagnosis of vitamin  $B_{12}$  deficiency, which can result in an increased risk of progressive, unrecognized neurological damage.

To reduce the risk of neural tube defects, women able to become pregnant should take 400  $\mu\text{g}$  of folic acid daily from fortified foods, supplements, or both, in addition to consuming food folate from a varied diet. It is important to note that this recommendation specifically calls for folic acid, which is more bioavailable than food folate. Since foods fortified to a level of 400  $\mu\text{g}$  are not available in Canada, the recommendation is to consume a multivitamin containing 400  $\mu\text{g}$  of folic acid every day in addition to the amount of folate in a healthful diet.

## FOLATE AND THE BODY

### Function

Folate is a water-soluble B-complex vitamin that functions as a coenzyme in the metabolism of nucleic and amino acids. The term folate refers to two forms: naturally occurring folates in food, referred to here as food folates (pteroylpolyglutamates), and folic acid (pteroylmonoglutamic acid), which is rarely naturally found in foods but is the form used in dietary supplements and fortified foods. Folic acid is the most stable form of folate.

### Absorption, Metabolism, Storage, and Excretion

Folate is absorbed from the gut across the intestinal mucosa via a saturable, pH-dependent active transport process. When pharmacological doses of folic acid are consumed, it is also absorbed by nonsaturable passive diffusion. Folate is taken up from the portal circulation by the liver, where it is metabolized and retained or released into the blood or bile. Approximately two-thirds of folate in plasma is bound to protein. Some folate is excreted in the urine, bile, and feces.

## DETERMINING DRIS

### Determining Requirements

The requirements for folate are based on the amount of dietary folate equivalents (DFEs) needed to maintain erythrocyte folate; ancillary data on plasma homocysteine and plasma folate concentrations were also considered. DFEs adjust for the nearly 50 percent lower bioavailability of food folate compared with that of folic acid (see “Bioavailability”), such that:

1 DFE = 1 µg food folate = 0.6 µg of folic acid from fortified food or as a supplement consumed with food = 0.5 µg of folic acid from a supplement taken on an empty stomach

Currently, nutrition labels do not distinguish between sources of folate (food folate and folic acid) or express the folate content in DFEs. Although epidemiological evidence suggests that folate may protect against vascular disease, cancer, and mental disorders, the evidence was not sufficient to use risk reduction of these conditions as a basis for setting folate requirements.

## Special Considerations

**Individuals with increased needs:** Intakes of folate higher than the RDA may be needed by women who are carrying more than one fetus, mothers nursing more than one infant, individuals with chronic heavy intake of alcohol, and individuals on chronic anticonvulsant or methotrexate therapy.

To reduce the risk of neural tube defects, women able to become pregnant should take 400 µg of folic acid daily from fortified foods, supplements, or both, in addition to consuming food folate from a varied diet. It is important to note that this recommendation specifically calls for folic acid, which is more bioavailable than food folate. Since foods fortified to a level of 400 µg are not available in Canada, the recommendation is to consume a multivitamin containing 400 µg of folic acid every day in addition to the amount of folate in a healthful diet.

## Intake of Folate

Currently nutrient databases and nutrition labels do not express the folate content of food in DFEs, which take into account the different bioavailabilities of folate sources. (See Box 1 for information on how DFEs and types of folate are

### BOX 1 The Relationship Between DFEs and Types of Folate

DFEs and types of folate are related as follows:

1 µg of DFEs	= 1.0 µg of food folate
	= 0.6 µg of folate added to foods (as a fortificant or folate supplement with food)
	= 0.5 µg of folate taken as a supplement (on an empty stomach)
1 µg food folate	= 1.0 µg of DFEs
1 µg of folate added as a fortificant or as a supplement consumed with meals	= 1.7 µg of DFEs
1 µg of folate supplement taken on an empty stomach	= 2.0 µg of DFEs

When intakes of folate in an individual's diet are assessed, it is possible to approximate the DFE intake by estimating the amount present that has been added in fortification and the amount present that naturally occurs as food folate by using the relationship of 1 µg of folate added as a fortificant = 1.7 µg of DFEs (the reciprocal of 1 µg of DFEs = 0.6 µg folate added to food).

related.) Thus, nutrient intake data substantially underestimates the actual current intake. This is due to problems associated with analyzing the folate content of food, underreported intake, and the change in U.S. fortification laws instituted in 1998 (see “Dietary Sources” for information on fortification).

### **Criteria for Determining Folate Requirements, by Life Stage Group**

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Human milk content
7 through 12 mo	Extrapolation from younger infants and from adults
1 through 18 y	Extrapolation from adults
19 through > 70 y	Maintenance of normal erythrocyte folate, plasma homocysteine, plasma or serum folate

<i>Pregnancy</i>	
≤ 18 y through 50 y	Maintenance of normal erythrocyte and serum folate levels

<i>Lactation</i>	
≤ 18 y through 50 y	Folate intake necessary to replace folate secreted in human milk + folate needed to maintain folate status

### **The UL**

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Members of the general population should not routinely consume more than the UL. The UL for folate is from fortified foods or dietary supplements, or both. The UL does not include naturally occurring food folate and is based on the precipitation or exacerbation of neuropathy in vitamin B<sub>12</sub>-deficient individuals as the critical endpoint. It has been recognized that excessive intake of folate supplements may obscure or mask and potentially delay the diagnosis of vitamin B<sub>12</sub> deficiency.

The intake of folate in the United States is currently higher than indicated by the National Health and Nutrition Examination Survey (NHANES III, 1988–1994) because enriched cereal grains in the U.S. food supply, to which no folate was added previously, are now fortified with folate at 140 µg/100 g of cereal grain. The Food and Drug Administration (FDA) estimated that those who follow the guidance of the U.S. Food Guide Pyramid (1992) and consume cereal grains at the upper end of the recommended range might obtain an additional 440 µg/day of folate under the U.S. fortification regulations. Using this estimate and with the assumption of regular use of an over-the-counter supplement (400

μg per dose), it is unlikely that the intake of folate would regularly exceed 1,000 μg/day for members of any life stage or gender group.

## Special Considerations

**Individuals at increased risk:** People who are at risk of vitamin B<sub>12</sub> deficiency include those who follow a vegan diet, older adults with atrophic gastritis, and those with pernicious anemia and bacterial overgrowth of the gut. These individuals may place themselves at an increased risk of neurological disorders if they consume excess folate because folate may mask vitamin B<sub>12</sub> deficiency.

**Females of childbearing age:** In general, the prevalence of vitamin B<sub>12</sub> deficiency in women of the childbearing years is very low and the consumption of supplemental folate at or above the UL in this subgroup is unlikely to produce adverse effects.

## DIETARY SOURCES

### Foods

Rich food sources of folate include fortified grain products, dark green vegetables, and beans and legumes. According to data from the Continuing Survey of Food Intakes by Individuals (CSFII, 1994–1996), the greatest contribution to folate intake in U.S. adults came from fortified ready-to-eat cereals and a category called “other vegetables.” This category includes vegetables such as green beans, green peas, lettuces, cabbages, and vegetable soups. Many of the vegetables in the “other vegetables” category have lower folate content than dark green vegetables, but are so commonly eaten that their contribution to total folate intake is relatively high compared to other sources such as citrus juices and legumes.

During the period when data were collected for CSFII (1994–1996), the only grain products fortified with folate were mainly hot and cold breakfast cereals. However, as of January 1, 1998, in the United States, all enriched cereal grains, such as bread, pasta, flour, breakfast cereal, and rice, are required to be fortified with folic acid at 1.4 mg/kg of grain. In Canada, the fortification of all white flour and cornmeal with folate is at a level of 1.5 mg/kg and fortification of alimentary paste is at a level of at least 2.0 mg/kg. Because enriched grains are widely consumed in Canada and the United States, these foods are now an important contributor to folate intake.

It is estimated that folate fortification will increase the folate intake of most U.S. women by 80 μg/day (136 μg DFE/day) or more. This amount could be provided by 1 cup of pasta plus 1 slice of bread. Depending on the cereal grains

chosen and the amount consumed, 5 servings daily might add 220 µg/day or more of folate from fortified foods (nearly 400 µg DFE/day) to the diet.

## Dietary Supplements

Folic acid supplements in doses of 400 µg are widely available over the counter. Supplements containing 1,000 µg or more are available by prescription in the United States and Canada.

In a nationwide telephone survey conducted by the Centers for Disease Control and Prevention (CDC) during January and February 1997, 43 percent of women of childbearing age reported taking some form of vitamin supplement containing folic acid; 32 percent reported taking a folic acid supplement daily and 12 percent reported taking a supplement less frequently.

## Bioavailability

The bioavailability of folate varies, depending on the form of the vitamin ingested and whether it is consumed with or without food. Folic acid supplements taken on an empty stomach are nearly 100 percent bioavailable. No published information was found regarding the effect of food on the bioavailability of folate supplements. Folate in the form of folic acid added to foods is about 85 percent bioavailable. Naturally occurring food folates are about 50 percent bioavailable.

## Dietary Interactions

There is evidence that folate may interact with certain nutrients, dietary substances, and drugs (see Table 2).

## INADEQUATE INTAKE AND DEFICIENCY

Inadequate folate intake first leads to a decrease in serum folate concentration, then to a decrease in erythrocyte folate concentration, a rise in homocysteine concentration, and megaloblastic changes in the bone marrow and other tissues with rapidly dividing cells. These changes ultimately lead to macrocytic anemia, at first evidenced by a low erythrocyte count and eventually by a low hematocrit and hemoglobin, as well. The effects of moderate to severe macrocytic anemia may include the following:

- Weakness
- Fatigue
- Difficulty in concentrating
- Irritability

**TABLE 2 Potential Interactions with Other Dietary Substances**

Substance	Potential Interaction	Notes
<b>SUBSTANCES THAT AFFECT FOLATE</b>		
Alcohol	Inadequate folate intake in people with chronic alcoholism leads to folate deficiency.	Ethanol intake may aggravate folate deficiency by impairing intestinal folate absorption and hepatobiliary metabolism and by increasing renal folate excretion.
Cigarettes	Chronic smoking may lead to folate deficiency.	Low intake, rather than an increased requirement, in smokers may account for the poorer folate status of smokers.
Nonsteroidal anti-inflammatory drugs (NSAIDS): aspirin, ibuprofen, and acetaminophen	Very large therapeutic doses (e.g., 3,900 mg/day) of NSAIDS may exert antifolate activity.	Routine use of low doses of these drugs has not been reported to impair folate status.
Anticonvulsant drugs	Chronic use of anti-convulsant drugs, such as diphenhydantoin and phenobarbital, may impair folate status.	Few studies have controlled for folate intake between groups of anticonvulsant users. Therefore, definitive conclusions could not be drawn regarding the potential adverse effects of these drugs on folate status.
Methotrexate	Chronic methotrexate therapy may impair folate status.	It has been recommended that patients undergoing chronic methotrexate therapy for rheumatoid arthritis increase their folate consumption or consider folate supplements (1 mg/day).
Other drugs with antifolate activity	Pyrimethamine (for malaria), trimethoprim (for bacterial infections), triamterene (for hypertension), trimetrexate (for <i>Pneumocystis carinii</i> infection), and sulfasalazine (for chronic ulcerative colitis) have been shown to exert antifolate activity.	

- Headache
- Palpitations
- Shortness of breath
- Atrophic glossitis

## Special Considerations

*Coexisting deficiencies:* Coexisting iron or vitamin B<sub>12</sub> deficiencies may interfere with the diagnosis of folate deficiency. In contrast to folate deficiency, iron deficiency leads to a decrease in mean cell volume. When there is a deficiency of both iron and folate, the interpretation of hematological changes may be unclear. A vitamin B<sub>12</sub> deficiency results in the same hematological changes that occur with folate deficiency because the vitamin B<sub>12</sub> deficiency results in a secondary folate deficiency.

## EXCESS INTAKE

No adverse effects have been associated with the excess consumption of the amounts of folate normally found in fortified foods. The adverse effect that may result from excess intake of supplemental folate is the onset or progression of neurological complications in people with vitamin B<sub>12</sub> deficiency. Excess folate may obscure or mask and thus potentially delay the diagnosis of vitamin B<sub>12</sub> deficiency, which can result in an increased risk of progressive, unrecognized neurological damage.

## KEY POINTS FOR FOLATE

- ✓ Folate is a B vitamin that functions as a coenzyme in the metabolism of nucleic and amino acids.
- ✓ Folate is a generic term that includes both the naturally occurring form of the vitamin (food folate) and the monoglutamate form (folic acid), which is used in fortified foods and dietary supplements.
- ✓ The requirements for folate are based on the amount of DFEs needed to maintain erythrocyte folate; plasma homocysteine and plasma folate concentrations were also considered. The UL is based on precipitation or exacerbation of neuropathy in vitamin B<sub>12</sub>-deficient individuals as the critical endpoint.
- ✓ Although epidemiological evidence suggests that folate may protect against vascular disease, cancer, and mental disorders, the evidence was not sufficient to use risk reduction of these conditions as a basis for setting folate requirements.

- ✓ DFEs adjust for the nearly 50 percent lower bioavailability of food folate compared with that of folic acid, such that 1 DFE = 1 µg food folate = 0.6 µg of folic acid from fortified food or as a supplement consumed with food = 0.5 µg of folic acid from a supplement taken on an empty stomach.
- ✓ The UL for adults is from fortified foods or supplements. The UL does not include naturally occurring food folate.
- ✓ To reduce the risk of neural tube defects, women able to become pregnant should take 400 µg of folic acid daily from fortified foods, supplements, or both, in addition to consuming food folate from a varied diet. It is important to note that this recommendation specifically calls for folic acid, which is more bioavailable than food folate.
- ✓ Rich food sources of folate include fortified grain products, dark green vegetables, and beans and legumes.
- ✓ Chronic inadequate folate intake results in macrocytic anemia.
- ✓ Coexisting iron or vitamin B<sub>12</sub> deficiency may interfere with the diagnosis of folate deficiency.
- ✓ No adverse effects have been associated with the excess consumption of the amounts of folate normally found in fortified foods.
- ✓ The adverse effect that may result from excess intake of supplemental folate is the onset or progression of neurological complications in people with vitamin B<sub>12</sub> deficiency. Excess folate can obscure or mask and thus potentially delay the diagnosis of vitamin B<sub>12</sub> deficiency, which can result in an increased risk of progressive, unrecognized neurological damage.

**TABLE 1 Dietary Reference Intakes for Vitamin K by Life Stage Group**

Life stage group	DRI values (μg /day)	
	AI <sup>a</sup>	UL <sup>b</sup>
	males	females
<b>Pregnancy</b>		
≤ 18 y		75
19 through 50 y		90
<b>Lactation</b>		
≤ 18 y		75
19 through 50 y		90

<sup>a</sup> AI = Adequate Intake.<sup>b</sup> UL = Tolerable Upper Intake Level. Data were insufficient to set a UL. In the absence of a UL, extra caution may be warranted in consuming levels above the recommended intake.

# VITAMIN K

**V**itamin K functions as a coenzyme for biological reactions involved in blood coagulation and bone metabolism. Phylloquinone, the plant form of vitamin K, is the major form in the diet. Menaquinone forms are produced by bacteria in the lower bowel.

Since data were insufficient to set an Estimated Average Requirement (EAR) and thus calculate a Recommended Dietary Allowance (RDA) for vitamin K, an Adequate Intake (AI) was instead developed. The AIs for vitamin K are based on median intakes of the nutrient. Data were insufficient to set a Tolerable Upper Intake Level (UL). DRI values are listed by life stage group in Table 1.

Rich dietary sources of vitamin K include leafy green vegetables, soy and canola oils, and margarine. Vegetables particularly rich in vitamin K include collard greens, spinach, and salad greens. Clinically significant vitamin K deficiency is extremely rare in the general population, with cases being limited to individuals with malabsorption syndromes or to those treated with drugs known to interfere with vitamin K metabolism. No adverse effects have been reported with high intakes of vitamin K from food or supplements.

## **VITAMIN K AND THE BODY**

### **Function**

Vitamin K functions as a coenzyme for biological reactions involved in blood coagulation and bone metabolism. It also plays an essential role in the conversion of certain residues in proteins into biologically active forms. These proteins include plasma prothrombin (coagulation factor II) and the plasma procoagulants, factors VII, IX, and X. Two structurally related vitamin K-dependent proteins have received recent attention as being proteins with possible roles in the prevention of chronic disease. They are osteocalcin, found in bone, and matrix Gla protein, originally found in bone, but now known to be more widely distributed.

### **Absorption, Metabolism, Storage, and Excretion**

Phylloquinone is the major form of vitamin K in the diet. It is absorbed in the small intestine in a process that is enhanced by the presence of dietary fat and dependent on the normal flow of bile and pancreatic juice. The absorbed phyl-

loquinone is then secreted into the lymph and enters the circulation as a component of chylomicrons. The circulating vitamin K is taken up by the liver and other tissues.

The liver, which contains the highest concentration of vitamin K in the body, rapidly accumulates ingested phylloquinone. Skeletal muscle contains little phylloquinone, but significant concentrations are found in the heart and some other tissues. Turnover in the liver is rapid and hepatic reserves are rapidly depleted when dietary intake of vitamin K is restricted. Vitamin K is excreted primarily in the bile, but also, to a lesser extent, in the urine.

Menaquinone forms of vitamin K are produced by bacteria in the lower bowel, where the forms appear in large amounts. However, their contribution to the maintenance of vitamin K status has been difficult to assess. Although the content is extremely variable, the human liver contains about 10 times as much vitamin K as a mixture of menaquinones than as phylloquinone.

## DETERMINING DRIS

### Determining Requirements

Since data were insufficient to set an EAR and thus calculate an RDA for vitamin K, an AI was instead developed. The AIs for vitamin K are based on the median intakes of the nutrient indicated by the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994).

It has been suggested that vitamin K may have roles in osteoporosis and vascular health. However, this is difficult to establish on the basis of the studies performed thus far. Clinical intervention studies investigating the relationship between vitamin K and osteoporosis are currently being conducted in North America and Europe. Whether vitamin K status within the range of normal intake plays a significant role in the development of atherosclerosis requires further investigation and should be verified in studies that employ rigorous experimental designs.

### Special Considerations

**Newborns:** Vitamin K is poorly transported across the placenta, which puts newborn infants at risk for vitamin K deficiency. Poor vitamin K status, added to the fact that the concentrations of most plasma clotting factors are low at the time of birth, increases the risk of bleeding during the first few weeks of life, a condition known as hemorrhagic disease of the newborn (HDNB). Because HDNB can be effectively prevented by administering vitamin K, infants born in the United States and Canada routinely receive 0.5–1 mg of phylloquinone

intramuscularly or 2.0 mg orally within 6 hours of birth. This practice is supported by both U.S. and Canadian pediatric societies.

## **Criteria for Determining Vitamin K Requirements, by Life Stage Group**

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Average vitamin K intake from human milk
7 through 12 mo	Extrapolation from 0 through 6 mo AI
1 through > 70 y	Median intake of vitamin K from NHANES III
<i>Pregnancy</i>	
≤ 18 y	Adolescent female median intake
19 through 50 y	Adult female median intake
<i>Lactation</i>	
≤ 18 y	Adolescent female median intake
19 through 50 y	Adult female median intake

## **The UL**

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all healthy people. Data were insufficient to set a UL for vitamin K.

## **DIETARY SOURCES**

### **Foods**

Only a relatively small number of food items substantially contribute to the dietary phylloquinone intake of most people. A few green vegetables (collards, spinach, and salad greens) contain in excess of 300 µg of phylloquinone/100 g, while broccoli, brussels sprouts, cabbage, and bib lettuce contain between 100 and 200 µg of phylloquinone/100 g. Other green vegetables contain smaller amounts.

Plant oils and margarine are the second major source of phylloquinone in the diet. The phylloquinone content of plant oils varies, with soybean and canola oils containing greater than 100 µg of phylloquinone/100 g. Cottonseed oil and olive oil contain about 50 µg/100 g, and corn oil contains less than 5 µg/100 g. According to the Food and Drug Administration's (FDA's) Total Diet Study (1991–1997), spinach, collard greens, broccoli, and iceberg lettuce are the major contributors of vitamin K in the diets of U.S. adults and children.

The hydrogenation of plant oils to form solid shortenings results in some conversion of phylloquinone to 2',3'-dihydrophylloquinone. This form of vitamin K is more prevalent in margarines, infant formulas, and processed foods, and it can represent a substantial portion of total vitamin K in some diets. Some cheeses may also supply a substantial amount of vitamin K (40–80 µg/100 g) in the form of menaquinone. However, as earlier mentioned, the contribution of menaquinones to the maintenance of vitamin K status has been difficult to assess.

## Dietary Supplements

According to data from NHANES III, median intakes of vitamin K from food and supplements were 93–119 µg/day for men and 82–90 mg/day for women (for those who reported consuming supplements).

## Bioavailability

Studies on the bioavailability of vitamin K (in the form of phylloquinone) have been limited. Until more data are available, the bioavailability of phylloquinone obtained from vegetables should not be considered to be more than 20 percent as available as phylloquinone obtained from supplements. It is known, however, that the absorption of vitamin K from vegetables is enhanced by the presence of dietary fat.

## Dietary Interactions

The main interaction of concern regarding vitamin K involves anticoagulant medications, such as warfarin. Chronic use of these drugs results in an acquired cellular vitamin K deficiency and a decrease in the synthesis of vitamin K-dependent clotting factors. Alterations in vitamin K intake can influence the efficacy of these drugs.

Individuals on chronic warfarin therapy may require dietary counseling on how to maintain steady vitamin K intake levels. Because habitual vitamin K intake may modulate warfarin dosage in patients using this anticoagulant, these individuals should maintain their normal dietary and supplementation patterns once an effective dose of warfarin has been established. Short-term, day-to-day variations in vitamin K intake from food sources do not appear to interfere with anticoagulant status and therefore do not need to be carefully monitored. However, changes in supplemental vitamin K intake should be avoided, since the bioavailability of synthetic (supplemental) phylloquinone is considerably greater than the bioavailability of phylloquinone from food sources.

There is evidence that vitamin K may also interact with other nutrients and dietary substances (see Table 2).

**TABLE 2 Potential Interactions with Other Dietary Substances**

<i>Substance</i>	<i>Potential Interaction</i>	<i>Notes</i>
<b>SUBSTANCES THAT AFFECT VITAMIN K</b>		
Vitamin E	Elevated intakes of vitamin E may antagonize the action of vitamin K.	Increased intakes of vitamin E have not been reported to antagonize vitamin K status in healthy humans. However, in one study, patients receiving anticoagulation therapy who were supplemented with approximately 400 IU/day of $\alpha$ -tocopherol experienced nonstatistically significant decreases in prothrombin time over a 4-week period. The metabolic basis for the potential antagonism of vitamin K by vitamin E has not been completely determined.

## INADEQUATE INTAKE AND DEFICIENCY

Studies conducted over a number of years have indicated that the simple restriction of vitamin K intake to levels almost impossible to achieve in any nutritionally adequate, self-selected diet does not impair normal hemostatic control in healthy subjects. Although there is some interference in the hepatic synthesis of the vitamin K-dependent clotting factors that can be measured by sensitive assays, standard clinical measures of procoagulant potential are not changed. In general, clinically significant vitamin K deficiency is extremely rare in the general population, with cases being limited to individuals with various lipid malabsorption syndromes or to those treated with drugs known to interfere with vitamin K metabolism. However, a clinically significant vitamin K deficiency has usually been defined as a vitamin K-responsive hypoprothrombinemia and is associated with an increase in prothrombin time and, in severe cases, bleeding.

There have also been case reports of bleeding occurring in patients taking antibiotics, and the use of these drugs has often been associated with an acquired vitamin K deficiency resulting from a suppression of menaquinone-synthesizing organisms. But the reports are complicated by the possibility of general malnutrition in this given patient population and by the antiplatelet action of many of the same drugs.

## EXCESS INTAKE

No adverse effects have been reported with high intakes of vitamin K from food or supplements in healthy individuals who are not intentionally blocking vita-

min K activity with anticoagulation medications. A search of the literature revealed no evidence of toxicity associated with the intake of either the phylloquinone or the menaquinone forms of vitamin K. Menadione, a synthetic form of the vitamin, has been associated with liver damage and is no longer therapeutically used.

## KEY POINTS FOR VITAMIN K

- ✓ Vitamin K functions as a coenzyme for biological reactions involved in blood coagulation and bone metabolism.
- ✓ Since data were insufficient to set an EAR and thus calculate an RDA for vitamin K, an AI was instead developed.
- ✓ The AIs for vitamin K are based on the median intakes indicated by NHANES III.
- ✓ Infants born in the United States and Canada routinely receive 0.5–1 mg of phylloquinone intramuscularly or 2.0 mg orally within 6 hours of birth. This practice is supported by both U.S. and Canadian pediatric societies.
- ✓ Data were insufficient to set a UL.
- ✓ Although epidemiological evidence indicates that vitamin K may play a role in osteoporosis prevention, more research in this area is needed.
- ✓ Only a relatively small number of food items contribute substantially to the dietary phylloquinone intake of most people. A few green vegetables (collards, spinach, and salad greens) contain in excess of 300 µg of phylloquinone/100 g, while broccoli, brussels sprouts, cabbage, and bib lettuce contain between 100 and 200 µg of phylloquinone/100 g.
- ✓ The main interaction of concern regarding vitamin K involves anticoagulant medications, such as warfarin. Patients on chronic warfarin therapy may require dietary counseling on how to maintain steady vitamin K intake levels.
- ✓ In general, clinically significant vitamin K deficiency is extremely rare in the general population, with cases being limited to individuals with malabsorption syndromes or those treated with drugs known to interfere with vitamin K metabolism. However, the classic sign of vitamin K deficiency is a vitamin K-responsive increase in prothrombin time and, in severe cases, bleeding.
- ✓ No adverse effects have been reported with high intakes of vitamin K from food or supplements in healthy individuals who are not intentionally blocking vitamin K activity with anticoagulation medications.

**TABLE 1 Dietary Reference Intakes for Niacin by Life Stage Group**

Life stage group	DRI values (mg/day)			
	EAR <sup>a,b</sup>		RDA <sup>a,c</sup>	
	males	females	males	females
0 through 6 mo			2	ND <sup>g</sup>
7 through 12 mo			4	ND
1 through 3 y	5	5	6	6
4 through 8 y	6	6	8	8
9 through 13 y	9	9	12	12
14 through 18 y	12	11	16	14
19 through 30 y	12	11	16	14
31 through 50 y	12	11	16	14
51 through 70 y	12	11	16	14
> 70 y	12	11	16	14
<b>Pregnancy</b>				
≤ 18 y		14	18	30
19 through 50 y		14	18	35
<b>Lactation</b>				
≤ 18 y		13	17	30
19 through 50 y		13	17	35

<sup>a</sup> As niacin equivalents (NE). 1 mg of niacin = 60 mg of tryptophan; 0–6 months = preformed niacin (not NE).

<sup>b</sup> **EAR** = Estimated Average Requirement.

<sup>c</sup> **RDA** = Recommended Dietary Allowance.

<sup>d</sup> **AI** = Adequate Intake.

<sup>e</sup> **UL** = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.

<sup>f</sup> The UL for niacin applies to synthetic forms obtained from supplements, fortified foods, or a combination of the two. The UL is not expressed in NEs.

<sup>g</sup> **ND** = Not determinable. This value is not determinable due to the lack of data of adverse effects in this age group and concern regarding the lack of ability to handle excess amounts. Source of intake should only be from food to prevent high levels of intake.

# NIACIN

The term niacin refers to nicotinamide (nicotinic acid amide), nicotinic acid (pyridine-3-carboxylic acid), and derivatives that exhibit the biological activity of nicotinamide. Niacin is involved in many biological reactions, including intracellular respiration and fatty acid synthesis. The amino acid tryptophan is converted in part into nicotinamide and thus can contribute to meeting the requirement for niacin.

The primary method used to estimate the requirements for niacin intake relates intake to the urinary excretion of niacin metabolites. The requirements are expressed in niacin equivalents (NEs), allowing for some conversion of the amino acid tryptophan to niacin (1 mg niacin = 60 mg tryptophan). The Tolerable Upper Intake Level (UL) is based on flushing as the critical adverse effect. The UL applies to synthetic forms obtained from supplements, fortified foods, or a combination of the two. (The UL is in mg of preformed niacin and is not expressed in NEs.) DRI values are listed by life stage group in Table 1.

Meat, liver, poultry, and fish are rich sources of niacin. Other contributors to niacin intake include enriched and whole-grain breads and bread products and fortified ready-to-eat cereals. The classic disease of niacin deficiency is pellagra, which in industrialized nations generally only occurs in people with chronic alcoholism or conditions that inhibit the metabolism of tryptophan. There are no adverse effects associated with the excess consumption of naturally occurring niacin in foods, but they can result from excess intakes from dietary supplements, fortified foods, and pharmacological agents. The potential adverse effects of excess niacin intake include flushing, nausea, vomiting, liver toxicity, blurred vision, and impaired glucose tolerance.

## NIACIN AND THE BODY

### Function

The term niacin refers to nicotinamide, nicotinic acid, and derivatives that exhibit the biological activity of nicotinamide. Niacin acts as a donor or acceptor of a hydride ion in many biological reduction–oxidation reactions, including intracellular respiration, the oxidation of fuel molecules, and fatty acid and steroid synthesis. The amino acid tryptophan is converted in part into nicotinamide and thus can contribute to meeting the requirement for niacin.

## Absorption, Metabolism, Storage, and Excretion

Absorption of niacin from the stomach and intestine is rapid. At low concentrations, absorption is mediated by sodium ion–dependent facilitated diffusion. At higher concentrations, absorption is by passive diffusion. Niacin is stored in various body tissues. The niacin coenzymes NAD (nicotinamide adenine dinucleotide) and NADP (nicotinamide adenine dinucleotide phosphate) are synthesized in all body tissues from nicotinic acid or nicotinamide.

The body's niacin requirement is met not only by nicotinic acid and nicotinamide present in the diet, but also by conversion from dietary protein containing tryptophan.

## DETERMINING DRIS

### Determining Requirements

The requirements for niacin are based on the urinary excretion of niacin metabolites. The EAR and RDA are expressed in niacin equivalents (NEs), allowing for some conversion of the amino acid tryptophan to niacin (1 mg niacin = 60 mg tryptophan).

### Special Considerations

**Individuals with increased needs:** The RDAs for niacin are not expected to be sufficient to meet the needs of people with Hartnup's disease, liver cirrhosis, or carcinoid syndrome, or the needs of individuals on long-term isoniazid treatment for tuberculosis. Extra niacin may also be required by those being treated with hemodialysis or peritoneal dialysis, those with malabsorption syndrome, and women who are carrying more than one fetus or breastfeeding more than one infant.

### Criteria for Determining Niacin Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Human milk content
7 through 12 mo	Extrapolation from adults
1 through 18 y	Extrapolation from adults
19 through > 70 y	Excretion of niacin metabolites

<i>Pregnancy</i>	
≤ 18 y through 50 y	Age-specific requirement + increased energy utilization and growth needs during pregnancy

*Lactation*

≤ 18 y through 50 y      Age-specific requirement + energy expenditure of human milk production

## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Members of the general population should not routinely consume more than the UL. The UL for niacin represents preformed niacin and is based on flushing as the critical adverse effect. The UL developed for niacin applies to all forms of niacin added to foods or taken as supplements (e.g., immediate-release, slow- or sustained-release nicotinic acid, and niacinamide [nicotinamide]). Individuals who take over-the-counter niacin to treat themselves, such as for high blood cholesterol, for example, might exceed the UL on a chronic basis. The UL is not meant to apply to individuals who are receiving niacin under medical supervision. Niacin intake data indicate that only a small percentage of the U.S. population is likely to exceed the UL for niacin.

## Special Considerations

**Individuals susceptible to adverse effects:** People with the following conditions are particularly susceptible to the adverse effects of excess niacin intake: liver dysfunction or a history of liver disease, diabetes mellitus, active peptic ulcer disease, gout, cardiac arrhythmias, inflammatory bowel disease, migraine headaches, and alcoholism. Individuals with these conditions might not be protected by the UL for niacin for the general population.

## DIETARY SOURCES

### Foods

Data from the Continuing Survey of Food Intakes by Individuals (CSFII, 1994–1996) indicated that the greatest contribution to the niacin intake of the U.S. adult population came from mixed dishes high in meat, fish, or poultry; poultry as an entree; enriched and whole-grain breads and bread products; and fortified ready-to-eat cereals. Most flesh foods are rich sources of niacin.

### Dietary Supplements

In the 1986 National Health Interview Survey (NHIS), approximately 26 percent of all adults reported taking a supplement containing niacin. For adults who took supplements and participated in the Boston Nutritional Status Sur-

vey (1981–1984), median supplemental niacin intakes were 20 mg/day for men and 30 mg/day for women. Supplements containing up to about 400 mg of niacin are available without a prescription in the United States.

### Bioavailability

Niacin from meat, liver, beans, and fortified or enriched foods appears to be highly bioavailable, whereas niacin from unfortified cereal grains is bound and only about 30 percent available (although alkali treatment of the grains increases the percentage absorbed). Niacin added during enrichment or fortification is in the free form of niacin; foods that contain this free form include beans and liver.

The conversion efficiency of tryptophan to niacin, although assumed to be 60:1, varies depending on a number of dietary and metabolic factors. The efficiency of conversion is decreased by deficiencies in some other nutrients (see “Dietary Interactions”). Individual differences also account for a substantial difference in conversion efficiency.

### Dietary Interactions

There is some evidence that inadequate iron, riboflavin, or vitamin B<sub>6</sub> status increases niacin needs by decreasing the conversion of tryptophan to niacin. Data were not available to quantitatively assess the effects of these nutrient-nutrient interactions on the niacin requirement.

## INADEQUATE INTAKE AND DEFICIENCY

The classic disease of severe niacin deficiency is pellagra, which is characterized by the following signs and symptoms:

- Pigmented rash
- Vomiting, constipation, or diarrhea
- Bright red tongue
- Depression
- Apathy
- Headache
- Fatigue
- Memory loss

Pellagra was common in the United States and parts of Europe in the early 20th century in areas where corn or maize (low in both niacin and tryptophan) was the dietary staple. Now it is occasionally seen in developing nations, such as in India, China, and Africa. In industrialized nations, it is generally only

associated with chronic alcoholism and in individuals with conditions that disrupt the metabolism of tryptophan. Deficiencies of other micronutrients, such as pyridoxine and iron, which are required to convert tryptophan to niacin, may also contribute to the appearance of pellagra.

## **EXCESS INTAKE**

There is no evidence of adverse effects associated with the excess consumption of naturally occurring niacin in foods. But adverse effects may result from excess niacin intake from dietary supplements, pharmaceutical preparations, and fortified foods. Most of the data concerning adverse effects of niacin has come from studies and case reports involving patients with hyperlipidemia or other disorders who were treated with pharmacological preparations that contained immediate-release nicotinic acid or slow- or sustained-release nicotinic acid. The potential adverse effects of excess niacin intake include the following:

- Flushing (the first observed adverse effect observed; generally occurs at lower doses than do other adverse effects)
- Nausea and vomiting
- Liver toxicity
- Blurred vision
- Impaired glucose tolerance

## KEY POINTS FOR NIACIN

- ✓ Niacin is involved in many biological reactions, including intracellular respiration and fatty acid synthesis. The amino acid tryptophan is converted in part into nicotinamide and thus can contribute to meeting the requirement for niacin.
- ✓ The requirements for niacin are based on the urinary excretion of niacin metabolites. The UL is based on flushing as the critical adverse effect.
- ✓ The requirements are expressed in niacin equivalents (NEs), allowing for some conversion of the amino acid tryptophan to niacin (1 mg niacin = 60 mg tryptophan).
- ✓ The UL for niacin represents preformed niacin (the UL is not expressed in NEs) and applies to synthetic forms obtained from supplements, fortified foods, or a combination of the two.
- ✓ Niacin intake data indicate that only a small percentage of the U.S. population is likely to exceed the UL for niacin.
- ✓ People with an increased need for niacin include those with Hartnup's disease, liver cirrhosis, carcinoid syndrome, and malabsorption syndrome, as well as those on long-term isoniazid treatment for tuberculosis or on hemodialysis or peritoneal dialysis. Also, pregnant females who are carrying more than one fetus or breastfeeding more than one infant may require additional niacin.
- ✓ Meat, liver, poultry, and fish are rich sources of niacin. Other contributors to niacin intake include enriched and whole-grain breads and bread products and fortified ready-to-eat cereals.
- ✓ The classic disease of severe niacin deficiency is pellagra, which in industrialized nations generally only occurs in people with chronic alcoholism or conditions that inhibit the metabolism of tryptophan.

- ✓ There is no evidence of adverse effects associated with the excess consumption of naturally occurring niacin in foods. But adverse effects may result from excess niacin intake from dietary supplements, pharmaceutical preparations, and fortified foods.
- ✓ The adverse effects of excess niacin intake include flushing, nausea and vomiting, liver toxicity, and impaired glucose tolerance. However, most of the data on adverse effects has come from research with patients with special conditions who were treated with pharmacological preparations.

**TABLE 1 Dietary Reference Intakes for Pantothenic Acid by Life Stage Group**

Life stage group <sup>c</sup>	DRI values (mg/day)	
	AI <sup>a</sup>	UL <sup>b</sup>
<b>Life stage group<sup>c</sup></b>		
0 through 6 mo	1.7	
7 through 12 mo	1.8	
1 through 3 y	2	
4 through 8 y	3	
9 through 13 y	4	
14 through 18 y	5	
19 through 30 y	5	
31 through 50 y	5	
51 through 70 y	5	
> 70 y	5	
<b>Pregnancy</b>		
≤ 18 y	6	
19 through 50 y	6	
<b>Lactation</b>		
≤ 18 y	7	
19 through 50 y	7	

<sup>a</sup> AI = Adequate Intake.<sup>b</sup> UL = Tolerable Upper Intake Level. Data were insufficient to set a UL. In the absence of a UL, extra caution may be warranted in consuming levels above the recommended intake.<sup>c</sup> All groups except Pregnancy and Lactation represent males and females.

# PANTOTHENIC ACID

**P**antothenic acid functions as a component of coenzyme A (CoA), which is involved in fatty acid metabolism. Pantothenic acid is widely distributed in foods and is essential to almost all forms of life.

Since data were insufficient to set an Estimated Average Requirement (EAR) and thus calculate a Recommended Dietary Allowance (RDA) for pantothenic acid, an Adequate Intake (AI) was instead developed. The AIs for pantothenic acid are based on pantothenic acid intake sufficient to replace urinary excretion. Data were insufficient to set a Tolerable Upper Intake Level (UL). DRI values are listed by life stage group in Table 1.

Major food sources of pantothenic acid include chicken, beef, potatoes, oat cereals, tomato products, liver, kidney, yeast, egg yolk, broccoli, and whole grains. Pantothenic acid deficiency is rare, and no adverse effects have been associated with high intakes.

## PANTOTHENIC ACID AND THE BODY

### Function

Pantothenic acid is involved in the synthesis of coenzyme A (CoA), which is involved in the synthesis of fatty acids and membrane phospholipids, amino acids, steroid hormones, vitamins A and D, porphyrin and corrin rings, and neurotransmitters.

### Absorption, Metabolism, Storage, and Excretion

Pantothenic acid is absorbed in the small intestine by active transport at low concentrations of the vitamin and by passive transport at higher concentrations. Because the active transport system is saturable, absorption is less efficient at higher concentrations of intake. However, the exact intake levels at which absorption decreases in humans are not known. Pantothenic acid is excreted in the urine in amounts that are proportional with dietary intake over a wide range of intake values.

## DETERMINING DRIS

### Determining Requirements

Since data were insufficient to set an EAR and thus calculate an RDA, an AI was instead developed. The AIs for pantothenic acid are based on pantothenic acid intake sufficient to replace urinary excretion.

## Criteria for Determining Pantothenic Acid Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Human milk content
7 through 12 mo	Mean of extrapolation from younger infants and from adults
1 through 18 y	Extrapolation from adults
19 through > 70 y	Pantothenic acid intake sufficient to replace urinary excretion

<i>Pregnancy</i>	
≤ 18 y through 50 y	Mean intake of pregnant women

<i>Lactation</i>	
≤ 18 y through 50 y	Pantothenic acid sufficient to replace amount excreted in milk + amount needed to maintain concentration of maternal blood levels

## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Due to insufficient data on adverse effects of oral pantothenic acid consumption, a UL for pantothenic acid could not be determined.

## DIETARY SOURCES

### Foods

Data on the pantothenic acid content of food are very limited. Foods that are reported to be major sources include chicken, beef, potatoes, oat cereals, tomato products, liver, kidney, yeast, egg yolk, broccoli, and whole grains. Food processing, including the refining of whole grains and the freezing and canning of vegetables, fish, meat, and dairy products, lowers the pantothenic acid content of these foods.

### Dietary Supplements

Results from the 1986 National Health Interview Survey (NHIS) indicated that 22 percent of U.S. adults took a supplement that contained pantothenic acid.

### Bioavailability

Little information exists on the bioavailability of dietary pantothenic acid. Values of 40–61 percent (average of 50 percent) have been reported for absorbed food-bound pantothenic acid.

## Dietary Interactions

This information was not provided at the time the DRI values for this nutrient were set.

## INADEQUATE INTAKE AND DEFICIENCY

Pantothenic acid deficiency is rare and has only been observed in individuals who were fed diets devoid of the vitamin or who were given a pantothenic-acid metabolic antagonist. The signs and symptoms of deficiency may include the following:

- Irritability and restlessness
- Fatigue
- Apathy
- Malaise
- Sleep disturbances
- Nausea, vomiting, and abdominal cramps
- Neurobiological symptoms, such as numbness, paresthesias, muscle cramps, and staggering gait
- Hypoglycemia and increased sensitivity to insulin

## EXCESS INTAKE

No adverse effects have been associated with high intakes of pantothenic acid.

## KEY POINTS FOR PANTOTHENIC ACID

- ✓ Pantothenic acid functions as a component of coenzyme A (CoA), which is involved in fatty acid metabolism.
- ✓ Since data were insufficient to set an EAR and thus calculate an RDA for pantothenic acid, an AI was instead developed.
- ✓ The AIs for pantothenic acid are based on pantothenic acid intake sufficient to replace urinary excretion.
- ✓ Data were insufficient to set a UL.
- ✓ Major food sources of pantothenic acid include chicken, beef, potatoes, oat cereals, tomato products, liver, kidney, yeast, egg yolk, broccoli, and whole grains.
- ✓ Pantothenic acid deficiency is rare and has only been observed in individuals who were fed diets devoid of the vitamin or who were given a pantothenic acid metabolic antagonist.
- ✓ No adverse effects have been associated with high intakes of pantothenic acid.

**TABLE 1 Dietary Reference Intakes for Riboflavin by Life Stage Group**

Life stage group	DRI values (mg/day)			
	EAR <sup>a</sup>		RDA <sup>b</sup>	
	males	females	males	females
0 through 6 mo				0.3
7 through 12 mo				0.4
1 through 3 y	0.4	0.4	0.5	0.5
4 through 8 y	0.5	0.5	0.6	0.6
9 through 13 y	0.8	0.8	0.9	0.9
14 through 18 y	1.1	0.9	1.3	1.0
19 through 30 y	1.1	0.9	1.3	1.1
31 through 50 y	1.1	0.9	1.3	1.1
51 through 70 y	1.1	0.9	1.3	1.1
> 70 y	1.1	0.9	1.3	1.1
<b>Pregnancy</b>				
≤ 18 y		1.2		1.4
19 through 50 y		1.2		1.4
<b>Lactation</b>				
≤ 18 y		1.3		1.6
19 through 50 y		1.3		1.6

<sup>a</sup> EAR = Estimated Average Requirement.<sup>b</sup> RDA = Recommended Dietary Allowance.<sup>c</sup> AI = Adequate Intake.<sup>d</sup> UL = Tolerable Upper Intake Level. Data were insufficient to set a UL. In the absence of a UL, extra caution may be warranted in consuming levels above the recommended intake.

# RIBOFLAVIN

**R**iboflavin (vitamin B<sub>2</sub>) functions as a coenzyme for numerous oxidation–reduction reactions in several metabolic pathways and in energy production. The rate of absorption is proportional to intake, and it increases when riboflavin is ingested along with other foods and in the presence of bile salts.

The requirements for riboflavin are based on intake in relation to a combination of indicators, including the excretion of riboflavin and its metabolites, blood values for riboflavin, and the erythrocyte glutathione reductase activity coefficient. Data were insufficient to set a Tolerable Upper Intake Level (UL). DRI values are listed by life stage group in Table 1.

Major food sources of riboflavin for the U.S. adult population include milk and milk drinks, bread products, and fortified cereals. Riboflavin deficiency (riboflavinosis) is most often accompanied by other nutrient deficiencies, and it may lead to deficiencies of vitamin B<sub>6</sub> and niacin, in particular. Diseases such as cancer, cardiac disease, and diabetes mellitus are known to precipitate or exacerbate riboflavin deficiency. There is no evidence of adverse effects from excess riboflavin intake. Its apparent nontoxic nature may be due its limited absorption in the gut and its rapid excretion in the urine.

## RIBOFLAVIN AND THE BODY

### Function

Riboflavin functions as a coenzyme for numerous oxidation–reduction reactions in several metabolic pathways and in energy production. The primary form of the vitamin is as an integral component of the coenzymes flavin mononucleotide and flavin-adenine dinucleotide. It is in these bound coenzymes that riboflavin functions as a catalyst for redox reactions.

### Absorption, Metabolism, Storage, and Excretion

Primary absorption of riboflavin occurs in the small intestine via a rapid, saturable transport system. A small amount is absorbed in the large intestine. The rate of absorption is proportional to intake, and it increases when riboflavin is ingested along with other foods and in the presence of bile salts. At low intake levels, most absorption of riboflavin occurs via an active or facilitated trans-

port system. At higher levels of intake, riboflavin can be absorbed by passive diffusion.

In the plasma, a large portion of riboflavin associates with other proteins, mainly immunoglobulins, for transport. Pregnancy increases the level of carrier proteins available for riboflavin, which results in a higher rate of riboflavin uptake at the maternal surface of the placenta.

The metabolism of riboflavin is a tightly controlled process that depends on a person's riboflavin status. Riboflavin is converted to coenzymes within most tissues, but primarily in the small intestine, liver, heart, and kidneys.

When riboflavin is absorbed in excess, very little is stored in the body. The excess is excreted primarily in the urine. Urinary excretion of riboflavin varies with intake, metabolic events, and age. In healthy adults who consume well-balanced diets, riboflavin accounts for 60–70 percent of the excreted urinary flavins. In newborns, urinary excretion is slow; however, the cumulative amount excreted is similar to the amount excreted by older infants.

## DETERMINING DRIS

### Determining Requirements

The requirements for riboflavin are based on intake in relation to a combination of indicators, including the excretion of riboflavin and its metabolites, blood values for riboflavin, and the erythrocyte glutathione reductase activity coefficient.

### Special Considerations

**Individuals with increased needs:** People undergoing hemodialysis or peritoneal dialysis and those with severe malabsorption are likely to require extra riboflavin. Women who are carrying more than one fetus or breastfeeding more than one infant are also likely to require more riboflavin. It is possible that individuals who are ordinarily extremely physically active may also have increased needs for riboflavin.

### Criteria for Determining Riboflavin Requirements, by Life Stage Group

Life stage group	Criterion
0 through 6 mo	Human milk content
7 through 12 mo	Extrapolation from younger infants and from adults
1 through 18 y	Extrapolation from adults

19 through 70 y	Excretion of riboflavin and its metabolites, blood values for riboflavin, and the erythrocyte glutathione reductase activity coefficient
> 70 y	Extrapolation from younger adults

*Pregnancy*

≤ 18 y through 50 y	Age-specific requirement + increased energy utilization and growth needs during pregnancy
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*Lactation*

≤ 18 y through 50 y	Age-specific requirement + energy expenditure of human milk production
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## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Due to insufficient data on adverse effects of excess riboflavin consumption, a UL for riboflavin could not be determined. Although no adverse effects have been associated with excess riboflavin intake, this does not mean that there is no potential for adverse effects to occur with high intakes. Because data on adverse effects are limited, caution may be warranted.

## DIETARY SOURCES

### Foods

Most plant and animal tissues contain at least small amounts of riboflavin. Data from the Continuing Survey of Food Intakes by Individuals (CSFII, 1994–1996) indicate that the greatest contribution to the riboflavin intake by the U.S. adult population came from milk and milk beverages, followed by bread products and fortified cereals. Organ meats are also good sources of riboflavin. (It should be noted that the riboflavin content of milk is decreased if the milk is exposed to light.)

### Dietary Supplements

Approximately 26 percent of all adults reported taking a supplement containing riboflavin, according to the 1986 National Health Interview Survey (NHIS). For adults who took supplements and participated in the Boston Nutritional Status Survey (1981–1984), median supplemental riboflavin intakes were 1.9 mg/day for men and 2.9 mg/day for women.

## Bioavailability

Approximately 95 percent of food flavin is bioavailable, up to a maximum of about 27 mg absorbed per single meal or dose. More than 90 percent of riboflavin is estimated to be in the form of readily digestible flavocoenzymes.

## Dietary Interactions

Riboflavin interrelates with other B vitamins: notably niacin, which requires riboflavin for its formation from tryptophan, and vitamin B<sub>6</sub>, which also requires riboflavin for a conversion to a coenzyme form. These interrelationships are not known to affect the requirement for riboflavin.

## INADEQUATE INTAKE AND DEFICIENCY

Riboflavin deficiency (ariboflavinosis) has been documented in industrialized and developing nations and across various demographic groups. Riboflavin deficiency is most often accompanied by other nutrient deficiencies, and it may lead to deficiencies of vitamin B<sub>6</sub> and niacin, in particular. The signs and symptoms of riboflavin deficiency include the following:

- Sore throat
- Hyperemia and edema of the pharyngeal and oral mucous membranes
- Cheilosis
- Angular stomatitis
- Glossitis (magenta tongue)
- Seborrheic dermatitis (dandruff)
- Normocytic anemia associated with pure erythrocyte cytoplasia of the bone marrow

## Special Considerations

*Conditions that increase deficiency risk:* Diseases such as cancer, cardiac disease, and diabetes mellitus are known to precipitate or exacerbate riboflavin deficiency.

## EXCESS INTAKE

No adverse effects associated with excess riboflavin consumption from food or supplements have been reported. However, studies involving large doses of riboflavin have not been designed to systematically evaluate adverse effects. The apparent lack of harm resulting from high oral doses of riboflavin may be due to its limited solubility and limited capacity for absorption in the human gastrointestinal tract and its rapid excretion in the urine.

## KEY POINTS FOR RIBOFLAVIN

- ✓ Riboflavin (vitamin B<sub>2</sub>) functions as a coenzyme in numerous oxidation-reduction reactions in several metabolic pathways and in energy production.
- ✓ The metabolism of riboflavin is a tightly controlled process that depends on a person's riboflavin status.
- ✓ The requirements for riboflavin are based on intake in relation to a combination of indicators, including the excretion of riboflavin and its metabolites, blood values for riboflavin, and the erythrocyte glutathione reductase activity coefficient.
- ✓ Data were insufficient to set a UL.
- ✓ Certain individuals may have an increased need for riboflavin, including those undergoing dialysis, those with severe malabsorption, and women who are carrying more than one fetus or breastfeeding more than one infant.
- ✓ Major food sources of riboflavin for the U.S. adult population include milk and milk beverages, bread products, and fortified cereals.
- ✓ Riboflavin deficiency is most often accompanied by other nutrient deficiencies, and it may lead to deficiencies of vitamin B<sub>6</sub> and niacin, in particular.
- ✓ The signs and symptoms of riboflavin deficiency include sore throat, hyperemia and edema of the pharyngeal and oral mucous membranes, cheilosis, angular stomatitis, glossitis, seborrheic dermatitis, and normocytic anemia associated with pure erythrocyte cytoplasia of the bone marrow.
- ✓ Diseases such as cancer, cardiac disease, and diabetes mellitus are known to precipitate or exacerbate riboflavin deficiency.
- ✓ There is no evidence of adverse effects from excess riboflavin intake. Its apparent nontoxic nature may be due to its limited absorption in the gut and rapid excretion in the urine.

**TABLE 1 Dietary Reference Intakes for Thiamin by Life Stage Group**

Life stage group	DRI values (mg/day)			
	EAR <sup>a</sup>		RDA <sup>b</sup>	
	males	females	males	females
0 through 6 mo				0.2
7 through 12 mo				0.3
1 through 3 y	0.4	0.4	0.5	0.5
4 through 8 y	0.5	0.5	0.6	0.6
9 through 13 y	0.7	0.7	0.9	0.9
14 through 18 y	1.0	0.9	1.2	1.0
19 through 30 y	1.0	0.9	1.2	1.1
31 through 50 y	1.0	0.9	1.2	1.1
51 through 70 y	1.0	0.9	1.2	1.1
> 70 y	1.0	0.9	1.2	1.1
<b>Pregnancy</b>				
≤ 18 y			1.2	1.4
19 through 50 y			1.2	1.4
<b>Lactation</b>				
≤ 18 y			1.2	1.4
19 through 50 y			1.2	1.4

<sup>a</sup> EAR = Estimated Average Requirement.<sup>b</sup> RDA = Recommended Dietary Allowance.<sup>c</sup> AI = Adequate Intake.<sup>d</sup> UL = Tolerable Upper Intake Level. Data were insufficient to set a UL. In the absence of a UL, extra caution may be warranted in consuming levels above the recommended intake.

# THIAMIN

**T**hiamin, also known as vitamin B<sub>1</sub> and aneurin, functions as a coenzyme in the metabolism of carbohydrates and branched-chain amino acids. Only a small percentage of a high dose of thiamin is absorbed, and elevated serum values result in active urinary excretion of the vitamin.

The adult requirements for thiamin are based on the amount of the vitamin needed to achieve and maintain normal erythrocyte transketolase activity, while avoiding excessive thiamin excretion. Data were insufficient to set a Tolerable Upper Intake Level (UL). DRI values are listed by life stage group in Table 1.

Food sources of thiamin include grain products, pork, ham, and fortified meat substitutes. The classic disease of thiamin deficiency is beriberi, which is sometimes seen in developing countries. Severe thiamin deficiency in industrialized nations is often associated with chronic heavy alcohol consumption, where it presents as Wernicke-Korsakoff syndrome. Evidence of adverse effects from excess thiamin consumption is extremely limited. The apparent lack of toxicity of supplemental thiamin may be explained by the rapid decline in absorption that occurs at intakes above 5 mg and the rapid urinary excretion of the vitamin.

## THIAMIN AND THE BODY

### Function

Thiamin (also known as vitamin B<sub>1</sub> and aneurin) was the first B vitamin to be identified. It functions as a coenzyme in the metabolism of carbohydrates and branched-chain amino acids.

### Absorption, Metabolism, Storage, and Excretion

Absorption of thiamin occurs mainly in the jejunum. At low concentrations of thiamin, absorption occurs by an active transport system that involves phosphorylation; at higher concentrations, absorption occurs by passive diffusion. Only a small percentage of a high dose of thiamin is absorbed, and elevated serum values result in active urinary excretion of the vitamin.

Total thiamin content of the adult human is approximately 30 mg, and the biological half-life of the vitamin is in the range of 9 to 18 days. Thiamin is transported in blood in both erythrocytes and plasma and is excreted in the urine.

## DETERMINING DRIS

### Determining Requirements

The adult requirements for thiamin are based on metabolic studies in which urinary thiamin was measured during depletion–repletion, along with the measurement of erythrocyte transketolase activity.

### Special Considerations

*Individuals with increased needs:* People who may have increased needs for thiamin include those being treated with hemodialysis or peritoneal dialysis, individuals with malabsorption syndrome, and women who are carrying more than one fetus or breastfeeding more than one infant. It was concluded that under normal conditions, physical activity does not appear to influence thiamin requirements to a substantial degree. However, those who engage in physically demanding occupations or who spend much time training for active sports may require additional thiamin.

### Criteria for Determining Thiamin Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Human milk content
7 through 12 mo	Extrapolation from adults
1 through 18 y	Extrapolation from adults
19 through 50 y	Maintenance of normal erythrocyte transketolase activity and urinary thiamin excretion
51 through > 70 y	Extrapolation from younger adults

<i>Pregnancy</i>	
≤ 18 y through 50 y	Age-specific requirement + increased energy utilization and growth needs during pregnancy

<i>Lactation</i>	
≤ 18 y through 50 y	Age-specific requirement + energy expenditure of human milk production

### The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Due to insufficient data on adverse effects of excess thiamin consumption, a UL for

thiamin could not be determined. Although no adverse effects have been associated with excess intake of thiamin from food or supplements, this does not mean that there is no potential for adverse effects resulting from high intakes.

## **DIETARY SOURCES**

### **Foods**

According to the Continuing Survey of Food Intakes by Individuals (CSFII, 1994–1996), the greatest contribution to thiamin intake by U.S. adults came from the following enriched, fortified, or whole-grain products: bread and bread products, mixed foods whose main ingredient is grain, and ready-to-eat cereals. Other dietary sources of thiamin included pork and ham products, as well as fortified cereals and fortified meat substitutes.

### **Dietary Supplements**

Approximately 27 percent of adults surveyed took a thiamin-containing supplement, according to the 1986 National Health Interview Survey (NHIS). For adults over age 60 years who took supplements and participated in the Boston Nutritional Status Survey (1981–1984), median supplemental thiamin intakes were 2.4 mg/day for men and 3.2 mg/day for women.

### **Bioavailability**

Data on the bioavailability of thiamin in humans were extremely limited. No adjustments for bioavailability were judged necessary for deriving the EAR for thiamin.

### **Dietary interactions**

This information was not provided at the time the DRI values for this nutrient were set.

## **INADEQUATE INTAKE AND DEFICIENCY**

Early stages of thiamin deficiency may be accompanied by nonspecific signs and symptoms that may be overlooked or easily misinterpreted. Signs and symptoms of thiamine deficiency include the following:

- Anorexia
- Weight loss

- Mental changes such as apathy, decreased short-term memory, confusion, and irritability
- Muscle weakness
- Cardiovascular effects such as enlarged heart

In developing nations, thiamin deficiency often manifests as beriberi. In “wet beriberi,” edema occurs. In “dry beriberi,” muscle wasting is obvious. In infants, cardiac failure may occur rather suddenly.

Severe thiamin deficiency in industrialized countries is likely to be related to heavy alcohol consumption with limited food consumption, where it presents as Wernicke-Korsakoff syndrome. In severe cases of this syndrome, renal and cardiovascular complications can become life threatening.

## EXCESS INTAKE

There are no reports of adverse effects from the consumption of excess thiamin from food or supplements. Supplements that contain up to 50 mg/day of thiamin are widely available without a prescription, but the possible occurrence of adverse effects resulting from this level or more of intake has not been studied systematically.

The apparent lack of toxicity of supplemental thiamin may be explained by the rapid decline in absorption that occurs at intakes above 5 mg and the rapid urinary excretion of the vitamin.

## KEY POINTS FOR THIAMIN

- ✓ Thiamin (also known as vitamin B<sub>1</sub> and aneurin) functions as a coenzyme in the metabolism of carbohydrates and branched-chain amino acids.
- ✓ The adult requirements for thiamin are based on the amount of the vitamin needed to achieve and maintain normal erythrocyte transketolase activity, while avoiding excessive thiamin excretion.
- ✓ Data were insufficient to set a UL.
- ✓ Food sources of thiamin include grain products, pork, ham, and fortified meat substitutes.
- ✓ The classic disease of thiamin deficiency is beriberi, which is sometimes seen in developing countries.
- ✓ Severe thiamin deficiency in industrialized nations is often associated with chronic heavy alcohol consumption and presents as Wernicke-Korsakoff syndrome.
- ✓ There are no reports of adverse effects from excess thiamin consumption from food or supplements.
- ✓ The apparent lack of toxicity of supplemental thiamin may be explained by the rapid decline in absorption that occurs at intakes above 5 mg and the rapid urinary excretion of the vitamin.

**TABLE 1 Dietary Reference Intakes for Calcium by Life Stage Group**

<b>Life stage group<sup>c</sup></b>	<b>DRI values (mg/day)</b>	
	<b>AI<sup>a</sup></b>	<b>UL<sup>b</sup></b>
<b>Life stage group<sup>c</sup></b>		
0 through 6 mo	210	ND <sup>d</sup>
7 through 12 mo	270	ND
1 through 3 y	500	2,500
4 through 8 y	800	2,500
9 through 13 y	1,300	2,500
14 through 18 y	1,300	2,500
19 through 30 y	1,000	2,500
31 through 50 y	1,000	2,500
51 through 70 y	1,200	2,500
> 70 y	1,200	2,500
<b>Pregnancy</b>		
≤ 18 y	1,300	2,500
19 through 50 y	1,000	2,500
<b>Lactation</b>		
≤ 18 y	1,300	2,500
19 through 50 y	1,000	2,500

<sup>a</sup> AI = Adequate Intake.<sup>b</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.<sup>c</sup> All groups except Pregnancy and Lactation represent males and females.<sup>d</sup> ND = Not determinable. This value is not determinable due to the lack of data of adverse effects in this age group and concern regarding the lack of ability to handle excess amounts. Source of intake should only be from food to prevent high levels of intake.

# CALCIUM

**C**alcium plays a key role in bone health. In fact, more than 99 percent of total body calcium is found in the bones and teeth. Calcium is also involved in vascular, neuromuscular, and glandular functions in the body.

Since data were inadequate to determine an Estimated Average Requirement (EAR) and thus calculate a Recommended Dietary Allowance (RDA) for calcium, an Adequate Intake (AI) was instead developed. The AIs for calcium are based on desirable rates of calcium retention (as determined from balance studies), factorial estimates of requirements, and limited data on changes in bone mineral density (BMD) and bone mineral content (BMC). The Tolerable Upper Intake Level (UL) is based on milk-alkali syndrome as the critical endpoint. DRI values are listed by life stage group in Table 1.

Foods rich in calcium include milk, yogurt, cheese, calcium-set tofu, calcium-fortified orange juice, Chinese cabbage, kale, and broccoli. Calcium may be poorly absorbed from foods that are rich in oxalic acid or phytic acid. The effects of calcium deficiency include osteopenia, osteoporosis, and an increased risk of bone fractures. The effects of excess intake include kidney stones, hypercalcemia with renal insufficiency, and a decreased absorption of certain minerals.

## CALCIUM AND THE BODY

### Function

Calcium's primary role in the body is to form the structure of bones and teeth. More than 99 percent of total body calcium is stored in the skeleton, where it exists primarily in the form of hydroxyapatite. The remainder is found in the blood, extracellular fluid, muscle, and other tissues, where it is involved in vascular contraction and vasodilation, muscle contraction, neural transmission, and glandular secretion.

### Absorption, Metabolism, Storage, and Excretion

Calcium is absorbed by active transport and passive diffusion across the intestinal mucosa. Active transport of calcium into the intestine requires the active form of vitamin D (1,25-dihydroxyvitamin D) and accounts for most of the

absorption of calcium at low and moderate intake levels, as well as at times of great need, such as growth, pregnancy, or lactation. Passive diffusion becomes more important at high calcium intakes.

As calcium intake decreases, the efficiency of calcium absorption increases (and vice versa). However, this increased efficiency of calcium absorption, or fractional calcium absorption, is generally not sufficient to offset the loss of absorbed calcium that occurs with a decrease in dietary calcium intake. Calcium absorption declines with aging in both men and women. Calcium is excreted in the urine and feces.

## DETERMINING DRIS

### Determining Requirements

There is no biochemical assay that reflects calcium nutritional status. Except in extreme circumstances, such as severe malnutrition or hyperparathyroidism, circulating levels of blood calcium can actually be normal during chronic calcium deficiency because calcium is resorbed from the skeleton to maintain a normal circulating concentration. Since data were inadequate to determine an EAR and thus calculate an RDA for calcium, an AI was instead developed. Therefore, the adult AIs for calcium are based on desirable rates of calcium retention (as determined from balance studies), factorial estimates of requirements, and limited data on changes in bone mineral density (BMD) and bone mineral content (BMC). These indicators were chosen as reasonable surrogate markers to reflect changes in skeletal calcium content and, therefore, calcium retention.

The AI represents the approximate calcium intake that appears sufficient to maintain calcium nutriture, while recognizing that lower intakes may be adequate for some. However, this evaluation must await additional studies on calcium balance over broad ranges of intakes or long-term measures of calcium sufficiency, or both.

During pregnancy, the maternal skeleton is not used as a reserve for fetal calcium needs. Calcium-regulating hormones adjust maternal calcium absorption efficiency so that the AI does not have to be increased during pregnancy. Although increased dietary calcium intake will not prevent the loss of calcium from the maternal skeleton during lactation, the calcium that is lost appears to be regained following weaning. Thus, the AI for calcium in lactating women is the same as that of nonlactating women.

## Criteria for Determining Calcium Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion<sup>a</sup></i>
0 through 6 mo	Human milk content
7 through 12 mo	Human milk + solid food
1 through 3 y	Extrapolation of data on desirable calcium retention from 4 through 8 year olds
4 through 8 y	Calcium accretion / $\Delta$ BMC / calcium balance
9 through 18 y	Desirable calcium retention / factorial / $\Delta$ BMC
19 through 30 y	Desirable calcium retention / factorial
31 through 50 y	Calcium balance
51 through 70 y	Desirable calcium retention / factorial / $\Delta$ BMD
> 70 y	Extrapolation of desirable calcium retention from 51 through 70 year age group / $\Delta$ BMD / fracture rate

### *Pregnancy*

$\leq$ 18 y through 50 y	Bone mineral mass
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### *Lactation*

$\leq$ 18 y through 50 y	Bone mineral mass
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<sup>a</sup>  $\Delta$  BMC is the change in bone mineral mass.  $\Delta$  BMD is the change in bone mineral density.

## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Members of the general population should not routinely exceed the UL. The UL value for calcium is based on milk-alkali syndrome (characterized by hypercalcemia and renal insufficiency) as the critical endpoint and is derived from case studies of people who consumed large doses of calcium, mostly in the form of supplements. The UL for calcium represents total intake from food, water, and supplements.

Although the 95th percentile of daily intake did not exceed the UL for any age group in the Continuing Survey of Food Intakes by Individuals (CSFII, 1994–1996), people with very high caloric intakes, especially if intakes of dairy products are also high, may exceed the UL of 2,500 mg/day. Although users of dietary supplements of any kind tend to also have higher intakes of calcium from food than nonusers, it is unlikely that the same person would fall at the upper end of both ranges. Prevalence of usual intakes, from foods plus supplements, above the UL is well below 5 percent, even for age groups with relatively

high intakes. However, with calcium-fortified foods becoming more common, it is important to maintain surveillance of these foods in the marketplace and to monitor their impact on calcium intake.

## DIETARY SOURCES

### Foods

Dairy products, such as milk, yogurt, and cheese, are the most calcium-rich foods in Western diets. Other calcium-rich foods include calcium-set tofu, calcium-fortified plant-based beverages, Chinese cabbage, kale, calcium-fortified fruit juices, and broccoli.

Although grains are not particularly rich in calcium, the use of calcium-containing additives in these foods accounts for a substantial proportion of the calcium ingested by people who consume a large amount of grains. Among Mexican Americans, corn tortillas are the second most important source of calcium, after milk. White bread is the second most important source among Puerto Rican adults.

### Dietary Supplements

According to U.S. data from the 1986 National Health Interview Survey (NHIS), 14 percent of men, 25 percent of women, and 7.5 percent of children 2 to 6 years of age took supplements that contained calcium. Data from 11,643 adults who participated in the 1992 NHIS showed that calcium intakes were higher for men and women who took daily supplements with calcium (of any kind) compared with those who seldom or never took supplements. (This difference was only statistically significant for women.) However, adults who took calcium supplements did not have higher intakes of food calcium.

### Bioavailability

With regard to food sources of calcium, bioavailability is generally less important than the overall calcium content of the food. Calcium absorption efficiency is fairly similar for most foods, including milk products and grains, both of which represent major sources of calcium in North American diets. Calcium may be poorly absorbed from foods rich in oxalic acid (such as spinach, sweet potatoes, rhubarb, and beans) and from foods rich in phytic acid (such as unleavened bread, raw beans, seeds, nuts, grains, and soy isolates). Although soybeans contain large amounts of phytic acid, calcium absorption from these legumes is relatively high compared with other foods rich in phytic acid. Compared with calcium absorption from milk, calcium absorption from dried beans is about half; from spinach it is about one-tenth.

As for dietary supplements, the bioavailability of calcium depends on the size of the dose, the form, and the presence or absence of a meal, with the former improving absorption. Tablet disintegration of supplements is crucial, and the efficiency of calcium absorption from supplements is greatest when calcium is taken in doses of 500 mg or less.

## Dietary Interactions

There is evidence that calcium may interact with certain other nutrients and dietary substances (see Table 2).

## INADEQUATE INTAKE AND DEFICIENCY

Chronic calcium deficiency can result from inadequate intake or poor intestinal absorption. During chronic calcium deficiency, the mineral is resorbed from the skeleton to maintain a normal circulating concentration, thereby compromising bone health. Consequently, chronic calcium deficiency is one of several important causes of reduced bone mass and osteoporosis. In the United States each year, approximately 1.5 million fractures are associated with osteoporosis; in Canada in 1993, there were approximately 76,000 such fractures. The potential effects of calcium deficiency include the following:

- Osteopenia (lower than normal bone-mineral density)
- Osteoporosis (very low bone-mineral density)
- An increased risk of fractures

## Special Considerations

**Amenorrhea:** Induced by exercise or anorexia nervosa, amenorrhea results in reduced calcium retention and net calcium absorption, respectively, along with lower bone mass.

**Menopause:** Decreased estrogen production at menopause is associated with accelerated bone loss for about 5 years. Lower levels of estrogen are accompanied by decreased calcium absorption efficiency and increased rates of bone turnover. However, available evidence suggests that the calcium intake requirement for women does not appear to change acutely with menopause.

**Lactose intolerance:** People with lactose intolerance who avoid dairy products and do not consume calcium-rich lactose-free foods may be at risk for calcium deficiency. Although lactose intolerance may influence intake, lactose-intolerant individuals absorb calcium normally from milk.

**TABLE 2 Potential Interactions with Other Dietary Substances**

<i>Substance</i>	<i>Potential Interaction</i>	<i>Notes</i>
<b>SUBSTANCES THAT AFFECT CALCIUM</b>		
Caffeine	Caffeine may increase urinary loss of calcium and decrease calcium absorption. These effects are modest.	Accelerated bone loss associated with caffeine consumption has been seen only in postmenopausal women with low calcium intakes. Available evidence does not warrant different calcium intake recommendations for people with different caffeine intakes.
Magnesium	Magnesium deficiency may cause hypocalcemia.	In general, magnesium deficiency must become moderate to severe before symptomatic hypocalcemia develops. However, a 3-week study of dietary-induced experimental magnesium depletion in humans demonstrated that even a mild degree of magnesium depletion may result in a significant decrease in serum calcium concentration.
Oxalic acid	Oxalic acid may inhibit calcium absorption.	Foods rich in oxalic acid include spinach, sweet potatoes, rhubarb, and beans.
Phosphorus	Excess intake of phosphorus may interfere with calcium absorption.	This is less likely to pose a problem if calcium intake is adequate. Foods rich in phosphorus include dairy foods, colas or other soft drinks, and meats.
Phytic acid	Phytic acid may inhibit calcium absorption.	Foods rich in phytic acid include unleavened bread, raw beans, seeds, nuts, grains, and soy isolates.
Protein	Protein may increase urinary loss of calcium.	The effect of dietary protein on calcium retention is controversial. Available evidence does not warrant adjusting calcium intake recommendations based on dietary protein intake.
Sodium	Moderate and high sodium intake may increase urinary loss of calcium.	High sodium chloride (salt) intake results in an increased loss of urinary calcium. There is indirect evidence that dietary sodium chloride has a negative effect on the skeleton. However, direct evidence linking sodium intake with bone loss and fracture is lacking. Available evidence does not warrant different calcium intake requirements for individuals based on their salt consumption.

**TABLE 2 Continued**

<i>Substance</i>	<i>Potential Interaction</i>	<i>Notes</i>
<b>CALCIUM AFFECTING OTHER SUBSTANCES</b>		
Iron	Calcium may decrease iron absorption.	Calcium inhibits iron absorption in a dose-dependent and dose-saturable fashion. However, the available human data fail to show cases of iron deficiency or even reduced iron stores as a result of calcium intake.
Magnesium	High intakes of calcium may decrease magnesium absorption.	Most human studies of the effects of dietary calcium on magnesium absorption have shown no effect, but one has reported decreased magnesium absorption rates. Calcium intakes of as much as 2,000 mg/day (in adult men) did not affect magnesium absorption. Calcium intakes in excess of 2,600 mg/day have been reported to decrease magnesium balance. Several studies have found that high sodium and calcium intake may result in increased renal magnesium excretion. Overall, at the dietary levels recommended in this publication, the interaction of magnesium with calcium is not of concern.
Phosphorus	Pharmacological doses of calcium carbonate may interfere with phosphorus absorption.	Calcium in the normal adult intake range is not likely to pose a problem for phosphorus absorption.
Zinc	Calcium may decrease zinc absorption.	Dietary calcium may decrease zinc absorption, but there is not yet definitive evidence. Human studies have found that calcium phosphate (1,360 mg/day of calcium) decreased zinc absorption, whereas calcium in the form of a citrate–malate complex (1,000 mg/day of calcium) had no statistically significant effect on zinc absorption. Data suggest that consuming a calcium-rich diet does not lower zinc absorption in people who consume adequate zinc. The effect of calcium on zinc absorption in people with low zinc intakes has not been extensively studied.

**Vegetarian diets:** Vegetarian diets, which may have relatively high contents of oxalic acid and phytic acid (see Table 2), may reduce calcium bioavailability.

**Mothers who breastfeed multiple infants:** Due to the increased milk production of a mother while breastfeeding multiple infants, increased intakes of calcium during lactation, as with magnesium, should be considered.

## EXCESS INTAKE

The available data on the adverse effects of excess calcium intake in humans have primarily come from the study of nutrient supplements. Of the many possible adverse effects of excessive calcium intake, the three most widely studied and biologically important are the following:

- Kidney stones
- Hypercalcemia and renal insufficiency (also known as milk-alkali syndrome)
- The interaction of calcium with absorption of other minerals (see Table 2)

Although these are not the only adverse effects associated with excess calcium intake, they do constitute the vast majority of reported effects.

## Special Considerations

**Individuals susceptible to adverse effects:** Some people may be at greater risk for adverse effects related to calcium. They include those with renal failure, those who take thiazide diuretics, and those with low intakes of minerals that interact with calcium (see Table 2).

## KEY POINTS FOR CALCIUM

- ✓ Calcium plays a key role in bone health. In fact, more than 99 percent of total body calcium found in the teeth and bones.
- ✓ As calcium intake decreases, the efficiency of calcium absorption increases (and vice versa). However, this increased efficiency of calcium absorption is generally not sufficient to offset the loss of absorbed calcium that occurs with a decrease in dietary calcium intake.
- ✓ There is no biochemical assay that reflects calcium nutritional status. During chronic calcium deficiency, the mineral is resorbed from the skeleton to keep the circulating concentration normal, thereby compromising bone health.
- ✓ Since data were inadequate to determine an EAR and thus calculate an RDA for calcium, an AI was instead developed.
- ✓ The adult AIs for calcium are based on desirable rates of calcium retention (as determined from balance studies), factorial estimates of requirements, and limited data on changes in bone mineral density (BMD) and bone mineral content (BMC). The UL is based on milk-alkali syndrome as the critical endpoint.
- ✓ Calcium absorption declines with aging in both men and women.
- ✓ Although increased dietary calcium intake will not prevent the loss of calcium from the maternal skeleton during lactation, the calcium that is lost appears to be regained following weaning. Thus, the AI for calcium in lactating women is the same as that of nonlactating women.
- ✓ The UL value is derived from case studies of people who consumed large doses of calcium, mostly in the form of supplements.
- ✓ Foods rich in calcium include milk, yogurt, cheese, calcium-set tofu, calcium-fortified orange juice, Chinese cabbage, kale, and broccoli. Calcium may be poorly absorbed from foods that are rich in oxalic acid or phytic acid.
- ✓ Calcium deficiency can result from inadequate intake or poor intestinal absorption and can cause osteopenia, osteoporosis, and an increased risk of fractures.
- ✓ Excessive calcium intake can cause kidney stones, hypercalcemia with renal insufficiency, and decreased absorption of certain other minerals.

**TABLE 1 Dietary Reference Intakes for Chromium by Life Stage Group**

Life stage group	DRI values ( $\mu\text{g}/\text{day}$ )	
	AI <sup>a</sup>	
	males	females
0 through 6 mo	0.2	0.2
7 through 12 mo	5.5	5.5
1 through 3 y	11	11
4 through 8 y	15	15
9 through 13 y	25	21
14 through 18 y	35	24
19 through 30 y	35	25
31 through 50 y	35	25
51 through 70 y	30	20
> 70 y	30	20
<b>Pregnancy</b>		
≤ 18 y		29
19 through 50 y		30
<b>Lactation</b>		
≤ 18 y		44
19 through 50 y		45

<sup>a</sup> AI = Adequate Intake.<sup>b</sup> UL = Tolerable Upper Intake Level. Data were insufficient to set a UL. In the absence of a UL, extra caution may be warranted in consuming levels above the recommended intake.

# CHROMIUM

**C**romium potentiates the action of insulin and may improve glucose tolerance. The form of chromium found in foods is trivalent chromium, or chromium III, which is the form discussed in this chapter.

Since data were insufficient to set an Estimated Average Requirement (EAR) and thus calculate a Recommended Dietary Allowance (RDA) for chromium, an Adequate Intake (AI) was instead developed. Data were insufficient to set a Tolerable Upper Intake Level (UL). The AIs for chromium are based on estimated intakes of chromium derived from the average amount of chromium/1,000 kcal of balanced diets and average energy intake. DRI values are listed by life stage group in Table 1.

Rich sources of chromium include cereals, particularly some high-bran cereals. Whole grains have more chromium than do refined grains. Some beers and wines are also high in chromium. The clinical signs and symptoms of deficiency include impaired plasma glucose utilization and an increased need for insulin. Few serious adverse effects have been associated with excess intake of chromium from foods.

## CHROMIUM AND THE BODY

### Function

The form of chromium found in foods is trivalent chromium, or chromium III, which is the form discussed in this chapter. (Another form, hexavalent chromium, or chromium VI, is found in the environment as a chemical by-product and has been shown to be carcinogenic when inhaled.)

Dietary chromium potentiates the action of insulin. Early studies identified chromium as the element that restores glucose tolerance in rats. A number of studies have demonstrated beneficial effects of chromium on circulating glucose, insulin, and lipids, although the potential mechanisms of action are still being investigated. Progress in the field has been limited by the difficulty in producing chromium deficiency in animals and also by the lack of a simple, widely accepted method for identifying subjects who are chromium depleted and, thus, who would be expected to respond to chromium supplementation.

## Absorption, Metabolism, Storage, and Excretion

Chromium absorption by the body is generally low, with absorption estimates ranging from 0.4 to 2.5 percent. Some studies suggest that chromium absorption increases with exercise, but further research is necessary. Chromium is stored in the liver, spleen, soft tissue, and bone. Most absorbed chromium is excreted rapidly in the urine, and most unabsorbed chromium is excreted in the feces.

## DETERMINING DRIS

### Determining Requirements

Since data were insufficient to set an EAR and thus calculate an RDA for chromium, an AI was instead developed. The AIs for chromium are based on estimated intakes of chromium derived from the average amount of chromium/1,000 kcal of balanced diets and average energy intake taken from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994).

### Criteria for Determining Chromium Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Average chromium intake from human milk
7 through 12 mo	Average chromium intake from human milk and complementary foods
1 through 18 y	Extrapolation from adult AI
19 through > 70 y	Average chromium intake based on the chromium content of foods/1,000 kcal and average energy intake <sup>a</sup>
<i>Pregnancy</i>	
≤ 18 y	Extrapolation from adolescent female AI based on body weight
19 through 50 y	Extrapolation from adult female AI based on body weight
<i>Lactation</i>	
≤ 18 y	Adolescent female intake plus average amount of chromium secreted in human milk
19 through 50 y	Adult female intake plus average amount of chromium secreted in human milk

<sup>a</sup> The average chromium content in well-balanced diets was determined to be 13.4 µg/1,000 kcal, and the average energy intake for adults was obtained from NHANES III.

## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Data were insufficient to set a UL for chromium. No adverse effects have been convincingly associated with excess intake from food or supplements, but this does not mean that there is no potential for adverse effects resulting from high intakes. Since data were limited, caution may be warranted.

## DIETARY SOURCES

### Foods

Chromium is widely distributed throughout the food supply, but many foods contribute less than 1–2 µg per serving. Determining the chromium content of foods requires rigorous contamination control because standard methods of sample preparation contribute substantial amounts of chromium to the foods being analyzed. In addition, the chromium content of individual foods widely varies and may be influenced by geochemical factors. Consequently, dietary chromium intakes cannot be determined using any existing databases.

The chromium content of foods may increase or decrease with processing. Refined grains have been shown to have less chromium than whole grains; conversely, acidic foods have been shown to gain chromium content during processing that involves the use of stainless steel containers or utensils.

Cereals tend to be a significant contributor of chromium to diets. High-bran cereals are generally, but not always, high in chromium. Most dairy products are low in chromium and provide less than 0.6 µg per serving. Meats, poultry, and fish generally contribute 1–2 µg per serving, but processed meats are higher in chromium and may acquire it from exogenous sources. Chromium concentrations of fruits and vegetables highly vary. Some brands of beer and some French wines, particularly red wines, are high in chromium. Wines have not been analyzed for chromium in the United States.

### Dietary Supplements

According to U.S. data from the 1986 National Health Interview Survey (NHIS), 8 percent of adults consumed supplements that contained chromium. Based on data from NHANES III, the median supplemental intake of chromium was 23 µg/day for those who took supplements, an amount similar to the average dietary chromium intake.

## Bioavailability

Most chromium compounds are soluble at the pH of the stomach, but less soluble hydroxides may form as pH is increased. The environment of the gastrointestinal tract and ligands provided by food and supplements are important for mineral absorption. Several dietary factors may affect the bioavailability of chromium (see “Dietary Interactions”).

## Dietary Interactions

There is evidence that chromium may interact with certain other nutrients and dietary substances (see Table 2).

**TABLE 2 Potential Interactions with Other Dietary Substances**

Substance	Potential Interaction	Notes
<b>SUBSTANCES THAT AFFECT CHROMIUM</b>		
Vitamin C	Vitamin C may enhance the absorption of chromium.	In one study, plasma chromium concentrations in three women were consistently higher when they were given 1 mg chromium as CrCl <sub>3</sub> with 100 mg ascorbic acid than when given chromium without ascorbic acid.
Simple sugars	Diets high in simple sugars (35 percent of total kcal) may increase urinary excretion of chromium.	Urinary chromium excretion was found to be related to the insulinogenic properties of carbohydrates.
Phytate	Phytate may decrease chromium absorption.	In rats, phytate at high levels had adverse effects on chromium absorption, but lower levels of phytate did not have detrimental effects on chromium status.
Medications	Antacids and other drugs that alter stomach acidity or gastrointestinal prostaglandins may affect chromium absorption.	When rats were dosed with physiological doses of chromium and prostaglandin inhibitors, such as aspirin, chromium levels in the blood, tissues, and urine markedly increased. Medications, such as antacids, reduced chromium absorption and retention.

## INADEQUATE INTAKE AND DEFICIENCY

Chromium deficiency has been reported in three patients who did not receive supplemental chromium in their total parenteral nutrition (TPN) solutions. Their clinical signs and symptoms included unexplained weight loss, peripheral neuropathy, impaired plasma glucose removal, increased insulin requirements, elevated plasma free fatty acids, and low respiratory quotient.

Because chromium is known to potentiate the action of insulin and because these chromium-deficient TPN patients were observed to have impaired glucose utilization and increased insulin requirements, it has been hypothesized that poor chromium status contributes to the incidence of impaired glucose tolerance and Type II diabetes (prevalence of impaired glucose tolerance was 15.8 percent in adults aged 40 to 74 years in NHANES III). However, addressing this hypothesis is difficult because of the current lack of information about the variability in dietary chromium intakes and because there is not a simple, widely acceptable method that identifies potential study subjects with poor chromium status.

## EXCESS INTAKE

Ingested chromium has a low level of toxicity that is partially due to its very poor absorption. Although no adverse effects have been convincingly associated with the excess intake of chromium from food or supplements, this does not mean that the potential for adverse effects does not exist. Because data on the adverse effects of chromium intake were limited, caution may be warranted.

## Special Considerations

***Individuals susceptible to adverse effects:*** Data suggest that people with preexisting renal and liver disease may be particularly susceptible to the adverse effects of excess chromium. These individuals should be particularly careful to limit their chromium intake.



## KEY POINTS FOR CHROMIUM

- ✓ Chromium potentiates the action of insulin and may improve glucose tolerance.
- ✓ Since data were insufficient to set an EAR and thus calculate an RDA for chromium, an AI was instead developed.
- ✓ The AIs for chromium are based on estimated intakes of chromium derived from the average amount of chromium/1,000 kcal of balanced diets and average energy intake.
- ✓ Data were insufficient to set a UL.
- ✓ Although no adverse effects have been convincingly associated with the excess intake of chromium from food or supplements, this does not mean that the potential for adverse effects does not exist.
- ✓ The form of chromium found in the diet is trivalent chromium, or chromium III. Another form, hexavalent chromium, or chromium VI, is found in the environment as a chemical by-product and has been shown to be carcinogenic when inhaled.
- ✓ Dietary chromium intakes cannot be determined using any existing databases.
- ✓ Rich sources of chromium include cereals, particularly all-bran cereals. Whole grains have more chromium than do refined grains.
- ✓ Because chromium is known to potentiate the action of insulin and because some chromium-deficient TPN patients have been observed to have impaired glucose utilization and increased insulin requirements, it has been hypothesized that poor chromium status contributes to the incidence of impaired glucose tolerance and Type II diabetes. The potential relationship between chromium and Type II diabetes remains under study.
- ✓ Ingested chromium has a low level of toxicity that is partially due to its very poor absorption.
- ✓ Data suggest that people with preexisting renal and liver disease may be particularly susceptible to the adverse effects of excess chromium.

**TABLE 1 Dietary Reference Intakes for Copper by Life Stage Group**

Life stage group	DRI values (μg/day)					
	EAR <sup>a</sup>		RDA <sup>b</sup>		AI <sup>c</sup>	UL <sup>d</sup>
	males	females	males	females		
0 through 6 mo					200	ND <sup>e</sup>
7 through 12 mo					220	ND
1 through 3 y	260	260	340	340		1,000
4 through 8 y	340	340	440	440		3,000
9 through 13 y	540	540	700	700		5,000
14 through 18 y	685	685	890	890		8,000
19 through 30 y	700	700	900	900		10,000
31 through 50 y	700	700	900	900		10,000
51 through 70 y	700	700	900	900		10,000
> 70 y	700	700	900	900		10,000
<b>Pregnancy</b>						
≤ 18 y		785		1,000		8,000
19 through 50 y		800		1,000		10,000
<b>Lactation</b>						
≤ 18 y		985		1,300		8,000
19 through 50 y		1,000		1,300		10,000

<sup>a</sup> EAR = Estimated Average Requirement.<sup>b</sup> RDA = Recommended Dietary Allowance.<sup>c</sup> AI = Adequate Intake.<sup>d</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.<sup>e</sup> ND = Not determinable. This value is not determinable due to the lack of data of adverse effects in this age group and concern regarding the lack of ability to handle excess amounts. Source of intake should only be from food to prevent high levels of intake.

# COPPER

**C**opper functions as a component of several metalloenzymes, which act as oxidases in the reduction of molecular oxygen. The activities of some copper metalloenzymes have been shown to decrease in human copper depletion.

The requirements for copper are based on a combination of indicators, including plasma copper and ceruloplasmin concentrations, erythrocyte superoxide dismutase activity, and platelet copper concentration in controlled human depletion/repletion studies. The Tolerable Upper Intake Level (UL) is based on protection from liver damage as the critical adverse event. DRI values are listed by life stage group in Table 1.

Sources of copper include organ meats, seafood, nuts, seeds, wheat-bran cereals, and whole-grain products. Frank copper deficiency in humans is rare. Symptoms associated with deficiency include normocytic, hypochromic anemia; leucopenia; and neutropenia; and, in copper-deficient infants and growing children, osteoporosis. Copper toxicity is generally rare except in individuals genetically susceptible to the increased risk of adverse effects from excess copper intake.

## COPPER AND THE BODY

### Function

Copper functions as a component of several metalloenzymes, which act as oxidases in the reduction of molecular oxygen. Some of the principal copper metalloenzymes found in humans include the following:

- Diamine oxidase, which inactivates the histamine released during allergic reactions
- Monoamine oxidase (MAO), which is important in serotonin degradation and in the metabolism of epinephrine, norepinephrine, and dopamine; MAO inhibitors are used as antidepressant drugs
- Ferroxidases, which are copper enzymes found in the plasma and function in ferrous iron oxidation that is needed to bind iron to transferrin
- Dopamine  $\beta$ -monooxygenase, which uses ascorbate, copper, and  $O_2$  to convert dopamine to norepinephrine

- Copper/zinc superoxide dismutase (Cu/Zn SOD), which defends against oxidative damage; mutations in the Cu/Zn SOD gene, which alter the protein's redox behavior, produce amyotrophic lateral sclerosis (Lou Gehrig's disease)

## Absorption, Metabolism, Storage, and Excretion

Copper absorption primarily occurs in the small intestine via both saturable-mediated and nonsaturable-nonmediated mechanisms. The Menkes P-type ATPase (MNK; ATP7A) is believed to be responsible for copper trafficking to the secretory pathway for efflux from cells, including enterocytes. A defective MNK gene causes Menkes' disease, which is characterized by reduced copper absorption and placental copper transport. The extent of copper absorption varies with dietary copper intake; it ranges from more than 50 percent at an intake of less than 1 mg/day to less than 20 percent at intakes above 5 mg/day. About 35 percent of a 2 mg/day intake is absorbed and transported via the portal vein to the liver, bound to albumin, for uptake by liver parenchymal cells.

Nearly two-thirds of body copper content is found in the skeleton and muscle, but the liver appears to be the key site in maintaining plasma copper concentration. Biliary copper excretion is adjusted to maintain balance. Copper is released via the plasma to extrahepatic sites, where up to 95 percent of the copper is bound to ceruloplasmin.

Urinary copper excretion is normally very low (< 0.1 mg/day) over a wide range of dietary intakes. As with other trace elements, renal dysfunction can lead to increased urinary losses.

## DETERMINING DRIS

### Determining Requirements

The primary criterion used to estimate the requirements for copper is based on a combination of indicators, including plasma copper and ceruloplasmin concentrations, erythrocyte superoxide dismutase activity, and platelet copper concentration in controlled human depletion/repletion studies.

### Criteria for Determining Copper Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Average copper intake from human milk
7 through 12 mo	Average copper intake from human milk and complementary foods

1 through 18 y	Extrapolation from adult EAR
19 through 50 y	Plasma copper, serum ceruloplasmin, and platelet copper concentrations and erythrocyte superoxide dismutase activity
51 through > 70 y	Extrapolation from 19 through 50 y
<i>Pregnancy</i>	
≤ 18 y	Adolescent female EAR plus fetal accumulation of copper
19 through 50 y	Adult female EAR plus fetal accumulation of copper
<i>Lactation</i>	
≤ 18 y	Adolescent female EAR plus average amount of copper secreted in human milk
19 through 50 y	Adult female EAR plus average amount of copper secreted in human milk

## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Members of the general population should not routinely exceed the UL. The UL for copper is based on liver damage as the critical endpoint and represents intake from food, water, and supplements.

Based on data from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994), the highest median intakes of copper from the diet and supplements for any gender and life stage group were approximately 1,700 µg/day for men aged 19 through 50 years and approximately 1,900 µg/day for lactating women. The highest reported intake from food and supplements at the 99th percentile was 4,700 µg/day, also in lactating women. The next highest reported intake at the 99th percentile was 4,600 µg/day in pregnant women and men aged 50 through 70 years. The risk of adverse effects resulting from excess intake of copper from food, water, and supplements appears to be low in the highest intakes noted above.

## DIETARY SOURCES

### Foods

Copper is widely distributed in foods. The accumulation of copper in plants is not affected by the copper content of the soil in which they are grown. Major contributors of copper include organ meats, seafood, nuts, and seeds. Wheat-bran cereals and whole-grain products are also sources of copper. Foods that contribute substantial amounts of copper to the U.S. diet include those high in

copper, such as organ meats, grains, and cocoa products, as well as foods relatively low in copper, but which are consumed in substantial amounts, such as tea, potatoes, milk, and chicken.

## Dietary Supplements

According to U.S. data from the 1986 National Health Interview Survey (NHIS) approximately 15 percent of adults in the United States consumed supplements that contained copper. Based on data from the NHANES III, the median dietary plus supplemental copper intake was similar to the intake from food alone. The mean intake of dietary and supplemental copper (1.3–2.2 mg/day) was approximately 0.3–0.5 mg/day greater for men and women than the mean intake from food (1.0–1.7 mg/day).

## Bioavailability

The bioavailability of copper is markedly influenced by the amount of copper in the diet, rather than by the diet's composition. Bioavailability ranges from 75 percent of dietary copper absorbed by the body when the diet contains only 400 µg/day to 12 percent absorbed when the diet contains 7.5 mg/day. The absolute amount of copper absorbed is higher with increased intake. In addition, the excretion of copper into the gastrointestinal tract regulates copper retention. As more copper is absorbed, turnover is faster and more copper is excreted into the gastrointestinal tract. This excretion is probably the primary point of regulation of total body copper. This efficient homeostatic regulation of absorption and retention helps protect against copper deficiency and toxicity.

## Dietary Interactions

Copper homeostasis is affected by interactions among zinc, copper, iron, and molybdenum. In addition, the level of dietary protein, interacting cations, and sulfate all can influence the absorption and utilization of copper. Some evidence that copper may interact with certain nutrients and dietary substances appears in Table 2.

## INADEQUATE INTAKE AND DEFICIENCY

Frank copper deficiency in humans is rare, but it has been found in a number of special conditions. It has also been observed in premature infants fed milk formulas deficient in copper, infants recovering from malnutrition associated with chronic diarrhea and fed cow milk, and patients with prolonged total

**TABLE 2 Potential Interactions with Other Dietary Substances**

<i>Substance</i>	<i>Potential Interaction</i>	<i>Notes</i>
<b>SUBSTANCES THAT AFFECT COPPER</b>		
Zinc	Zinc (at very high intakes) may decrease copper absorption.	This usually only occurs at intakes well in excess of the amount of zinc normally found in the diet.
Iron	High iron may interfere with copper absorption in infants.	Infants fed a formula that contained low concentrations of iron absorbed more copper than infants who consumed the same formula with a higher iron concentration. Such an interaction has been reported to produce reduced copper status in infants.

parenteral nutrition (TPN). In these cases, serum copper and ceruloplasmin concentrations were as low as 0.5 μmol/L and 35 mg/L, respectively, compared with reported normal ranges of 10–25 μmol/L for serum copper concentration and 180–400 mg/L for ceruloplasmin concentration. Supplementation with copper resulted in rapid increases in serum copper and ceruloplasmin concentrations. The symptoms associated with copper deficiency include the following:

- Normocytic, hypochromic anemia
- Leukopenia
- Neutropenia
- Osteoporosis (in copper-deficient infants and growing children)

## **EXCESS INTAKE**

The long-term toxicity of copper has not been well studied in humans, but it is rare in normal populations without some hereditary defect in copper homeostasis. Potential adverse effects have been associated with excess intake of soluble copper salts in both supplements and drinking water, although most have only been reported based on acute and not chronic intakes. The consumption of drinking water or other beverages containing high levels of copper has resulted mostly in gastrointestinal illness, including abdominal pain, cramps, nausea, diarrhea, and vomiting.

## Special Considerations

*Individuals susceptible to adverse effects:* Liver damage in humans due to excess intake of copper is observed almost exclusively in individuals with Wilson's disease, idiopathic copper toxicosis (ICT), and children with Indian childhood cirrhosis (ICC). Thus, these individuals will be at an increased risk of adverse effects from excess copper intake.

## KEY POINTS FOR COPPER

- ✓ Copper functions as a component of several metalloenzymes, which act as oxidases in the reduction of molecular oxygen.
- ✓ The requirements for copper are based on a combination of indicators, including plasma copper and ceruloplasmin concentrations, erythrocyte superoxide dismutase activity, and platelet copper concentration in controlled human depletion/repletion studies. The UL is based on protection from liver damage as the critical adverse event.
- ✓ The risk of adverse effects resulting from excess intake of copper from food, water, and supplements appears to be low.
- ✓ Good sources of copper include organ meats, seafood, nuts, seeds, wheat-bran cereals, and whole-grain products.
- ✓ Frank copper deficiency in humans is rare. The signs and symptoms of deficiency include normocytic, hypochromic anemia; leucopenia; and neutropenia; and, in copper-deficient children, osteoporosis.
- ✓ The long-term toxicity of copper has not been well studied in humans, but it is rare in normal populations without some hereditary defect in copper homeostasis. Potential adverse effects have been associated with excess intake of soluble copper salts in both supplements and drinking water, although most have only been reported based on acute and not chronic intakes.
- ✓ People at an increased risk of adverse effects from excess copper intake include individuals with Wilson's disease (homozygous and heterozygous), idiopathic copper toxicosis (ICT), and Indian childhood cirrhosis (ICC).

**TABLE 1 Dietary Reference Intakes for Fluoride by Life Stage Group**

Life stage group	DRI values (mg/day)		
	AI <sup>a</sup>		UL <sup>b</sup>
	males	females	
0 through 6 mo	0.01	0.01	0.7
7 through 12 mo	0.5	0.5	0.9
1 through 3 y	0.7	0.7	1.3
4 through 8 y	1	1	2.2
9 through 13 y	2	2	10
14 through 18 y	3	3	10
19 through 30 y	4	3	10
31 through 50 y	4	3	10
51 through 70 y	4	3	10
> 70 y	4	3	10
<b>Pregnancy</b>			
≤ 18 y		3	10
19 through 50 y		3	10
<b>Lactation</b>			
≤ 18 y		3	10
19 through 50 y		3	10

<sup>a</sup> AI = Adequate Intake.<sup>b</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.

# FLUORIDE

**F**luoride is vital for the health of teeth and bones. About 99 percent of body fluoride is found in calcified tissues, where it protects against dental caries and can stimulate new bone formation.

Since data were inadequate to determine an Estimated Average Requirement (EAR) and thus calculate a Recommended Dietary Allowance (RDA) for fluoride, an Adequate Intake (AI) was instead developed. The AIs for fluoride (for people aged 7 months and older) are based on the prevention of dental caries. The Tolerable Upper Intake (UL) was derived using data on the risk of developing early signs of skeletal fluorosis. DRI values are listed by life stage group in Table 1.

Fluoridated water is a primary source of dietary fluoride intake. Average fluoride intakes tend to be higher in communities with fluoridated water compared with those with nonfluoridated water. The primary effect of inadequate fluoride intake is an increased risk of dental caries. The potential effects of excess intake are discolored or pitted teeth (in children who consume excess amounts of fluoride prior to the eruption of teeth) and skeletal fluorosis, a very rare effect characterized by elevated bone-ash fluoride concentrations. In the United States and Canada, it is unlikely that older children and adults are exceeding the UL for fluoride.

## FLUORIDE AND THE BODY

### Function

Fluoride is vital for the health of teeth and bones. Ingesting fluoride during the pre-eruptive phase of tooth development can help prevent dental caries. This is due to the uptake of fluoride in the dental enamel and the formation of fluorhydroxyapatite. Even after teeth have erupted, fluoride can protect against dental caries, but this protection requires frequent exposure to fluoride throughout a person's lifetime to achieve and maintain adequate concentrations of the ion in dental plaque and enamel.

### Absorption, Metabolism, Storage, and Excretion

In general, 50 percent of dietary fluoride is absorbed from the gastrointestinal tract. In the absence of calcium, which may bind with fluoride, absorption

typically increases to about 80 percent or more. Because of fluoride's affinity for calcium, about 99 percent of body fluoride is found in calcified tissues. Elimination of absorbed fluoride occurs through the kidneys.

The body's retention of fluoride changes throughout life. In young children, whose skeletons and teeth are still growing, as much as 80 percent of absorbed fluoride may be retained and only 20 percent excreted. In healthy young and middle-aged adults, approximately 50 percent of absorbed fluoride is retained in the skeleton and 50 percent is excreted in the urine. In older adults, it is likely that the fraction of fluoride excreted is greater than the fraction retained.

Under most dietary conditions, fluoride balance is positive. When fluoride intake is chronically insufficient to maintain plasma concentrations, fluoride excretion in both infants and adults can exceed the amounts ingested due to mobilization from calcified tissues.

## DETERMINING DRIS

### Determining Requirements

For fluoride, the data are strong on risk reduction, but the evidence upon which to base an actual requirement is scant. Since data were inadequate to determine an EAR and thus calculate an RDA, an AI was instead developed. The AIs for fluoride (for people aged 7 months and older), are based on the intake values that maximally reduce the occurrence of dental caries in a group of individuals without causing unwanted effects including moderate tooth enamel mottling known as dental fluorosis.

### Special Considerations

*Nonfluoridated water:* Infants and children who live in areas with nonfluoridated water will not easily achieve the AI for fluoride. Therefore, the American Dental Association, the American Academy of Pediatrics, and the Canadian Paediatric Society have recommended fluoride supplements for these children, with daily doses based on a child's age and the fluoride concentration of his or her main drinking water source.

## Criteria for Determining Fluoride Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Human milk content
For all other life stage groups	Caries prevention

### The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Members of the general population should not routinely exceed the UL. The UL value for fluoride represents total intake from food, water, and supplements.

The UL for fluoride for individuals aged 9 years and older was derived using data on the risk of developing early signs of skeletal fluorosis, which is associated with a fluoride intake greater than 10 mg/day for a period of 10 years or longer. The UL for infants and children younger than 8 years old was based on a critical adverse effect of developing fluorosis of the anterior teeth, not skeletal fluorosis.

Data from studies of fluoride exposure from dietary sources or work environments showed that a UL of 10 mg/day for a period of 10 years or longer carries only a small risk for an individual to develop preclinical or stage 1 skeletal fluorosis (see “Excess Intake”).

Although the prevalence of enamel fluorosis in both fluoridated and nonfluoridated communities in the United States and Canada is substantially higher than it was when the original epidemiological studies were done some 60 years ago, the severity remains largely limited to the very mild and mild categories. Based on several U.S. studies done in the 1980s, it is estimated that approximately 1 in 100 children exceed the UL in areas where the water fluoride concentration is 1.0 mg/L or slightly higher. Any additional intake by children who are at risk of enamel fluorosis is almost certainly derived from the use of fluoride-containing dental products, especially if they are inadvertently swallowed. The virtual absence of evidence showing skeletal changes consistent with a diagnosis of skeletal fluorosis indicates that the UL for older children and adults is not being exceeded in the United States and Canada.

## DIETARY SOURCES

### Foods and Water

Most foods have fluoride concentrations well below 0.05 mg/100 g. Exceptions to this include fluoridated water, beverages (including teas), some ma-

rine fish (especially if eating with bones, e.g., sardines), and some infant formulas that are made or reconstituted with fluoridated water. Because tea leaves can accumulate fluoride to concentrations exceeding 10 mg/100 g dry weight, brewed tea contains fluoride at concentrations of 1–6 mg/L, depending on the amount of dry tea used, the fluoride concentration of the water, and brewing time. Decaffeinated teas have roughly twice the fluoride concentration of caffeinated teas.

## Dietary Supplements

Fluoride supplements are intended for use by children living in areas with low water fluoride concentrations so that their intake is similar to that of children with access to water fluoride concentrations of approximately 1.0 mg/L. Based on the 1986 National Health Interview Survey (NHIS) data, in the United States approximately 15 percent of children up to age 5 years and 8 percent of those aged 5 to 17 years are given dietary fluoride supplements. Supplements are rarely prescribed for adults.

## Dental Products

Fluoride intake from dental products (such as toothpaste and mouth rinse) can add considerable fluoride content to the diet, often approaching or exceeding intake from foods and water. This is a particular concern in young children who may inadvertently swallow toothpaste or mouth rinses.

## Bioavailability

The bioavailability of fluoride is generally high, but it can be affected by the method in which it is ingested. When a soluble compound such as sodium fluoride is ingested from fluoridated water, absorption is nearly complete. If it is ingested with milk, infant formula, or foods, particularly those with high concentrations of calcium or certain divalent or trivalent ions that form insoluble compounds, absorption may be reduced by 10–25 percent. The absorption of fluoride from ingested toothpaste, whether added as sodium fluoride or monofluorophosphate, is nearly 100 percent.

## Dietary Interactions

There is evidence that fluoride may interact with certain nutrients and dietary substances (see Table 2).

**TABLE 2 Potential Interactions with Other Dietary Substances**

<i>Substance</i>	<i>Potential Interaction</i>	<i>Notes</i>
<b>SUBSTANCES THAT AFFECT FLUORIDE</b>		
Calcium	High concentrations of calcium ingested with fluoride may reduce fluoride absorption.	The rate and extent of fluoride absorption from the gastrointestinal tract are somewhat reduced by ingestion with solid foods and some liquids, particularly those rich in calcium, such as milk or infant formulas.

## INADEQUATE INTAKE AND DEFICIENCY

The primary effect of inadequate fluoride intake is an increased risk of dental caries. The results of many studies conducted prior to the availability of fluoride-containing dental products showed that the prevalence of dental caries in communities with optimal water fluoride concentrations was 40–60 percent lower than in areas with low water fluoride concentrations. In a later survey conducted in 1986–1987, the National Caries Program of the National Institute of Dental Research found that the overall difference in caries prevalence between fluoridated and nonfluoridated regions in the United States was 18 percent. The exclusion of children with reported exposure to fluoride supplements increased the difference to 25 percent.

## EXCESS INTAKE

The primary adverse effects associated with chronic excess fluoride intake are the following:

- Enamel fluorosis, which occurs during the pre-eruptive development of teeth and results in mainly cosmetic effects in the form of discolored or pitted teeth
- Skeletal fluorosis, which results in elevated bone-ash fluoride concentrations and potentially debilitating symptoms. The following are stages of skeletal fluorosis:

*Stage 1 skeletal fluorosis:* Characterized by occasional stiffness or pain in the joints and some osteosclerosis of the pelvis and vertebrae. Bone-ash fluoride concentrations usually range from 6,000 to 7,000 mg/kg.

*Stages 2 and 3 skeletal fluorosis:* Symptoms are more severe and may include the calcification of ligaments, osteosclerosis, exostoses, possible osteoporosis of long bones, muscle wasting, and neurological defects due to the hypercalcification of vertebrae. Bone-ash fluoride concentrations typically exceed 7,500–8,000 mg/kg.

The development and severity of skeletal fluorosis directly relate to the level and duration of fluoride exposure. Most epidemiological evidence indicates that an intake of at least 10 mg/day for a period of 10 years or longer is needed to produce clinical signs of the condition's milder forms. Crippling skeletal fluorosis is extremely rare in the United States and Canada.

## Special Considerations

**Tropical climates:** Reports of relatively marked osteofluorotic signs and symptoms have been associated with concentrations of fluoride in drinking water of approximately 3 mg/L in tropical climates. These adverse effects have been attributed to poor nutrition and hard manual labor leading to excessive sweat loss and compensatory high levels of water intake. Therefore, an increased risk for skeletal fluorosis from excess fluoride intake may exist for malnourished individuals who live in hot climates or tropical environments.

## KEY POINTS FOR FLUORIDE

- ✓ Fluoride is vital for the health of teeth and bones. About 99 percent of body fluoride is found in calcified tissues, where it protects against dental caries and can stimulate new bone formation.
- ✓ Since data were inadequate to determine an EAR and thus calculate an RDA for fluoride, an AI was instead developed.
- ✓ The AIs for fluoride are based on the prevention of dental caries. The UL for adults was derived using data on the risk of developing early signs of skeletal fluorosis.
- ✓ Infants and children who live in nonfluoridated water areas will not easily achieve the AI for fluoride. Thus, fluoride supplements have been recommended based on life stage and level of water fluoridation.
- ✓ Fluoridated water is a primary source of dietary fluoride intake.
- ✓ The primary effect of inadequate intake is an increased risk of dental caries.
- ✓ The primary adverse effects associated with chronic excess fluoride intake are enamel fluorosis and skeletal fluorosis.
- ✓ Dental products such as toothpaste and mouth rinses can significantly increase fluoride intake, a particular concern in young children if they inadvertently swallow these products.
- ✓ In the United States and Canada, it is unlikely that older children and adults are exceeding the UL for fluoride.

**TABLE 1 Dietary Reference Intakes for Iodine by Life Stage Group**

Life stage group	DRI values (μg/day)					
	EAR <sup>a</sup>		RDA <sup>b</sup>		AI <sup>c</sup>	UL <sup>d</sup>
	males	females	males	females		
<b>Pregnancy</b>						
≤ 18 y		160		220		900
19 through 50 y		160		220		1,100
<b>Lactation</b>						
≤ 18 y		209		290		900
19 through 50 y		209		290		1,100

<sup>a</sup> EAR = Estimated Average Requirement.<sup>b</sup> RDA = Recommended Dietary Allowance.<sup>c</sup> AI = Adequate Intake.<sup>d</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.

<sup>e</sup> ND = Not determinable. This value is not determinable due to the lack of data of adverse effects in this age group and concern regarding the lack of ability to handle excess amounts. Source of intake should only be from food to prevent high levels of intake.

# IODINE

Iodine is an essential component of thyroid hormones that are involved in the regulation of various enzymes and metabolic processes. These hormones regulate many key biochemical reactions, including protein synthesis and enzymatic activity. Major organs that are affected by these processes include the brain, muscles, heart, pituitary gland, and kidneys.

The requirements for iodine are based on thyroid iodine accumulation and turnover. The Tolerable Upper Intake Level (UL) is based on serum thyrotropin concentration in response to varying levels of ingested iodine. DRI values are listed by life stage group in Table 1.

The iodine content of most food sources is low and can be affected by soil content, irrigation, and fertilizers. Seafood has high concentrations; processed foods may also have high levels due to the addition of iodized salt or additives that contain iodine. In North America where much of the iodine consumed is from salt iodized with potassium iodide, symptoms of iodine deficiency are rare. However, severe iodine deficiency can result in impaired cognitive development in children and goiter in adults. For the general population, high iodine intakes from food, water, and supplements have been associated with thyroiditis, goiter, hypothyroidism, hyperthyroidism, sensitivity reactions, thyroid papillary cancer, and acute responses in some individuals. However, most individuals are very tolerant of excess iodine intake from foods.

## IODINE AND THE BODY

### Function

Iodine is an essential component of the thyroid hormones thyroxine (T4) and triiodothyronine (T3), comprising 65 and 59 percent of their respective weights. These hormones regulate many key biochemical reactions, including protein synthesis and enzymatic activity. Major organs that are affected by these processes include the brain, muscles, heart, pituitary gland, and kidneys.

### Absorption, Metabolism, Storage, and Excretion

Iodine is ingested in a variety of chemical forms. Most ingested iodine is reduced in the gut to iodide and absorbed almost completely. Some iodine-containing compounds (e.g., thyroid hormones) are absorbed intact. Iodate,

widely used in many countries as an additive to salt, is rapidly reduced to iodide and completely absorbed. Once in the circulation, iodide is principally removed by the thyroid gland and kidneys. The thyroid selectively concentrates iodide in amounts required for adequate thyroid hormone synthesis; most of the remaining iodine is excreted in the urine.

A sodium/iodide transporter in the thyroïdal basal membrane transfers iodide from the circulation into the thyroid gland at a concentration gradient of about 20 to 50 times that of the plasma. This ensures that the thyroid gland obtains adequate amounts of iodine for hormone synthesis. During iodine deficiency, the thyroid gland concentrates a majority of the iodine available from the plasma. The thyroid of an average adult from an iodine-sufficient geographical region contains about 15 mg of iodine. Most excretion of iodine occurs through the urine, with the remainder excreted in the feces.

## **DETERMINING DRIS**

### **Determining Requirements**

The requirements for iodine are based on thyroid iodine accumulation and turnover.

### **Special Considerations**

*Individuals susceptible to adverse effects:* People with autoimmune thyroid disease (AITD) and iodine deficiency respond adversely to intakes that are considered safe for the general population. AITD is common in the U.S. population and particularly in older women. Individuals with AITD who are treated for iodine deficiency or nodular goiter may have an increased sensitivity to the adverse effects of iodine intake.

### **Criteria for Determining Iodine Requirements, by Life Stage Group**

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Average iodine intake from human milk
7 through 12 mo	Extrapolation from 0 to 6 mo AI
1 through 8 y	Balance data on children
9 through 18 y	Extrapolation from adult EAR
19 through 50 y	Thyroid iodine accumulation and turnover
51 through > 70 y	Extrapolation of iodine turnover studies from 19 through 50 y

*Pregnancy*

≤ 18 y through 50 y      Balance data during pregnancy

*Lactation*

≤ 18 y                      Adolescent female EAR plus average amount of iodine secreted  
                                  in human milk

19 through 50 y            Adult female EAR plus average amount of iodine secreted  
                                  in human milk

## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all healthy people. Members of the general population should not routinely exceed the UL. The UL for iodine is based on thyroid dysfunction, characterized by elevated serum thyrotropin (also known as TSH) concentrations in response to increasing levels of ingested iodine; it represents intake from food, water, and supplements. A high urinary iodine excretion distinguishes this hypothyroidism from that produced in iodine deficiency. The UL is not meant to apply to individuals who are receiving iodine under medical supervision.

Based on the Food and Drug Administration's Total Diet Study, the highest intake of dietary iodine for any life stage or gender group at the 95th percentile was approximately 1.14 mg/day, which is equivalent to the UL for adults. The iodine intake from the diet and supplements at the 95th percentile was approximately 1.15 mg/day. For most people, iodine intake from usual foods and supplements is unlikely to exceed the UL.

## Special Considerations

**Goiter:** In certain regions of the world where goiter is present, therapeutic doses may exceed the UL.

**AITD:** The UL for iodine does not apply to individuals with AITD (see “Determining Requirements”). Due to inadequate data, a UL could not be set for these individuals.

## DIETARY SOURCES

### Foods

The iodine content of most food sources is low and can be affected by soil content, irrigation, and fertilizers. Most foods provide 3–75 µg per serving. Seafood has higher concentrations of iodine because marine animals can con-

centrate iodine from seawater. Processed foods may also have higher levels due to the addition of iodized salt or additives such as calcium iodate, potassium iodate, potassium iodide, and cuprous iodide. Both the United States and Canada iodize salt with potassium iodide at 100 ppm (76 mg iodine/kg salt). Iodized salt is mandatory in Canada and discretionary in the United States. Iodized salt is optionally used by about 50 percent of the U.S. population.

## Dietary Supplements

According to the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994), the median intake of iodine from supplements was approximately 140 µg/day for adults. The 1986 National Health Interview Survey (NHIS) reported that approximately 12 percent of men and 15 percent of nonpregnant women took a supplement that contained iodine.

## Bioavailability

Under normal conditions, the absorption of dietary iodine by the body is greater than 90 percent. The bioavailability of orally administered thyroxine is approximately 75 percent.

Soya flour has been shown to inhibit iodine absorption, and goiter and hypothyroidism were reported in several infants who consumed infant formula containing soya flour. However, if iodine was added to this formula, no goiter appeared.

Some foods contain goitrogens, which interfere with thyroid hormone production or utilization. These foods, which include cassava, millet, and cruciferous vegetables (e.g., cabbage), generally are of no clinical significance unless there is a coexisting iodine deficiency. Water from shallow or polluted streams and wells may also contain goitrogens. Deficiencies of vitamin A, selenium, or iron can each exacerbate the effects of iodine deficiency.

Some ingested substances contain large amounts of iodine that can interfere with proper thyroid function. They include radiocontrast media, food coloring, certain medications (e.g., amiodarone), water purification tablets, and skin and dental disinfectants.

## Dietary Interactions

This information was not provided at the time the DRI values for this nutrient were set.

## **INADEQUATE INTAKE AND DEFICIENCY**

In North America, where much of the iodine consumed is from salt iodized with potassium iodide, symptoms of iodine deficiency are rare. However, most countries currently have some degree of iodine deficiency, including some industrialized countries in Western Europe. Of historical note, during the early part of the 20th century iodine deficiency was a significant problem in the United States and Canada, particularly in the interior, the Great Lakes region, and the Pacific Northwest.

The clinical signs and symptoms of iodine deficiency that result from inadequate thyroid hormone production due to a lack of sufficient iodine, include the following:

- Goiter (thyroid enlargement; usually the earliest clinical feature of deficiency)
- Mental retardation
- Hypothyroidism (elevated thyroid stimulating hormone [TSH])
- Cretinism (extreme form of neurological damage from fetal hypothyroidism; can be reversed with iodine treatment, especially when begun early)
- Growth and developmental abnormalities

The most damaging effect of iodine deficiency involves the developing brain. Thyroid hormone is particularly important for myelination of the central nervous system, which is most active in the perinatal period and during fetal and early postnatal development. Numerous population studies have correlated an iodine-deficient diet with an increased incidence of mental retardation. The effects of iodine deficiency on brain development are similar to those of hypothyroidism from any other cause.

Other consequences of iodine deficiency across populations include impaired reproductive outcome, increased childhood mortality, decreased learning ability, and economic stagnation. Major international efforts have produced dramatic improvements in the correction of iodine deficiency, mainly through the use of iodized salt in iodine-deficient countries.

## **EXCESS INTAKE**

Most people are very tolerant of excess iodine intake from food. For the general population, high iodine intakes (in excess of the UL) from food, water, and supplements have been associated with the following adverse effects:

- Thyroiditis
- Goiter
- Hypothyroidism (elevated thyroid stimulating hormone [TSH])
- Hyperthyroidism
- Sensitivity reactions
- Thyroid papillary cancer
- Acute effects of iodine poisoning, such as burning of the mouth, throat, and stomach; abdominal pain; fever; nausea; vomiting; diarrhea; weak pulse; cardiac irritability; coma; and cyanosis (These symptoms are quite rare and are usually associated with doses of many grams.)

## KEY POINTS FOR IODINE

- ✓ Iodine is an essential component of thyroid hormones that are involved in the regulation of various enzymes and metabolic processes.
- ✓ The requirements for iodine are based on thyroid iodine accumulation and turnover. The UL is based on serum thyrotropin concentration in response to varying levels of ingested iodine.
- ✓ Certain subpopulations, such as those with autoimmune thyroid disease (AITD) and iodine deficiency, respond adversely to intakes that are considered safe for the general population. AITD is common in the U.S. population and particularly in older women.
- ✓ For most people, iodine intake from usual foods and supplements is unlikely to exceed the UL. In certain regions of the world where goiter is present, therapeutic doses may exceed the UL.
- ✓ The iodine content of most food sources is low and can be affected by soil content, irrigation, and fertilizers. Most foods provide 3–75 µg per serving. Seafood has higher concentrations of iodine because marine animals can concentrate iodine from seawater.
- ✓ Processed foods may also have higher levels due to the addition of iodized salt or additives that contain iodine. Iodized salt is mandatory in Canada and optionally used by about 50 percent of the U.S. population.

- ✓ In North America, where much of the iodine consumed is from salt iodized with potassium iodide, symptoms of iodine deficiency are rare. However, most countries currently have some degree of iodine deficiency, including some industrialized countries in Western Europe.
- ✓ The clinical signs and symptoms of iodine deficiency include goiter, mental retardation, hypothyroidism, cretinism, and growth and developmental abnormalities.
- ✓ The use of iodized salt has helped reduce iodine deficiency.
- ✓ Most people are very tolerant of excess iodine intake from food and supplements.
- ✓ The potential adverse effects of iodine intakes in excess of the UL include thyroiditis, goiter, hypothyroidism, hyperthyroidism, sensitivity reactions, thyroid papillary cancer, and acute responses in some individuals.

**TABLE 1 Dietary Reference Intakes for Iron by Life Stage Group**

Life stage group	DRI values (mg/day)					
	EAR <sup>a</sup>		RDA <sup>b</sup>		AI <sup>c</sup>	UL <sup>d</sup>
	males	females	males	females		
<b>Pregnancy</b>						
≤ 18 y		23		27		45
19 through 50 y		22		27		45
<b>Lactation</b>						
≤ 18 y		7		10		45
19 through 50 y		6.5		9		45

<sup>a</sup> EAR = Estimated Average Requirement.<sup>b</sup> RDA = Recommended Dietary Allowance.<sup>c</sup> AI = Adequate Intake.<sup>d</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.

# IRON

Iron is a critical component of several proteins, including enzymes, cytochromes, myoglobin, and hemoglobin, the latter of which transports oxygen throughout the body. Almost two-thirds of the body's iron is found in hemoglobin that is present in circulating erythrocytes and involved in the transport of oxygen from the environment to tissues throughout the body for metabolism. Iron can exist in various oxidation states, including the ferrous, ferric, and ferryl states.

The requirements for iron are based on factorial modeling using the following factors: basal iron losses; menstrual losses; fetal requirements in pregnancy; increased requirement during growth for the expansion of blood volume; and increased tissue and storage iron. The Tolerable Upper Intake Level (UL) is based on gastrointestinal distress as the critical adverse effect. DRI values are listed by life stage group in Table 1.

About half of the iron from meat, poultry, and fish is heme iron, which is highly bioavailable; the remainder is nonheme, which is less readily absorbed by the body. Iron in dairy foods, eggs, and all plant-based foods is entirely nonheme. Particularly rich sources of nonheme iron are fortified plant-based foods, such as breads, cereals, and breakfast bars.

Iron deficiency anemia is the most common nutritional deficiency in the world. Adverse effects associated with excessive iron intake include gastrointestinal distress, secondary iron overload, and acute toxicity.

## IRON AND THE BODY

### Function

Iron is a component of several proteins, including enzymes, cytochromes, myoglobin, and hemoglobin. Almost two-thirds of the body's iron is found in hemoglobin that is present in circulating erythrocytes and involved in the transport of oxygen from the environment to tissues throughout the body for metabolism. A readily mobilizable iron store contains another 25 percent. Most of the remaining 15 percent is in the myoglobin of muscle tissue. Iron can exist in various oxidation states, including the ferrous, ferric, and ferryl states.

Four major classes of iron-containing proteins exist in the mammalian system: iron-containing heme proteins (hemoglobin, myoglobin, cytochromes),

iron-sulfur enzymes (flavoproteins, heme-flavoproteins), proteins for iron storage and transport (transferrin, lactoferrin, ferritin), and other iron-containing or activated enzymes (sulfur, nonheme enzymes).

## Absorption, Metabolism, Storage, and Excretion

The iron content of the body is highly conserved and strongly influenced by the size of a person's iron stores. The greater the stores, the less iron that is absorbed.

Adult men need to absorb about 1 mg/day to maintain iron balance. Menstruating women need to absorb about 1.5 mg/day, with a small proportion of this group needing to absorb as much as 3.4 mg/day. Menstrual losses highly vary among women and explain why iron requirements in menstruating women are not symmetrically distributed. The median amount of iron lost through menstruation in adult women is approximately 0.51 mg/day; in adolescent girls it is approximately 0.45 mg/day. Women in the late stages of pregnancy must absorb 4–5 mg/day to maintain iron balance. Requirements are also higher in childhood, particularly during periods of rapid growth in early childhood (6 to 24 months of age) and adolescence.

Iron absorption occurs in the upper small intestine via pathways that allow the absorption of heme and nonheme iron. Heme iron is more highly bioavailable than nonheme iron (see “Bioavailability” and “Dietary Sources”). Many factors can affect iron absorption (see “Dietary Interactions”). Therefore, exact figures for absorption of heme and nonheme iron are unknown. A conservative estimate for heme iron absorption is 25 percent; for nonheme iron the mean percentage of absorption is estimated to be approximately 16.8 percent. Absorption of bioavailable iron occurs by an energy-dependent carrier-mediated process; the iron is then intracellularly transported and transferred into the plasma.

Iron that enters the cells may be incorporated into functional compounds, stored as ferritin, or used to regulate future cellular iron metabolism. The liver, spleen, and bone marrow are the primary sites of iron storage in the body. The majority of iron that is absorbed into enterocytes, but not taken up by transferrin, is excreted in the feces, since these intestinal cells are sloughed off every 3 to 5 days. Little iron is excreted into the urine. In the absence of bleeding (including menstruation) or pregnancy, only a small quantity of iron is lost each day. As stated above, iron is also lost through menstrual bleeding, and these losses can widely vary among premenopausal women.

## DETERMINING REQUIREMENTS

### Determining Requirements

The requirements for iron are based on factorial modeling using the following factors: basal iron losses; menstrual losses; fetal requirements in pregnancy; increased requirements during growth for the expansion of blood volume; and increased tissue and storage iron.

It is important to note that iron requirements are known to be skewed rather than normally distributed for menstruating women. Information on the distribution of iron requirements can be found in Appendix G.

### Special Considerations

**Individuals susceptible to iron deficiency:** People with decreased stomach acidity, such as those who overconsume antacids, ingest alkaline clay, or have pathological conditions, such as achlorhydria or partial gastrectomy, may have impaired iron absorption and be at greater risk for deficiency.

**Infants:** Because cow milk is a poor source of bioavailable iron, it is not recommended for infants under the age of 1 year; in Canada, the recommendation is 9 months of age. Early inappropriate ingestion of cow milk is associated with a higher risk of iron deficiency anemia. U.S. and Canadian pediatric societies have concluded that infants who are not, or only partially, fed human milk should receive an iron-fortified formula. Supplementation is also recommended for preterm infants as their iron stores are low.

**Age of menarche:** The RDA for iron for girls increases from 8 mg/day to 15 mg/day at the age of 14 years to account for menstruation. For girls who have reached this age, but are not yet menstruating, the requirement is approximately 10.5 mg/day, rather than 15 mg/day.

**Adolescent and preadolescent growth spurt:** The rate of growth during the growth spurt can be more than double the average rate for boys and up to 50 percent higher for girls. The increased requirement for dietary iron for boys and girls in the growth spurt is 2.9 mg/day and 1.1 mg/day, respectively.

**Use of oral contraceptives and hormone replacement therapy (HRT):** The use of oral contraceptives lowers menstrual blood loss. As a result, adolescent girls and women using oral contraceptives may have lower iron requirements. HRT may cause some uterine bleeding in some women. In this situation, women

who are on HRT may have higher iron requirements than postmenopausal women who are not.

**Vegetarian diets:** Because heme iron is more bioavailable than nonheme iron (milk products and eggs are of animal origin, but they contain only nonheme iron), it is estimated that the bioavailability of iron from a vegetarian diet is approximately 10 percent, rather than the 18 percent from a mixed Western diet. Hence, the requirement for iron is 1.8 times higher for vegetarians. It is important to emphasize that lower bioavailability diets (approaching 5 percent overall absorption) may be encountered with very strict vegetarian diets.

**Intestinal parasitic infection:** A common problem in developing nations, intestinal parasites can cause significant blood loss, thereby increasing an individual's iron requirement.

**Blood donation:** A 500 mL donation just once a year translates to an additional iron loss of approximately 0.6 mg/day over the year. People who frequently donate blood have higher iron requirements.

**Regular, intense physical activity:** Studies show that iron status is often marginal or inadequate in many individuals, particularly females, who engage in regular, intense physical activity. The requirement of these individuals may be as much as 30–70 percent greater than those who do not participate in regular strenuous exercise.

### Criteria for Determining Iron Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Average iron intake from human milk
7 through 12 mo	Factorial modeling
1 through 70 y	Factorial modeling
> 70 y	Extrapolation of factorial analysis from 51 through 70 y

<i>Pregnancy</i>	
≤ 18 y through 50 y	Factorial modeling

<i>Lactation</i>	
≤ 18 y through 50 y	Adolescent female EAR minus menstrual losses plus average amount of iron secreted in human milk

## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all healthy people. Members of the general population should not routinely exceed the UL. This value is based on gastrointestinal distress as the critical adverse effect and represents intake from food, water, and supplements.

According to the National Health and Nutrition Examination Survey (NHANES III, 1988–1994), the highest intake from food and supplements at the 90th percentile reported for any life stage and gender groups, excluding pregnancy and lactation, was approximately 34 mg/day for men 51 years of age and older. This value is below the UL of 45 mg/day. Between 50 and 75 percent of pregnant and lactating women consumed iron from food and supplements at a greater level than 45 mg/day, but iron supplementation is usually supervised in prenatal and postnatal care programs. Based on a UL of 45 mg/day of iron for adults, the risk of adverse effects from dietary sources appears to be low.

## Special Considerations

**Individuals susceptible to adverse effects:** People with the following conditions are susceptible to the adverse effects of excess iron intake: hereditary hemochromatosis; chronic alcoholism; alcoholic cirrhosis and other liver diseases; iron-loading abnormalities, particularly thalassemias; congenital atransferrinemia; and aceruloplasminemia. These individuals may not be protected by the UL for iron. A UL for subpopulations such as persons with hereditary hemochromatosis cannot be determined until information on the relationship between iron intake and the risk of adverse effects from excess iron stores becomes available.

## DIETARY SOURCES

### Foods

About half of the iron from meat, fish, and poultry is a rich source of heme iron, which is highly bioavailable; the remainder is nonheme, which is less readily absorbed by the body. However, heme iron represents only 8–12 percent of dietary iron for boys and men and 7–10 percent of dietary iron for girls and women. Plant-based foods, such as vegetables, fruits, whole-grain breads, or whole-grain pasta contain 0.1–1.4 mg of nonheme iron per serving. Fortified products, including breads, cereals, and breakfast bars can contribute high amounts of nonheme iron to the diet. In the United States, some fortified cereals contain as much as 24 mg of iron (nonheme) per 1-cup serving, while in Canada most cereals are formulated to contain 4 mg per serving.

## Dietary Supplements

The 1986 National Health Interview Survey (NHIS) reported that approximately 21–25 percent of women and 16 percent of men consumed a supplement containing iron. According to NHANES III, the median intake of iron from supplements was approximately 1 mg/day for men and women. The median iron intake from food plus supplements by pregnant women was approximately 21 mg/day.

## Bioavailability

Heme iron, from meat, poultry, and fish, is generally very well absorbed by the body and only slightly influenced by other dietary factors. The absorption of nonheme iron, present in all foods, including meat, poultry, and fish, is strongly influenced by its solubility and interaction with other meal components that promote or inhibit its absorption (see “Dietary Interactions”).

Because of the many factors that influence iron bioavailability, 18 percent bioavailability was used to estimate the average requirement of iron for non-pregnant adults, adolescents, and children over the age of 1 year consuming typical North American diets. The intake was assumed to contain some meat-based foods. Because the diets of children under the age of 1 year contain little meat and are rich in cereal and vegetables, a bioavailability of 10 percent was assumed in setting the requirements. During pregnancy, iron absorption was assumed to be 25 percent.

## Dietary Interactions

There is evidence that iron may interact with other nutrients and dietary substances (see Table 2).

**TABLE 2 Potential Interactions with Other Dietary Substances**

Substance	Potential Interaction	Notes
<b>SUBSTANCES THAT AFFECT IRON</b>		
Ascorbic acid	Ascorbic acid strongly enhances the absorption of nonheme iron.	There appears to be a linear relation between ascorbic acid intake and iron absorption up to at least 100 mg of ascorbic acid per meal. Because ascorbic acid improves iron absorption through the release of nonheme iron bound to inhibitors, the enhanced iron absorption effect is most marked when ascorbic acid is consumed with foods containing high levels of inhibitors, including phytate and tannins.

**TABLE 2 Continued**

<i>Substance</i>	<i>Potential Interaction</i>	<i>Notes</i>
Animal muscle tissue	Meat, fish, and poultry improve nonheme iron absorption.	The mechanism of this enhancing effect is poorly studied, but is likely to involve low molecular weight peptides that are released during digestion.
Phytate	Phytate inhibits nonheme iron absorption.	The absorption of iron from foods high in phytate, such as soybeans, black beans, lentils, mung beans, and split peas, has been shown to be very low (0.84–0.91 percent) and similar to each other. Unrefined rice and grains also contain phytate.
Polyphenols	Polyphenols inhibit nonheme iron absorption.	Polyphenols, such as those in tea, inhibit iron absorption through the binding of iron to tannic acids in the intestine. The inhibitory effects of tannic acid are dose-dependent and reduced by the addition of ascorbic acid. Polyphenols are also found in many grain products, red wine, and herbs such as oregano.
Vegetable proteins	Vegetable proteins inhibit nonheme iron absorption.	This effect is independent of the phytate content of the food.
Calcium	Calcium inhibits the absorption of both heme and nonheme iron.	This interaction is not well understood; however, it has been suggested that calcium inhibits heme and nonheme iron absorption during transfer through the mucosal cell. Despite the significant reduction of iron absorption by calcium in single meals, little effect has been observed on serum ferritin concentrations in supplementation trials with calcium supplementation at levels of 1,000–1,500 mg/day.
<b>IRON AFFECTING OTHER SUBSTANCES</b>		
Zinc	High iron intakes may reduce zinc absorption.	In general, data indicate that supplemental iron may inhibit zinc absorption if both are taken without food, but does not inhibit zinc absorption if it is consumed with food.

## INADEQUATE INTAKE AND DEFICIENCY

Iron deficiency anemia is the most common nutritional deficiency in the world. The most important functional indicators of iron deficiency are reduced physical work capacity, delayed psychomotor development in infants, impaired cognitive function, and adverse effects for both the mother and the fetus (such as maternal anemia, premature delivery, low birth weight, and increased perinatal infant mortality).

A series of laboratory indicators can be used to precisely characterize iron status and to categorize the severity of iron deficiency. Three levels of iron deficiency are customarily identified:

- Depleted iron stores, but where there appears to be no limitation in the supply of iron to the functional compartment
- Early functional iron deficiency (iron-deficient erythropoiesis), where the supply of iron to the functional compartment is suboptimal but not sufficiently reduced to cause measurable anemia
- Iron deficiency anemia, where there is a measurable deficit in the most accessible functional compartment, the erythrocyte

Available laboratory tests can be used in combination with each other to identify the evolution of iron deficiency through these three stages (see Table 3).

**TABLE 3 Laboratory Measurements Commonly Used in the Evaluation of Iron Status**

Stage of Iron Deficiency	Indicator	Diagnostic Range
Depleted stores	Stainable bone marrow iron	Absent
	Total iron binding capacity	> 400 µg/dL
	Serum ferritin concentration	< 12 µg/L
Early functional iron deficiency	Transferrin saturation	< 16%
	Free erythrocyte protoporphyrin	> 70 µg/dL erythrocyte
	Serum transferrin receptor	> 8.5 mg/L
Iron deficiency anemia	Hemoglobin concentration	< 130 g/L (male) < 120 g/L (female)
	Mean cell volume	< 80 fL

## **EXCESS INTAKE**

The risk of adverse effects of excessive iron intake from dietary sources appears to be low in the general population. Adverse effects may include the following:

- Acute toxicity with vomiting and diarrhea, followed by cardiovascular, central nervous system, kidney, liver, and hematological effects.
- Gastrointestinal effects associated with high-dose supplements, such as constipation, nausea, vomiting, and diarrhea
- Secondary iron overload, which occurs when body iron stores are increased as a consequence of parenteral iron administration, repeated blood transfusions, or hematological disorders that increase the rate of iron absorption

## **Special Considerations**

*Men and postmenopausal women:* Currently the relationship between excessive iron intake and measure of iron status (e.g., serum ferritin concentrations) and both coronary heart disease and cancer is unclear. Nevertheless, the association between a high iron intake and iron overload in sub-Saharan Africa makes it prudent to recommend that men and postmenopausal women avoid iron supplements and highly fortified foods.

## KEY POINTS FOR IRON

- ✓ Iron is a critical component of several proteins, including cytochromes, myoglobin, and hemoglobin, the latter of which transports oxygen throughout the body.
- ✓ The requirements for iron are based on factorial modeling using the following factors: basal iron losses; menstrual losses; fetal requirements in pregnancy; increased requirement during growth for the expansion of blood volume; and increased tissue and storage iron. The UL is based on gastrointestinal distress as the critical adverse effect.
- ✓ Special populations and situations in which iron requirements may vary include infants who do not receive human milk (0–6 months), preterm infants, teens/preteens in the growth spurt, oral contraceptive users, postmenopausal women using cyclic HRT, vegetarians, athletes, and blood donors.
- ✓ People with the following conditions are susceptible to the adverse effects of excess iron intake: hereditary hemochromatosis; chronic alcoholism; alcoholic cirrhosis, and other liver diseases; iron-loading abnormalities, particularly thalassemias; congenital transferrinemia; and aceruloplasminemia. These individuals may not be protected by the UL for iron.
- ✓ About half of the iron from meat, poultry, and fish is heme iron, which is highly bioavailable; the remainder is nonheme, which is less readily absorbed by the body.
- ✓ Particularly rich sources of nonheme iron are fortified plant-based foods, such as breads, cereals, and breakfast bars. The absorption of nonheme iron is enhanced when it is consumed with foods that contain ascorbic acid (vitamin C) or meat, poultry, and fish.
- ✓ Iron deficiency anemia is the most common nutritional deficiency in the world.
- ✓ The most important functional indicators of iron deficiency are reduced physical work capacity, delayed psychomotor development in infants, impaired cognitive function, and adverse effects for both the mother and the fetus (such as maternal anemia, premature delivery, low birth weight, and increased perinatal infant mortality).

- ✓ Three levels of iron deficiency are customarily identified: depleted iron stores, early functional iron deficiency, and iron deficiency anemia.
- ✓ Adverse effects associated with excessive iron intake include acute toxicity, gastrointestinal distress, and secondary iron overload.
- ✓ Currently the relationship between excessive iron intake and high serum ferritin concentrations and both coronary heart disease and cancer is unclear. Nevertheless, the association between a high iron intake and iron overload in sub-Saharan Africa makes it prudent to recommend that men and post-menopausal women avoid iron supplements and highly fortified foods.

**TABLE 1 Dietary Reference Intakes for Magnesium by Life Stage Group**

Life stage group	DRI values (mg/day)							
	EAR <sup>a</sup>		RDA <sup>b</sup>		AI <sup>c</sup>		UL <sup>d,e</sup>	
	males	females	males	females	males	females	males	females
<b>Pregnancy</b>								
≤ 18 y		335		400			350	
19 through 30 y		290		350			350	
31 through 50 y		300		360			350	
<b>Lactation</b>								
≤ 18 y		300		360			350	
19 through 30 y		255		310			350	
31 through 50 y		265		320			350	

<sup>a</sup> EAR = Estimated Average Requirement.<sup>b</sup> RDA = Recommended Dietary Allowance.<sup>c</sup> AI = Adequate Intake.<sup>d</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.<sup>e</sup> The ULs for magnesium represent intake from pharmacological agents only and do not include intake from food and water.<sup>f</sup> ND = Not determinable. This value is not determinable due to the lack of data of adverse effects in this age group and concern regarding the lack of ability to handle excess amounts. Source of intake should only be from food to prevent high levels of intake.

# MAGNESIUM

**M**agnesium is involved in more than 300 enzymatic processes in the body, as well as in bone health and in the maintenance of intracellular levels of potassium and calcium. Magnesium also plays a role in the development and maintenance of bone and other calcified tissues.

Magnesium requirements for adults are based primarily on balance studies. The Tolerable Upper Intake Level (UL) is based on diarrhea as the critical endpoint and was derived from several studies on adults evaluating the effect of high magnesium intake from nonfood sources. DRI values are listed by life stage group in Table 1.

Foods rich in magnesium include green leafy vegetables, whole grains, and nuts. Magnesium may be poorly absorbed from foods that are high in fiber and phytic acid. Magnesium deficiency may result in muscle cramps, hypertension, and coronary and cerebral vasospasms. Adverse effects from excess intake of magnesium from food sources are rare, but the use of pharmacological doses of magnesium from nonfood sources can result in magnesium toxicity, which is characterized by diarrhea, metabolic alkalosis, hypokalemia, paralytic ileus, and cardiorespiratory arrest.

## MAGNESIUM AND THE BODY

### Function

Magnesium is involved in more than 300 enzymatic processes in the body, as well as in the maintenance of intracellular levels of potassium and calcium. Magnesium also plays a role in the development and maintenance of bone and other calcified tissues.

### Absorption, Metabolism, Storage, and Excretion

Magnesium is absorbed along the entire intestinal tract, with maximal absorption likely occurring at the distal jejunum and ileum. In both children and adults, fractional magnesium absorption is inversely proportional to the amount of magnesium consumed. That is, the more magnesium consumed, the lower the proportion that is absorbed (and vice versa). This may be explained by how magnesium is absorbed in the intestine, which is via an unsaturable passive and saturable active transport system.

To a small extent, vitamin D appears to enhance intestinal magnesium absorption. The body's level of magnesium is maintained primarily by the kidneys, where magnesium is filtered and reabsorbed. Approximately 50–60 percent of total body magnesium is stored in bone. Magnesium intake in excess of need is efficiently excreted in urine.

## DETERMINING DRIS

### Determining Requirements

The adult requirements for magnesium are based on dietary balance studies of magnesium. Although several magnesium balance studies have been performed, not all have met the requirements of a well-designed investigation. The minimum requirements for the balance studies used to determine the EAR included either an adaptation period of at least 12 days or a determination of balance made while subjects consume self-selected diets. The disadvantage of the latter is that they do not provide the two levels of intakes needed to determine the dose-response relationship.

### Criteria for Determining Magnesium Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Human milk content
7 through 12 mo	Human milk + solid food
1 through 8 y	Extrapolation of balance studies in older children
9 through 70 y	Balance studies
> 70 y	Intracellular studies; decreases in absorption; balance studies in other adult ages
<i>Pregnancy</i>	
≤ 18 y through 50 y	Age-specific requirement + gain in lean mass
<i>Lactation</i>	
≤ 18 y through 50 y	Balance studies

## The UL

The Tolerable Upper Intake Level (UL) is the highest level of magnesium taken acutely without food that is likely to pose no risk of adverse effects for almost all people. Members of the general population should not routinely exceed the UL.

When ingested as a naturally occurring substance in foods, magnesium has not been shown to exert any adverse effects. However, adverse effects of

excessive magnesium intake have been observed with intakes from nonfood sources, such as various magnesium salts used for pharmacological purposes. Therefore, the UL for magnesium represents acute intake from pharmacological agents and does not include intake from food and water. The UL for adults is based on diarrhea as the critical endpoint and was derived from several studies on adults that evaluated the effects of excessive magnesium intake from non-food sources.

Although a few studies have noted mild diarrhea and other mild gastrointestinal complaints in a small percentage of patients at levels of 360–380 mg/day, it is noteworthy that many other individuals have not encountered such effects, even when receiving substantially more than this amount of supplementary magnesium.

Using data from the 1986 National Health Interview Survey (NHIS), it is estimated that almost 1 percent of all adults in the United States took a nonfood magnesium supplement that exceeded the UL of 350 mg/day. The data on supplement use also indicated that at least 5 percent of young children who used magnesium supplements exceeded the UL for magnesium at 5 mg/kg/day. However, based on the reported frequency of intake in children, fewer than 1 percent of all children would be at risk for adverse effects. More information on supplement use by specific ages is needed.

## Special Considerations

**Individuals with certain conditions:** People with neonatal tetany, hyperuricemia, hyperlipidemia, lithium toxicity, hyperthyroidism, pancreatitis, hepatitis, phlebitis, coronary artery disease, arrhythmia, and digitalis intoxication may benefit from the clinically prescribed use of magnesium in quantities exceeding the UL.

## DIETARY SOURCES

### Foods

Foods rich in magnesium include green leafy vegetables, whole grains, and nuts. Meats, starches, and milk are intermediate in magnesium content, and refined foods generally have the lowest magnesium content. According to the 1989 Total Diet Study of the U.S. Food and Drug Administration, approximately 45 percent of dietary magnesium was obtained from vegetables, fruits, grains, and nuts, whereas approximately 29 percent was obtained from milk, meat, and eggs.

With the increased consumption of refined and processed foods, dietary magnesium intake appears to have decreased over the years. Total magnesium

intake usually depends on calorie intake, which explains the higher intake levels generally seen in young children and adult males and the lower intake levels seen in women and the elderly. Water is a variable source of magnesium intake. Typically, “hard” water has a higher concentration of magnesium salts than “soft” water.

## Dietary Supplements

According to the 1986 NHIS, about 14 percent of men and 17 percent of women took supplements that contained magnesium, while approximately 8 percent of young children (2 to 6 years of age) did so. Women and men who used magnesium supplements took similar doses, about 100 mg/day, although the 95th percentile of intake was somewhat higher for women (400 mg/day) than it was for men (350 mg/day). Children who took magnesium had a median daily intake of 23 mg and a 95th-percentile daily supplemental intake of 117 mg.

## Bioavailability

In a typical diet, approximately 50 percent of the magnesium consumed will be absorbed. High levels of dietary fiber from fruits, vegetables, and grains decrease magnesium absorption or retention, or both.

## Dietary Interactions

There is evidence that magnesium may interact with certain other nutrients and dietary substances (see Table 2).

**TABLE 2 Potential Interactions with Other Dietary Substances**

Substance	Potential Interaction	Notes
<b>SUBSTANCES THAT AFFECT MAGNESIUM</b>		
Phytic acid and fiber	Phytic acid, or phytate, may decrease magnesium absorption.	Foods high in fiber, which contain phytic acid, may decrease intestinal magnesium absorption, likely by binding magnesium to phosphate groups on phytic acid.
Phosphorus	Phosphorus may decrease magnesium absorption.	Studies of subjects on high-phosphate diets have shown that phosphate binding to magnesium may explain decreases in intestinal magnesium absorption.

**TABLE 2 Continued**

<i>Substance</i>	<i>Potential Interaction</i>	<i>Notes</i>
Calcium	High intakes of calcium may decrease magnesium absorption.	Most human studies of the effects of dietary calcium on magnesium absorption have shown no effect. Calcium intakes of as much as 2,000 mg/day (in adult men) did not affect magnesium balance. However, calcium intakes in excess of 2,600 mg/day have been reported to decrease magnesium balance. Several studies have found that high sodium and calcium intake may result in increased renal magnesium excretion. Overall, at the dietary levels recommended in this report, the interaction of magnesium with calcium is not a concern.
Protein	Protein may affect magnesium absorption.	Magnesium absorption has been shown to be lower when protein intake is less than 30 g/day. A higher protein intake may increase renal magnesium excretion, perhaps because an increased acid load increases urinary magnesium excretion. Studies in adolescents have shown improved magnesium absorption and retention when protein intakes were higher (93 vs. 43 g/day).
<b>MAGNESIUM AFFECTING OTHER SUBSTANCES</b>		
Calcium	Magnesium deficiency may cause hypocalcemia.	In general, magnesium deficiency must become moderate to severe before symptomatic hypocalcemia develops. However, a 3-week study of dietary-induced experimental magnesium depletion in humans demonstrated that even a mild degree of magnesium depletion may result in a significant decrease in serum calcium concentration.
Vitamin D	Magnesium deficiency may affect the body's response to pharmacological vitamin D.	Individuals with hypocalcemia and magnesium deficiency are resistant to pharmacological doses of vitamin D, 1,α-hydroxyvitamin D, and 1,25-dihydroxyvitamin D.

## INADEQUATE INTAKE AND DEFICIENCY

Severe magnesium depletion leads to specific biochemical abnormalities and clinical manifestations that can be easily detected. The potential effects of inadequate magnesium intake or deficiency include the following:

- Symptomatic hypocalcemia (A prominent manifestation of magnesium deficiency in humans, symptomatic hypocalcemia develops when magnesium deficiency becomes moderate to severe. See Table 2.)
- Muscle cramps
- Interference with vitamin D metabolism (see Table 2)
- Neuromuscular hyperexcitability (often the initial problem cited in individuals who have or are developing magnesium deficiency)
- Latent tetany
- Spontaneous carpal-pedal spasm
- Seizures

Magnesium depletion may be found in several cardiovascular and neuromuscular diseases, malabsorption syndromes, diabetes mellitus, renal wasting syndromes, osteoporosis, and chronic alcoholism.

### Special Considerations

**Excessive alcohol intake:** Excessive alcohol intake has been shown to cause renal magnesium wasting. Individuals who consume marginal amounts of magnesium and who excessively consume alcohol could be at risk for magnesium depletion. However, current evidence does not support the suggestion that magnesium deficiency causes alcoholism.

**Medications:** A growing number of medications have been found to result in increased renal magnesium excretion. Diuretics, which are commonly used to treat hypertension, heart failure, and edema, may cause hypermagnesuria.

**Mothers who breastfeed multiple infants:** Due to the increased milk production of a mother while breastfeeding multiple infants, increased intakes of magnesium during lactation, as with calcium, should be considered.

**The elderly:** Several studies have found that elderly people have relatively low dietary intakes of magnesium. This may be due to several factors. With aging, intestinal magnesium absorption tends to decrease and urinary magnesium excretion tends to increase. Other factors include poor appetite, diminished senses of taste or smell (or both), poorly fitting dentures, and difficulty in

shopping for and preparing meals. It should also be noted that meals served by some long-term care facilities may provide less than the recommended levels of magnesium.

## EXCESS INTAKE

Excess intake of magnesium from food sources is not associated with adverse effects. However, adverse effects have been observed with excessive intake from nonfood sources that are used acutely for pharmacological purposes, such as magnesium salts. They include the following:

- Diarrhea (primary symptom)
- Nausea
- Abdominal cramps

More severe adverse effects may occur with very large pharmacological doses of magnesium. They include the following:

- Metabolic alkalosis
- Hypokalemia
- Paralytic ileus

## Special Considerations

**Impaired renal function:** Individuals with impaired renal function are at greater risk of magnesium toxicity (from nonfood sources).



## KEY POINTS FOR MAGNESIUM

- ✓ Magnesium is involved in more than 300 enzymatic processes in the body, as well as in bone health and in the maintenance of intracellular levels of potassium and calcium.
- ✓ The more magnesium consumed, the lower the proportion that is absorbed (and vice versa).
- ✓ The adult requirements for magnesium are based primarily on balance studies. The UL for adults was based on diarrhea as the critical endpoint and was derived from several studies on adults evaluating the effect of high magnesium intake from nonfood sources. The UL is based on intake from pharmacological sources of magnesium, rather than from food and water.
- ✓ Foods rich in magnesium include green leafy vegetables, whole grains, and nuts; population intakes of magnesium have declined with decreased intakes of these foods.
- ✓ Magnesium deficiency can result in hypocalcemia, muscle cramps, and seizures, as well as interfere with vitamin D metabolism.
- ✓ No adverse effects of magnesium intake from food sources have been demonstrated.
- ✓ Acute excessive intake of magnesium from nonfood sources, such as pharmacological doses of magnesium salts, can cause metabolic alkalosis, hypokalemia, and paralytic ileus.

**TABLE 1 Dietary Reference Intakes for Manganese by Life Stage Group**

Life stage group	DRI values (mg/day)		
	AI <sup>a</sup>		UL <sup>b</sup>
	males	females	
<b>Pregnancy</b>			
≤ 18 y	2.0	9	
19 through 50 y	2.0	11	
<b>Lactation</b>			
≤ 18 y	2.6	9	
19 through 50 y	2.6	11	

<sup>a</sup> AI = Adequate Intake.<sup>b</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.<sup>c</sup> ND = Not determinable. This value is not determinable due to the lack of data of adverse effects in this age group and concern regarding the lack of ability to handle excess amounts. Source of intake should only be from food to prevent high levels of intake.

# MANGANESE

**M**anganese is involved in the formation of bone and in specific reactions related to amino acid, cholesterol, and carbohydrate metabolism. Manganese metalloenzymes include arginase, glutamine synthetase, phosphoenolpyruvate decarboxylase, and manganese superoxide dismutase.

Since data were insufficient to set an Estimated Average Requirement (EAR) and thus calculate a Recommended Dietary Allowance (RDA) for manganese, an Adequate Intake (AI) was instead developed. The AIs for manganese are based on intakes in healthy individuals, using the median manganese intakes reported from the Food and Drug Administration's (FDA's) Total Diet Study (1991–1997). The Tolerable Upper Intake Level (UL) is based on elevated blood manganese concentrations and neurotoxicity as the critical adverse effects. DRI values are listed by life stage group in Table 1.

The highest contributors of manganese to the diet are grains, beverages (tea), and vegetables. Although a manganese deficiency may contribute to one or more clinical symptoms, a clinical deficiency has not been clearly associated with poor dietary intakes of healthy individuals. Neurotoxicity of orally ingested manganese at relatively low doses is controversial, but evidence suggests that elevated blood manganese levels and neurotoxicity are possible.

## MANGANESE AND THE BODY

### Function

Manganese is an essential nutrient involved in the formation of bone and in specific reactions related to amino acid, cholesterol, and carbohydrate metabolism. Manganese metalloenzymes include arginase, glutamine synthetase, phosphoenolpyruvate decarboxylase, and manganese superoxide dismutase.

### Absorption, Metabolism, Storage, and Excretion

Only a small percentage of dietary manganese is absorbed by the body. Some studies indicate that manganese is absorbed via active transport mechanisms, while other studies suggest that passive diffusion via a nonsaturable process occurs. Much of absorbed manganese is excreted very rapidly into the gut via the bile, and only a small amount is retained.

Manganese is taken up from the blood by the liver and transported to ex-

trahepatic tissues by transferrin and possibly  $\alpha_2$ -macroglobulin and albumin. Excretion primarily occurs in the feces. Urinary excretion of manganese is low and has not been found to be sensitive to dietary intake. Therefore, the potential risk for manganese toxicity is highest when bile excretion is low, such as in the neonate or in liver disease.

## DETERMINING DRIS

### Determining Requirements

Since data were insufficient to set an EAR and thus calculate an RDA for manganese, an AI was instead developed. The AIs for manganese are based on intakes in healthy individuals, using the median manganese intake from the FDA's Total Diet Study (1991–1997).

### Special Considerations

**Gender:** Men have been shown to absorb significantly less manganese compared to women. This may be related to iron status, as men generally have higher serum ferritin concentrations than do women (see “Dietary Interactions”).

### Criteria for Determining Manganese Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Average manganese intake from human milk
7 through 12 mo	Extrapolation from adult AI
1 through > 70 y	Median manganese intake from the Total Diet Study
<i>Pregnancy</i>	
≤ 18 y	Extrapolation from adolescent female AI based on body weight
19 through 50 y	Extrapolation from adult female AI based on body weight
<i>Lactation</i>	
< 18 y through 50 y	Median manganese intake from the Total Diet Study

### The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all healthy people. Members of the general population should not routinely exceed the UL. This value is based on elevated blood manganese and neurotoxicity as the critical adverse effects and represents intake from food, water, and supplements.

Based on the Total Diet Study, the highest dietary manganese intake at the 95th percentile was 6.3 mg/day, which was the level consumed by men aged 31 to 50 years. Data from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994) indicated that the highest supplemental intake of manganese at the 95th percentile was approximately 5 mg/day, which was consumed by adults, including pregnant women. The risk of an adverse effect resulting from excess intake of manganese from food and supplements appears to be low at these intakes.

## **DIETARY SOURCES**

### **Foods**

Based on the Total Diet Study, grain products contributed 37 percent of dietary manganese, while beverages (tea) and vegetables contributed 20 and 18 percent, respectively, to the adult male diet.

### **Dietary Supplements**

According to U.S. data from the 1986 National Health Interview Survey (NHIS), 12 percent of adults consumed supplements that contained manganese. Based on data from NHANES III, the median supplemental intake of manganese was 2.4 mg/day for those adults who took supplements, an amount similar to the average dietary manganese intake.

### **Bioavailability**

Several factors may affect the bioavailability of manganese (see “Dietary Interactions”).

### **Dietary Interactions**

There is evidence that manganese may interact with certain other nutrients and dietary substances (see Table 2).

## **INADEQUATE INTAKE AND DEFICIENCY**

Although a manganese deficiency may contribute to one or more clinical symptoms, a clinical deficiency has not been clearly associated with poor dietary intakes of healthy individuals. In limited studies on induced manganese depletion in humans, subjects developed scaly dermatitis and hypocholesterolemia. Studies in various animal species observed signs and symptoms of deficiency, including impaired growth and skeletal development, impaired reproductive

**TABLE 2 Potential Interactions with Other Dietary Substances**

<i>Substance</i>	<i>Potential Interaction</i>	<i>Notes</i>
<b>SUBSTANCES THAT AFFECT MANGANESE</b>		
Calcium	Calcium may reduce manganese absorption.	In one study, adding calcium to human milk reduced the absorption of manganese from 4.9 percent to 3.0 percent.
Iron	Iron status may affect manganese absorption: low serum ferritin concentration may increase manganese absorption.	Low ferritin concentrations are associated with increased manganese absorption, thereby having a gender effect on manganese bioavailability (because women tend to have lower ferritin concentrations compared with men).
Phytate	Phytate may decrease manganese absorption.	In a study of infant formula, the soy-based formula without phytate produced manganese absorption of 1.6 percent, whereas a formula with phytate produced an absorption of 0.7 percent.

function, impaired glucose tolerance, and alterations in carbohydrate and lipid metabolism.

## EXCESS INTAKE

Manganese toxicity, which causes central nervous system effects similar to those of Parkinson's disease, is a well-recognized occupational hazard for people who inhale manganese dust. The totality of evidence in animals and humans supports a causal association between elevated blood manganese concentrations and neurotoxicity.

## Special Considerations

**Individuals susceptible to adverse effects:** People with chronic liver disease may be distinctly susceptible to the adverse effects of excess manganese intake, probably because elimination of manganese in bile is impaired. Also, manganese in drinking water and supplements may be more bioavailable than food manganese. Therefore, individuals who take manganese supplements, particularly those who already consume large amounts of manganese from diets high in plant products, should take extra caution.

Plasma manganese concentrations can become elevated in infants with cholestatic liver disease who are given supplemental manganese in total parenteral nutrition (TPN).

## KEY POINTS FOR MANGANESE

- ✓ Manganese is an essential nutrient involved in the formation of bone and in specific reactions related to amino acid, cholesterol, and carbohydrate metabolism.
- ✓ Since data were insufficient to set an EAR and thus calculate an RDA for manganese, an AI was instead developed.
- ✓ The AIs for manganese are based on the intakes of healthy individuals, using median manganese intakes reported from the FDA's Total Diet Study. The UL is based on elevated blood manganese concentrations and neurotoxicity as the critical adverse effects.
- ✓ The risk of an adverse effect resulting from excess intake of manganese from food and supplements appears to be low.
- ✓ The highest contributors of manganese to the diet are grain products, beverages (tea), and vegetables.
- ✓ Although a manganese deficiency may contribute to one or more clinical symptoms, a clinical deficiency has not been clearly associated with poor dietary intakes of healthy individuals. In limited studies on induced manganese depletion in humans, subjects developed scaly dermatitis and hypcholesterolemia.
- ✓ Manganese toxicity, which causes central nervous system effects similar to those of Parkinson's disease, is a well-recognized occupational hazard for people who inhale manganese dust. Neurotoxicity of orally ingested manganese at relatively low doses is more controversial, but evidence suggests that elevated blood manganese levels and neurotoxicity are possible.
- ✓ Plasma manganese concentrations can become elevated in infants with cholestatic liver disease who are given supplemental manganese in total parenteral nutrition.

**TABLE 1 Dietary Reference Intakes for Molybdenum by Life Stage Group**

Life stage group	DRI values (μg /day)					
	EAR <sup>a</sup>		RDA <sup>b</sup>		AI <sup>c</sup>	UL <sup>d</sup>
	males	females	males	females		
0 through 6 mo					2	ND <sup>e</sup>
6 through 12 mo					3	ND
1 through 3 y	13	13	17	17		300
4 through 8 y	17	17	22	22		600
9 through 13 y	26	26	34	34		1,100
14 through 18 y	33	33	43	43		1,700
19 through 30 y	34	34	45	45		2,000
31 through 50 y	34	34	45	45		2,000
51 through 70 y	34	34	45	45		2,000
> 70 y	34	34	45	45		2,000
<b>Pregnancy</b>						
≤ 18 y		40		50		1,700
19 through 50 y		40		50		2,000
<b>Lactation</b>						
≤ 18 y		35		50		1,700
19 through 50 y		36		50		2,000

<sup>a</sup> EAR = Estimated Average Requirement.<sup>b</sup> RDA = Recommended Dietary Allowance.<sup>c</sup> AI = Adequate Intake.<sup>d</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.<sup>e</sup> ND = Not determinable. This value is not determinable due to the lack of data of adverse effects in this age group and concern regarding the lack of ability to handle excess amounts. Source of intake should only be from food to prevent high levels of intake.

# MOLYBDENUM

**M**olybdenum functions as a cofactor for several enzymes, including sulfite oxidase, xanthine oxidase, and aldehyde oxidase. The requirements for molybdenum are based on controlled balance studies with specific amounts of molybdenum consumed. Adjustments were made for the bioavailability of molybdenum. The Tolerable Upper Intake Level (UL) is based on impaired reproduction and growth in animals. DRI values are listed by life stage group in Table 1.

Legumes, grain products, and nuts are the major contributors of dietary molybdenum. Molybdenum deficiency has not been observed in healthy people. Molybdenum compounds appear to have low toxicity in humans.

## MOLYBDENUM AND THE BODY

### Function

Molybdenum, in a form called molybdopterin, acts as a cofactor for several enzymes, including sulfite oxidase, xanthine oxidase, and aldehyde oxidase. These enzymes are involved in catabolism of sulfur amino acids and heterocyclic compounds such as purines and pyrimidines. A clear molybdenum deficiency syndrome that produces physiological signs of molybdenum restriction has not been achieved in animals, despite major reduction in the activity of these molybdoenzymes. Rather, the essential nature of molybdenum is based on a genetic defect that prevents sulfite oxidase synthesis. Because sulfite is not oxidized to sulfate, severe neurological damage leading to early death occurs with this inborn error of metabolism.

### Absorption, Metabolism, Storage, and Excretion

The absorption of molybdenum is highly efficient over a wide range of intakes, which suggests that the mechanism of action is a passive (nonmediated) diffusion process. However, the exact mechanism and location within the gastrointestinal tract of molybdenum absorption have not been studied. Protein-bound molybdenum constitutes 83–97 percent of the total molybdenum in erythrocytes. Potential plasma molybdenum transport proteins include  $\alpha$ -macroglobulin.

Evidence suggests that the kidneys are the primary site of molybdenum homeostatic regulation. Excretion is primarily through the urine and is directly related to dietary intake. When molybdenum intake is low, about 60 percent of ingested molybdenum is excreted in the urine, but when molybdenum intake is high, more than 90 percent is excreted in the urine. Although related to dietary intake, urinary molybdenum alone does not reflect status.

## DETERMINING DRIS

### Determining Requirements

The requirements for molybdenum are based on controlled balance studies with specific amounts of molybdenum consumed. Adjustments were made for the bioavailability of molybdenum. Information on dietary intake of molybdenum is limited because of lack of a simple and reliable analytical method for determining molybdenum in foods.

### Criteria for Determining Molybdenum Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Average molybdenum intake from human milk
7 through 12 mo	Extrapolation from 0 through 6 mo AI
1 through 18 y	Extrapolation from adult EAR
19 through 30 y	Balance data
31 through > 70 y	Extrapolation of balance data from 19 through 30 y
<i>Pregnancy</i>	
≤ 18 y	Extrapolation of adolescent female EAR based on body weight
19 through 50 y	Extrapolation of adult female EAR based on body weight
<i>Lactation</i>	
≤ 18 y	Adolescent female EAR plus average amount of molybdenum secreted in human milk
19 through 50 y	Adult female EAR plus average amount of molybdenum secreted in human milk

### The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Members of the general population should not routinely exceed the UL. Inadequate data exist to identify a causal association between excess molybdenum

intake in normal, apparently healthy individuals and any adverse health outcomes. In addition, studies have identified levels of dietary molybdenum intake that appear to be associated with no harm. Thus, the UL is based on adverse reproductive effects in rats fed high levels of molybdenum. The UL applies to all forms of molybdenum from food, water, and supplements. More soluble forms of molybdenum have greater toxicity than insoluble or less soluble forms.

National surveys do not provide percentile data on the dietary intake of molybdenum. Data available from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994) indicate that the average U.S. intakes from molybdenum supplements at the 95th percentile were 80 µg/day for men and 84 µg/day for women. Because there was no information from national surveys on percentile distribution of molybdenum intakes, the risk of adverse effects could not be characterized.

## DIETARY SOURCES

### Foods

The molybdenum content of plant-based foods depends on the content of the soil in which the foods were grown. Legumes, grain products, and nuts are the major contributors of dietary molybdenum. Animal products, fruits, and many vegetables are generally low in molybdenum.

### Dietary Supplements

Data from NHANES III indicated that the median intakes of molybdenum from supplements were 23 µg/day for men and 24 µg/day for women.

### Bioavailability

Little is known about the bioavailability of molybdenum, except that it has been demonstrated to be less efficiently absorbed from soy than from other food sources (as is the case with other minerals). It is unlikely that molybdenum in other commonly consumed foods would be less available than the molybdenum in soy. The utilization of absorbed molybdenum appears to be similar regardless of food source.

### Dietary Interactions

This information was not provided at the time the DRI values for this nutrient were set.

## INADEQUATE INTAKE AND DEFICIENCY

Molybdenum deficiency has not been observed in healthy people. A rare metabolic defect called molybdenum cofactor deficiency results from the deficiency of molybdoenzymes. Few infants with this defect survive the first days of life, and those who do have severe neurological and other abnormalities.

## EXCESS INTAKE

Molybdenum compounds appear to have a low toxicity in humans. Possible reasons for the presumed low toxicity of molybdenum include its rapid excretion in the urine, especially at higher intake levels. More soluble forms of molybdenum have greater toxicity than insoluble or less soluble forms.

There are limited toxicity data for molybdenum in humans; most of the data apply to animals. In the absence of adequate human studies, it is impossible to determine which adverse effects might be considered most relevant to humans.

## Special Considerations

*Individuals susceptible to adverse effects:* People who are deficient in dietary copper or who have some dysfunction in copper metabolism that makes them copper-deficient could be at increased risk of molybdenum toxicity. However, the effect of molybdenum intake on copper status in humans remains to be clearly established.

## KEY POINTS FOR MOLYBDENUM

- ✓ Molybdenum functions as a cofactor for certain enzymes, including sulfite oxidase, xanthine oxidase, and aldehyde oxidase.
- ✓ The requirements for molybdenum are based on controlled balance studies with specific amounts of molybdenum consumed. The UL is based on impaired reproduction and growth in animals.
- ✓ Information on dietary intake of molybdenum is limited because of lack of a simple and reliable analytical method for determining molybdenum in food. Usual intake is well above the dietary molybdenum requirement.
- ✓ The molybdenum content of plant-based foods depends on the content of the soil in which the foods were grown. Legumes, grain products, and nuts are the major contributors of dietary molybdenum.
- ✓ Molybdenum deficiency has not been observed in healthy people. A rare and usually fatal metabolic defect called molybdenum cofactor deficiency results from the deficiency of molybdoenzymes.
- ✓ Molybdenum compounds appear to have a low toxicity in humans.
- ✓ There are limited toxicity data for molybdenum in humans; most of the data apply to animals.
- ✓ Possible reasons for the presumed low toxicity of molybdenum include its rapid excretion in the urine, especially at higher intake levels.

**TABLE 1 Dietary Reference Intakes for Phosphorus by Life Stage Group**

Life stage group	DRI values (mg /day)					
	EAR <sup>a</sup>		RDA <sup>b</sup>		AI <sup>c</sup>	UL <sup>d</sup>
	males	females	males	females		
<b>Life stage group</b>						
0 through 6 mo					100	ND <sup>e</sup>
7 through 12 mo					275	ND
1 through 3 y	380	380	460	460		3,000
4 through 8 y	405	405	500	500		3,000
9 through 13 y	1,055	1,055	1,250	1,250		4,000
14 through 18 y	1,055	1,055	1,250	1,250		4,000
19 through 30 y	580	580	700	700		4,000
31 through 50 y	580	580	700	700		4,000
51 through 70 y	580	580	700	700		4,000
> 70 y	580	580	700	700		3,000
<b>Pregnancy</b>						
≤ 18 y		1,055		1,250		3,500
19 through 50 y		580		700		3,500
<b>Lactation</b>						
≤ 18 y		1,055		1,250		4,000
19 through 50 y		580		700		4,000

<sup>a</sup> EAR = Estimated Average Requirement.<sup>b</sup> RDA = Recommended Dietary Allowance.<sup>c</sup> AI = Adequate Intake.<sup>d</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.<sup>e</sup> ND = Not determinable. This value is not determinable due to the lack of data of adverse effects in this age group and concern regarding the lack of ability to handle excess amounts. Source of intake should only be from food to prevent high levels of intake.

# PHOSPHORUS

The element phosphorus is found in nature (e.g., foods, water, and living tissues) primarily as phosphate ( $\text{PO}_4^{3-}$ ). It is a major component of bones and teeth. In fact, 85 percent of total body phosphorus is found in bone. Phosphorus helps maintain a normal pH in the body and is involved in metabolic processes.

The adult requirements for phosphorus are based on studies of serum inorganic phosphate concentration in adults. The Tolerable Upper Intake Level (UL) was derived using data on the normal adult range for serum inorganic phosphate concentration. DRI values are listed by life stage group in Table 1.

Nearly all foods contain phosphorus, and it is also common in food additives. Phosphorus deficiency is generally not a problem; the average adult diet contains about 62 mg phosphorus per 100 kcal. Excess phosphorus intake is expressed as hyperphosphatemia, and essentially all adverse effects of phosphorus excess are due to the elevated inorganic phosphorus in the extracellular fluid (ECF).

## PHOSPHORUS AND THE BODY

### Function

Phosphorus is a major component of bones and teeth. Its main functions are to maintain a normal pH (by buffering excesses of acid or alkali), temporarily store and transfer energy derived from metabolic fuels, and activate catalytic proteins via phosphorylation. Structurally, phosphorus occurs in the body as phospholipids (a major component of biological membranes) and as nucleotides and nucleic acids. Dietary phosphorus supports tissue growth and replaces phosphorus stores that are lost through excretion and the shedding of skin cells.

### Absorption, Metabolism, Storage, and Excretion

Phosphorus found in foods is a mixture of organic and inorganic forms, and most phosphorus absorption occurs as inorganic phosphate. Approximately 55–70 percent of dietary phosphorus is absorbed in adults and about 65–90 percent in infants and children. The majority of phosphorus absorption occurs through passive concentration-dependent processes.

The amount of phosphorus ingested does not appear to affect absorption efficiency, which suggests that this efficiency does not improve with low intakes (unlike calcium absorption). By the same token, when serum phosphorus is abnormally high, even dangerously so, phosphorus continues to be absorbed from the diet at a rate only slightly lower than normal. Phosphorus absorption is reduced by aluminum-containing antacids and pharmacological doses of calcium carbonate. However, when consumed at intakes in the typical adult range, calcium does not significantly interfere with phosphorus absorption.

In adults, 85 percent of phosphorus is found in bone, with the remaining 15 percent distributed through the soft tissues. Excretion is achieved mainly through the kidneys. In healthy adults, the amount of phosphorus excreted in the urine is essentially equal to the amount absorbed through diet, less small amounts lost in the shedding of skin cells and intestinal mucosa.

## DETERMINING DRIS

### Determining Requirements

The adult requirements for phosphorus are based on studies of serum inorganic phosphate concentration. The EAR, and hence the RDA, for healthy adolescents aged 9 through 18 years is based on a factorial approach and is higher than the adult value. This is because this age range brackets a period of intense growth, with growth rate, absorption efficiency, and normal values of inorganic phosphorus in the extracellular fluid changing during this time.

### Criteria for Determining Phosphorus Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 12 mo	Human milk content
1 through 18 y	Factorial approach
19 through 50 y	Serum $P_i$ (serum inorganic phosphate concentration)
51 through > 70 y	Extrapolation of serum $P_i$ from 19 through 50 years

<i>Pregnancy</i>	
$\leq 18$ y	Factorial approach
19 through 50 y	Serum $P_i$

<i>Lactation</i>	
$\leq 18$ y	Factorial approach
19 through 50 y	Serum $P_i$

## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Members of the general population should not routinely exceed the UL. The UL value for phosphorus was derived using data on the normal adult range for serum inorganic phosphate concentration and represents total intake from food, water, and supplements.

Phosphorus exposure data, based on data from the Continuing Survey of Food Intakes by Individuals (CSFII, 1994–1996) and the 1986 National Health Interview Survey (NHIS), indicated that only a small percentage of the population was likely to routinely exceed the UL for phosphorus; however, because food composition data do not always indicate phosphorus from food additives, the full extent of phosphorus intake is not known.

## DIETARY SOURCES

### Foods

Phosphorus is found naturally in many foods in the form of phosphate ( $\text{PO}_4$ ) and as a food additive in the form of various phosphate salts, which are used for nonnutritive functions during food processing, such as moisture retention, smoothness, and binding.

According to data from the National Health Survey (1976–1980), the phosphorus content of the average adult diet for both men and women is about 62 mg/100 kcal. Dietary intake of phosphorus appears to be affected more by total food intake and less by differences in food composition. People with a high intake of dairy products will have diets with higher phosphorus density values because the phosphorus density of cow milk is higher than for most other foods. People who consume several servings per day of colas or a few other soft drinks that contain phosphoric acid also tend to have high phosphorus intake. A 12-ounce serving of such beverages contains about 50 mg, which is only 5 percent of the typical intake by an adult woman. However, when consumed in a quantity of 5 or more servings per day, such beverages may contribute substantially to total phosphate intake.

### Dietary Supplements

Phosphorus supplements are not widely used in the United States. Based on the 1986 NHIS study, about 10 percent of adults and 6 percent of children aged 2 to 6 years took supplements containing phosphorus. Supplement usage and

dosage was similar for men and women, with a median intake from supplements of 120 mg/day.

### Bioavailability

Most foods exhibit good phosphorus bioavailability. However, foods derived from plant seeds (e.g., beans, peas, cereals, and nuts) contain phytic acid (also called phytate), a stored form of phosphorus that is not directly available to humans. Absorption of this form requires the presence of phytase, an enzyme found in some foods and in some colonic bacteria. Because yeasts can hydrolyze phytate, whole grains that are incorporated into leavened bread products have higher phosphorus bioavailability than do grains used in unleavened bread or breakfast cereals. Also, unabsorbed calcium in the digestive tract combines with phytic acid and interferes with its digestion and absorption. This may partly explain why calcium interferes with phosphorus absorption.

In infants, phosphorus bioavailability is highest from human milk (85–90 percent), intermediate from cow milk (72 percent), and lowest from soy formulas, which contain phytic acid (59 percent). However, the higher amounts of phosphorus contained in cow milk and soy formulas offset this decreased bioavailability.

### Dietary Interactions

There is evidence that phosphorus may interact with certain nutrients and dietary substances (see Table 2).

## INADEQUATE INTAKE AND DEFICIENCY

Phosphorus deficiency is generally not a problem. This is because phosphorus is so ubiquitous in the diet that near total starvation is required to produce dietary phosphorus deficiency. However, if inadequate phosphorus intake does occur, such as in individuals recovering from alcoholic bouts, from diabetic ketoacidosis, and from refeeding with calorie-rich sources without paying attention to phosphorus needs, it is realized as hypophosphatemia. The effects of hypophosphatemia include the following:

- Anorexia
- Anemia
- Muscle weakness
- Bone pain
- Rickets (in children) and osteomalacia (in adults)
- General debility

**TABLE 2 Potential Interactions with Other Dietary Substances**

<i>Substance</i>	<i>Potential Interaction</i>	<i>Notes</i>
<b>SUBSTANCES THAT AFFECT PHOSPHORUS</b>		
Calcium	Pharmacological doses of calcium carbonate may interfere with phosphorus absorption.	Calcium in the normal adult intake range is not likely to pose a problem for phosphorus absorption.
Aluminum	When taken in large doses, antacids that contain aluminum may interfere with phosphorus absorption.	
<b>PHOSPHORUS AFFECTING OTHER SUBSTANCES</b>		
Calcium	Excess intake of phosphorus may interfere with calcium absorption.	This is less likely to pose a problem if calcium intake is adequate.

- Increased susceptibility to infection
- Paresthesias
- Ataxia
- Confusion
- Possible death

## Special Considerations

**Antacids:** Antacids that contain aluminum can bind with dietary phosphorus and, when consumed in large doses, produce hypophosphatemia.

**Treating malnutrition:** The refeeding of energy-depleted individuals, either orally or parenterally, must supply adequate inorganic phosphate. Otherwise, severe and perhaps fatal hypophosphatemia may occur.

## EXCESS INTAKE

Excess phosphorus intake from any source can result in hyperphosphatemia, the adverse effects of which are due to an elevated concentration of inorganic phosphate in the extracellular fluid. Hyperphosphatemia from dietary causes becomes a problem mainly in individuals with end-stage renal disease or in such conditions as vitamin D intoxication. The potential effects of hyperphosphatemia include the following:

- Reduced calcium absorption (less problematic with adequate calcium intake)
- Calcification of nonskeletal tissues, particularly the kidneys

Concern about high phosphorus intake has been raised because of a probable population-level increase in phosphorus intake through colas and a few other soft drinks that contain phosphoric acid and processed foods containing phosphate additives. High intakes of polyphosphates found in additives may interfere with the absorption of iron, copper, and zinc. However, further research is necessary in this area.

## KEY POINTS FOR PHOSPHORUS

- ✓ The element phosphorus is found in nature primarily as phosphate ( $\text{PO}_4$ ). It is a major component of bones and teeth. In fact, 85 percent of total body phosphorus is found in bone.
- ✓ Phosphorus helps maintain a normal pH in the body and is involved in metabolic processes. Dietary phosphorus supports tissue growth and replaces phosphorus stores that are lost through excretion and the shedding of skin cells.
- ✓ The adult requirements for phosphorus are based on studies of serum inorganic phosphate concentration. The UL was derived using data on the normal adult range for serum inorganic phosphate concentration.
- ✓ Nearly all foods contain phosphorus; dairy products are a particularly rich source.
- ✓ Foods derived from plant seeds (e.g., beans, peas, cereals, and nuts) contain phytic acid (also called phytate), a stored form of phosphorus that is poorly absorbed in humans.
- ✓ Phosphorus deficiency is generally not a problem; the average adult diet contains about 62 mg phosphorus per 100 kcal.
- ✓ Excess phosphorus intake from any source can result in hyperphosphatemia, the adverse effects of which are due to an elevated concentration of inorganic phosphate in the extracellular fluid. Hyperphosphatemia from dietary causes becomes a problem mainly in individuals with end-stage renal disease or in such conditions as vitamin D intoxication.
- ✓ There is concern about the population-level increase in phosphorus intake through colas and a few other soft drinks that contain phosphoric acid and processed foods containing phosphates. High intakes of polyphosphates found in additives may interfere with the absorption of iron, copper, and zinc. However, further research is necessary in this area.

**TABLE 1 Dietary Reference Intakes for Potassium by Life Stage Group**

Life stage group <sup>c</sup>	DRI values (g/day)	
	AI <sup>a</sup>	UL <sup>b</sup>
<b>Life stage group<sup>c</sup></b>		
0 through 6 mo	0.4	
7 through 12 mo	0.7	
1 through 3 y	3.0	
4 through 8 y	3.8	
9 through 13 y	4.5	
14 through 18 y	4.7	
19 through 30 y	4.7	
31 through 50 y	4.7	
51 through 70 y	4.7	
> 70 y	4.7	
<b>Pregnancy</b>		
≤18 y	4.7	
19 through 50 y	4.7	
<b>Lactation</b>		
≤18 y	5.1	
19 through 50 y	5.1	

<sup>a</sup> AI = Adequate Intake.<sup>b</sup> UL = Tolerable Upper Intake Level. Data were insufficient to set a UL. In the absence of a UL, extra caution may be warranted in consuming levels above the recommended intake.<sup>c</sup> All groups except Pregnancy and Lactation represent males and females.

# POTASSIUM

The mineral potassium is the main intracellular cation in the body and is required for normal cellular function. The ratio of extracellular to intracellular potassium affects nerve transmission, muscle contraction, and vascular tone.

Since data were inadequate to determine an Estimated Average Requirement (EAR) and thus calculate a Recommended Dietary Allowance (RDA) for potassium, an Adequate Intake (AI) was instead developed. The AIs for potassium are based on a level of dietary intake that should maintain lower blood pressure levels, reduce the adverse effects of sodium chloride intake on blood pressure, reduce the risk of recurrent kidney stones, and possibly decrease bone loss. In healthy people, excess potassium above the AI is readily excreted in the urine; therefore a UL was not set. DRI values are listed by life stage group in Table 1.

Fruits and vegetables, particularly leafy greens, vine fruit, and root vegetables, are good food sources of potassium. Although uncommon in the general population, the main effect of severe potassium deficiency is hypokalemia. Hypokalemia can cause cardiac arrhythmias, muscle weakness, and glucose intolerance. Moderate potassium deficiency, which typically occurs without hypokalemia, is characterized by elevated blood pressure, increased salt sensitivity, an increased risk of kidney stones, and increased bone turnover. An inadequate intake of potassium may also increase the risk of cardiovascular disease, particularly stroke.

There is no evidence that a high intake of potassium from foods has adverse effects in healthy people. However, for individuals whose urinary excretion of potassium is impaired, a potassium intake below the AI is appropriate because adverse cardiac effects (arrhythmias) can occur as a result of hyperkalemia (markedly elevated serum potassium concentration). Such individuals are typically under medical supervision.

## POTASSIUM AND THE BODY

### Function

Potassium is the major intracellular cation in the body. Although the mineral is found in both the intracellular and the extracellular fluids, it is more concentrated in the intracellular fluid (about 145 mmol/L). Even small changes in the

concentration of extracellular potassium can greatly affect the ratio between extracellular and intracellular potassium. This, in turn, affects neural transmission, muscle contraction, and vascular tone.

## Absorption, Metabolism, Storage, and Excretion

In unprocessed foods, potassium occurs mainly in association with bicarbonate-generating precursors like citrate and, to a lesser extent, phosphate. When potassium is added to foods during processing or to supplements, it is in the form of potassium chloride.

Healthy people absorb about 85 percent of the dietary potassium that they consume. The high intracellular concentration of potassium is maintained by the sodium-potassium-ATPase pump. Because insulin stimulates this pump, changes in the plasma insulin concentration can affect extracellular potassium concentration and thus plasma concentration of potassium.

About 77–90 percent of dietary potassium is excreted in the urine. This is because, in a steady state, the correlation between dietary potassium intake and urinary potassium content is high. The rest is excreted mainly in the feces, and much smaller amounts are lost through sweat.

## DETERMINING DRIS

### Determining Requirements

In unprocessed foods, the conjugate anions of potassium are organic anions, such as citrate, which are converted in the body to bicarbonate. Bicarbonate acts as a buffer, neutralizing diet-derived acids such as sulfuric acid generated from sulfur-containing amino acids found in meats and other high-protein foods. When the intake of bicarbonate precursors is inadequate, buffers in the bone matrix neutralize excess diet-derived acids. Bone becomes demineralized in the process. The resulting adverse consequences are increased bone turnover and calcium-containing kidney stones. In processed foods to which potassium has been added, and in supplements, the conjugate anion is typically chloride, which does not act as a buffer.

Because the demonstrated effects of potassium often depend on the accompanying anion and because it is difficult to separate the effects of potassium from the effects of its accompanying anion, this publication focuses on nonchloride forms of potassium naturally found in fruits, vegetables, and other potassium-rich foods.

Since data were inadequate to determine an EAR and thus calculate an RDA for potassium, an AI was instead developed. The AIs for potassium are based on a level of dietary intake that should maintain lower blood pressure

levels, reduce the adverse effects of sodium chloride intake on blood pressure, reduce the risk of recurrent kidney stones, and possibly decrease bone loss.

## Special Considerations

**African Americans:** Because African Americans have lower intakes of potassium and a higher prevalence of elevated blood pressure and salt sensitivity, this population subgroup would especially benefit from an increased intake of potassium. (In general terms, salt sensitivity is expressed as either the reduction in blood pressure in response to a lower salt intake or the rise in blood pressure in response to sodium loading.)

**Individuals with certain conditions:** Individuals with Type I diabetes and individuals taking cyclo-oxygenase-2 (COX-2) inhibitors or other nonsteroidal anti-inflammatory (NSAID) drugs should consume levels of potassium recommended by their health care professional. These levels may well be lower than the AI.

**Impaired urinary potassium excretion:** Common drugs that can substantially impair potassium excretion are angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), and potassium-sparing diuretics. Medical conditions associated with impaired urinary potassium excretion include diabetes, chronic renal insufficiency, end-stage renal disease, severe heart failure, and adrenal insufficiency. Elderly individuals are at an increased risk of hyperkalemia because they often have one or more of these conditions or are treated with one of these medications.

Because arrhythmias due to hyperkalemia can be life-threatening, the AI does not apply to people with the above medical conditions or to those taking drugs that impair potassium excretion. In such cases, a potassium intake below the AI is often appropriate. In addition, salt substitutes containing potassium chloride should be cautiously used by these individuals, for whom medical supervision is also advised.

## Criteria for Determining Potassium Requirements, by Life Stage Group

Life Stage Group	Criterion
0 through 6 months	Average consumption from human milk
7 through 12 months	Average consumption from human milk + complementary foods
1 through 18 y	Extrapolation of adult AI based on energy intake
19 through >70 y	Intake level to lower blood pressure, reduce the extent of salt sensitivity, and minimize the risk of kidney stones in adults

*Pregnancy*

≤ 18 through 50 y      Age-specific value

*Lactation*

≤ 18 through 50 y      Age-specific values + average amount of potassium estimated in breast milk during the first 6 months (0.4 g/day)

## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. In otherwise healthy individuals (i.e., individuals without impaired urinary potassium excretion due to a medical condition or drug therapy), there is no evidence that a high level of potassium from foods has adverse effects. Therefore, a UL for potassium from foods has not been set. However, supplemental potassium can lead to acute toxicity, as well as adverse effects due to chronic consumption (see “Excess Intake”). Although no UL for potassium was set, potassium supplements should only be provided under medical supervision.

## SOURCES OF POTASSIUM

### Foods

Fruits and vegetables, particularly leafy greens, vine fruit (such as tomatoes, cucumbers, zucchini, eggplant, and pumpkin), and root vegetables, are good sources of potassium and bicarbonate precursors. Although meat, milk, and cereal products contain potassium, they do not contain enough bicarbonate precursors to adequately balance their acid-forming precursors, such as sulfur-containing amino acids. Nutrient tables of the citrate and bicarbonate content of foods are lacking, making it difficult to estimate the amount consumed of these other food components.

### Dietary Supplements

The maximum amount of potassium found in over-the-counter, multivitamin-mineral supplements is generally less than 100 mg.

### Bioavailability

This information was not provided at the time the DRI values for this nutrient were set.

**TABLE 2 Potential Interactions with Other Dietary Substances**

<i>Substance</i>	<i>Potential Interaction</i>	<i>Notes</i>
<b>POTASSIUM AFFECTING OTHER SUBSTANCES</b>		
Sodium chloride	Potassium bicarbonate mitigates the pressor effect of sodium chloride. Dietary potassium increases the urinary excretion of sodium chloride.	Supplemental potassium bicarbonate mitigates the effects of dietary sodium chloride. The effects seem to be more prominent in African Americans, who have a higher prevalence of hypertension and of salt sensitivity and a lower intake of potassium than non-African Americans.
Sodium:potassium ratio	The sodium:potassium ratio is typically more closely associated with blood pressure than with the intake of either substance alone.  The incidence of kidney stones has been shown to increase with an increased sodium:potassium ratio.	Although blood pressure is inversely associated with potassium intake and directly associated with sodium intake and the sodium:potassium ratio, the ratio typically is more influential. Given the interrelatedness of sodium and potassium, the requirement for potassium may depend on dietary sodium intake. However, currently there are not enough data on which to make recommendations.

## Dietary Interactions

There is evidence that potassium may interact with certain other nutrients and dietary substances (see Table 2).

## INADEQUATE INTAKE AND DEFICIENCY

The adverse effects of inadequate potassium intake can result from a deficiency of potassium per se, a deficiency of the anion that accompanies it (e.g., citrate), or both. Severe potassium deficiency is characterized by hypokalemia, a condition marked by a serum potassium concentration of less than 3.5 mmol/L. The adverse consequences of hypokalemia include cardiac arrhythmias, muscle weakness, and glucose intolerance. Moderate potassium deficiency, which typically occurs without hypokalemia, is characterized by increased blood pressure, increased salt sensitivity, an increased risk of kidney stones, increased bone turnover, and a possible increased risk of cardiovascular disease, particularly stroke.

Processed foods and unprocessed foods differ in their composition of conjugate anions, which in turn, can affect bone mineralization. In unprocessed foods, the conjugate anions of potassium are mainly organic anions, such as citrate, which are converted in the body to bicarbonate. Consequently, an inadequate intake of potassium is also associated with a reduced intake of bicarbonate precursors. Bicarbonate acts as a buffer, neutralizing diet-derived noncarbonic acids such as sulfuric acid generated from sulfur-containing amino acids found in meats and other high-protein foods. If the intake of bicarbonate precursors is inadequate, buffers in the bone matrix neutralize the excess diet-derived acids. Bone becomes demineralized in the process. In processed foods to which potassium has been added, and in supplements, the conjugate anion is typically chloride, which does not act as a buffer.

Excess diet-derived acid titrates bone, leading to increased urinary calcium and reduced urinary citrate excretion. The possible adverse consequences are increased bone demineralization and an increased risk of calcium-containing kidney stones.

## Special Considerations

**Climate and physical activity:** Heat exposure and exercise can increase potassium loss, primarily through sweat, thereby increasing potassium requirements.

**Diuretics:** Often used to treat hypertension and congestive heart failure, thiazide-type diuretics increase urinary potassium excretion and can lead to hypokalemia. For this reason, potassium supplements are often prescribed. Potassium-sparing diuretics prevent diuretic-induced potassium loss and are often concurrently used with thiazide-type diuretics. Individuals who take diuretics should have their serum potassium levels regularly checked by their health care providers.

**Very low-carbohydrate, high-protein diets:** Low-grade metabolic acidosis occurs with the consumption of very low-carbohydrate, high-protein diets to promote and maintain weight loss. These diets, which may be adequate in potassium due to their high protein content, are inadequate as a source of alkali because fruits are often excluded from them.

## EXCESS INTAKE

For healthy individuals, there is no evidence that a high level of potassium intake from foods can have adverse effects. However, potassium supplements can cause acute toxicity in healthy people. Chronic consumption of high levels of supplemental potassium can lead to hyperkalemia (markedly elevated serum

potassium) in people with an impaired ability to excrete potassium. The most serious potential effect of hyperkalemia is cardiac arrhythmia.

Gastrointestinal discomfort has been reported with some forms of potassium supplements. The specific product or vehicle in which the potassium supplement is provided is the critical determinant of the risk of gastrointestinal side effects.

## **Special Considerations**

***Problem pregnancy:*** High levels of potassium should be consumed with care by pregnant women with preeclampsia. The hormone progesterone, which is elevated during pregnancy, may make women with undetected kidney problems or decreased glomerular filtration rate (a side effect of preeclampsia) more likely to develop hyperkalemia when potassium intake is high.

## KEY POINTS FOR POTASSIUM

- ✓ Potassium is the main intracellular cation in the body and is required for normal cellular function. The ratio of extracellular to intracellular potassium levels affects neural transmission, muscle contraction, and vascular tone.
- ✓ The AIs for potassium are based on a level of dietary intake that should maintain lower blood pressure levels, reduce the adverse effects of sodium chloride intake on blood pressure, reduce the risk of recurrent kidney stones, and possibly decrease bone loss.
- ✓ Since data were inadequate to determine an EAR and thus calculate an RDA for potassium, an AI was instead developed.
- ✓ Individuals with Type I diabetes; individuals with chronic renal insufficiency, who may take certain medications; and individuals taking cyclo-oxygenase-2 (COX-2) inhibitors or other nonsteroidal anti-inflammatory (NSAID) drugs should consume levels of potassium recommended by their health care professional. These levels may well be lower than the AI.
- ✓ Because African Americans have lower intakes of potassium and a higher prevalence of elevated blood pressure and salt sensitivity, this population subgroup would especially benefit from an increased intake of potassium.
- ✓ In healthy individuals, excess potassium above the AI is readily excreted in the urine; therefore, a UL was not set.
- ✓ Good food sources of potassium include fruits and vegetables, particularly leafy greens, vine fruit, and root vegetables.
- ✓ Although uncommon in the general population, the main effect of severe potassium deficiency is hypokalemia, which can cause cardiac arrhythmias, muscle weakness, and glucose intolerance.
- ✓ Moderate potassium deficiency, which typically occurs without hypokalemia, is characterized by elevated blood pressure, increased salt sensitivity, an increased risk of kidney stones, and increased bone turnover.

- ✓ Chronic consumption of high levels of potassium can lead to hyperkalemia in people with an impaired ability to excrete potassium. The most serious potential effect of hyperkalemia is cardiac arrhythmia.
- ✓ Elderly individuals are often at increased risk of hyperkalemia.

**TABLE 1 Dietary Reference Intakes for Selenium by Life Stage Group**

	DRI values (μg/day)			
	EAR <sup>a</sup>	RDA <sup>b</sup>	AI <sup>c</sup>	UL <sup>d</sup>
<b>Life stage group<sup>e</sup></b>				
0 through 6 mo			15	45
7 through 12 mo			20	60
1 through 3 y	17	20		90
4 through 8 y	23	30		150
9 through 13 y	35	40		280
14 through 18 y	45	55		400
19 through 30 y	45	55		400
31 through 50 y	45	55		400
51 through 70 y	45	55		400
> 70 y	45	55		400
<b>Pregnancy</b>				
≤ 18 y	49	60		400
19 through 50 y	49	60		400
<b>Lactation</b>				
≤ 18 y	59	70		400
19 through 50 y	59	70		400

<sup>a</sup> EAR = Estimated Average Requirement.<sup>b</sup> RDA = Recommended Dietary Allowance.<sup>c</sup> AI = Adequate Intake.<sup>d</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.<sup>e</sup> All groups except Pregnancy and Lactation represent males and females.

# SELENIUM

Selenium is an antioxidant nutrient involved in the defense against oxidative stress. Selenoproteins regulate thyroid hormone actions and the redox status of vitamin C and other molecules. Most selenium found in animal tissue is in the form of selenomethionine (the major dietary form of selenium) or selenocysteine, both of which are well absorbed.

The method used to estimate the requirements for selenium relates to the intake needed to maximize the activity of the plasma selenoprotein glutathione peroxidase, an oxidant defense enzyme. The Tolerable Upper Intake Level (UL) is based on the adverse effect of selenosis, and pertains to intakes from food and supplements. Although some studies indicate a potential anticancer effect of selenium, the data were inadequate to set dietary selenium requirements based on this potential effect. DRI values are listed by life stage group in Table 1.

Food sources of selenium include meat, seafood, grains, dairy products, fruits, and vegetables, and the major dietary forms of selenium appear to be highly bioavailable. However, the selenium content of foods greatly varies depending on the selenium content of the soil where the animal was raised or where the plant was grown. Neither selenium deficiency nor toxicity appears to be common in U.S. and Canadian populations.

## SELENIUM AND THE BODY

### Function

Selenium functions through selenoproteins, several of which defend against oxidative stress; and as such, it plays a role as a dietary antioxidant. Although the function of all selenoproteins has not yet been characterized, selenium has been found to regulate both thyroid hormone actions and the redox status of vitamin C and other molecules.

### Absorption, Metabolism, Storage, and Excretion

Most dietary selenium is in the form of selenomethionine (the major dietary form of selenium) or selenocysteine, both of which are well absorbed. Other forms of selenium include selenate and selenite, which are not major dietary constituents, but are commonly used in fortified foods and dietary supplements. Two pools of reserve selenium are present in the body. The first is as

selenomethionine, which is not known to have a physiological function separate from that of methionine. The second reserve pool is the selenium found in liver glutathione peroxidase.

Ingested selenite, selenate, and selenocysteine are all metabolized directly to selenide, the reduced form of selenium. Selenomethionine can also be metabolized to selenide. Selenide can be metabolized to a precursor of other reactions or be converted into an excretory metabolite. Selenium is excreted mainly through the urine. The breath may also contain volatile metabolites when large amounts of selenium are being excreted.

## DETERMINING DRIS

### Determining Requirements

The adult requirements for selenium are based on the criterion of maximizing plasma glutathione peroxidase activity, as assessed by plateau concentration of plasma selenoproteins. Although some studies indicate a potential anticancer effect of selenium, the data were inadequate to set dietary selenium requirements based on this potential effect. Further large-scale trials are necessary.

### Criteria for Determining Selenium Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Human milk content
7 through 12 mo	Human milk + solid food
1 through 18 y	Extrapolation from adult
19 through 30 y	Maximizing plasma glutathione peroxidase activity
31 through >70 y	Extrapolation of plasma glutathione peroxidase activity from 19 through 30 y

*Pregnancy*  
≤ 18 y through 50 y      Age-specific requirement + saturation of fetal selenoprotein

*Lactation*  
≤ 18 y through 50 y      Age-specific requirement + human milk content requirement

### The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Members of the general population should not routinely exceed the UL. The

UL for selenium is based on selenosis as the adverse effect and represents total intake from food, water, and supplements. The most frequently reported features of selenosis (chronic toxicity) are hair and nail brittleness and loss and thus were selected as the critical endpoints on which to base a UL.

The extensive food distribution systems in Canada and the U.S. ensure that individuals do not eat diets that originate solely from one locality. This moderates the selenium content of diets, even in high-selenium areas. The risk of selenium intake above the UL for U.S. and Canadian populations appears to be small, and there is no known seleniferous area in the United States and Canada with recognized cases of selenosis.

## **DIETARY SOURCES**

### **Foods**

Dietary sources of selenium include meat, seafood, cereals and grains, dairy products, and fruits and vegetables. (Drinking water does not supply nutritionally significant amounts of selenium.)

However, the selenium content of food can greatly vary depending on the selenium content of the soil where the animal was raised or where the plant was grown. Food animals in the United States and Canada usually have controlled diets to which selenium is added, and thus, the amounts found in muscle meats, milk, and eggs are more consistent than for plant-based foods.

Dietary intake of selenium in the United States and Canada varies by geographical origin, based on the selenium content of the soil and meat content of the diet. This variation is buffered by a large food-distribution system, in which the extensive transport of food throughout North America prevents decreased intakes in people living in low-selenium areas. Although the food distribution systems in the United States and Canada ensure a mix of plant- and animal-based foods originating from a broad range of soil selenium conditions, local foods (e.g., from farmers' markets) may considerably vary from the mean values in food composition databases.

The content of selenium in plants depends on the availability of the element in the soil where the plant was grown. Unlike plants, animals require selenium, and so meat and seafood are reliable dietary sources of selenium. Therefore, the lowest selenium intakes are in populations that eat vegetarian diets comprising plants grown in low-selenium areas.

## Dietary Supplements

Selenium is widely available in a variety of supplements and multivitamin preparations. In the 1986 National Health Interview Survey (NHIS), 9 percent of all adults reported the use of supplements containing selenium.

## Bioavailability

Most dietary selenium is highly bioavailable, although its bioavailability from fortified foods and supplements is lower than for naturally occurring dietary forms of selenium.

## Dietary Interactions

This information was not provided at the time the DRI values for this nutrient were set.

## INADEQUATE INTAKE AND DEFICIENCY

Selenium deficiency in otherwise well-nourished individuals is not likely to cause overt symptoms. However, selenium deficiency may lead to biochemical changes that can predispose a person to illness associated with other stresses, such as:

- Keshan disease, a cardiomyopathy found only in selenium-deficient children that appears to be triggered by an additional stress, possibly an infection or chemical exposure
- Kashin-Beck disease, an endemic disease of cartilage that occurs in preadolescence or adolescence, has been reported in some of the low-selenium areas of Asia, although the pathogenesis remains uncertain

## EXCESS INTAKE

The limited data available on humans suggest that chronic toxicities from inorganic and organic forms of selenium have similar clinical features, but differ in the rapidity of onset and the relationship to tissue selenium concentrations. Inorganic selenium can cause toxicity at tissue levels of selenium that are much lower than those seen with similar intakes of dietary selenium as selenomethionine. The signs and symptoms of chronic selenosis, or selenium toxicity, are the following:

- Hair and nail brittleness and loss (most frequently reported symptoms)
- Gastrointestinal disturbances

- Skin rash
- Garlic breath odor
- Fatigue
- Irritability
- Nervous system abnormalities

## Special Considerations

**Soil variations:** There are high-selenium regions in the United States, such as western South Dakota and eastern Wyoming, but the U.S. Department of Agriculture has identified them and proscribed their use for raising animals for food. No evidence of selenosis has been found in these areas of high selenium content, even in the subjects consuming the most selenium.

## KEY POINTS FOR SELENIUM

- ✓ Selenium functions through selenoproteins, several of which defend against oxidative stress and as such, plays a role as a dietary antioxidant.
- ✓ The requirements for selenium are based on the criterion of maximizing plasma glutathione peroxidase activity. The UL is based on the critical endpoints of hair and nail brittleness and loss.
- ✓ Although some studies indicate a potential anticancer effect of selenium, the data were inadequate to set dietary selenium requirements based on this potential effect.
- ✓ Food sources of selenium include meat, seafood, cereals and grains, dairy products, and fruits and vegetables.
- ✓ The lowest selenium intakes are in populations that eat vegetarian diets comprising plants grown in low-selenium geographic areas.
- ✓ The selenium content of foods can greatly vary depending on the selenium content of the soil where the animal was raised or where the plant was grown.
- ✓ Selenium deficiency in otherwise well-nourished individuals is not likely to cause overt symptoms.
- ✓ The limited data available on humans suggest that chronic toxicities from inorganic and organic forms of selenium have similar clinical features but differ in rapidity of onset and relationship to tissue selenium concentrations.

**TABLE 1 Dietary Reference Intakes for Sodium and Chloride by Life Stage Group**

Life stage group <sup>c</sup>	DRI values (g/day)			
	Sodium		Chloride	
	AI <sup>a</sup>	UL <sup>b</sup>	AI	UL
0 through 6 mo	0.12	ND <sup>d</sup>	0.18	ND
7 through 12 mo	0.37	ND	0.57	ND
1 through 3 y	1.0	1.5	1.5	2.3
4 through 8 y	1.2	1.9	1.9	2.9
9 through 13 y	1.5	2.2	2.3	3.4
14 through 18 y	1.5	2.3	2.3	3.6
19 through 30 y	1.5	2.3	2.3	3.6
31 through 50 y	1.5	2.3	2.3	3.6
51 through 70 y	1.3	2.3	2.0	3.6
> 70 y	1.2	2.3	1.8	3.6
<b>Pregnancy</b>				
≤18 y	1.5	2.3	2.3	3.6
19 through 50 y	1.5	2.3	2.3	3.6
<b>Lactation</b>				
≤18 y	1.5	2.3	2.3	3.6
19 through 50 y	1.5	2.3	2.3	3.6

<sup>a</sup> AI = Adequate Intake.<sup>b</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.<sup>c</sup> All groups except Pregnancy and Lactation represent males and females.<sup>d</sup> ND = Not determinable. This value is not determinable due to the lack of data of adverse effects in this age group and concern regarding the lack of ability to handle excess amounts. Source of intake should only be from food to prevent high levels of intake.

## SODIUM AND CHLORIDE

**S**odium and chloride are necessary to maintain extracellular fluid volume and plasma osmolality. The cation sodium and the anion chloride are normally found in most foods together as sodium chloride (salt). For this reason, this publication presents data on the requirements for and the effects of sodium and chloride together.

Since data were inadequate to determine Estimated Average Requirements (EARs) and thus calculate Recommended Dietary Allowances (RDAs) for sodium and chloride, Adequate Intakes (AIs) were instead developed. The AIs for sodium are set at an intake that ensures that the overall diet provides an adequate intake of other important nutrients and covers sodium sweat losses in unacclimated individuals who are exposed to high temperatures or who become physically active. The AIs for chloride are set at a level equivalent on a molar basis to that of sodium, since almost all dietary chloride comes with sodium added during the processing or consumption of foods. The AIs for sodium do not apply to individuals who lose large volumes of sodium in sweat, such as competitive athletes and workers exposed to extreme heat stress (e.g., foundry workers and firefighters).

The adverse effects of higher levels of sodium intake on blood pressure provide the scientific rationale for setting the Tolerable Upper Intake Level (UL) for sodium and chloride. DRI values are listed by life stage group in Table 1.

In the United States, sodium chloride accounts for about 90 percent of total sodium intake in the United States. Most of the sodium chloride found in the typical diet is added to food during processing. Examples of high-sodium processed foods include luncheon meats and hot dogs, canned vegetables, processed cheese, potato chips, Worcestershire sauce, and soy sauce.

Overall, there is little evidence of any adverse effect of low dietary sodium intake on serum or plasma sodium concentrations in healthy people. Likewise, chloride deficiency is rarely seen because most foods that contain sodium also provide chloride. The primary adverse effect related to increased sodium chloride intake is elevated blood pressure, which is directly related to cardiovascular disease and end-stage renal disease. Individuals with hypertension, diabetes, and chronic kidney disease, as well as African Americans and older people, tend to be more sensitive than others to the blood pressure-raising effect of sodium chloride intake.

## SODIUM AND CHLORIDE AND THE BODY

### Function

About 95 percent of the body's sodium content is found in the extracellular fluid, where it serves as the primary cation. Sodium regulates extracellular fluid volume and plasma volume and also plays an important role in the membrane potential of cells (the electrical potential difference across a cell's plasma membrane) and the active transport of molecules across cell membranes.

Chloride, in association with sodium, is the primary osmotically active anion in the extracellular fluid. It plays a key role in maintaining fluid and electrolyte balance. In addition, chloride, in the form of hydrochloric acid, is an important component of gastric juice.

### Absorption, Metabolism, Storage, and Excretion

Sodium and chloride ions are typically consumed as sodium chloride. About 98 percent of ingested sodium chloride is absorbed, mainly in the small intestine. Absorbed sodium and chloride remain in the extracellular compartments, which include the plasma, interstitial fluid, and plasma water. As long as sweating is not excessive, most of this sodium chloride is excreted in the urine. In people with "steady-state" sodium and fluid balance, and minimal sweat loss, the amount of sodium excreted in urine is roughly equal to the amount consumed, when other obligatory sodium losses are small.

A number of systems and hormones influence sodium and chloride balance, some of which are shown in Table 2.

## DETERMINING DRIS

### Determining Requirements

Since data were inadequate to determine EARs and thus calculate RDAs for sodium and chloride, AIs were instead developed. The AIs for sodium are set at an intake that ensures that the overall diet provides an adequate intake of other important nutrients and also covers sodium sweat losses in unacclimated individuals who are exposed to high temperatures or who become physically active (as recommended in Part II, "Physical Activity"). The AIs for chloride are set at a level equivalent on a molar basis to that of sodium, since almost all dietary chloride comes with the sodium added during processing or consumption of foods.

Concerns have been raised that a low level of sodium intake adversely affects blood lipids, insulin resistance, and cardiovascular disease risk. However, at the level of the AI, the preponderance of evidence does not support this

**TABLE 2 Major Systems and Hormones That Influence Sodium Chloride Balance**

System or Hormones	Activators	Effect
Renin-angiotensin-aldosterone axis	<ul style="list-style-type: none"> <li>• Reduced salt intake</li> <li>• Reduced blood volume</li> <li>• Reduced blood pressure<sup>a</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Promotes retention of sodium and chloride by the kidneys</li> <li>• Promotes renal reabsorption of sodium</li> </ul>
Atrial natriuretic peptide (counter-regulatory system to renin-angiotensin-aldosterone axis)	<ul style="list-style-type: none"> <li>• Elevated blood volume</li> <li>• Increased salt intake</li> <li>• Increased blood pressure</li> </ul>	<ul style="list-style-type: none"> <li>• Increases glomerular filtration rate</li> <li>• Reduces blood volume</li> <li>• Reduces blood pressure</li> <li>• Increases sodium excretion</li> </ul>
Sympathetic nervous system	<ul style="list-style-type: none"> <li>• Reduced salt intake</li> <li>• Reduced blood volume</li> <li>• Reduced blood pressure</li> </ul>	<ul style="list-style-type: none"> <li>• Reduces sodium reabsorption</li> <li>• Reduces water reabsorption in the kidneys</li> </ul>

<sup>a</sup> When the renin-angiotensin-aldosterone system is less responsive, as with advanced age, a greater decrease in blood pressure results from reduced sodium chloride intake.

contention. A potential indicator of an adverse effect of inadequate sodium is an increase in plasma renin activity. However, in contrast to the well-accepted benefits of blood pressure reduction, the clinical relevance of modest rises in plasma renin activity as a result of sodium reduction is uncertain.

It is well recognized that the current intake of sodium for most individuals in the United States and Canada greatly exceeds both the AI and the UL. Progress in achieving a reduced sodium intake will likely be gradual, requiring changes in personal behavior toward salt consumption, which includes the replacement of high sodium foods with lower sodium alternatives, as well as increased collaboration between the food industry and public health officials. Also required will be a broad spectrum of additional research that includes the development of reduced sodium foods that maintain flavor, texture, consumer acceptability, and low cost.

## Special Considerations

**Excessive sweat loss:** The AI for sodium does not apply to individuals who lose large volumes of sodium in sweat, such as competitive athletes and workers exposed to extreme heat stress (e.g., foundry workers and firefighters).

## Criteria for Determining Sodium and Chloride Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 months	Average consumption of sodium from human milk
7 through 12 months	Average consumption of sodium from human milk + complementary foods
1 through 18 y	Extrapolation of adult AI based on median energy intake level from CSFII
19 though 50 y	Intake level to cover possible daily losses, provide adequate intakes of other nutrients, and maintain normal function
> 50 y	Extrapolation from younger adults based on median energy intake level from CSFII
<i>Pregnancy</i>	
≤ 18 through 50 y	Age-specific AI
<i>Lactation</i>	
≤ 18 through 50 y	Age-specific AI

## The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Members of the general population should not routinely exceed the UL. The major adverse effect of increased sodium chloride intake is elevated blood pressure. High blood pressure has been shown to be a risk factor for heart disease, stroke, and kidney disease.

The scientific rationale for setting the UL is based on the impact of sodium on blood pressure and represents total intake from food, water, and supplements. However, because the relationship between sodium intake and blood pressure is progressive and continuous without an apparent threshold, it is difficult to precisely set a UL, especially since other environmental factors (weight, exercise, potassium intake, dietary pattern, and alcohol intake) and genetic factors also affect blood pressure. There was inadequate evidence to support a different upper level of sodium intake in pregnant women from that of nonpregnant women as a means to prevent hypertensive disorders of pregnancy.

Data from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994) indicated that more than 95 percent of men and 75 percent of women in the United States consumed sodium chloride in excess of the UL. According to NHANES III, 24.7 percent of men and 24.3 percent of

women aged 18 years and older had hypertension, indicating that a substantial number of individuals appear to experience this adverse effect.

Data on Canadian consumption indicated that 90–95 percent of younger men (aged 19 to 50 years) and between 50 and 75 percent of younger women in the same age range had usual intakes above the UL. Neither of these surveys included discretionary salt usage (e.g., from the salt shaker).

### **Special Considerations:**

**Sensitive individuals:** The UL may be even lower for people whose blood pressure is most sensitive to increased sodium intake (e.g., older people; African Americans; and individuals with hypertension, diabetes, or chronic kidney disease) and who also have an especially high incidence of heart disease related to high blood pressure.

**Physical activity and temperature:** In contrast, people unaccustomed to prolonged strenuous physical activity in a hot environment may have sodium needs that exceed the UL because of sodium loss through sweat.

## **DIETARY SOURCES OF SODIUM AND CHLORIDE**

### **Foods**

Sodium chloride (salt) accounts for about 90 percent of total sodium intake in the United States. As Table 3 shows, most of the sodium chloride found in the typical diet is added to food during processing.

Because salt is naturally present in only a few foods, such as celery and milk, the reduction of dietary salt does not cause diets to be inadequate in other nutrients. Although sodium chloride is the primary source of dietary sodium, other forms often found in foods as food additives include monosodium

**TABLE 3 Sources of Dietary Sodium Chloride**

Source of Salt	Percent of Total Sodium Chloride Intake
Added to food during processing	77
Naturally occurring in foods	12
Added while eating	6
Added during cooking	5
Tap water	< 1

glutamate, sodium benzoate, sodium nitrite, and sodium acid pyrophosphate. Sodium bicarbonate and sodium citrate are found in many antacids, which are sometimes consumed in large amounts.

Foods that are processed or canned tend to have high levels of additives that contain sodium. Examples include luncheon meats and hot dogs, canned vegetables, processed cheese, and potato chips. Condiments such as Worcestershire sauce, soy sauce, and ketchup also contain substantial amounts of sodium.

## Dietary Supplements

This information was not provided at the time the DRI values for this nutrient were set.

## Bioavailability

This information was not provided at the time the DRI values for this nutrient were set.

## Dietary Interactions

There is evidence that sodium and chloride may interact with certain other nutrients and dietary substances (see Table 4).

## INADEQUATE INTAKE AND DEFICIENCY

Overall, there is little evidence of any adverse effect of low dietary sodium intake on serum or plasma sodium concentrations in healthy people. Chloride loss usually accompanies sodium loss. Excess chloride depletion causes hypochloremic metabolic alkalosis, a syndrome seen in individuals with significant vomiting. In such cases, the chloride depletion is mainly due to the loss of hydrochloric acid. However, chloride deficiency is rarely seen in healthy people because most foods that contain sodium also provide chloride.

## Special Considerations

**Physical activity and temperature:** Extremely vigorous physical activity performed in high temperatures can potentially affect sodium chloride balance due to the loss of sodium through sweat. The loss depends on a number of factors, including overall diet, sodium intake, sweating rate, hydration status, and one's degree of acclimation to the heat. People who are accustomed to heat exposure lose less sodium through their sweat than those unaccustomed to high temperatures.

**TABLE 4 Potential Interactions with Other Dietary Substances**

Substance	Potential Interaction	Notes
<b>SUBSTANCES THAT AFFECT SODIUM AND CHLORIDE</b>		
Potassium	Increased potassium intake increases urinary excretion of sodium chloride and blunts the rise in blood pressure resulting from excess sodium intake.	Potassium may inhibit sodium reabsorption in the kidneys, thereby reducing extracellular fluid and plasma volumes. This is considered to be an important aspect of the antihypertensive effect of potassium.
<b>SODIUM AND CHLORIDE AFFECTING OTHER SUBSTANCES</b>		
Sodium: potassium ratio	Sodium:potassium ratio is typically more closely associated with blood pressure than the intake of either substance alone, especially in older adults.	Clinical trials have shown that increased potassium intake lowers blood pressure, and the effects of potassium in reducing blood pressure appear to be greatest when sodium is concurrently high. Increased potassium intake also reduces the sensitivity of blood pressure changes to sodium intake.
	The incidence of kidney stones has been shown to increase with an increased sodium:potassium ratio.	Currently, there are not enough data to set different intake recommendations based on the sodium:potassium ratio.

**Diuretics:** Diuretics increase urinary excretion of water, sodium, and chloride, sometimes causing low blood levels of sodium (hyponatremia) and chloride (hypochloremia). Some people have experienced severe hyponatremia as a result of taking thiazide-type diuretics. However, this appears to be due to impaired water excretion rather than excessive sodium loss since it can be corrected by water restriction.

**Cystic fibrosis:** This genetic disorder is characterized by the body's production of abnormally thick, viscous mucus due to the faulty membrane transport of sodium chloride. As a result, the sodium and chloride content of sweat is very high. Although the increased amount of sodium and chloride required by people with cystic fibrosis is unknown, the needs are particularly high for those who exercise and therefore lose additional sodium and chloride through sweat.

**Diabetes:** High blood glucose levels increase renal excretion of sodium and water. In instances of acute hyperglycemia (e.g., diabetic ketoacidosis), low blood

levels of sodium may occur and can generally be treated with intravenous sodium chloride and water along with insulin. Some hypoglycemic medications, such as chlorpropamide, have been associated with low blood sodium levels. In some elderly people with diabetes, hyporeninemic hypoaldosteronism may increase renal sodium loss.

## EXCESS INTAKE

The major adverse effect of increased sodium chloride intake is elevated blood pressure, which has been shown to be an etiologically related risk factor for cardiovascular and renal diseases. On average, blood pressure rises progressively with increased sodium chloride intake. The dose-dependent rise in blood pressure appears to occur throughout the spectrum of sodium intake. However, the relationship is nonlinear in that the blood pressure response to changes in sodium intake is greater at sodium intakes below 2.3 g/day than above this level. The strongest dose-response evidence comes from clinical trials that specifically examined the effects of at least three levels of sodium intake on blood pressure. The range of sodium intake in these studies varied from 0.23 to 34.5 g/day. Several trials included sodium intake levels close to 1.5 g/day and 2.3 g/day.

## Special Considerations

**Special populations:** Although blood pressure, on average, rises with increased sodium intake, there is well-recognized heterogeneity in the blood pressure response to changes in sodium chloride intake. Individuals with hypertension, diabetes, and chronic kidney disease, as well as older people and African Americans, tend to be more sensitive to the blood-pressure-raising effects of sodium chloride intake (defined as salt sensitivity) than others. Genetic factors also influence the blood pressure response to sodium chloride.

There is considerable evidence that salt sensitivity is modifiable. In research studies, different techniques and quantitative criteria have been used to define salt sensitivity. In general terms, salt sensitivity is expressed as either the reduction in blood pressure in response to a lower salt intake or the rise in blood pressure in response to sodium loading. Salt sensitivity differs among population subgroups and among individuals within a subgroup.

The rise in blood pressure from increased sodium chloride intake is blunted in the setting of a diet that is high in potassium or low in fat, and rich in minerals. Nonetheless, a dose-response relationship between sodium intake and blood pressure still persists. In nonhypertensive individuals, a reduced salt intake can decrease the risk of developing hypertension (typically defined as systolic blood pressure  $\geq 140$  mm Hg or diastolic blood pressure  $\geq 90$  mm Hg).

## KEY POINTS FOR SODIUM AND CHLORIDE

- ✓ Sodium and chloride are necessary to maintain extracellular fluid volume and plasma osmolality. The cation sodium and the anion chloride are normally found in most foods together as sodium chloride (salt). About 98 percent of the sodium chloride consumed is absorbed.
- ✓ Since data were inadequate to determine EARs and thus calculate RDAs for sodium and chloride, AIs were instead developed.
- ✓ The AIs for sodium are set at an intake that ensures that the overall diet provides an adequate intake of other important nutrients and also covers sodium sweat losses in unacclimated individuals who are exposed to high temperatures or who become physically active. The AIs for chloride are set at a level equivalent on a molar basis to that of sodium. The UL is set based on the impact of sodium on blood pressure.
- ✓ It is well recognized that the current intake of sodium for most individuals in the United States and Canada greatly exceeds both the AI and the UL.
- ✓ There is inadequate evidence to support a different upper intake level of sodium intake in pregnant women from that of nonpregnant women as a means to prevent hypertensive disorders of pregnancy.
- ✓ The UL may be even lower among people whose blood pressure is most sensitive to increased sodium intake (e.g., older persons; African Americans; and individuals with hypertension, diabetes, or chronic kidney disease) and who also have an especially high incidence of heart disease related to high blood pressure.
- ✓ In contrast, people who are not accustomed to prolonged strenuous physical activity in a hot environment may have sodium needs that exceed the UL because of sodium losses through sweat.
- ✓ Sodium chloride (salt) accounts for about 90 percent of total sodium intake in the United States. Most of the sodium chloride found in the typical diet is added to food during processing. Examples include luncheon meats and hot dogs, canned vegetables, processed cheese, and potato chips. Condiments such as Worcestershire sauce, soy sauce, and ketchup also contain substantial amounts of sodium.

- ✓ There is little evidence of any adverse effect of low dietary sodium intake. Chloride deficiency is rarely seen because most foods that contain sodium also provide chloride.
- ✓ Diuretics increase urinary excretion of water, sodium, and chloride, sometimes causing low blood levels of sodium (hyponatremia) and chloride (hypochloremia).
- ✓ The primary adverse effect related to excessive sodium chloride intake is high blood pressure, which is a risk factor for heart disease, stroke, and kidney disease.
- ✓ On average, blood pressure rises progressively with increased sodium chloride intake. However, this relationship is nonlinear.

# SULFATE

One of sulfate's key roles in the body is in the synthesis of 3'-phosphoadenosine-5'-phosphosulfate (PAPS), also known as active sulfate. In the body, active sulfate is used in the synthesis of many essential compounds, some of which are not absorbed intact when consumed in foods.

Sulfate requirements are met when intakes include recommended levels of sulfur amino acids. Therefore, neither an Estimated Average Requirement (EAR), and thus a Recommended Dietary Allowance (RDA), nor an Adequate Intake (AI) has been established for sulfate. Overall, there were insufficient data to set a Tolerable Upper Intake Level (UL) for sulfate.

About 19 percent of total sulfate intake comes from inorganic sulfate in foods and another 17 percent comes from inorganic sulfate in drinking water and beverages. Foods found to be high in sulfate include dried fruits, certain commercial breads, soya flour, and sausages. Beverages found to be high in sulfate include select juices, beers, wines, and ciders. Sulfate is also present in many other sulfur-containing compounds in foods, providing the remaining approximately 64 percent of total sulfate available for bodily needs.

Sulfate deficiency is not found in people who consume normal protein intakes containing adequate sulfur amino acids. Adverse effects have been noted in individuals whose drinking water source contains high levels of inorganic sulfate. Osmotic diarrhea that results from unabsorbed sulfate has been described and may be of particular concern in infants who consume fluids derived from water sources with high levels of sulfate.

## SULFATE AND THE BODY

### Function

Sulfate (inorganic sulfate  $\text{SO}_4^{2-}$ ) is required by the body for the biosynthesis of 3'-phosphoadenosine-5'-phosphosulfate (PAPS), also known as active sulfate. PAPS is used in the biosynthesis of chondroitin sulfate, cerebroside sulfate, and many other important sulfur-containing compounds, some of which are not absorbed intact when consumed in foods.

## Absorption, Metabolism, Storage, and Excretion

Sulfate can be absorbed in the stomach, small intestine, and colon. Absorption is a sodium-dependent active process. When sulfate is consumed in the form of soluble sulfate salts, such as potassium sulfate or sodium sulfate, more than 80 percent is absorbed. When sulfate is consumed as insoluble salts, such as barium sulfate, almost no absorption occurs. Unabsorbed sulfate is excreted in the feces, reabsorbed in the colon, or reduced by anaerobic bacteria to metabolites. The primary route of excretion is through the urine.

In addition to dietary sulfate intake from food and water, sulfate is derived in the body from methionine and cysteine found in dietary protein and the cysteine component of glutathione. In fact, most body sulfate is produced from the amino acids methionine and cysteine, both of which contain sulfur and are obtained from dietary protein and body protein turnover.

## DETERMINING DRIS

### Determining Requirements

Dietary inorganic sulfate in food and water, together with sulfate derived from methionine and cysteine found in dietary protein, as well as the cysteine component of glutathione, provide sulfate for use in PAPS biosynthesis. Sulfate requirements are thus met when intakes include recommended levels of sulfur amino acids. For this reason, neither an EAR, and thus an RDA, nor an AI for sulfate has been established.

### The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Overall, there was insufficient information available to set a UL for sulfate.

Because there is no information from national surveys on sulfate intakes or on supplement usage, the risk of adverse effects within the United States or Canada cannot be characterized.

## DIETARY SOURCES

### Foods and Water

About 19 percent of total sulfate intake comes from inorganic sulfate in foods and another 17 percent comes from inorganic sulfate in drinking water and beverages. The remaining approximately 64 percent comes from organic com-

pounds such as methionine, cysteine, glutathione, and taurine. Foods found to be high in inorganic sulfate include dried fruits, certain commercial breads, soya flour, and sausages. Beverages found to be high in sulfate include select juices, beers, wines, and ciders. An analysis of the sulfate content of various diets using foods purchased at supermarkets suggested a large variation in daily inorganic sulfate intake, ranging from 0.2–1.5 g (2.1–15.8 mmol)/day.

The sulfate content of drinking water highly varies depending on where in the country it was obtained. Distilled water contains very little, if any, sulfate, and deionized water contains no sulfate. However, an intake of inorganic sulfate as high as 1.3 g/day can be obtained from water and other beverages ( $0.5\text{ g/L} \times 2.6\text{ L/day}$ ).

## Dietary Supplements

Some people self-prescribe sulfur-containing compounds such as chondroitin sulfate, glucosamine sulfate, and methylsulfonylmethane as possible aids to bones and joints. Evidence has been presented suggesting that the beneficial effects of glucosamine sulfate for osteoarthritis may be due more to the sulfate than to the glucosamine contained in the compound. No data were available on the intake of sulfur-containing compounds.

## Bioavailability

This information was not provided at the time the DRI values for this nutrient were set.

## Dietary Interactions

This information was not provided at the time the DRI values for this nutrient were set.

## INADEQUATE INTAKE AND DEFICIENCY

Unlike most other nutrients, the body's need for sulfate can be met by consuming other required nutrients that contain sulfur amino acids. Thus, a deficiency of sulfate is not found in people who consume normal protein intakes containing adequate sulfur amino acids. Ingestion of methionine, cysteine, and glutathione in foods, along with consumption of other sulfated compounds in both food and beverages, is sufficient to meet the body's requirement for sulfate.

Research with animals has shown that growth is stunted when dietary sulfate is removed from the food and water supply, and when sulfur amino acids,

particularly cysteine, are provided at levels that result in deficiency signs. Reintroducing sulfate to the diet prompts growth to resume.

## EXCESS INTAKE

Adverse effects have been noted in individuals whose drinking-water source contains high levels of inorganic sulfate. Osmotic diarrhea resulting from unabsorbed sulfate has been reported and may be of particular concern in infants who consume fluids that are derived from water sources with high levels of sulfate.

Sulfate and undigested sulfur compounds have been implicated in the etiology of ulcerative colitis. High levels of hydrogen sulfide, produced in the colon from sulfate by sulfate-reducing bacteria, are thought to overburden mucosal detoxification systems, causing the colonic epithelial inflammation of ulcerative colitis. However, the possible link between dietary sulfate, colonic hydrogen sulfide levels, and ulcerative colitis has not been adequately evaluated.

## Special Considerations

*Kidney failure:* Increased blood sulfate levels are a common feature of kidney failure. High serum sulfate levels may play a role in parathyroid stimulation and homocystinemia, both of which commonly occur in people with chronic kidney disease.

## KEY POINTS FOR SULFATE

- ✓ Sulfate is used in the biosynthesis of many essential compounds, some of which are not absorbed intact when consumed in foods. Inorganic sulfate is needed for the synthesis of 3'-phosphoadenosine-5'-phosphosulfate (PAPS), or active sulfate.
- ✓ Neither an EAR, and thus an RDA, nor an AI has been established for sulfate because most people consume adequate sulfate from foods and from sulfate produced in the body.
- ✓ Overall, there were insufficient data to set a UL for sulfate.
- ✓ About 19 percent of total sulfate intake comes from inorganic sulfate in foods and another 17 percent comes from inorganic sulfate in drinking water and beverages. Foods found to be high in inorganic sulfate include dried fruits, certain commercial breads, soya flour, and sausages. Beverages found to be high in sulfate include select juices, beers, wines, and ciders. Sulfate is also present in many other sulfur-containing compounds in foods, providing the remaining approximately 64 percent of total sulfate available for bodily needs.
- ✓ Unlike most other nutrients, the body's need for sulfate can be met by consuming other required nutrients that contain sulfur amino acids. Thus, a deficiency of sulfate is not found in people who consume normal protein intakes containing adequate sulfur amino acids.
- ✓ Osmotic diarrhea has been reported in people whose drinking water contains high levels of inorganic sulfate.
- ✓ Some association between increased hydrogen sulfide production and the risk of ulcerative colitis has been noted; however, this possible link has not been adequately evaluated.

**TABLE 1 Dietary Reference Intakes for Zinc by Life Stage Group**

Life stage group	DRI values (mg/day)					
	EAR <sup>a</sup>		RDA <sup>b</sup>		AI <sup>c</sup>	UL <sup>d</sup>
	males	females	males	females		
0 through 6 mo					2	4
7 through 12 mo	2.5	2.5	3	3		5
1 through 3 y	2.5	2.5	3	3		7
4 through 8 y	4.0	4.0	5	5		12
9 through 13 y	7.0	7.0	8	8		23
14 through 18 y	8.5	7.3	11	9		34
19 through 50 y	9.4	6.8	11	8		40
≥ 51 y	9.4	6.8	11	8		40
<b>Pregnancy</b>						
14 through 18 y		10.5		12		34
19 through 50 y		9.5		11		40
<b>Lactation</b>						
14 through 18 y		10.9		13		34
19 through 50 y		10.4		12		40

<sup>a</sup> EAR = Estimated Average Requirement.<sup>b</sup> RDA = Recommended Dietary Allowance.<sup>c</sup> AI = Adequate Intake.<sup>d</sup> UL = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.

# ZINC

**Z**inc is crucial for growth and development. It facilitates several enzymatic processes related to the metabolism of protein, carbohydrates, and fats. Zinc also helps form the structure of proteins and enzymes, and is involved in the regulation of gene expression.

The adult requirements for zinc are based on metabolic studies of zinc absorption, defined as the minimum amount of dietary zinc necessary to offset total daily losses of the nutrient. The Tolerable Upper Intake Level (UL) is based on a zinc-induced decrease in copper absorption that is manifest as a reduction in erythrocyte copper–zinc superoxide dismutase activity. DRI values are listed by life stage group in Table 1.

Foods rich in zinc include meat, some shellfish, legumes, fortified cereals, and whole grains. Overt human zinc deficiency is rare, and the signs and symptoms of mild deficiency are diverse due to zinc's ubiquitous involvement in metabolic processes. There is no evidence of adverse effects from intake of naturally occurring zinc in food. The adverse effects associated with chronic intake of supplemental zinc include acute gastrointestinal effects and headaches, impaired immune function, changes in lipoprotein and cholesterol levels, reduced copper status, and zinc–iron interactions.

## ZINC AND THE BODY

### Function

Zinc is essential for proper growth and development. Its biological functions can be divided into catalytic, structural, and regulatory. Zinc serves as a catalyst for nearly 100 specific enzymes, including alcohol dehydrogenase, alkaline phosphatase, and RNA polymerases. It is necessary for the structure of certain proteins, some of which are involved in gene expression as deoxyribonucleic acid–binding transcription factors. Examples include retinoic acid receptors and vitamin D receptors. Zinc also provides a structural function for some enzymes, the most notable of which is copper–zinc superoxide dismutase. Additionally, zinc plays a role in gene expression and has been shown to influence both apoptosis and protein kinase C activity.

## Absorption, Metabolism, Storage, and Excretion

During digestion, zinc is absorbed by the small intestine through a transcellular process, with the jejunum being the site with the greatest transport rate. The mechanism of absorption appears to be saturable and there is an increase in transport velocity with zinc depletion. The absorbed zinc is bound to albumin and transferred from the intestine via the portal system.

More than 85 percent of the body's total zinc is stored in the skeletal muscle and bone; only about 0.1 percent of total body zinc is found in the plasma. However, the body tightly regulates plasma zinc concentrations to keep them steady at about 10–15  $\mu\text{mol/L}$ . Factors such as stress, acute trauma, and infection can cause plasma zinc levels to drop. In humans, plasma zinc concentrations will remain relatively stable when zinc intake is restricted or increased, unless these changes in intake are severe and prolonged. This tight regulation also means that small amounts of zinc are more efficiently absorbed than large amounts and that people in poor zinc status can absorb the nutrient more efficiently than those in good status.

Zinc is excreted from the body primarily through the feces. Normal zinc losses may range from less than 1 mg/day with a zinc-poor diet to greater than 5 mg/day with a zinc-rich diet. Zinc loss through the urine represents only a fraction (less than 10 percent) of normal zinc losses, although urinary losses may increase with conditions such as starvation or trauma. Other modes of zinc loss from the body include skin cell turnover, sweat, semen, hair, and menstruation.

## DETERMINING DRIS

### Determining Requirements

The adult requirements for zinc are based on factorial analysis of metabolic studies of zinc absorption. Zinc absorption is defined for this purpose as the minimum amount of absorbed zinc necessary to match total daily zinc losses. The dietary intake corresponding to this average minimum quantity of absorbed zinc is the EAR.

### Special Considerations

*Children aged 3 years and under:* The absorption of zinc from human milk is higher than from cow milk-based infant formula and cow milk. The zinc bioavailability from soy formulas is significantly lower than from milk-based formulas. Zinc nutriture in later infancy is quite different from that in the younger infant. Human milk provides only 0.5 mg/day of zinc by 7 months postpartum,

and the concentration declines even further by 12 months. It is apparent, therefore, that human milk alone is an inadequate source of zinc after the first 6 months.

**Vegetarian diets:** Cereals are the primary source of dietary zinc for vegetarian diets. The bioavailability of zinc in vegetarian diets is reduced if phytate content in the diet is high, resulting in low zinc status (see “Dietary Interactions”). Zinc intake from vegetarian diets has been found to be similar to or lower than intake from nonvegetarian diets. Among vegetarians, zinc concentrations in the serum, plasma, hair, urine, and saliva are either the same as or lower than in individuals consuming nonvegetarian diets.

The variations found in these status indicators are most likely due in part to the amount of phytate, fiber, calcium, or other zinc absorption inhibitors in vegetarian diets. Even so, individuals consuming vegetarian diets were found to be in positive zinc balance. Yet, the requirement for dietary zinc may be as much as 50 percent greater for vegetarians, particularly for strict vegetarians whose major food staples are grains and legumes and whose dietary phytate:zinc molar ratio exceeds 15:1. This is due to poor absorption of zinc from vegetarian sources.

**Alcohol intake:** Long-term alcohol consumption is associated with impaired zinc absorption and increased urinary zinc excretion. Low zinc status is observed in approximately 30–50 percent of people with alcoholism. Thus, with long-term alcohol consumption, the daily requirement for zinc will be greater than that estimated by the factorial approach.

## Criteria for Determining Zinc Requirements, by Life Stage Group

<i>Life stage group</i>	<i>Criterion</i>
0 through 6 mo	Average zinc intake from human milk
7 through 12 mo	Factorial analysis
1 through 50 y	Factorial analysis
≥ 51 y	Extrapolation of factorial data from 19 through 50 y

### *Pregnancy*

14 through 18 y	Adolescent female EAR plus fetal accumulation of zinc
19 through 50 y	Adult female average requirement plus fetal accumulation of zinc

*Lactation*

14 through 18 y	Adolescent female EAR plus average amount of zinc secreted in human milk
19 through 50 y	Adult female EAR plus average amount of zinc secreted in human milk

**The UL**

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all healthy people. Members of the general population should not routinely exceed the UL. The adverse effect of excess zinc on copper metabolism (i.e., reduced copper status) was chosen as the critical effect on which to base a UL for total daily intake of zinc from food, water, and supplements. The UL for zinc represents total intake from food, water, and supplements.

According to data from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994), the highest reported zinc intake (from food) at the 95th percentile for all adults was 24 mg/day in men aged 19 to 30 years, which is lower than the UL. The 95th percentile of intake from food and supplements for adult men and nonpregnant women was approximately 25–32 mg/day; for pregnant and lactating women the 95th percentile of intake was 40 mg/day and 47 mg/day, respectively. The risk of adverse effects resulting from excess zinc intake appears to be low at these intake levels.

**DIETARY SOURCES****Foods**

Zinc is widely distributed in foods. Zinc-rich foods include red meat, some seafood, whole grains, and some fortified breakfast cereals. Because zinc is mainly found in the germ and bran portions of grain, as much as 80 percent of total zinc is lost during milling. This is why whole grains tend to be richer in zinc than unfortified refined grains.

**Dietary Supplements**

According to U.S. data from the 1986 National Health Interview Survey (NHIS), approximately 16 percent of Americans took supplements containing zinc. The median total (food plus supplements) zinc intakes by adults who took the supplements were similar to those adults who did not. However, the use of zinc supplements greatly increased the intakes of those in the upper quartile of intake level compared with those who did not take supplements.

**TABLE 2 Qualitative Bioavailability of Zinc According to Diet Characteristics<sup>a</sup>**

Bioavailability	Dietary Characteristics
High	Refined diets low in cereal fiber and phytic acid, with adequate protein primarily from meats and fish Phytate/zinc molar ratio < 5
Medium	Mixed diets containing animal or fish protein Vegetarian diets not based primarily on unrefined, unfermented cereal grains Phytate/zinc molar ratio 5–15
Low	Diets high in unrefined, unfermented, and ungerminated cereal grains, especially when animal protein intake is negligible High-phytate soy protein products are the primary protein source Diets in which ≥ 50 percent of energy is provided by high-phytate foods (high extraction rate [90 percent] flours and grains, legumes) Phytate/zinc molar ratio > 15 High intake of inorganic calcium (> 1 g/day) potentiates the inhibitory effects of these diets, especially when animal protein intake is low

<sup>a</sup> The phytate content of foods is provided by Hallberg and Hulthen (2000). The zinc content of foods is available from the U.S. Department of Agriculture at <http://www.nal.usda.gov/fnic/foodcomp>.

Evidence of the efficacy of zinc lozenges in reducing the duration of common colds remains unclear.

## Bioavailability

The bioavailability of zinc can be affected by many factors at many sites and is a function of the extent of digestion. The intestine is the major organ in which variations in bioavailability affect dietary zinc requirements. Dietary substances such as phytate can reduce zinc bioavailability (see “Dietary Interactions”). To date, a useful algorithm for establishing dietary zinc requirements based on the presence of other nutrients and food components has not been established, and much information is still needed to develop one that can predict zinc bioavailability. Algorithms for estimating dietary zinc bioavailability will need to include the dietary content of phytic acid, protein, zinc, and possibly calcium, iron, and copper. (Characteristics associated with diets varying in zinc bioavailability are summarized in Table 2.)

## Dietary Interactions

There is evidence that zinc may interact with certain other nutrients and dietary substances (see Table 3).

**TABLE 3 Potential Interactions with Other Dietary Substances**

<i>Substance</i>	<i>Potential Interaction</i>	<i>Notes</i>
<b>NUTRIENTS THAT AFFECT ZINC</b>		
Iron	Iron may decrease zinc absorption.	In general, data indicate that high intakes of supplemental iron inhibit zinc absorption if both are taken without food, but do not inhibit zinc absorption if they are consumed with food. This relationship is of some concern in the management of iron supplementation during pregnancy and lactation.
Calcium and phosphorus	Calcium and phosphorus may decrease zinc absorption.	Dietary calcium may decrease zinc absorption, but there is not yet definitive evidence. Human studies have found that calcium phosphate supplements (1,360 mg/day of calcium) decreased zinc absorption, whereas calcium supplements in the form of a citrate-malate complex (1,000 mg/day of calcium) had no statistically significant effect on zinc absorption. Currently, data suggest that consuming a calcium-rich diet does not lower zinc absorption in people who consume adequate zinc. The effect of calcium on zinc absorption in people with low zinc intakes has not been extensively studied. Certain dietary sources of phosphorus, including phytate and phosphorus-rich proteins, such as milk casein, decrease zinc absorption.
Protein	Protein may affect zinc absorption.	The amount and type of dietary protein may affect zinc absorption. In general, zinc absorption is higher in diets rich in animal protein versus those rich in plant protein. The markedly greater bioavailability of zinc from human milk than from cow milk is an example of how protein digestibility, which is much lower in casein-rich cow milk than in human milk, influences zinc absorption.
Phytic acid and fiber	Phytic acid, or phytate, may reduce zinc absorption.	Phytic acid, which is found in many plant-based foods, including grains and legumes, binds to zinc and reduces its absorption in the gastrointestinal tract. Phytate binding of zinc has been demonstrated as a contributing factor for zinc deficiency related to the consumption of unleavened bread seen in certain population groups in the Middle East. Although high-fiber foods tend also to be phytate-rich, fiber alone may not have a major effect on zinc absorption.

**TABLE 3 Continued**

<i>Substance</i>	<i>Potential Interaction</i>	<i>Notes</i>
Picolinic acid	Picolinic acid may promote negative zinc balance.	Picolinic acid has a high metal binding affinity. People do not consume picolinic acid through food, but through dietary supplements, such as zinc picolinate or chromium picolinate. Zinc picolinate as a zinc source for humans has not received extensive investigation, but in an animal model, picolinic acid supplementation promoted negative zinc balance, presumably by promoting urinary zinc excretion.
<b>ZINC AFFECTING OTHER NUTRIENTS</b>		
Copper	Increased zinc intake may lead to reduced copper absorption.	Reduced copper status has been associated with increased zinc intake. Doses of 60 mg/day (50 mg from supplements and 10 mg from food) for 10 weeks have shown this effect. This interaction also derives from the therapeutic effect of zinc in reducing copper absorption in patients with Wilson's disease.
Folate	Low zinc intake may decrease folate absorption.	Some studies have shown that low zinc intake may decrease folate absorption and folate status, whereas other studies have found that low zinc intake did not affect folate nutriture and that folate supplementation does not adversely affect zinc status. However, extensive studies on this potential relationship have not been carried out in women, and because both of the nutrients are important for fetal and postnatal development, further research is warranted.
Iron	Zinc may reduce iron absorption.	High intakes of supplemental zinc may reduce iron absorption. One study found a 56 percent decline in iron absorption when a supplemental dose of zinc and iron (administered in water) contained five times as much zinc as iron. However, when the same dose was given in a hamburger meal, no effect on iron absorption was noted.

## INADEQUATE INTAKE AND DEFICIENCY

Overt human zinc deficiency is rare. Because zinc is involved in so many core areas of metabolism, the signs and symptoms of mild deficiency are diverse and inconsistent. Impaired growth velocity is the primary clinical feature and can be corrected with zinc supplementation. Other functions that respond to zinc supplementation include pregnancy outcome and immune function. Other basic and nonspecific signs and symptoms include the following:

- Growth retardation
- Alopecia
- Diarrhea
- Delayed sexual maturation and impotence
- Eye and skin lesions
- Impaired appetite

It is noteworthy that zinc homeostasis within the body is such that zinc deficiency can occur with only modest degrees of dietary zinc restriction, while circulating zinc concentrations are indistinguishable from normal.

## Special Considerations

**Individuals susceptible to zinc deficiency:** People with malabsorption syndromes, including sprue, Crohn's disease, and short bowel syndrome are at risk of zinc deficiency due to malabsorption of zinc and increased urinary zinc losses. Acrodermatitis enteropathica, an autosomal recessive trait, is a zinc malabsorption problem of an undetermined genetic basis. The mutation causes severe skin lesions and cognitive dysfunction.

## EXCESS INTAKE

There is no evidence of adverse effects from the excess intake of naturally occurring zinc in food. The adverse effects associated with chronic intake of supplemental zinc include suppression of the immune system, a decrease in high density lipoprotein (HDL) cholesterol, and reduced copper status. Other adverse effects include the following:

- **Acute effects:** Acute adverse effects of excess zinc include acute epigastric pain, nausea, vomiting, loss of appetite, abdominal cramps, diarrhea, and headaches. Doses of 225–450 mg of zinc have been estimated to

cause vomiting. Gastrointestinal distress has been reported at doses of 50–150 mg/day of zinc

- *Impaired immune function:* Intake of 300 mg/day of supplemental zinc for 6 weeks has been shown to cause impaired immune function

## **SPECIAL CONSIDERATIONS**

***Individuals susceptible to adverse effects:*** People with Menke's disease may be distinctly susceptible to the adverse effects of excess zinc intake. Because Menke's disease is a defect in the ATPase involved in copper efflux from enterocytes, supplying extra zinc will likely further limit copper absorption.

## KEY POINTS FOR ZINC

- ✓ Zinc functions as a component of various enzymes in the maintenance of the structural integrity of proteins and in the regulation of gene expression. Factors such as stress, acute trauma, and infection can cause plasma zinc levels to drop.
- ✓ In humans, plasma zinc concentrations will remain relatively stable when zinc intake is restricted or increased, unless these changes in intake are severe and prolonged.
- ✓ The adult requirements for zinc are based on metabolic studies of zinc absorption, defined as the minimum amount of dietary zinc necessary to offset total daily losses of zinc. The adverse effect of excess zinc on copper metabolism (i.e., reduced copper status) was chosen as the critical effect on which to base a UL for total daily intake of zinc from food, water, and supplements.
- ✓ The bioavailability of zinc in vegetarian diets is reduced if phytate content in the diet is high, which may result in low zinc status.
- ✓ Zinc interacts with many other nutrients and dietary substances. To date, a useful algorithm for establishing dietary zinc requirements based on the presence of other nutrients and food components has not been established, and much information is still needed to develop one that can predict zinc bioavailability.
- ✓ Zinc-rich foods include red meat, some seafood, whole grains, and some fortified breakfast cereals. Whole grains tend to be richer in zinc than unfortified refined grains. This is because zinc, mainly found in the germ and bran portions of grains, is lost during the milling process.
- ✓ Overt human zinc deficiency is rare.
- ✓ Because zinc is involved in so many core areas of metabolism, the signs and symptoms of mild deficiency are diverse and inconsistent. Impaired growth velocity is the primary clinical feature and can be corrected with zinc supplementation.
- ✓ The signs and symptoms of zinc deficiency include impaired growth, alopecia, diarrhea, delayed sexual maturation and impotence, eye and skin lesions, loss of appetite, altered immune function, and adverse pregnancy outcomes.

- ✓ It is noteworthy that zinc homeostasis within the body is such that zinc deficiency can occur with only modest degrees of dietary zinc restriction, while circulating zinc concentrations are indistinguishable from normal.
- ✓ People with malabsorption syndromes, including sprue, Crohn's disease, and short bowel syndrome are at risk of zinc deficiency due to malabsorption of zinc and increased urinary zinc losses.
- ✓ There is no evidence of adverse effects from the excess intake of naturally occurring zinc in food. The adverse effects associated with chronic intake of excess supplemental zinc include acute gastrointestinal effects and headaches, impaired immune function, changes in lipoprotein and cholesterol levels.

**TABLE 1 Dietary Reference Intakes for Boron, Nickel, and Vanadium by Life Stage Group<sup>a</sup>**

	DRI values (mg/day)		
	Boron	Nickel	Vanadium <sup>c</sup>
	UL <sup>b</sup>	UL	UL
<b>Life stage group<sup>d</sup></b>			
0 through 6 mo	ND <sup>e</sup>	ND	ND
7 through 12 mo	ND	ND	ND
1 through 3 y	3	0.2	ND
4 through 8 y	6	0.3	ND
9 through 13 y	11	0.6	ND
14 through 18 y	17	1.0	ND
19 through 30 y	20	1.0	1.8
31 through 50 y	20	1.0	1.8
51 through 70 y	20	1.0	1.8
> 70 y	20	1.0	1.8
<b>Pregnancy</b>			
≤ 18 y	17	1.0	ND
19 through 50 y	20	1.0	ND
<b>Lactation</b>			
≤ 18 y	17	1.0	ND
19 through 50 y	20	1.0	ND

<sup>a</sup> Data were insufficient to set a UL for arsenic and for silicon. Although a UL was not determined for arsenic, there is no justification for adding it to food or supplements. In addition, although silicon has not been shown to cause adverse effects in humans, there is no justification for adding it to supplements.

<sup>b</sup> **UL** = Tolerable Upper Intake Level. Unless otherwise specified, the UL represents total intake from food, water, and supplements.

<sup>c</sup> Although vanadium in food has not been shown to cause adverse effects in humans, there is no justification for adding it to food, and vanadium supplements should be used with caution. The UL is based on adverse effects in laboratory animals and these data could be used to set a UL for adults, but not for children or adolescents.

<sup>d</sup> All groups except for Pregnancy and Lactation represent males and females.

<sup>e</sup> **ND** = Not determinable. This value is not determinable due to the lack of data of adverse effects in this age group and concern regarding the lack of ability to handle excess amounts. Source of intake should only be from food to prevent high levels of intake.

# ARSENIC, BORON, NICKEL, SILICON, AND VANADIUM

There is evidence that the minerals arsenic, boron, nickel, silicon, and vanadium play a beneficial role in some physiological processes of certain animal species. For boron, silicon, and vanadium, measurable responses by human subjects to dietary intake variations have also been demonstrated. However, the available data were not as extensive and the responses were not as consistently observed as with vitamins and other minerals. Therefore, data were insufficient to determine Estimated Average Requirements (EARs), and thus Recommended Dietary Allowances (RDAs), for these minerals.

Estimates of dietary intakes of arsenic, boron, nickel, silicon, and vanadium by the North American adult population were available and could have been used to establish Adequate Intakes (AIs). However, establishing an AI also requires a clearly defined, reproducible indicator in humans who are sensitive to a range of intakes. Indicators that meet this criterion for establishing an AI were not available for any of these minerals, and therefore no AIs were set.

ULs were set for boron, nickel, and vanadium based on animal data. DRI values are listed by life stage group in Table 1. There were insufficient data to set Tolerable Upper Intake Levels (ULs) for arsenic and silicon.

Observations of deficiency effects (e.g., on growth and development) in multiple animal species and data from limited human studies suggest beneficial roles for arsenic, boron, nickel, silicon, and vanadium in human health. However, the data indicate a need for continued study of these elements to determine their metabolic role, identify sensitive indicators, and more fully characterize their specific functions in human health.

## ARSENIC, BORON, NICKEL, SILICON, AND VANADIUM AND THE BODY

### Function

**Arsenic:** There have been no studies performed to determine the nutritional importance of arsenic for humans. Animal studies suggest a role for arsenic in the metabolism of methionine, in growth and reproduction, and in gene expression.

**Boron:** A collective body of evidence has yet to establish a clear biological function for boron in humans. Although some evidence does suggest a role in the metabolism of vitamin D and estrogen, further research is necessary.

**Nickel:** The possible nutritional importance or biochemical function of nickel in humans has not been established. Nickel may serve as a cofactor or structural component of specific metalloenzymes of various functions, including hydrolysis and redox reactions and gene expression. Nickel may also serve as a cofactor facilitating iron absorption or metabolism.

**Silicon:** A functional role for silicon in humans has not yet been identified, although animal studies show that silicon may be involved in the formation of bone.

**Vanadium:** A functional role for vanadium in humans has not been identified. There are some reports that vanadium may increase the action of insulin, but the potential mechanism of action is uncertain. Vanadium also stimulates cell proliferation and differentiation and inhibits various ATPases, phosphatases, and phosphoryl-transfer enzymes.

## Absorption, Metabolism, Storage, and Excretion

**Arsenic:** Approximately 90 percent of inorganic arsenic from water is absorbed by the body; the amount absorbed of dietary arsenic is approximately 60–70 percent. Once absorbed, inorganic arsenic is transported to the liver, where it is reduced to arsenite and then methylated. Most ingested arsenic is rapidly excreted in the urine.

**Boron:** With normal intakes, about 90 percent of dietary boron is absorbed. The mechanism of absorption has not been confirmed, but a passive (nonmediated) diffusion process is likely. The excretory form of boron has not been studied.

**Nickel:** The absorption of dietary nickel is less than 10 percent and is affected by certain foods, including milk, coffee, tea, orange juice, and ascorbic acid. Nickel is transported through the blood bound primarily to albumin. Most organs and tissues do not accumulate nickel, but in humans the thyroid and adrenal glands have relatively high concentrations. Because of the poor absorption of nickel, most ingested nickel is excreted in the feces. Absorbed nickel is excreted in the urine, with minor amounts secreted in the sweat and bile.

**Silicon:** Findings indicating that as much as 50 percent of ingested silicon is excreted in the urine suggest that some dietary forms of silicon are well absorbed. Silicon in the blood exists almost entirely as silicic acid and is not bound to proteins. Most body silicon is found in the various connective tissues including the aorta, trachea, bone, tendons, and skin. Excretion is primarily through the urine.

**Vanadium:** Less than 5 percent of ingested vanadium is absorbed. Absorbed vanadate is converted to the vanadyl cation, which can complex with ferritin and transferrin in plasma and body fluids. Very little absorbed vanadium remains in the body; whatever does remain is found primarily in the liver, kidneys, and bone. Because of the low absorption of ingested vanadium, most excretion occurs through the feces.

## **DETERMINING DRIS**

### **Determining Requirements**

Data were insufficient to estimate EARs, RDAs, or AIs for arsenic, boron, nickel, silicon, and vanadium.

### **The UL**

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse health effects for almost all individuals. Although members of the general healthy population should be advised not to routinely exceed the UL, intake above the UL may be appropriate for investigation within well-controlled clinical trials. The UL is not meant to apply to individuals receiving any of these elements under medical supervision.

**Arsenic:** Data were insufficient to set a UL for arsenic. Although a UL was not determined for arsenic, there is no justification for adding it to food or supplements.

Although no UL was set for arsenic, there may be a risk of adverse effects with the consumption of organic arsenic in food or with the intake of inorganic arsenic in water supplies at the current maximum contamination level of 50 µg/L, set in the United States.

**Boron:** The UL for boron is based on reproductive and developmental effects in animals as the critical endpoint and represents intake from food, water, and supplements.

According to data from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994) at the 95th percentile, intake of boron from the diet and supplements was approximately 2.8 mg/day. Adding to that a maximum intake from water of 2 mg/day provides a total intake of less than 5 mg/day of boron at this percentile. At the 95th percentile intake, no segment of the U.S. population had a *total* (dietary, water, and supplemental) intake greater than 5 mg/day, according to NHANES III and the Continuing Survey of Food Intakes by Individuals (CSFII, 1994–1996) data. Those who take body-building supplements could consume an additional 1.5–20 mg/day. Therefore, this supplemental intake may exceed the UL of 20 mg/day.

**Nickel:** The UL for nickel is based on general systemic toxicity (in the form of decreased body-weight gain reported in rat studies) as the critical endpoint. Because there were no data on the adverse effects of nickel consumption from a normal diet, the UL for nickel applies to excess nickel intake as soluble nickel salts.

Individuals with preexisting nickel hypersensitivity (from previous dermal exposure) and kidney dysfunction are distinctly susceptible to the adverse effects of excess nickel intake and may not be protected by the UL set for the general population.

Based on the Food and Drug Administration's (FDA's) Total Diet Study (1991–1997), 0.5 mg/day was the highest intake at the 99th percentile of nickel (from food) reported for any life stage and gender group; this was also the reported intake for pregnant females. Nickel intake from supplements provided only 9.6–15 µg/day at the 99th percentile for all age and gender groups, according to NHANES III. The risk of adverse effects resulting from excess intake of nickel from food and supplements appears to be very low at the highest intakes noted above. Increased risks are likely to occur from environmental exposures or from the consumption of contaminated water.

**Silicon:** Data were insufficient to set a UL for silicon. Although silicon has not been shown to cause adverse effects in humans, there is no justification for adding it to supplements.

**Vanadium:** The UL for vanadium is based on renal toxicity in animals as the critical adverse effect. Since the forms of vanadium found in food and supplements are the same, the UL applies to total vanadium intake from food, water, and supplements. Due to insufficient data, no UL was set for pregnant and lactating women, children, and infants. Caution should be exercised regarding the consumption of vanadium supplements by these individuals.

Because of the widespread use of high-dose (60 mg/day) supplemental vanadium by athletes and other subgroups (e.g., borderline diabetics) that are

considered part of the apparently healthy general population, further research on vanadium toxicity is needed.

Vanadium in the forms of vanadyl sulfate (100 mg/day) and sodium metavanadate (125 mg/day) has been used as a supplement for diabetic patients. Although insulin requirements were decreased in patients with Type I diabetes, the doses of vanadium used in the supplements were about 100 times the usual intakes and greatly exceeded the UL for vanadium.

Although percentile data were not available for dietary vanadium intakes from U.S. surveys, the highest mean intake of vanadium for the U.S. population was 18 µg/day. The average intake of supplemental vanadium at the 99th percentile by adults was 20 µg/day, which is significantly lower than the adult UL. The risk of adverse effects resulting from excess intake of vanadium from food is very unlikely. Because of the high doses of vanadium present in some supplements, increased risks are likely to result from excess intake.

## **DIETARY SOURCES**

### **Foods**

**Arsenic:** Dairy products contribute as much as 31 percent of dietary arsenic; meat, poultry, fish, grains, and cereal products collectively contribute approximately 56 percent. Based on a national survey conducted in six Canadian cities from 1985 to 1988, the foods that contained the highest concentrations of arsenic were fish, meat and poultry, bakery goods and cereals, and fats and oils. Most of the arsenic found in fish is in the organic form. Major contributors of inorganic arsenic are raw rice, flour, grape juice, and cooked spinach.

**Boron:** Fruit-based beverages and products, tubers, and legumes have been found to have the highest concentrations of boron. Other studies have reported that the top ten foods with the highest concentration of boron were avocado, peanut butter, peanuts, prune and grape juices, chocolate powder, wine, pecans, and granola-raisin and raisin-bran cereals. When both content and total food consumption (amount and frequency) were considered, the five major contributors were found to be coffee, milk, apples, dried beans, and potatoes, which collectively accounted for 27 percent of the dietary boron consumption. Coffee and milk are generally low in boron, but they tend to be high dietary contributors because of the volume at which they are consumed.

**Nickel:** Nuts and legumes have the highest concentrations of nickel, followed by sweeteners, including chocolate powder and chocolate candy. Major contributors to nickel intake are mixed dishes and soups (19–30 percent), grains and grain products (12–30 percent), vegetables (10–24 percent), legumes (3–

16 percent), and desserts (4–18 percent). Major contributors of nickel to the Canadian diet include meat and poultry (37 percent), bakery goods and cereals (19 percent), soups (15 percent), and vegetables (11 percent). Cooking acidic foods in stainless-steel cookware can increase the nickel content of these foods.

**Silicon:** Plant-based foods contain higher concentrations of silicon than do animal-based foods. Beer, coffee, and water appear to be the major contributors of silicon to the diet, followed by grains and vegetables. Silicate additives that have been increasingly used as antifoaming and anticaking agents in foods can raise the silicon content of foods, but the bioavailability of these additives is low.

**Vanadium:** Foods rich in vanadium include mushrooms, shellfish, black pepper, parsley, dill seed, and certain prepared foods. Processed foods contain more vanadium than unprocessed foods. Beer and wine may also contribute appreciable amounts to the diet. The Total Diet Study showed grains and grain products contributed 13–30 percent of the vanadium in adult diets; beverages, which contributed 26–57 percent, were an important source for adults and elderly men. Canned apple juice and cereals have been shown to be major contributors to vanadium intake in infants and toddlers.

## Dietary Supplements

**Arsenic:** This information was not provided at the time the DRI values for this nutrient were set.

**Boron:** In NHANES III, the adult median intake of boron from supplements was approximately 0.14 mg/day.

**Nickel:** In NHANES III, the adult median intake of nickel from supplements was approximately 5 µg/day.

**Silicon:** In NHANES III, the adult median intake of silicon from supplements was approximately 2 mg/day.

**Vanadium:** In NHANES III, the adult median intake of vanadium from supplements was approximately 9 µg/day.

## Bioavailability

This information was not provided at the time the DRI values for these nutrients were set.

## **INADEQUATE INTAKE AND DEFICIENCY**

This information was not provided at the time the DRI values for these nutrients were set.

## **EXCESS INTAKE**

**Arsenic:** Arsenic occurs in both inorganic and organic forms, with the inorganic forms that contain trivalent arsenite (III) or pentavalent arsenate (V) having the greatest toxicological significance. No data were found on the possible adverse effects, including cancer, of organic arsenic compounds from food. Because organic forms of arsenic are less toxic than inorganic forms, any increased health risks from the intake of organic arsenic from food is unlikely.

In contrast, inorganic arsenic is an established human poison, and acute adverse effects such as anemia and hepatotoxicity can occur in doses of 1 mg/kg/day or greater. The ingestion of acute doses greater than 10 mg/kg/day leads to encephalopathy and gastrointestinal symptoms. Chronic intake of 10 µg/kg/day or greater of inorganic arsenic produces arsenicism, a condition characterized by keratosis and the alteration of skin pigmentation. Intermediate and chronic exposures of arsenic up to levels of 11 mg/L of water are associated with symmetrical peripheral neuropathy.

The ingestion of inorganic arsenic is also associated with the risk of skin, bladder, and lung cancers. Most studies indicating a positive association with cancer involved intakes of inorganic arsenic from drinking water, as reported in areas of Taiwan, Japan, Argentina, and Chile. Studies of U.S. populations exposed to arsenic in drinking water have not identified cancer increases. Occupational exposure to inorganic forms of arsenic, in environments such as smelters and chemical plants, occurs primarily by inhalation (where the predominate form is arsenic trioxide dust).

**Boron:** No data were available on adverse health effects from ingestion of large amounts of boron from food and water. However, animal data suggest that reproductive and developmental effects may occur.

**Nickel:** There is no evidence in humans of adverse effects associated with exposure to nickel through a normal diet. The acute effects of ingesting large doses of soluble nickel salts include nausea, abdominal pain, diarrhea, vomiting, and shortness of breath. In animal studies, the signs and symptoms of general systemic toxicity include lethargy, ataxia, irregular breathing, hypothermia, and salivation, as well as decreased body-weight gain and impaired reproduction.

**Silicon:** There is no evidence that naturally occurring silicon in food and water produces adverse health effects. Limited reports indicate that magnesium trisilicate (6.5 mg of elemental silicon per tablet) used as an antacid in large amounts for long periods (i.e., several years) may be associated with the development of silicon-containing kidney stones.

**Vanadium:** There is no evidence of adverse effects associated with vanadium intake from food, which is the major source of exposure for the general population; no special subpopulations are distinctly susceptible. In animal studies, renal toxicity has occurred. Most vanadium toxicity reports involve industrial exposure to high levels of airborne vanadium. Vanadyl sulfate supplements are used by some weight-training athletes to increase performance; in addition, vanadium supplements have been studied for the treatment of diabetes. For these reasons, further research on vanadium toxicity is necessary.

### KEY POINTS FOR ARSENIC, BORON, NICKEL, SILICON, AND VANADIUM

- ✓ Data were insufficient to set EARs, RDAs, or AIs for arsenic, boron, nickel, silicon, and vanadium.
- ✓ There were insufficient data to set ULs for arsenic and silicon. However, ULs based on animal data were set for boron, nickel, and vanadium.
- ✓ Although a UL was not determined for arsenic, there is no justification for adding it to food or supplements.
- ✓ Although silicon has not been shown to cause adverse effects in humans, there is no justification for adding it to supplements.
- ✓ Observations of deficiency effects (e.g., on growth and development) in multiple animal species and data from limited human studies suggest that there are beneficial roles for arsenic, boron, nickel, silicon, and vanadium in human health. However, the data indicate a need for continued study of these elements to determine their metabolic role, identify sensitive indicators, and more fully characterize their specific functions in human health.

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# A

## ACKNOWLEDGMENTS

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# C METHODS

The general methods for examining and interpreting the evidence on requirements for nutrients are presented in this appendix, with special attention given to approaches used to provide Dietary Reference Intakes (DRIs) where data are lacking for specific subgroups of the population (typically for infants, children, pregnant and lactating women, and older adults). Included as well are discussions of methodological problems in assessing requirements and estimating intakes from dietary survey data.

## METHODOLOGICAL CONSIDERATIONS

### Types of Data Used

The scientific data for developing the Dietary Reference Intakes (DRIs) have essentially come from observational and experimental studies in humans. Observational studies include single-case and case-series reports and cross-sectional, cohort, and case-control studies. Experimental studies include randomized and nonrandomized prevention trials and controlled dose-response, balance, turnover, and depletion-repletion physiological studies. Results from animal experiments are generally not applicable to the establishment of DRIs, but selected animal studies are considered in the absence of human data.

### ANIMAL MODELS

Basic research using experimental animals affords considerable advantage in terms of control of nutrient exposures, environmental factors, and even genetics. In contrast, the relevance to free-living humans may be unclear. In addition, dose levels and routes of administration that are practical in animal experiments may differ greatly from those relevant to humans. Nevertheless, animal feeding experiments were sometimes included in the evidence reviewed to determine the ability to specify DRIs.

### HUMAN FEEDING STUDIES

Controlled feeding studies, usually in a confined setting such as a metabolic unit, can yield valuable information on the relationship between nutrient con-

sumption and health-related biomarkers. Much of the understanding of human nutrient requirements to prevent deficiencies is based on studies of this type. Studies in which the subjects are confined allow for close control of both intake and activities. Complete collections of nutrient losses through urine and feces are possible, as are recurring sampling of biological materials such as blood. Nutrient balance studies measure nutrient status in relation to intake. Depletion–repletion studies, by contrast, measure nutrient status while subjects are maintained on diets containing marginally low or deficient levels of a nutrient; then the deficit is corrected with measured amounts of that nutrient. Unfortunately, these two types of studies have several limitations. Typically they are limited in time to a few days or weeks, and so longer-term outcomes cannot be measured with the same level of accuracy. In addition, subjects may be confined, and findings are therefore not always generalizable to free-living individuals. Finally, the time and expense involved in such studies usually limit the number of subjects and the number of doses or intake levels that can be tested.

In spite of these limitations, feeding studies play an important role in understanding nutrient needs and metabolism. Such data were considered in the DRI process and were given particular attention in the absence of reliable data to directly relate nutrient intake to disease risk.

### OBSERVATIONAL STUDIES

In comparison to human feeding studies, observational epidemiological studies are frequently of direct relevance to free-living humans, but they lack the controlled setting. Hence they are useful in establishing evidence of an association between the consumption of a nutrient and disease risk but are limited in their ability to ascribe a causal relationship. A judgment of causality may be supported by a consistency of association among studies in diverse populations, and it may be strengthened by the use of laboratory-based tools to measure exposures and confounding factors, such as personal interviews, rather than other means of data collection. In recent years, rapid advances in laboratory technology have made possible the increased use of biomarkers of exposure, susceptibility, and disease outcome in molecular epidemiological research. For example, one area of great potential in advancing current knowledge of the effects of diet on health is the study of genetic markers of disease susceptibility (especially polymorphisms in genes encoding metabolizing enzymes) in relation to dietary exposures. This development is expected to provide more accurate assessments of the risk associated with different levels of intake of both nutrients and nonnutritive food constituents.

While analytic epidemiological studies (studies that relate exposure to disease outcomes in individuals) have provided convincing evidence of an associative relationship between selected nondietary exposures and disease risk, there

are a number of other factors that limit study reliability in research relating nutrient intakes to disease risk.

First, the variation in nutrient intake may be rather limited in populations selected for study. This feature alone may yield modest relative risk trends across intake categories in the population, even if the nutrient is an important factor in explaining large disease rate variations among populations.

A second factor, one that gives rise to particular concerns about confounding, is the human diet's complex mixture of foods and nutrients that includes many substances that may be highly correlated. Third, many cohort and case-control studies have relied on self-reports of diet, typically food records, 24-hour recalls, or diet history questionnaires. Repeated application of such instruments to the same individuals shows considerable variation in nutrient consumption estimates from one time period to another with correlations often in the 0.3 to 0.7 range. In addition, there may be systematic bias in nutrient consumption estimates from self-reports as the reporting of food intakes and portion sizes may depend on individual characteristics such as body mass, ethnicity, and age. For example, total energy consumption may tend to be substantially underreported (30 to 50 percent) among obese persons, with little or no underreporting among lean persons. Such systematic bias, in conjunction with random measurement error and limited intake range, has the potential to greatly impact analytic epidemiological studies based on self-reported dietary habits. Note that cohort studies using objective (biomarker) measures of nutrient intake may have an important advantage in the avoidance of systematic bias, though important sources of bias (e.g., confounding) may remain.

### **RANDOMIZED CLINICAL TRIALS**

By randomly allocating subjects to the (nutrient) exposure of interest, clinical trials eliminate the confounding that may be introduced in observational studies by self-selection. The unique strength of randomized trials is that if the sample is large enough, the study groups will be similar with respect not only to those confounding variables known to the investigators, but also to any unknown factors that might be related to risk of the disease. Thus, randomized trials achieve a degree of control of confounding that is simply not possible with any observational design strategy, and thus they allow for the testing of small effects that are beyond the ability of observational studies to detect reliably.

Although randomized controlled trials represent the accepted standard for studies of nutrient consumption in relation to human health, they too possess important limitations. Specifically, persons agreeing to be part of a randomized trial may be a select subset of the population of interest, thus limiting the generalization of trial results. For practical reasons, only a small number of nutri-

ents or nutrient combinations at a single intake level are generally studied in a randomized trial (although a few intervention trials to compare specific dietary patterns have been initiated in recent years). In addition, the follow-up period will typically be short relative to the preceding time period of nutrient consumption that may be relevant to the health outcomes under study, particularly if chronic disease endpoints are sought. Also, dietary intervention or supplementation trials tend to be costly and logistically difficult, and the maintenance of intervention adherence can be a particular challenge.

Because of the many complexities in conducting studies among free-living human populations and the attendant potential for bias and confounding, it is the totality of the evidence from both observational and intervention studies, appropriately weighted, that must form the basis for conclusions about causal relationships between particular exposures and disease outcomes.

### WEIGHING THE EVIDENCE

As a principle, only studies published in peer-reviewed journals were used in the original DRI series and, thus, used as the basis for this book. However, studies published in other scientific journals or readily available reports were considered if they appeared to provide important information not documented elsewhere. To the extent possible, original scientific studies have been used to derive the DRIs. On the basis of a thorough review of the scientific literature, clinical, functional, and biochemical indicators of nutritional adequacy and excess were evaluated for each nutrient.

The quality of the study was considered in weighing the evidence. The characteristics examined included the study design and the representativeness of the study population; the validity, reliability, and precision of the methods used for measuring intake and indicators of adequacy or excess; the control of biases and confounding factors; and the power of the study to demonstrate a given difference or correlation. Publications solely expressing opinions were not used in setting DRIs. The assessment acknowledged the inherent reliability of each type of study design as described above, and it applied standard criteria from Hill concerning the strength, dose-response, and temporal pattern of estimated nutrient-disease or adverse effect associations, the consistency of associations among studies of various types, and the specificity and biological plausibility of the suggested relationships. For example, biological plausibility would not be sufficient in the presence of a weak association and lack of evidence that exposure preceded the effect.

Data were examined to determine whether similar estimates of the requirement resulted from the use of different indicators and different types of studies. In the DRI model described in Part I, for a single nutrient, the criterion for setting the Estimated Average Requirement (EAR) may differ from one life stage

group to another because the critical function or the risk of disease may be different. When no or very poor data are available for a given life stage group, extrapolation is made from the EAR or Adequate Intake (AI) set for another group (see section later on extrapolation); explicit and logical assumptions on relative requirements were made. Because EARs can be used for multiple purposes, unlike AIs, they are established whenever sufficient supporting data were available.

### **DATA LIMITATIONS**

Although the reference values in the original DRI report series were based on data, the data were often scanty or drawn from studies that had limitations in addressing the various questions that confronted the DRI panels. Therefore, many of the questions raised about the requirements for and recommended intakes of these nutrients cannot be answered fully. Apart from studies of overt deficiency diseases, there is a dearth of studies that address specific effects of inadequate intakes on specific indicators of health status, and thus a research agenda was proposed in each of the original DRI series reports. For many of the nutrients in the DRI reports, estimated requirements are based on factorial, balance, and biochemical indicator data because there is little information relating health status indicators to functional sufficiency or insufficiency. Thus, after careful review and analysis of the evidence, including examination of the extent of congruent findings, scientific judgment was used to determine the basis for establishing the values.

### **Method for Determining the Adequate Intake for Infants**

The AI for young infants is generally taken to be the average intake by full-term infants who are born to healthy, well-nourished mothers and who are exclusively fed human milk. The extent to which intake of a nutrient from human milk may exceed the actual requirements of infants is not known, and ethics of experimentation preclude testing the levels known to be potentially inadequate. Using the infant exclusively fed human milk as a model is in keeping with the basis for earlier recommendations for intake. It also supports the recommendation that exclusive intake of human milk is the preferred method of feeding for normal full-term infants for the first 4 to 6 months of life. This recommendation has been made by the Canadian Paediatric Society, the American Academy of Pediatrics, the Institute of Medicine, and many other expert groups, even though most U.S. babies no longer receive human milk by age 6 months.

In general, this book does not cover possible variations in physiological need during the first month after birth or the variations in intake of nutrients

from human milk that result from differences in milk volume and nutrient concentration during early lactation.

In keeping with the decision made by the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, there were not specific recommended intakes to meet the needs of formula-fed infants. The use of formula introduces a large number of complex issues, one of which is the bioavailability of different forms of the nutrient in different formula types.

### AGES 0 THROUGH 6 MONTHS

To derive the AI for infants ages 0 through 6 months, the mean intake of a nutrient was calculated based on (1) the average concentration of the nutrient from 2 to 6 months of lactation using consensus values from several reported studies, if possible, and (2) an average volume of milk intake of 0.78 L/day. This volume was reported from studies that used test weighing of full-term infants. In this procedure, the infant is weighed before and after each feeding. Because there is variation in both the composition of milk and the volume consumed, the computed value represents the mean. It is expected that infants will consume increased volumes of human milk during growth spurts.

### AGES 7 THROUGH 12 MONTHS

During the period of infant growth and gradual weaning to a mixed diet of human milk and solid foods from ages 7 through 12 months, there is no evidence for markedly different nutrient needs. The AI can be derived for this age group by calculating the sum of (1) the content of the nutrient provided by 0.6 L/day of human milk, which is the average volume of milk reported from studies of infants receiving human milk in this age category and (2) that provided by the usual intakes of complementary weaning foods consumed by infants in this age category. Such an approach is in keeping with the current recommendations of the Canadian Paediatric Society, the American Academy of Pediatrics, and the Institute of Medicine for continued feeding of infants with human milk through 9 to 12 months of age with appropriate introduction of solid foods. The World Health Organization recommends the introduction of solid foods after 6 months of age.

For some of the nutrients in other DRI reports, two other approaches were considered as well: (1) extrapolation downward from the EAR for young adults by adjusting for metabolic or total body size and growth and adding a factor for variability and (2) extrapolation upward from the AI for infants ages 0 through 6 months by using the same type of adjustment. Both of these methods are described below. The results of the methods are evaluated in the process of setting the AI.

## Method for Extrapolating Data from Younger to Older Infants

When information is not available on the nutrient intake of older infants, intake data can be extrapolated from young to older infants. Using the metabolic weight ratio method to extrapolate data from younger to older infants involves metabolic scaling but does not include an adjustment for growth because it is based on a value for a growing infant. To extrapolate from the AI for infants ages 0 through 6 months to an AI for infants ages 7 through 12 months, the following formula is used:

$$AI_{7-12 \text{ mo}} = AI_{0-6 \text{ mo}} \times F,$$

where  $F = (\text{Weight}_{7-12 \text{ mo}} / \text{Weight}_{0-6 \text{ mo}})^{0.75}$ .

## Method for Extrapolating Data from Adults to Children

### SETTING THE AI FOR CHILDREN

When data are lacking to set an EAR or AI for children and adolescents, the values can often be extrapolated from adult values. The EAR or AI can be extrapolated down by scaling requirements to the 0.75 power of body mass, which adjusts for metabolic differences demonstrated to be related to body weight. Other approaches include extrapolating down based on the reference body weights, which has been done in developing ULs for some nutrients, and extrapolating on the basis of energy intake.

## Methods for Determining Increased Needs for Pregnancy

It is known that the placenta actively transports certain nutrients from the mother to the fetus against a concentration gradient. However, for many nutrients, experimental data that could be used to set an EAR and RDA or an AI for pregnancy are lacking. In these cases, the potential increased need for these nutrients during pregnancy is based on theoretical considerations, including obligatory fetal transfer, if data are available, and on increased maternal needs related to increases in energy or protein metabolism, as applicable. Thus, in some cases, the EAR can be determined by the additional weight gained during pregnancy.

## Methods for Determining Increased Needs for Lactation

For most nutrients, it is assumed that the total nutrient requirements for lactating women equal the requirements for nonpregnant, nonlactating women of similar age plus an increment to cover the amount needed for milk production.

## ESTIMATES OF NUTRIENT INTAKES

Reliable and valid methods of food composition analysis are crucial in determining the intake of a nutrient needed to meet a requirement.

## Methodological Considerations

The quality of nutrient intake data varies widely across studies. The most valid intake data are those collected from the metabolic study protocols in which all food is provided by the researchers, amounts consumed are measured accurately, and the nutrient composition of the food is determined by reliable and valid laboratory analyses. Such protocols are usually possible with only a few subjects. Thus, in many studies, intake data are self-reported (e.g., through 24-hour recalls of food intake, diet records, or food frequency questionnaires).

Potential sources of error in self-reported intake data include over- or underreporting of portion sizes and frequency of intake, omission of foods, and inaccuracies related to the use of food composition tables. In addition, because a high percentage of the food consumed in the United States and Canada is not prepared from scratch in the home, errors can occur due to a lack of information on how a food was manufactured, prepared, and served. Therefore, the values reported by nationwide surveys or studies that rely on self-report are often inaccurate and possibly biased, with a greater tendency to underestimate actual intake.

## Adjusting for Day-to-Day Variation

Because of day-to-day variation in dietary intakes, the distribution of 1-day (or 2-day) intakes for a group is wider than the distribution of usual intakes even though the mean of the intakes may be the same. To reduce this problem, statistical adjustments have been developed that require at least 2 days of dietary data from a representative subsample of the population of interest. However, no accepted method is available to adjust for the underreporting of intake, which may average as much as 20 percent for energy.

## **DIETARY INTAKES IN THE UNITED STATES AND CANADA**

### **Sources of Dietary Intake Data**

At the time the original DRI reports were published, the major sources of current dietary intake data for the U.S. population were the National Health and Nutrition Examination Survey (NHANES), which was conducted by the U.S. Department of Health and Human Services, and the Continuing Survey of Food Intakes by Individuals (CSFII), which was conducted by the U.S. Department of Agriculture (USDA). Both surveys used the food composition database developed by USDA to calculate nutrient intakes. National survey data for Canada for these nutrients was collected in 10 provinces.

### **Sources of Supplement Intake Data**

Data on supplement use was obtained via the 1986 National Health Interview Survey, involving 11,558 adults and 1,877 children. Participants were asked about their use of supplements during the previous two weeks, and supplement composition was obtained from product labels whenever possible.

### **Food Sources**

For some nutrients, two types of information are provided about food sources: identification of the foods that are the major contributors of the nutrients to diets in the United States and Canada and identification of the foods that contain the highest amounts of the nutrient. The determination of foods that are major contributors depends on both nutrient content of a food and total consumption of the food (amount and frequency). Therefore, a food that has a relatively low concentration of the nutrient might still be a large contributor to total intake if that food is consumed in relatively large amounts.

## **METHODS TO DETERMINE UPPER LEVELS**

The Tolerable Upper Intake Level (UL) refers to the highest level of daily nutrient intake that is likely to pose no risk of adverse health effects for almost all people in a population. As intake increases above the UL, the potential risk of adverse effects increases.

### **Risk Assessment Model**

The model used to derive the ULs consists of a set of scientific factors that are considered explicitly. The factors are organized into a framework called risk

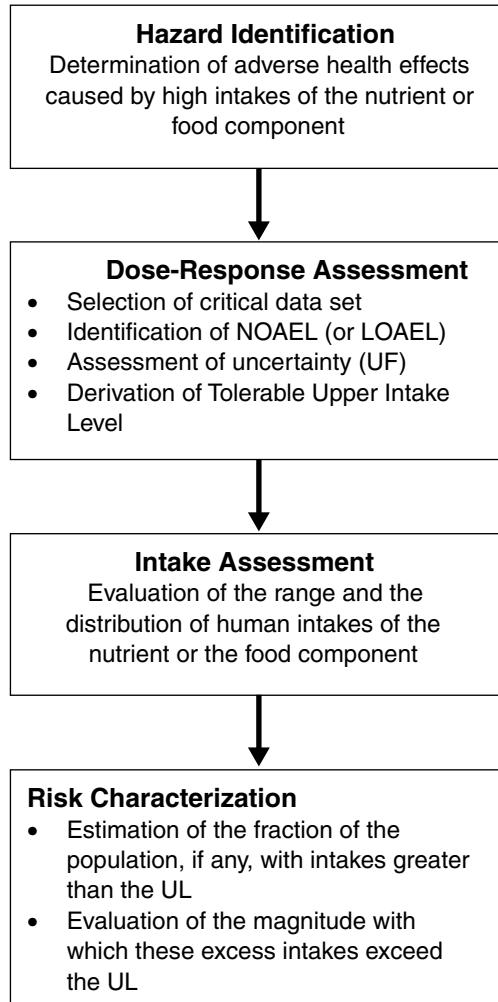


FIGURE C-1 Risk assessment model for nutrient toxicity.

assessment. In determining ULs, risk assessment is used to systematically evaluate the likelihood of adverse effects due to excess exposure to a nutrient.

The steps used in risk assessment are summarized in Figure C-1 and explained in more detail in the text that follows.

### STEP 1: HAZARD IDENTIFICATION

In this step, a thorough review of the scientific literature is conducted to identify adverse health effects caused by consuming excess amounts of the nutrient

in question. Data from human, animal, and in vitro research is examined, and scientific judgment is used to determine which observed effects are adverse. In addition, adverse nutrient–nutrient interactions are considered in defining an adverse effect. When available, data regarding the rate of nutrient absorption, distribution, metabolism, and excretion may also be used to help identify potential hazards. Any available knowledge of the molecular and cellular mechanisms by which a nutrient causes an adverse effect may also be identified. The scientific quality and quantity of the database evaluated as well. Finally, distinct subgroups that are highly sensitive to the adverse effects of high nutrient intake are identified.

### STEP 2: DOSE–RESPONSE ASSESSMENT

At this stage, the most critical data pertaining to the UL are selected. These data are chosen based on their relevance to human route of expected intake, and expected magnitude and duration of intake.

Once the critical data have been chosen, a threshold “dose,” or intake, is determined. For nutrients, a key assumption underlying risk assessment is that no risk of adverse effects is expected unless the threshold dose, or intake, is exceeded.

When possible, a no-observed-adverse-effect level (NOAEL) is identified. This is the highest intake (or experimental oral dose) of a nutrient at which no adverse effects have been observed in the people studied. If there are not enough data to select a NOAEL, then a lowest-observed-adverse-effect level (LOAEL) may be used. The LOAEL is the lowest intake (or experimental dose) at which an adverse effect has been identified.

### Uncertainty Factors

Because the UL is intended to be an estimate of the level of intake that will protect the health of virtually all healthy members of a population, a critical part of risk assessment is accounting for uncertainty that is inherent in the process. In addition, the fact that excessive levels of a nutrient can cause more than one adverse effect must be considered. The NOAELs and LOAELs for these unique effects will typically differ.

To help account for such variations, an uncertainty factor (UF) is selected. The UF is intended to incorporate all potential sources of uncertainties. In general, the UFs are lower when the available data are high quality and when the adverse effects of the nutrient are extremely mild and reversible. When determining a UF, the following potential sources of uncertainty are generally considered:

- Individual variations in sensitivity to a nutrient
- Extrapolation from data from experimental animal studies to humans, when animal data constitute the primary evidence available
- Absence of NOAEL (to account for uncertainty of deriving a UL from the LOAEL)
- Use of data showing effects of subchronic nutrient exposures (NOAEL) to predict the potential effects of chronic exposure

The UL is derived by dividing the NOAEL (or LOAEL) by a single UF that incorporates all the relevant uncertainties. Scientific judgment is used to derive the appropriate NOAELs, LOAELs, and UFs. The considerations and uncertainties that are accounted for in the setting of ULs are detailed in the original DRI reports.

### **STEP 3: INTAKE ASSESSMENT**

Information on the nutrient intake of the population is assessed. In cases where the UL pertains only to supplemental intake of the nutrient (as opposed to intake from food), the assessment is directed at supplement intakes only.

### **STEP 4: RISK CHARACTERIZATION**

Several factors are considered to determine whether nutrient intakes create a risk of adverse effects to a population:

- The fraction of the group consistently consuming the nutrient at levels in excess of the UL
- The seriousness of the adverse effects associated with the nutrient
- The extent to which the effect is reversible when intakes are reduced to levels less than the UL
- The fraction of the population with consistent intakes above the NOAEL or even the LOAEL

**D****GLOSSARY AND ACRONYMS**

AAP	American Academy of Pediatrics
ACC	Acetyl-CoA carboxylase
Accommodation	An adaptative response that allows survival, but at the expense of some more or less serious consequences on health or physiological function
ACE	Angiotensin converting enzyme
Action	Demonstrated effects in various biological systems that may or may not have physiological significance
Acute exposure	An exposure to a toxin or excess amount of a nutrient that is short term, perhaps as short as one day or one dose. In this report it generally refers to total exposure (diet plus supplements) on a single day.
Adaptation	Maintenance of essentially unchanged functional capacity despite some alterations in steady-state conditions
ADD	Attention deficit disorder
Adequacy of nutrient intake	Intake of a nutrient that meets the individual's requirement for that nutrient
ADP	Adenosine diphosphate
Adverse effect	Any significant alteration in the structure or function of the human organism, or any impairment of a physiologically important function, that could lead to an adverse health effect
AI	Adequate Intake; a category of Dietary Reference Intakes
AITD	Autoimmune thyroid disease
AMDR	Acceptable Macronutrient Distribution Range
ANP	Atrial natriuretic peptide
Antioxidant	See Dietary Antioxidant
ARB	Angiotensin II receptor blocker
Association	Potential interaction derived from epidemiological studies of the relationship between a specific nutrient and chronic disease
ASTDR	Agency for Toxic Substances and Disease Registry
ATBC	Alpha-Tocopherol, Beta-Carotene (Cancer Prevention Study)

ATP	Adenosine triphosphate
AUC	Area under the curve
BEE	Basal energy expenditure
Bias	Used in a statistical sense, referring to a tendency of an estimate to deviate from a true value (as by reason of nonrandom sampling). To be unbiased, a statistic would have an expected value equal to a population parameter being estimated.
Bioavailability	Accessibility of a nutrient to participate in unspecified metabolic or physiological processes
BMI	Body mass index
BMR	Basal metabolic rate
CARET	Carotene and Retinol Efficacy Trial
Carotenodermia	Yellow discoloration of the skin with elevated plasma carotene concentrations
CDC	Centers for Disease Control and Prevention; an agency of the U.S. Department of Health and Human Services
CF	Cystic fibrosis
CHAOS	Cambridge Heart Antioxidant Study
CHD	Coronary heart disease
Chronic exposure	Exposure to a chemical compound such as a nutrient for a long period of time, perhaps as long as every day for the lifetime of an individual
CI	Confidence interval
CID	Cold-induced diuresis
CLAS	Cholesterol Lowering Atherosclerosis Study
Cluster analysis	A general approach to multivariate problems, the aim of which is to determine whether individuals fall into groups or clusters
CoA	Coenzyme A
Cr	Elemental symbol for chromium
CRBP	Cellular retinol binding protein
CSFII	Continuing Survey of Food Intakes by Individuals; a survey conducted periodically by the Agricultural Research Service, U.S. Department of Agriculture
Cut-point	The exact point when something stops or changes. The EAR is used as a cut-point in the EAR cut-point method of assessing the prevalence of inadequacy for a group.
CV	Coefficient of variation—standard deviation divided by the square root of $n$ , where $n$ is the sample size
CVD	Cardiovascular disease; includes heart disease and stroke

DASH Diet	Dietary Approaches to Stop Hypertension Diet; a diet rich in fruits, vegetables, and low-fat dairy products and reduced in saturated fat, total fat, and cholesterol
DASH-Sodium Trial	A clinical trial that tested the effects on blood pressure of three different sodium levels in two distinct diets
DASH Trial	A clinical trial that tested the effects of different dietary patterns on blood pressure
DDS	Delayed dermal sensitivity
Deficiency	An abnormal physiological condition resulting from inadequate intake of a nutrient or multiple nutrients.
Dehydration	The process of decreasing total body water; lower than normal total body water (euhydration) (see Hypohydration)
DEXA	Dual energy X-ray absorptiometry
DFE	Dietary folate equivalent
DHA	Docosahexaenoic acid
Dietary antioxidant	A dietary antioxidant is a substance in foods that significantly decreases the adverse effects of reactive species, such as reactive oxygen and nitrogen species, on normal physiological function in humans.
Dietary status	The condition of an individual or group as a result of food and nutrient intake. Dietary status also refers to the sum of dietary intake measurements for an individual or a group.
Disappearance data	Data that refer to food and nutrients that disappear from the marketplace. The term refers to food and nutrient availability for a population that is calculated from national or regional statistics by the inventory-style method. Usually taken into account are the sum of food remaining from the previous year, food imports, and agricultural production; from this sum is subtracted the sum of food remaining at the end of the year, food exports, food waste, and food used for non-food purposes. Disappearance data do not always take account of food that does not enter commerce, such as home food production, wild food harvests, etc.
Distribution of observed intakes	The observed dietary or nutrient intake distribution representing the variability of <i>observed</i> intakes in the population of interest. For example, the distribution of observed intakes may be obtained from dietary survey data such as 24-hour recalls.
Distribution of requirements	The distribution reflecting the individual-to-individual variability in requirements. Variability exists because not all individuals in a (sub) population have the same requirements for a nutrient (even if individuals are grouped into homogeneous classes, such as Hispanic men aged 19 to 50 years).

Distribution of usual intakes	The distribution of long-run average dietary or nutrient intakes of individuals in the population. The distribution should reflect only the individual-to-individual variability in intakes. Statistical procedures may be used to adjust the distribution of observed intakes by partially removing the day-to-day variability in individual intakes, so the adjusted distribution more closely reflects a usual intake distribution.
DLW	Doubly labeled water
DNA	Deoxyribonucleic acid
Dose-response assessment	Second step in a risk assessment in which the relationship between nutrient intake and an adverse effect (in terms of incidence or severity of the effect) is determined
DRI	Dietary Reference Intakes
DTH	Delayed-type hypersensitivity
EAR	Estimated Average Requirement; a category of Dietary Reference Intakes
EAR cut-point method	A method of assessing the nutrient adequacy of groups. It consists of assessing the proportion of individuals in the group whose usual nutrient intakes are below the EAR.
ECF	Extracellular fluid
ECG	Electrocardiogram
EEG	Electroencephalogram
EEPA	Energy expenditure of physical activity
EER	Estimated energy requirement
EGR	Erythrocyte glutathione reductase
EGRAC	Erythrocyte glutathione reductase activity coefficient
EPA	U.S. Environmental Protection Agency
EPOC	Excess post-exercise oxygen consumption
Error in measurement	Mistake made in the observation or recording of data
Erythrocyte	A red blood cell
Euhydration	Normal hydration
FAO	Food and Agriculture Organization of the United Nations
FASEB	Federation of American Societies for Experimental Biology
FDA	Food and Drug Administration; an agency of the U.S. Department of Health and Human Services
Fe	Elemental symbol for iron
FFA	Free fatty acids
FFM	Fat-free mass
FM	Fat mass
FNB	Food and Nutrition Board; a division of the Institute of Medicine of the National Academies

Food balance sheet	See Disappearance data
Fore milk	Human milk collected at the beginning of an infant feeding
Former RDA and RNI	Recommended daily dietary intake level of a nutrient sufficient to meet the nutrient requirement of nearly all healthy persons in a particular life stage and gender group. These standards were last issued in the United States in 1989 (RDA, Recommended Dietary Allowance) and in Canada in 1990 (RNI, Recommended Nutrient Intake).
FQ	Food quotient
Function	Role played by a nutrient in growth, development, and maturation
GFR	Glomerular filtration rate
Gravid	Pregnant
H <sub>2</sub> O <sub>2</sub>	Hydrogen peroxide
Hazard identification	First step in a risk assessment, which is concerned with the collection, organization, and evaluation of all information pertaining to the toxic properties of a nutrient
HDL	High density lipoprotein
Health Canada	The federal department in Canada responsible for maintaining and improving the health of Canadian people
Hind milk	Human milk collected at the end of an infant feeding
HIV	Human immunodeficiency virus
HOPE	Heart Outcomes Prevention Evaluation
Household	Individuals sharing in the purchase, preparation, and consumption of foods. Usually this will represent individuals living as a family in one home, including adults and children. A household may be the unit of observation rather than the independent individuals within it.
HPLC	High-performance liquid chromatography
HPV	Human papilloma virus
HRT	Hormone replacement therapy
Hyperhydration	Higher than normal total body water (euhydration)
Hyperkalemia	Serum potassium concentration > 5.0 mEq/L or mmol/L
Hypernatremia	Serum sodium concentration > 145 mEq/L or mmol/L
Hypertension	Systolic blood pressure ≥ 140 or diastolic blood pressure ≥ 90 mm Hg
Hypohydration	Lower than normal total body water (euhydration) (see Dehydration)
Hypokalemia	Serum potassium concentration < 3.5 mEq/L or mmol/L
Hyponatremia	Serum sodium concentration < 135 mEq/L or mmol/L

IAEA	International Atomic Energy Agency
IARC	International Agency for Research on Cancer
ICC	Indian childhood cirrhosis
ICCIDD	International Council for the Control of Iodine Deficiency Disorders
ICF	Intracellular fluid
ICT	Idiopathic copper toxicosis
IM	Intramuscular
Inadequacy of nutrient intake	Intake of a nutrient that fails to meet the individual's requirement for that nutrient
Interindividual variability	Variability from person to person
Intraindividual variability	Variability within one person. The term is generally used to refer to day-to-day variation in reported intakes, also called the within-person variation or standard deviation within ( $SD_{within}$ ).
IOM	Institute of Medicine
IPCS	International Programme on Chemical Safety
IR	Insulin receptor
IRE	Iron response element
IRP	Iron response proteins
IU	International unit
Joint distribution	Simultaneous distribution of both requirements (y-axis) and usual intakes (x-axis) for a single nutrient by individuals within a population or group
Kashin-Beck disease	Human cartilage disease found in some of the low-selenium intake areas in Asia
Keshan disease	Human cardiomyopathy that occurs only in selenium-deficient children
Lacto-ovo-vegetarian	A person who consumes milk (lacto), eggs (ovo), and plant foods and products, but no meat or fish
LBM	Lean body mass
LCAT	Lecithin-cholesterol acyltransferase
LDL	Low-density lipoprotein
Likelihood	Probability
LMWCr	Low molecular weight chromium-binding substance
LOAEL	Lowest-observed-adverse-effect level; the lowest intake (or experimental dose) of a nutrient at which an adverse effect has been identified
LPL	Lipoprotein lipase
LSRO	Life Sciences Research Office
Lycopenodermia	Deep orange discoloration of the skin resulting from high intakes of lycopene-rich food

MAP	Mean arterial pressure; diastolic pressure times 2 plus systolic pressure over 3; the average pressure during a cardiac cycle
MCH	Mean corpuscular hemoglobin—the amount of hemoglobin in erythrocytes (red blood cells)
MCL	Maximum contaminant level; a level set by the U.S. Environmental Protection Agency for environmental contaminants
MCV	Mean corpuscular volume—the volume of the average erythrocyte
Mean intake	Average intake of a particular nutrient or food for a group or population of individuals. Also average intake of a nutrient or food over two or more days for an individual.
Mean requirement	Average requirement of a particular nutrient for a group or population of individuals.
MET	Metabolic equivalent—a rate of energy expenditure sustained by a rate of oxygen consumption of 3.5 mL/kg of body weight/min
MHC	Major histocompatibility complex
MI	Myocardial infarction
Mn	Elemental symbol for manganese
MPOD	Macular pigment optical density
MUFA	Monounsaturated fatty acid
MVP	Mitral valve prolapse
NAD	Nicotinamide adenine dinucleotide
NADH	Nicotinamide adenine dinucleotide hydride; a coenzyme
NADPH	Nicotinamide adenine dinucleotide phosphate
NAS	National Academy of Sciences
NE	Niacin equivalent
NEC	Necrotizing enterocolitis
NFCS	Nationwide Food Consumption Survey; a food consumption survey conducted through 1965 by the U.S. Department of Agriculture
NHANES	National Health and Nutrition Examination Survey; a survey conducted periodically by the National Center for Health Statistics, Centers for Disease Control and Prevention
NHIS	National Health Interview Survey
NO	Nitric oxide
NOAEL	No-observed-adverse-effect level; the highest intake (or experimental dose) of a nutrient at which no adverse effect has been observed

Normal distribution	In the statistical sense, refers to a specific type of distribution of the values for a parameter within a group or population. The distribution is symmetrical and the mean $\pm$ 2 standard deviations will encompass the parameter for 95 percent of the individuals in the group.
NRC	National Research Council
NTD	Neural tube defect
Nutrient requirement	The lowest continuing intake level of a nutrient that will maintain a defined level of nutriture in a healthy individual; also called individual requirement
Nutritional status	Condition of an individual or group resulting from nutrient intake and utilization of a nutrient at the tissue level
ORAC	Oxygen radical absorbance capacity
OTA	Office of Technology Assessment
Oxidative stress	Imbalance between the production of various reactive species and the ability of the organism's natural protective mechanisms to cope with these reactive compounds and prevent adverse effects
OxLDL	Oxidized low density lipoprotein
PAI	Physical activity index
PAL	Physical activity level
PAPS	3'-Phosphoadenosine-5'-phosphosulfate
Phylloquinone	Plant form of vitamin K and a major form of this vitamin in the human diet
PHS	Physicians' Health Study
PL	Pyridoxal
PLP	Pyridoxal phosphate
PM	Pyridoxamine
PMP	Pyridoxamine phosphate
PN	Pyridoxine
PNP	Pyridoxine phosphate
Population	A large group; in this report, a large group of people
Prevalence	The percentage of a defined population that is affected by a specific condition at the same time
Prevalence of inadequate intakes	The percentage of a population that has intakes below requirements
Probability approach	A method of assessing the nutrient adequacy of groups. It uses the distribution of usual intakes and the distribution of requirements to estimate the prevalence of inadequate intakes in a group. Also known as the NRC approach.

Probability of inadequacy	Outcome of a calculation that compares an individual's usual intake to the distribution of requirements for persons of the same life stage and gender to determine the probability that the individual's intake does not meet his or her requirement.
Provitamin A carotenoids	$\alpha$ -Carotene, $\beta$ -carotene, and $\beta$ -cryptoxanthin
Psychogenic polydipsia	The excessive consumption of fluid, especially water, among chronic psychiatric patients, particularly those with schizophrenia
PUFA	Polyunsaturated fatty acid
RAR	Retinoic acid receptor
RBC	Red blood cell
RDA	Recommended Dietary Allowance; a category of Dietary Reference Intakes
RE	Retinol equivalent
REE	Resting Energy Expenditure
Requirement	The lowest continuing intake level of a nutrient that will maintain a defined level of nutriture in a healthy individual
Rhabdomyolysis	Injury to skeletal muscle tissue that results in the destruction of skeletal muscle cells and allows for the escape of cellular contents into the extracellular fluid, leading to renal failure and compartment syndromes
Risk	The probability or likelihood that some unwanted effect will occur; in this report, refers to an unwanted effect from too small or too large an intake of a nutrient
Risk assessment	The organized framework for evaluating scientific information that has as its objective a characterization of the nature and likelihood of harm resulting from excess human exposure to an environmental agent (in this case, a nutrient); it includes the development of both qualitative and quantitative expressions of risk
Risk characterization	The final step in a risk assessment, which summarizes the conclusions from steps 1 through 3 of the assessment (hazard identification, dose response, and estimate of exposure) and evaluates the risk; this step also includes a characterization of the degree of scientific confidence that can be placed in the Tolerable Upper Intake Level
Risk curve	Used to demonstrate inadequacy or excess of a particular nutrient. As defined in the usual statistical sense, a risk curve is in contrast to the concept of probability curve.

Risk management	Process by which risk assessment results are integrated with other information to make decisions about the need for, method of, and extent of risk reduction; in addition, it considers such issues as the public health significance of the risk, the technical feasibility of achieving various degrees of risk control, and the economic and social costs of this control
Risk of excess	In relation to the DRIs, the likelihood that an individual will exceed the UL for a particular nutrient
Risk of exposure	In the toxicological sense, the likelihood that individuals will experience contact with a toxin (or consume levels of a nutrient above the UL)
Risk of inadequacy	The likelihood that an individual will have usual intake of a particular nutrient that is less than the individual's requirement
RMR	Resting metabolic rate
RNA	Ribonucleic acid
RNI	Recommended Nutrient Intake
RNS	Reactive nitrogen species
ROS	Reactive oxygen species
RQ	Respiratory quotient
RXR	Retinoid X receptor
Salt sensitivity	The extent of blood pressure change in response to a reduction in salt intake; the term “salt-sensitive blood pressure” applies to those individuals or subgroups who experience the greatest reduction in blood pressure from a given reduction in salt intake
SD	Standard deviation
SDA	Specific dynamic action
SE	Standard error
Selenite and selenate	Inorganic selenium, the forms found in many dietary supplements
Selenomethionine and selenocysteine	Major dietary forms of selenium
Selenosis	Selenium toxicity characterized by hair loss and nail sloughing
SEM	Standard error of the mean
Sensitivity analysis	Technique of varying the implicit assumptions or presumed conditions of an analysis approach to see how much this affects the overall outcome
SHRSP	Stroke-prone spontaneously hypertensive (inbred strain of rats)
Skewed distribution	A distribution that is not symmetrical around its mean. For example, a skewed distribution can have a long tail to the right (right-skewed distribution) or to the left (left-skewed distribution).

SMR	Sleeping metabolic rate
SOD	Superoxide dismutase
sTfr	Soluble transferrin receptor
Symmetrical distribution	A distribution that has the same number of values (observations) above and below the mean and has equal proportions of these values around the mean
TBW	Total body water
TDS	Total Diet Study; a study conducted by the Food and Drug Administration
$\alpha$ -TE	$\alpha$ -Tocopherol equivalent
TEE	Total energy expenditure
TEF	Thermic effect of food
Threshold	The point in a dose-response curve that is accepted as the point beyond which a risk of adverse effects occurs
TIBC	Total iron binding capacity
TMA	Trimethylamine
$\alpha$ -Tocopherol	The only form of vitamin E that is maintained in human plasma and thus it is the only form utilized to estimate the vitamin E requirement
Total water	Includes drinking water, water in beverages, and water that is part of food
Toxicity	An adverse condition relating to or caused by a toxin
TPN	Total parenteral nutrition
TPP	Thiamin pyrophosphate
TRH	Thyrotropin-releasing hormone
True prevalence	The actual prevalence of a condition assuming no error in measurement of either requirements or intakes that would result in false negative or false positive classifications
TSH	Thyroid stimulating hormone, also known as thyrotropin
$\alpha$ -TTP	$\alpha$ -Tocopherol transfer protein
UF	Uncertainty factor; the number by which the NOAEL (or LOAEL) is divided to obtain the Tolerable Upper Intake Level; the size of the UF varies depending on the confidence in the data and the nature of the adverse effect
UL	Tolerable Upper Intake Level; a category of Dietary Reference Intakes
Unit of observation	The level of aggregation at which data are collected. For example, the unit of observation for dietary assessment may be the individual, the household, or the population
Univariate distribution	The distribution of a single variable
USDA	U.S. Department of Agriculture
USP	U.S. Pharmacopeia

Usual intake	The long-run average intake of food, nutrients, or a specific nutrient for an individual
Variance of usual intakes or requirements	In the statistical sense, reflects the spread of the distribution of usual intakes or requirements on both sides of the mean intake or requirement. When the variance of a distribution is low, the likelihood of seeing values that are far away from the mean is low; in contrast, when the variance is large, the likelihood of seeing values that are far away from the mean is high. For usual intakes and requirements, variance reflects the person-to-person variability in the group.
Vitamin E	The 2 <i>R</i> -stereoisomeric forms of $\alpha$ -tocopherol ( <i>RRR</i> -, <i>RSR</i> -, <i>RRS</i> -, and <i>RSS</i> - $\alpha$ -tocopherol)
VLDL	Very low density lipoprotein
WHO	World Health Organization

# E

## DRI VALUES FOR INDISPENSABLE AMINO ACIDS BY LIFE STAGE AND GENDER GROUP

### AI for Infants Ages 0 through 6 Months

0–6 mo	214 mg/d or 36 mg/kg/d of histidine 529 mg/d or 88 mg/kg/d of isoleucine 938 mg/d or 156 mg/kg/d of leucine 640 mg/d or 107 mg/kg/d of lysine 353 mg/d or 59 mg/kg/d of methionine + cysteine 807 mg/d or 135 mg/kg/d of phenylalanine + tyrosine 436 mg/d or 73 mg/kg/d of threonine 167 mg/d or 28 mg/kg/d of tryptophan 519 mg/d or 87 mg/kg/d of valine
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### Infants Ages 7 through 12 Months

EAR for 7–12 mo	22 mg/kg/d of histidine 30 mg/kg/d of isoleucine 65 mg/kg/d of leucine 62 mg/kg/d of lysine 30 mg/kg/d of methionine + cysteine 58 mg/kg/d of phenylalanine + tyrosine 34 mg/kg/d of threonine 9 mg/kg/d of tryptophan 39 mg/kg/d of valine
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RDA for 7–12 mo	32 mg/kg/d of histidine 43 mg/kg/d of isoleucine 93 mg/kg/d of leucine 89 mg/kg/d of lysine 43 mg/kg/d of methionine + cysteine 84 mg/kg/d of phenylalanine + tyrosine 49 mg/kg/d of threonine 13 mg/kg/d of tryptophan 58 mg/kg/d of valine
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**Children Ages 1 through 3 Years**

EAR for 1–3 y	16 mg/kg/d of histidine 22 mg/kg/d of isoleucine 48 mg/kg/d of leucine 45 mg/kg/d of lysine 22 mg/kg/d of methionine + cysteine 41 mg/kg/d of phenylalanine + tyrosine 24 mg/kg/d of threonine 6 mg/kg/d of tryptophan 28 mg/kg/d of valine
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RDA for 1–3 y	21 mg/kg/d of histidine 28 mg/kg/d of isoleucine 63 mg/kg/d of leucine 58 mg/kg/d of lysine 28 mg/kg/d of methionine + cysteine 54 mg/kg/d of phenylalanine + tyrosine 32 mg/kg/d of threonine 8 mg/kg/d of tryptophan 37 mg/kg/d of valine
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**Children Ages 4 through 8 Years**

EAR for 4–8 y	13 mg/kg/d of histidine 18 mg/kg/d of isoleucine 40 mg/kg/d of leucine 37 mg/kg/d of lysine 18 mg/kg/d of methionine + cysteine 33 mg/kg/d of phenylalanine + tyrosine 19 mg/kg/d of threonine 5 mg/kg/d of tryptophan 23 mg/kg/d of valine
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RDA for 4–8 y	16 mg/kg/d of histidine 22 mg/kg/d of isoleucine 49 mg/kg/d of leucine 46 mg/kg/d of lysine 22 mg/kg/d of methionine + cysteine 41 mg/kg/d of phenylalanine + tyrosine 24 mg/kg/d of threonine 6 mg/kg/d of tryptophan 28 mg/kg/d of valine
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## **Boys Ages 9 through 13 Years**

### **Boys**

EAR for 9–13 y	13 mg/kg/d of histidine 18 mg/kg/d of isoleucine 40 mg/kg/d of leucine 37 mg/kg/d of lysine 18 mg/kg/d of methionine + cysteine 33 mg/kg/d of phenylalanine + tyrosine 19 mg/kg/d of threonine 5 mg/kg/d of tryptophan 23 mg/kg/d of valine
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### **Boys**

RDA for 9–13 y	17 mg/kg/d of histidine 22 mg/kg/d of isoleucine 49 mg/kg/d of leucine 46 mg/kg/d of lysine 22 mg/kg/d of methionine + cysteine 41 mg/kg/d of phenylalanine + tyrosine 24 mg/kg/d of threonine 6 mg/kg/d of tryptophan 28 mg/kg/d of valine
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## **Girls Ages 9 through 13 Years**

### **Girls**

EAR for 9–13 y	12 mg/kg/d of histidine 17 mg/kg/d of isoleucine
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38 mg/kg/d of leucine  
 35 mg/kg/d of lysine  
 17 mg/kg/d of methionine + cysteine  
 31 mg/kg/d of phenylalanine + tyrosine  
 18 mg/kg/d of threonine  
 5 mg/kg/d of tryptophan  
 22 mg/kg/d of valine

**GIRLS**

RDA for 9–13 y      15 mg/kg/d of histidine  
                           21 mg/kg/d of isoleucine  
                           47 mg/kg/d of leucine  
                           43 mg/kg/d of lysine  
                           21 mg/kg/d of methionine + cysteine  
                           38 mg/kg/d of phenylalanine + tyrosine  
                           22 mg/kg/d of threonine  
                           6 mg/kg/d of tryptophan  
                           27 mg/kg/d of valine

**Boys Ages 14 through 18 Years****Boys**

EAR for 14–18 y      12 mg/kg/d of histidine  
                           17 mg/kg/d of isoleucine  
                           38 mg/kg/d of leucine  
                           35 mg/kg/d of lysine  
                           17 mg/kg/d of methionine + cysteine  
                           31 mg/kg/d of phenylalanine + tyrosine  
                           18 mg/kg/d of threonine  
                           5 mg/kg/d of tryptophan  
                           22 mg/kg/d of valine

**Boys**

RDA for 14–18 y      15 mg/kg/d of histidine  
                           21 mg/kg/d of isoleucine  
                           47 mg/kg/d of leucine  
                           43 mg/kg/d of lysine  
                           21 mg/kg/d of methionine + cysteine

38 mg/kg/d of phenylalanine + tyrosine  
22 mg/kg/d of threonine  
6 mg/kg/d of tryptophan  
27 mg/kg/d of valine

## Girls Ages 14 through 18 Years

### GIRLS

EAR for 14–18 y	12 mg/kg/d of histidine
	16 mg/kg/d of isoleucine
	35 mg/kg/d of leucine
	32 mg/kg/d of lysine
	16 mg/kg/d of methionine + cysteine
	28 mg/kg/d of phenylalanine + tyrosine
	17 mg/kg/d of threonine
	4 mg/kg/d of tryptophan
	20 mg/kg/d of valine

### GIRLS

RDA for 14–18 y	14 mg/kg/d of histidine
	19 mg/kg/d of isoleucine
	44 mg/kg/d of leucine
	40 mg/kg/d of lysine
	19 mg/kg/d of methionine + cysteine
	35 mg/kg/d of phenylalanine + tyrosine
	21 mg/kg/d of threonine
	5 mg/kg/d of tryptophan
	24 mg/kg/d of valine

## Adults Ages 19 Years and Older

### EAR FOR ADULTS

19 y and older	11 mg/kg/d of histidine
	15 mg/kg/d of isoleucine
	34 mg/kg/d of leucine
	31 mg/kg/d of lysine
	15 mg/kg/d of methionine + cysteine
	27 mg/kg/d of phenylalanine + tyrosine
	16 mg/kg/d of threonine

4 mg/kg/d of tryptophan  
19 mg/kg/d of valine

### RDA FOR ADULTS

19 y and older	14 mg/kg/d of histidine 19 mg/kg/d of isoleucine 42 mg/kg/d of leucine 38 mg/kg/d of lysine 19 mg/kg/d of methionine + cysteine 33 mg/kg/d of phenylalanine + tyrosine 20 mg/kg/d of threonine 5 mg/kg/d of tryptophan 24 mg/kg/d of valine
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### Pregnancy

#### EAR FOR PREGNANCY

For all ages	15 mg/kg/d of histidine 20 mg/kg/d of isoleucine 45 mg/kg/d of leucine 41 mg/kg/d of lysine 20 mg/kg/d of methionine + cysteine 36 mg/kg/d of phenylalanine + tyrosine 21 mg/kg/d of threonine 5 mg/kg/d of tryptophan 25 mg/kg/d of valine
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#### RDA FOR PREGNANCY

For all ages	18 mg/kg/d of histidine 25 mg/kg/d of isoleucine 56 mg/kg/d of leucine 51 mg/kg/d of lysine 25 mg/kg/d of methionine + cysteine 44 mg/kg/d of phenylalanine + tyrosine 26 mg/kg/d of threonine 7 mg/kg/d of tryptophan 31 mg/kg/d of valine
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## Lactation

### EAR FOR LACTATION

For all ages	15 mg/kg/d of histidine 24 mg/kg/d of isoleucine 50 mg/kg/d of leucine 42 mg/kg/d of lysine 21 mg/kg/d of methionine + cysteine 41 mg/kg/d of phenylalanine + tyrosine 24 mg/kg/d of threonine 7 mg/kg/d of tryptophan 28 mg/kg/d of valine
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### RDA FOR LACTATION

For all ages	19 mg/kg/d of histidine 30 mg/kg/d of isoleucine 62 mg/kg/d of leucine 52 mg/kg/d of lysine 26 mg/kg/d of methionine + cysteine 51 mg/kg/d of phenylalanine + tyrosine 30 mg/kg/d of threonine 9 mg/kg/d of tryptophan 35 mg/kg/d of valine
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**TABLE F-1 Conversions****Water**

1 L = 33.8 fluid oz; 1 L = 1.06 qt; 1 cup = 8 fluid oz

**Vitamin A and Carotenoids**

- $\mu\text{g RAE} = 1 \mu\text{g all}-trans\text{-retinol}$
- $\mu\text{g RAE} = 2 \mu\text{g supplemental all}-trans\text{-}\beta\text{-carotene}$
- $\mu\text{g RAE} = 12 \mu\text{g dietary all}-trans\text{-}\beta\text{-carotene}$
- $\mu\text{g RAE} = 24 \mu\text{g other dietary provitamin A carotenoids}$
- $\mu\text{g RAE} = \mu\text{g RE in foods containing only preformed Vitamin A (retinol)}$
- $\mu\text{g RAE} = \mu\text{g RE in foods containing only plant sources (provitamin A carotenoids) of vitamin A (e.g., carrots)} \div 2$
- One IU of retinol =  $0.3 \mu\text{g of retinol, or } 0.3 \mu\text{g RAE}$
- One IU of supplemental  $\beta$ -carotene =  $0.5 \text{ IU of retinol or } 0.15 \mu\text{g RAE } (0.3 \times 0.5)$
- One IU of dietary  $\beta$ -carotene =  $0.165 \text{ IU retinol or } 0.05 \mu\text{g RAE } (0.3 \times 0.165)$
- One IU of other dietary provitamin A carotenoids =  $0.025 \mu\text{g RAE}$

**Vitamin D**

$1 \mu\text{g cholecalciferol} = 40 \text{ IU vitamin D}$

**Vitamin E**

- mg of  $\alpha$ -tocopherol in a meal = mg of  $\alpha$ -tocopherol equivalents in a meal  $\times 0.8$
- mg of  $\alpha$ -tocopherol in food, fortified food, or multivitamin  
 $= \text{IU of the } RRR\text{-}\alpha\text{-tocopherol compound} \times 0.67$   
or  
 $= \text{IU of the } all\text{ }rac\text{-}\alpha\text{-tocopherol compound} \times 0.45$

**Folate**

$1 \mu\text{g of DFEs}$	$= 1.0 \mu\text{g of food folate}$
	$= 0.6 \mu\text{g of folate added to foods (as a fortificant or folate supplement with food)}$
	$= 0.5 \mu\text{g of folate taken as a supplement (without food).}$

$1 \mu\text{g of food folate} = 1.0 \mu\text{g of DFEs}$

$1 \mu\text{g of folate added as a fortificant or as a supplement consumed with meals} = 1.7 \mu\text{g of DFEs}$

$1 \mu\text{g of folate supplement taken without food} = 2.0 \mu\text{g of DFEs.}$

**Niacin**

As niacin equivalents (NEs).  $1 \text{ mg of niacin} = 60 \text{ mg of tryptophan}$

# F **CONVERSIONS**

## **WATER**

Conversion factors: 1 L = 33.8 fluid oz; 1 L = 1.06 qt; 1 cup = 8 fluid oz.

## **VITAMIN A AND CAROTENOIDS**

A major change in the extent to which provitamin A carotenoids can be used to form vitamin A is the replacement of retinol equivalents ( $\mu\text{g}$  RE) with retinol activity equivalents ( $\mu\text{g}$  RAE) for the provitamin A carotenoids. The RAEs for dietary  $\beta$ -carotene,  $\alpha$ -carotene, and  $\beta$ -cryptoxanthin are 12, 24, and 24  $\mu\text{g}$ , respectively, compared to corresponding REs of 6, 12, and 12  $\mu\text{g}$  reported by the National Research Council in 1989.

### **DETERMINING THE VITAMIN A CONTENT OF FOODS WITH SOME NUTRIENT DATABASES**

Newer nutrient databases provide vitamin A activity in RAE. Even if a database does not, it is still possible to estimate total vitamin A activity in  $\mu\text{g}$  RAE from existing tables using  $\mu\text{g}$  RE. For foods, such as liver, containing only vitamin A activity from preformed vitamin A (retinol), no adjustment is necessary. Vitamin A values for foods containing only plant sources (provitamin A carotenoids) of vitamin A (e.g., carrots) can be adjusted by dividing the  $\mu\text{g}$  RE by two. For foods that are mixtures containing both plant and animal sources of vitamin A (e.g., a casserole containing meat and vegetables), the adjustment process is more complex. If the recipe for a mixture is known, the new vitamin A value may be calculated after adjusting the vitamin A content of each ingredient, as necessary. Alternatively, if the nutrient database contains values as  $\mu\text{g}$  RE for both total vitamin A and carotenoids, then it is possible to calculate a new value both for carotenoids and for total vitamin A. To determine a revised total vitamin A value, the retinol value is calculated as the difference between the original total vitamin A value and the original carotenoid value. The revised total vitamin A content is then calculated as the sum of the retinol value and the adjusted carotenoid value, which is the original carotenoid value in  $\mu\text{g}$  RE di-

vided by two. As discussed in the following section, this same procedure may be used to adjust intake data that have been analyzed using other databases.

Supplemental  $\beta$ -carotene has a higher bioconversion to vitamin A than does dietary  $\beta$ -carotene. With low doses, the conversion is as high as 2:1. Little is known about the bioconversion of the forms of  $\beta$ -carotene that are added to foods, so fortification forms of  $\beta$ -carotene should be assumed to have the same bioconversion as food forms, which is 12:1. Food and supplement labels usually state vitamin A levels in International Units (IU). One IU of retinol is equivalent to 0.3  $\mu\text{g}$  of retinol, or 0.3  $\mu\text{g}$  RAE. One IU of  $\beta$ -carotene in supplements is equivalent to 0.5 IU of retinol or 0.15  $\mu\text{g}$  RAE ( $0.3 \times 0.5$ ). One IU of dietary  $\beta$ -carotene is equivalent to 0.165 IU retinol or 0.05  $\mu\text{g}$  RAE ( $0.3 \times 0.165$ ). One IU of other dietary provitamin A carotenoids is equivalent 0.025  $\mu\text{g}$  RAE.

### INTERPRETING PUBLISHED DATA ON VITAMIN A INTAKES OF VARIOUS POPULATION GROUPS

Existing data on vitamin A intakes of individuals and groups will need to be reinterpreted because of the changes in the retinol molar equivalency ratios for carotenoids to  $\mu\text{g}$  RAE. Two scenarios are possible: (1) the existing data provide values for both total vitamin A and carotenoid intake, and (2) the existing data provide values only for total vitamin A intake.

#### EXISTING DATA PROVIDE VALUES FOR BOTH TOTAL VITAMIN A AND CAROTENOID

The data manipulations required depend on the type of information that is sought (for example, mean intakes versus the proportion of a group with inadequate intakes). A way to approximate the mean intake of a group follows:

1a. Find the group mean intake for total vitamin A intake (e.g., for women aged 30 to 39 years in the Continuing Survey of Food Intakes by Individuals [CSFII, 1994–1996], mean intake was 895  $\mu\text{g}$  RE). Subtract the group mean intake of carotenoids (e.g., for women aged 30 to 39 years in the CSFII, mean carotene intake was 500  $\mu\text{g}$  RE). Thus, preformed vitamin A intake would be estimated as 395  $\mu\text{g}$  ( $895 - 500$ ).

1b. Divide the group mean intake of carotenoids by 2 (in this example,  $500 \div 2 = 250 \mu\text{g}$  RAE). This represents the corrected value for provitamin A intake.

1c. Add the corrected provitamin A intake determined in Step 1b to the preformed vitamin A intake determined in Step 1a. In this example, the mean vitamin A intake of women aged 30 to 39 years in the CSFII would be 645  $\mu\text{g}$  RAE ( $250 + 395$ ).

### EXISTING DATA PROVIDE VALUES FOR ONLY TOTAL VITAMIN A INTAKE

In this situation, there will be more uncertainty associated with estimates of both group mean intakes and the proportion of a group with inadequate intakes. This is because of the lack of information on the proportion of the total vitamin A intake that was derived from carotenoids. In this situation, a possible approach to approximating group mean intakes follows:

2a. Use other published data from a similar subject life stage and gender group that provide intakes of both total vitamin A and carotenoids to perform the calculations in Steps 1a through 1c above. For example, if the group of interest was 30- to 39-year-old women, data for this group from the CSFII could be used.

2b. Calculate the adjusted vitamin A intake for this group as a percentage of the unadjusted mean intake. For the example of 30- to 39-year-old women, the adjusted mean intake was 645 µg, and the unadjusted mean was 895 µg. Thus the adjusted vitamin A intake would be 0.72 ( $645 \div 895$ ), or 72 percent.

2c. Apply the adjustment factor to the mean intake of the group of interest. For example, if the group's mean intake had been reported as 1,100 µg RE, the adjusted intake would be 792 µg RAE ( $1,100 \times 0.72$ ).

### IMPLICATIONS ARISING FROM THE DEVELOPMENT OF RETINOL ACTIVITY EQUIVALENTS (RAE)

The vitamin A activity of provitamin A carotenoids found in darkly colored fruits and green leafy vegetables is half that previously assumed. Consequently, individuals who rely on plant foods for the majority of their vitamin A needs should ensure that they consume foods that are rich in carotenoids (specifically, deep yellow and green vegetables and fruits) on a regular basis.

Another implication of the reduced contribution from the provitamin A carotenoids is that vitamin A intakes of most population groups are lower than was previously believed. For example, in the CSFII survey, the reported mean proportion of vitamin A derived from carotenoids was 47 percent. Using the new conversion factors would thus reduce the population mean vitamin A intake by about 23 to 24 percent, or from 982 µg RE to 751 µg RAE.

## VITAMIN D

As cholecalciferol. 1 µg cholecalciferol = 40 IU vitamin D.

## VITAMIN E

The EARs, RDAs, and AIs for vitamin E are based on  $\alpha$ -tocopherol only and do not include amounts obtained from the other seven naturally occurring forms of vitamin E ( $\beta$ -,  $\gamma$ -,  $\delta$ -tocopherol and the four tocotrienols). Although absorbed, these forms do not contribute to meeting the vitamin E requirement because they are not converted to  $\alpha$ -tocopherol. Only the 2R-stereoisomeric forms of  $\alpha$ -tocopherol are preferentially secreted by the liver into the plasma for transport to tissues. Since the 2S-stereoisomeric forms of  $\alpha$ -tocopherol are not maintained in human plasma or tissues, vitamin E is defined in this publication as limited to the 2R-stereoisomeric forms of  $\alpha$ -tocopherol to establish recommended intakes. However, all eight stereoisomers of supplemental  $\alpha$ -tocopherol are used as the basis for establishing the Tolerable Upper Intake Level (UL) for vitamin E.

Newer nutrient databases provide values for  $\alpha$ -tocopherol. Older ones do not distinguish among all the different forms of vitamin E in food. These databases often present the data as  $\alpha$ -tocopherol equivalents ( $\alpha$ -TE) and thus include the contribution of all eight naturally occurring forms of vitamin E, after adjustment for bioavailability using previously determined equivalencies (e.g.,  $\alpha$ -tocopherol has been usually assumed to have only 10 percent of the availability of  $\alpha$ -tocopherol) based on fetal resorption assays. It is recommended that the use of  $\alpha$ -TE be abandoned due to the lack of evidence of bioavailability via transport in plasma or tissues. Because these other forms of vitamin E occur in foods (e.g.,  $\gamma$ -tocopherol is present in widely consumed oils such as soybean and corn oils), the intake of  $\alpha$ -TE is greater than the intake of  $\alpha$ -tocopherol alone.

All  $\alpha$ -tocopherol in foods is RRR- $\alpha$ -tocopherol, but the *all rac*- $\alpha$ -tocopherol in fortified foods and supplements is an equal mix of the 2R- and 2S-stereoisomers. The EARs, RDAs, and AIs given in the Vitamin E chapter apply only to the intake of the RRR- $\alpha$ -tocopherol from food and the 2R-stereoisomeric forms of  $\alpha$ -tocopherol (RRR-, RSR-, RRS-, and RSS- $\alpha$ -tocopherol) that occur in fortified foods and supplements. The UL applies to all eight stereoisomeric forms of  $\alpha$ -tocopherol that occur in fortified foods and supplements.

### CONVERSION FACTOR FOR VITAMIN E IN FOOD AND SUPPLEMENTS

To estimate the  $\alpha$ -tocopherol intake from food surveys in the United States in which food intake data are presented as  $\alpha$ -TE, the  $\alpha$ -TE should be multiplied by 0.8.

$$\begin{aligned} \text{mg of } \alpha\text{-tocopherol in a meal} &= \\ \text{mg of } \alpha\text{-tocopherol equivalents in a meal} \times 0.8. \end{aligned}$$

In addition, the amount of chemically synthesized *all rac*- $\alpha$ -tocopherol compounds added to foods and multivitamin supplements in milligrams should be estimated at 50 percent to calculate the intake of the 2R-stereoisomers of  $\alpha$ -tocopherol when assessing intakes to meet requirements.

If vitamin E in foods, fortified foods, and multivitamin supplements is reported in international units (IUs), the activity in milligrams of  $\alpha$ -tocopherol may be calculated by multiplying the number of IUs by 0.67 if the form of vitamin E is *RRR*- $\alpha$ -tocopherol (natural vitamin E) (historically and incorrectly labeled *d*- $\alpha$ -tocopherol), and by 0.45 if the form is *all rac*- $\alpha$ -tocopherol (synthetic vitamin E) (historically and incorrectly labeled *dl*- $\alpha$ -tocopherol compounds).

$$\begin{aligned} \text{mg of } \alpha\text{-tocopherol in food, fortified food, or multivitamin} \\ = \text{IU of the } RRR\text{-}\alpha\text{-tocopherol compound} \times 0.67 \\ \text{or} \\ = \text{IU of the } all\ rac\text{-}\alpha\text{-tocopherol compound} \times 0.45 \end{aligned}$$

For example, a person with intake from food of 15 mg/day of  $\alpha$ -TE would have consumed approximately 12 mg/day of  $\alpha$ -tocopherol ( $15 \times 0.8 = 12$ ). If this person took a daily multivitamin supplement with 30 IU of *RRR*- $\alpha$ -tocopheryl acetate, an additional 20 mg/day of  $\alpha$ -tocopherol would have been consumed ( $30 \times 0.67 = 20$ ). Thus, this person would have an effective total intake of 32 mg/day of  $\alpha$ -tocopherol (12 + 20). If the daily multivitamin supplement contained 30 IU of *all rac*- $\alpha$ -tocopherol, it would be equivalent to 13.5 mg/day of  $\alpha$ -tocopherol ( $30 \times 0.45 = 13.5$ ), and the person's total intake of  $\alpha$ -tocopherol would be 25.5 mg/day (12 + 13.5).

## FOLATE

### DIETARY FOLATE EQUIVALENTS AND FOLATE SOURCES

Currently, nutrition labels do not distinguish between sources of folate (food folate and folic acid) or express the folate content of food in dietary folate equivalents (DFEs), which take into account the different bioavailabilities of folate sources. DFEs and types of folate are related as follows:

$$\begin{aligned} 1 \mu\text{g of DFEs} \\ = 1.0 \mu\text{g of food folate} \\ = 0.6 \mu\text{g of folate added to foods (as a fortificant or folate supplement with food)} \\ = 0.5 \mu\text{g of folate taken as a supplement (without food)} \end{aligned}$$

1 µg of food folate	=	1.0 µg of DFEs
1 µg of folate added as a fortificant or as a supplement consumed with meals	=	1.7 µg of DFEs
1 µg of folate supplement taken without food	=	2.0 µg of DFEs

**Diet Assessment of Individuals.** When intakes of folate in the diet of an individual are assessed, it is possible to approximate the DFE intake by estimating the amount added in fortification and the amount present naturally as food folate by using the relationship 1 µg of folate added as a fortificant = 1.7 µg of DFEs (the reciprocal of 1 µg of DFEs = 0.6 µg folate added to food).

The following four-step method is proposed to approximate DFEs when estimating the dietary intake of an individual:

1. Group foods into (a) fortified cereal grain foods and specially fortified foods and (b) all others.

2. If other current data are not available for cereal grains, assume the following levels of fortification (read the label of the product to determine whether folate has been added in amounts greater than the required fortification level; this primarily refers to cereals):

- one slice of bread provides 20 µg of added folate;
- one serving (about 1 cup) of cooked pasta provides 60 µg of added folate; and
- one serving (about 1 cup) of cooked cereal or rice provides 60 µg of added folate.

Moderately fortified ready-to-eat cereals provide approximately 25 percent of the daily value per serving according to the product label, which is currently equivalent to 100 µg of added folate (25 percent of 400 µg). Highly fortified ready-to-eat cereals provide 100 percent of the daily value per serving, or 400 µg of added folate. Serving sizes of ready-to-eat cereals vary widely.

3. Combine the folate contributed by all the fortified cereal grains and multiply the result by 1.7 to obtain DFEs from folate added to foods.

4. Add DFEs from cereal grains to the folate content (in µg) from all other foods obtained from existing nutrient databases to obtain the total folate content in DFEs. For example, if the fortified cereal grains consumed were

- 8 slices of bread at 20 µg of added folate per slice (160 µg of total folate),
- 1 serving of moderately fortified ready-to-eat cereal (100 µg of folate), and
- 1 one-cup serving of pasta (60 µg of folate).

the total content would be 320 µg of added folate. The other foods in the diet—fruits, vegetables, meats, legumes, and milk products—provide 250 µg of food folate as determined by food composition data.

Therefore, total folate intake in DFEs =  $(1.7 \times 320) + 250 = 794$  µg of DFEs.

**Diet Assessment of Populations.** If dietary folate intake has been reported for groups without adjusting for DFEs and if members of the group have consumed foods fortified with folate, the amount of available folate will be higher than reported for those group members. Adjustments can be made only at the individual level, not at the group level.

## NIACIN

As niacin equivalents (NEs). 1 mg of niacin = 60 mg of tryptophan.

**G**

**IRON INTAKES AND  
ESTIMATED PERCENTILES  
OF THE DISTRIBUTION OF  
IRON REQUIREMENTS FROM  
THE CONTINUING SURVEY  
OF FOOD INTAKES BY  
INDIVIDUALS (CSFII),  
1994–1996**

**TABLE G-1 Iron Content of Foods Consumed by Infants 7 to 12 Months of Age, CSFII, 1994–1996**

Foods	Iron Content (mg/100 kcal)	Absorption (%)	Amount of Iron <sup>a</sup>	Estimate of Iron Absorbed (mg)	Weighted Mean Absorption (%) <sup>b</sup>
Human breast milk <sup>c</sup>	0.04	50	0.18	0.09	0.65
Meat and poultry	1.2	20	0.36	0.07	0.52
Fruits	0.4	5	0.27	0.13	0.10
Vegetables	1.2	5	0.56	0.03	0.20
Cereals <sup>d</sup>	8.75	6	12.1	0.73	5.24
Noodles	0.6	5	0.38	0.02	0.14
Total			13.85	1.07	6.85

<sup>a</sup> Based on a total daily energy intake of 845 kcal.<sup>b</sup> Calculation based on the proportion of iron in each of the six food groups.<sup>c</sup> Assumes an intake of 670 mL/day.<sup>d</sup> Refers to iron-fortified infant cereals containing 35 mg iron/100 g of dry cereal.

**TABLE G-2 Contribution of Iron from the 14 Food Groups for Children Aged 1 to 3 and 4 to 8 Years, CSFII, 1994–1996**

Food Group	Iron Content (mg/100 kcal) <sup>a</sup>	Amount of Iron (mg) 1–3 y <sup>b</sup>	Amount of Iron (mg) 4–8 y <sup>c</sup>
Meat	1.19	1.57	2.17
Fruits	0.36	0.23	0.25
Vegetables	1.22	1.14	1.87
Cereals	2.65	8.64	11.98
Vegetables plus meat	0.7	0.17	0.18
Grain plus meat	0.78	1.12	1.53
Cheese	0.15	0.04	0.05
Eggs	0.9	0.22	0.19
Ice cream, yogurt, etc.	0.13	0.06	0.01
Fats, candy	0.05	0.03	0.05
Milk	0.08	0.18	0.15
Formula	1.8	0.18	0.00
Juices	0.44	0.34	0.22
Other beverages	0.11	0.07	0.12
Total		14.27	18.77

<sup>a</sup> Source: Whitney EN, Rolfes SR. 1996. *Understanding Nutrition*, 7th ed. St. Paul: West Publishing; Pennington JAT. 1998. *Bowes and Church's Food Values of Portions Commonly Used*, 17th ed. Philadelphia: Lippincott

<sup>b</sup> The CSFII database provides total food energy (average of 2 days) and the proportion of energy from each of 14 food groups. The iron content of each food was determined from appropriate references (expressed as iron content per 100 kcal), thus the iron content of each food was calculated. The results are based on a total daily energy intake of 1,345 kcal ( $n = 1,868$ ) as reported in CSFII.

<sup>c</sup> Calculated as shown above. Based on a total daily energy intake of 1,665 kcal ( $n = 1,711$ ) as reported in CSFII. According to the Third National Health and Nutrition Examination Survey, the median intake of iron by infants is 15.5 mg/day; the iron mainly comes from fortified formulas and cereals, with smaller amounts from vegetables, pureed meats, and poultry. It is estimated that the absorption of iron from fortified cereals is in the range of 6 percent, from breast milk 50 percent, and from meat 20 percent.

**TABLE G-3 Estimated Percentiles of the Distribution of Iron Requirements (mg/d) in Young Children and Adolescent and Adult Males, CSFII, 1994–1996**

Estimated Percentile of Requirements	Young Children, Both Sexes <sup>a</sup>			Male Adolescents and Adults		
	0.5–1 y <sup>b</sup>	1–3 y <sup>c</sup>	4–8 y <sup>c</sup>	9–13 y <sup>c</sup>	14–18 y <sup>c</sup>	Adult <sup>c</sup>
2.5	3.01	1.01	1.33	3.91	5.06	3.98
5	3.63	1.24	1.64	4.23	5.42	4.29
10	4.35	1.54	2.05	4.59	5.85	4.64
20	5.23	1.96	2.63	5.03	6.43	5.09
30	5.87	2.32	3.13	5.36	6.89	5.44
40	6.39	2.66	3.62	5.64	7.29	5.74
50 <sup>d</sup>	6.90	3.01	4.11	5.89	7.69	6.03
60	7.41	3.39	4.65	6.15	8.08	6.32
70	7.93	3.82	5.27	6.43	8.51	6.65
80	8.57	4.39	6.08	6.76	9.03	7.04
90	9.44	5.26	7.31	7.21	9.74	7.69
95	10.15	6.06	8.45	7.58	10.32	8.06
97.5 <sup>e</sup>	10.78	6.81	9.52	7.91	10.83	8.49

<sup>a</sup> Based on pooled estimates of requirement components; presented Estimated Average Requirement (EAR) and Recommended Dietary Allowance (RDA) based on the higher estimates obtained for males.

<sup>b</sup> Based on 10 percent bioavailability.

<sup>c</sup> Based on 18 percent bioavailability.

<sup>d</sup> Fiftieth percentile = EAR.

<sup>e</sup> Ninety-seven and one-half percentile = RDA.

**TABLE G-4 Estimated Percentiles of the Distribution of Iron Requirements (mg/d) for Female Adolescents and Adults, CSFII, 1994–1996**

Estimated Percentile of Requirement	9–13 y	14–18 y	Oral Contraceptive User, <sup>a</sup> Adolescent
2.5	3.24	4.63	4.11
5	3.60	5.06	4.49
10	4.04	5.61	4.97
20	4.59	6.31	5.57
30	4.98	6.87	6.05
40	5.33	7.39	6.48
50 <sup>c</sup>	5.66	7.91	6.89
60	6.00	8.43	7.34
70	6.36	9.15	7.84
80	6.78	10.03	8.47
90	7.38	11.54	9.47
95	7.88	13.08	10.42
97.5 <sup>d</sup>	8.34	14.80	11.44

<sup>a</sup> Based on 60 percent reduction in menstrual blood loss.<sup>b</sup> Mixed population assumes 17 percent oral contraceptive users, 83 percent nonusers, all menstruating.<sup>c</sup> Fiftieth percentile = Estimated Average Requirement.<sup>d</sup> Ninety-seven and one-half percentile = Recommended Dietary Allowance.

Mixed Adolescent Population <sup>b</sup>	Menstruating Adult	Oral Contraceptive User, <sup>a</sup> Adult	Mixed Adult Population <sup>b</sup>	Post Menopause
4.49	4.42	3.63	4.18	2.73
4.92	4.88	4.00	4.63	3.04
5.45	5.45	4.45	5.19	3.43
6.14	6.22	5.06	5.94	3.93
6.69	6.87	5.52	6.55	4.30
7.21	7.46	5.94	7.13	4.64
7.71	8.07	6.35	7.73	4.97
8.25	8.76	6.79	8.39	5.30
8.92	9.63	7.27	9.21	5.68
9.77	10.82	7.91	10.36	6.14
11.21	13.05	8.91	12.49	6.80
12.74	15.49	9.90	14.85	7.36
14.39	18.23	10.94	17.51	7.88

**TABLE G-5 Probabilities of Inadequate Iron Intakes<sup>a</sup> and Associated Ranges of Usual Intake for Infants and Children 1 through 8 Years, CSFII, 1994–1996**

Probability of Inadequacy	Associated Range of Usual Intakes (mg/d)		
	Infants 8–12 mo	Children 1–3 y	Children 4–8 y
1.0 <sup>b</sup>	< 3.01	< 1.0	< 1.33
0.96	3.02–3.63	1.1–1.24	1.34–1.64
0.93	3.64–4.35	1.25–1.54	1.65–2.05
0.85	4.36–5.23	1.55–1.96	2.07–2.63
0.75	5.24–5.87	1.97–2.32	2.64–3.13
0.65	5.88–6.39	2.33–2.66	3.14–3.62
0.55	6.40–6.90	2.67–3.01	3.63–4.11
0.45	6.91–7.41	3.02–3.39	4.12–4.64
0.35	7.42–7.93	3.40–3.82	4.65–5.27
0.25	7.94–8.57	3.83–4.38	5.28–6.08
0.15	8.58–9.44	4.39–5.25	6.09–7.31
0.08	9.45–10.17	5.26–6.06	7.32–8.45
0.04	10.18–10.78	6.07–6.81	8.46–9.52
0 <sup>b</sup>	> 10.78	> 6.81	> 9.52

<sup>a</sup> Probability of inadequate intake = probability that requirement is greater than the usual intake. Derived from Table G-3.

<sup>b</sup> For population assessment purposes, a probability of 1 has been assigned to all usual intakes falling below the two and one-half percentile of requirement and a probability of 0 has been assigned to all usual intakes falling above the ninety-seven and one-half percentile of requirement. This enables the assessment of population risk where precise estimates are impractical and effectively without impact.

**TABLE G-6 FOLLOWS**

**TABLE G-6 Probabilities of Inadequate Iron Intakes<sup>a</sup> (mg/d) and Associated Ranges of Usual Intake in Adolescent Males and in Girls Using or Not Using Oral Contraceptives (OC), CSFII, 1994-1996**

Probability of Inadequacy	9-13 y	
	Male	Female
1.0 <sup>d</sup>	< 3.91	< 3.24
0.96	3.91-4.23	3.24-3.60
0.93	4.24-4.59	3.61-4.04
0.85	4.60-5.03	4.05-4.59
0.75	5.04-5.36	4.60-4.98
0.65	5.37-5.64	4.99-5.33
0.55	5.65-5.89	5.34-5.66
0.45	5.90-6.15	5.67-6.00
0.35	6.16-6.43	6.01-6.36
0.25	6.44-6.76	6.37-6.78
0.15	6.77-7.21	6.79-7.38
0.08	7.22-7.58	7.39-7.88
0.04	7.59-7.91	7.89-8.34
0 <sup>d</sup>	> 7.91	> 8.34

<sup>a</sup> Probability of inadequate intake = probability that requirement is greater than the usual intake. May be used in simple computer programs to evaluate adjusted distributions of usual intakes. See Institute of Medicine. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press, for method of adjusting observed intake distributions. Not to be applied in the assessment of individuals. Derived from Tables G-3 and G-4.

<sup>b</sup> Assumes 60 percent reduction in menstrual iron loss.

<sup>c</sup> Mixed population represents 17 percent oral contraceptive users and 83 percent nonoral contraceptive users.

<sup>d</sup> For population assessment purposes, a probability of 1 has been assigned to all usual intakes falling below the two and one-half percentile of requirement and a probability of 0 has been assigned to all usual intakes falling above the ninety-seven and one-half percentile of requirement. This enables the assessment of population risk where precise estimates are impractical and effectively without impact.

14–18 y

Male	Female		
	Non-OC Users	OC Users <sup>b</sup>	Mixed Population <sup>c</sup>
< 5.06	< 4.63	< 4.11	< 4.49
5.06–5.42	4.64–5.06	4.11–4.49	4.49–4.92
5.43–5.85	5.07–5.61	4.50–4.97	4.93–5.45
5.86–6.43	5.62–6.31	4.98–5.57	5.46–6.14
6.44–6.89	6.32–6.87	5.58–6.05	6.15–6.69
6.90–7.29	6.88–7.39	6.06–6.48	6.70–7.21
7.30–7.69	7.40–7.91	6.49–6.89	7.22–7.71
7.70–8.08	7.92–8.48	6.90–7.34	7.72–8.25
8.09–8.51	8.49–9.15	7.35–7.84	8.26–8.92
8.52–9.03	9.16–10.03	7.85–8.47	8.93–9.77
9.04–9.74	10.04–11.54	8.48–9.47	9.78–11.21
9.75–10.32	11.55–13.08	9.48–10.42	11.22–12.74
10.33–10.83	13.09–14.80	10.43–11.44	12.75–14.39
> 10.83	> 14.80	> 11.44	> 14.39

**TABLE G-7 Probabilities of Inadequate Iron Intakes<sup>a</sup> (mg/d) and Associated Ranges of Usual Intake in Adult Men and Women Using and Not Using Oral Contraceptives (OC) , CSFII, 1994–1996**

Probability of Inadequacy	Adult Men	Menstruating Women			
		Non-OC Users	OC Users <sup>b</sup>	Mixed Population <sup>c</sup>	Postmenopausal Women
1.0 <sup>d</sup>	< 3.98	< 4.42	< 3.63	< 4.18	< 2.73
0.96	3.98–4.29	4.42–4.88	3.63–4.00	4.18–4.63	2.73–3.04
0.93	4.30–4.64	4.89–5.45	4.01–4.45	4.64–5.19	3.05–3.43
0.85	4.65–5.09	5.46–6.22	4.46–5.06	5.20–5.94	3.44–3.93
0.75	5.10–5.44	6.23–6.87	5.07–5.52	5.95–6.55	3.94–4.30
0.65	5.45–5.74	6.88–7.46	5.53–5.94	6.56–7.13	4.31–4.64
0.55	5.75–6.03	7.47–8.07	5.95–6.35	7.14–7.73	4.65–4.97
0.45	6.04–6.32	8.08–8.76	6.36–6.79	7.74–8.39	4.98–5.30
0.35	6.33–6.65	8.77–9.63	6.80–7.27	8.40–9.21	5.31–5.68
0.25	6.66–7.04	9.64–10.82	7.28–7.91	9.22–10.36	5.69–6.14
0.15	7.05–7.69	10.83–13.05	7.92–8.91	10.37–12.49	6.15–6.80
0.08	7.70–8.06	13.06–15.49	8.92–9.90	12.50–14.85	6.81–7.36
0.04	8.07–8.49	15.50–18.23	9.91–10.94	14.86–17.51	7.37–7.88
0 <sup>d</sup>	> 8.49	> 18.23	> 10.94	> 17.51	> 7.88

<sup>a</sup> Probability of inadequate intake = probability that requirement is greater than the usual intake. May be used in simple computer programs to evaluate adjusted distributions of usual intakes. See Institute of Medicine. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press, for method of adjusting observed intake distributions. Not to be applied in the assessment of individuals. Derived from Tables G-3 and G-4.

<sup>b</sup> Assumes 60 percent reduction in menstrual iron loss.

<sup>c</sup> Mixed population represents 17 percent oral contraceptive users and 83 percent nonoral contraceptive users.

<sup>d</sup> For population assessment purposes, a probability of 1 has been assigned to all usual intakes falling below the two and one-half percentile of requirement and a probability of 0 has been assigned to all usual intakes falling above the ninety-seven and one-half percentile of requirement. This enables the assessment of population risk where precise estimates are impractical and effectively without impact.

# H

## STANDARD DEVIATION OF REQUIREMENTS FOR NUTRIENTS WITH AN EAR

Standard Deviation (SD) of requirements is calculated from the Coefficient of Variation (CV) and the Estimated Average Requirement (EAR) as:

$$SD = CV \times EAR$$

Nutrient with an EAR	CV (percent)	Basis if not 10 percent <sup>a</sup>
<b>MACRONUTRIENTS</b>		
Dietary Carbohydrate	15	Variation in brain glucose utilization
Protein	12	Skewed distribution; calculated as half distance from 16th to 84th percentile of protein requirement distribution <sup>b</sup>
<b>VITAMINS</b>		
Vitamin A	20	Half-life for liver vitamin A in adults
Vitamin B <sub>6</sub>	10	
Vitamin B <sub>12</sub>	10	
Vitamin C	10	
Vitamin E	10	
Folate	10	

Nutrient with an EAR	CV (percent)	Basis if not 10 percent <sup>a</sup>
Niacin	15	Limited studies suggest greater variation than 10 percent, partly from wide variation in conversion efficiency of tryptophan to niacin
Riboflavin	10	
Thiamin	10	
<b>MINERALS</b>		
Copper	15	Limited data to set EAR
Iodine	20	Calculation that subtracts out variation due to experimental design
Iron		Skewed distribution; calculated by modeling components of requirement distribution, estimating the requirement for absorbed iron at the 97.5 percentile, and with use of an upper limit of 18 percent iron absorption, and rounding
Magnesium	10	
Molybdenum	15	Limited data to set EAR (few Mo levels in depletion/repletion study and small number of subjects)
Phosphorus	10	
Selenium	10	
Zinc	10	

<sup>a</sup> The assumption of 10 percent is based on extensive data on the variation in basal metabolic rate and on a similar CV of 12 percent for protein requirements in adults.

<sup>b</sup> Rand and colleagues demonstrated that the natural logarithm of requirements in mg nitrogen/kg/day has a normal distribution with a mean of 4.65 and a standard deviation of 0.12. From this and because the skewness is not extreme, an approximate standard deviation can be calculated.

I

# **ESTIMATES OF WITHIN-SUBJECT VARIATION IN INTAKE**

**TABLE I-1 Estimates of Within-Subject Variation in Intake, Expressed as Standard Deviation (*SD*)<sup>a</sup> and Coefficient of Variation (CV) for Vitamins and Minerals in Adults Aged 19 and Over**

Nutrient <sup>b</sup>	Adults Ages 19–50 y				Adults, Ages 51 y and Over			
	Females ( <i>n</i> = 2,480) <sup>c</sup>		Males ( <i>n</i> = 2,538)		Females ( <i>n</i> = 2,162)		Males ( <i>n</i> = 2,280)	
	<i>SD</i>	CV (%)	<i>SD</i>	CV (%)	<i>SD</i>	CV (%)	<i>SD</i>	CV (%)
Vitamin A (μg)	1,300	152	1,160	115	1,255	129	1,619	133
Carotene (RE)	799	175	875	177	796	147	919	153
Vitamin E (mg)	5	76	7	176	6	65	9	60
Vitamin C (mg)	73	87	93	92	61	69	72	71
Thiamin (mg)	0.6	47	0.9	46	0.5	41	0.7	40
Riboflavin (mg)	0.6	50	1.0	44	0.6	42	0.8	40
Niacin (mg)	9	47	12	44	7	42	9	39
Vitamin B <sub>6</sub> (mg)	0.8	53	1.0	48	0.6	44	0.8	42
Folate (μg) <sup>d</sup>	131	62	180	61	12	52	150	53
Vitamin B <sub>12</sub> (μg)	12	294	13	212	10	237	14	226
Calcium (mg)	325	51	492	54	256	44	339	44
Phosphorus (mg)	395	39	573	38	313	33	408	32
Magnesium (mg)	86	38	122	38	74	33	94	32
Iron (mg)	7	53	9	51	5	44	7	44
Zinc (mg)	6	61	9	63	5	58	8	66
Copper (mg)	0.6	53	0.7	48	0.5	53	0.7	56
Sodium (mg)	1,839	44	1,819	43	1,016	41	1,323	38
Potassium (mg)	851	38	1,147	36	723	31	922	31

NOTE: When the CV is larger than 60 to 70 percent the distribution of daily intakes is nonnormal and the methods presented here are unreliable.

<sup>a</sup> Square root of the residual variance after accounting for subject, and sequence of observation (gender and age controlled by classifications).

<sup>b</sup> Nutrient intakes are for food only, data do not include intake from supplements.

<sup>c</sup> Sample size was inadequate to provide separate estimates for pregnant or lactating women.

<sup>d</sup> Folate reported in μg rather than as the new dietary folate equivalents (DFE).

SOURCE: Data from Continuing Survey of Food Intakes by Individuals 1994–1996.

**TABLE I-2 Estimates of Within-Subject Variation in Intake, Expressed as Standard Deviation (*SD*)<sup>a</sup> and Coefficient of Variation (CV) for Vitamins and Minerals in Adolescents and Children**

Nutrient <sup>b</sup>	Adolescents, Ages 9–18 y				Children, Ages 4–8 y			
	Females (n = 1,002)		Males (n = 998)		Females (n = 817)		Males (n = 883)	
	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Vitamin A (μg)	852	109	898	91	808	103	723	86
Carotene (RE)	549	180	681	197	452	167	454	166
Vitamin E (mg)	4	67	5	62	3	54	3	57
Vitamin C (mg)	81	90	93	89	61	69	74	76
Thiamin (mg)	0.6	43	0.8	42	0.5	35	0.5	37
Riboflavin (mg)	0.7	42	1.0	41	0.6	35	0.7	35
Niacin (mg)	8	46	11	43	6	36	7	38
Vitamin B <sub>6</sub> (μg)	0.7	49	1.0	49	0.6	42	0.7	43
Folate (μg) <sup>c</sup>	128	58	176	60	99	48	117	50
Vitamin B <sub>12</sub> (μg)	5.5	142	5.0	93	9.6	254	4.7	118
Calcium (mg)	374	48	505	48	313	40	353	41
Phosphorus (mg)	410	38	542	37	321	32	352	32
Magnesium (mg)	86	41	109	39	61	31	71	33
Iron (mg)	6	47	9	50	5	45	6	43
Zinc (mg)	5	50	8	58	3	41	4	42
Copper (mg)	0.5	52	0.6	48	0.4	47	0.4	41
Sodium (mg)	1,313	45	1,630	42	930	38	957	35
Potassium (mg)	866	41	1,130	41	631	32	750	35

NOTE: When the CV is larger than 60 to 70 percent the distribution of daily intakes is nonnormal and the methods presented here are unreliable.

<sup>a</sup> Square root of the residual variance after accounting for subject, and sequence of observation (gender and age controlled by classifications).

<sup>b</sup> Nutrient intakes are for food only, data do not include intake from supplements.

<sup>c</sup> Folate reported in μg rather than as the new dietary folate equivalents (DFE).

SOURCE: Data from Continuing Survey of Food Intakes by Individuals 1994–1996.

**TABLE I-3 Estimates of Within-Subject Variation in Intake, Expressed as Standard Deviation (*SD*)<sup>a</sup> and Coefficient of Variation (CV) for Macronutrients in Adults Aged 19 and Over**

Nutrient <sup>b</sup>	Adults, Ages 19–50 y				Adults, Ages 51 y and Over			
	Females ( <i>n</i> = 2,480) <sup>c</sup>		Males ( <i>n</i> = 2,583)		Females ( <i>n</i> = 2,162)		Males ( <i>n</i> = 2,280)	
	<i>SD</i>	CV (%)	<i>SD</i>	CV (%)	<i>SD</i>	CV (%)	<i>SD</i>	CV (%)
Energy (kcal)	576	34	854	34	448	31	590	29
Fat (total, g)	29.9	48	42.7	44	24.0	45	31.8	42
Fat (saturated, g)	10.9	52	15.9	49	8.6	50	11.4	45
Fat (mono-unsaturated, g)	12.0	50	17.4	46	9.7	48	13.0	44
Fat (poly-unsaturated, g)	8.4	64	11.3	59	7.0	61	8.8	57
Carbohydrate (g)	75.2	35	109	35	59.9	32	79.5	32
Protein (g)	26.6	42	40.4	41	22.1	37	28.6	35
Fiber (g)	6.5	49	9.2	51	5.9	43	7.7	43
Cholesterol (mg)	168	77	227	66	144	70	201	66

NOTE: When the CV is larger than 60 to 70 percent the distribution of daily intakes is nonnormal and the methods presented here are unreliable.

<sup>a</sup> Square root of the residual variance after accounting for subject, and sequence of observation (gender and age controlled by classifications).

<sup>b</sup> Nutrient intakes are for food only, data do not include intake from supplements.

<sup>c</sup> Sample size was inadequate to provide separate estimates for pregnant or lactating women.

SOURCE: Data from Continuing Survey of Food Intakes by Individuals 1994–1996.

**TABLE I-4 Estimates of Within-Subject Variation in Intake, Expressed as Standard Deviation (*SD*)<sup>a</sup> and Coefficient of Variation (CV) for Macronutrients in Adolescents and Children**

Nutrient <sup>b</sup>	Adolescents Ages 9–18 y				Children Ages 4–8 y			
	Females ( <i>n</i> = 1,002)		Males ( <i>n</i> = 998)		Females ( <i>n</i> = 817)		Males ( <i>n</i> = 833)	
	<i>SD</i>	CV (%)	<i>SD</i>	CV (%)	<i>SD</i>	CV (%)	<i>SD</i>	CV (%)
Energy (kcal)	628	34	800	33	427	27	478	27
Fat (total, g)	29.8	45	38.2	42	21.3	37	23.9	37
Fat (saturated, g)	11.3	48	15.3	48	8.5	40	9.6	40
Fat (mono-unsaturated, g)	12.4	48	15.5	44	8.6	39	9.9	41
Fat (poly-unsaturated, g)	7.3	60	8.7	55	5.1	52	5.5	52
Carbohydrate (g)	88.1	35	113	35	61.7	29	70.8	30
Protein (g)	26.2	42	33.9	39	19.2	34	20.4	33
Fiber (g)	6.2	51	8.7	56	4.6	43	5.3	45
Cholesterol (mg)	145	72	199	71	129	70	137	66

NOTE: When the CV is larger than 60 to 70 percent the distribution of daily intakes is nonnormal and the methods presented here are unreliable.

<sup>a</sup> Square root of the residual variance after accounting for subject, and sequence of observation (gender and age controlled by classifications).

<sup>b</sup> Nutrient intakes are for food only, data do not include intake from supplements.

SOURCE: Data from Continuing Survey of Food Intakes by Individuals 1994–1996.



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**Dietary Reference Intakes (DRIs): Estimated Average Requirements**  
 Food and Nutrition Board, Institute of Medicine, National Academies

Life Stage Group	CHO (g/d)	Protein (g/kg/d)	Vit A (µg/d) <sup>a</sup>	Vit C (mg/d)	Vit E (mg/d) <sup>b</sup>	Thiamin (mg/d)	Riboflavin (mg/d)	Niacin (mg/d)	Vit B <sub>6</sub> (mg/d) <sup>c</sup>
<b>Infants</b>									
7–12 mo			1.0						
<b>Children</b>									
1–3 y	100	0.87	210	13	5	0.4	0.4	5	0.4
4–8 y	100	0.76	275	22	6	0.5	0.5	6	0.5
<b>Males</b>									
9–13 y	100	0.76	445	39	9	0.7	0.8	9	0.8
14–18 y	100	0.73	630	63	12	1.0	1.1	12	1.1
19–30 y	100	0.66	625	75	12	1.0	1.1	12	1.1
31–50 y	100	0.66	625	75	12	1.0	1.1	12	1.1
51–70 y	100	0.66	625	75	12	1.0	1.1	12	1.4
> 70 y	100	0.66	625	75	12	1.0	1.1	12	1.4
<b>Females</b>									
9–13 y	100	0.76	420	39	9	0.7	0.8	9	0.8
14–18 y	100	0.71	485	56	12	0.9	0.9	11	1.0
19–30 y	100	0.66	500	60	12	0.9	0.9	11	1.1
31–50 y	100	0.66	500	60	12	0.9	0.9	11	1.1
51–70 y	100	0.66	500	60	12	0.9	0.9	11	1.3
> 70 y	100	0.66	500	60	12	0.9	0.9	11	1.3
<b>Pregnancy</b>									
14–18 y	135	0.88	530	66	12	1.2	1.2	14	1.6
19–30 y	135	0.88	550	70	12	1.2	1.2	14	1.6
31–50 y	135	0.88	550	70	12	1.2	1.2	14	1.6
<b>Lactation</b>									
14–18 y	160	1.05	885	96	16	1.2	1.3	13	1.7
19–30 y	160	1.05	900	100	16	1.2	1.3	13	1.7
31–50 y	160	1.05	900	100	16	1.2	1.3	13	1.7

NOTE: An Estimated Average Requirement (EAR) is the average daily nutrient intake level estimated to meet the requirements of half of the healthy individuals in a group. EARs have not been established for vitamin D, vitamin K, pantothenic acid, biotin, choline, calcium, chromium, fluoride, manganese, or other nutrients not yet evaluated via the DRI process.

<sup>a</sup> As retinol activity equivalents (RAEs). 1 RAE = 1 µg retinol, 12 µg β-carotene, 24 µg α-carotene, or 24 µg β-cryptoxanthin. The RAE for dietary provitamin A carotenoids is twofold greater than retinol equivalents (RE), whereas the RAE for preformed vitamin A is the same as RE.

<sup>b</sup> As α-tocopherol. α-Tocopherol includes *RRR*-α-tocopherol, the only form of α-tocopherol that occurs naturally in foods, and the *2R*-stereoisomeric forms of α-tocopherol (*RRR*, *RSR*, *RRS*, and *RSS*-α-tocopherol) that occur in fortified foods and supplements. It does not include the *2S*-stereoisomeric forms of α-tocopherol (*SRR*, *SSR*, *SRS*, and *SSS*-α-tocopherol), also found in fortified foods and supplements.

Folate ( $\mu\text{g}/\text{d}$ ) <sup>d</sup>	Vit B <sub>12</sub> ( $\mu\text{g}/\text{d}$ )	Copper ( $\mu\text{g}/\text{d}$ )	Iodine ( $\mu\text{g}/\text{d}$ )	Iron ( $\text{mg}/\text{d}$ )	Magnes- ium ( $\text{mg}/\text{d}$ )	Molyb- denum ( $\mu\text{g}/\text{d}$ )	Phos- phorus ( $\text{mg}/\text{d}$ )	Sele- nium ( $\mu\text{g}/\text{d}$ )	Zinc ( $\text{mg}/\text{d}$ )
				6.9					2.5
120	0.7	260	65	3.0	65	13	380	17	2.5
160	1.0	340	65	4.1	110	17	405	23	4.0
250	1.5	540	73	5.9	200	26	1,055	35	7.0
330	2.0	685	95	7.7	340	33	1,055	45	8.5
320	2.0	700	95	6	330	34	580	45	9.4
320	2.0	700	95	6	350	34	580	45	9.4
320	2.0	700	95	6	350	34	580	45	9.4
320	2.0	700	95	6	350	34	580	45	9.4
250	1.5	540	73	5.7	200	26	1,055	35	7.0
330	2.0	685	95	7.9	300	33	1,055	45	7.3
320	2.0	700	95	8.1	255	34	580	45	6.8
320	2.0	700	95	8.1	265	34	580	45	6.8
320	2.0	700	95	5	265	34	580	45	6.8
320	2.0	700	95	5	265	34	580	45	6.8
520	2.2	785	160	23	335	40	1,055	49	10.5
520	2.2	800	160	22	290	40	580	49	9.5
520	2.2	800	160	22	300	40	580	49	9.5
450	2.4	985	209	7	300	35	1,055	59	10.9
450	2.4	1,000	209	6.5	255	36	580	59	10.4
450	2.4	1,000	209	6.5	265	36	580	59	10.4

<sup>c</sup>As niacin equivalents (NE). 1 mg of niacin = 60 mg of tryptophan.

<sup>d</sup>As dietary folate equivalents (DFE). 1 DFE = 1  $\mu\text{g}$  food folate = 0.6  $\mu\text{g}$  of folic acid from fortified food or as a supplement consumed with food = 0.5  $\mu\text{g}$  of a supplement taken on an empty stomach.

SOURCES: *Dietary Reference Intakes for Calcium, Phosphorous, Magnesium, Vitamin D, and Fluoride* (1997); *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline* (1998); *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids* (2000); *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc* (2001), and *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* (2002/2005). These reports may be accessed via [www.nap.edu](http://www.nap.edu).

**Dietary Reference Intakes (DRIs): Recommended Dietary Allowances and Adequate Intakes, Vitamins**

Food and Nutrition Board, Institute of Medicine, National Academies

Life Stage Group	Vitamin A (µg/d) <sup>a</sup>	Vitamin C (mg/d)	Vitamin D (µg/d) <sup>b,c</sup>	Vitamin E (mg/d) <sup>d</sup>	Vitamin K (µg/d)	Thiamin (mg/d)
<b>Infants</b>						
0–6 mo	400*	40*	5*	4*	2.0*	0.2*
7–12 mo	500*	50*	5*	5*	2.5*	0.3*
<b>Children</b>						
1–3 y	<b>300</b>	<b>15</b>	5*	<b>6</b>	30*	<b>0.5</b>
4–8 y	<b>400</b>	<b>25</b>	5*	<b>7</b>	55*	<b>0.6</b>
<b>Males</b>						
9–13 y	<b>600</b>	<b>45</b>	5*	<b>11</b>	60*	<b>0.9</b>
14–18 y	<b>900</b>	<b>75</b>	5*	<b>15</b>	75*	<b>1.2</b>
19–30 y	<b>900</b>	<b>90</b>	5*	<b>15</b>	120*	<b>1.2</b>
31–50 y	<b>900</b>	<b>90</b>	5*	<b>15</b>	120*	<b>1.2</b>
51–70 y	<b>900</b>	<b>90</b>	10*	<b>15</b>	120*	<b>1.2</b>
> 70 y	<b>900</b>	<b>90</b>	15*	<b>15</b>	120*	<b>1.2</b>
<b>Females</b>						
9–13 y	<b>600</b>	<b>45</b>	5*	<b>11</b>	60*	<b>0.9</b>
14–18 y	<b>700</b>	<b>65</b>	5*	<b>15</b>	75*	<b>1.0</b>
19–30 y	<b>700</b>	<b>75</b>	5*	<b>15</b>	90*	<b>1.1</b>
31–50 y	<b>700</b>	<b>75</b>	5*	<b>15</b>	90*	<b>1.1</b>
51–70 y	<b>700</b>	<b>75</b>	10*	<b>15</b>	90*	<b>1.1</b>
> 70 y	<b>700</b>	<b>75</b>	15*	<b>15</b>	90*	<b>1.1</b>
<b>Pregnancy</b>						
14–18 y	<b>750</b>	<b>80</b>	5*	<b>15</b>	75*	<b>1.4</b>
19–30 y	<b>770</b>	<b>85</b>	5*	<b>15</b>	90*	<b>1.4</b>
31–50 y	<b>770</b>	<b>85</b>	5*	<b>15</b>	90*	<b>1.4</b>
<b>Lactation</b>						
14–18 y	<b>1,200</b>	<b>115</b>	5*	<b>19</b>	75*	<b>1.4</b>
19–30 y	<b>1,300</b>	<b>120</b>	5*	<b>19</b>	90*	<b>1.4</b>
31–50 y	<b>1,300</b>	<b>120</b>	5*	<b>19</b>	90*	<b>1.4</b>

**NOTE:** This table (taken from the DRI reports, see [www.nap.edu](http://www.nap.edu)) presents Recommended Dietary Allowances (RDA) in **bold type** or Adequate Intakes (AI) in ordinary type followed by an asterisk (\*). An RDA is the average daily dietary intake level sufficient to meet the nutrient requirements of nearly all (97-98 percent) healthy individuals in a group. It is calculated from an Estimated Average Requirement (EAR). If sufficient scientific evidence is not available to establish an EAR, and thus calculate an RDA, an AI is usually developed. For healthy breastfed infants, the AI is the mean intake. The AI for other life stage and gender groups is believed to cover the needs of all healthy individuals in the group, but lack of data or uncertainty in the data prevent being able to specify with confidence the percentage of individuals covered by this intake.

<sup>a</sup> As retinol activity equivalents (RAEs). 1 RAE = 1 µg retinol, 12 µg β-carotene, 24 µg α-carotene, or 24 µg β-cryptoxanthin. The RAE for dietary provitamin A carotenoids is two-fold greater than retinol equivalents (RE), whereas the RAE for preformed vitamin A is the same as RE.

<sup>b</sup> As cholecalciferol. 1 µg cholecalciferol = 40 IU vitamin D.

<sup>c</sup> In the absence of adequate exposure to sunlight.

<sup>d</sup> As α-tocopherol. α-Tocopherol includes *RRR*-α-tocopherol, the only form of α-tocopherol that occurs naturally in foods, and the *2R*-stereoisomeric forms of α-tocopherol (*RRR*, *RSR*, *RRS*, and *RSS*-α-tocopherol) that occur in fortified foods and supplements. It does not include the *2S*-stereoisomeric forms of α-tocopherol (*SRR*, *SSR*, *SRS*, and *SSS*-α-tocopherol), also found in fortified foods and supplements.

<sup>e</sup> As niacin equivalents (NE). 1 mg of niacin = 60 mg of tryptophan; 0–6 months = pre-formed niacin (not NE).

Riboflavin (mg/d)	Niacin (mg/d) <sup>e</sup>	Vitamin B <sub>6</sub> (mg/d)	Folate (µg/d) <sup>f</sup>	Vitamin B <sub>12</sub> (µg/d)	Pantothenic Acid (mg/d)	Biotin (µg/d)	Choline (mg/d) <sup>g</sup>
0.3*	2*	0.1*	65*	0.4*	1.7*	5*	125*
0.4*	4*	0.3*	80*	0.5*	1.8*	6*	150*
0.5	6	0.5	150	0.9	2*	8*	200*
0.6	8	0.6	200	1.2	3*	12*	250*
0.9	12	1.0	300	1.8	4*	20*	375*
1.3	16	1.3	400	2.4	5*	25*	550*
1.3	16	1.3	400	2.4	5*	30*	550*
1.3	16	1.3	400	2.4	5*	30*	550*
1.3	16	1.7	400	2.4 <sup>h</sup>	5*	30*	550*
1.3	16	1.7	400	2.4 <sup>h</sup>	5*	30*	550*
0.9	12	1.0	300	1.8	4*	20*	375*
1.0	14	1.2	400 <sup>i</sup>	2.4	5*	25*	400*
1.1	14	1.3	400 <sup>i</sup>	2.4	5*	30*	425*
1.1	14	1.3	400 <sup>i</sup>	2.4	5*	30*	425*
1.1	14	1.5	400	2.4 <sup>h</sup>	5*	30*	425*
1.1	14	1.5	400	2.4 <sup>h</sup>	5*	30*	425*
1.4	18	1.9	600 <sup>j</sup>	2.6	6*	30*	450*
1.4	18	1.9	600 <sup>j</sup>	2.6	6*	30*	450*
1.4	18	1.9	600 <sup>j</sup>	2.6	6*	30*	450*
1.6	17	2.0	500	2.8	7*	35*	550*
1.6	17	2.0	500	2.8	7*	35*	550*
1.6	17	2.0	500	2.8	7*	35*	550*

<sup>f</sup>As dietary folate equivalents (DFE). 1 DFE = 1 µg food folate = 0.6 µg of folic acid from fortified food or as a supplement consumed with food = 0.5 µg of a supplement taken on an empty stomach.

<sup>g</sup>Although AIs have been set for choline, there are few data to assess whether a dietary supply of choline is needed at all stages of the life cycle, and it may be that the choline requirement can be met by endogenous synthesis at some of these stages.

<sup>h</sup>Because 10 to 30 percent of older people may malabsorb food-bound B<sub>12</sub>, it is advisable for those older than 50 years to meet their RDA mainly by consuming foods fortified with B<sub>12</sub> or a supplement containing B<sub>12</sub>.

<sup>i</sup>In view of evidence linking folate intake with neural tube defects in the fetus, it is recommended that all women capable of becoming pregnant consume 400 µg from supplements or fortified foods in addition to intake of food folate from a varied diet.

<sup>j</sup>It is assumed that women will continue consuming 400 µg from supplements or fortified food until their pregnancy is confirmed and they enter prenatal care, which ordinarily occurs after the end of the periconceptional period—the critical time for formation of the neural tube.

SOURCES: *Dietary Reference Intakes for Calcium, Phosphorous, Magnesium, Vitamin D, and Fluoride* (1997); *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline* (1998); *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids* (2000); *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc* (2001); and *Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate* (2005). These reports may be accessed via <http://www.nap.edu>.

**Dietary Reference Intakes (DRIs): Recommended Dietary Allowances and Adequate Intakes, Elements**

Food and Nutrition Board, Institute of Medicine, National Academies

Life Stage Group	Calcium (mg/d)	Chromium (µg/d)	Copper (µg/d)	Fluoride (mg/d)	Iodine (µg/d)	Iron (mg/d)	Magnesium (mg/d)
<b>Infants</b>							
0–6 mo	210*	0.2*	200*	0.01*	110*	0.27*	30*
7–12 mo	270*	5.5*	220*	0.5*	130*	<b>11</b>	75*
<b>Children</b>							
1–3 y	500*	11*	<b>340</b>	0.7*	<b>90</b>	<b>7</b>	<b>80</b>
4–8 y	800*	15*	<b>440</b>	1*	<b>90</b>	<b>10</b>	<b>130</b>
<b>Males</b>							
9–13 y	1,300*	25*	<b>700</b>	2*	<b>120</b>	<b>8</b>	<b>240</b>
14–18 y	1,300*	35*	<b>890</b>	3*	<b>150</b>	<b>11</b>	<b>410</b>
19–30 y	1,000*	35*	<b>900</b>	4*	<b>150</b>	<b>8</b>	<b>400</b>
31–50 y	1,000*	35*	<b>900</b>	4*	<b>150</b>	<b>8</b>	<b>420</b>
51–70 y	1,200*	30*	<b>900</b>	4*	<b>150</b>	<b>8</b>	<b>420</b>
> 70 y	1,200*	30*	<b>900</b>	4*	<b>150</b>	<b>8</b>	<b>420</b>
<b>Females</b>							
9–13 y	1,300*	21*	<b>700</b>	2*	<b>120</b>	<b>8</b>	<b>240</b>
14–18 y	1,300*	24*	<b>890</b>	3*	<b>150</b>	<b>15</b>	<b>360</b>
19–30 y	1,000*	25*	<b>900</b>	3*	<b>150</b>	<b>18</b>	<b>310</b>
31–50 y	1,000*	25*	<b>900</b>	3*	<b>150</b>	<b>18</b>	<b>320</b>
51–70 y	1,200*	20*	<b>900</b>	3*	<b>150</b>	<b>8</b>	<b>320</b>
> 70 y	1,200*	20*	<b>900</b>	3*	<b>150</b>	<b>8</b>	<b>320</b>
<b>Pregnancy</b>							
14–18 y	1,300*	29*	<b>1,000</b>	3*	<b>220</b>	<b>27</b>	<b>400</b>
19–30 y	1,000*	30*	<b>1,000</b>	3*	<b>220</b>	<b>27</b>	<b>350</b>
31–50 y	1,000*	30*	<b>1,000</b>	3*	<b>220</b>	<b>27</b>	<b>360</b>
<b>Lactation</b>							
14–18 y	1,300*	44*	<b>1,300</b>	3*	<b>290</b>	<b>10</b>	<b>360</b>
19–30 y	1,000*	45*	<b>1,300</b>	3*	<b>290</b>	<b>9</b>	<b>310</b>
31–50 y	1,000*	45*	<b>1,300</b>	3*	<b>290</b>	<b>9</b>	<b>320</b>

**NOTE:** This table (taken from the DRI reports, see [www.nap.edu](http://www.nap.edu)) presents Recommended Dietary Allowances (RDA) in **bold type** or Adequate Intakes (AI) in ordinary type followed by an asterisk (\*). An RDA is the average daily dietary intake level sufficient to meet the nutrient requirements of nearly all (97–98 percent) healthy individuals in a group. It is calculated from an Estimated Average Requirement (EAR). If sufficient scientific evidence is not available to establish an EAR, and thus calculate an RDA, an AI is usually developed. For healthy breastfed infants, the AI is the mean intake. The AI for other life stage and gender groups is believed to cover the needs of all healthy individuals in the group, but lack of data or uncertainty in the data prevent being able to specify with confidence the percentage of individuals covered by this intake.

Manganese (mg/d)	Molybdenum (µg/d)	Phosphorus (mg/d)	Selenium (µg/d)	Zinc (mg/d)	Potassium (g/d)	Sodium (g/d)	Chloride (g/d)
0.003*	2*	100*	15*	2*	0.4*	0.12*	0.18*
0.6*	3*	275*	20*	3	0.7*	0.37*	0.57*
1.2*	<b>17</b>	<b>460</b>	<b>20</b>	<b>3</b>	3.0*	1.0*	1.5*
1.5*	<b>22</b>	<b>500</b>	<b>30</b>	<b>5</b>	3.8*	1.2*	1.9*
1.9*	<b>34</b>	<b>1,250</b>	<b>40</b>	<b>8</b>	4.5*	1.5*	2.3*
2.2*	<b>43</b>	<b>1,250</b>	<b>55</b>	<b>11</b>	4.7*	1.5*	2.3*
2.3*	<b>45</b>	<b>700</b>	<b>55</b>	<b>11</b>	4.7*	1.5*	2.3*
2.3*	<b>45</b>	<b>700</b>	<b>55</b>	<b>11</b>	4.7*	1.5*	2.3*
2.3*	<b>45</b>	<b>700</b>	<b>55</b>	<b>11</b>	4.7*	1.3*	2.0*
2.3*	<b>45</b>	<b>700</b>	<b>55</b>	<b>11</b>	4.7*	1.2*	1.8*
1.6*	<b>34</b>	<b>1,250</b>	<b>40</b>	<b>8</b>	4.5*	1.5*	2.3*
1.6*	<b>43</b>	<b>1,250</b>	<b>55</b>	<b>9</b>	4.7*	1.5*	2.3*
1.8*	<b>45</b>	<b>700</b>	<b>55</b>	<b>8</b>	4.7*	1.5*	2.3*
1.8*	<b>45</b>	<b>700</b>	<b>55</b>	<b>8</b>	4.7*	1.5*	2.3*
1.8*	<b>45</b>	<b>700</b>	<b>55</b>	<b>8</b>	4.7*	1.3*	2.0*
1.8*	<b>45</b>	<b>700</b>	<b>55</b>	<b>8</b>	4.7*	1.2*	1.8*
2.0*	<b>50</b>	<b>1,250</b>	<b>60</b>	<b>12</b>	4.7*	1.5*	2.3*
2.0*	<b>50</b>	<b>700</b>	<b>60</b>	<b>11</b>	4.7*	1.5*	2.3*
2.0*	<b>50</b>	<b>700</b>	<b>60</b>	<b>11</b>	4.7*	1.5*	2.3*
2.6*	<b>50</b>	<b>1,250</b>	<b>70</b>	<b>13</b>	5.1*	1.5*	2.3*
2.6*	<b>50</b>	<b>700</b>	<b>70</b>	<b>12</b>	5.1*	1.5*	2.3*
2.6*	<b>50</b>	<b>700</b>	<b>70</b>	<b>12</b>	5.1*	1.5*	2.3*

SOURCES: *Dietary Reference Intakes for Calcium, Phosphorous, Magnesium, Vitamin D, and Fluoride* (1997); *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline* (1998); *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids* (2000); *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc* (2001); and *Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate* (2005). These reports may be accessed via <http://www.nap.edu>.

**Dietary Reference Intakes (DRIs): Recommended Dietary Allowances and Adequate Intakes, Total Water and Macronutrients**  
 Food and Nutrition Board, Institute of Medicine, National Academies

Life Stage Group	Total Water <sup>a</sup> (L/d)	Carbo-hydrate (g/d)	Total Fiber (g/d)	Fat (g/d)	Linoleic Acid (g/d)	α-Linolenic Acid (g/d)	Protein <sup>b</sup> (g/d)
<b>Infants</b>							
0–6 mo	0.7*	60*	ND	31*	4.4*	0.5*	9.1*
7–12 mo	0.8*	95*	ND	30*	4.6*	0.5*	<b>11.0+</b>
<b>Children</b>							
1–3 y	1.3*	<b>130</b>	19*	ND <sup>c</sup>	7*	0.7*	<b>13</b>
4–8 y	1.7*	<b>130</b>	25*	ND	10*	0.9*	<b>19</b>
<b>Males</b>							
9–13 y	2.4*	<b>130</b>	31*	ND	12*	1.2*	<b>34</b>
14–18 y	3.3*	<b>130</b>	38*	ND	16*	1.6*	<b>52</b>
19–30 y	3.7*	<b>130</b>	38*	ND	17*	1.6*	<b>56</b>
31–50 y	3.7*	<b>130</b>	38*	ND	17*	1.6*	<b>56</b>
51–70 y	3.7*	<b>130</b>	30*	ND	14*	1.6*	<b>56</b>
> 70 y	3.7*	<b>130</b>	30*	ND	14*	1.6*	<b>56</b>
<b>Females</b>							
9–13 y	2.1*	<b>130</b>	26*	ND	10*	1.0*	<b>34</b>
14–18 y	2.3*	<b>130</b>	26*	ND	11*	1.1*	<b>46</b>
19–30 y	2.7*	<b>130</b>	25*	ND	12*	1.1*	<b>46</b>
31–50 y	2.7*	<b>130</b>	25*	ND	12*	1.1*	<b>46</b>
51–70 y	2.7*	<b>130</b>	21*	ND	11*	1.1*	<b>46</b>
> 70 y	2.7*	<b>130</b>	21*	ND	11*	1.1*	<b>46</b>
<b>Pregnancy</b>							
14–18 y	3.0*	<b>175</b>	28*	ND	13*	1.4*	<b>71</b>
19–30 y	3.0*	<b>175</b>	28*	ND	13*	1.4*	<b>71</b>
31–50 y	3.0*	<b>175</b>	28*	ND	13*	1.4*	<b>71</b>
<b>Lactation</b>							
14–18 y	3.8*	<b>210</b>	29*	ND	13*	1.3*	<b>71</b>
19–30 y	3.8*	<b>210</b>	29*	ND	13*	1.3*	<b>71</b>
31–50 y	3.8*	<b>210</b>	29*	ND	13*	1.3*	<b>71</b>

**NOTE:** This table (taken from the DRI reports, see [www.nap.edu](http://www.nap.edu)) presents Recommended Dietary Allowances (RDA) in **bold type** or Adequate Intakes (AI) in ordinary type followed by an asterisk (\*). An RDA is the average daily dietary intake level sufficient to meet the nutrient requirements of nearly all (97-98 percent) healthy individuals in a group. It is calculated from an Estimated Average Requirement (EAR). If sufficient scientific evidence is not available to establish an EAR, and thus calculate an RDA, an AI is usually developed. For healthy breastfed infants, the AI is the mean intake. The AI for other life stage and gender groups is believed to cover the needs of all healthy individuals in the group, but lack of data or uncertainty in the data prevent being able to specify with confidence the percentage of individuals covered by this intake.

<sup>a</sup> Total water includes all water contained in food, beverages, and drinking water.

<sup>b</sup> Based on g protein per kg of body weight for the reference body weight, e.g., for adults 0.8 g/kg body weight for the reference body weight.

<sup>c</sup> Not determined.

SOURCES: *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* (2002/2005); *Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate* (2005). These reports may be accessed via <http://www.nap.edu>.

**Dietary Reference Intakes (DRIs): Acceptable Macronutrient Distribution Ranges**  
 Food and Nutrition Board, Institute of Medicine, National Academies

Macronutrient	Range (percent of energy)		
	Children, 1–3 y	Children, 4–18 y	Adults
Fat	30–40	25–35	20–35
<i>n</i> -6 Polyunsaturated fatty acids <sup>a</sup> (linoleic acid)	5–10	5–10	5–10
<i>n</i> -3 Polyunsaturated fatty acids <sup>a</sup> ( $\alpha$ -linolenic acid)	0.6–1.2	0.6–1.2	0.6–1.2
Carbohydrate	45–65	45–65	45–65
Protein	5–20	10–30	10–35

<sup>a</sup> Approximately 10 percent of the total can come from longer-chain *n*-3 or *n*-6 fatty acids.

SOURCE: *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* (2002/2005).

**Dietary Reference Intakes (DRIs): Additional Macronutrient Recommendations**  
 Food and Nutrition Board, Institute of Medicine, National Academies

Macronutrient	Recommendation
Dietary cholesterol	As low as possible while consuming a nutritionally adequate diet
Trans fatty acids	As low as possible while consuming a nutritionally adequate diet
Saturated fatty acids	As low as possible while consuming a nutritionally adequate diet
Added sugars <sup>a</sup>	Limit to no more than 25% of total energy

<sup>a</sup> Not a recommended intake. A daily intake of added sugars that individuals should aim for to achieve a healthful diet was not set.

SOURCE: *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* (2002/2005).

**Dietary Reference Intakes (DRIs): Tolerable Upper Intake Levels, Vitamins**  
 Food and Nutrition Board, Institute of Medicine, National Academies

Life Stage Group		Vitamin A (µg/d) <sup>a</sup>	Vitamin C (mg/d)	Vitamin D (µg/d)	Vitamin E (mg/d) <sup>b,c</sup>	Vitamin K	Thiamin
<b>Infants</b>							
0–6 mo	600	ND <sup>e</sup>	25	ND	ND	ND	ND
7–12 mo	600	ND	25	ND	ND	ND	ND
<b>Children</b>							
1–3 y	600	400	50	200	ND	ND	ND
4–8 y	900	650	50	300	ND	ND	ND
<b>Males, Females</b>							
9–13 y	1,700	1,200	50	600	ND	ND	ND
14–18 y	2,800	1,800	50	800	ND	ND	ND
19–70 y	3,000	2,000	50	1,000	ND	ND	ND
> 70 y	3,000	2,000	50	1,000	ND	ND	ND
<b>Pregnancy</b>							
14–18 y	2,800	1,800	50	800	ND	ND	ND
19–50 y	3,000	2,000	50	1,000	ND	ND	ND
<b>Lactation</b>							
14–18 y	2,800	1,800	50	800	ND	ND	ND
19–50 y	3,000	2,000	50	1,000	ND	ND	ND

**NOTE:** A Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse health effects to almost all individuals in the general population. Unless otherwise specified, the UL represents total intake from food, water, and supplements. Due to lack of suitable data, ULs could not be established for vitamin K, thiamin, riboflavin, vitamin B<sub>12</sub>, pantothenic acid, biotin, and carotenoids. In the absence of a UL, extra caution may be warranted in consuming levels above recommended intakes. Members of the general population should be advised not to routinely exceed the UL. The UL is not meant to apply to individuals who are treated with the nutrient under medical supervision or to individuals with predisposing conditions that modify their sensitivity to the nutrient.

<sup>a</sup>As preformed vitamin A only.

<sup>b</sup>As α-tocopherol; applies to any form of supplemental α-tocopherol.

<sup>c</sup>The ULs for vitamin E, niacin, and folate apply to synthetic forms obtained from supplements, fortified foods, or a combination of the two.

Riboflavin	Niacin (mg/d) <sup>c</sup>	Vitamin B <sub>6</sub> (mg/d)	Folate (μg/d) <sup>c</sup>	Vitamin B <sub>12</sub>	Pantothenic Acid	Biotin	Choline (g/d)	Carotenoids <sup>d</sup>
ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	10	30	300	ND	ND	ND	1.0	ND
ND	15	40	400	ND	ND	ND	1.0	ND
ND	20	60	600	ND	ND	ND	2.0	ND
ND	30	80	800	ND	ND	ND	3.0	ND
ND	35	100	1,000	ND	ND	ND	3.5	ND
ND	35	100	1,000	ND	ND	ND	3.5	ND
ND	30	80	800	ND	ND	ND	3.0	ND
ND	35	100	1,000	ND	ND	ND	3.5	ND
ND	30	80	800	ND	ND	ND	3.0	ND
ND	35	100	1,000	ND	ND	ND	3.5	ND

<sup>d</sup> β-Carotene supplements are advised only to serve as a provitamin A source for individuals at risk of vitamin A deficiency.

<sup>e</sup> ND = Not determinable due to lack of data of adverse effects in this age group and concern with regard to lack of ability to handle excess amounts. Source of intake should be from food only to prevent high levels of intake.

SOURCES: *Dietary Reference Intakes for Calcium, Phosphorous, Magnesium, Vitamin D, and Fluoride* (1997); *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline* (1998); *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids* (2000); and *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc* (2001). These reports may be accessed via <http://www.nap.edu>.

**Dietary Reference Intakes (DRIs): Tolerable Upper Intake Levels, Elements**  
 Food and Nutrition Board, Institute of Medicine, National Academies

Life Stage Group	Arsenic <sup>a</sup>	Boron (mg/d)	Calci- um (g/d)	Chro- mium (µg/d)	Copper (µg/d)	Fluo- ride (mg/d)	Iodine (µg/d)	Iron (mg/d)	Magne- sium (mg/d) <sup>b</sup>
<b>Infants</b>									
0–6 mo	ND <sup>c</sup>	ND	ND	ND	ND	0.7	ND	40	ND
7–12 mo	ND	ND	ND	ND	ND	0.9	ND	40	ND
<b>Children</b>									
1–3 y	ND	3	2.5	ND	1,000	1.3	200	40	65
4–8 y	ND	6	2.5	ND	3,000	2.2	300	40	110
<b>Males, Females</b>									
9–13 y	ND	11	2.5	ND	5,000	10	600	40	350
14–18 y	ND	17	2.5	ND	8,000	10	900	45	350
19–70 y	ND	20	2.5	ND	10,000	10	1,100	45	350
> 70 y	ND	20	2.5	ND	10,000	10	1,100	45	350
<b>Pregnancy</b>									
14–18 y	ND	17	2.5	ND	8,000	10	900	45	350
19–50 y	ND	20	2.5	ND	10,000	10	1,100	45	350
<b>Lactation</b>									
14–18 y	ND	17	2.5	ND	8,000	10	900	45	350
19–50 y	ND	20	2.5	ND	10,000	10	1,100	45	350

**NOTE:** A Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse health effects to almost all individuals in the general population. Unless otherwise specified, the UL represents total intake from food, water, and supplements. Due to lack of suitable data, ULs could not be established for vitamin K, thiamin, riboflavin, vitamin B<sub>12</sub>, pantothenic acid, biotin, and carotenoids. In the absence of a UL, extra caution may be warranted in consuming levels above recommended intakes. Members of the general population should be advised not to routinely exceed the UL. The UL is not meant to apply to individuals who are treated with the nutrient under medical supervision or to individuals with predisposing conditions that modify their sensitivity to the nutrient.

<sup>a</sup> Although the UL was not determined for arsenic, there is no justification for adding arsenic to food or supplements.

<sup>b</sup> The ULs for magnesium represent intake from a pharmacological agent only and do not include intake from food and water.

<sup>c</sup> Although silicon has not been shown to cause adverse effects in humans, there is no justification for adding silicon to supplements.

Manganese (mg/d)	Molybdenum (µg/d)	Nickel (mg/d)	Phosphorus (g/d)	Potassium (µg/d)	Selenium (µg/d)	Silicon <sup>c</sup> concentration (mg/d)	Sulfate (mg/d)	Vanadium (mg/d) <sup>d</sup>	Zinc (mg/d)	Sodium (g/d)	Chloride (g/d)
ND	ND	ND	ND	ND	45	ND	ND	ND	4	ND	ND
ND	ND	ND	ND	ND	60	ND	ND	ND	5	ND	ND
2	300	0.2	3.0	ND	90	ND	ND	ND	7	1.5	2.3
3	600	0.3	3.0	ND	150	ND	ND	ND	12	1.9	2.9
6	1,100	0.6	4.0	ND	280	ND	ND	ND	23	2.2	3.4
9	1,700	1.0	4.0	ND	400	ND	ND	ND	34	2.3	3.6
11	2,000	1.0	4.0	ND	400	ND	ND	1.8	40	2.3	3.6
11	2,000	1.0	3.0	ND	400	ND	ND	1.8	40	2.3	3.6
9	1,700	1.0	3.5	ND	400	ND	ND	ND	34	2.3	3.6
11	2,000	1.0	3.5	ND	400	ND	ND	ND	40	2.3	3.6
9	1,700	1.0	4.0	ND	400	ND	ND	ND	34	2.3	3.6
11	2,000	1.0	4.0	ND	400	ND	ND	ND	40	2.3	3.6

<sup>d</sup> Although vanadium in food has not been shown to cause adverse effects in humans, there is no justification for adding vanadium to food and vanadium supplements should be used with caution. The UL is based on adverse effects in laboratory animals and these data could be used to set a UL for adults but not children and adolescents.

<sup>e</sup> ND = Not determinable due to lack of data of adverse effects in this age group and concern with regard to lack of ability to handle excess amounts. Source of intake should be from food only to prevent high levels of intake.

SOURCES: *Dietary Reference Intakes for Calcium, Phosphorous, Magnesium, Vitamin D, and Fluoride* (1997); *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline* (1998); *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids* (2000); *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc* (2001); and *Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate* (2005). These reports may be accessed via <http://www.nap.edu>.



## REFERENCES

Full references, which also appear in the parent report series, the *Dietary Reference Intakes*, are not printed in this book but are provided online at <http://www.nap.edu/catalog/11537.html>.



# References

## INTRODUCTION TO THE DIETARY REFERENCE INTAKES

*Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*  
(ISBN 0-309-08537-3), Chapter 1, pp. 36–37.

- AAP (American Academy of Pediatrics). 1997. Breastfeeding and the use of human milk. *Pediatrics* 100:1035–1039.
- Atkinson SA, Alston-Mills BP, Lonnerdal B, Neville MC, Thompson M. 1995. Major minerals and ionic constituents of human and bovine milk. In: Jensen RJ, ed. *Handbook of Milk Composition*. San Diego, CA: Academic Press. Pp. 593–619.
- Butte NF, Garza C, Smith EO, Nichols BL. 1984. Human milk intake and growth in exclusively breast-fed infants. *J Pediatr* 104:187–195.
- Chandra RK. 1984. Physical growth of exclusively breast-fed infants. *Nutr Res* 2:275–276.
- COMA (Committee on Medical Aspects of Food Policy). 1991. *Dietary Reference Values for Food Energy and Nutrients in the United Kingdom*. Report on Health and Social Subjects, No. 41. London: HMSO.
- FAO/WHO/UNA (Food and Agriculture Organization of the United Nations/World Health Organization/United Nations Association). 1985. *Energy and Protein Requirements. Report of a Joint FAO/WHO/UNA Expert Consultation*. Technical Report Series. No. 724. Geneva: WHO.
- Garby L, Lammert O. 1984. Within-subjects between-days-and-weeks variation in energy expenditure at rest. *Hum Nutr Clin Nutr* 38:395–397.
- Health Canada. 1990. *Nutrition Recommendations. The Report of the Scientific Review Committee 1990*. Ottawa: Canadian Government Publishing Centre.
- Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. 1993. Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: The DARLING Study. *Am J Clin Nutr* 58:152–161.

- Herman-Giddens ME, Slora EJ, Wasserman RC, Bourdony CJ, Bhapkar MV, Koch GG, Hasemeier CM. 1997. Secondary sexual characteristics and menses in young girls seen in office practice: A study from the Pediatric Research in Office Settings Network. *Pediatrics* 99:505–512.
- Hofvander Y, Hagman U, Hillervik C, Sjolin S. 1982. The amount of milk consumed by 1–3 months old breast- or bottle-fed infants. *Acta Paediatr Scand* 71:953–958.
- IOM (Institute of Medicine). 1991. *Nutrition During Lactation*. Washington, DC: National Academy Press.
- IOM. 1997. *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. Washington, DC: National Academy Press.
- IOM. 1998. *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline*. Washington, DC: National Academy Press.
- IOM. 2000a. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- IOM. 2000b. *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*. Washington, DC: National Academy Press.
- IOM. 2001. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Washington, DC: National Academy Press.
- Kuczmarski RJ, Ogden CL, Grummer-Strawn LM, Flegal KM, Guo SS, Wei R, Mei Z, Curtin LR, Roche AF, Johnson CL. 2000. CDC growth charts: United States. *Adv Data* 314:1–28.
- Neville MC, Keller R, Seacat J, Lutes V, Neifert M, Casey C, Allen J, Archer P. 1988. Studies in human lactation: Milk volumes in lactating women during the onset of lactation and full lactation. *Am J Clin Nutr* 48:1375–1386.
- NRC (National Research Council). 1989. *Recommended Dietary Allowances*, 10th ed. Washington, DC: National Academy Press.
- Specker BL, Beck A, Kalkwarf H, Ho M. 1997. Randomized trial of varying mineral intake on total body bone mineral accretion during the first year of life. *Pediatrics* 99:E12.
- Tanner JM. 1990. *Growth at Adolescence*. Oxford: Oxford University Press.
- WHO (World Health Organization). 1996. *Trace Elements in Human Nutrition and Health*. Geneva: WHO.

Ibid., Chapter 4, pp. 105–106.

- Dourson ML, Stara JF. 1983. Regulatory history and experimental support of uncertainty (safety) factors. *Regul Toxicol Pharmacol* 3:224–238.
- FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization). 1982. *Evaluation of Certain Food Additives and Contaminants*. Twenty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series No. 683. Geneva: WHO.
- FAO/WHO. 1995. *The Application of Risk Analysis to Food Standard Issues*. Recommendations to the Codex Alimentarius Commission (ALINORM 95/9, Appendix 5). Geneva: WHO.
- Health Canada. 1993. *Health Risk Determination—The Challenge of Health Protection*. Ottawa: Health Canada, Health Protection Branch.

- Hill AB. 1971. *Principles of Medical Statistics*, 9th ed. New York: Oxford University Press.
- Klaassen CD, Amdur MO, Doull J. 1986. *Casarett and Doull's Toxicology: The Basic Science of Poisons*, 3rd ed. New York: Macmillan.
- Mertz W, Abernathy CO, Olin SS. 1994. *Risk Assessment of Essential Elements*. Washington, DC: ILSI Press.
- NRC (National Research Council). 1983. *Risk Assessment in the Federal Government: Managing the Process*. Washington, DC: National Academy Press.
- NRC. 1994. *Science and Judgment in Risk Assessment*. Washington, DC: National Academy Press.
- OTA (Office of Technology Assessment). 1993. *Researching Health Risks*. Washington, DC: OTA.
- WHO (World Health Organization). 1987. *Principles for the Safety Assessment of Food Additives and Contaminants in Food*. Environmental Health Criteria 70. Geneva: WHO.
- WHO. 1996. *Trace Elements in Human Nutrition and Health*. Geneva: WHO.
- Zielhuis RL, van der Kreek FW. 1979. The use of a safety factor in setting health-based permissible levels for occupational exposure. *Int Arch Occup Environ Health* 42:191–201.

*Dietary Reference Intakes: Applications in Dietary Assessment* (ISBN 0-309-07183-6), Chapter 10, pp. 168–177.

- Aickin M, Ritenbaugh C. 1991. Estimation of the true distribution of vitamin A intake by the unmixing algorithm. *Communications Stat Simulations* 20:255–280.
- Aksnes L, Aarskog D. 1982. Plasma concentrations of vitamin D metabolites in puberty: Effect of sexual maturation and implications for growth. *J Clin Endocrinol Metab* 55:94–101.
- Aloia JF, Vaswani A, Yeh JK, Ross PL, Flaster E, Dilmanian FA. 1994. Calcium supplementation with and without hormone replacement therapy to prevent postmenopausal bone loss. *Ann Intern Med* 120:97–103.
- AR (Army Regulation) 40-25. 1985. See U.S. Departments of the Army, the Navy, and the Air Force, 1985.
- Baran D, Sorensen A, Grimes J, Lew R, Karella A, Johnson B, Roche J. 1990. Dietary modification with dairy products for preventing vertebral bone loss in premenopausal women: A three-year prospective study. *J Clin Endocrinol Metab* 70:264–270.
- Barr SI, Janelle KC, Prior JC. 1995. Energy intakes are higher during the luteal phase of ovulatory menstrual cycles. *Am J Clin Nutr* 61:39–43.
- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Beaton GH. 1991. Interpretation of results from dietary studies. In: Kohlmeier L, ed. *The Diet History Method: Proceedings of the 2nd Berlin Meeting on Nutritional Epidemiology*. London: Smith-Gordon/Nishimura. Pp. 15–38.
- Beaton GH. 1994. Criteria of an adequate diet. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*, 8th edition. Philadelphia: Lea & Febiger. Pp. 1491–1505.

- Beaton GH. 1999. Recommended dietary intakes: Individuals and populations. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th edition. Baltimore: Williams & Wilkins. Pp. 1705–1725.
- Beaton GH, Chery A. 1988. Protein requirements of infants: A reexamination of concepts and approaches. *Am J Clin Nutr* 48:1403–1412.
- Beaton GH, Milner J, Corey P, McGuire V, Cousins M, Stewart E, deRamos M, Hewitt D, Grambsch PV, Kassim N, Little JA. 1979. Sources of variance in 24-hour dietary recall data: Implications for nutrition study design and interpretation. *Am J Clin Nutr* 32:2546–2559.
- Beaton GH, Milner J, McGuire V, Feather TE, Little JA. 1983. Source of variance in 24-hour dietary recall data: Implications for nutrition study design and interpretation. Carbohydrate sources, vitamins, and minerals. *Am J Clin Nutr* 37:986–995.
- Black AE, Prentice AM, Goldberg GR, Jebb SA, Bingham SA, Livingstone MB, Coward WA. 1993. Measurements of total energy expenditure provide insights into the validity of dietary measurements of energy intake. *J Am Diet Assoc* 93:572–579.
- Block G, Hartman AM, Dresser CM, Carroll MD, Gannon J, Gardner L. 1986. A data-based approach to diet questionnaire design and testing. *Am J Epidemiol* 124:453–469.
- Bolland JE, Ward JY, Bolland TW. 1990. Improved accuracy of estimating food quantities up to 4 weeks after training. *J Am Diet Assoc* 90:1402–1404, 1407.
- Bull NL, Buss DH. 1982. Biotin, pantothenic acid and vitamin E in the British household food supply. *Hum Nutr Appl Nutr* 36:190–196.
- Burk MC, Pao EM. 1976. Methodology for large-scale surveys of household and individual diets. *Home Econ Res Rep* No. 40. Washington, DC: Agricultural Research Service/U.S. Department of Agriculture.
- Burke BS. 1947. The dietary history as a tool in research. *J Am Diet Assoc* 23:1041–1046.
- Buzzard IM, Price KS, Warren RA. 1991. Considerations for selecting nutrient-calculation software: Evaluation of the nutrient database. *Am J Clin Nutr* 54:7–9.
- Cameron ME, Van Staveren W. 1988. *Manual on Methodology for Food Consumption Studies*. New York, NY: Oxford University Press.
- Canadian Council on Nutrition. 1938. *Canadian Dietary Standards*. Ottawa: Department of Pensions and National Health.
- Carriquiry AL. 1999. Assessing the prevalence of nutrient inadequacy. *Public Health Nutr* 2:23–33.
- Carriquiry AL, Dodd KW, Nusser SM. 1997. Estimating Adjusted Intake and Biochemical Measurement Distributions for NHANES III. Final report prepared for the National Center for Health Statistics.
- Chan GM, Hoffman K, McMurry M. 1995. Effects of dairy products on bone and body composition in pubertal girls. *J Pediatr* 126:551–556.
- Chen C. 1999. Spline Estimators of the Distribution Function of a Variable Measured with Error. Unpublished PhD dissertation. Department of Statistics, Iowa State University, Ames.
- Chevalley T, Rizzoli R, Nydegger V, Slosman D, Rapin CH, Michel JP, Vasey H, Bonjour JP. 1994. Effects of calcium supplements on femoral bone mineral density and vertebral fracture rate in vitamin-D-replete elderly patients. *Osteoporos Int* 4:245–252.

- COMA (Committee on Medical Aspects of Food Policy). 1991. *Dietary Reference Values for Food Energy and Nutrients for the United Kingdom. Report on Health and Social Subjects*, No. 41. London: Her Majesty's Stationery Office.
- Crane NT, Green NR. 1980. Food habits and food preferences of Vietnamese refugees living in northern Florida. *J Am Diet Assoc* 76:591–593.
- Dabeka RW, McKenzie AD, Conacher HBS, Kirkpatrick DC. 1982. Determination of fluoride in Canadian infant foods and calculation of fluoride intakes by infants. *Can J Public Health* 73:188–191.
- Dabeka RW, McKenzie AD, Lecroix GM. 1987. Dietary intakes of lead, cadmium, arsenic and fluoride by Canadian adults: A 24-hour duplicate diet study. *Food Addit Contam* 4:89–101.
- Dawson-Hughes B, Dallal GE, Krall EA, Sadowski L, Sahyoun N, Tannenbaum S. 1990. A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women. *N Engl J Med* 323:878–883.
- Dawson-Hughes B, Dallal GE, Krall EA, Harris S, Sokoll LJ, Falconer G. 1991. Effect of vitamin D supplementation on wintertime and overall bone loss in healthy postmenopausal women. *Ann Intern Med* 115:505–512.
- Dawson-Hughes B, Harris SS, Krall EA, Dallal GE, Falconer G, Green CL. 1995. Rates of bone loss in postmenopausal women randomly assigned to one of two dosages of vitamin D. *Am J Clin Nutr* 61:1140–1145.
- Demirjian A. 1980. *Anthropometry Report. Height, Weight, and Body Dimensions: A Report from Nutrition Canada*. Ottawa: Minister of National Health and Welfare, Health and Promotion Directorate, Health Services and Promotion Branch.
- Dewey KG, Beaton GH, Fjeld C, Lonnerdal B, Reeds P. 1996. Protein requirements of infants and children. *Eur J Clin Nutr* 50:S119–S150.
- Dodd KW. 1996. *A Technical Guide to C-SIDE: Software for Intake Distribution Estimation Version 1.0*. Technical Report 96-TR 32. Ames, IA: Center for Agricultural and Rural Development, Iowa State University.
- Domel SB. 1997. Self-reports of diet: How children remember what they have eaten. *Am J Clin Nutr* 65:1148S–1152S.
- Dwyer J. 1999. Dietary assessment. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th edition. Baltimore: Williams & Wilkins. Pp. 937–959.
- Dwyer JT, Coleman KA. 1997. Insights into dietary recall from a longitudinal study: Accuracy over four decades. *Am J Clin Nutr* 65:1153S–1158S.
- Eckert RS, Carroll RJ, Wang N. 1997. Transformations to additivity in measurement error models. *Biometrics* 53:262–272.
- Eissenstat BR, Wyse BW, Hansen RG. 1986. Pantothenic acid status of adolescents. *Am J Clin Nutr* 44:931–937.
- Elders PJ, Netelenbos JC, Lips P, van Ginkel FC, Kho E, Leeuwenkamp OR, Hackeng WH, van der Stelt PF. 1991. Calcium supplementation reduces vertebral bone loss in perimenopausal women: A controlled trial in 248 women between 46 and 55 years of age. *J Clin Endocrinol Metab* 73:533–540.
- Elders PJ, Lips P, Netelenbos JC, van Ginkel FC, Kho E, van der Vijgh WJ, van der Stelt PF. 1994. Long-term effect of calcium supplementation on bone loss in perimenopausal women. *J Bone Miner Res* 9:963–970.
- FAO (Food and Agriculture Organization). 1998. *FAO Food Balance Sheets 1994–1996 Average*. Rome: FAO.

- FAO/WHO (Food and Agriculture Organization/World Health Organization). 1970. *Requirements of Ascorbic Acid, Vitamin D, Vitamin B<sub>12</sub>, Folate, and Iron*. Report of a Joint FAO/WHO Expert Group. WHO Technical Report Series No. 452. FAO Nutrition Meetings Report Series No. 47. Geneva: WHO.
- FAO/WHO (Food and Agriculture Organization/World Health Organization). 1988. *Requirements of Vitamin A, Iron, Folate, and Vitamin B<sub>12</sub>*. Report of a Joint FAO/WHO Expert Consultation. FAO Food and Nutrition Series No. 23. Rome: FAO.
- FAO/WHO/UNU (Food and Agriculture Organization/World Health Organization/United Nations University). 1985. *Energy and Protein Requirements*. Report of a Joint FAO/WHO/UNU Expert Consultation. Technical Report Series No. 724. Geneva: WHO.
- Fuller WA. 1987. *Measurement Error Models*. Wiley Series in Probability and Mathematical Statistics. New York: Wiley.
- Gibson RS. 1990. *Principles of Nutritional Assessment*. New York: Oxford University Press.
- Gibson RS, Gibson IL, Kitching J. 1985. A study of inter- and intrasubject variability in seven-day weighed dietary intakes with particular emphasis on trace elements. *Biol Trace Elem Res* 8:79–91.
- Gloth FM III, Gundberg CM, Hollis BW, Haddad JG Jr, Tobin JD. 1995. Vitamin D deficiency in homebound elderly persons. *J Am Med Assoc* 274:1683–1686.
- Gordon AR, Devaney BL, Burghardt JA. 1995. Dietary effects of the National School Lunch Program and the School Breakfast Program. *Am J Clin Nutr* 61:221S–231S.
- Greenfield H, Southgate DAT. 1992. *Food Composition Data; Production, Management and Use*. London: Elsevier Applied Science.
- Greer FR, Searcy JE, Levin RS, Steichen JJ, Steichen-Asche PS, Tsang RC. 1982. Bone mineral content and serum 25-hydroxyvitamin D concentrations in breast-fed infants with and without supplemental vitamin D: One-year follow-up. *J Pediatr* 100:919–922.
- Greger JL, Baligar P, Abernathy RP, Bennett OA, Peterson T. 1978. Calcium, magnesium, phosphorus, copper, and manganese balance in adolescent females. *Am J Clin Nutr* 31:117–121.
- Guenther PM, Kott PS, Carriquiry AL. 1997. Development of an approach for estimating usual nutrient intake distributions at the population level. *J Nutr* 127:1106–1112.
- Gultekin A, Ozalp I, Hasanoglu A, Unal A. 1987. Serum-25-hydroxycholecalciferol levels in children and adolescents. *Turk J Pediatr* 29:155–162.
- Guthrie HA. 1984. Selection and quantification of typical food portions by young adults. *J Am Diet Assoc* 84:1440–1444.
- Hallberg L, Hogdahl AM, Nilsson L, Rybo G. 1966. Menstrual blood loss—A population study. Variation at different ages and attempts to define normality. *Acta Obstet Gynecol Scand* 45:320–351.
- Hankin JH, Wilkens LR. 1994. Development and validation of dietary assessment methods for culturally diverse populations. *Am J Clin Nutr* 59:198S–200S.
- Haraldsdottir J, Tjønneland A, Overvad K. 1994. Validity of individual portion size estimates in a food frequency questionnaire. *Int J Epidemiol* 23:787–796.
- Hartman AM, Block G, Chan W, Williams J, McAdams M, Banks WL Jr, Robbins A. 1996. Reproducibility of a self-administered diet history questionnaire administered three times over three different seasons. *Nutr Cancer* 25:305–315.

- Hasling C, Charles P, Jensen FT, Mosekilde L. 1990. Calcium metabolism in postmenopausal osteoporosis: The influence of dietary calcium and net absorbed calcium. *J Bone Miner Res* 5:939–946.
- Health and Welfare Canada. 1990. *Nutrition Recommendations*. The Report of the Scientific Review Committee. Ottawa: Canadian Government Publishing Centre.
- Heaney RP, Recker RR. 1982. Effects of nitrogen, phosphorus, and caffeine on calcium balance in women. *J Lab Clin Med* 99:46–55.
- Heaney RP, Recker RR, Saville PD. 1977. Calcium balance and calcium requirements in middle-aged women. *Am J Clin Nutr* 30:1603–1611.
- Heaney RP, Recker RR, Saville PD. 1978. Menopausal changes in calcium balance performance. *J Lab Clin Med* 92:953–963.
- Hebert JR, Ma Y, Clemow L, Ockene IS, Saperia G, Stanek EJ, Merriam PA, Ockene JK. 1997. Gender differences in social desirability and social approval bias in dietary self-report. *Am J Epidemiol* 146:1046–1055.
- Hirano M, Honma K, Daimatsu T, Hayakawa K, Oizumi J, Zaima K, Kanke Y. 1992. Longitudinal variations of biotin content in human milk. *Int J Vitam Nutr Res* 62:281–282.
- Immink MDC, Sanjur D, Burgos M. 1983. Nutritional consequences of U.S. migration patterns among Puerto Rican women. *Ecol Food Nutr* 13:139–147.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Food and Nutrition Board. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1997. *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1998a. *Dietary Reference Intakes: A Risk Assessment Model for Establishing Upper Intake Levels for Nutrients*. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1998b. *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline*. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 2000. *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*. Washington, DC: National Academy Press.
- Jackman LA, Millane SS, Martin BR, Wood OB, McCabe GP, Peacock M, Weaver CM. 1997. Calcium retention in relation to calcium intake and postmenarcheal age in adolescent females. *Am J Clin Nutr* 66:327–333.
- James WPT, Schofield EC. 1990. *Human Energy Requirements: A Manual for Planners and Nutritionists*. Oxford: Oxford University Press.
- Joachim G. 1997. The influence of time on dietary data: Differences in reported summer and winter food consumption. *Nutr Health* 12:33–43.
- Johnson RK, Soultanakis RP, Matthews DE. 1998. Literacy and body fatness are associated with underreporting of energy intake in U.S. low-income women using the multiple-pass 24-hour recall: A doubly labeled water study. *J Am Diet Assoc* 98:1136–1140.
- Johnston CC, Miller JZ, Slemenda CW, Reister TK, Hui S, Christian JC, Peacock M. 1992. Calcium supplementation and increases in bone mineral density in children. *N Engl J Med* 327:82–87.
- Juni RP. 1996. How should nutrient databases be evaluated? *J Am Diet Assoc* 96:120, 122.
- Kathman JV, Kies C. 1984. Pantothenic acid status of free living adolescent and young adults. *Nutr Res* 4:245–250.

- Kinyamu HK, Gallagher JC, Balhorn KE, Petranick KM, Rafferty KA. 1997. Serum vitamin D metabolites and calcium absorption in normal young and elderly free-living women and in women living in nursing homes. *Am J Clin Nutr* 65:790–797.
- Kohlmeier L, Bellach B. 1995. Exposure assessment error and its handling in nutritional epidemiology. *Annu Rev Public Health* 16:43–59.
- Kohlmeier L, Simonsen N, Mottus K. 1995. Dietary modifiers of carcinogenesis. *Environ Health Perspect* 103:177–184.
- Kohlmeier L, Mendez M, McDuffie J, Miller M. 1997. Computer-assisted self-interviewing: A multimedia approach to dietary assessment. *Am J Clin Nutr* 65:1275S–1281S.
- Krall EA, Sahyoun N, Tannenbaum S, Dallal GE, Dawson-Hughes B. 1989. Effect of vitamin D intake on seasonal variations in parathyroid hormone secretion in postmenopausal women. *N Engl J Med* 321:1777–1783.
- Kramer L, Osis D, Wiatrowski E, Spenser H. 1974. Dietary fluoride in different areas in the United States. *Am J Clin Nutr* 27:590–594.
- Kristal AR, Abrams BF, Thornquist MD, Disogra L, Croyle RT, Shattuck AL, Henry HJ. 1990. Development and validation of a food use checklist for evaluation of community nutrition interventions. *Am J Public Health* 80:1318–1322.
- Kristal AR, Feng Z, Coates RJ, Oberman A, George V. 1997. Associations of race/ethnicity, education, and dietary intervention with the validity and reliability of a food frequency questionnaire: The Women's Health Trial Feasibility Study in Minority Populations. *Am J Epidemiol* 146:856–869.
- Kuhnlein HV. 1992. Change in the use of traditional foods by the Nuxalk native people of British Columbia. *Ecol Food Nutr* 27:259–282.
- Kuhnlein HV, Soueida R. 1992. Use and nutrient composition of traditional Baffin Inuit foods. *J Food Comp Anal* 5:112–126.
- Kuhnlein HV, Soueida R, Receveur O. 1996. Dietary nutrient profiles of Canadian Baffin Island Inuit differ by food source, season, and age. *J Am Diet Assoc* 96:155–162.
- Leung SSF, Lui S, Swaminathan R. 1989. Vitamin D status of Hong Kong Chinese infants. *Acta Paediatr Scand* 78:303–306.
- Lichtman SW, Pisarska K, Berman ER, Pestone M, Dowling H, Offenbacher E, Weisel H, Heshka S, Matthews DE, Heymsfield SB. 1992. Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. *N Engl J Med* 327:1893–1898.
- Liu K. 1988. Consideration of and compensation for intra-individual variability in nutrient intakes. In: Kohlmeier L, Helsing E, eds. *Epidemiology Nutrition and Health: Proceedings of the First Berlin Meeting on Nutritional Epidemiology*. London: Smith-Gordon/Nishimura. Pp. 87–106.
- Liu K, Stamler J, Dyer A, McKeever J, McKeever P. 1978. Statistical methods to assess and minimize the role of intra-individual variability in obscuring the relationship between dietary lipids and serum cholesterol. *J Chronic Dis* 31:399–418.
- Lloyd T, Andon MB, Rollings N, Martel JK, Landis R, Demers LM, Eggle DF, Kieselhorst K, Kulin HE. 1993. Calcium supplementation and bone mineral density in adolescent girls. *J Am Med Assoc* 270:841–844.
- Looker AC, Sempos CT, Liu K, Johnson CL, Gunter EW. 1990. Within-person variance in biochemical indicators of iron status: Effects on prevalence estimates. *Am J Clin Nutr* 52:541–547.

- LSRO (Life Sciences Research Office). 1986. *Guidelines for Use of Dietary Intake Data*. Bethesda, MD: LSRO/FASEB.
- Markestad T, Elzouki AY. 1991. Vitamin D-deficiency rickets in northern Europe and Libya. In: Glorieux FH, ed. *Rickets: Nestle Nutrition Workshop Series*, Vol 21. New York, NY: Raven Press.
- Marshall DH, Nordin BEC, Speed R. 1976. Calcium, phosphorus and magnesium requirement. *Proc Nutr Soc* 35:163–173.
- Martin AD, Bailey DA, McKay HA. 1997. Bone mineral and calcium accretion during puberty. *Am J Clin Nutr* 66:611–615.
- Matkovic V. 1991. Calcium metabolism and calcium requirements during skeletal modeling and consolidation of bone mass. *Am J Clin Nutr* 54:245S–260S.
- Matkovic V, Heaney RP. 1992. Calcium balance during human growth: Evidence for threshold behavior. *Am J Clin Nutr* 55:992–996.
- Matkovic V, Fontana D, Tominac C, Goel P, Chesnut CH III. 1990. Factors that influence peak bone mass formation: A study of calcium balance and the inheritance of bone mass in adolescent females. *Am J Clin Nutr* 52:878–888.
- McClure FJ. 1943. Ingestion of fluoride and dental caries. Quantitative relations based on food and water requirements of children one to twelve years old. *Am J Dis Child* 66:362–369.
- McDowell MA. 1994. The NHANES III Supplemental Nutrition Survey of older Americans. *Am J Clin Nutr* 59:224S–226S.
- Mertz W, Kelsay JL. 1984. Rationale and design of the Beltsville one-year dietary intake study. *Am J Clin Nutr* 40:1323–1326.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- Nieman DC, Butterworth DE, Nieman CN, Lee KE, Lee RD. 1992. Comparison of six microcomputer dietary analysis systems with the USDA Nutrient Data Base for Standard Reference. *J Am Diet Assoc* 92:48–56.
- NRC (National Research Council). 1941. *Recommended Dietary Allowances: Protein, Calcium, Iron, Vitamin A, Vitamin B (Thiamin), Vitamin C (Ascorbic Acid), Riboflavin, Nicotinic Acid, Vitamin D*. Washington, DC: National Research Council.
- NRC (National Research Council). 1968. *Recommended Dietary Allowances*, 7th Ed. Washington, DC: National Academy of Sciences.
- NRC (National Research Council). 1980. *Recommended Dietary Allowances*, 9th Ed. Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC (National Research Council). 1989. *Recommended Dietary Allowances*, 10th Ed. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- O'Dowd KJ, Clemens TL, Kelsey JL, Lindsay R. 1993. Exogenous calciferol (vitamin D) and vitamin D endocrine status among elderly nursing home residents in the New York City area. *J Am Geriatr Soc* 41:414–421.
- Ohlson MA, Brewer WD, Jackson L, Swanson PP, Roberts PH, Mangel M, Leverton RM, Chaloupka M, Gram MR, Reynolds MS, Lutz R. 1952. Intakes and retentions of nitrogen, calcium and phosphorus by 136 women between 30 and 85 years of age. *Fed Proc* 11:775–783.

- Oliveira V, Gunderson C. 2000. *WIC and the Nutrient Intake of Children*. Food Assistance and Nutrition Research Report No. 5. Beltsville, MD: U.S. Department of Agriculture, Economic Research Service, Food and Rural Economics Division.
- Ophaug RH, Singer L, Harland BF. 1980a. Estimated fluoride intake of 6-month-old infants in four dietary regions of the United States. *Am J Clin Nutr* 33:324–327.
- Ophaug RH, Singer L, Harland BF. 1980b. Estimated fluoride intake of average two-year-old children in four dietary regions of the United States. *J Dent Res* 59:777–781.
- Ophaug RH, Singer L, Harland BF. 1985. Dietary fluoride intake of 6-month and 2-year-old children in four dietary regions of the United States. *Am J Clin Nutr* 42:701–707.
- Orwoll ES, Oviatt SK, McClung MR, Deftos LJ, Sexton G. 1990. The rate of bone mineral loss in normal men and the effects of calcium and cholecalciferol supplementation. *Ann Intern Med* 112:29–34.
- Osis D, Kramer L, Wiatrowski E, Spencer H. 1974. Dietary fluoride intake in man. *J Nutr* 104:1313–1318.
- Prince R, Smith M, Dick IM, Price RI, Webb PG, Henderson NK, Harris MM. 1991. Prevention of postmenopausal osteoporosis. A comparative study of exercise, calcium supplementation, and hormone-replacement therapy. *N Engl J Med* 325:1189–1195.
- Prince R, Devine A, Dick I, Criddle A, Kerr D, Kent N, Price R, Randell A. 1995. The effects of calcium supplementation (milk powder or tablets) and exercise on bone density in postmenopausal women. *J Bone Miner Res* 10:1068–1075.
- Rand WM, Pennington JAT, Murphy SP, Klensin JC. 1991. *Compiling Data for Food Composition Data Bases*. Tokyo: United Nations University Press.
- Receveur O, Boulay M, Kuhnlein HV. 1997. Decreasing traditional food use affects diet quality for adult Dene/Metis in 16 communities of the Canadian Northwest Territories. *J Nutr* 127:2179–2186.
- Recker RR, Hinders S, Davies KM, Heaney RP, Stegman MR, Lappe JM, Kimmel DB. 1996. Correcting calcium nutritional deficiency prevents spine fractures in elderly women. *J Bone Miner Res* 11:1961–1966.
- Reid IR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. 1995. Long-term effects of calcium supplementation on bone loss and fractures in postmenopausal women: A randomized controlled trial. *Am J Med* 98:331–335.
- Riis B, Thomsen K, Christiansen C. 1987. Does calcium supplementation prevent postmenopausal bone loss? *N Engl J Med* 316:173–177.
- Rose D, Habicht JP, Devaney B. 1998. Household participation in the Food Stamp and WIC programs increases the nutrient intakes of preschool children. *J Nutr* 128:548–555.
- Salmenpera L, Perheentupa J, Pispa JP, Siimes MA. 1985. Biotin concentrations in maternal plasma and milk during prolonged lactation. *Int J Vitam Nutr Res* 55:281–285.
- Selby PL. 1994. Calcium requirement—A reappraisal of the methods used in its determination and their application to patients with osteoporosis. *Am J Clin Nutr* 60:944–948.
- Sempers CT, Johnson NE, Smith EL, Gilligan C. 1985. Effects of intraindividual and interindividual variation in repeated dietary records. *Am J Epidemiol* 121:120–130.

- Sims LS. 1996. Uses of the Recommended Dietary Allowances: A commentary. *J Am Diet Assoc* 96:659–662.
- Singer L, Ophaug R. 1979. Total fluoride intakes of infants. *Pediatrics* 63:460–466.
- Singer L, Ophaug RH, Harland BF. 1980. Fluoride intakes of young male adults in the United States. *Am J Clin Nutr* 33:328–332.
- Singer L, Ophaug RH, Harland BF. 1985. Dietary fluoride intake of 15–19-year-old male adults residing in the United States. *J Dent Res* 64:1302–1305.
- Smith AF, Jobe JB, Mingay DJ. 1991a. Retrieval from memory of dietary information. *Appl Cognitive Psychol* 5:269–296.
- Smith CJ, Schakel SF, Nelson RG. 1991b. Selected traditional and contemporary foods currently used by the Pima Indians. *J Am Diet Assoc* 91:338–341.
- Snedecor GW, Cochran WG. 1980. *Statistical Methods*, 7th edition. Ames, Iowa: Iowa State University Press.
- Specker BL, Ho ML, Oestreich A, Yin TA, Shui QM, Chen XC, Tsang RC. 1992. Prospective study of vitamin D supplementation and rickets in China. *J Pediatr* 120:733–739.
- Spencer H, Kramer L, Lesniak M, DeBartolo M, Norris C, Osis D. 1984. Calcium requirements in humans. Report of original data and a review. *Clin Orthop Relat Res* 184:270–280.
- Spencer H, Osis D, Lender M. 1981. Studies of fluoride metabolism in man. A review and report of original data. *Sci Total Environ* 17:1–12.
- Srinivasan V, Christensen N, Wyse BW, Hansen RG. 1981. Pantothenic acid nutritional status in the elderly—Institutionalized and noninstitutionalized. *Am J Clin Nutr* 34:1736–1742.
- Stefanski LA, Bay JM. 1996. Simulation extrapolation deconvolution of finite population cumulative distribution function estimators. *Biometrika* 83:407–417.
- Subar AF, Frey CM, Harlan LC, Kahle L. 1994. Differences in reported food frequency by season of questionnaire administration: The 1987 National Health Interview Survey. *Epidemiology* 5:226–233.
- Tarasuk V, Beaton GH. 1991a. Menstrual-cycle patterns in energy and macronutrient intake. *Am J Clin Nutr* 53:442–447.
- Tarasuk V, Beaton GH. 1991b. The nature and individuality of within-subject variation in energy intake. *Am J Clin Nutr* 54:464–470.
- Tarasuk V, Beaton GH. 1992. Statistical estimation of dietary parameters: Implications of patterns in within-subject variation—A case study of sampling strategies. *Am J Clin Nutr* 55:22–27.
- Tarr JB, Tamura T, Stokstad EL. 1981. Availability of vitamin B<sub>6</sub> and pantothenate in an average American diet in man. *Am J Clin Nutr* 34:1328–1337.
- Taves DR. 1983. Dietary intake of fluoride ashed (total fluoride) v. unashed (inorganic fluoride) analysis of individual foods. *Br J Nutr* 49:295–301.
- Teufel NI. 1997. Development of culturally competent food-frequency questionnaires. *Am J Clin Nutr* 65:1173S–1178S.
- Thompson CH, Head MK, Rodman SM. 1987. Factors influencing accuracy in estimating plate waste. *J Am Diet Assoc* 87:1219–1220.
- Thompson FE, Byers T. 1994. Dietary assessment resource manual. *J Nutr* 124:2245S–2317S.
- Tsubono Y, Kobayashi M, Takahashi T, Iwase Y, Itoi Y, Akabane M, Tsugane S. 1997. Within- and between-person variations in portion sizes of foods consumed by the Japanese population. *Nutr Cancer* 29:140–145.
- USDA (U.S. Department of Agriculture, Human Nutrition Information Service). 1992. The Food Guide Pyramid. Home and Garden Bulletin No. 252, 32 pp.

- USDA (U.S. Department of Agriculture, Agricultural Research Service). 1999. USDA Nutrient Database for Standard Reference, Release 13. Nutrient Data Laboratory Home Page. Available from: <<http://www.nal.usda.gov/fnic/foodcomp>>.
- U.S. Departments of the Army, the Navy, and the Air Force. 1985. Army Regulation 40-25/Navy Command Medical Instruction 10110.1/Air Force Regulation 160-95. *Nutritional Allowances, Standards, and Education*. May 15. Washington, D.C.
- Van Staveren WA, Hautvast JG, Katan MB, Van Montfort MA, Van Oosten-Van der Goes HG. 1982. Dietary fiber consumption in an adult Dutch population. *J Am Diet Assoc* 80:324–330.
- Van Staveren WA, Deurenberg P, Burema J, de Groot LC, Hautvast JG. 1986. Seasonal variation in food intake, pattern of physical activity and change in body weight in a group of young adult Dutch women consuming self-selected diets. *Int J Obes* 10:133–145.
- Van Staveren WA, de Groot LC, Blauw YH, van der Wielen RPJ. 1994. Assessing diets of elderly people: Problems and approaches. *Am J Clin Nutr* 59:221S–223S.
- Watt BK, Merrill AL, Pecot RK. 1963. *Composition of Foods; Raw, Processed, Prepared*. Agriculture Handbook No. 8. Washington, DC: U.S. Department of Agriculture.
- Welsh S, Davis C, Shaw A. 1992. Development of the food guide pyramid. *Nutr Today* 27:12–23.
- Willett WC, Reynolds RD, Cottrell-Hoehner S, Sampson L, Browne ML. 1987. Validation of a semi-quantitative food frequency questionnaire: Comparison with a 1-year diet record. *J Am Diet Assoc* 87:43–47.
- Wolter KM. 1985. *Introduction to Variance Estimation*. New York: Springer-Verlag.
- Yang W, Read M. 1996. Dietary pattern changes of Asian immigrants. *Nutr Res* 16:1277–1293.
- Young CM. 1981. Dietary methodology. In: *Assessing Changing Food Consumption Patterns*. Food and Nutrition Board, National Research Council. Washington, DC: National Academy Press. Pp. 89–118.
- Zeisel SH, da Costa K-A, Franklin PD, Alexander EA, Lamont JT, Sheard NF, Beiser A. 1991. Choline, an essential nutrient for humans. *FASEB J* 5:2093–2098.

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- Aickin M, Ritenbaugh C. 1991. Estimation of the true distribution of vitamin A intake by the unmixing algorithm. *Communications Stat Simulations* 20:255–280.
- Aksnes L, Aarskog D. 1982. Plasma concentrations of vitamin D metabolites in puberty: Effect of sexual maturation and implications for growth. *J Clin Endocrinol Metab* 55:94–101.
- Aloia JF, Vaswani A, Yeh JK, Ross PL, Flaster E, Dilmanian FA. 1994. Calcium supplementation with and without hormone replacement therapy to prevent postmenopausal bone loss. *Ann Intern Med* 120:97–103.
- AR (Army Regulation) 40-25. 1985. See U.S. Departments of the Army, the Navy, and the Air Force, 1985.
- Baran D, Sorensen A, Grimes J, Lew R, Karella A, Johnson B, Roche J. 1990. Dietary modification with dairy products for preventing vertebral bone loss in premenopausal women: A three-year prospective study. *J Clin Endocrinol Metab* 70:264–270.
- Barr SI, Janelle KC, Prior JC. 1995. Energy intakes are higher during the luteal phase of ovulatory menstrual cycles. *Am J Clin Nutr* 61:39–43.
- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Beaton GH. 1991. Interpretation of results from dietary studies. In: Kohlmeier L, ed. *The Diet History Method: Proceedings of the 2nd Berlin Meeting on Nutritional Epidemiology*. London: Smith-Gordon/Nishimura. Pp. 15–38.
- Beaton GH. 1994. Criteria of an adequate diet. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*, 8th edition. Philadelphia: Lea & Febiger. Pp. 1491–1505.
- Beaton GH. 1999. Recommended dietary intakes: Individuals and populations. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th edition. Baltimore: Williams & Wilkins. Pp. 1705–1725.
- Beaton GH, Chery A. 1988. Protein requirements of infants: A reexamination of concepts and approaches. *Am J Clin Nutr* 48:1403–1412.
- Beaton GH, Milner J, Corey P, McGuire V, Cousins M, Stewart E, deRamos M, Hewitt D, Grambsch PV, Kassim N, Little JA. 1979. Sources of variance in 24-hour dietary recall data: Implications for nutrition study design and interpretation. *Am J Clin Nutr* 32:2546–2559.
- Beaton GH, Milner J, McGuire V, Feather TE, Little JA. 1983. Source of variance in 24-hour dietary recall data: Implications for nutrition study design and interpretation. Carbohydrate sources, vitamins, and minerals. *Am J Clin Nutr* 37:986–995.
- Black AE, Prentice AM, Goldberg GR, Jebb SA, Bingham SA, Livingstone MB, Coward WA. 1993. Measurements of total energy expenditure provide insights into the validity of dietary measurements of energy intake. *J Am Diet Assoc* 93:572–579.
- Block G, Hartman AM, Dresser CM, Carroll MD, Gannon J, Gardner L. 1986. A data-based approach to diet questionnaire design and testing. *Am J Epidemiol* 124:453–469.

- Bolland JE, Ward JY, Bolland TW. 1990. Improved accuracy of estimating food quantities up to 4 weeks after training. *J Am Diet Assoc* 90:1402–1404, 1407.
- Bull NL, Buss DH. 1982. Biotin, pantothenic acid and vitamin E in the British household food supply. *Hum Nutr Appl Nutr* 36:190–196.
- Burk MC, Pao EM. 1976. Methodology for large-scale surveys of household and individual diets. *Home Econ Res Rep* No. 40. Washington, DC: Agricultural Research Service/U.S. Department of Agriculture.
- Burke BS. 1947. The dietary history as a tool in research. *J Am Diet Assoc* 23:1041–1046.
- Buzzard IM, Price KS, Warren RA. 1991. Considerations for selecting nutrient-calculation software: Evaluation of the nutrient database. *Am J Clin Nutr* 54:7–9.
- Cameron ME, Van Staveren W. 1988. *Manual on Methodology for Food Consumption Studies*. New York, NY: Oxford University Press.
- Canadian Council on Nutrition. 1938. *Canadian Dietary Standards*. Ottawa: Department of Pensions and National Health.
- Carriquiry AL. 1999. Assessing the prevalence of nutrient inadequacy. *Public Health Nutr* 2:23–33.
- Carriquiry AL, Dodd KW, Nusser SM. 1997. Estimating Adjusted Intake and Biochemical Measurement Distributions for NHANES III. Final report prepared for the National Center for Health Statistics.
- Chan GM, Hoffman K, McMurry M. 1995. Effects of dairy products on bone and body composition in pubertal girls. *J Pediatr* 126:551–556.
- Chen C. 1999. Spline Estimators of the Distribution Function of a Variable Measured with Error. Unpublished PhD dissertation. Department of Statistics, Iowa State University, Ames.
- Chevalley T, Rizzoli R, Nydegger V, Slosman D, Rapin CH, Michel JP, Vasey H, Bonjour JP. 1994. Effects of calcium supplements on femoral bone mineral density and vertebral fracture rate in vitamin-D-replete elderly patients. *Osteoporos Int* 4:245–252.
- COMA (Committee on Medical Aspects of Food Policy). 1991. *Dietary Reference Values for Food Energy and Nutrients for the United Kingdom. Report on Health and Social Subjects*, No. 41. London: Her Majesty's Stationery Office.
- Crane NT, Green NR. 1980. Food habits and food preferences of Vietnamese refugees living in northern Florida. *J Am Diet Assoc* 76:591–593.
- Dabeka RW, McKenzie AD, Conacher HBS, Kirkpatrick DC. 1982. Determination of fluoride in Canadian infant foods and calculation of fluoride intakes by infants. *Can J Public Health* 73:188–191.
- Dabeka RW, McKenzie AD, Lacroix GM. 1987. Dietary intakes of lead, cadmium, arsenic and fluoride by Canadian adults: A 24-hour duplicate diet study. *Food Addit Contam* 4:89–101.
- Dawson-Hughes B, Dallal GE, Krall EA, Sadowski L, Sahyoun N, Tannenbaum S. 1990. A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women. *N Engl J Med* 323:878–883.
- Dawson-Hughes B, Dallal GE, Krall EA, Harris S, Sokoll LJ, Falconer G. 1991. Effect of vitamin D supplementation on wintertime and overall bone loss in healthy postmenopausal women. *Ann Intern Med* 115:505–512.
- Dawson-Hughes B, Harris SS, Krall EA, Dallal GE, Falconer G, Green CL. 1995. Rates of bone loss in postmenopausal women randomly assigned to one of two dosages of vitamin D. *Am J Clin Nutr* 61:1140–1145.

- Demirjian A. 1980. *Anthropometry Report. Height, Weight, and Body Dimensions: A Report from Nutrition Canada*. Ottawa: Minister of National Health and Welfare, Health and Promotion Directorate, Health Services and Promotion Branch.
- Dewey KG, Beaton GH, Fjeld C, Lonnerdal B, Reeds P. 1996. Protein requirements of infants and children. *Eur J Clin Nutr* 50:S119–S150.
- Dodd KW. 1996. *A Technical Guide to C-SIDE: Software for Intake Distribution Estimation Version 1.0*. Technical Report 96-TR 32. Ames, IA: Center for Agricultural and Rural Development, Iowa State University.
- Domel SB. 1997. Self-reports of diet: How children remember what they have eaten. *Am J Clin Nutr* 65:1148S–1152S.
- Dwyer J. 1999. Dietary assessment. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th edition. Baltimore: Williams & Wilkins. Pp. 937–959.
- Dwyer JT, Coleman KA. 1997. Insights into dietary recall from a longitudinal study: Accuracy over four decades. *Am J Clin Nutr* 65:1153S–1158S.
- Eckert RS, Carroll RJ, Wang N. 1997. Transformations to additivity in measurement error models. *Biometrics* 53:262–272.
- Eissenstat BR, Wyse BW, Hansen RG. 1986. Pantothenic acid status of adolescents. *Am J Clin Nutr* 44:931–937.
- Elders PJ, Netelenbos JC, Lips P, van Ginkel FC, Khoe E, Leeuwenkamp OR, Hackeng WH, van der Stelt PF. 1991. Calcium supplementation reduces vertebral bone loss in perimenopausal women: A controlled trial in 248 women between 46 and 55 years of age. *J Clin Endocrinol Metab* 73:533–540.
- Elders PJ, Lips P, Netelenbos JC, van Ginkel FC, Khoe E, van der Vijgh WJ, van der Stelt PF. 1994. Long-term effect of calcium supplementation on bone loss in perimenopausal women. *J Bone Miner Res* 9:963–970.
- FAO (Food and Agriculture Organization). 1998. *FAO Food Balance Sheets 1994–1996 Average*. Rome: FAO.
- FAO/WHO (Food and Agriculture Organization/World Health Organization). 1970. *Requirements of Ascorbic Acid, Vitamin D, Vitamin B<sub>12</sub>, Folate, and Iron*. Report of a Joint FAO/WHO Expert Group. WHO Technical Report Series No. 452. FAO Nutrition Meetings Report Series No. 47. Geneva: WHO.
- FAO/WHO (Food and Agriculture Organization/World Health Organization). 1988. *Requirements of Vitamin A, Iron, Folate, and Vitamin B<sub>12</sub>*. Report of a Joint FAO/WHO Expert Consultation. FAO Food and Nutrition Series No. 23. Rome: FAO.
- FAO/WHO/UNU (Food and Agriculture Organization/World Health Organization/United Nations University). 1985. *Energy and Protein Requirements*. Report of a Joint FAO/WHO/UNU Expert Consultation. Technical Report Series No. 724. Geneva: WHO.
- Fuller WA. 1987. *Measurement Error Models*. Wiley Series in Probability and Mathematical Statistics. New York: Wiley.
- Gibson RS. 1990. *Principles of Nutritional Assessment*. New York: Oxford University Press.
- Gibson RS, Gibson IL, Kitching J. 1985. A study of inter- and intrasubject variability in seven-day weighed dietary intakes with particular emphasis on trace elements. *Biol Trace Elem Res* 8:79–91.
- Gloth FM III, Gundberg CM, Hollis BW, Haddad JG Jr, Tobin JD. 1995. Vitamin D deficiency in homebound elderly persons. *J Am Med Assoc* 274:1683–1686.

- Gordon AR, Devaney BL, Burghardt JA. 1995. Dietary effects of the National School Lunch Program and the School Breakfast Program. *Am J Clin Nutr* 61:221S–231S.
- Greenfield H, Southgate DAT. 1992. *Food Composition Data; Production, Management and Use*. London: Elsevier Applied Science.
- Greer FR, Searcy JE, Levin RS, Steichen JJ, Steichen-Asche PS, Tsang RC. 1982. Bone mineral content and serum 25-hydroxyvitamin D concentrations in breast-fed infants with and without supplemental vitamin D: One-year follow-up. *J Pediatr* 100:919–922.
- Greger JL, Baligar P, Abernathy RP, Bennett OA, Peterson T. 1978. Calcium, magnesium, phosphorus, copper, and manganese balance in adolescent females. *Am J Clin Nutr* 31:117–121.
- Guenther PM, Kott PS, Carriquiry AL. 1997. Development of an approach for estimating usual nutrient intake distributions at the population level. *J Nutr* 127:1106–1112.
- Gultekin A, Ozalp I, Hasanoglu A, Unal A. 1987. Serum-25-hydroxycholecalciferol levels in children and adolescents. *Turk J Pediatr* 29:155–162.
- Guthrie HA. 1984. Selection and quantification of typical food portions by young adults. *J Am Diet Assoc* 84:1440–1444.
- Hallberg L, Hogdahl AM, Nilsson L, Rybo G. 1966. Menstrual blood loss—A population study. Variation at different ages and attempts to define normality. *Acta Obstet Gynecol Scand* 45:320–351.
- Hankin JH, Wilkens LR. 1994. Development and validation of dietary assessment methods for culturally diverse populations. *Am J Clin Nutr* 59:198S–200S.
- Haraldsdottir J, Tjønneland A, Overvad K. 1994. Validity of individual portion size estimates in a food frequency questionnaire. *Int J Epidemiol* 23:787–796.
- Hartman AM, Block G, Chan W, Williams J, McAdams M, Banks WL Jr, Robbins A. 1996. Reproducibility of a self-administered diet history questionnaire administered three times over three different seasons. *Nutr Cancer* 25:305–315.
- Hasling C, Charles P, Jensen FT, Mosekilde L. 1990. Calcium metabolism in post-menopausal osteoporosis: The influence of dietary calcium and net absorbed calcium. *J Bone Miner Res* 5:939–946.
- Health and Welfare Canada. 1990. *Nutrition Recommendations*. The Report of the Scientific Review Committee. Ottawa: Canadian Government Publishing Centre.
- Heaney RP, Recker RR. 1982. Effects of nitrogen, phosphorus, and caffeine on calcium balance in women. *J Lab Clin Med* 99:46–55.
- Heaney RP, Recker RR, Saville PD. 1977. Calcium balance and calcium requirements in middle-aged women. *Am J Clin Nutr* 30:1603–1611.
- Heaney RP, Recker RR, Saville PD. 1978. Menopausal changes in calcium balance performance. *J Lab Clin Med* 92:953–963.
- Hebert JR, Ma Y, Clemow L, Ockene IS, Saperia G, Stanek EJ, Merriam PA, Ockene JK. 1997. Gender differences in social desirability and social approval bias in dietary self-report. *Am J Epidemiol* 146:1046–1055.
- Hirano M, Honma K, Daimatsu T, Hayakawa K, Oizumi J, Zaima K, Kanke Y. 1992. Longitudinal variations of biotin content in human milk. *Int J Vitam Nutr Res* 62:281–282.
- Immink MDC, Sanjur D, Burgos M. 1983. Nutritional consequences of U.S. migration patterns among Puerto Rican women. *Ecol Food Nutr* 13:139–147.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Food and Nutrition Board. Washington, DC: National Academy Press.

- IOM (Institute of Medicine). 1997. *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1998a. *Dietary Reference Intakes: A Risk Assessment Model for Establishing Upper Intake Levels for Nutrients*. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1998b. *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline*. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 2000. *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*. Washington, DC: National Academy Press.
- Jackman LA, Millane SS, Martin BR, Wood OB, McCabe GP, Peacock M, Weaver CM. 1997. Calcium retention in relation to calcium intake and postmenarcheal age in adolescent females. *Am J Clin Nutr* 66:327–333.
- James WPT, Schofield EC. 1990. *Human Energy Requirements: A Manual for Planners and Nutritionists*. Oxford: Oxford University Press.
- Joachim G. 1997. The influence of time on dietary data: Differences in reported summer and winter food consumption. *Nutr Health* 12:33–43.
- Johnson RK, Soultanakis RP, Matthews DE. 1998. Literacy and body fatness are associated with underreporting of energy intake in U.S. low-income women using the multiple-pass 24-hour recall: A doubly labeled water study. *J Am Diet Assoc* 98:1136–1140.
- Johnston CC, Miller JZ, Slemenda CW, Reister TK, Hui S, Christian JC, Peacock M. 1992. Calcium supplementation and increases in bone mineral density in children. *N Engl J Med* 327:82–87.
- Juni RP. 1996. How should nutrient databases be evaluated? *J Am Diet Assoc* 96:120, 122.
- Kathman JV, Kies C. 1984. Pantothenic acid status of free living adolescent and young adults. *Nutr Res* 4:245–250.
- Kinyamu HK, Gallagher JC, Balhorn KE, Petranick KM, Rafferty KA. 1997. Serum vitamin D metabolites and calcium absorption in normal young and elderly free-living women and in women living in nursing homes. *Am J Clin Nutr* 65:790–797.
- Kohlmeier L, Bellach B. 1995. Exposure assessment error and its handling in nutritional epidemiology. *Annu Rev Public Health* 16:43–59.
- Kohlmeier L, Simonsen N, Mottus K. 1995. Dietary modifiers of carcinogenesis. *Environ Health Perspect* 103:177–184.
- Kohlmeier L, Mendez M, McDuffie J, Miller M. 1997. Computer-assisted self-interviewing: A multimedia approach to dietary assessment. *Am J Clin Nutr* 65:1275S–1281S.
- Krall EA, Sahyoun N, Tannenbaum S, Dallal GE, Dawson-Hughes B. 1989. Effect of vitamin D intake on seasonal variations in parathyroid hormone secretion in postmenopausal women. *N Engl J Med* 321:1777–1783.
- Kramer L, Osis D, Wiatrowski E, Spenser H. 1974. Dietary fluoride in different areas in the United States. *Am J Clin Nutr* 27:590–594.
- Kristal AR, Abrams BF, Thornquist MD, Disogra L, Croyle RT, Shattuck AL, Henry HJ. 1990. Development and validation of a food use checklist for evaluation of community nutrition interventions. *Am J Public Health* 80:1318–1322.
- Kristal AR, Feng Z, Coates RJ, Oberman A, George V. 1997. Associations of race/ethnicity, education, and dietary intervention with the validity and reliability of a food frequency questionnaire: The Women's Health Trial Feasibility Study in Minority Populations. *Am J Epidemiol* 146:856–869.

- Kuhnlein HV. 1992. Change in the use of traditional foods by the Nuxalk native people of British Columbia. *Ecol Food Nutr* 27:259–282.
- Kuhnlein HV, Soueida R. 1992. Use and nutrient composition of traditional Baffin Inuit foods. *J Food Comp Anal* 5:112–126.
- Kuhnlein HV, Soueida R, Receveur O. 1996. Dietary nutrient profiles of Canadian Baffin Island Inuit differ by food source, season, and age. *J Am Diet Assoc* 96:155–162.
- Leung SSF, Lui S, Swaminathan R. 1989. Vitamin D status of Hong Kong Chinese infants. *Acta Paediatr Scand* 78:303–306.
- Lichtman SW, Pisarska K, Berman ER, Pestone M, Dowling H, Offenbacher E, Weisel H, Heshka S, Matthews DE, Heymsfield SB. 1992. Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. *N Engl J Med* 327:1893–1898.
- Liu K. 1988. Consideration of and compensation for intra-individual variability in nutrient intakes. In: Kohlmeier L, Helsing E, eds. *Epidemiology Nutrition and Health: Proceedings of the First Berlin Meeting on Nutritional Epidemiology*. London: Smith-Gordon/Nishimura. Pp. 87–106.
- Liu K, Stamler J, Dyer A, McKeever J, McKeever P. 1978. Statistical methods to assess and minimize the role of intra-individual variability in obscuring the relationship between dietary lipids and serum cholesterol. *J Chronic Dis* 31:399–418.
- Lloyd T, Andon MB, Rollings N, Martel JK, Landis R, Demers LM, Eggle DF, Kieselhorst K, Kulin HE. 1993. Calcium supplementation and bone mineral density in adolescent girls. *J Am Med Assoc* 270:841–844.
- Looker AC, Sempos CT, Liu K, Johnson CL, Gunter EW. 1990. Within-person variance in biochemical indicators of iron status: Effects on prevalence estimates. *Am J Clin Nutr* 52:541–547.
- LSRO (Life Sciences Research Office). 1986. *Guidelines for Use of Dietary Intake Data*. Bethesda, MD: LSRO/FASEB.
- Markestad T, Elzouki AY. 1991. Vitamin D-deficiency rickets in northern Europe and Libya. In: Glorieux FH, ed. *Rickets: Nestle Nutrition Workshop Series*, Vol 21. New York, NY: Raven Press.
- Marshall DH, Nordin BEC, Speed R. 1976. Calcium, phosphorus and magnesium requirement. *Proc Nutr Soc* 35:163–173.
- Martin AD, Bailey DA, McKay HA. 1997. Bone mineral and calcium accretion during puberty. *Am J Clin Nutr* 66:611–615.
- Matkovic V. 1991. Calcium metabolism and calcium requirements during skeletal modeling and consolidation of bone mass. *Am J Clin Nutr* 54:245S–260S.
- Matkovic V, Heaney RP. 1992. Calcium balance during human growth: Evidence for threshold behavior. *Am J Clin Nutr* 55:992–996.
- Matkovic V, Fontana D, Tominac C, Goel P, Chesnut CH III. 1990. Factors that influence peak bone mass formation: A study of calcium balance and the inheritance of bone mass in adolescent females. *Am J Clin Nutr* 52:878–888.
- McClure FJ. 1943. Ingestion of fluoride and dental caries. Quantitative relations based on food and water requirements of children one to twelve years old. *Am J Dis Child* 66:362–369.
- McDowell MA. 1994. The NHANES III Supplemental Nutrition Survey of older Americans. *Am J Clin Nutr* 59:224S–226S.
- Mertz W, Kelsay JL. 1984. Rationale and design of the Beltsville one-year dietary intake study. *Am J Clin Nutr* 40:1323–1326.

- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- Nieman DC, Butterworth DE, Nieman CN, Lee KE, Lee RD. 1992. Comparison of six microcomputer dietary analysis systems with the USDA Nutrient Data Base for Standard Reference. *J Am Diet Assoc* 92:48–56.
- NRC (National Research Council). 1941. *Recommended Dietary Allowances: Protein, Calcium, Iron, Vitamin A, Vitamin B (Thiamin), Vitamin C (Ascorbic Acid), Riboflavin, Nicotinic Acid, Vitamin D*. Washington, DC: National Research Council.
- NRC (National Research Council). 1968. *Recommended Dietary Allowances*, 7th Ed. Washington, DC: National Academy of Sciences.
- NRC (National Research Council). 1980. *Recommended Dietary Allowances*, 9th Ed. Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC (National Research Council). 1989. *Recommended Dietary Allowances*, 10th Ed. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- O'Dowd KJ, Clemens TL, Kelsey JL, Lindsay R. 1993. Exogenous calciferol (vitamin D) and vitamin D endocrine status among elderly nursing home residents in the New York City area. *J Am Geriatr Soc* 41:414–421.
- Ohlson MA, Brewer WD, Jackson L, Swanson PP, Roberts PH, Mangel M, Leverton RM, Chaloupka M, Gram MR, Reynolds MS, Lutz R. 1952. Intakes and retentions of nitrogen, calcium and phosphorus by 136 women between 30 and 85 years of age. *Fed Proc* 11:775–783.
- Oliveira V, Gunderson C. 2000. *WIC and the Nutrient Intake of Children*. Food Assistance and Nutrition Research Report No. 5. Beltsville, MD: U.S. Department of Agriculture, Economic Research Service, Food and Rural Economics Division.
- Ophaug RH, Singer L, Harland BF. 1980a. Estimated fluoride intake of 6-month-old infants in four dietary regions of the United States. *Am J Clin Nutr* 33:324–327.
- Ophaug RH, Singer L, Harland BF. 1980b. Estimated fluoride intake of average two-year-old children in four dietary regions of the United States. *J Dent Res* 59:777–781.
- Ophaug RH, Singer L, Harland BF. 1985. Dietary fluoride intake of 6-month and 2-year-old children in four dietary regions of the United States. *Am J Clin Nutr* 42:701–707.
- Orwoll ES, Oviatt SK, McClung MR, Deftos LJ, Sexton G. 1990. The rate of bone mineral loss in normal men and the effects of calcium and cholecalciferol supplementation. *Ann Intern Med* 112:29–34.
- Osis D, Kramer L, Wiatrowski E, Spencer H. 1974. Dietary fluoride intake in man. *J Nutr* 104:1313–1318.
- Prince R, Smith M, Dick IM, Price RI, Webb PG, Henderson NK, Harris MM. 1991. Prevention of postmenopausal osteoporosis. A comparative study of exercise, calcium supplementation, and hormone-replacement therapy. *N Engl J Med* 325:1189–1195.

- Prince R, Devine A, Dick I, Criddle A, Kerr D, Kent N, Price R, Randell A. 1995. The effects of calcium supplementation (milk powder or tablets) and exercise on bone density in postmenopausal women. *J Bone Miner Res* 10:1068–1075.
- Rand WM, Pennington JAT, Murphy SP, Klensin JC. 1991. *Compiling Data for Food Composition Data Bases*. Tokyo: United Nations University Press.
- Receveur O, Boulay M, Kuhnlein HV. 1997. Decreasing traditional food use affects diet quality for adult Dene/Metis in 16 communities of the Canadian Northwest Territories. *J Nutr* 127:2179–2186.
- Recker RR, Hinders S, Davies KM, Heaney RP, Stegman MR, Lappe JM, Kimmel DB. 1996. Correcting calcium nutritional deficiency prevents spine fractures in elderly women. *J Bone Miner Res* 11:1961–1966.
- Reid IR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. 1995. Long-term effects of calcium supplementation on bone loss and fractures in postmenopausal women: A randomized controlled trial. *Am J Med* 98:331–335.
- Riis B, Thomsen K, Christiansen C. 1987. Does calcium supplementation prevent postmenopausal bone loss? *N Engl J Med* 316:173–177.
- Rose D, Habicht JP, Devaney B. 1998. Household participation in the Food Stamp and WIC programs increases the nutrient intakes of preschool children. *J Nutr* 128:548–555.
- Salmenpera L, Perheentupa J, Pispa JP, Siimes MA. 1985. Biotin concentrations in maternal plasma and milk during prolonged lactation. *Int J Vitam Nutr Res* 55:281–285.
- Selby PL. 1994. Calcium requirement—A reappraisal of the methods used in its determination and their application to patients with osteoporosis. *Am J Clin Nutr* 60:944–948.
- Sempos CT, Johnson NE, Smith EL, Gilligan C. 1985. Effects of intraindividual and interindividual variation in repeated dietary records. *Am J Epidemiol* 121:120–130.
- Sims LS. 1996. Uses of the Recommended Dietary Allowances: A commentary. *J Am Diet Assoc* 96:659–662.
- Singer L, Ophaug R. 1979. Total fluoride intakes of infants. *Pediatrics* 63:460–466.
- Singer L, Ophaug RH, Harland BF. 1980. Fluoride intakes of young male adults in the United States. *Am J Clin Nutr* 33:328–332.
- Singer L, Ophaug RH, Harland BF. 1985. Dietary fluoride intake of 15–19-year-old male adults residing in the United States. *J Dent Res* 64:1302–1305.
- Smith AF, Jobe JB, Mingay DJ. 1991a. Retrieval from memory of dietary information. *Appl Cognitive Psychol* 5:269–296.
- Smith CJ, Schakel SF, Nelson RG. 1991b. Selected traditional and contemporary foods currently used by the Pima Indians. *J Am Diet Assoc* 91:338–341.
- Snedecor GW, Cochran WG. 1980. *Statistical Methods*, 7th edition. Ames, Iowa: Iowa State University Press.
- Specker BL, Ho ML, Oestreich A, Yin TA, Shui QM, Chen XC, Tsang RC. 1992. Prospective study of vitamin D supplementation and rickets in China. *J Pediatr* 120:733–739.
- Spencer H, Kramer L, Lesniak M, DeBartolo M, Norris C, Osis D. 1984. Calcium requirements in humans. Report of original data and a review. *Clin Orthop Relat Res* 184:270–280.
- Spencer H, Osis D, Lender M. 1981. Studies of fluoride metabolism in man. A review and report of original data. *Sci Total Environ* 17:1–12.

- Srinivasan V, Christensen N, Wyse BW, Hansen RG. 1981. Pantothenic acid nutritional status in the elderly—Institutionalized and noninstitutionalized. *Am J Clin Nutr* 34:1736–1742.
- Stefanski LA, Bay JM. 1996. Simulation extrapolation deconvolution of finite population cumulative distribution function estimators. *Biometrika* 83:407–417.
- Subar AF, Frey CM, Harlan LC, Kahle L. 1994. Differences in reported food frequency by season of questionnaire administration: The 1987 National Health Interview Survey. *Epidemiology* 5:226–233.
- Tarasuk V, Beaton GH. 1991a. Menstrual-cycle patterns in energy and macronutrient intake. *Am J Clin Nutr* 53:442–447.
- Tarasuk V, Beaton GH. 1991b. The nature and individuality of within-subject variation in energy intake. *Am J Clin Nutr* 54:464–470.
- Tarasuk V, Beaton GH. 1992. Statistical estimation of dietary parameters: Implications of patterns in within-subject variation—A case study of sampling strategies. *Am J Clin Nutr* 55:22–27.
- Tarr JB, Tamura T, Stokstad EL. 1981. Availability of vitamin B<sub>6</sub> and pantothenate in an average American diet in man. *Am J Clin Nutr* 34:1328–1337.
- Taves DR. 1983. Dietary intake of fluoride ashed (total fluoride) v. unashed (inorganic fluoride) analysis of individual foods. *Br J Nutr* 49:295–301.
- Teufel NI. 1997. Development of culturally competent food-frequency questionnaires. *Am J Clin Nutr* 65:1173S–1178S.
- Thompson CH, Head MK, Rodman SM. 1987. Factors influencing accuracy in estimating plate waste. *J Am Diet Assoc* 87:1219–1220.
- Thompson FE, Byers T. 1994. Dietary assessment resource manual. *J Nutr* 124:2245S–2317S.
- Tsubono Y, Kobayashi M, Takahashi T, Iwase Y, Itoi Y, Akabane M, Tsugane S. 1997. Within- and between-person variations in portion sizes of foods consumed by the Japanese population. *Nutr Cancer* 29:140–145.
- USDA (U.S. Department of Agriculture, Human Nutrition Information Service). 1992. The Food Guide Pyramid. Home and Garden Bulletin No. 252, 32 pp.
- USDA (U.S. Department of Agriculture, Agricultural Research Service). 1999. USDA Nutrient Database for Standard Reference, Release 13. Nutrient Data Laboratory Home Page. Available from: <<http://www.nal.usda.gov/fnic/foodcomp>>.
- U.S. Departments of the Army, the Navy, and the Air Force. 1985. Army Regulation 40-25/Navy Command Medical Instruction 10110.1/Air Force Regulation 160-95. *Nutritional Allowances, Standards, and Education*. May 15. Washington, D.C.
- Van Staveren WA, Hautvast JG, Katan MB, Van Montfort MA, Van Oosten-Van der Goes HG. 1982. Dietary fiber consumption in an adult Dutch population. *J Am Diet Assoc* 80:324–330.
- Van Staveren WA, Deurenberg P, Burema J, de Groot LC, Hautvast JG. 1986. Seasonal variation in food intake, pattern of physical activity and change in body weight in a group of young adult Dutch women consuming self-selected diets. *Int J Obes* 10:133–145.
- Van Staveren WA, de Groot LC, Blauw YH, van der Wielen RPJ. 1994. Assessing diets of elderly people: Problems and approaches. *Am J Clin Nutr* 59:221S–223S.
- Watt BK, Merrill AL, Pecot RK. 1963. *Composition of Foods; Raw, Processed, Prepared*. Agriculture Handbook No. 8. Washington, DC: U.S. Department of Agriculture.

- Welsh S, Davis C, Shaw A. 1992. Development of the food guide pyramid. *Nutr Today* 27:12–23.
- Willett WC, Reynolds RD, Cottrell-Hoehner S, Sampson L, Browne ML. 1987. Validation of a semi-quantitative food frequency questionnaire: Comparison with a 1-year diet record. *J Am Diet Assoc* 87:43–47.
- Wolter KM. 1985. *Introduction to Variance Estimation*. New York: Springer-Verlag.
- Yang W, Read M. 1996. Dietary pattern changes of Asian immigrants. *Nutr Res* 16:1277–1293.
- Young CM. 1981. Dietary methodology. In: *Assessing Changing Food Consumption Patterns*. Food and Nutrition Board, National Research Council. Washington, DC: National Academy Press. Pp. 89–118.
- Zeisel SH, da Costa K-A, Franklin PD, Alexander EA, Lamont JT, Sheard NF, Beiser A. 1991. Choline, an essential nutrient for humans. *FASEB J* 5:2093–2098.

*Dietary Reference Intakes: Applications in Dietary Planning* (ISBN 0-309-08714-7), Chapter 8, pp. 156–161.

- ACC/SCN (Administrative Committee on Coordination/Sub-Committee on Nutrition). 2000. *Fourth Report on The World Nutrition Situation*. Geneva: ACC/SCN in collaboration with IFPRI. Pp. 27–29.
- Aickin M, Ritenbaugh C. 1991. Estimation of the true distribution of vitamin A intake by the unmixing algorithm. *Commun Stat Sim* 20:255–280.
- ARS (Agriculture Research Service). 1998. *Continuing Survey of Food Intakes by Individuals (CSFII) 1994–96, 1998*. CD-ROM. Beltsville, MD: ARS.
- Bandini LG, Schoeller DA, Cry HN, Dietz WH. 1990. Validity of reported energy intake in obese and nonobese adolescents. *Am J Clin Nutr* 52:421–425.
- Beaton GH. 1994. Criteria of an adequate diet. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*, 8th ed. Philadelphia: Lea & Febiger. Pp. 1491–1505.
- Beaton GH, Milner J, McGuire V, Feather TE, Little JA. 1983. Source of variance in 24-hour dietary recall data: Implications for nutrition study design and interpretation. Carbohydrate sources, vitamins, and minerals. *Am J Clin Nutr* 37:986–995.
- Beaton GH, Burema J, Ritenbaugh C. 1997. Errors in interpretation of dietary assessments. *Am J Clin Nutr* 65:1100S–1107S.
- Becker W, Welten D. 2001. Under-reporting in dietary surveys—implications for development of food-based dietary guidelines. *Public Health Nutr* 4:683–687.
- Becker W, Foley S, Shelley E, Gibney M. 1999. Energy under-reporting in Swedish and Irish dietary surveys: Implications for food-based dietary guidelines. *Br J Nutr* 81:S127–S131.
- Berner LA, Clydesdale FM, Douglass JS. 2001. Fortification contributed greatly to vitamin and mineral intakes in the United States, 1989–1991. *J Nutr* 131:2177–2183.
- Black AE, Cole TJ. 2001. Biased over- or under-reporting is characteristic of individuals whether over time or by different assessment methods. *J Am Diet Assoc* 101:70–80.
- Black AE, Goldberg GR, Jebb SA, Livingstone MBE, Cole TJ, Prentice AM. 1991. Critical evaluation of energy intake data using fundamental principles of energy physiology: 2. Evaluating the results of published surveys. *Eur J Clin Nutr* 45:583–599.

- Black AE, Prentice AM, Goldberg GR, Jebb SA, Bingham SA, Livingstone MB, Conward WA. 1993. Measurements of total energy expenditure provide insights into the validity of dietary measurements of energy intake. *J Am Diet Assoc* 93:572–579.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Nutrition Examination Survey: Underreporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Burghardt JA, Gordon AR, Fraker TM. 1995. Meals offered in the national school lunch program and the school breakfast program. *Am J Clin Nutr* 61:187S–198S.
- CDC/NCHS (Centers for Disease Control and Prevention/National Center for Health Statistics). 2000. *2000 CDC Growth Charts*. Online. Available at <http://www.cdc.gov/growthcharts/>. Accessed December 3, 2002.
- CFIA (Canadian Food Inspection Agency). 1996. *Guide to Food Labelling and Advertising*. Online. Available at <http://www.inspection.gc.ca/english/bureau/labeti/guide/guidee.shtml>. Accessed December 3, 2002.
- COMA (Committee on Medical Aspects of Food Policy). 1991. *Dietary Reference Values for Food Energy and Nutrients for the United Kingdom*. Report on Health and Social Subjects, No. 41. London: Her Majesty's Stationery Office.
- Consumer and Corporate Affairs Canada. 1988. *Guide for Food Manufacturers and Advertisers*. Ottawa: Consumer Products Branch, Bureau of Consumer Affairs.
- Demirjian A. 1980. *Anthropometry Report. Height, Weight, and Body Dimensions: A Report from Nutrition Canada*. Ottawa: Minister of National Health and Welfare, Health and Promotion Directorate, Health Services and Promotion Branch.
- Devaney BL, Gordon AR, Burghardt JA. 1995. Dietary intakes of students. *Am J Clin Nutr* 61:205S–221S.
- FAO/WHO (Food and Agriculture Organization/World Health Organization). 1970. *Requirements of Ascorbic Acid, Vitamin D, Vitamin B<sub>12</sub>, Folate, and Iron. Report of a Joint FAO/WHO Expert Group*. WHO Technical Report Series No. 452. Geneva: WHO.
- FAO/WHO. 1988. *Requirements of Vitamin A, Iron, Folate, and Vitamin B<sub>12</sub>. Report of a Joint FAO/WHO Expert Consultation*. FAO Food and Nutrition Series No. 23. Rome: FAO.
- FAO/WHO/UNU (United Nations University). 1985. *Energy and Protein Requirements. Report of a Joint FAO/WHO/UNU Expert Consultation*. Technical Report Series No. 724. Geneva: WHO.
- FDA (U.S. Food and Drug Administration). 1999. *The Food Label*. FDA Backgrounder. May 1999. Online. Center for Food Safety and Applied Nutrition. Available at <http://www.cfsan.fda.gov/~dms/fdnewlab.html>. Accessed November 18, 2002.
- FDA. 2000. *Guidance on How to Understand and Use the Nutrition Facts Panel on Food Labels*. Online. Center for Food Safety and Applied Nutrition. Available at <http://www.cfsan.fda.gov/~dms/foodlab.html>. Accessed May 16, 2002.
- Fox MK, Crepinsek MK, Connor P, Battaglia M. 2001. *School Nutrition Dietary Assessment Study: II. Final Report*. Washington, DC: U.S. Department of Agriculture, Food and Nutrition Service.
- Gentle JE. 1998. *Random Number Generation and Monte Carlo Methods*. New York: Springer-Verlag.
- Goldberg GR, Black AE, Jebb SA, Cole TJ, Murgatroyd PR, Conward WA, Prentice AM. 1991. Critical evaluation of energy intake data using fundamental principles of energy physiology: 1. Derivation of cut-off limits to identify under-recording. *Eur J Clin Nutr* 45:569–581.

- Goris AHC, Westerterp-Plantenga MS, Westerterp KR. 2000. Undereating and underrecording of habitual food intake in obese men: Selective underreporting of fat intake. *Am J Clin Nutr* 71:130–134.
- Goyeneche JJ, Carriquiry A, Fuller WA. 1997. Estimating bivariate usual intake distributions. *ASA Proceedings of the Biometrics Section*. Alexandria, VA: American Statistical Association.
- Guenther PM, Kott PS, Carriquiry AL. 1997. Development of an approach for estimating usual nutrient intake distributions at the population level. *J Nutr* 127:1106–1112.
- Health Canada. 1990a. *Action Towards Healthy Eating. Canada's Guidelines for Healthy Eating and Recommended Strategies for Implementation*. The Report of the Communications/Implementation Committee. Ottawa: Public Works and Government Service Canada.
- Health Canada. 1990b. *Nutrition Recommendations*. The Report of the Scientific Review Committee 1990. Ottawa: Canadian Government Publishing Centre.
- Health Canada. 1991. *Canada's Food Guide to Healthy Eating*. Ottawa: Minister of Supply and Services.
- Health Canada. 1997. *Using the Food Guide*. Ottawa: Public Works and Government Service Canada.
- Health Canada. 1998. *Handbook for Canada's Physical Activity Guide to Healthy Active Living*. Ottawa: Health Canada and the Canadian Society for Exercise Physiology.
- Health Canada. 1999. *The Addition of Vitamins and Minerals to Foods: Proposed Policy Recommendations*. Ottawa: Bureau of Nutritional Sciences, Food Directorate, Health Protection Branch.
- Health Canada. 2002. *Nutrition Labels*. Online. Available at [http://www.hc-sc.gc.ca/hppb/nutrition/labels/e\\_before.html](http://www.hc-sc.gc.ca/hppb/nutrition/labels/e_before.html). Accessed November 27, 2002.
- Herman-Giddens ME, Slora EJ, Wasserman RC, Bourdony CJ, Bhapkar MV, Koch GG, Hasemeier CM. 1997. Secondary sexual characteristics and menses in young girls seen in office practice: A study from the Pediatric Research in Office Settings Network. *Pediatrics* 99:505–512.
- HHS (U.S. Department of Health and Human Services). 1996. *Physical Activity and Health: A Report of the Surgeon General*. Atlanta: Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion.
- Hoffmann K, Boeing H, Dufour A, Volatier JL, Telman J, Virtanen M, Becker S, DeHenauw S. 2002. Estimating the distribution of usual dietary intake by short-term measures. *Eur J Clin Nutr* 56:S53–S62.
- Hunt JR, Roughead ZK. 1999. Nonheme-iron absorption, fecal ferritin excretion, and blood indexes of iron status in women consuming controlled lactoovo-vegetarian diets for 8 wk. *Am J Clin Nutr* 69:944–952.
- Hunt JR, Matthys LA, Johnson LK. 1998. Zinc absorption, mineral balance, and blood lipids in women consuming controlled lactoovo-vegetarian and omnivorous diets for 8 wk. *Am J Clin Nutr* 67:421–430.
- IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy: Part I: Weight Gain, Part II: Nutrient Supplements*. Washington, DC: National Academy Press.
- IOM. 1992. *Nutrition During Pregnancy and Lactation: An Implementation Guide*. Washington, DC: National Academy Press.
- IOM. 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- IOM. 1995. *Estimated Mean per Capita Energy Requirements for Planning Emergency Food Aid Rations*. Washington, DC: National Academy Press.

- IOM. 1997. *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. Washington, DC: National Academy Press.
- IOM. 1998a. *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline*. Washington, DC: National Academy Press.
- IOM. 1998b. *Prevention of Micronutrient Deficiencies: Tools for Policymakers and Public Health Workers*. Washington, DC: National Academy Press.
- IOM. 1999. *Dietary Reference Intakes: A Risk Assessment Model for Establishing Upper Intake Levels for Nutrients*. Washington, DC: National Academy Press.
- IOM. 2000a. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- IOM. 2000b. *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*. Washington, DC: National Academy Press.
- IOM. 2001. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Washington, DC: National Academy Press.
- IOM. 2002a. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*. Washington, DC: National Academy Press.
- IOM. 2002b. *High-Energy, Nutrient-Dense Emergency Relief Food Product*. Washington, DC: National Academy Press.
- Jacques PF, Bostom AG, Williams RR, Ellison RC, Eckfeldt JH, Rosenberg IH, Selhub J, Rozen R. 1996. Relation between folate status, a common mutation in methylenetetrahydrofolate reductase, and plasma homocysteine concentrations. *Circulation* 93:7–9.
- Johansson L, Solvoll K, Aa Bjorneboe G-E, Drevon CA. 1998. Under- and over-reporting of energy intake related to weight status and lifestyle in a nationwide sample. *Am J Clin Nutr* 68:266–274.
- Johnson RK, Soultanakis RP, Matthews DE. 1998. Literacy and body fatness are associated with underreporting of energy intake in US low-income women using the multiple-pass 24-hour recall: A doubly labeled water study. *J Am Diet Assoc* 98:1136–1140.
- Kaczkowski CH, Jones PJH, Feng J, Bayley HS. 2000. Four-day multimedia diet records underestimate energy needs in middle-aged and elderly women as determined by doubly-labeled water. *J Nutr* 130:802–805.
- Krebs-Smith SM, Graubard BI, Kahle LL, Subar AF, Cleveland LE, Ballard-Barbash R. 2000. Low energy reporters vs. others: A comparison of reported food intakes. *Eur J Clin Nutr* 54:281–287.
- Kuczmarski MF, Kuczmarski RJ, Najjar M. 2001. Effects of age on validity of self-reported height, weight, and body mass index: Findings from the Third National Health and Nutrition Examination Survey, 1988–1994. *J Am Diet Assoc* 101:28–34.
- Kuczmarski RJ, Ogden CL, Grummer-Strawn LM, Flegal KM, Guo SS, Wei R, Mei Z, Curtin LR, Roche AF, Johnson CL. 2000. CDC growth charts: United States. *Advance Data from Vital and Health Statistics* 314:1–28.
- Ladizesky M, Lu Z, Oliveri B, San Roman N, Diaz S, Holick MF, Mautalen C. 1995. Solar ultraviolet B radiation and photoproduction of vitamin D<sub>3</sub> in central and southern areas of Argentina. *J Bone Miner Res* 10:545–549.
- Larsson CL, Westerterp KR, Johansson GK. 2002. Validity of reported energy expenditure and energy and protein intakes in Swedish adolescent vegans and omnivores. *Am J Clin Nutr* 75:268–274.

- Lewis CJ, Crane NT, Wilson DB, Yetley EA. 1999. Estimated folate intakes: Data updated to reflect food fortification, increased bioavailability, and dietary supplement use. *Am J Clin Nutr* 70:198–207.
- MacLaughlin J, Holick MF. 1985. Aging decreases the capacity of human skin to produce vitamin D. *J Clin Invest* 76:1536–1538.
- Martin LJ, Su W, Jones PJ, Lockwood GA, Tritchler DL, Boyd NF. 1996. Comparison of energy intakes determined by food records and doubly labeled water in women participating in a dietary-intervention trial. *Am J Clin Nutr* 63:483–490.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- Mertz W, Abernathy CO, Olin SS. 1994. *Risk Assessment of Essential Elements*. Washington, DC: ILSI Press.
- Messina VK, Burke KI. 1997. Position of the American Dietetic Association: Vegetarian diets. *J Am Diet Assoc* 97:1317–1321.
- Monsen ER, Hallberg L, Layrisse M, Hegsted DM, Cook JD, Mertz W, Finch CA. 1978. Estimation of available dietary iron. *Am J Clin Nutr* 31:134–141.
- Northwest Territories Aboriginal Head Start Program. 2002. *N.W.T. Food Guide*. Online. Available at [www.nwtheadstart.org/comp\\_nutrition\\_food\\_guide.htm](http://www.nwtheadstart.org/comp_nutrition_food_guide.htm). Accessed August 16, 2002.
- NRC (National Research Council). 1968. *Recommended Dietary Allowances*, 7th ed. Washington, DC: National Academy Press.
- NRC. 1986. *Nutrient Adequacy: Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC. 1989. *Recommended Dietary Allowances*, 10th ed. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- PCRM (Physicians Committee for Responsible Medicine). 1997. The origin of U.S. Dietary Guidelines. Online. *Good Medicine*. Available at <http://www.pcrm.org/magazine/GM97Autumn/GM97Autumn2.html>. Accessed November 27, 2002.
- Pett LB, Ogilvie GH. 1956. The Canadian Weight-Height Survey. *Hum Biol* 28:177–188.
- Prentice AM, Black AE, Coward WA, Davies HL, Goldberg GR, Murgatroyd PR, Ashford J, Sawyer M, Whitehead RG. 1986. High levels of energy expenditure in obese women. *Br Med J* 292:983–987.
- Saint L, Maggiore P, Hartmann PE. 1986. Yield and nutrient content of milk in eight women breast-feeding twins and one woman breast-feeding triplets. *Br J Nutr* 56:49–58.
- Sawaya AL, Tucker K, Tsay R, Willett W, Saltzman E, Dallal GE, Roberts SB. 1996. Evaluation of four methods for determining energy intake in young and older women: Comparison with doubly labeled water measurements of total energy expenditure. *Am J Clin Nutr* 63:491–499.
- Shaw A, Fulton L, Davis C, Hogbin M. 1996. *Using the Food Guide Pyramid: A Resource for Nutrition Education*. Washington, DC: U.S. Department of Agriculture, Food, Nutrition and Consumer Services, Center for Nutrition Policy and Promotion.
- Sichert-Hellert W, Kersting M, Schöh G. 1999. Consumption of fortified foods between 1985 and 1996 in 2- to 14-year-old German children and adolescents. *Int J Food Sci Nutr* 50:65–72.

- Stallone DD, Brunner EJ, Bingham SA, Marmot MG. 1997. Dietary assessment in Whitehall II: The influence of reporting bias on apparent socioeconomic variation in nutrient intakes. *Eur J Clin Nutr* 51:815–825.
- Steel RGD, Torrie JH, Dickey DA. 1997. *Principles and Procedures of Statistics. A Biometrical Approach*, 3rd ed. Boston: WCB McGraw-Hill. P. 612.
- Subar AF, Harlan LC, Mattson ME. 1990. Food and nutrient intake differences between smokers and non-smokers in the US. *Am J Public Health* 80:1323–1329.
- Tarasuk VS, Beaton GH. 1999. Women's dietary intakes in the context of household food insecurity. *J Nutr* 129:672–679.
- Tomoyasu NJ, Toth MJ, Poehlman ET. 1999. Misreporting of total energy intake in older men and women. *J Am Geriatr Soc* 47:710–715.
- USDA (U.S. Department of Agriculture). 1992. *The Food Guide Pyramid*. Home and Garden Bulletin No. 252. Washington, DC: U.S. Government Printing Office.
- USDA/ARS (Agricultural Research Service). 1997. *1994–96 Continuing Survey of Food Intakes by Individuals (CSFII 1994–96)*. Riverdale, MD: USDA.
- USDA/HHS (U.S. Department of Health and Human Services). 1980. *Nutrition and Your Health: Dietary Guidelines for Americans*. Home and Garden Bulletin No. 232. Washington, DC: U.S. Government Printing Office.
- USDA/HHS. 2000. *Nutrition and Your Health: Dietary Guidelines for Americans*, 5th ed. Home and Garden Bulletin No. 232. Washington, DC: U.S. Government Printing Office.
- Welsh SO, Davis C, Shaw A. 1993. *USDA's Food Guide: Background and Development*. Miscellaneous Publication No. 1514. Hyattsville, MD: USDA.
- Webb AR, Kline L, Holick MF. 1988. Influence of season and latitude on the cutaneous synthesis of vitamin D<sub>3</sub>: Exposure to winter sunlight in Boston and Edmonton will not promote vitamin D<sub>3</sub> synthesis in human skin. *J Clin Endocrinol Metab* 67:373–378.
- Whittaker P, Tufaro PR, Rader JL. 2001. Iron and folate in fortified cereals. *J Am Coll Nutr* 20:247–254.
- Willett W, Stampfer MJ. 1986. Total energy intake: Implications for epidemiologic analyses. *Am J Epidemiol* 124:17–27.

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*Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* (ISBN 0-309-08537-3), Chapter 3, pp. 66–83.

- Abbott WGH, Boyce VL, Grundy SM, Howard BV. 1989. Effects of replacing saturated fat with complex carbohydrate in diets of subjects with NIDDM. *Diabetes Care* 12:102–107.
- Albert CM, Hennekens CH, O'Donnell CJ, Ajani UA, Carey VJ, Willett WC, Ruskin JN, Manson JE. 1998. Fish consumption and risk of sudden cardiac death. *J Am Med Assoc* 279:23–28.
- Alberts DS, Martínes ME, Roe DJ, Guillén-Rodríguez JM, Marshall JR, van Leeuwen JB, Reid ME, Ritenbaugh C, Vargas PA, Bhattacharyya AB, Earnest DL, Sampliner RE. 2000. Lack of effect of a high-fiber cereal supplement on the recurrence of colorectal adenomas. *N Engl J Med* 342:1156–1162.
- Anderson JJ. 2000. The important role of physical activity in skeletal development: How exercise may counter low calcium intake. *Am J Clin Nutr* 71:1384–1386.
- Anderson JW. 1999. Nutritional management of diabetes mellitus. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th ed. Baltimore, MD: Williams and Wilkins. Pp. 1365–1394.
- Anderson JW, Johnstone BM, Cook-Newell ME. 1995. Meta-analysis of the effects of soy protein intake on serum lipids. *N Engl J Med* 333:276–282.
- Andersson S-O, Wolk A, Bergström R, Giovannucci E, Lindgren C, Baron J, Adami H-O. 1996. Energy, nutrient intake and prostate cancer risk: A population-based case-control study in Sweden. *Int J Cancer* 68:716–722.
- Anti M, Marra G, Armelao F, Bartoli GM, Ficarelli R, Percesepe A, De Vitis I, Maria G, Sofo L, Rapaccini GL. 1992. Effect of omega-3 fatty acids on rectal mucosal cell proliferation in subjects at risk for colon cancer. *Gastroenterology* 103:883–891.
- Araújo-Vilar D, Osifo E, Kirk M, García-Estevez DA, Cabezas-Cerrato J, Hockaday TDR. 1997. Influence of moderate physical exercise on insulin-mediated and non-insulin-mediated glucose uptake in healthy subjects. *Metabolism* 46:203–209.
- Armstrong B, Doll R. 1975. Environmental factors and cancer incidence and mortality in different countries, with special reference to dietary practices. *Int J Cancer* 15:617–631.
- Arntzenius AC, Kromhout D, Barth JD, Reiber JHC, Bruschke AVG, Buis B, van Gent CM, Kempen-Voogd N, Strikwerda S, van der Velde EA. 1985. Diet, lipoproteins, and the progression of coronary atherosclerosis. The Leiden Intervention Trial. *N Engl J Med* 312:805–811.
- Arraiz GA, Wigle DT, Mao Y. 1992. Risk assessment of physical activity and physical fitness in the Canada Health Survey Mortality Follow-up Study. *J Clin Epidemiol* 45:419–428.
- Arroll B, Beaglehole R. 1992. Does physical activity lower blood pressure: A review of the clinical trials. *J Clin Epidemiol* 45:439–447.

- Ascherio A, Rimm EB, Giovannucci EL, Colditz GA, Rosner B, Willett WC, Sacks F, Stampfer MJ. 1992. A prospective study of nutritional factors and hypertension among US men. *Circulation* 86:1475–1484.
- Ascherio A, Hennekens CH, Buring JE, Master C, Stampfer MJ, Willett WC. 1994. Trans-fatty acids intake and risk of myocardial infarction. *Circulation* 89:94–101.
- Ascherio A, Rimm EB, Stampfer MJ, Giovannucci EL, Willett WC. 1995. Dietary intake of marine n-3 fatty acids, fish intake, and the risk of coronary disease among men. *N Engl J Med* 332:977–982.
- Ascherio A, Hennekens C, Willett WC, Sacks F, Rosner B, Manson J, Witteman J, Stampfer MJ. 1996a. Prospective study of nutritional factors, blood pressure, and hypertension among US women. *Hypertension* 27:1065–1072.
- Ascherio A, Rimm EB, Giovannucci EL, Spiegelman D, Stampfer M, Willett WC. 1996b. Dietary fat and risk of coronary heart disease in men: Cohort follow up study in the United States. *Br Med J* 313:84–90.
- Ascherio A, Katan MB, Zock PL, Stampfer MJ, Willett WC. 1999. Trans fatty acids and coronary heart disease. *N Engl J Med* 340:1994–1998.
- Astrup A. 1999. Macronutrient balances and obesity: The role of diet and physical activity. *Public Health Nutr* 2:341–347.
- Astrup A, Vrist E, Quaade F. 1990. Dietary fibre added to very low calorie diet reduces hunger and alleviates constipation. *Int J Obes* 14:105–112.
- Astrup A, Toubro S, Raben A, Skov AR. 1997. The role of low-fat diets and fat substitutes in body weight management: What have we learned from clinical studies? *J Am Diet Assoc* 97:S82–S87.
- Austin MA. 1989. Plasma triglyceride as a risk factor for coronary heart disease. The epidemiologic evidence and beyond. *Am J Epidemiol* 129:249–259.
- Austin MA, Rodriguez BL, McKnight B, McNeely MJ, Edwards KL, Curb DJ, Sharp DS. 2000. Low-density lipoprotein particle size, triglycerides, and high-density lipoprotein cholesterol as risk factors for coronary heart disease in older Japanese-American men. *Am J Cardiol* 86:412–416.
- Bainton D, Miller NE, Bolton CH, Yarnell JWG, Sweetnam PM, Baker IA, Lewis B, Elwood PC. 1992. Plasma triglyceride and high density lipoprotein cholesterol as predictors of ischaemic heart disease in British men. The Caerphilly and Speedwell Collaborative Heart Disease Studies. *Br Heart J* 68:60–66.
- Bakhit RM, Klein BP, Essex-Sorlie D, Ham JO, Erdman JW, Potter SM. 1994. Intake of 25 g of soybean protein with or without soybean fiber alters plasma lipids in men with elevated cholesterol concentrations. *J Nutr* 124:213–222.
- Ballor DL, Keesey RE. 1991. A meta-analysis of the factors affecting exercise-induced changes in body mass, fat mass and fat-free mass in males and females. *Int J Obes* 15:717–726.
- Barbone F, Austin H, Partridge EE. 1993. Diet and endometrial cancer: A case-control study. *Am J Epidemiol* 137:393–403.
- Baron JA, Schori A, Crow B, Carter R, Mann JI. 1986. A randomized controlled trial of low carbohydrate and low fat/high fiber diets for weight loss. *Am J Public Health* 76:1293–1296.
- Barrett-Connor E. 1989. Epidemiology, obesity, and non-insulin-dependent diabetes mellitus. *Epidemiol Rev* 11:172–181.
- Bartsch H, Nair J, Owen RW. 1999. Dietary polyunsaturated fatty acids and cancers of the breast and colorectum: Emerging evidence for their role as risk modifiers. *Carcinogenesis* 20:2209–2218.

- Batty D, Thune I. 2000. Does physical activity prevent cancer? Evidence suggests protection against colon cancer and probably breast cancer. *Br Med J* 321:1424–1425.
- Becker N, Illingworth R, Alaupovic P, Connor WE, Sundberg EE. 1983. Effects of saturated, monounsaturated, and ω-6 polyunsaturated fatty acids on plasma lipids, lipoproteins, and apoproteins in humans. *Am J Clin Nutr* 37:355–360.
- Behall KM. 1990. Effect of soluble fibers on plasma lipids, glucose tolerance and mineral balance. *Adv Exp Med Biol* 270:7–16.
- Bell EA, Castellanos VH, Pelkman CL, Thorwart ML, Rolls BJ. 1998. Energy density of foods affects energy intake in normal-weight women. *Am J Clin Nutr* 67:412–420.
- Benito R, Obrador A, Stiggebout A, Bosch FX, Mulet M, Muñoz N, Kaldor J. 1990. A population-based case-control study of colorectal cancer in Majorca. I. Dietary factors. *Int J Cancer* 45:69–76.
- Bergman BC, Butterfield GE, Wolfel EE, Lopaschuk GD, Casazza GA, Horning MA, Brooks GA. 1999. Muscle net glucose uptake and glucose kinetics after endurance training in men. *Am J Physiol* 277:E81–E92.
- Bergmann JF, Chassany O, Petit A, Triki R, Caulin C, Segrestaa JM. 1992. Correlation between echographic gastric emptying and appetite: Influence of psyllium. *Gut* 33:1042–1043.
- Billman GE, Kang JX, Leaf A. 1999. Prevention of sudden cardiac death by dietary pure ω-3 polyunsaturated fatty acids in dogs. *Circulation* 99:2452–2457.
- Birketvedt GS, Aaseth J, Florholmen JR, Ryttig K. 2000. Long term effect of fibre supplement and reduced energy intake on body weight and blood lipids in overweight subjects. *Acta Medica (Hradec Králové)* 43:129–132.
- Birt DF, Shull JD, Yaktine AL. 1999. Chemoprevention of cancer. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th ed. Baltimore, MD: Williams and Wilkins. Pp. 1263–1295.
- Björntorp P, Sjöström L, Sullivan L. 1979. The role of physical exercise in the management of obesity. In: Munro JF, ed. *The Treatment of Obesity*. Baltimore, MD: University Park Press. Pp. 123–138.
- Blair SN, Kohl HW, Barlow CE. 1993. Physical activity, physical fitness, and all-cause mortality in women: Do women need to be active? *J Am Coll Nutr* 12:368–371.
- Bolton-Smith C, Woodward M. 1994. Dietary composition and fat to sugar ratios in relation to obesity. *Int J Obes Relat Metab Disord* 18:820–828.
- Bonanome A, Grundy SM. 1988. Effect of dietary stearic acid on plasma cholesterol and lipoprotein levels. *N Engl J Med* 318:1244–1248.
- Bonithon-Kopp C, Kronborg O, Giacosa A, Råth U, Faivre J. 2000. Calcium and fibre supplementation in prevention of colorectal adenoma recurrence: A randomised intervention trial. *Lancet* 356:1300–1306.
- Borkman M, Campbell LV, Chisholm DJ, Storlien LH. 1991. Comparison of the effects on insulin sensitivity of high carbohydrate and high fat diets in normal subjects. *J Clin Endocrinol Metab* 72:432–437.
- Bowman SA. 1999. Diets of individuals based on energy intakes from added sugars. *Fam Econ Nutr Rev* 12:31–38.
- Bray GA, Popkin BM. 1998. Dietary fat intake does affect obesity! *Am J Clin Nutr* 68:1157–1173.
- Brooks GA, Fahey TD, White TP, Baldwin KM. 2000. *Exercise Physiology: Human Bioenergetics and its Applications*, 3rd ed. Mountain View, CA: Mayfield Publishing.

- Brussaard JH, Katan MB, Groot PHE, Havekes LM, Hautvast JGAJ. 1982. Serum lipoproteins of healthy persons fed a low-fat diet or a polyunsaturated fat diet for three months. A comparison of two cholesterol-lowering diets. *Atherosclerosis* 42:205–219.
- Bruunsgaard H, Jensen MS, Schjerling P, Halkjaer-Kristensen J, Ogawa K, Skinhøj P, Pedersen BK. 1999. Exercise induces recruitment of lymphocytes with an activated phenotype and short telomeres in young and elderly humans. *Life Sci* 65:2623–2633.
- Calviello G, Palozza P, Piccioni E, Maggiano N, Frattucci A, Franceschelli P, Baroli GM. 1998. Dietary supplementation with eicosapentaenoic and docosahexaenoic acid inhibits growth of Morris hepatocarcinoma 3924A in rats: Effects on proliferation and apoptosis. *Int J Cancer* 75:699–705.
- Carlson LA, Böttiger LE. 1972. Ischaemic heart-disease in relation to fasting values of plasma triglycerides and cholesterol. Stockholm Prospective Study. *Lancet* 1:865–868.
- Carroll KK. 1998. Obesity as a risk factor for certain types of cancer. *Lipids* 33:1055–1059.
- Castelli WP. 1996. Lipids, risk factors and ischaemic heart disease. *Atherosclerosis* 124:S1–S9.
- Caygill CPJ, Hill MJ. 1995. Fish, n-3 fatty acids and human colorectal and breast cancer mortality. *Eur J Cancer Prev* 4:329–332.
- Caygill CPJ, Charlett A, Hill MJ. 1996. Fat, fish, fish oil and cancer. *Br J Cancer* 74:159–164.
- Clarke R, Frost C, Collins R, Appleby P, Peto R. 1997. Dietary lipids and blood cholesterol: Quantitative meta-analysis of metabolic ward studies. *Br Med J* 314:112–117.
- Cohen JC, Schall R. 1988. Reassessing the effects of simple carbohydrates on the serum triglyceride responses to fat meals. *Am J Clin Nutr* 48:1031–1034.
- Colbert LH, Hartman TJ, Malila N, Limburg PJ, Pietinen P, Virtamo J, Taylor PR, Albanes D. 2001. Physical activity in relation to cancer of the colon and rectum in a cohort of male smokers. *Cancer Epidemiol Biomarkers Prev* 10:265–268.
- Colditz GA, Willett WC, Stampfer MJ, Manson JE, Hennekens CH, Arky RA, Speizer FE. 1990. Weight as a risk factor for clinical diabetes in women. *Am J Epidemiol* 132:501–513.
- Colditz GA, Manson JE, Stampfer MJ, Rosner B, Willett WC, Speizer FE. 1992. Diet and risk of clinical diabetes in women. *Am J Clin Nutr* 55:1018–1023.
- Coulston AM, Liu GC, Reaven GM. 1983. Plasma glucose, insulin and lipid responses to high-carbohydrate low-fat diets in normal humans. *Metabolism* 32:52–56.
- Daviglus ML, Stamler J, O'renica AJ, Dyer AR, Liu K, Greenland P, Walsh MK, Morris D, Shekelle RB. 1997. Fish consumption and the 30-year risk of fatal myocardial infarction. *N Engl J Med* 336:1046–1053.
- Davy KP, Horton T, Davy BM, Bessessen D, Hill JO. 2001. Regulation of macronutrient balance in healthy young and older men. *Int J Obes Relat Metab Disord* 25:1497–1502.
- De Caterina R, Liao JK, Libby P. 2000. Fatty acid modulation of endothelial activation. *Am J Clin Nutr* 71:213–223.
- Denke MA. 1994. Effects of cocoa butter on serum lipids in humans: Historical highlights. *Am J Clin Nutr* 60:1014S–1016S.

- Depaola DP, Faine MP, Palmer CA. 1999. Nutrition in relation to dental medicine. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th ed. Baltimore, MD: Williams and Wilkins. Pp. 1099–1124.
- Després J-P, Tremblay A, Nadeau A, Bouchard C. 1988. Physical training and changes in regional adipose tissue distribution. *Acta Med Scand Suppl* 723: 205–212.
- De Stefani E, Deneo-Pellegrini H, Mendilaharsu M, Carzoglio JC, Ronco A. 1997a. Dietary fat and lung cancer: A case-control study in Uruguay. *Cancer Causes Control* 8:913–921.
- De Stefani E, Mendilaharsu M, Deneo-Pellegrini H, Ronco A. 1997b. Influence of dietary levels of fat, cholesterol, and calcium on colorectal cancer. *Nutr Cancer* 29:83–89.
- Diabetes Prevention Program Research Group. 2002. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 346:393–403.
- Dolecek TA. 1992. Epidemiological evidence of relationships between dietary polyunsaturated fatty acids and mortality in the Multiple Risk Factor Intervention Trial. *Proc Soc Exp Med Biol* 200:177–182.
- Dreon DM, Frey-Hewitt B, Ellsworth N, Williams PT, Terry RB, Wood PD. 1988. Dietary fat:carbohydrate ratio and obesity in middle-aged men. *Am J Clin Nutr* 47:995–1000.
- Dunnigan MG, Fyfe T, McKiddie MT, Crosbie SM. 1970. The effects of isocaloric exchange of dietary starch and sucrose on glucose tolerance, plasma insulin and serum lipids in man. *Clin Sci* 38:1–9.
- Eliasson K, Ryttig KR, Hylander B, Rossner S. 1992. A dietary fibre supplement in the treatment of mild hypertension. A randomized, double-blind, placebo-controlled trial. *J Hypertens* 10:195–199.
- El-Sayed MS. 1996. Effects of exercise on blood coagulation, fibrinolysis and platelet aggregation. *Sports Med* 22:282–298.
- Fasching P, Ratheiser K, Schneeweiss B, Rohac M, Nowotny P, Waldhausl W. 1996. No effect of short-term dietary supplementation of saturated and poly- and monounsaturated fatty acids on insulin secretion and sensitivity in healthy men. *Ann Nutr Metab* 40:116–122.
- Fehily AM, Phillips KM, Yarnell JWG. 1984. Diet, smoking, social class, and body mass index in the Caerphilly Heart Disease Study. *Am J Clin Nutr* 40:827–833.
- Feskens EJM, Loeber JG, Kromhout D. 1994. Diet and physical activity as determinants of hyperinsulinemia: The Zutphen Elderly Study. *Am J Epidemiol* 140: 350–360.
- Frankel S, Gunnell DJ, Peters TJ, Maynard M, Smith GD. 1998. Childhood energy intake and adult mortality from cancer: The Boyd Orr Cohort Study. *Br Med J* 316:499–504.
- French SA, Fulkerson JA, Story M. 2000. Increasing weight-bearing physical activity and calcium intake for bone mass growth in children and adolescents: A review of intervention trials. *Prev Med* 31:722–731.
- Friday KE, Childs MT, Tsunehara CH, Fujimoto WY, Bierman EL, Ensinck JW. 1989. Elevated plasma glucose and lowered triglyceride levels from omega-3 fatty acid supplementation in type II diabetes. *Diabetes Care* 12:276–281.
- Frost G, Leeds A, Trew G, Margara R, Dornhorst A. 1998. Insulin sensitivity in women at risk of coronary heart disease and the effect of a low glycemic diet. *Metabolism* 47:1245–1251.

- Fuchs CS, Giovannucci EL, Colditz GA, Hunter DJ, Stampfer MJ, Rosner B, Speizer FE, Willett WC. 1999. Dietary fiber and the risk of colorectal cancer and adenoma in women. *N Engl J Med* 340:169–176.
- Fukagawa NK, Anderson JW, Hageman G, Young VR, Minaker KL. 1990. High-carbohydrate, high-fiber diets increase peripheral insulin sensitivity in healthy young and old adults. *Am J Clin Nutr* 52:524–528.
- Gardner CD, Kraemer HC. 1995. Monounsaturated versus polyunsaturated dietary fat and serum lipids. A meta-analysis. *Arterioscler Thromb Vasc Biol* 15:1917–1927.
- Gartside PS, Glueck CJ. 1993. Relationship of dietary intake to hospital admission for coronary heart and vascular disease: The NHANES II National Probability Study. *J Am Coll Nutr* 6:676–684.
- Gerber M. 1998. Fibre and breast cancer. *Eur J Cancer Prev* 7:S63–S67.
- Gibson SA. 1993. Consumption and sources of sugars in the diets of British schoolchildren: Are high-sugar diets nutritionally inferior? *J Hum Nutr Diet* 6:355–371.
- Gibson SA. 1996a. Are diets high in non-milk extrinsic sugars conducive to obesity? An analysis from the Dietary and Nutritional Survey of British Adults. *J Hum Nutr Diet* 9:283–292.
- Gibson SA. 1996b. Are high-fat, high-sugar foods and diets conducive to obesity? *Int J Food Sci Nutr* 47:405–415.
- Gibson SA. 1997. Non-milk extrinsic sugars in the diets of pre-school children: Association with intakes of micronutrients, energy, fat and NSP. *Br J Nutr* 78:367–378.
- Giovannucci E, Willett WC. 1994. Dietary factors and risk of colon cancer. *Ann Med* 26:443–452.
- Giovannucci E, Stampfer MJ, Colditz G, Rimm EB, Willett WC. 1992. Relationship of diet to risk of colorectal adenoma in men. *J Natl Cancer Inst* 84:91–98.
- Giovannucci E, Rimm EB, Colditz GA, Stampfer MJ, Ascherio A, Chute CC, Willett WC. 1993. A prospective study of dietary fat and risk of prostate cancer. *J Natl Cancer Inst* 85:1571–1579.
- Giovannucci E, Rimm EB, Stampfer MJ, Colditz GA, Ascherio A, Willett WC. 1994. Intake of fat, meat, and fiber in relation to risk of colon cancer in men. *Cancer Res* 54:2390–2397.
- Glauber H, Wallace P, Griver K, Brechtel G. 1988. Adverse metabolic effect of omega-3 fatty acids in non-insulin-dependent diabetes mellitus. *Ann Intern Med* 108:663–668.
- Goodman MT, Kolonel LN, Yoshizawa CN, Hankin JH. 1988. The effect of dietary cholesterol and fat on the risk of lung cancer in Hawaii. *Am J Epidemiol* 128:1241–1255.
- Goodman MT, Wilkens LR, Hankin JH, Lyu L-C, Wu AH, Kolonel LN. 1997. Association of soy and fiber consumption with the risk of endometrial cancer. *Am J Epidemiol* 146:294–306.
- Goran MI. 2001. Metabolic precursors and effects of obesity in children: A decade of progress, 1990–1999. *Am J Clin Nutr* 73:158–171.
- Gordon T, Castelli WP, Hjortland MC, Kannel WB, Dawber TR. 1977. High density lipoprotein as a protective factor against coronary heart disease. The Framingham Study. *Am J Med* 62:707–714.
- Gordon T, Kagan A, Garcia-Palmieri M, Kannel WB, Zukel WJ, Tillotson J, Sorlie P, Hjortland M. 1981. Diet and its relation to coronary heart disease and death in three populations. *Circulation* 63:500–515.

- Grammatikos SI, Subbaiah PV, Victor TA, Miller WM. 1994. *n*-3 And *n*-6 fatty acid processing and growth effects in neoplastic and non-cancerous human mammary epithelial cell lines. *Br J Cancer* 70:219–227.
- Gray GE, Pike MC, Henderson BE. 1979. Breast-cancer incidence and mortality rates in different countries in relation to known risk factors and dietary practices. *Br J Cancer* 39:1–7.
- Hallfrisch J, Scholfield DJ, Behall KM. 1995. Diets containing soluble oat extracts improve glucose and insulin responses of moderately hypercholesterolemic men and women. *Am J Clin Nutr* 61:379–384.
- Hambrecht R, Wolf A, Gielen S, Linke A, Hofer J, Erbs S, Schoene N, Schuler G. 2000. Effect of exercise on coronary endothelial function in patients with coronary artery disease. *N Engl J Med* 342:454–460.
- Harker LA, Kelly AB, Hanson SR, Krupski W, Bass A, Osterud B, Fitzgerald GA, Goodnight SH, Connor WE. 1993. Interruption of vascular thrombus formation and vascular lesion formation by dietary *n*-3 fatty acids in fish oil in non-human primates. *Circulation* 87:1017–1029.
- Harris PJ, Ferguson LR. 1993. Dietary fibre: Its composition and role in protection against colorectal cancer. *Mutat Res* 290:97–110.
- Harris WS. 1989. Fish oils and plasma lipid and lipoprotein metabolism in humans: A critical review. *J Lipid Res* 30:785–807.
- Hegsted DM. 1986. Serum-cholesterol response to dietary cholesterol: A re-evaluation. *Am J Clin Nutr* 44:299–305.
- Hegsted DM, Ausman LM, Johnson JA, Dallal GE. 1993. Dietary fat and serum lipids: An evaluation of the experimental data. *Am J Clin Nutr* 57:875–883.
- Helmrich SP, Ragland DR, Leung RW, Paffenbarger RS. 1991. Physical activity and reduced occurrence of non-insulin-dependent diabetes mellitus. *N Engl J Med* 325:147–152.
- Hennekens CH. 1998. Risk factors for coronary heart disease in women. *Cardiol Clin* 16:1–8.
- Hill MJ. 1997. Cereals, cereal fibre and colorectal cancer risk: A review of the epidemiological literature. *Eur J Cancer Prev* 6:219–225.
- Hinkle LE, Thaler HT, Merke DP, Renier-Berg D, Morton NE. 1988. The risk factors for arrhythmic death in a sample of men followed for 20 years. *Am J Epidemiol* 127:500–515.
- Hoff G, Moen IE, Trygg K, Frølich W, Sauar J, Vatn M, Gjone E, Larsen S. 1986. Epidemiology of polyps in the rectum and sigmoid colon. Evaluation of nutritional factors. *Scand J Gastroenterol* 21:199–204.
- Hopkins PN. 1992. Effects of dietary cholesterol on serum cholesterol: A meta-analysis and review. *Am J Clin Nutr* 55:1060–1070.
- Horton ES. 1986. Exercise and physical training: Effects on insulin sensitivity and glucose metabolism. *Diabetes Metab Rev* 2:1–17.
- Horton ES. 1991. Exercise and decreased risk of NIDDM. *N Engl J Med* 325:196–197.
- Howard BV, Abbott WGH, Swinburn BA. 1991. Evaluation of metabolic effects of substitution of complex carbohydrates for saturated fat in individuals with obesity and NIDDM. *Diabetes Care* 14:786–795.
- Howe GR, Friedenreich CM, Jain M, Miller AB. 1991. A cohort study of fat intake and risk of breast cancer. *J Natl Cancer Inst* 83:336–340.

- Howe GR, Aronson KJ, Benito E, Castelleto R, Cornée J, Duffy S, Gallagher RP, Iscovich JM, Deng-ao J, Kaaks R, Kune GA, Kune S, Lee HP, Lee M, Miller AB, Peters RK, Potter JD, Riboli E, Slattery ML, Trichopoulos D, Tuyns A, Tzonou A, Watson LF, Whittemore AS, Wu-Willimas AH, Shu Z. 1997. The relationship between dietary fat intake and risk of colorectal cancer: Evidence from the combined analysis of 13 case-control studies. *Cancer Causes Control* 8:215–228.
- Howell WH, McNamara DJ, Tosca MA, Smith BT, Gaines JA. 1997. Plasma lipid and lipoprotein responses to dietary fat and cholesterol: A meta-analysis. *Am J Clin Nutr* 65:1747–1764.
- Hu FB, Stampfer MJ, Manson JE, Rimm E, Colditz GA, Rosner BA, Hennekens CH, Willett WC. 1997. Dietary fat intake and the risk of coronary heart disease in women. *N Engl J Med* 337:1491–1499.
- Hu FB, Stampfer MJ, Manson JE, Rimm E, Colditz GA, Speizer FE, Hennekens CH, Willett WC. 1999a. Dietary protein and risk of ischemic heart disease in women. *Am J Clin Nutr* 70:221–227.
- Hu FB, Stampfer MJ, Rimm EB, Manson JE, Ascherio A, Colditz GA, Rosner BA, Spiegelman D, Speizer FE, Sacks FM, Hennekens CH, Willett WC. 1999b. A prospective study of egg consumption and risk of cardiovascular disease in men and women. *J Am Med Assoc* 281:1387–1394.
- Hulley SB, Rosenman RH, Bawol RD, Brand RJ. 1980. Epidemiology as a guide to clinical decisions. The association between triglyceride and coronary heart disease. *N Engl J Med* 302:1383–1389.
- Hunter DJ, Spiegelman D, Adami H-O, Beeson L, van den Brandt PA, Folsom AR, Fraser GE, Goldbohm A, Graham S, Howe GR, Kushi LH, Marshall JR, McDermott A, Miller AB, Speizer FE, Wolk A, Yaun S-S, Willett W. 1996. Cohort studies of fat intake and the risk of breast cancer—A pooled analysis. *N Engl J Med* 334:356–361.
- Hurley BR, Roth SM. 2000. Strength training in the elderly. Effects on risk factors for age-related diseases. *Sports Med* 30:249–268.
- Huttunen JK, Länsimies E, Voutilainen E, Ehnholm C, Hietanen E, Penttilä I, Siiton O, Rauranaa R. 1979. Effect of moderate physical exercise on serum lipoproteins. A controlled clinical trial with special reference to serum high-density lipoproteins. *Circulation* 60:1220–1229.
- IARC (International Agency for Research on Cancer). 2002. *IARC Handbooks of Cancer Prevention. Volume 6: Weight Control and Physical Activity*. Lyon, France: IARC Press.
- Jacobs DR, Meyer KA, Kushi LH, Folsom AR. 1998. Whole-grain intake may reduce the risk of ischemic heart disease death in postmenopausal women: The Iowa Women's Health Study. *Am J Clin Nutr* 68:248–257.
- Jacobs LR. 1986. Relationship between dietary fiber and cancer: Metabolic, physiologic, and cellular mechanisms. *Proc Soc Exp Biol Med* 183:299–310.
- James MJ, Gibson RA, Cleland LG. 2000. Dietary polyunsaturated fatty acids and inflammatory mediator production. *Am J Clin Nutr* 71:343S–348S.
- Jenkins DJA, Wolever TMS, Leeds AR, Gassull MA, Haisman P, Dilawari J, Goff DV, Metz GL, Alberti KGMM. 1978. Dietary fibres, fibre analogues, and glucose tolerance: Importance of viscosity. *Br Med J* 1:1392–1394.
- Jenkins DJA, Wolever TMS, Buckley G, Lam KY, Giudici S, Kalmusky J, Jenkins AL, Patten RL, Bird J, Wong GS, Josse RG. 1988. Low-glycemic-index starchy food in the diabetic diet. *Am J Clin Nutr* 48:248–254.

- Jeppesen J, Schaaf P, Jones C, Zhou M-Y, Chen Y-DI, Reaven GM. 1997. Effects of low-fat, high-carbohydrate diets on risk factors for ischemic heart disease in postmenopausal women. *Am J Clin Nutr* 65:1027–1033.
- Johnson RK. 2000. What are people really eating and why does it matter? *Nutr Today* 35:40–45.
- Jones DY, Schatzkin A, Green SB, Block G, Brinton LA, Ziegler RG, Hoover R, Taylor PR. 1987. Dietary fat and breast cancer in the National Health and Nutrition Examination Survey I. Epidemiologic follow-up study. *J Natl Cancer Inst* 79:465–471.
- Jousilahti P, Vartiainen E, Pekkanen J, Tuomilehto J, Sundvall J, Puska P. 1998. Serum cholesterol distribution and coronary heart disease risk. Observations and predictions among middle-aged population in eastern Finland. *Circulation* 97:1087–1094.
- Kaizer L, Boyd NF, Kriukov V, Tritchler D. 1989. Fish consumption and breast cancer risk: An ecologic study. *Nutr Cancer* 12:61–68.
- Kang JX, Leaf A. 1996. Antiarrhythmic effects of polyunsaturated fatty acids: Recent studies. *Circulation* 94:1774–1780.
- Kannel WB, Sorlie P. 1979. Some health benefits of physical activity. The Framingham Study. *Arch Intern Med* 139:857–861.
- Kannel WB, Belanger A, D'Agostino R, Israel I. 1986. Physical activity and physical demand on the job and risk of cardiovascular disease and death: The Framingham Study. *Am Heart J* 112:820–825.
- Kasim SE, Stern B, Khilnani S, McLin P, Baciorowski S, Jen K-LC. 1988. Effects of omega-3 fish oils on lipid metabolism, glycemic control, and blood pressure in type II diabetic patients. *J Clin Endocrinol Metab* 67:1–5.
- Kasim SE, Martino S, Kim P-N, Khilnani S, Boomer A, Depper J, Reading BA, Heilbrun LK. 1993. Dietary and anthropometric determinants of plasma lipoproteins during a long-term low-fat diet in healthy women. *Am J Clin Nutr* 57:146–153.
- Kendall A, Levitsky DA, Strupp BJ, Lissner L. 1991. Weight loss on a low-fat diet: Consequence of the imprecision of the control of food intake in humans. *Am J Clin Nutr* 53:1124–1129.
- Keys A, Menotti A, Karvonen MJ, Aravanis C, Blackburn H, Buzina R, Djordjevic BS, Dontas AS, Fidanza F, Keys MH, Kromhout D, Nedeljkovic S, Punsar S, Seccareccia F, Toshima H. 1986. The diet and 15-year death rate in the seven countries study. *Am J Epidemiol* 124:903–915.
- Khan K, McKay HA, Haapasalo H, Bennell KL, Forwood MR, Kannus P, Wark JD. 2000. Does childhood and adolescence provide a unique opportunity for exercise to strengthen the skeleton? *J Sci Med Sport* 3:150–164.
- King H, Taylor R, Zimmet P, Pargeter K, Raper LR, Beriki T, Tekanene J. 1984. Non-insulin-dependent diabetes (NIDDM) in a newly independent Pacific nation: The Republic of Kiribati. *Diabetes Care* 7:409–415.
- Klurfeld DM. 1992. Dietary fiber-mediated mechanisms in carcinogenesis. *Cancer Res* 52:2055S–2059S.
- Koutsari C, Karpe F, Humphreys SM, Frayn KN, Hardman AE. 2001. Exercise prevents the accumulation of triglyceride-rich lipoproteins and their remnants seen when changing to a high-carbohydrate diet. *Arterioscler Thromb Vasc Biol* 21:1520–1525.
- Krauss RM, Drewn DM. 1995. Low-density-lipoprotein subclasses and response to a low-fat diet in healthy men. *Am J Clin Nutr* 62:478S–487S.

- Kromhout D, de Lezenne Coulander C. 1984. Diet, prevalence and 10-year mortality from coronary heart disease in 871 middle-aged men. *Am J Epidemiol* 119:733–741.
- Kromhout D, Bosschieter EB, de Lezenne Coulander C. 1985. The inverse relation between fish consumption and 20-year mortality from coronary heart disease. *N Engl J Med* 312:1205–1209.
- Kromhout D, Feskens EJM, Bowles CH. 1995. The protective effect of a small amount of fish on coronary heart disease mortality in an elderly population. *Int J Epidemiol* 24:340–345.
- Kushi LH, Lew RA, Stare FJ, Ellison CR, el Lozy M, Bourke G, Daly L, Graham I, Hickey N, Mulcahy R, Kevaney J. 1985. Diet and 20-year mortality from coronary heart disease. The Ireland-Boston Diet-Heart Study. *N Engl J Med* 312:811–818.
- Kushi LH, Sellers TA, Potter JD, Nelson CL, Munger RG, Kaye SA, Folsom AR. 1992. Dietary fat and postmenopausal breast cancer. *J Natl Cancer Inst* 84:1092–1099.
- Lai PBS, Ross JA, Fearson KCH, Anderson JD, Carter DC. 1996. Cell cycle arrest and induction of apoptosis in pancreatic cancer cells exposed to eicosapentaenoic acid in vitro. *Br J Cancer* 74:1375–1383.
- Lanza E. 1990. National Cancer Institute Satellite Symposium on Fiber and Colon Cancer. In: Kritchevsky D, Bonfield C, Anderson JW, eds. *Dietary Fiber: Chemistry, Physiology, and Health Effects*. New York: Plenum Press. Pp. 383–387.
- Layne JE, Nelson ME. 1999. The effects of progressive resistance training on bone density: A review. *Med Sci Sports Exerc* 21:25–30.
- Leclerc I, Davignon I, Lopez D, Garrel DR. 1993. No change in glucose tolerance and substrate oxidation after a high-carbohydrate, low-fat diet. *Metabolism* 42:365–370.
- Lewis CJ, Park YK, Dexter PB, Yetley EA. 1992. Nutrient intakes and body weights of persons consuming high and moderate levels of added sugars. *J Am Diet Assoc* 92:708–713.
- Liljeberg HGM, Åkerberg AKE, Björck IME. 1999. Effect of the glycemic index and content of indigestible carbohydrates of cereal-based breakfast meals on glucose tolerance at lunch in healthy subjects. *Am J Clin Nutr* 69:647–655.
- Lindsted KD, Tonstad S, Kuzma JW. 1991. Self-report of physical activity and patterns of mortality in Seventh-day Adventist men. *J Clin Epidemiol* 44:355–364.
- Lissner L, Heitmann BL. 1995. Dietary fat and obesity: Evidence from epidemiology. *Eur J Clin Nutr* 49:79–90.
- Lissner L, Levitsky DA, Strupp BJ, Kalkwarf HJ, Roe DA. 1987. Dietary fat and the regulation of energy intake in human subjects. *Am J Clin Nutr* 46:886–892.
- Lissner L, Helgesson Ö, Bengtsson C, Lapidus L, Hultén B, Branehög I, Holmberg E. 1992. Energy and macronutrient intake in relation to cancer incidence among Swedish women. *Eur J Clin Nutr* 46:501–507.
- Lissner L, Heitmann BL, Bengtsson C. 2000. Population studies of diet and obesity. *Br J Nutr* 83:S21–S24.
- Little J, Logan RFA, Hawtin PG, Hardcastle JD, Turner ID. 1993. Colorectal adenomas and diet: A case-control study of subjects participating in the Nottingham Faecal Occult Blood Screening Programme. *Br J Cancer* 67:177–84.

- Lundgren H, Bengtsson C, Blohmé G, Isaksson B, Lapidus L, Lenner RA, Saaek A, Winther E. 1989. Dietary habits and incidence of noninsulin-dependent diabetes mellitus in a population study of women in Gothenburg, Sweden. *Am J Clin Nutr* 49:708–712.
- Lyon JL, Mahoney AW, West DW, Gardner JW, Smith KR, Sorenson AW, Stanish W. 1987. Energy intake: Its relationship to colon cancer risk. *J Natl Cancer Inst* 78:853–861.
- Macquart-Moulin G, Riboli E, Cornée J, Charnay B, Berthezène P, Day N. 1986. Case-control study on colorectal cancer and diet in Marseilles. *Int J Cancer* 38:183–191.
- Macquart-Moulin G, Riboli E, Cornée J, Kaaks R, Berthezène P. 1987. Colorectal polyps and diet: A case-control study in Marseilles. *Int J Cancer* 40:179–188.
- Madsen KL, Adams WC, Van Loan MD. 1998. Effects of physical activity, body weight and composition, and muscular strength on bone density in young women. *Med Sci Sports Exerc* 30:114–120.
- Mann JI, Watermeyer GS, Manning EB, Randles J, Truswell AS. 1973. Effects on serum lipids of different dietary fats associated with a high sucrose diet. *Clin Sci* 44:601–604.
- Mann JI, Appleby PN, Key TJ, Thorogood M. 1997. Dietary determinants of ischaemic heart disease in health conscious individuals. *Heart* 78:450–455.
- Manson JE, Rimm EB, Stampfer MJ, Colditz GA, Willett WC, Krolewski AS, Rosner B, Hennekens CH, Speizer FE. 1991. Physical activity and incidence of non-insulin-dependent diabetes mellitus in women. *Lancet* 338:774–778.
- Manson JE, Nathan DM, Krolewski AS, Stampfer MJ, Willett WC, Hennekens CH. 1992. A prospective study of exercise and incidence of diabetes among US male physicians. *J Am Med Assoc* 268:63–67.
- Marckmann P, Raben A, Astrup A. 2000. Ad libitum intake of low-fat diets rich in either starchy foods or sucrose: Effects on blood lipids, factor VII coagulant activity, and fibrinogen. *Metabolism* 49:731–735.
- Marniemi J, Seppänen A, Hakala P. 1990. Long-term effects on lipid metabolism of weight reduction on lactovegetarian and mixed diet. *Int J Obes* 14:113–125.
- Marshall JA, Hamman RF, Baxter J. 1991. High-fat, low-carbohydrate diet and the etiology of non-insulin-dependent diabetes mellitus: The San Luis Valley Diabetes Study. *Am J Epidemiol* 134:590–603.
- Masironi R. 1970. Dietary factors and coronary heart disease. *Bull World Health Organ* 42:103–114.
- Mayer-Davis EJ, Monaco JH, Hoen HM, Carmichael S, Vitolins MZ, Rewers MJ, Haffner SM, Ayad MF, Bergman RN, Karter AJ. 1997. Dietary fat and insulin sensitivity in a triethnic population: The role of obesity. The Insulin Resistance Arteriosclerosis Study (IRAS). *Am J Clin Nutr* 65:79–87.
- Mayer-Davis EJ, D'Agostino R, Karter AJ, Haffner SM, Rewers MJ, Saad M, Bergman RN. 1998. Intensity and amount of physical activity in relation to insulin sensitivity. The Insulin Resistance Atherosclerosis Study. *J Am Med Assoc* 279:669–674.
- Mazzeo RS, Rajkumar C, Rolland J, Blaher B, Jennings G, Esler M. 1998. Immune response to a single bout of exercise in young and elderly subjects. *Mech Ageing Dev* 100:121–132.
- McLennan PL. 1993. Relative effects of dietary saturated, monounsaturated, and polyunsaturated fatty acids on cardiac arrhythmias in rats. *Am J Clin Nutr* 57:207–212.

- Meinertz H, Nilausen K, Faergeman O. 1989. Soy protein and casein in cholesterol-enriched diets: Effects on plasma lipoproteins in normolipidemic subjects. *Am J Clin Nutr* 50:786–793.
- Mensink RP, Katan MB. 1992. Effect of dietary fatty acids on serum lipids and lipoproteins. A meta-analysis of 27 trials. *Arterioscler Thromb* 12:911–919.
- Mensink RP, Temme EH, Hornstra G. 1994. Dietary saturated and trans fatty acids and lipoprotein metabolism. *Ann Med* 26:461–464.
- Meyer KA, Kushi LH, Jacobs DR, Slavin J, Sellers TA, Folsom AR. 2000. Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. *Am J Clin Nutr* 71:921–930.
- Michaud DS, Giovannucci E, Willett WC, Colditz GA, Stampfer MJ, Fuchs CS. 2001. Physical activity, obesity, height, and the risk of pancreatic cancer. *J Am Med Assoc* 286:921–929.
- Miller AB, Kelly A, Choi NW, Matthews V, Morgan RW, Munan L, Burch JD, Feather J, Howe GR, Jain M. 1978. A study of diet and breast cancer. *Am J Epidemiol* 107:499–509.
- Miller WC, Lindeman AK, Wallace J, Niederpruem M. 1990. Diet composition, energy intake, and exercise in relation to body fat in men and women. *Am J Clin Nutr* 52:426–430.
- Morris MC, Sacks F, Rosner B. 1993. Does fish oil lower blood pressure? A meta-analysis of controlled trials. *Circulation* 88:523–533.
- Must A, Lipman RD. 1999. Childhood energy intake and cancer mortality in adulthood. *Nutr Rev* 57:21–24.
- Neaton JD, Wentworth D. 1992. Serum cholesterol, blood pressure, cigarette smoking, and death from coronary heart disease. Overall findings and differences by age for 316,099 white men. *Arch Intern Med* 152:56–64.
- Neugut AI, Garbowski GC, Lee WC, Murray T, Nieves JW, Forde KA, Treat MR, Waye JD, Fenoglio-Preiser C. 1993. Dietary risk factors for the incidence and recurrence of colorectal adenomatous polyps. A case-control study. *Ann Intern Med* 118:91–95.
- NHLBI/NIDDK (National Heart, Lung, and Blood Institute/National Institute of Diabetes and Digestive and Kidney Diseases). 1998. *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. The Evidence Report*. NIH Publication No. 98-4083. Bethesda, MD: National Institutes of Health.
- Nikkilä EA, Taskinen M-R, Rehunen S, Häkkinen M. 1978. Lipoprotein lipase activity in adipose tissue and skeletal muscle of runners: Relation to serum lipoproteins. *Metabolism* 27:1661–1671.
- Obarzanek E, Velletri PA, Cutler JA. 1996. Dietary protein and blood pressure. *J Am Med Assoc* 275:1598–1603.
- Paffenbarger RS, Hyde RT, Jung DL, Wing AL. 1984. Epidemiology of exercise and coronary heart disease. *Clin Sports Med* 3:297–318.
- Parker DR, Weiss ST, Troisi R, Cassano PA, Vokonas PS, Landsberg L. 1993. Relationship of dietary saturated fatty acids and body habitus to serum insulin concentrations: The Normative Aging Study. *Am J Clin Nutr* 58:129–136.
- Parks EJ, Hellerstein MK. 2000. Carbohydrate-induced hypertriglycerolemia: Historical perspective and review of biological mechanisms. *Am J Clin Nutr* 71:412–433.
- Parmley WW. 1997. Nonlipoprotein risk factors for coronary heart disease: Evaluation and management. *Am J Med* 102:7–14.

- Pietinen P, Rimm EB, Korhonen P, Hartman AM, Willett WC, Albanes D, Virtamo J. 1996. Intake of dietary fiber and risk of coronary heart disease in a cohort of Finnish men. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. *Circulation* 94:2720–2727.
- Pietinen P, Ascherio A, Korhonen P, Hartman AM, Willett WC, Albanes D, Virtamo J. 1997. Intake of fatty acids and risk of coronary heart disease in a cohort of Finnish men. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. *Am J Epidemiol* 145:876–887.
- Pi-Sunyer FX, Woo R. 1985. Effect of exercise on food intake in human subjects. *Am J Clin Nutr* 42:983–990.
- Platz EA, Giovannucci E, Rimm EB, Rickett HRH, Stampfer MJ, Colditz GA, Willett WC. 1997. Dietary fiber and distal colorectal adenoma in men. *Cancer Epidemiol Biomarkers Prev* 6:661–670.
- Purnell JQ, Kahn SE, Albers JJ, Nevin DN, Brunzell JD, Schwartz RS. 2000. Effect of weight loss with reduction of intra-abdominal fat on lipid metabolism in older men. *J Clin Endocrinol Metab* 85:977–982.
- Ramon JM, Bou R, Romea S, Alkiza ME, Jacas M, Ribes J, Oromi J. 2000. Dietary fat intake and prostate cancer risk: A case-control study in Spain. *Cancer Causes Control* 11:679–685.
- Rath R, Mas'ek J, Kujalová V, Slabochová Z. 1974. Effect of a high sugar intake on some metabolic and regulatory indicators in young men. *Nahrung* 18:343–353.
- Reiser S, Hallfrisch J. 1987. Lipogenesis and blood lipids. In: *Metabolic Effects of Dietary Fructose*. Boca Raton, FL: CRC Press. Pp. 83–111.
- Reiser S, Hallfrisch J, Michaelis OE, Lazar FL, Martin RE, Prather ES. 1979. Isocaloric exchange of dietary starch and sucrose in humans. I. Effects on levels of fasting blood lipids. *Am J Clin Nutr* 32:1659–1669.
- Richter EA, Ruderman NB, Schneider SH. 1981. Diabetes and exercise. *Am J Med* 70:201–209.
- Rigaud D, Ryttig KR, Angel LA, Apfelbaum M. 1990. Overweight treated with energy restriction and a dietary fibre supplement: A 6-month randomized, double-blind, placebo-controlled trial. *Int J Obes* 14:763–769.
- Risch HA, Jain M, Marrett LD, Howe GR. 1994. Dietary fat intake and risk of epithelial ovarian cancer. *J Natl Cancer Inst* 86:1409–1415.
- Rivellese A, Riccardi G, Giacco A, Pacioni D, Genovese S, Mattioli PL, Mancini M. 1980. Effect of dietary fibre on glucose control and serum lipoproteins in diabetic patients. *Lancet* 2:447–450.
- Roberfroid M. 1993. Dietary fiber, inulin, and oligofructose: A review comparing their physiological effects. *Crit Rev Food Sci Nutr* 33:103–148.
- Roche HM, Zampelas A, Jackson KG, Williams CM, Gibney MJ. 1998. The effect of test meal monounsaturated fatty acid:saturated fatty acid ratio on postprandial lipid metabolism. *Br J Nutr* 79:419–424.
- Rohan TE, Howe GR, Friedenreich CM, Jain M, Miller AB. 1993. Dietary fiber, vitamins A, C, and E, and risk of breast cancer: A cohort study. *Cancer Causes Control* 4:29–37.
- Rose DP. 1997. Dietary fatty acids and cancer. *Am J Clin Nutr* 66:998S–1003S.
- Rose DP, Connolly JM. 2000. Regulation of tumor angiogenesis by dietary fatty acids and eicosanoids. *Nutr Cancer* 37:119–127.
- Rose DP, Boyar AP, Wynder EL. 1986. International comparisons of mortality rates for cancer of the breast, ovary, prostate, and colon, and per capita food consumption. *Cancer* 58:2363–2371.

## ONLINE REFERENCES

## 585

- Rose DP, Goldman M, Connolly JM, Strong LE. 1991. High-fiber diet reduces serum estrogen concentrations in premenopausal women. *Am J Clin Nutr* 54:520–525.
- Rössner S, von Zweigbergk D, Öhlin A, Ryttig K. 1987. Weight reduction with dietary fibre supplements. Results of two double-blind randomized studies. *Acta Med Scand* 222:83–88.
- Ryttig KR, Tellnes G, Haegh L, Boe E, Fagerthun H. 1989. A dietary fibre supplement and weight maintenance after weight reduction: A randomized, double-blind, placebo-controlled long-term trial. *Int J Obes* 13:165–171.
- Salmerón J, Ascherio A, Rimm EB, Colditz GA, Spiegelman D, Jenkins DJ, Stampfer MJ, Wing AL, Willett WC. 1997a. Dietary fiber, glycemic load, and risk of NIDDM in men. *Diabetes Care* 20:545–550.
- Salmerón J, Manson JE, Stampfer MJ, Colditz GA, Wing AL, Willett WC. 1997b. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. *J Am Med Assoc* 277:472–477.
- Saltzman E, Dallal GE, Roberts SB. 1997. Effect of high-fat and low-fat diets on voluntary energy intake and substrate oxidation: Studies in identical twins consuming diets matched for energy density, fiber, and palatability. *Am J Clin Nutr* 66:1332–1339.
- Sasaki S, Horacek M, Kesteloot H. 1993. An ecological study of the relationship between dietary fat intake and breast cancer mortality. *Prev Med* 22:187–202.
- Schatzkin A, Lanza E, Corle D, Lance P, Iber F, Caan B, Shike M, Weissfeld J, Burt R, Cooper MR, Kikendall JW, Cahill J. 2000. Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas. *N Engl J Med* 342:1149–1155.
- Schneider SH, Amorosa LF, Khachadurian AK, Ruderman NB. 1984. Studies on the mechanism of improved glucose control during regular exercise in type 2 (non-insulin-dependent) diabetes. *Diabetologia* 26:355–360.
- Schuurman AG, van den Brandt PA, Dorant E, Brants HAM, Goldbohm RA. 1999. Association of energy and fat intake with prostate carcinoma risk. Results from the Netherlands Cohort Study. *Cancer* 86:1019–1027.
- Shephard RJ. 1990. Physical activity and cancer. *Int J Sports Med* 11:413–420.
- Shephard RJ. 1996. Exercise and cancer: Linkages with obesity? *Crit Rev Food Sci Nutr* 36:321–339.
- Sonnenberg LM, Quatromoni PA, Gagnon DR, Cupples LA, Franz MM, Ordovas JM, Wilson PWF, Schaefer EJ, Millen BE. 1996. Diet and plasma lipids in women. II. Macronutrients and plasma triglycerides, high-density lipoprotein, and the ratio of total to high-density lipoprotein cholesterol in women: The Framingham Nutrition Studies. *J Clin Epidemiol* 49:665–672.
- Sorkin JD, Andres R, Muller DC, Baldwin HL, Fleg JL. 1992. Cholesterol as a risk factor for coronary heart disease in elderly men. The Baltimore Longitudinal Study of Aging. *Ann Epidemiol* 2:59–67.
- Stacpoole PW, Alig J, Ammon L, Crockett SE. 1989. Dose-response effects of dietary marine oil on carbohydrate and lipid metabolism in normal subjects and patients with hypertriglyceridemia. *Metabolism* 38:946–956.
- Stamler J. 1979. Population studies. In: Levy R, Rifkind B, Dennis B, Ernst N, eds. *Nutrition, Lipids, and Coronary Heart Disease*. New York: Raven Press. Pp. 25–88.
- Stamler J, Wentworth D, Neaton JD. 1986. Is relationship between serum cholesterol and risk of premature death from coronary heart disease continuous and graded? Findings in 356,222 primary screenees of the Multiple Risk Factor Intervention Trial (MRFIT). *J Am Med Assoc* 256:2823–2828.

- Stampfer MJ, Krauss RM, Ma J, Blanche PJ, Holl LG, Sacks FM, Hennekens CH. 1996. A prospective study of triglyceride level, low-density lipoprotein particle diameter, and risk of myocardial infarction. *J Am Med Assoc* 276:882–888.
- Stemmermann GN, Nomura AM, Heilbrun LK. 1985. Cancer risk in relation to fat and energy intake among Hawaii Japanese: A prospective study. *Princess Takamatsu Symp* 16:265–274.
- Straznicky NE, O'Callaghan CJ, Barrington VE, Louis WJ. 1999. Hypotensive effect of low-fat, high-carbohydrate diet can be independent of changes in plasma insulin concentrations. *Hypertension* 34:580–585.
- Stubbs RJ, Ritz P, Coward WA, Prentice AM. 1995. Covert manipulation of the ratio of dietary fat to carbohydrate and energy density: Effect on food intake and energy balance in free-living men eating ad libitum. *Am J Clin Nutr* 62:330–337.
- Stubbs RJ, Harbron CG, Prentice AM. 1996. Covert manipulation of the dietary fat to carbohydrate ratio of isoenergetically dense diets: Effect on food intake in feeding men ad libitum. *Int J Obes Relat Metab Disord* 20:651–660.
- Swinburn BA, Boyce VL, Bergman RN, Howard BV, Bogardus C. 1991. Deterioration in carbohydrate metabolism and lipoprotein changes induced by modern, high fat diet in Pima Indians and Caucasians. *J Clin Endocrinol Metab* 73:156–165.
- Takahashi M, Przetakiewicz M, Ong A, Borek C, Lowenstein JM. 1992. Effect of omega 3 and omega 6 fatty acids on transformation of cultured cells by irradiation and transfection. *Cancer Res* 52:154–162.
- Tannenbaum A. 1942. The genesis and growth of tumors. II. Effects of caloric restriction per se. *Cancer Res* 2:460–467.
- Tannenbaum A, Silverstone H. 1957. Nutrition and the genesis of tumours. In: Raven RW, ed. *Cancer*, Vol. 1. London: Butterworth. Pp. 306–334.
- Taylor RJ, Bennett PH, LeGonidec G, Lacoste J, Combe D, Joffres M, Uili R, Charpin M, Zimmet PZ. 1983. The prevalence of diabetes mellitus in a traditional-living Polynesian population: The Wallis Island Survey. *Diabetes Care* 6:334–340.
- Thomsen C, Rasmussen O, Christiansen C, Pedersen E, Vesterlund M, Storm H, Ingerslev J, Hermansen K. 1999. Comparison of the effects of a mono-unsaturated fat diet and a high carbohydrate diet on cardiovascular risk factors in first degree relatives to type-2 diabetic subjects. *Eur J Clin Nutr* 52:818–823.
- Trichopoulou A, Katsouyanni K, Stuver S, Tzala L, Gnardellis C, Rimm E, Trichopoulos D. 1995. Consumption of olive oil and specific food groups in relation to breast cancer risk in Greece. *J Natl Cancer Inst* 87:110–116.
- Trock B, Lanza E, Greenwald P. 1990. Dietary fiber, vegetables, and colon cancer: Critical review and meta-analyses of the epidemiologic evidence. *J Natl Cancer Inst* 82:650–661.
- Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hääläinen H, Ilanne-Parikka P, Keinänen-Kiukaanniemi S, Laakso M, Louheranta A, Rastas M, Salminen V, Uusitupa M. 2001. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 344:1343–1350.
- Tuyns AJ, Kaaks R, Haelterman M. 1988. Colorectal cancer and the consumption of foods: A case-control study in Belgium. *Nutr Cancer* 11:189–204.
- Tzonou A, Hsieh C-C, Polychronopoulou A, Kaprinis G, Toupadaki N, Trichopoulou A, Karakatsani A, Trichopoulos D. 1993. Diet and ovarian cancer: A case-control study in Greece. *Int J Cancer* 55:411–414.

- Vainio H, Bianchini F. 2001. Physical activity and cancer prevention—Is ‘no pain, no gain’ passé? *Eur J Cancer Prev* 10:301–302.
- van den Brandt PA, van’t Veer P, Goldbohm RA, Dorant E, Volovics A, Hermus RJJ, Sturmans F. 1993. A prospective cohort study on dietary fat and the risk of postmenopausal breast cancer. *Cancer Res* 53:75–82.
- Van Munster IP, Nagengast FM. 1993. The role of carbohydrate fermentation in colon cancer prevention. *Scand J Gastroenterol* 200:80–86.
- van Raaij JMA, Katan MB, West CE, Hautvast JGAJ. 1982. Influence of diets containing casein, soy isolate, and soy concentrate on serum cholesterol and lipoproteins in middle-aged volunteers. *Am J Clin Nutr* 35:925–934.
- van Stratum P, Lussenburg RN, van Wezel LA, Vergroesen AJ, Cremer HD. 1978. The effect of dietary carbohydrate:fat ratio on energy intake by adult women. *Am J Clin Nutr* 31:206–212.
- van’t Veer P, Kok FJ, Brants HAM, Ockhuizen T, Sturmans F, Hermus RJJ. 1990. Dietary fat and the risk of breast cancer. *Int J Epidemiol* 19:12–18.
- Veierød MB, Laake P, Thelle DS. 1997a. Dietary fat intake and risk of lung cancer: A prospective study of 51,452 Norwegian men and women. *Eur J Cancer Prev* 6:540–549.
- Veierød MB, Laake P, Thelle DS. 1997b. Dietary fat intake and risk of prostate cancer: A prospective study of 25,708 Norwegian men. *Int J Cancer* 73:634–638.
- Velie E, Kulldorff M, Schairer C, Block G, Albanes D, Schatzkin A. 2000. Dietary fat, fat subtypes, and breast cancer in postmenopausal women: A prospective cohort study. *J Natl Cancer Inst* 92:833–839.
- Vessby B. 2000. Dietary fat and insulin action in humans. *Br J Nutr* 83:S91–S96.
- Vessby B, Uusitupa M, Hermansen K, Riccardi G, Rivellese AA, Tapsell LC, Nälsén C, Berglund L, Louheranta A, Rasmussen BM, Calvert GD, Maffetone A, Pedersen E, Gustafsson I-B, Storlien LH. 2001. Substituting dietary saturated for monounsaturated fat impairs insulin sensitivity in healthy men and women: The KANWU study. *Diabetologia* 44:312–319.
- Visek WJ. 1978. Diet and cell growth modulation by ammonia. *Am J Clin Nutr* 31:S216–S220.
- von Schacky C, Angerer P, Kothny W, Theisen K, Mudra H. 1999. The effect of dietary ω-3 fatty acids on coronary atherosclerosis. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 130:554–562.
- Walker ARP, Cleaton-Jones PE. 1992. Sugar intake and dental caries. *Br Dent J* 172:7.
- Wang G-S, Olsson JM, Eriksson LC, Stål P. 2000. Diet restriction increases ubiquinone contents and inhibits progression of hepatocellular carcinoma in the rat. *Scand J Gastroenterol* 35:83–89.
- West CE, Sullivan DR, Katan MB, Halferkamps IL, van der Torre HW. 1990. Boys from populations with high-carbohydrate intake have higher fasting triglyceride levels than boys from populations with high-fat intake. *Am J Epidemiol* 131:271–282.
- West DB, York B. 1998. Dietary fat, genetic predisposition, and obesity: Lessons from animal models. *Am J Clin Nutr* 67:505S–512S.
- White E, Jacobs EJ, Daling JR. 1996. Physical activity in relation to colon cancer in middle-aged men and women. *Am J Epidemiol* 144:42–50.
- Willett WC. 1997. Specific fatty acids and risks of breast and prostate cancer: Dietary intake. *Am J Clin Nutr* 66:1557S–1563S.
- Willett WC. 1998. Is dietary fat a major determinant of body fat? *Am J Clin Nutr* 67:556S–562S.

- Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Hennekens CH, Speizer FE. 1987. Dietary fat and the risk of breast cancer. *N Engl J Med* 316:22–28.
- Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Speizer FE. 1990. Relation of meat, fat, and fiber intake to the risk of colon cancer in a prospective study among women. *N Engl J Med* 323:1664–1672.
- Willett WC, Hunter DJ, Stampfer MJ, Colditz G, Manson JE, Spiegelman D, Rosner B, Hennekens CH, Speizer FE. 1992. Dietary fat and fiber in relation to risk of breast cancer. An 8-year follow-up. *J Am Med Assoc* 268:2037–2044.
- Willett WC, Stampfer MJ, Mason JE, Colditz GA, Speizer FE, Rosner BA, Sampson LA, Hennekens CH. 1993. Intake of *trans* fatty acids and risk of coronary heart disease among women. *Lancet* 341:581–585.
- Williams PT. 1997. Relationship of distance run per week to coronary heart disease risk factors in 8283 male runners. The National Runners' Health Study. *Arch Intern Med* 157:191–198.
- Williams PT, Wood PD, Krauss RM, Haskell WL, Vranizan KM, Blair SN, Terry R, Farquhar JW. 1983. Does weight loss cause the exercise-induced increase in plasma high density lipoproteins? *Atherosclerosis* 47:173–185.
- Williams PT, Krauss RM, Wood PD, Lindgren FT, Giotas C, Vranizan KM. 1986. Lipoprotein subfractions of runners and sedentary men. *Metabolism* 35:45–52.
- Williams PT, Krauss RM, Vranizan KM, Wood PDS. 1990. Changes in lipoprotein subfractions during diet-induced and exercise-induced weight loss in moderately overweight men. *Circulation* 81:1293–1304.
- Williams PT, Krauss RM, Vranizan KM, Albers JJ, Wood PDS. 1992. Effects of weight-loss by exercise and by diet on apolipoproteins A-I and A-II and the particle-size distribution of high-density lipoproteins in men. *Metabolism* 41:441–449.
- Williams PT, Stefanick ML, Vranizan KM, Wood PD. 1994. The effects of weight loss by exercise or by dieting on plasma high-density lipoprotein (HDL) levels in men with low, intermediate, and normal-to-high HDL at baseline. *Metabolism* 43:917–924.
- Williamson DF, Madans J, Anda RF, Kleinman JC, Kahn HS, Byers T. 1993. Recreational physical activity and ten-year weight change in a US national cohort. *Int J Obes Relat Metab Disord* 17:279–286.
- Wolever TMS, Jenkins DJA. 1993. Effect of dietary fiber and foods on carbohydrate metabolism. In: Spiller G, ed. *CRC Handbook of Dietary Fiber in Human Nutrition*. Boca Raton, FL: CRC Press. Pp. 111–162.
- Wolever TMS, Jenkins DJA, Ocana AM, Rao VA, Collier GR. 1988. Second-meal effect: Low-glycemic-index foods eaten at dinner improve subsequent breakfast glycemic response. *Am J Clin Nutr* 48:1041–1047.
- Wolfe BMJ, Piché LA. 1999. Replacement of carbohydrate by protein in a conventional-fat diet reduces cholesterol and triglyceride concentrations in healthy normolipidemic subjects. *Clin Invest Med* 22:140–148.
- Wood PD, Stefanick ML, Dreon DM, Frey-Hewitt B, Garay SC, Williams PT, Superko HR, Fortmann SP, Albers JJ, Vranizan KM, Ellsworth NM, Terry RB, Haskell WL. 1988. Changes in plasma lipids and lipoproteins in overweight men during weight loss through dieting as compared with exercise. *N Engl J Med* 319:1173–1179.
- Wood PJ, Braaten JT, Scott FW, Riedel KD, Wolynetz MS, Collins MW. 1994. Effect of dose and modification of viscous properties of oat gum on plasma glucose and insulin following an oral glucose load. *Br J Nutr* 72:731–743.

- Wu Y, Zheng W, Sellars TA, Kushi LH, Bostick RM, Potter JD. 1994. Dietary cholesterol, fat, and lung cancer incidence among older women: The Iowa Women's Health Study (United States). *Cancer Causes Control* 5:395–400.
- Yost TJ, Jensen DR, Haugen BR, Eckel RH. 1998. Effect of dietary macronutrient composition on tissue-specific lipoprotein lipase activity and insulin action in normal-weight subjects. *Am J Clin Nutr* 68:296–302.
- Yu S, Derr J, Etherton TD, Kris-Etherton PM. 1995. Plasma cholesterol-predictive equations demonstrate that stearic acid is neutral and monounsaturated fatty acids are hypocholesterolemic. *Am J Clin Nutr* 61:1129–1139.
- Yudkin J, Eisa O, Kang SS, Meraji S, Bruckdorfer KR. 1986. Dietary sucrose affects plasma HDL cholesterol concentration in young men. *Ann Nutr Metab* 30: 261–266.
- Yu-Poth S, Zhao G, Etherton T, Naglak M, Jonnalagadda S, Kris-Etherton PM. 1999. Effects of the National Cholesterol Education Program's Step I and Step II dietary intervention programs on cardiovascular disease risk factors: A meta-analysis. *Am J Clin Nutr* 69:632–646.
- Zambon S, Friday KE, Childs MT, Fujimoto WY, Bierman EL, Ensinck JW. 1992. Effect of glyburide and ω3 fatty acid dietary supplements on glucose and lipid metabolism in patients with non-insulin-dependent diabetes mellitus. *Am J Clin Nutr* 56:447–454.
- Zhu Z, Jiang W, Thompson HJ. 1999. Effect of energy restriction on tissue size regulation during chemically induced mammary carcinogenesis. *Carcinogenesis* 20:1721–1726.

Ibid., Chapter 11, pp. 845–879.

- Abate N, Garg A, Peshock RM, Stray-Gundersen J, Adams-Huet B, Grundy SM. 1996. Relationship of generalized and regional adiposity to insulin sensitivity in men with NIDDM. *Diabetes* 45:1684–1693.
- Abbey M, Belling GB, Noakes M, Hirata F, Nestel PJ. 1993. Oxidation of low-density lipoproteins: Intraindividual variability and the effect of dietary linoleate supplementation. *Am J Clin Nutr* 57:391–398.
- Abbott WGH, Boyce VL, Grundy SM, Howard BV. 1989. Effects of replacing saturated fat with complex carbohydrate in diets of subjects with NIDDM. *Diabetes Care* 12:102–107.
- Adams SO, Barr GD, Huenemann RL. 1978. Effect of nutritional supplementation in pregnancy. I. Outcome of pregnancy. *J Am Diet Assoc* 72:144–147.
- Ågren JJ, Hänninen O, Julkunen A, Fogelholm L, Vidgren H, Schwab U, Pynnönen O, Uusitupa M. 1996. Fish diet, fish oil and docosahexaenoic acid rich oil lower fasting and postprandial plasma lipid levels. *Eur J Clin Nutr* 50:765–771.
- Albert CM, Hennekens CH, O'Donnell CJ, Ajani UA, Carey VJ, Willett WC, Ruskin JN, Manson JE. 1998. Fish consumption and risk of sudden cardiac death. *J Am Med Assoc* 279:23–28.
- Allen LH, Oddoye EA, Margen S. 1979. Protein-induced calciuria: A longer term study. *Am J Clin Nutr* 32:741–749.
- Allison DB, Egan K, Barraj LM, Caughman C, Infante M, Heimbach J. 1999. Estimated intakes of *trans* fatty and other fatty acids in the US population. *J Am Diet Assoc* 99:166–174.
- American Diabetes Association. 2001. Screening for diabetes. *Diabetes Care* 24:S21–S24.

- Anderson S, Brenner BM. 1986. Effects of aging on the renal glomerulus. *Am J Med* 80:435–442.
- Anderson S, Brenner BM. 1987. The aging kidney: Structure, function, mechanisms, and therapeutic implications. *J Am Geriatr Soc* 35:590–593.
- Andreassi M, Forleo P, Di Lorio A, Masci S, Abate G, Amerio P. 1997. Efficacy of  $\gamma$ -linolenic acid in the treatment of patients with atopic dermatitis. *J Int Med Res* 25:266–274.
- Annuzzi G, Rivelles A, Capaldo B, Di Marino L, Iovine C, Marotta G, Riccardi G. 1991. A controlled study on the effects of *n*-3 fatty acids on lipid and glucose metabolism in non-insulin-dependent diabetic patients. *Atherosclerosis* 87:65–73.
- Anti M, Marra G, Armelao F, Bartoli GM, Ficarelli R, Percesepe A, De Vitis I, Maria G, Sofo L, Rapaccini GL. 1992. Effect of omega-3 fatty acids on rectal mucosal cell proliferation in subjects at risk for colon cancer. *Gastroenterology* 103:883–891.
- Arntzenius AC, Kromhout D, Barth JD, Reiber JHC, Bruschke AVG, Buis B, van Gent CM, Kempen-Voogd N, Strikwerda S, van der Velde EA. 1985. Diet, lipoproteins, and the progression of coronary atherosclerosis. The Leiden Intervention Trial. *N Engl J Med* 312:805–811.
- ARS (Agricultural Research Service). 1998. *Food and Nutrient Intakes by Individuals in the United States, by Sex and Age, 1994–96*. Washington, DC: U.S. Department of Agriculture.
- Ascherio A, Rimm EB, Stampfer MJ, Giovannucci EL, Willett WC. 1995. Dietary intake of marine *n*-3 fatty acids, fish intake, and the risk of coronary disease among men. *N Engl J Med* 332:977–982.
- Ascherio A, Rimm EB, Giovannucci EL, Spiegelman D, Stampfer M, Willett WC. 1996. Dietary fat and risk of coronary heart disease in men: Cohort follow up study in the United States. *Br Med J* 313:84–90.
- Astrup A, Grunwald GK, Melanson EL, Saris WH, Hill JO. 2000. The role of low-fat diets in body weight control: A meta-analysis of ad libitum dietary intervention studies. *Int J Obes Relat Metab Disord* 24:1545–1552.
- Atkin L-M, Davies PSW. 2000. Diet composition and body composition in pre-school children. *Am J Clin Nutr* 72:15–21.
- Austin MA, King MC, Vranizan KM, Krauss RM. 1990. Atherogenic lipoprotein phenotype: A proposed genetic marker for coronary heart disease risk. *Circulation* 82:495–506.
- Axelrod L, Camuso J, Williams E, Kleinman K, Briones E, Schoenfeld D. 1994. Effects of a small quantity of  $\omega$ -3 fatty acids on cardiovascular risk factors in NIDDM. *Diabetes Care* 17:37–44.
- Badaloo A, Boyne M, Reid M, Persaud C, Forrester T, Millward DJ, Jackson AA. 1999. Dietary protein, growth and urea kinetics in severely malnourished children and during recovery. *J Nutr* 129:969–979.
- Baer JT. 1993. Improved plasma cholesterol levels in men after a nutrition education program at the worksite. *J Am Diet Assoc* 93:658–663.
- Ballew C, Kuester S, Gillespie C. 2000. Beverage choices affect adequacy of children's nutrient intakes. *Arch Pediatr Adolesc Med* 154:1148–1152.
- Bang HO, Dyerberg J, Hjørne N. 1976. The composition of food consumed by Greenland Eskimos. *Acta Med Scand* 200:69–73.
- Banni S, Angioni E, Casu V, Melis MP, Carta G, Corongiu FP, Thompson H, Ip C. 1999. Decrease in linoleic acid metabolites as a potential mechanism in cancer risk reduction by conjugated linoleic acid. *Carcinogenesis* 20:1019–1024.

- Barbone F, Austin H, Partridge EE. 1993. Diet and endometrial cancer: A case-control study. *Am J Epidemiol* 137:393–403.
- Barinagarrementeria F, González-Duarte A, Cantú-Brito C. 1998. Prothrombic states and cerebral ischemia. *Rev Neurol* 26:85–91.
- Bartsch H, Nair J, Owen RW. 1999. Dietary polyunsaturated fatty acids and cancers of the breast and colorectum: Emerging evidence for their role as risk modifiers. *Carcinogenesis* 20:2209–2218.
- Barzel US, Massey LK. 1998. Excess dietary protein can adversely affect bone. *J Nutr* 128:1051–1053.
- Bassett DR, Abel M, Moellering RC, Rosenblatt G, Stokes J. 1969. Coronary heart disease in Hawaii: Dietary intake, depot fat, “stress,” smoking, and energy balance in Hawaiian and Japanese men. *Am J Clin Nutr* 22:1483–1503.
- Becker N, Illingworth R, Alaupovic P, Connor WE, Sundberg EE. 1983. Effects of saturated, monounsaturated, and ω-6 polyunsaturated fatty acids on plasma lipids, lipoproteins, and apoproteins in humans. *Am J Clin Nutr* 37:355–360.
- Beck-Nielsen H, Pedersen O, Lindskov HO. 1980. Impaired cellular insulin binding and insulin sensitivity induced by high-fructose feeding in normal subjects. *Am J Clin Nutr* 33:273–278.
- Behall KM, Scholfield DJ, Lee K, Powell AS, Moser PB. 1987. Mineral balance in adult men: Effect of four refined fibers. *Am J Clin Nutr* 46:307–314.
- Bennett PH, Knowler WC, Baird HR, Butler WJ, Pettitt DJ, Reid JM. 1984. Diet and the development of noninsulin-dependent diabetes mellitus: An epidemiological perspective. In: Pozza G, ed. *Diet, Diabetes, and Atherosclerosis*. New York: Raven Press. Pp. 109–119.
- Berenson GS, Wattigney WA, Tracy RE, Newman WP, Srinivasan SR, Webber LS, Dalferves ER, Strong JP. 1992. Atherosclerosis of the aorta and coronary arteries and cardiovascular risk factors in persons aged 6 to 30 years and studied at necropsy (The Bogalusa Heart Study). *Am J Cardiol* 70:851–858.
- Berry EM, Eisenberg S, Haratz D, Friedlander Y, Norman Y, Kaufmann NA, Stein Y. 1991. Effects of diets rich in monounsaturated fatty acids on plasma lipoproteins—The Jerusalem Nutrition Study: High MUFA vs high PUFA. *Am J Clin Nutr* 53:899–907.
- Berry EM, Eisenberg S, Friedlander Y, Haratz D, Kaufmann NA, Norman Y, Stein Y. 1992. Effects of diets rich in monounsaturated fatty acids on plasma lipoproteins—The Jerusalem Nutrition Study. II. Monounsaturated fatty acids vs carbohydrates. *Am J Clin Nutr* 56:394–403.
- Bhathena SJ, Berlin E, Judd JT, Kim YC, Law JS, Bhagavan HN, Ballard-Barbash R, Nair PP. 1991. Effects of ω3 fatty acids and vitamin E on hormones involved in carbohydrate and lipid metabolism in men. *Am J Clin Nutr* 54:684–688.
- Billman GE, Kang JX, Leaf A. 1999. Prevention of sudden cardiac death by dietary pure ω-3 polyunsaturated fatty acids in dogs. *Circulation* 99:2452–2457.
- Black HS, Herd JA, Goldberg LH, Wolf JE, Thornby JI, Rosen T, Bruce S, Tschen JA, Foreyt JP, Scott LW, Jaax S, Andrews K. 1994. Effect of a low-fat diet on the incidence of actinic keratosis. *N Engl J Med* 330:1272–1275.
- Bladbjerg EM, Marckmann P, Sandström B, Jespersen J. 1994. Non-fasting factor VII coagulant activity (FVII:C) increased by high fat diet. *Thromb Haemost* 71:755–758.
- Blankson H, Stakkestad JA, Fagertun H, Thom E, Wadstein J, Gudmundsen O. 2000. Conjugated linoleic acid reduces body fat mass in overweight and obese humans. *J Nutr* 130:2943–2948.

- Bloemberg BPM, Kromhout D, Goddijn HE, Jansen A, Obermann-de Boer GL. 1991. The impact of the Guidelines for a Healthy Diet of the Netherlands Nutrition Council on total and high density lipoprotein cholesterol in hypercholesterolemic free-living men. *Am J Epidemiol* 134:39–48.
- Blundell JE, Burley VJ, Cotton JR, Lawton CL. 1993. Dietary fat and the control of energy intake: Evaluating the effects of fat on meal size and postmeal satiety. *Am J Clin Nutr* 57:772S–778S.
- Bobroff EM, Kissileff HR. 1986. Effects of changes in palatability on food intake and the cumulative food intake curve in man. *Appetite* 7:85–96.
- Bolton-Smith C. 1996. Intake of sugars in relation to fatness and micronutrient adequacy. *Int J Obes Relat Metab Disord* 20:S31–S33.
- Bolton-Smith C, Woodward M. 1994. Coronary heart disease: Prevalence and dietary sugars in Scotland. *J Epidemiol Community Health* 48:119–122.
- Bolton-Smith C, Woodward M. 1995. Antioxidant vitamin adequacy in relation to consumption of sugars. *Eur J Clin Nutr* 49:124–133.
- Bønaa KH, Bjerve KS, Nordøy A. 1992. Habitual fish consumption, plasma phospholipid fatty acids, and serum lipids: The Tromsø Study. *Am J Clin Nutr* 55:1126–1134.
- Bonanome A, Pagnan A, Biffanti S, Opportuno A, Sorgato F, Dorella M, Maiorino M, Ursini F. 1992. Effect of dietary monounsaturated and polyunsaturated fatty acids on the susceptibility of plasma low density lipoproteins to oxidative modification. *Arterioscler Thromb* 12:529–533.
- Borkman M, Campbell LV, Chisholm DJ, Storlien LH. 1991. Comparison of the effects on insulin sensitivity of high carbohydrate and high fat diets in normal subjects. *J Clin Endocrinol Metab* 72:432–437.
- Borkman M, Storlien LH, Pan DA, Jenkins AB, Chisholm DJ, Campbell LV. 1993. The relation between insulin sensitivity and the fatty-acid composition of skeletal-muscle phospholipids. *N Engl J Med* 328:238–244.
- Boulton TJC, Magarey AM. 1995. Effects of differences in dietary fat on growth, energy and nutrient intake from infancy to eight years of age. *Acta Paediatr* 84:146–150.
- Boutron MC, Wilpart M, Faivre J. 1991. Diet and colorectal cancer. *Eur J Cancer Prev* 1:13–20.
- Bowman MP, Van Doren J, Taper LJ, Thye FW, Ritchey SJ. 1988. Effect of dietary fat and cholesterol on plasma lipids and lipoprotein fractions in normolipidemic men. *J Nutr* 118:555–560.
- Bowman SA. 1999. Diets of individuals based on energy intakes from added sugars. *Fam Econ Nutr Rev* 12:31–38.
- Boyar AP, Rose DP, Loughridge JR, Engle A, Palgi A, Laakso K, Kinne D, Wynder EL. 1988. Response to a diet low in total fat in women with postmenopausal breast cancer: A pilot study. *Nutr Cancer* 11:93–99.
- Boyd NF, Cousins M, Beaton M, Kriukov V, Lockwood G, Tritchler D. 1990. Quantitative changes in dietary fat intake and serum cholesterol in women: Results from a randomized, controlled trial. *Am J Clin Nutr* 52:470–476.
- Boyd NF, Martin LJ, Noffel M, Lockwood GA, Tritchler DL. 1993. A meta-analysis of studies of dietary fat and breast cancer risk. *Br J Cancer* 68:627–636.
- Bray GA, Popkin BM. 1998. Dietary fat intake does affect obesity! *Am J Clin Nutr* 68:1157–1173.
- Breillout F, Antoine E, Poupon MF. 1990. Methionine dependency of malignant tumors: A possible approach for therapy. *J Natl Cancer Inst* 82:1628–1632.

- Brodie AE, Manning VA, Ferguson KR, Jewell DE, Hu CY. 1999. Conjugated linoleic acid inhibits differentiation of pre- and post-confluent 3T3-L1 preadipocytes but inhibits cell proliferation only in preconfluent cells. *J Nutr* 129:602–606.
- Brussaard JH, Katan MB, Groot PHE, Havekes LM, Hautvast JGAJ. 1982. Serum lipoproteins of healthy persons fed a low-fat diet or a polyunsaturated fat diet for three months. A comparison of two cholesterol-lowering diets. *Atherosclerosis* 42:205–219.
- Budohoski L, Panczenko-Kresowska B, Langfort J, Zernicka E, Dubaniewicz A, Zieman'ski S, Challiss RAJ, Newsholme WA. 1993. Effects of saturated and polyunsaturated fat enriched diet on the skeletal muscle insulin sensitivity in young rats. *J Physiol Pharmacol* 44:391–398.
- Buell P. 1973. Changing incidence of breast cancer in Japanese-American women. *J Natl Cancer Inst* 51:1479–1483.
- Buell P, Dunn JE. 1965. Cancer mortality among Japanese Issei and Nisei of California. *Cancer* 18:656–664.
- Buemann B, Tremblay A, Bouchard C. 1995. Social class interacts with the association between macronutrient intake and subcutaneous fat. *Int J Obes Relat Metab Disord* 19:770–775.
- Burmeister LA, Valdivia T, Nuttal FQ. 1991. Adult hereditary fructose intolerance. *Arch Intern Med* 151:773–776.
- Burr ML, Fehily AM, Gilbert JF, Rogers S, Holliday RM, Sweetnam PM, Elwood PC, Deadman NM. 1989a. Effects of changes in fat, fish, and fibre intakes on death and myocardial reinfarction: Diet and Reinfarction Trial (DART). *Lancet* 2:757–761.
- Burr ML, Fehily AM, Rogers S, Welsby E, King S, Sandham S. 1989b. Diet and Reinfarction Trial (DART): Design, recruitment, and compliance. *Eur Heart J* 10:558–567.
- Burr ML, Sweetnam PM, Fehily AM. 1994. Diet and reinfarction. *Eur Heart J* 15:1152–1153.
- Buzzard IM, Asp EH, Chlebowski RT, Boyar AP, Jeffery RW, Nixon DW, Blackburn GL, Jochimsen PR, Scanlon EF, Insull W, Elashoff RM, Butram R, Wynder EL. 1990. Diet intervention methods to reduce fat intake: Nutrient and food group composition of self-selected low-fat diets. *J Am Diet Assoc* 90:42–50, 53.
- Calbet JA, MacLean DA. 1997. Role of caloric content on gastric emptying in humans. *J Physiol* 498:553–559.
- Calviello G, Palozza P, Piccioni E, Maggiano N, Frattucci A, Franceschelli P, Baroli GM. 1998. Dietary supplementation with eicosapentaenoic and docosahexaenoic acid inhibits growth of Morris hepatocarcinoma 3924A in rats: Effects on proliferation and apoptosis. *Int J Cancer* 75:699–705.
- Campbell TC, Parpia B, Chen J. 1998. Diet, lifestyle, and the etiology of coronary artery disease: The Cornell China Study. *Am J Cardiol* 82:18T–21T.
- Castelli WP, Anderson K, Wilson PWF, Levy D. 1992. Lipids and risk of coronary heart disease. The Framingham Study. *Ann Epidemiol* 2:23–28.
- Caygill CPJ, Hill MJ. 1995. Fish, n-3 fatty acids and human colorectal and breast cancer mortality. *Eur J Cancer Prev* 4:329–332.
- Caygill CPJ, Charlett A, Hill MJ. 1996. Fat, fish, fish oil and cancer. *Br J Cancer* 74:159–164.
- CDC (Centers for Disease Control and Prevention). 1994. Daily dietary fat and total food-energy intakes—Third National Health and Nutrition Examination Survey, Phase 1, 1988–91. *Morb Mortal Wkly Rep* 43:116–117, 123–125.

- Cesano A, Visonneau S, Scimeca JA, Kritchevsky D, Santoli D. 1998. Opposite effects of linoleic acid and conjugated linoleic acid on human prostatic cancer in SCID mice. *Anticancer Res* 18:833–838.
- Chandra RK. 1972. Immunocompetence in undernutrition. *J Pediatr* 81:1194–1200.
- Chandra RK. 1991. 1990 McCollum Award lecture. Nutrition and immunity: Lessons from the past and new insights into the future. *Am J Clin Nutr* 53:1087–1101.
- Chandra RK, Newberne PM. 1977. *Nutrition, Immunity, and Infection: Mechanisms of Interactions*. New York: Plenum Press.
- Chandra RK, Chandra S, Gupta S. 1984. Antibody affinity and immune complexes after immunization with tetanus toxoid in protein-energy malnutrition. *Am J Clin Nutr* 40:131–134.
- Chen M, Bergman RN, Porte D. 1988. Insulin resistance and β-cell dysfunction in aging: The importance of dietary carbohydrate. *J Clin Endocrinol Metab* 67:951–957.
- Chicco A, D'Alessandro ME, Karabatas L, Gutman R, Lombardo YB. 1996. Effect of moderate levels of dietary fish oil on insulin secretion and sensitivity, and pancreas insulin content in normal rats. *Ann Nutr Metab* 40:61–70.
- Chilton-Lopez T, Surette ME, Swan DD, Fonteh AN, Johnson MM, Chilton FH. 1996. Metabolism of gammalinolenic acid in human neutrophils. *J Immunol* 156:2941–2947.
- Chisholm KW, O'Dea K. 1987. Effect of short-term consumption of a high fat diet on glucose tolerance and insulin sensitivity in the rat. *J Nutr Sci Vitaminol* 3:377–390.
- Chisolm GM, Steinberg D. 2000. The oxidative modification hypothesis of atherosclerosis: An overview. *Free Radic Biol Med* 28:1815–1826.
- Chiu BC, Cerhan JR, Folsom AR, Sellers TA, Kushi LH, Wallace RB, Zheng W, Potter JD. 1996. Diet and risk of non-Hodgkin lymphoma in older women. *J Am Med Assoc* 275:1315–1321.
- Choi Y, Kim Y-C, Han Y-B, Park Y, Pariza M, Ntambi JM. 2000. The *trans*-10,*cis*-12 isomer of conjugated linoleic acid downregulates stearoyl-CoA desaturase 1 gene expression in 3T3-L1 adipocytes. *J Nutr* 130:1920–1924.
- Chow WH, Gridley G, McLaughlin JK, Mandel JS, Wacholder S, Blot WJ, Niwa S, Fraumeni JF. 1994. Protein intake and risk of renal cell cancer. *J Natl Cancer Inst* 86:1131–1139.
- Christensen JH, Gustenhoff P, Korup E, Aarøe J, Møller JM, Rasmussen K, Dyerberg J, Schmidt EB. 1997. n-3 Polyunsaturated fatty acids, heart rate variability and ventricular arrhythmias in patients with previous myocardial infarcts. *Ugeskr Laeger* 159:5525–5529.
- Christensen JH, Christensen MS, Dyerberg J, Schmidt EB. 1999. Heart rate variability and fatty acid content of blood cell membranes: A dose-response study with n-3 fatty acids. *Am J Clin Nutr* 70:331–337.
- Clarke R, Frost C, Collins R, Appleby P, Peto R. 1997. Dietary lipids and blood cholesterol: Quantitative meta-analysis of metabolic ward studies. *Br Med J* 314:112–117.
- Clinton SK. 1993. Dietary protein and the origins of human cancer. In: Liepa GU, Beitz DC, Beynen AC, Gorman MA, eds. *Dietary Proteins: How They Alleviate Disease and Promote Better Health*. Champaign, IL: American Oil Chemists' Society. Pp. 84–122.

## ONLINE REFERENCES

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- Clore JN, Li J, Gill R, Gupta S, Spencer R, Azzam A, Zuelzer W, Rizzo WB, Blackard WG. 1998. Skeletal muscle phosphatidylcholine fatty acids and insulin sensitivity in normal humans. *Am J Physiol* 275:E665–E670.
- Colditz GA, Willett WC, Stampfer MJ, London SJ, Segal MR, Speizer FE. 1990. Patterns of weight change and their relation to diet in a cohort of healthy women. *Am J Clin Nutr* 51:1100–1105.
- Colditz GA, Manson JE, Stampfer MJ, Rosner B, Willett WC, Speizer FE. 1992. Diet and risk of clinical diabetes in women. *Am J Clin Nutr* 55:1018–1023.
- Collins CL, Wasa M, Souba WW, Abcouwer SF. 1998. Determinants of glutamine dependence and utilization by normal and tumor-derived breast cell lines. *J Cell Physiol* 176:166–178.
- Coudray C, Bellanger J, Castiglia-Delavaud C, Rémesy C, Vermorel M, Rayssignuier Y. 1997. Effect of soluble or partly soluble dietary fibres supplementation on absorption and balance of calcium, magnesium, iron and zinc in healthy young men. *Eur J Clin Nutr* 51:375–380.
- Coulston AM, Liu GC, Reaven GM. 1983. Plasma glucose, insulin and lipid responses to high-carbohydrate low-fat diets in normal humans. *Metabolism* 32:52–56.
- Coulston AM, Hollenbeck CB, Swislocki AL, Chen YD, Reaven GM. 1987. Deleterious metabolic effects of high-carbohydrate, sucrose-containing diets in patients with non-insulin-dependent diabetes mellitus. *Am J Med* 82:213–220.
- Cunningham DC, Harrison LY, Shultz TD. 1997. Proliferative responses of normal human mammary and MCF-7 breast cancer cells to linoleic acid, conjugated linoleic acid and eicosanoid synthesis inhibitors in culture. *Anticancer Res* 17:197–204.
- Curb JD, Wergowske G, Dobbs JC, Abbott RD, Huang B. 2000. Serum lipid effects of a high-monounsaturated fat diet based on macadamia nuts. *Arch Intern Med* 160:1154–1158.
- Curhan GC, Willet WC, Rimm EB, Stampfer MJ. 1996. A prospective study of dietary calcium and other nutrients and the risk of kidney stones in men: 8 Year follow-up. In: Pak CY, Resnick MI, Preminger GM, eds. *Urolithiasis*. Dallas, TX: Millet. Pp. 164–166.
- Czarnecki SK, Kritchevsky D. 1993. Dietary protein and atherosclerosis. In: Liepa GU, Beitz DC, Beynen AC, Gorman MA, eds. *Dietary Proteins: How They Alleviate Disease and Promote Better Health*. Champaign, IL: American Oil Chemists' Society. Pp. 42–56.
- Davies PS. 1997. Diet composition and body mass index in pre-school children. *Eur J Clin Nutr* 51:443–448.
- Daviglus ML, Stamler J, O'renica AJ, Dyer AR, Liu K, Greenland P, Walsh MK, Morris D, Shekelle RB. 1997. Fish consumption and the 30-year risk of fatal myocardial infarction. *N Engl J Med* 336:1046–1053.
- Dawson-Hughes B, Harris SS. 2002. Calcium intake influences the association of protein intake with rates of bone loss in elderly men and women. *Am J Clin Nutr* 75:773–779.
- Decarli A, Favero A, La Vecchia C, Russo A, Ferraroni M, Negri E, Franceschi S. 1997. Macronutrients, energy intake, and breast cancer risk: Implications from different models. *Epidemiology* 8:425–428.
- De Caterina R, Liao JK, Libby P. 2000. Fatty acid modulation of endothelial activation. *Am J Clin Nutr* 71:213–223.
- de Deckere EAM, van Amelsvoort JMM, McNeill GP, Jones P. 1999. Effects of conjugated linoleic acid (CLA) isomers on lipid levels and peroxisome proliferation in the hamster. *Br J Nutr* 82:309–317.

- DeLany JP, Vivian VM, Snook JT, Anderson PA. 1990. Effects of fish oil on serum lipids in men during a controlled feeding trial. *Am J Clin Nutr* 52:477–485.
- de Lorgeril M, Renaud S, Mamelle N, Salen P, Martin J-L, Monjaud I, Guidollet J, Touboul P, Delaye J. 1994. Mediterranean alpha-linolenic acid-rich diet in secondary prevention of coronary heart disease. *Lancet* 343:1454–1459.
- de Lorgeril M, Salen P, Martin J-L, Monjaud I, Delaye J, Mamelle N. 1999. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction. Final report of the Lyon Diet Heart Study. *Circulation* 99:779–785.
- Delzenne N, Aertssens J, Verplaetse H, Roccaro M, Roberfroid M. 1995. Effect of fermentable fructo-oligosaccharides on mineral, nitrogen and energy digestive balance in the rat. *Life Sci* 57:1579–1587.
- Demigné C, Levrat M-A, Rémésy C. 1989. Effects of feeding fermentable carbohydrates on the cecal concentrations of minerals and their fluxes between the cecum and blood plasma in the rat. *J Nutr* 119:1625–1630.
- Deschner EE, Lytle JS, Wong G, Ruperto JF, Newmark HL. 1990. The effect of dietary omega-3 fatty acids (fish oil) on azoxymethanol-induced focal areas of dysplasia and colon tumor incidence. *Cancer* 66:2350–2356.
- Després J-P. 1993. Abdominal obesity as important component of insulin-resistance syndrome. *Nutrition* 9:452–459.
- De Stefani E, Deneo-Pellegrini H, Mendilaharsu M, Carzoglio JC, Ronco A. 1997a. Dietary fat and lung cancer: A case-control study in Uruguay. *Cancer Causes Control* 8:913–921.
- De Stefani E, Mendilaharsu M, Deneo-Pellegrini H, Ronco A. 1997b. Influence of dietary levels of fat, cholesterol, and calcium on colorectal cancer. *Nutr Cancer* 29:83–89.
- De Stefani E, Ronco A, Mendilaharsu M, Deneo-Pellegrini H. 1999. Diet and risk of cancer of the upper aerodigestive tract. II. Nutrients. *Oral Oncol* 35:22–26.
- Djoussé L, Pankow JS, Eckfeldt JH, Folsom AR, Hopkins PN, Province MA, Hong Y, Ellison RC. 2001. Relation between dietary linolenic acid and coronary artery disease in the National Heart, Lung, and Blood Institute Family Heart Study. *Am J Clin Nutr* 74:612–619.
- Dolecek TA. 1992. Epidemiological evidence of relationships between dietary polyunsaturated fatty acids and mortality in the Multiple Risk Factor Intervention Trial. *Proc Soc Exp Med Biol* 200:177–182.
- Dreon DM, Frey-Hewitt B, Ellsworth N, Williams PT, Terry RB, Wood PD. 1988. Dietary fat:carbohydrate ratio and obesity in middle-aged men. *Am J Clin Nutr* 47:995–1000.
- Drewnowski A. 1999. Intense sweeteners and energy density of foods: Implications for weight control. *Eur J Clin Nutr* 53:757–763.
- Drewnowski A, Greenwood MR. 1983. Cream and sugar: Human preferences for high-fat foods. *Physiol Behav* 30:629–633.
- Duncan KH, Bacon JA, Weinsier RL. 1983. The effects of high and low energy density diets on satiety, energy intake, and eating time of obese and nonobese subjects. *Am J Clin Nutr* 37:763–767.
- Dunnigan MG, Fyfe T, McKiddie MT, Crosbie SM. 1970. The effects of isocaloric exchange of dietary starch and sucrose on glucose tolerance, plasma insulin and serum lipids in man. *Clin Sci* 38:1–9.
- Durrant M, Royston P. 1979. Short-term effects of energy density on salivation, hunger and appetite in obese subjects. *Int J Obes* 3:335–347.

- Dyerberg J, Bang HO. 1979. Haemostatic function and platelet polyunsaturated fatty acids in Eskimos. *Lancet* 2:433–435.
- Emmett PM, Heaton KW. 1995. Is extrinsic sugar a vehicle for dietary fat? *Lancet* 345:1537–1540.
- Eritsland J, Arnesen H, Seljeflot I, Høstmark AT. 1994a. Long-term metabolic effects of n-3 polyunsaturated fatty acids in patients with coronary artery disease. *Am J Clin Nutr* 61:831–836.
- Eritsland J, Seljeflot I, Abdelnoor M, Arnesen H, Torjesen PA. 1994b. Long-term effects of n-3 fatty acids on serum lipids and glycaemic control. *Scand J Clin Lab Invest* 54:273–280.
- Ernst N, Fisher M, Smith W, Gordon T, Rifkind BM, Little JA, Mishkel MA, Williams OD. 1980. The association of plasma high-density lipoprotein cholesterol with dietary intake and alcohol consumption. The Lipid Research Clinics Program Prevalence Study. *Circulation* 62:IV41–IV52.
- Fairweather-Tait SM, Wright AJA. 1990. The effects of sugar-beet fibre and wheat bran on iron and zinc absorption in rats. *Br J Nutr* 64:547–552.
- FAO/WHO (Food and Agricultural Organization/World Health Organization). 1996. *Sixth World Food and Nutrition Survey*. Rome: FAO.
- Farrell TG, Bashir Y, Cripps T, Malik M, Poloniecki J, Bennett ED, Ward DE, Camm AJ. 1991. Risk stratification for arrhythmic events in postinfarction patients based on heart rate variability, ambulatory electrocardiographic variables and the signal-averaged electrocardiogram. *J Am Coll Cardiol* 18:687–697.
- Farris RP, Nicklas TA, Myers L, Berenson GS. 1998. Nutrient intake and food group consumption of 10-year-olds by sugar intake level: The Bogalusa Heart Study. *J Am Coll Nutr* 17:579–585.
- Fasching P, Ratheiser K, Waldhäusl W, Rohac M, Osterrode W, Nowotny P, Vierhapper H. 1991. Metabolic effects of fish-oil supplementation in patients with impaired glucose tolerance. *Diabetes* 40:583–589.
- Fasching P, Ratheiser K, Schneeweiss B, Rohac M, Nowotny P, Waldhausl W. 1996. No effect of short-term dietary supplementation of saturated and poly- and monounsaturated fatty acids on insulin secretion and sensitivity in healthy men. *Ann Nutr Metab* 40:116–122.
- Fehily AM, Yarnell JWG, Bolton CH, Butland BK. 1988. Dietary determinants of plasma lipids and lipoproteins: The Caerphilly Study. *Eur J Clin Nutr* 42:405–413.
- Fernandez ML, Wilson TA, Conde K, Vergara-Jimenez M, Nicolosi RJ. 1999. Hamsters and guinea pigs differ in their plasma lipoprotein cholesterol distribution when fed diets varying in animal protein, soluble fiber, or cholesterol content. *J Nutr* 129:1323–1332.
- Feskens EJM, Bowles CH, Kromhout D. 1991a. Carbohydrate intake and body mass index in relation to the risk of glucose tolerance in an elderly population. *Am J Clin Nutr* 54:136–140.
- Feskens EJ, Bowles CH, Kromhout D. 1991b. Inverse association between fish intake and risk of glucose intolerance in normoglycemic elderly men and women. *Diabetes Care* 14:935–941.
- Feskens EJM, Loeber JG, Kromhout D. 1994. Diet and physical activity as determinants of hyperinsulinemia: The Zutphen Elderly Study. *Am J Epidemiol* 140:350–360.
- Feskens EJM, Virtanen SM, Räsänen L, Tuomilehto J, Stengard J, Pekkanen J, Nissinen A, Kromhout D. 1995. Dietary factors determining diabetes and impaired glucose tolerance: A 20-year follow-up of the Finnish and Dutch cohorts of the Seven Countries Study. *Diabetes Care* 18:1104–1112.

- Fischer DR, Morgan KJ, Zabik ME. 1985. Cholesterol, saturated fatty acids, polyunsaturated fatty acids, sodium, and potassium intakes of the United States population. *J Am Coll Nutr* 4:207–224.
- Flaten H, Høstmark AT, Kierulf P, Lystad E, Trygg K, Bjerkedal T, Osland A. 1990. Fish-oil concentrate: Effects on variables related to cardiovascular disease. *Am J Clin Nutr* 52:300–306.
- Flegal KM. 1999. The obesity epidemic in children and adults: Current evidence and research issues. *Med Sci Sports Exerc* 31:S509–S514.
- Flint A, Raben A, Blundell JE, Astrup A. 2000. Reproducibility, power and validity of visual analogue scales in assessment of appetite sensations in single test meal studies. *Int J Obes Relat Metab Disord* 24:3–48.
- Fomon SJ, Thomas LN, Filer LJ, Anderson TA, Nelson SE. 1976. Influence of fat and carbohydrate content of diet on food intake and growth of male infants. *Acta Paediatr Scand* 65:136–144.
- Forshee RA, Storey ML. 2001. The role of added sugars in the diet quality of children and adolescents. *J Am Coll Nutr* 20:32–43.
- Franceschi S, Levi F, Conti E, Talamini R, Negri E, Dal Maso L, Boyle P, Decarli A, La Vecchia C. 1999. Energy intake and dietary pattern in cancer of the oral cavity and pharynx. *Cancer Causes Control* 10:439–444.
- Friedman MI. 1995. Control of energy intake by energy metabolism. *Am J Clin Nutr* 62:1096S–1100S.
- Fukagawa NK, Anderson JW, Hageman G, Young VR, Minaker KL. 1990. High-carbohydrate, high-fiber diets increase peripheral insulin sensitivity in healthy young and old adults. *Am J Clin Nutr* 52:524–528.
- Gao YT, McLaughlin JK, Gridley G, Blot WJ, Ji BT, Dai Q, Fraumeni JF. 1994. Risk factors for esophageal cancer in Shanghai, China. II. Role of diet and nutrients. *Int J Cancer* 58:197–202.
- Garg A, Bonanome A, Grundy SM, Zhang Z-J, Unger RH. 1988. Comparison of a high-carbohydrate diet with a high-monounsaturated-fat diet in patients with non-insulin-dependent diabetes mellitus. *N Engl J Med* 319:829–834.
- Garg A, Grundy SM, Koffler M. 1992a. Effect of high carbohydrate intake on hyperglycemia, islet function, and plasma lipoproteins in NIDDM. *Diabetes Care* 15:1572–1580.
- Garg A, Grundy SM, Unger RH. 1992b. Comparison of effects of high and low carbohydrate diets on plasma lipoproteins and insulin sensitivity in patients with mild NIDDM. *Diabetes* 41:1278–1285.
- Garg A, Bantle JP, Henry RR, Coulston AM, Griver KA, Raatz SK, Brinkley L, Chen Y-DI, Grundy SM, Huet BA, Reaven GM. 1994. Effects of varying carbohydrate content of diet in patients with non-insulin-dependent diabetes mellitus. *J Am Med Assoc* 271:1421–1428.
- Gartside PS, Glueck CJ. 1993. Relationship of dietary intake to hospital admission for coronary heart and vascular disease: The NHANES II National Probability Study. *J Am Coll Nutr* 6:676–684.
- Gazzaniga JM, Burns TL. 1993. Relationship between diet composition and body fatness, with adjustment for resting energy expenditure and physical activity, in preadolescent children. *Am J Clin Nutr* 58:21–28.
- George V, Tremblay A, Després JP, Leblanc C, Bouchard C. 1990. Effect of dietary fat content on total and regional adiposity in men and women. *Int J Obes* 14:1085–1094.

- Gerhard GT, Connor SL, Wander RC, Connor WE. 2000. Plasma lipid and lipoprotein responsiveness to dietary fat and cholesterol in premenopausal African American and white women. *Am J Clin Nutr* 72:56–63.
- Giannini S, Nobile M, Sartori L, Dalle Carbonare L, Ciuffreda M, Corro P, D'Angelo A, Calo L, Crepaldi G. 1999. Acute effects of moderate dietary protein restriction in patients with idiopathic hypercalciuria and calcium nephrolithiasis. *Am J Clin Nutr* 69:267–271.
- Gibney M, Sigman-Grant M, Stanton JL, Keast DR. 1995. Consumption of sugars. *Am J Clin Nutr* 62:178S–194S.
- Gibson SA. 1993. Consumption and sources of sugars in the diets of British schoolchildren: Are high-sugar diets nutritionally inferior? *J Hum Nutr Diet* 6:355–371.
- Gibson SA. 1997. Non-milk extrinsic sugars in the diets of pre-school children: Association with intakes of micronutrients, energy, fat and NSP. *Br J Nutr* 78:367–378.
- Gillum RF, Mussolino ME, Madans JH. 1996. The relationship between fish consumption and stroke incidence. The NHANES I epidemiologic follow-up study. *Arch Intern Med* 156:537–542.
- Ginsberg HN, Barr SL, Gilbert A, Karmally W, Deckelbaum R, Kaplan K, Ramakrishnan R, Holleran S, Dell RB. 1990. Reduction of plasma cholesterol levels in normal men on an American Heart Association Step 1 diet or a Step 1 diet with added monounsaturated fat. *N Engl J Med* 322:574–579.
- Giovannucci E, Willett WC. 1994. Dietary factors and risk of colon cancer. *Ann Med* 26:443–452.
- Giovannucci E, Rimm EB, Colditz GA, Stampfer MJ, Ascherio A, Chute CC, Willett WC. 1993. A prospective study of dietary fat and risk of prostate cancer. *J Natl Cancer Inst* 85:1571–1579.
- Giovannucci E, Rimm EB, Stampfer MJ, Colditz GA, Ascherio A, Willett WC. 1994. Intake of fat, meat, and fiber in relation to risk of colon cancer in men. *Cancer Res* 54:2390–2397.
- GISSI-Prevenzione Investigators. 1999. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: Results of the GISSI-Prevenzione trial. *Lancet* 354:447–455.
- Glanz K, Basil M, Maibach E, Goldberg J, Snyder D. 1998. Why Americans eat what they do: Taste, nutrition, cost, convenience, and weight control concerns as influences on food consumption. *J Am Diet Assoc* 98:1118–1126.
- Glueck CJ, Hastings MM, Allen C, Hogg E, Baehler L, Gartside PS, Phillips D, Jones M, Hollenbach EJ, Braun B, Anastasia JV. 1982. Sucrose polyester and covert caloric dilution. *Am J Clin Nutr* 35:1352–1359.
- Goodman MT, Kolonel LN, Yoshizawa CN, Hankin JH. 1988. The effect of dietary cholesterol and fat on the risk of lung cancer in Hawaii. *Am J Epidemiol* 128:1241–1255.
- Göransson H, Forsum E, Thilén M. 1983. Calculation and determination of metabolizable energy in mixed diets to humans. *Am J Clin Nutr* 38:954–963.
- Gortmaker SL, Dietz WH, Sobol AM, Wehler CA. 1987. Increasing pediatric obesity in the United States. *Am J Dis Child* 141:535–540.
- Grammatikos SI, Subbaiah PV, Victor TA, Miller WM. 1994. n-3 and n-6 Fatty acid processing and growth effects in neoplastic and non-cancerous human mammary epithelial cell lines. *Br J Cancer* 70:219–227.
- Green SM, Burley VJ, Blundell JE. 1994. Effect of fat- and sucrose-containing foods on the size of eating episodes and energy intake in lean males: Potential for causing overconsumption. *Eur J Clin Nutr* 48:547–555.

- Grill V, Björklund A. 2001. Overstimulation and beta-cell function. *Diabetes* 50:S122–S124.
- Grimsgaard S, Bønaa KH, Hansen J-B, Nordøy A. 1997. Highly purified eicosapentaenoic acid and docosahexaenoic acid in humans have similar triacylglycerol-lowering effects but divergent effects on serum fatty acids. *Am J Clin Nutr* 66:649–659.
- Grundy SM. 1986. Comparison of monounsaturated fatty acids and carbohydrates for lowering plasma cholesterol. *N Engl J Med* 314:745–748.
- Grundy SM, Florentin L, Nix D, Whelan MF. 1988. Comparison of monounsaturated fatty acids and carbohydrates for reducing raised levels of plasma cholesterol in man. *Am J Clin Nutr* 47:965–969.
- Guallar E, Aro A, Jiménez FJ, Martín-Moreno JM, Salminen I, van't Veer P, Kardinaal AFM, Gómez-Aracena J, Martin BC, Kohlmeier L, Kark JD, Mazaev VP, Ringstad J, Guillén J, Riemersma RA, Huttunen JK, Thamm M, Kok FJ. 1999. Omega-3 fatty acids in adipose tissue and risk of myocardial infarction. The EURAMIC Study. *Arterioscler Thromb Vasc Biol* 19:1111–1118.
- Guenther PM. 1986. Beverages in the diets of American teenagers. *J Am Diet Assoc* 86:493–499.
- Guthrie JF. 1996. Dietary patterns and personal characteristics of women consuming recommended amounts of calcium. *Fam Econ Nutr Rev* 9:33–49.
- Guthrie JF, Derby B. 1998. Changes in consumers' knowledge of food guide recommendations, 1990–91 versus 1994–95. *Fam Econ Nutr Rev* 11:42–48.
- Ha YL, Storkson J, Pariza MW. 1990. Inhibition of benzo(a)pyrene-induced mouse forestomach neoplasia by conjugated dienoic derivatives of linoleic acid. *Cancer Res* 50:1097–1101.
- Haglund O, Wallin R, Luostarinen R, Saldeen T. 1990. Effects of a new fluid fish oil concentrate, ESKIMO-3, on triglycerides, cholesterol, fibrinogen and blood pressure. *J Intern Med* 227:347–353.
- Halliwell B, Chirico S. 1993. Lipid peroxidation: Its mechanism, measurement, and significance. *Am J Clin Nutr* 57:715S–725S.
- Hansen D, Michaelsen KF, Skovby F. 1992. Growth during treatment of familial hypercholesterolemia. *Acta Paediatr* 81:1023–1025.
- Harker LA, Kelly AB, Hanson SR, Krupski W, Bass A, Osterud B, Fitzgerald GA, Goodnight SH, Connor WE. 1993. Interruption of vascular thrombus formation and vascular lesion formation by dietary n-3 fatty acids in fish oil in non-human primates. *Circulation* 87:1017–1029.
- Harnack L, Stang J, Story M. 1999. Soft drink consumption among US children and adolescents: Nutritional consequences. *J Am Diet Assoc* 99:436–441.
- Harnack LJ, Jeffery RW, Boutelle KN. 2000. Temporal trends in energy intake in the United States: An ecologic perspective. *Am J Clin Nutr* 71:1478–1484.
- Harris WS. 1989. Fish oils and plasma lipid and lipoprotein metabolism in humans: A critical review. *J Lipid Res* 30:785–807.
- Harris WS. 1997. n-3 Fatty acids and serum lipoproteins: Human studies. *Am J Clin Nutr* 65:1645S–1654S.
- Health Canada. 1997. *Canada's Food Guide to Healthy Eating*. Ottawa: Minister of Public Works and Government Services Canada.
- Heaney RP. 1993. Protein intake and the calcium economy. *J Am Diet Assoc* 93:1259–1260.
- Heaney RP. 1998. Excess dietary protein may not adversely affect bone. *J Nutr* 128:1054–1057.

- Hegsted DM, Ausman LM, Johnson JA, Dallal GE. 1993. Dietary fat and serum lipids: An evaluation of the experimental data. *Am J Clin Nutr* 57:875–883.
- Heitmann BL, Lissner L, Sørensen TIA, Bengtsson C. 1995. Dietary fat intake and weight gain in women genetically predisposed for obesity. *Am J Clin Nutr* 61:1213–1217.
- Hiatt RA, Ettinger B, Caan B, Quesenberry CP, Duncan D, Citron JT. 1996. Randomized controlled trial of a low animal protein, high fiber diet in the prevention of recurrent calcium oxalate kidney stones. *Am J Epidemiol* 144:25–33.
- Hill AJ, Blundell JE. 1990. Sensitivity of the appetite control system in obese subjects to nutritional and serotonergic challenges. *Int J Obes* 14:219–233.
- Hill AJ, Leathwood PD, Blundell JE. 1987. Some evidence for short-term caloric compensation in normal weight human subjects: The effects of high- and low-energy meals on hunger, food preference and food intake. *Hum Nutr Appl Nutr* 41:244–257.
- Hill JO, Peters JC, Reed GW, Schlundt DG, Sharp T, Greene HL. 1991. Nutrient balance in humans: Effects of diet composition. *Am J Clin Nutr* 54:10–17.
- Hill JO, Melanson EL, Wyatt HT. 2000. Dietary fat intake and regulation of energy balance: Implications for obesity. *J Nutr* 130:284S–288S.
- Himaya A, Fantino M, Antoine JM, Bronel L, Louis-Sylvestre J. 1997. Satiety power of dietary fat: A new appraisal. *Am J Clin Nutr* 65:1410–1418.
- Hislop TG, Coldman AJ, Elwood JM, Brauer G, Kan L. 1986. Childhood and recent eating patterns and risk of breast cancer. *Cancer Detect Prev* 9:47–58.
- Holman RL, McGill HC, Strong JP, Greer JC. 1958. The natural history of atherosclerosis. The early aortic lesions as seen in New Orleans in the middle of the 20th century. *Am J Pathol* 34:209–235.
- Holmes MD, Hunter DJ, Colditz GA, Stampfer MJ, Hankinson SE, Speizer FE, Rosner B, Willett WC. 1999. Association of dietary intake of fat and fatty acids with risk of breast cancer. *J Am Med Assoc* 281:914–920.
- Holt SH, Miller JC, Petocz P, Farmakalidid E. 1995. A satiety index of common foods. *Eur J Clin Nutr* 49:675–690.
- Höppener JWM, Ahrén B, Lips CJM. 2000. Islet amyloid and type 2 diabetes mellitus. *N Engl J Med* 343:411–419.
- Horton TJ, Drougas H, Brachey A, Reed GW, Peters JC, Hill JO. 1995. Fat and carbohydrate overfeeding in humans: Different effects on energy storage. *Am J Clin Nutr* 62:19–29.
- Horvath PJ, Eagen CK, Fisher NM, Leddy JJ, Pendergast DR. 2000. The effects of varying dietary fat on performance and metabolism in trained male and female runners. *J Am Coll Nutr* 19:52–60.
- Howard BV, Abbott WGH, Swinburn BA. 1991. Evaluation of metabolic effects of substitution of complex carbohydrates for saturated fat in individuals with obesity and NIDDM. *Diabetes Care* 14:786–795.
- Howard BV, Hannah JS, Heiser CC, Jablonski KA, Paidi MC, Alarif L, Robbins DC, Howard WJ. 1995. Polyunsaturated fatty acids result in greater cholesterol lowering and less triacylglycerol elevation than do monounsaturated fatty acids in a dose-response comparison in a multiracial study group. *Am J Clin Nutr* 62:392–402.
- Howe GR, Hirohata T, Hislop TG, Iscovich JM, Yuan J-M, Katsouyanni K, Lubin F, Marubini E, Modan B, Rohan T, Toniolo P, Shunzhang Y. 1990. Dietary factors and risk of breast cancer: Combined analysis of 12 case-control studies. *J Natl Cancer Inst* 82:561–569.

- Howe GR, Friedenreich CM, Jain M, Miller AB. 1991. A cohort study of fat intake and risk of breast cancer. *J Natl Cancer Inst* 83:336–340.
- Howe GR, Aronson KJ, Benito E, Castelletto R, Cornée J, Duffy S, Gallagher RP, Iscovich JM, Deng-ao J, Kaaks R, Kune GA, Kune S, Lee HP, Lee M, Miller AB, Peters RK, Potter JD, Riboli E, Slattery ML, Trichopoulos D, Tuyns A, Tzonou A, Watson LF, Whittemore AS, Wu-Willimas AH, Shu Z. 1997. The relationship between dietary fat intake and risk of colorectal cancer: Evidence from the combined analysis of 13 case-control studies. *Cancer Causes Control* 8:215–228.
- Hu FB, Stampfer MJ, Manson JE, Rimm E, Colditz GA, Rosner BA, Hennekens CH, Willett WC. 1997. Dietary fat intake and the risk of coronary heart disease in women. *N Engl J Med* 337:1491–1499.
- Hu FB, Stampfer MJ, Manson JE, Rimm E, Colditz GA, Speizer FE, Hennekens CH, Willett WC. 1999. Dietary protein and risk of ischemic heart disease in women. *Am J Clin Nutr* 70:221–227.
- Hu FB, van Dam RM, Liu S. 2001. Diet and risk of type II diabetes: The role of types of fat and carbohydrate. *Diabetologia* 44:805–817.
- Hulshof T, De Graaf C, Weststrate JA. 1993. The effects of preloads varying in physical state and fat content on satiety and energy intake. *Appetite* 21:273–286.
- Hun CS, Hasegawa K, Kawabata T, Kato M, Shimokawa T, Kagawa Y. 1999. Increased uncoupling protein2 mRNA in white adipose tissue, and decrease in leptin, visceral fat, blood glucose, and cholesterol in KK-A<sup>y</sup> mice fed with eicosapentaenoic and docosahexaenoic acids in addition to linolenic acid. *Biochem Biophys Res Comm* 259:85–90.
- Hunter DJ, Spiegelman D, Adami H-O, Beeson L, van den Brandt PA, Folsom AR, Fraser GE, Goldbohn A, Graham S, Howe GR, Kushi LH, Marshall JR, McDermott A, Miller AB, Speizer FE, Wolk A, Yaun S-S, Willett W. 1996. Cohort studies of fat intake and the risk of breast cancer—A pooled analysis. *N Engl J Med* 334:356–361.
- Hursting SD, Thornquist M, Henderson MM. 1990. Types of dietary fat and the incidence of cancer at five sites. *Prev Med* 19:242–253.
- Ip C, Scimeca JA. 1997. Conjugated linoleic acid and linoleic acid are distinctive modulators of mammary carcinogenesis. *Nutr Cancer* 27:131–135.
- Ip C, Chin SF, Scimeca JA, Pariza MW. 1991. Mammary cancer prevention by conjugated dienoic derivative of linoleic acid. *Cancer Res* 51:6118–6124.
- Ip C, Ip MM, Loftus T, Shoemaker S, Shea-Eaton W. 2000. Induction of apoptosis by conjugated linoleic acid in cultured mammary tumor cells and premalignant lesions of the rat mammary gland. *Cancer Epidemiol Biomarkers Prev* 9:689–696.
- Ip MM, Masso-Welch PA, Shoemaker SF, Shea-Eaton WK, Ip C. 1999. Conjugated linoleic acid inhibits proliferation and induces apoptosis of normal rat mammary epithelial cells in primary culture. *Exp Cell Res* 250:22–34.
- Iso H, Rexrode KM, Stampfer MJ, Manson JE, Colditz GA, Speizer FE, Hennekens CH, Willett WC. 2001. Intake of fish and omega-3 fatty acids and risk of stroke in women. *J Am Med Assoc* 285:304–312.
- James MJ, Gibson RA, Cleland LG. 2000. Dietary polyunsaturated fatty acids and inflammatory mediator production. *Am J Clin Nutr* 71:343S–348S.
- Janelle KC, Barr SI. 1995. Nutrient intakes and eating behavior scores of vegetarian and nonvegetarian women. *J Am Diet Assoc* 95:180–196.
- Jansen S, Lopez-Miranda J, Salas J, Castro P, Paniagua JA, Lopez-Segura F, Ordovas JM, Jimenez-Pereperez JA, Blanco A, Perez-Jimenez F. 1998. Plasma lipid response to hypolipidemic diets in young healthy non-obese men varies with body mass index. *J Nutr* 128:1144–1149.

- Jayarajan P, Reddy V, Mohanram M. 1980. Effect of dietary fat on absorption of  $\beta$ -carotene from green leafy vegetables in children. *Indian J Med Res* 71:53–56.
- Jeppesen J, Schaaf P, Jones C, Zhou M-Y, Chen Y-DI, Reaven GM. 1997. Effects of low-fat, high-carbohydrate diets on risk factors for ischemic heart disease in postmenopausal women. *Am J Clin Nutr* 65:1027–1033.
- Jéquier E. 1999. Response to and range of acceptable fat intake in adults. *Eur J Clin Nutr* 53:S84–S93.
- Jessup W, Kritharides L. 2000. Metabolism of oxidized LDL by macrophages. *Curr Opin Lipidol* 11:473–481.
- Johnson MM, Swan DD, Surette ME, Stegner J, Chilton T, Fonteh AN, Chilton FH. 1997. Dietary supplementation with  $\gamma$ -linolenic acid alters fatty acid content and eicosanoid production in healthy humans. *J Nutr* 127:1435–1444.
- Johnson RK, Panely C, Wang MQ. 1998. The association between noon beverage consumption and the diet quality of school-age children. *J Child Nutr Manage* 22:95–100.
- Jones AE, Murphy JL, Stolinski M, Wootton SA. 1998. The effect of age and gender on the metabolic disposal of [ $1^{13}\text{C}$ ]palmitic acid. *Eur J Clin Nutr* 52:22–28.
- Jones DY, Schatzkin A, Green SB, Block G, Brinton LA, Ziegler RG, Hoover R, Taylor PR. 1987. Dietary fat and breast cancer in the National Health and Nutrition Examination Survey. I. Epidemiologic follow-up study. *J Natl Cancer Inst* 79:465–471.
- Jonnalagadda SS, Egan SK, Heimbach JT, Harris SS, Kris-Etherton PM. 1995. Fatty acid consumption pattern of Americans: 1987–1988 USDA Nationwide Food Consumption Survey. *Nutr Res* 15:1767–1781.
- Kahn SR, Solymoss S, Flegel KM. 1997. Nonvalvular atrial fibrillation: Evidence for a prothrombic state. *Can Med Assoc J* 157:673–681.
- Kaizer L, Boyd NF, Kriukov V, Tritchler D. 1989. Fish consumption and breast cancer risk: An ecologic study. *Nutr Cancer* 12:61–68.
- Kang JX, Leaf A. 1996. Antiarrhythmic effects of polyunsaturated fatty acids: Recent studies. *Circulation* 94:1774–1780.
- Kannel WB. 2000. The Framingham Study: Its 50-year legacy and future promise. *J Atheroscler Thromb* 6:60–66.
- Karmali RA. 1986. Eicosanoids and cancer. *Prog Clin Biol Res* 222:687–697.
- Karmali RA, Marsh J, Fuchs C. 1984. Effect of omega-3 fatty acids on growth of a rat mammary tumor. *J Natl Cancer Inst* 73:457–461.
- Karmali RA, Reichel P, Cohen LA, Terano T, Hirai A, Tamura Y, Yoshida S. 1987. The effects of dietary omega-3 fatty acids on the DU-145 transplantable human prostatic tumor. *Anticancer Res* 7:1173–1179.
- Kasim SE, Martino S, Kim P-N, Khilnani S, Boomer A, Depper J, Reading BA, Heilbrun LK. 1993. Dietary and anthropometric determinants of plasma lipoproteins during a long-term low-fat diet in healthy women. *Am J Clin Nutr* 57:146–153.
- Kasim-Karakas SE, Lane E, Almario R, Mueller W, Walzem R. 1997. Effects of dietary fat restriction on particle size of plasma lipoproteins in postmenopausal women. *Metabolism* 46:431–436.
- Kasim-Karakas SE, Almario RU, Mueller WM, Peerson J. 2000. Changes in plasma lipoproteins during low-fat, high-carbohydrate diets: Effects of energy intake. *Am J Clin Nutr* 71:1439–1447.
- Katan MB, Zock PL, Mensink RP. 1994. Effects of fats and fatty acids on blood lipids in humans: An overview. *Am J Clin Nutr* 60:1017S–1022S.

- Kato I, Akhmedkhanov A, Koenig K, Toniolo PG, Shore RE, Riboli E. 1997. Prospective study of diet and female colorectal cancer: The New York University Women's Health Study. *Nutr Cancer* 28:276–281.
- Kavanaugh CJ, Liu K-L, Belury MA. 1999. Effect of dietary conjugated linoleic acid on phorbol ester-induced PGE<sub>2</sub> production and hyperplasia in mouse epidermis. *Nutr Cancer* 33:132–138.
- Keli SO, Feskens EJ, Kromhout D. 1994. Fish consumption and risk of stroke. The Zutphen Study. *Stroke* 25:328–332.
- Kelleher CC. 1992. Plasma fibrinogen and factor VII as risk factors for cardiovascular disease. *Eur J Epidemiol* 8:79–82.
- Kendall A, Levitsky DA, Strupp BJ, Lissner L. 1991. Weight loss on a low-fat diet: Consequence of the imprecision of the control of food intake in humans. *Am J Clin Nutr* 53:1124–1129.
- Kerstetter JE, Mitnick ME, Gundberg CM, Caseria DM, Ellison AF, Carpenter TO, Insogna KL. 1999. Changes in bone turnover in young women consuming different levels of dietary protein. *J Clin Endocrinol Metab* 84:1052–1055.
- Kestin M, Clifton P, Belling GB, Nestel PJ. 1990. n-3 Fatty acids of marine origin lower systolic blood pressure and triglycerides but raise LDL cholesterol compared with n-3 and n-6 fatty acids from plants. *Am J Clin Nutr* 51:1028–1034.
- Keusch GT, Torun B, Johnson RB, Urrutia JJ. 1984. Impairment of hemolytic complement activation by both classical and alternative pathways in serum from patients with kwashiorkor. *J Pediatr* 105:434–436.
- Keys A, Aravanis C, Blackburn H, Buzina R, Djordević BS, Dontas AS, Fidanza F, Karvonen MJ, Kimura N, Menotti A, Mohaček I, Nedeljković S, Puddu V, Punzar S, Taylor HL, van Buchem FSP. 1980. *Seven Countries. A Multivariate Analysis of Death and Coronary Heart Disease*. Cambridge, MA: Harvard University Press.
- Keys A, Menotti A, Aravanis C, Blackburn H, Djordević BS, Buzinz R, Dontas AS, Fidanza F, Karvonen MJ, Kimura N, Mohaček I, Nedeljković S, Puddu V, Punzar S, Taylor HL, Conti S, Kromhout D, Toshima H. 1984. The Seven Countries Study: 2,289 deaths in 15 years. *Prev Med* 13:141–154.
- Keys A, Menotti A, Karvonen MJ, Aravanis C, Blackburn H, Buzina R, Djordjević BS, Dontas AS, Fidanza F, Keys MH. 1986. The diet and 15-year death rate in the Seven Countries Study. *Am J Epidemiol* 124:903–915.
- King JC. 2000. Physiology of pregnancy and nutrient metabolism. *Am J Clin Nutr* 71:1218S–1225S.
- Klesges RC, Klesges LM, Haddock CK, Eck LH. 1992. A longitudinal analysis of the impact of dietary intake and physical activity on weight change in adults. *Am J Clin Nutr* 55:818–822.
- Knopp RH, Walden CE, Retzlaff BM, McCann BS, Dowdy AA, Albers JJ, Gey GO, Cooper MN. 1997. Long-term cholesterol-lowering effects of 4 fat-restricted diets in hypercholesterolemic and combined hyperlipidemic men. *J Am Med Assoc* 278:1509–1515.
- Knuiman JT, Westenbrink S, van der Heyden L, West CE, Burema J, De Boer J, Hautvast JGAJ, Räsänen L, Virkkunen L, Viikari J, Lokko P, Pobee JOM, Ferro-Luzzi A, Ferrini AM, Scaccini C, Sette S, Villavieja GM, Bulatao-Jayne J. 1983. Determinants of total and high density lipoprotein cholesterol in boys from Finland, the Netherlands, Italy, the Philippines and Ghana with special reference to diet. *Hum Nutr Clin Nutr* 37:237–254.

- Knuiman JT, West CE, Katan MB, Hautvast JGAJ. 1987. Total cholesterol and high density lipoprotein cholesterol levels in populations differing in fat and carbohydrate intake. *Arteriosclerosis* 7:612–619.
- Krauss RM. 2001. Atherogenic lipoprotein phenotype and diet-gene interactions. *J Nutr* 131:340S–343S.
- Krauss RM, Drewn DM. 1995. Low-density-lipoprotein subclasses and response to a low-fat diet in healthy men. *Am J Clin Nutr* 62:478S–487S.
- Kris-Etherton PM (for the DELTA Investigators). 1996. Effects of replacing saturated fat (SFA) with monounsaturated fat (MUFA) or carbohydrate (CHO) on plasma lipids and lipoproteins in individuals with markers for insulin resistance. *FASEB J* 10:2666.
- Kris-Etherton PM, Derr J, Mitchell DC, Mustad VA, Russell ME, McDonnell ET, Salabsky D, Pearson TA. 1993. The role of fatty acid saturation on plasma lipids, lipoproteins, and apolipoproteins: I. Effects of whole food diets high in cocoa butter, olive oil, soybean oil, dairy butter, and milk chocolate on the plasma lipids of young men. *Metabolism* 42:121–129.
- Kris-Etherton PM, Pearson TA, Wan Y, Hargrove RL, Moriarty K, Fishell V, Etherton TD. 1999. High-monounsaturated fatty acid diets lower both plasma cholesterol and triacylglycerol concentrations. *Am J Clin Nutr* 70:1009–1015.
- Kris-Etherton PM, Zhao G, Pekman CL, Fishell VK, Coval SM. 2000. Beneficial effects of a diet high in monounsaturated fatty acids on risk factors for cardiovascular disease. *Nutr Clin Care* 3:153–162.
- Kritchevsky D, Tepper SA, Czarnecki SK, Klurfeld DM, Story JA. 1981. Experimental atherosclerosis in rabbits fed cholesterol-free diets. Part 9. Beef protein and textured vegetable protein. *Atherosclerosis* 39:169–175.
- Kromhout D, de Lezenne Coulander C. 1984. Diet, prevalence and 10-year mortality from coronary heart disease in 871 middle-aged men. *Am J Epidemiol* 119:733–741.
- Kromhout D, Bosscheriet EB, de Lezenne Coulander C. 1985. The inverse relation between fish consumption and 20-year mortality from coronary heart disease. *N Engl J Med* 312:1205–1209.
- Kromhout D, Feskens EJM, Bowles CH. 1995. The protective effect of a small amount of fish on coronary heart disease mortality in an elderly population. *Int J Epidemiol* 24:340–345.
- Kromhout D, Bloemberg BPM, Feskens EJM, Hertog MGL, Menotti A, Blackburn H. 1996. Alcohol, fish, fibre and antioxidant vitamins intake do not explain population differences in coronary heart disease mortality. *Int J Epidemiol* 25:753–759.
- Kushi LH, Lew RA, Stare FJ, Ellison CR, el Lozy M, Bourke G, Daly L, Graham I, Hickey N, Mulcahy R, Kevaney J. 1985. Diet and 20-year mortality from coronary heart disease. The Ireland–Boston Diet–Heart Study. *N Engl J Med* 312:811–888.
- Kushi LH, Sellers TA, Potter JD, Nelson CL, Munger RG, Kaye SA, Folsom AR. 1992. Dietary fat and postmenopausal breast cancer. *J Natl Cancer Inst* 84:1092–1099.
- Kwiterovich PO, Barton BA, McMahon RP, Obarzanek E, Hunsberger S, Simons-Morton D, Kimm SYS, Friedman LA, Lasser N, Robson A, Lauer R, Stevens V, Van Horn L, Gidding S, Snetselaar L, Hartmuller VW, Greenlick M, Franklin F. 1997. Effects of diet and sexual maturation on low-density lipoprotein cholesterol during puberty. The Dietary Intervention Study in Children (DISC). *Circulation* 96:2526–2533.

- Lagström H, Jokinen E, Seppänen R, Rönnemaa T, Viikari J, Välimäki I, Venetoklis J, Myyrinmaa A, Niinikoski H, Lapinleimu H, Simell O. 1997. Nutrient intakes by young children in a prospective randomized trial of a low-saturated fat, low-cholesterol diet. The STRIP Baby Project. *Arch Pediatr Adolesc Med* 151:181–188.
- Lagström H, Seppänen R, Jokinen E, Niinikoski H, Rönnemaa T, Viikari J, Simell O. 1999. Influence of dietary fat on the nutrient intake and growth of children from 1 to 5 y of age: The Special Turku Coronary Risk Factor Intervention Project. *Am J Clin Nutr* 69:516–523.
- Lai PBS, Ross JA, Fearson KCH, Anderson JD, Carter DC. 1996. Cell cycle arrest and induction of apoptosis in pancreatic cancer cells exposed to eicosapentaenoic acid in vitro. *Br J Cancer* 74:1375–1383.
- Lapinleimu H, Viikari J, Jokinen E, Salo P, Routi T, Leino A, Rönnemaa R, Seppänen R, Välimäki I, Simell O. 1995. Prospective randomised trial in 1062 infants of diet low in saturated fat and cholesterol. *Lancet* 345:471–476.
- Larsen LF, Bladbjerg E-M, Jespersen J, Marckmann P. 1997. Effects of dietary fat quality and quantity on postprandial activation of blood coagulation factor VII. *Arterioscler Thromb Vasc Biol* 17:2904–2909.
- Larson DE, Hunter GR, Williams MJ, Kekes-Szabo T, Nyikos I, Goran MI. 1996. Dietary fat in relation to body fat and intraabdominal adipose tissue: A cross-sectional analysis. *Am J Clin Nutr* 64:677–684.
- Larsson H, Elmståhl S, Berglund G, Ahrén B. 1999. Habitual dietary intake versus glucose tolerance, insulin sensitivity and insulin secretion in postmenopausal women. *J Intern Med* 245:581–591.
- Lauer RM, Obarzanek E, Hunsberger SA, Van Horn L, Hartmuller VW, Barton BA, Stevens VJ, Kwiterovich PO, Franklin FA, Kimm SYS, Lasser NL, Simons-Morton DG. 2000. Efficacy and safety of lowering dietary intake of total fat, saturated fat, and cholesterol in children with elevated LDL cholesterol: The Dietary Intervention Study in Children. *Am J Clin Nutr* 72:1332S–1342S.
- La Vecchia C, Negri E, Franceschi S, Decarli A, Giacosa A, Lipworth L. 1995. Olive oil, other dietary fats, and the risk of breast cancer (Italy). *Cancer Causes Control* 6:545–550.
- Lawton CL, Burley VJ, Wales JK, Blundell JE. 1993. Dietary fat and appetite control in obese subjects: Weak effects on satiation and satiety. *Int J Obes Relat Metab Disord* 17:409–416.
- Leclerc I, Davignon I, Lopez D, Garrel DR. 1993. No change in glucose tolerance and substrate oxidation after a high-carbohydrate, low-fat diet. *Metabolism* 42:365–370.
- Lee KN, Kritchevsky D, Pariza MW. 1994. Conjugated linoleic acid and atherosclerosis in rabbits. *Atherosclerosis* 108:19–25.
- Lee KN, Pariza MW, Ntambi JM. 1998. Conjugated linoleic acid decreases hepatic stearoyl-CoA desaturase mRNA expression. *Biochem Biophys Res Comm* 248:817–821.
- Lee-Han H, Cousins M, Beaton M, McGuire V, Kriukov V, Chipman M, Boyd N. 1988. Compliance in a randomized clinical trial of dietary fat reduction in patients with breast dysplasia. *Am J Clin Nutr* 48:575–586.
- Lei YX, Cai WC, Chen YZ, Du YX. 1996. Some lifestyle factors in human lung cancer: A case control study of 792 lung cancer cases. *Lung Cancer* 14:S121–S136.
- Leibel RL, Hirsch J, Appel BE, Checani GC. 1992. Energy intake required to maintain body weight is not affected by wide variation in diet composition. *Am J Clin Nutr* 55:350–355.

- Lemann J. 1999. Relationship between urinary calcium and net acid excretion as determined by dietary protein and potassium: A review. *Nephron* 81:18–25.
- Leventhal LJ, Boyce EG, Zurier RB. 1993. Treatment of rheumatoid arthritis with gammalinolenic acid. *Ann Intern Med* 119:867–873.
- Leventhal LJ, Boyce EG, Zurier RB. 1994. Treatment of rheumatoid arthritis with blackcurrant seed oil. *Br J Rheumatol* 33:847–852.
- Levrat M-A, Behr SR, Rémésy C, Demigné C. 1991a. Effects of soybean fiber on cecal digestion in rats previously adapted to a fiber-free diet. *J Nutr* 121:672–678.
- Levrat M-A, Rémésy C, Demigné C. 1991b. High propionic acid fermentations and mineral accumulation in the cecum of rats adapted to different levels of inulin. *J Nutr* 121:1730–1737.
- Lew SQ, Bosch JP. 1991. Effect of diet on creatinine clearance and excretion in young and elderly healthy subjects and in patients with renal disease. *J Am Soc Nephrol* 2:856–865.
- Lewis CL, Park YK, Dexter PB, Yetley EA. 1992. Nutrient intakes and body weights of persons consuming high and moderate levels of added sugars. *J Am Diet Assoc* 92:708–713.
- Liew C, Schut HAJ, Chin SF, Pariza MW, Dashwood RH. 1995. Protection of conjugated linoleic acids against 2-amino-3-methylimidazo[4,5-f]quinoline-induced colon carcinogenesis in the F344 rat: A study of inhibitory mechanisms. *Carcinogenesis* 16:3037–3043.
- Lifshitz F, Moses N. 1989. Growth failure. A complication of dietary treatment of hypercholesterolemia. *Am J Dis Child* 143:537–542.
- Lissner L, Heitmann BL. 1995. Dietary fat and obesity: Evidence from epidemiology. *Eur J Clin Nutr* 49:79–90.
- Lissner L, Levitsky DA, Strupp BJ, Kalkwarf HJ, Roe DA. 1987. Dietary fat and the regulation of energy intake in human subjects. *Am J Clin Nutr* 46:886–892.
- Lissner L, Heitmann BL, Bengtsson C. 2000. Population studies of diet and obesity. *Br J Nutr* 83:S21–S24.
- Litin L, Sacks F. 1993. Trans-fatty-acid content of common foods. *N Engl J Med* 329:1969–1970.
- Liu GC, Coulston AM, Reaven GM. 1983. Effect of high-carbohydrate-low-fat diets on plasma glucose, insulin and lipid responses in hypertriglyceridemic humans. *Metabolism* 32:750–753.
- Liu K, Stamler J, Trevisan M, Moss D. 1982. Dietary lipids, sugar, fiber, and mortality from coronary heart disease. Bivariate analysis of international data. *Arteriosclerosis* 2:221–227.
- Liu S, Willett WC, Stampfer MJ, Hu FB, Franz M, Sampson L, Hennekens CH, Manson JE. 2000. A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. *Am J Clin Nutr* 71:1455–1461.
- Lopes-Virella MF, Virella G. 1996. Modified lipoproteins, cytokines and macrovascular disease in non-insulin-dependent diabetes mellitus. *Ann Med* 28:347–354.
- Lopez-Segura F, Velasco F, Lopez-Miranda J, Castro P, Lopez-Pedrera R, Blanco A, Jimenez-Pereperez J, Torres A, Trujillo J, Ordovas JM, Perez-Jiminez F. 1996. Monounsaturated fatty acid-enriched diet decreases plasma plasminogen activator inhibitor type 1. *Atheroscler Thromb Vasc Biol* 16:82–88.
- Louheranta AM, Porkkala-Sarataho EK, Nyysönen MK, Salonen RM, Salonen JT. 1996. Linoleic acid intake and susceptibility of very-low-density and low density lipoproteins to oxidation in men. *Am J Clin Nutr* 63:698–703.

- Louis-Sylvestre J, Tournier A, Chapelot D, Chabert M. 1994. Effect of a fat-reduced dish in a meal on 24-h energy and macronutrient intake. *Appetite* 22:165–172.
- Lovejoy JC. 1999. Dietary fatty acids and insulin resistance. *Curr Atheroscler Rep* 1:215–220.
- Lovejoy J, DiGirolamo M. 1992. Habitual dietary intake and insulin sensitivity in lean and obese adults. *Am J Clin Nutr* 55:1174–1179.
- Lovell CR, Burton JL, Horrobin DF. 1981. Treatment of atopic eczema with evening primrose oil. *Lancet* 1:278.
- Lubin F, Wax Y, Modan B. 1986. Role of fat, animal protein, and dietary fiber in breast cancer etiology: A case-control study. *J Natl Cancer Inst* 77:605–612.
- Lubin JH, Burns PE, Blot WJ, Ziegler RG, Lees AW, Fraumeni JF. 1981. Dietary factors and breast cancer risk. *Int J Cancer* 28:685–689.
- Ludwig DS, Majzoub JA, Al-Zahrani A, Dallal GE, Blanco I, Roberts SB. 1999a. High glycemic index foods, overeating, and obesity. *Pediatrics* 103:E26.
- Ludwig DS, Pereira MA, Kroenke CH, Hilner JE, Van Horn L, Slattery ML, Jacobs DR. 1999b. Dietary fiber, weight gain, and cardiovascular disease risk factors in young adults. *J Am Med Assoc* 282:1539–1546.
- Luhman CM, Beitz DC. 1993. Dietary protein and blood cholesterol homeostasis. In: Liepa GU, Beitz DC, Beynen AC, Gorman MA, eds. *Dietary Proteins: How They Alleviate Disease and Promote Better Health*. Champaign, IL: American Oil Chemists' Society. Pp. 57–76.
- Lundgren H, Bengtsson C, Blohmé G, Isaksson B, Lapidus L, Lenner RA, Saaek A, Winther E. 1989. Dietary habits and incidence of noninsulin-dependent diabetes mellitus in a population study of women in Gothenburg, Sweden. *Am J Clin Nutr* 49:708–712.
- Lungerhausen YK, Abbey M, Nestel PJ, Howe PRC. 1994. Reduction of blood pressure and plasma triglycerides by omega-3 fatty acids in treated hypertensives. *J Hypertens* 12:1041–1045.
- Luo J, Rizkalla SW, Boillot J, Alamowitch C, Chaib H, Bruzzo F, Desplanque N, Dalix A-M, Durand G, Slama G. 1996. Dietary (*n*-3) polyunsaturated fatty acids improve adipocyte insulin action and glucose metabolism in insulin-resistant rats: Relation to membrane fatty acids. *J Nutr* 126:1951–1958.
- Luo J, Rizkalla SW, Vidal H, Oppert JM, Colas C, Boussari A, Guerre-Millo M, Chapuis A-S, Chevalier A, Durand G, Slama G. 1998. Moderate intake of *n*-3 fatty acids for 2 months has no detrimental effect on glucose metabolism and could ameliorate the lipid profile in type 2 diabetic men: Results of a controlled study. *Diabetes Care* 21:717–724.
- Maffeis C, Pinelli L, Schutz Y. 1996. Fat intake and adiposity in 8 to 11-year-old obese children. *Int J Obes Relat Metab Disord* 20:170–174.
- Maillard G, Charles MA, Lafay L, Thibault N, Vray M, Borys JM, Basdevant A, Eschwège E, Romon M. 2000. Macronutrient energy intake and adiposity in non obese prepubertal children aged 5–11 y (the Fleurbaix Laventie Ville Santé Study). *Int J Obes Relat Metab Disord* 24:1608–1617.
- Männistö S, Pietinen P, Virtanen M, Kataja V, Uusitupa M. 1999. Diet and the risk of breast cancer in a case-control study: Does the threat of disease have an influence on recall bias? *J Clin Epidemiol* 52:429–439.
- Marckmann P, Grønbaek M. 1999. Fish consumption and coronary heart disease mortality. A systematic review of prospective cohort studies. *Eur J Clin Nutr* 53:585–590.

- Marckmann P, Raben A, Astrup A. 2000. Ad libitum intake of low-fat diets rich in either starchy foods or sucrose: Effects on blood lipids, factor VII coagulant activity, and fibrinogen. *Metabolism* 49:731–735.
- Marshall JA, Hamman RF, Baxter J. 1991. High-fat, low-carbohydrate diet and the etiology of non-insulin-dependent diabetes mellitus: The San Luis Valley Diabetes Study. *Am J Epidemiol* 134:590–603.
- Marshall JA, Bessesen DH, Hamman RF. 1997. High saturated fat and low starch and fibre are associated with hyperinsulinemia in a non-diabetic population: The San Luis Valley Diabetes Study. *Diabetologia* 40:430–438.
- Martin-Moreno JM, Willett WC, Gorgojo L, Banegas JR, Rodriguez-Artalejo F, Fernandez-Rodriguez JC, Maisonneuve P, Boyle P. 1994. Dietary fat, olive oil intake and breast cancer risk. *Int J Cancer* 58:774–780.
- Masironi R. 1970. Dietary factors and coronary heart disease. *Bull World Health Organ* 42:103–114.
- Mattes R. 1990. Effects of aspartame and sucrose on hunger and energy intake in humans. *Physiol Behav* 47:1037–1044.
- Mattson FH, Grundy SM. 1985. Comparison of effects of dietary saturated, monounsaturated, and polyunsaturated fatty acids on plasma lipids and lipoproteins in man. *J Lipid Res* 26:194–202.
- Mayer EJ, Newman B, Quesenberry CP, Selby JV. 1993. Usual dietary fat intake and insulin concentrations in healthy women twins. *Diabetes Care* 16:1459–1469.
- Mayer-Davis EJ, Monaco JH, Hoen HM, Carmichael S, Vitolins MZ, Rewers MJ, Haffner SM, Ayad MF, Bergman RN, Karter AJ. 1997. Dietary fat and insulin sensitivity in a triethnic population: The role of obesity. The Insulin Resistance Atherosclerosis Study (IRAS). *Am J Clin Nutr* 65:79–87.
- McDevitt RM, Poppitt SD, Murgatroyd PR, Prentice AM. 2000. Macronutrient disposal during controlled overfeeding with glucose, fructose, sucrose, or fat in lean and obese women. *Am J Clin Nutr* 72:369–377.
- McDonald BE, Gerrard JM, Bruce VM, Corner EJ. 1989. Comparison of the effect of canola oil and sunflower oil on plasma lipids and lipoproteins and on in vivo thromboxane A<sub>2</sub> and prostacyclin production in healthy young men. *Am J Clin Nutr* 50:1382–1388.
- McDowell MA, Briefel RR, Alaimo K, Bischoff AM, Caughman CR, Carroll MD, Loria CM, Johnson CL. 1994. Energy and macronutrient intakes of persons ages 2 months and over in the United States: Third National Health and Nutrition Examination Survey, Phase 1, 1988–91. *Adv Data* 255:1–24.
- McGee DL, Reed DM, Yano K, Kagan A, Tillotson J. 1984. Ten-year incidence of coronary heart disease in the Honolulu Heart Program. Relationship to nutrient intake. *Am J Epidemiol* 119:667–676.
- McGill HC. 1968. Fatty streaks in the coronary arteries and aorta. *Lab Invest* 18:100–104.
- McGill HC, McMahan CA, Zieske AW, Sloop GD, Walcott JV, Troxclair DA, Malcom GT, Tracy RE, Oalmann MC, Strong JP. 2000a. Associations of coronary heart disease risk factors with the intermediate lesion of atherosclerosis in youth. *Arterioscler Thromb Vasc Biol* 20:1998–2004.
- McGill HC, McMahan CA, Zieske AW, Tracy RE, Malcom GT, Herderick EE, Strong JP. 2000b. Association of coronary heart disease risk factors with microscopic qualities of coronary atherosclerosis in youth. *Circulation* 102:374–379.
- McLennan PL. 1993. Relative effects of dietary saturated, monounsaturated, and polyunsaturated fatty acids on cardiac arrhythmias in rats. *Am J Clin Nutr* 57:207–212.

- Mensink RP, Katan MB. 1987. Effect of monounsaturated fatty acids versus complex carbohydrates on high-density lipoproteins in healthy men and women. *Lancet* 1:122–125.
- Mensink RP, Katan MB. 1992. Effect of dietary fatty acids on serum lipids and lipoproteins. A meta-analysis of 27 trials. *Arterioscler Thromb* 12:911–919.
- Mensink RP, Zock PL, Katan MB, Hornstra G. 1992. Effect of dietary *cis* and *trans* fatty acids on serum lipoprotein[a] levels in humans. *J Lipid Res* 33:1493–1501.
- Meyer KA, Kushi LH, Jacobs DR, Slavin J, Sellers TA, Folsom AR. 2000. Carbohydrates, dietary fiber, and incident of type 2 diabetes in older women. *Am J Clin Nutr* 71:921–930.
- Miles CW. 1992. The metabolizable energy of diets differing in dietary fat and fiber measured in humans. *J Nutr* 122:306–311.
- Miller AB, Kelly A, Choi NW, Matthews V, Morgan RW, Munan L, Burch JD, Feather J, Howe GR, Jain M. 1978. A study of diet and breast cancer. *Am J Epidemiol* 107:499–509.
- Miller GJ, Cruickshank JK, Ellis LJ, Thompson RL, Wilkes HC, Stirling Y, Mitropoulos KA, Allison JV, Fox TE, Walker AO. 1989. Fat consumption and factor VII coagulant activity in middle-aged men. An association between a dietary and thrombogenic coronary risk factor. *Atherosclerosis* 78:19–24.
- Miller WC, Lindeman AK, Wallace J, Niederpruem M. 1990. Diet composition, energy intake, and exercise in relation to body fat in men and women. *Am J Clin Nutr* 52:426–430.
- Mooy JM, Grootenhuis PA, de Vries H, Valkenburg HA, Bouter LM, Kostense PJ, Heine RJ. 1995. Prevalence and determinants of glucose intolerance in a Dutch Caucasian population. The Hoorn Study. *Diabetes Care* 18:1270–1273.
- Mori TA, Vandongen R, Masarei JRL, Rouse IL, Dunbar D. 1991. Comparison of diets supplemented with fish oil or olive oil on plasma lipoproteins in insulin-dependent diabetics. *Metabolism* 40:241–246.
- Mori TA, Beilin LJ, Burke V, Morris J, Ritchie J. 1997. Interactions between dietary fat, fish, and fish oils and their effects on platelet function in men at risk of cardiovascular disease. *Arterioscler Thromb Vasc Biol* 17:279–286.
- Morris MC. 1994. Dietary fats and blood pressure. *J Cardiovasc Risk* 1:21–30.
- Morris MC, Sacks F, Rosner B. 1993. Does fish oil lower blood pressure? A meta-analysis of controlled trials. *Circulation* 88:523–533.
- Morris MC, Manson JE, Rosner B, Buring JE, Willett WC, Hennekens CH. 1995. Fish consumption and cardiovascular disease in the Physicians' Health Study: A prospective study. *Am J Epidemiol* 142:166–175.
- Morton JF, Guthrie JF. 1998. Changes in children's total fat intakes and their food group sources of fat, 1989–91 versus 1994–95: Implications for diet quality. *Fam Econ Nutr Rev* 11:44–57.
- Murphy JL, Jones A, Brookes S, Wootton SA. 1995. The gastrointestinal handling and metabolism of [1-<sup>13</sup>C]palmitic acid in healthy women. *Lipids* 30:291–298.
- Nagata C, Takatsuka N, Kurisu Y, Shimizu H. 1998. Decreased serum total cholesterol concentration is associated with high intake of soy products in Japanese men and women. *J Nutr* 128:209–213.
- National Cholesterol Education Program. 2001. *Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III)*. NIH Publication No. 01-3670. Bethesda, MD: National Institutes of Health.

- Nelson GJ, Schmidt PC, Kelly DS. 1995. Low-fat diets do not lower plasma cholesterol levels in healthy men compared to high-fat diets with similar fatty acid composition at constant caloric intake. *Lipids* 30:969–976.
- Nelson GJ, Schmidt PC, Bartolini GL, Kelley DS, Kyle D. 1997a. The effect of dietary docosahexaenoic acid on plasma lipoproteins and tissue fatty acid composition in humans. *Lipids* 32:1137–1146.
- Nelson GJ, Schmidt PS, Bartolini GL, Kelley DS, Kyle D. 1997b. The effect of dietary docosahexaenoic acid on platelet function, platelet fatty acid composition, and blood coagulation in humans. *Lipids* 32:1129–1136.
- Nelson M. 1991. Food, vitamins and IQ. *Proc Nutr Soc* 50:29–35.
- Newman TB, Garber AM, Holtzman NA, Hulley SB. 1995. Problems with the report of the Expert Panel on blood cholesterol levels in children and adolescents. *Arch Pediatr Adolesc Med* 149:241–247.
- Newmark HL. 1999. Squalene, olive oil, and cancer risk: Review and hypothesis. *Ann NY Acad Sci* 889:193–203.
- Nguyen VT, Larson DE, Johnson RK, Goran MI. 1996. Fat intake and adiposity in children of lean and obese parents. *Am J Clin Nutr* 63:507–513.
- NHLBI/NIDDK (National Heart, Lung, and Blood Institute/National Institute of Diabetes and Digestive and Kidney Diseases). 1998. *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. The Evidence Report*. NIH Publication No. 98-4083. Bethesda, MD: National Institutes of Health.
- Nicklas TA, Webber LS, Koschak M, Berenson GS. 1992. Nutrient adequacy of low fat intakes for children: The Bogalusa Heart Study. *Pediatrics* 89:221–228.
- Nicklas TA, Myers L, Farris RP, Srinivasan SR, Berenson GS. 1996. Nutritional quality of a high carbohydrate diet as consumed by children: The Bogalusa Heart Study. *J Nutr* 126:1382–1388.
- Nicolosi RJ, Wilson TA. 1997. The anti-atherogenic effect of dietary soybean protein concentrate in hamsters. *Nutr Res* 17:1457–1467.
- Niinikoski H, Viikari J, Rönnemaa T, Lapinleimu H, Jokinen E, Salo P, Seppänen R, Leino A, Tuominen J, Välimäki I, Simell O. 1996. Prospective randomized trial of low-saturated-fat, low-cholesterol diet during the first 3 years of life. The STRIP Baby Project. *Circulation* 94:1386–1393.
- Niinikoski H, Lapinleimu H, Viikari J, Rönnemaa T, Jokinen E, Seppänen R, Terho P, Tuominen J, Välimäki I, Simell O. 1997a. Growth until 3 years of age in a prospective, randomized trial of a diet with reduced saturated fat and cholesterol. *Pediatrics* 99:687–694.
- Niinikoski H, Viikari J, Rönnemaa T, Helenius H, Jokinen E, Lapinleimu H, Routi T, Lagström H, Seppänen R, Välimäki I, Simell O. 1997b. Regulation of growth of 7- to 36-month-old children by energy and fat intake in the prospective, randomized STRIP baby trial. *Pediatrics* 100:810–816.
- Nobukata H, Ishikawa T, Obata M, Shibutani Y. 2000. Long-term administration of highly purified eicosapentaenoic acid ethyl ester prevents diabetes and abnormalities of blood coagulation in male WBN/Kob rats. *Metabolism* 49:912–919.
- Noguchi M, Rose DP, Earashi M, Miyazaki I. 1995. The role of fatty acids and eicosanoid synthesis inhibitors in breast carcinoma. *Oncology* 52:265–271.
- Norrish AE, Jackson RT, Sharpe SJ, Skeaff CM. 2000. Men who consume vegetable oils rich in monounsaturated fat: Their patterns and risk of prostate cancer (New Zealand). *Cancer Causes Control* 11:609–615.

- Obarzanek E, Schreiber GB, Crawford PB, Goldman SR, Barrier PM, Frederick MM, Lakatos E. 1994. Energy intake and physical activity in relation to indexes of body fat: The National Heart, Lung, and Blood Institute Growth and Health Study. *Am J Clin Nutr* 60:15–22.
- Obarzanek E, Velletri PA, Cutler JA. 1996. Dietary protein and blood pressure. *J Am Med Assoc* 275:1598–1603.
- Obarzanek E, Hunsberger SA, Van Horn L, Hartmuller VV, Barton BA, Stevens VJ, Kwiterovich PO, Franklin FA, Kimm SYS, Lasser NL, Simons-Morton DG, Lauer RM. 1997. Safety of a fat-reduced diet: The Dietary Intervention Study in Children (DISC). *Pediatrics* 100:51–59.
- Obarzanek E, Kimm SYS, Barton BA, Van Horn L, Kwiterovich PO, Simons-Morton DG, Hunsberger SA, Lasser NL, Robson AM, Franklin FA, Lauer RM, Stevens VJ, Friedman LA, Dorgan JF, Greenlick MR. 2001a. Long-term safety and efficacy of a cholesterol-lowering diet in children with elevated low-density lipoprotein cholesterol: Seven-year results of the Dietary Intervention Study in Children (DISC). *Pediatrics* 107:256–264.
- Obarzanek E, Sacks FM, Vollmer WM, Bray GA, Miller ER, Lin P-H, Karanja NM, Most-Windhauser MM, Moore TJ, Swain JF, Bales CW, Proschan MA. 2001b. Effects on blood lipids of a blood pressure-lowering diet: The Dietary Approaches to Stop Hypertension (DASH) Trial. *Am J Clin Nutr* 74:80–89.
- Ogden J, Wardle J. 1990. Cognitive restraint and sensitivity to cues for hunger and satiety. *Physiol Behav* 47:477–481.
- O'Hanesian MA, Rosner B, Bishop LM, Sacks FM. 1996. Effects of inherent responsiveness to diet and day-to-day diet variation on plasma lipoprotein concentrations. *Am J Clin Nutr* 64:53–59.
- Ohta A, Ohtsuki M, Baba S, Adachi T, Sakata T, Sakaguchi E. 1995. Calcium and magnesium absorption from the colon and rectum are increased in rats fed fructooligosaccharides. *J Nutr* 125:2417–2424.
- Okita M, Yoshida S, Yamamoto J, Suzuki K, Kaneyuki T, Kubota M, Sasagawa T. 1995. n-3 and n-6 Fatty acid intake and serum phospholipid fatty acid composition in middle-aged women living in rural and urban areas in Okayama Prefecture. *J Nutr Sci Vitaminol* 41:313–323.
- Olson RE. 2000. Is it wise to restrict fat in the diets of children? *J Am Diet Assoc* 100:28–32.
- Oomen CM, Feskens EJM, Räsänen L, Fidanza F, Nissinen AM, Menotti A, Kok FJ, Kromhout D. 2000. Fish consumption and coronary heart disease mortality in Finland, Italy, and the Netherlands. *Am J Epidemiol* 151:999–1006.
- Orencia AJ, Daviglus ML, Dyer AR, Shekelle RB, Stamler J. 1996. Fish consumption and stroke in men. 30-Year findings of the Chicago Western Electric Study. *Stroke* 27:204–209.
- Ostrowska E, Muralitharan M, Cross RF, Bauman DE, Dunshea FR. 1999. Dietary conjugated linoleic acids increase lean tissue and decrease fat deposition in growing pigs. *J Nutr* 129:2037–2042.
- Owen RW, Giacosa A, Hull WE, Haubner R, Spiegelhalder B, Bartsch H. 2000. The antioxidant/anticancer potential of phenolic compounds isolated from olive oil. *Eur J Cancer* 36:1235–1247.
- Parillo M, Rivelles AA, Ciardullo AV, Capaldo B, Giacco A, Genovese S, Riccardi G. 1992. A high-monounsaturated-fat/low-carbohydrate diet improves peripheral insulin sensitivity in non-insulin-dependent diabetic patients. *Metabolism* 41:1373–1378.

- Pariza MW, Park Y, Cook ME. 2001. The biologically active isomers of conjugated linoleic acid. *Prog Lipid Res* 40:283–298.
- Park Y, Albright KJ, Liu W, Storkson JM, Cook ME, Pariza MW. 1997. Effect of conjugated linoleic acid on body composition in mice. *Lipids* 32:853–858.
- Park Y, Storkson JM, Albright KJ, Liu W, Pariza MW. 1999. Evidence that the *trans*-10,*cis*-12 isomer of conjugated linoleic acid induces body composition changes in mice. *Lipids* 34:235–241.
- Parker DR, Weiss ST, Troisi R, Cassano PA, Vokonas PS, Landsberg L. 1993. Relationship of dietary saturated fatty acids and body habitus to serum insulin concentrations: The Normative Aging Study. *Am J Clin Nutr* 58:129–136.
- Parnaud G, Corpet DE. 1997. Colorectal cancer: Controversial role of meat consumption. *Bull Cancer* 84:899–911.
- Parrish CC, Pathy DA, Angel A. 1990. Dietary fish oils limit adipose tissue hypertrophy in rats. *Metabolism* 39:217–219.
- Parrish CC, Pathy DA, Parkes JG, Angel A. 1991. Dietary fish oils modify adipocyte structure and function. *J Cell Physiol* 148:493–502.
- Pearce ML, Dayton S. 1971. Incidence of cancer in men on a diet high in polyunsaturated fat. *Lancet* 1:464–467.
- Peiris AN, Struve MF, Mueller RA, Lee MB, Kisseebah AH. 1988. Glucose metabolism in obesity: Influence of body fat distribution. *J Clin Endocrinol Metab* 67:760–767.
- Pelkman CL, Coval SM, Mauger DT, Zhao G, Kris-Etherton PM. 2001. A meta-analysis of low-fat versus high-MUFA diets. *FASEB J* 15:394.
- Pelletier DL, Frongillo EA, Schroeder DG, Habicht J-P. 1995. The effects of malnutrition on child mortality in developing countries. *Bull World Health Organ* 73:443–448.
- Perez-Jimenez F, Espino A, Lopez-Segura F, Blanco J, Ruiz-Gutierrez V, Prada JL, Lopez-Miranda J, Jimenez-Pereperez J, Ordovas JM. 1995. Lipoprotein concentrations in normolipidemic males consuming oleic acid-rich diets from two different sources: Olive oil and oleic acid-rich sunflower oil. *Am J Clin Nutr* 62:769–775.
- Perez-Jimenez F, Catrso P, Lopez-Miranda J, Paz-Rojas E, Blanco A, Lopez-Segura F, Velasco F, Marin C, Fuentes F, Ordovas JM. 1999. Circulating levels of endothelial function are modulated by dietary monounsaturated fat. *Atherosclerosis* 145:351–358.
- Perez-Jimenez F, Lopez-Miranda J, Pinillos MD, Gomez P, Pas-Rojas E, Montilla P, Marin C, Velasco MJ, Blanco-Molina A, Jimenez Pereperez JA, Ordovas JM. 2001. A Mediterranean and a high-carbohydrate diet improves glucose metabolism in healthy young persons. *Diabetologica* 44:2038–2043.
- Peterson S, Sigman-Grant M. 1997. Impact of adopting lower-fat food choices on nutrient intake of American children. *Pediatrics* 100:E4.
- Pfeuffer M, Ahrens F, Hagemeyer H, Barth CA. 1988. Influence of casein versus soy protein isolate on lipid metabolism of minipigs. *Ann Nutr Metab* 32:83–89.
- Phillips RL. 1975. Role of life-style and dietary habits in risk of cancer among Seventh-Day Adventists. *Cancer Res* 35:3513–3522.
- Pietinen P, Ascherio A, Korhonen P, Hartman AM, Willett WC, Albanes D, Virtamo J. 1997. Intake of fatty acids and risk of coronary heart disease in a cohort of Finnish men. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. *Am J Epidemiol* 145:876–887.

- Poppitt SD, Swann DL. 1998. Dietary manipulation and energy compensation: Does the intermittent use of low-fat items in the diet reduce total energy intake in free-feeding lean men? *Int J Obes Relat Metab Disord* 22:1024–1031.
- Poppitt SD, Swann DL, Murgatroyd PR, Elia M, McDevitt RM, Prentice AM. 1998. Effect of dietary manipulation on substrate flux and energy balance in obese women taking the appetite suppressant dextroamphetamine. *Am J Clin Nutr* 68:1012–1021.
- Popp-Snijders C, Schouten JA, Heine RJ, van der Meer J, van der Veen EA. 1987. Dietary supplementation of omega-3 polyunsaturated fatty acids improves insulin sensitivity in non-insulin-dependent diabetes. *Diabetes Res* 4:141–147.
- Porrini M, Crovetti R, Riso P, Santangelo A, Testolin G. 1995. Effects of physical and chemical characteristics of food on specific and general satiety. *Physiol Behav* 57:461–468.
- Prentice AM. 2001. Overeating: The health risks. *Obes Res* 9:234S–238S.
- Price JM, Grinker J. 1973. Effects of degree of obesity, food deprivation, and palatability on eating behavior of humans. *J Comp Physiol Psychol* 85:265–271.
- Promislow JHE, Goodman-Gruen D, Slymen DJ, Barrett-Conner E. 2002. Protein consumption and bone mineral density in the elderly. The Rancho Bernardo Study. *Am J Epidemiol* 155:636–644.
- Proserpi C, Sparti A, Schutz Y, Di Vetta V, Milon H, Jéquier E. 1997. Ad libitum intake of a high-carbohydrate or high-fat diet in young men: Effects on nutrient balances. *Am J Clin Nutr* 66:539–545.
- Raben A, Macdonald I, Astrup A. 1997. Replacement of dietary fat by sucrose or starch: Effects on 14 d ad libitum energy intake, energy expenditure and body weight in formerly obese and never-obese subjects. *Int J Obes Relat Metab Disord* 21:846–859.
- Ramon JM, Bou R, Romea S, Alkiza ME, Jacas M, Ribes J, Oromi J. 2000. Dietary fat intake and prostate cancer risk: A case-control study in Spain. *Cancer Causes Control* 11:679–685.
- Rath R, Mašek J, Kujalová V, Slabochová Z. 1974. Effect of a high sugar intake on some metabolic and regulatory indicators in young men. *Nahrung* 18:343–353.
- Reaven GM. 1988. Banting lecture 1988. Role of insulin resistance in human disease. *Diabetes* 37:1595–1607.
- Reaven GM. 1995. Pathophysiology of insulin resistance in human disease. *Physiol Rev* 75:473–486.
- Reaven GM. 2001. Insulin resistance, compensatory hyperinsulinemia, and coronary heart disease: Syndrome X revisited. In: Jefferson LS, Cherrington AD, Goodman HM, eds. *Handbook of Physiology. Section 7: The Endocrine System. Volume II: The Endocrine Pancreas and Regulation of Metabolism*. Oxford: Oxford University Press. Pp. 1169–1197.
- Reaven P, Parthasarathy S, Grasse BJ, Miller E, Almazan F, Mattson FH, Khoo JC, Steinberg D, Witztum JL. 1991. Feasibility of using an oleate-rich diet to reduce the susceptibility of low-density lipoprotein to oxidative modification in humans. *Am J Clin Nutr* 54:701–706.
- Reaven P, Parthasarathy S, Grasse BJ, Miller E, Steinberg D, Witztum JL. 1993. Effects of oleate-rich and linoleate-rich diets on the susceptibility of low density lipoprotein to oxidative modification in mildly hypercholesterolemic subjects. *J Clin Invest* 91:668–676.

- Reaven PD, Grasse BJ, Tribble DL. 1994. Effects of linoleate-enriched and oleate-enriched diets in combination with alpha-tocopherol on the susceptibility of LDL and LDL subfractions to oxidative modification in humans. *Arterioscler Thromb* 14:557–566.
- Reddy BS. 1992. Dietary fat and colon cancer: Animal model studies. *Lipids* 27:807–813.
- Reddy BS, Burill C, Rigotti J. 1991. Effect of diets high in ω-3 and ω-6 fatty acids on initiation and postinitiation stages of colon carcinogenesis. *Cancer Res* 51:487–491.
- Reiser S, Handler HB, Gardner LB, Hallfrisch JG, Michaelis OE, Prather ES. 1979. Isocaloric exchange of dietary starch and sucrose in humans. II. Effect on fasting blood insulin, glucose, and glucagon and on insulin and glucose response to a sucrose load. *Am J Clin Nutr* 32:2206–2216.
- Rémésy C, Behr SR, Levrat M-A, Demigné C. 1992. Fiber fermentability in the rat cecum and its physiological consequences. *Nutr Res* 12:1235–1244.
- Renaud S, de Lorgeril M, Delaye J, Guidollet J, Jacquard F, Mamelle N, Martin JL, Monjaud I, Salen P, Toubol P. 1995. Creten Mediterranean diet for prevention of coronary heart disease. *Am J Clin Nutr* 61:1360S–1367S.
- Ricketts CD. 1997. Fat preferences, dietary fat intake and body composition in children. *Eur J Clin Nutr* 51:778–781.
- Rissanen AM, Heliövaara M, Knekt P, Reunanen A, Aromaa A. 1991. Determinants of weight gain and overweight in adult Finns. *Eur J Clin Nutr* 45:419–430.
- Robertson WG, Peacock M. 1982. The pattern of urinary stone disease in Leeds and in the United Kingdom in relation to animal protein intake during the period 1960–1980. *Urol Int* 37:394–399.
- Robertson WG, Heyburn PJ, Peacock M, Hanes FA, Swaminathan R. 1979. The effect of high animal protein intake on the risk of calcium stone-formation in the urinary tract. *Clin Sci* 57:285–288.
- Roche HM, Zampelas A, Jackson KG, Williams CM, Gibney MJ. 1998. The effect of test meal monounsaturated fatty acid:saturated fatty acid ratio on postprandial lipid metabolism. *Br J Nutr* 79:419–424.
- Rodier M, Colette C, Crastes de Paulet P, Crastes de Paulet A, Monnier L. 1993. Relationships between serum lipids, platelet membrane fatty acid composition and platelet aggregation in type 2 diabetes mellitus. *Diabète Metab* 19:560–565.
- Rolland-Cachera MF, Deheeger M, Akroud M, Bellisle F. 1995. Influence of macronutrients on adiposity development: A follow up study of nutrition and growth from 10 months to 8 years of age. *Int J Obes Relat Metab Disord* 19:573–578.
- Rolls BJ, Hetherington M, Burley VJ. 1988. The specificity of satiety: The influence of foods of different macronutrient content on the development of satiety. *Physiol Behav* 43:145–153.
- Rolls BJ, Lester LJ, Summerfelt A. 1989. Hunger and food intake following consumption of low-calorie foods. *Appetite* 13:115–127.
- Rolls BJ, Kim-Harris S, Fischman MW, Foltin RW, Moran TH, Stoner SA. 1994. Satiety after preloads with different amounts of fat and carbohydrate: Implications for obesity. *Am J Clin Nutr* 60:476–487.
- Romieu I, Willett WC, Stampfer MJ, Colditz GA, Sampson L, Rosner B, Hennekens CH, Speizer FE. 1988. Energy intake and other determinants of relative weight. *Am J Clin Nutr* 47:406–412.
- Rose DP, Connolly JM. 2000. Regulation of tumor angiogenesis by dietary fatty acids and eicosanoids. *Nutr Cancer* 37:119–127.

- Rugg-Gunn AJ, Hackett AF, Jenkins GN, Appleton DR. 1991. Empty calories? Nutrient intake in relation to sugar intake in English adolescents. *J Hum Nutr Diet* 4:101–111.
- Rush D, Stein Z, Susser M. 1980. A randomized controlled trial of prenatal nutrition supplementation in New York City. *Pediatrics* 65:683–697.
- Rustan AC, Hustvedt B-E, Drevon CA. 1993. Dietary supplementation of very long-chain *n*-3 fatty acids decreases whole body lipid utilization in the rat. *J Lipid Res* 34:1299–1309.
- Salmerón J, Manson JE, Stampfer MJ, Colditz GA, Wing AL, Willett WC. 1997. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. *J Am Med Assoc* 277:472–477.
- Salmerón J, Hu FB, Manson JE, Stampfer MJ, Colditz GA, Rimm EB, Willett WC. 2001. Dietary fat intake and risk of type 2 diabetes in women. *Am J Clin Nutr* 73:1019–1026.
- Salomon O, Steinberg DM, Zivelin A, Gitel S, Dardik R, Rosenberg N, Berliner S, Inbal A, Many A, Lubetsky A, Varon D, Martinowitz U, Seligsohn U. 1999. Single and combined prothrombotic factors in patients with idiopathic venous thromboembolism. Prevalence and risk assessment. *Arterioscler Thromb Vasc Biol* 19:511–518.
- Saltzman E, Dallal GE, Roberts SB. 1997. Effect of high-fat and low-fat diets on voluntary energy intake and substrate oxidation: Studies in identical twins consuming diets matched for energy density, fiber, and palatability. *Am J Clin Nutr* 66:1332–1339.
- Samaras K, Kelly PJ, Chiano MN, Arden N, Spector TD, Campbell LV. 1998. Genes versus environment. The relationship between dietary fat and total and central abdominal fat. *Diabetes Care* 21:2069–2076.
- Sanders TAB, Hinds A. 1992. The influence of a fish oil high in docosahexaenoic acid on plasma lipoprotein and vitamin E concentrations and haemostatic function in healthy male volunteers. *Br J Nutr* 68:163–173.
- Sanders TAB, Oakley FR, Miller GJ, Mitropoulos KA, Crook D, Oliver MF. 1997. Influence of *n*-6 versus *n*-3 polyunsaturated fatty acids in diets low in saturated fatty acids on plasma lipoproteins and hemostatic factors. *Arterioscler Thromb Vasc Biol* 17:3449–3460.
- Saris WHM, Astrup A, Prentice AM, Zunft HJF, Formiguera X, Verboeket-van de Venne WPHG, Raben A, Poppitt SD, Seppelt B, Johnston S, Vasilaras TH, Keogh GF. 2000. Randomized controlled trial of changes in dietary carbohydrate/fat ratio and simple vs complex carbohydrates on body weight and blood lipids: The CARMEN study. *Int J Obes Relat Metab Disord* 24:1310–1318.
- Sasaki S, Horacek M, Kesteloot H. 1993. An ecological study of the relationship between dietary fat intake and breast cancer mortality. *Prev Med* 22:187–202.
- Sawaya AL, Fuss PJ, Dallal GE, Tsay R, McCrory MA, Young V, Roberts SB. 2001. Meal palatability, substrate oxidation and blood glucose in young and older men. *Physiol Behav* 72:5–12.
- Saynor R, Gillott T. 1992. Changes in blood lipids and fibrinogen with a note on safety in a long term study on the effects of *n*-3 fatty acids in subjects receiving fish oil supplements and followed for seven years. *Lipids* 27:533–538.
- Schmidt EB, Lervang H-H, Varming K, Madsen P, Dyerberg J. 1992. Long-term supplementation with *n*-3 fatty acids. I: Effect on blood lipids, haemostasis and blood pressure. *Scand J Clin Lab Invest* 52:221–228.

- Schønberg S, Krokan HE. 1995. The inhibitory effect of conjugated dienoic derivates (CLA) of linoleic acid on the growth of human tumor cell lines is in part due to increased lipid peroxidation. *Anticancer Res* 15:1241–1246.
- Schuurman AG, van den Brandt PA, Dorant E, Brants HAM, Goldbohm RA. 1999. Association of energy and fat intake with prostate carcinoma risk. Results from the Netherlands Cohort Study. *Cancer* 86:1019–1027.
- Seagle HM, Davy BM, Grunwald G, Hill JO. 1997. Energy density of self-reported food intake: Variation and relationship to other food components. *Obes Res* 5:78S.
- Serdula MK, Ivery D, Coates RJ, Freedman DS, Williamson DF, Byers TE. 1993. Do obese children become obese adults? A review of the literature. *Prev Med* 22:167–177.
- Severson RK, Nomura AMY, Grove JS, Stemmermann GN. 1989. A prospective study of demographics, diet, and prostate cancer among men of Japanese ancestry in Hawaii. *Cancer Res* 49:1857–1860.
- Shannon BM, Tershakovec AM, Martel JK, Achterberg CL, Cortner JA, Smiciklas-Wright HS, Stallings VA, Stolley PD. 1994. Reduction of elevated LDL-cholesterol levels of 4- to 10-year-old children through home-based dietary education. *Pediatrics* 94:923–927.
- Shea S, Basch CE, Stein AD, Contento IR, Irigoyen M, Zybert P. 1993. Is there a relationship between dietary fat and stature or growth in children three to five years of age? *Pediatrics* 92:579–586.
- Sheppard L, Kristal AR, Kushi LH. 1991. Weight loss in women participating in a randomized trial of low-fat diets. *Am J Clin Nutr* 54:821–828.
- Shetty PS, Prentice AM, Goldberg GR, Murgatroyd PR, McKenna APM, Stubbs RJ, Volschenk PA. 1994. Alterations in fuel selection and voluntary food intake in response to isoenergetic manipulation of glycogen stores in humans. *Am J Clin Nutr* 60:534–543.
- Shide DJ, Rolls BJ. 1995. Information about the fat content of preloads influences energy intake in healthy women. *J Am Diet Assoc* 95:993–998.
- Shu XO, Zheng W, Potischman N, Brinton LA, Hatch MC, Gao YT, Fraumeni JF. 1993. A population-based case-control study of dietary factors and endometrial cancer in Shanghai, People's Republic of China. *Am J Epidemiol* 137:155–165.
- Shultz TD, Leklem JE. 1983. Dietary status of Seventh-day Adventists and non-vegetarians. *J Am Diet Assoc* 83:27–33.
- Shultz TD, Chew BP, Seaman WR, Luedcke LO. 1992. Inhibitory effect of conjugated dienoic derivates of linoleic acid and β-carotene on the in vitro growth of human cancer cells. *Cancer Lett* 63:125–133.
- Sierakowski R, Finlayson B, Landes RR, Finlayson CD, Sierakowski N. 1978. The frequency of urolithiasis in hospital discharge diagnoses in the United States. *Invest Urol* 15:438–441.
- Simell O, Niinikoski H, Rönnemaa T, Lapinleimu H, Routi T, Lagström H, Salo P, Jokinen E, Viikari J. 2000. Special Turku Coronary Risk Factor Intervention Project for Babies (STRIP). *Am J Clin Nutr* 72:1316S–1331S.
- Singh RB, Rastogi SS, Verma R, Laxmi B, Singh R, Ghosh S, Niaz MA. 1992. Randomised controlled trial of cardioprotective diet in patients with recent acute myocardial infarction: Results of one year follow up. *Br Med J* 304:1015–1019.
- Singh RB, Ghosh S, Niaz AM, Gupta S, Bishnoi I, Sharma JP, Agarwal P, Rastogi SS, Beegum R, Chibo H. 1995. Epidemiologic study of diet and coronary risk factors in relation to central obesity and insulin levels in rural and urban populations of north India. *Int J Cardiol* 47:245–255.

- Singh RB, Niaz MA, Sharma JP, Kumar R, Rastogi V, Moshiri M. 1997. Randomized, double-blind, placebo-controlled trial of fish oil and mustard oil in patients with suspected acute myocardial infarction: The Indian Experiment of Infarct Survival—4. *Cardiovasc Drugs Ther* 11:485–491.
- Siscovick DS, Raghunathan TE, King I, Weinmann S, Wicklund KG, Albright J, Bovbjerg V, Arbogast P, Smith H, Kushi LH, Cobb LA, Copass MK, Psaty BM, Lemaitre R, Retzlaff B, Childs M, Knopp RH. 1995. Dietary intake and cell membrane levels of long-chain  $\omega$ -3 polyunsaturated fatty acids and the risk of primary cardiac arrest. *J Am Med Assoc* 274:1363–1367.
- Skinner JD, Carruth BR, Moran J, Houck K, Coletta F. 1999. Fruit juice intake is not related to children's growth. *Pediatrics* 103:58–64.
- Skov AR, Toubro S, Ronn B, Holm L, Astrup A. 1999. Randomized trial on protein vs carbohydrate in ad libitum fat reduced diet for the treatment of obesity. *Int J Obes Relat Metab Disord* 23:528–536.
- Slattery ML, Potter JD, Sorenson AW. 1994. Age and risk factors for colon cancer (United States and Australia): Are there implications for understanding differences in case-control and cohort studies? *Cancer Causes Control* 5:557–563.
- Slattery ML, Caan BJ, Potter JD, Berry TD, Coates A, Duncan D, Edwards SL. 1997. Dietary energy sources and colon cancer risk. *Am J Epidemiol* 145:199–210.
- Sonko BJ, Prentice AM, Poppitt SD, Prentice A, Jequier E, Whitehead RG. 1994. Could dietary fat intake be an important determinant of seasonal weight changes in a rural subsistence farming community in The Gambia? In: *Nestlé Foundation for the Study of the Problems of Nutrition in the World. Annual Report 1994*. Lausanne, Switzerland: Nestlé Foundation. Pp. 74–87.
- Sonnenberg LM, Quatromoni PA, Gagnon DR, Cupples LA, Franz MM, Ordovas JM, Wilson PWF, Schaefer EJ, Millen BE. 1996. Diet and plasma lipids in women. II. Macronutrients and plasma triglycerides, high-density lipoprotein, and the ratio of total to high-density lipoprotein cholesterol in women: The Framingham Nutrition Studies. *J Clin Epidemiol* 49:665–672.
- Stamler J. 1979. Population studies. In: Levy R, Rifkind B, Dennis B, Ernst N, eds. *Nutrition, Lipids, and Coronary Heart Disease*. New York: Raven Press. Pp. 25–88.
- Stangl GI. 2000. Conjugated linoleic acids exhibit a strong fat-to-lean partitioning effect, reduce serum VLDL lipids and redistribute tissue lipids in food-restricted rats. *J Nutr* 130:1140–1146.
- Stary HC. 1989. Evolution and progression of atherosclerotic lesions in coronary arteries of children and young adults. *Arteriosclerosis* 9:I19–I32.
- Stefanick ML, Mackey S, Sheehan M, Ellsworth N, Haskell WL, Wood PD. 1998. Effects of diet and exercise in men and postmenopausal women with low levels of HDL cholesterol and high levels of LDL cholesterol. *N Engl J Med* 339:12–20.
- Steinberg D, Parthasarathy S, Carew TE, Khoo JC, Witztum JL. 1989. Beyond cholesterol. Modifications of low-density lipoprotein that increase its atherogenicity. *N Engl J Med* 320:915–924.
- Storlien LH, Kraegen EW, Chisholm DJ, Ford GL, Bruce DG, Pascoe WS. 1987. Fish oil prevents insulin resistance induced by high-fat feeding. *Science* 237:885–888.
- Storlien LH, Jenkins AB, Chisholm DJ, Pascoe WS, Khouri S, Kraegen EW. 1991. Influence of dietary fat composition on development of insulin resistance in rats. Relationship to muscle triglyceride and  $\omega$ -3 fatty acids in muscle phospholipid. *Diabetes* 40:280–289.

- Straznicky NE, O'Callaghan CJ, Barrington VE, Louis WJ. 1999. Hypotensive effect of low-fat, high-carbohydrate diet can be independent of changes in plasma insulin concentrations. *Hypertension* 34:580–585.
- Strong JP, Malcom GT, Newman WP, Oalmann MC. 1992. Early lesions of atherosclerosis in childhood and youth: Natural history and risk factors. *J Am Coll Nutr* 11:51S–54S.
- Stubbs RJ, Harbron CG, Murgatroyd PR, Prentice AM. 1995a. Covert manipulation of dietary fat and energy density: Effect on substrate flux and food intake in men eating ad libitum. *Am J Clin Nutr* 62:316–329.
- Stubbs RJ, Ritz P, Coward WA, Prentice AM. 1995b. Covert manipulation of the ratio of dietary fat to carbohydrate and energy density: Effect on food intake and energy balance in free-living men eating ad libitum. *Am J Clin Nutr* 62:330–337.
- Stubbs RJ, Harbron CG, Prentice AM. 1996. Covert manipulation of the dietary fat to carbohydrate ratio of isoenergetically dense diets: Effect on food intake in feeding men ad libitum. *Int J Obes Relat Metab Disord* 20:651–660.
- Sugano M, Tsujita A, Yamasaki M, Noguchi M, Yamada K. 1998. Conjugated linoleic acid modulates tissue levels of chemical mediators and immunoglobulins in rats. *Lipids* 33:521–527.
- Swinburn BA, Boyce VL, Bergman RN, Howard BV, Bogardus C. 1991. Deterioration in carbohydrate metabolism and lipoprotein changes induced by modern, high fat diet in Pima Indians and Caucasians. *J Clin Endocrinol Metab* 73:156–165.
- Swinburn BA, Metcalf PA, Ley SJ. 2001. Long-term (5-year) effects of a reduced-fat diet intervention in individuals with glucose intolerance. *Diabetes Care* 24:619–624.
- Takahashi M, Przetakiewicz M, Ong A, Borek C, Lowenstein JM. 1992. Effect of omega 3 and omega 6 fatty acids on transformation of cultured cells by irradiation and transfection. *Cancer Res* 52:154–162.
- Talamini R, Franceschi S, La Vecchia C, Serraino D, Barra S, Negri E. 1992. Diet and prostatic cancer: A case-control study in Northern Italy. *Nutr Cancer* 18:277–286.
- Tao SC, Huang ZD, Wu XG, Zhou BF, Xiao ZK, Hao JS, Li YH, Cen RC, Rao XX. 1989. CHD and its risk factors in the People's Republic of China. *Int J Epidemiol* 18:S159–S163.
- Tate G, Mandell BF, Laposata M, Ohliger D, Baker DG, Schumacher HR, Zurier RB. 1989. Suppression of acute and chronic inflammation by dietary gamma linolenic acid. *J Rheumatol* 16:729–733.
- Teixeira SR, Potter SM, Weigel R, Hannum S, Erdman JW, Hasler CM. 2000. Effects of feeding 4 levels of soy protein for 3 and 6 wk on blood lipids and apolipoproteins in moderately hypercholesterolemic men. *Am J Clin Nutr* 71:1077–1084.
- Terpstra AHM, Holmes JC, Nicolosi RJ. 1991. The hypocholesterolemic effect of dietary soybean protein vs. casein in hamsters fed cholesterol-free or cholesterol-enriched semipurified diets. *J Nutr* 121:944–947.
- Thomas CD, Peters JC, Reed GW, Abumrad NN, Sun M, Hill JO. 1992. Nutrient balance and energy expenditure during ad libitum feeding of high-fat and high-carbohydrate diets in humans. *Am J Clin Nutr* 55:934–942.
- Thomsen C, Rasmussen O, Christiansen C, Pedersen E, Vesterlund M, Storm H, Ingerslev J, Hermansen K. 1999. Comparison of the effects of a monounsaturated fat diet and a high carbohydrate diet on cardiovascular risk factors in first degree relatives to type-2 diabetic subjects. *Eur J Clin Nutr* 52:818–823.

- Tillotson JL, Grandits GA, Bartsch GE, Stamler J. 1997. Relation of dietary carbohydrates to blood lipids in the special intervention and usual care groups in the Multiple Risk Factor Intervention Trial. *Am J Clin Nutr* 65:314S–326S.
- Tobin J, Spector D. 1986. Dietary protein has no effect on future creatinine clearance (Ccr). *Gerontologist* 26:59A.
- Toft I, Bønaa KH, Ingebretnsen OC, Nordøy A, Jenssen T. 1995. Effects of n-3 polyunsaturated fatty acids on glucose homeostasis and blood pressure in essential hypertension. A randomized, controlled trial. *Ann Intern Med* 123:911–918.
- Toniolo P, Riboli E, Shore RE, Pasternack BS. 1994. Consumption of meat, animal products, protein, and fat and risk of breast cancer: A prospective cohort study in New York. *Epidemiology* 5:391–397.
- Tonstad S, Sivertsen M. 1997. Relation between dietary fat and energy and micronutrient intakes. *Arch Dis Child* 76:416–420.
- Torun B, Chew F. 1999. Protein-energy malnutrition. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th ed. Baltimore, MD: Williams and Wilkins. Pp. 963–988.
- Tremblay A, Plourde G, Despres JP, Bouchard C. 1989. Impact of dietary fat content and fat oxidation on energy intake in humans. *Am J Clin Nutr* 49:799–805.
- Tremblay A, Lavalée N, Almeras N, Allard L, Despres JP, Bouchard C. 1991. Nutritional determinants of the increase in energy intake associated with a high-fat diet. *Am J Clin Nutr* 53:1134–1137.
- Tremblay MS, Willms JD. 2000. Secular trends in the body mass index of Canadian children. *Can Med Assoc J* 163:1429–1433.
- Tremoli E, Maderna P, Marangoni F, Colli S, Eligini S, Catalano I, Angeli MT, Pazzucconi F, Gainfranceschi G, Davi G, Stragliotto E, Sirtori CR, Galli C. 1995. Prolonged inhibition of platelet aggregation after n-3 fatty acid ethyl ester ingestion by healthy volunteers. *Am J Clin Nutr* 61:607–613.
- Trevisan M, Krogh V, Freudenberg J, Blake A, Muti P, Panico S, Farinaro E, Mancini M, Menotti A, Ricci G. 1990. Consumption of olive oil, butter, and vegetable oils and coronary heart disease risk factors. The Research Group ATS-RF2 of the Italian National Research Council. *J Am Med Assoc* 263:688–692.
- Trichopoulou A, Katsouyanni K, Stuver S, Tzala L, Gnardellis C, Rimm E, Trichopoulos D. 1995. Consumption of olive oil and specific food groups in relation to breast cancer risk in Greece. *J Natl Cancer Inst* 87:110–116.
- Trinidad TP, Wolever TMS, Thompson LU. 1993. Interactive effects of Ca and SCFA on absorption in the distal colon of men. *Nutr Res* 13:417–425.
- Trinidad TP, Wolever TMS, Thompson LU. 1996. Effect of acetate and propionate on calcium absorption from the rectum and distal colon of humans. *Am J Clin Nutr* 63:574–578.
- Troiano RP, Flegal KM, Kuczmarski RJ, Campbell SM, Johnson CL. 1995. Overweight prevalence and trend for children and adolescents: The National Health and Nutrition Examination Surveys, 1963 to 1991. *Arch Pediatr Adolesc Med* 149:1085–1091.
- Tsuboyama-Kasaoka N, Takahashi M, Tanemura K, Kim H-J, Tange T, Okuyama H, Kasai M, Ikemoto S, Ezaki O. 2000. Conjugated linoleic acid supplementation reduces adipose tissue by apoptosis and develops lipodystrophy in mice. *Diabetes* 49:1534–1542.
- Tucker LA, Kano MJ. 1992. Dietary fat and body fat: A multivariate study of 205 adult females. *Am J Clin Nutr* 56:616–622.

- Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, Keinänen-Kiukaanniemi S, Laakso M, Louheranta A, Rastas M, Salminen V, Uusitupa M. 2001. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Eng J Med* 344:1343–1350.
- Turini ME, Powell WS, Behr SR, Holub BJ. 1994. Effects of a fish-oil and vegetable-oil formula on aggregation and ethanolamine-containing lysophospholipid generation in activated human platelets and on leukotriene production in stimulated neutrophils. *Am J Clin Nutr* 60:717–724.
- Turner NC, Clapham JC. 1998. Insulin resistance, impaired glucose tolerance and non-insulin-dependent diabetes, pathologic mechanisms and treatment: Current status and therapeutic possibilities. *Prog Drug Res* 51:33–94.
- Uauy R, Mize CE, Castillo-Duran C. 2000. Fat intake during childhood: Metabolic responses and effects on growth. *Am J Clin Nutr* 72:1354S–1360S.
- Uematsu T, Nagashima S, Niwa M, Kohno K, Sassa T, Ishii M, Tomono Y, Yamato C, Kanamaru M. 1996. Effect of dietary fat content on oral bioavailability of menatrenone in humans. *J Pharm Sci* 85:1012–1016.
- USDA (U.S. Department of Agriculture). 1996. *The Food Guide Pyramid*. Home and Garden Bulletin No. 252. Washington, DC: U.S. Government Printing Office.
- Uusitupa M, Schwab U, Mäkimattila S, Karhapää P, Sarkkinen E, Maliranta H, Ågren J, Penttilä I. 1994. Effects of two high-fat diets with different fatty acid compositions on glucose and lipid metabolism in healthy young women. *Am J Clin Nutr* 59:1310–1316.
- van Amelsvoort JM, van Stratum P, Kraal JH, Lussenburg RN, Houtsmuller UMT. 1989. Effects of varying the carbohydrate:fat ratio in a hot lunch on postprandial variables in male volunteers. *Br J Nutr* 61:267–283.
- van Amelsvoort JM, van Stratum P, Dubbelman GP, Lussenburg RN. 1990. Effects of meal size reduction on postprandial variables in male volunteers. *Ann Nutr Metab* 34:163–174.
- van den Berg JJM, Cook NE, Tribble DL. 1995. Reinvestigation of the antioxidant properties of conjugated linoleic acid. *Lipids* 30:599–605.
- van den Brandt PA, van't Veer P, Goldbohm RA, Dorant E, Volovics A, Hermus RJJ, Sturmans F. 1993. A prospective cohort study on dietary fat and the risk of postmenopausal breast cancer. *Cancer Res* 53:75–82.
- Van Dokkum W, Wesstra A, Schippers FA. 1982. Physiological effects of fibre-rich types of bread. 1. The effect of dietary fibre from bread on the mineral balance of young men. *Br J Nutr* 47:451–460.
- van Stratum P, Lussenburg RN, van Wezel LA, Vergroesen AJ, Cremer HD. 1978. The effect of dietary carbohydrate:fat ratio on energy intake by adult women. *Am J Clin Nutr* 31:206–212.
- van't Veer P, Kok FJ, Brants HAM, Ockhuizen T, Sturmans F, Hermus RJJ. 1990. Dietary fat and the risk of breast cancer. *Int J Epidemiol* 19:12–18.
- Vartiainen E, Puska P, Pietinen P, Nissinen A, Leino U, Uusitalo U. 1986. Effects of dietary fat modifications on serum lipids and blood pressure in children. *Acta Paediatr Scand* 75:396–401.
- Veierød MB, Laake P, Thelle DS. 1997a. Dietary fat intake and risk of lung cancer: A prospective study of 51,452 Norwegian men and women. *Eur J Cancer Prev* 6:540–549.
- Veierød MB, Laake P, Thelle DS. 1997b. Dietary fat intake and risk of prostate cancer: A prospective study of 25,708 Norwegian men. *Int J Cancer* 73:634–638.

- Velie E, Kulldorff M, Schairer C, Block G, Albanes D, Schatzkin A. 2000. Dietary fat, fat subtypes, and breast cancer in postmenopausal women: A prospective cohort study. *J Natl Cancer Inst* 92:833–839.
- Vessby B. 2000. Dietary fat and insulin action in humans. *Br J Nutr* 83:S91–S96.
- Vessby B, Uusitupa M, Hermansen K, Riccardi G, Rivellese AA, Tapsell LC, Nälsén C, Berglund L, Louheranta A, Rasmussen BM, Calvert GD, Maffetone A, Pedersen E, Gustafsson I-B, Storlien LH. 2001. Substituting dietary saturated for monounsaturated fat impairs insulin sensitivity in healthy men and women: The KANWU study. *Diabetologia* 44:312–319.
- Visonneau S, Cesano A, Tepper SA, Scimeca JA, Santoli D, Kritchevsky D. 1997. Conjugated linoleic acid suppresses the growth of human breast adenocarcinoma cells in SCID mice. *Anticancer Res* 17:969–974.
- Vobecky JS, Vobecky J, Normand L. 1995. Risk and benefit of low fat intake in childhood. *Ann Nutr Metab* 39:124–133.
- von Schacky C, Angerer P, Kothny W, Theisen K, Mudra H. 1999. The effect of dietary ω-3 fatty acids on coronary atherosclerosis. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 130:554–562.
- Walker AR, Walker BF. 1978. High high-density-lipoprotein cholesterol in African children and adults in a population free of coronary heart disease. *Br Med J* 2:1336–1337.
- Walser M. 1992. The relationship of dietary protein to kidney disease. In: Liepa GU, Beitz DC, Beynen AC, Gorman MA, eds. *Dietary Proteins: How They Alleviate Disease and Promote Better Health*. Champaign, IL: American Oil Chemists' Society. Pp. 168–178.
- Ward MH, Zahm SH, Weisenburger DD, Gridley G, Cantor KP, Saal RC, Blair A. 1994. Dietary factors and non-Hodgkin's lymphoma in Nebraska (United States). *Cancer Causes Control* 5:422–432.
- Waterlow JC. 1976. Classification and definition of protein-energy malnutrition. *Monogr Ser World Health Organ* 62:530–555.
- Weisburger JH. 1988. Comparison of nutrition as customary in the Western World, the Orient, and northern populations (Eskimos) in relation to specific disease risk. *Arctic Med Res* 47:110–120.
- West CE, Sullivan DR, Katan MB, Halferkamps IL, van der Torre HW. 1990. Boys from populations with high-carbohydrate intake have higher fasting triglyceride levels than boys from populations with high-fat intake. *Am J Epidemiol* 131:271–282.
- West KM, Kalbfleisch JM. 1971. Influence of nutritional factors on prevalence of diabetes. *Diabetes* 20:99–108.
- Westerterp KR, Verboeket-van de Venne WPHG, Westerterp-Plantenga MS, Velthuis-te Wierik EJM, de Graaf C, Weststrate JA. 1996. Dietary fat and body fat: An intervention study. *Int J Obes Relat Metab Disord* 20:1022–1026.
- Whigham LD, Cook ME, Atkinson RL. 2000. Conjugated linoleic acid: Implications for human health. *Pharmacol Res* 42:503–510.
- Whiting SJ, Anderson DJ, Weeks SJ. 1997. Calciuric effects of protein and potassium bicarbonate but not of sodium chloride or phosphate can be detected acutely in adult women and men. *Am J Clin Nutr* 65:1465–1472.
- Willett WC. 1997. Specific fatty acids and risks of breast and prostate cancer: Dietary intake. *Am J Clin Nutr* 66:1557S–1563S.
- Willett WC. 1998. Is dietary fat a major determinant of body fat? *Am J Clin Nutr* 67:556S–562S.

- Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Hennekens CH, Speizer FE. 1987. Dietary fat and the risk of breast cancer. *N Engl J Med* 316:22–28.
- Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Speizer FE. 1990. Relation of meat, fat, and fiber intake to the risk of colon cancer in a prospective study among women. *N Engl J Med* 323:1664–1672.
- Willett WC, Hunter DJ, Stampfer MJ, Colditz G, Manson JE, Spiegelman D, Rosner B, Hennekens CH, Speizer FE. 1992. Dietary fat and fiber in relation to risk of breast cancer. An 8-year follow-up. *J Am Med Assoc* 268:2037–2044.
- Williams CL, Bollella M. 1995. Is a high-fiber diet safe for children? *Pediatrics* 96:1014–1019.
- Wisen O, Hellstrom PM, Johansson C. 1993. Meal energy density as a determinant of postprandial gastrointestinal adaptation in man. *Scand J Gastroenterol* 28:737–743.
- Wisker E, Maltz A, Feldheim W. 1988. Metabolizable energy of diets low or high in dietary fiber from cereals when eaten by humans. *J Nutr* 118:945–952.
- Wolfe BMJ, Piché LA. 1999. Replacement of carbohydrate by protein in a conventional-fat diet reduced cholesterol and triglyceride concentrations in healthy normolipidemic subjects. *Clin Invest Med* 22:140–148.
- Wolk A, Bergström R, Hunter D, Willett W, Ljung H, Holmberg L, Bergkvist L, Bruce Å, Adami H-O. 1998. A prospective study of association of mono-unsaturated fat and other types of fat with risk of breast cancer. *Arch Intern Med* 158:41–45.
- Wooley SC. 1972. Physiologic versus cognitive factors in short term food regulation in the obese and nonobese. *Psychosom Med* 34:62–68.
- Wu Y, Zheng W, Sellars TA, Kushi LH, Bostick RM, Potter JD. 1994. Dietary cholesterol, fat, and lung cancer incidence among older women: The Iowa Women's Health Study (United States). *Cancer Causes Control* 5:395–400.
- Yao M, Roberts SB. 2001. Dietary energy density and weight regulation. *Nutr Rev* 59:247–258.
- Yeomans MR, Gray RW, Mitchell CJ, True S. 1997. Independent effects of palatability and within-meal pauses on intake and appetite ratings in human volunteers. *Appetite* 29:61–76.
- Yost TJ, Jensen DR, Haugen BR, Eckel RH. 1998. Effect of dietary macronutrient composition on tissue-specific lipoprotein lipase activity and insulin action in normal-weight subjects. *Am J Clin Nutr* 68:296–302.
- Yu-Poth S, Zhao G, Etherton T, Naglak M, Jonnalagadda S, Kris-Etherton PM. 1999. Effects of the National Cholesterol Education Program's Step I and Step II dietary intervention programs on cardiovascular disease risk factors: A meta-analysis. *Am J Clin Nutr* 69:632–646.
- Zambell KL, Keim NL, Van Loan MD, Gale B, Benito P, Kelley DS, Nelson GJ. 2000. Conjugated linoleic acid supplementation in humans: Effects of body composition and energy expenditure. *Lipids* 35:777–782.

- Zhang J, Sasaki S, Amano K, Kesteloot H. 1999. Fish consumption and mortality from all causes, ischemic heart disease, and stroke: An ecological study. *Prev Med* 28:520–529.
- Ziboh VA, Fletcher MP. 1992. Dose-response effects of dietary  $\gamma$ -linolenic acid-enriched oils on human polymorphonuclear-neutrophil biosynthesis of leukotriene B<sub>4</sub>. *Am J Clin Nutr* 55:39–45.
- Zock PL, Katan MB. 1992. Hydrogenation alternatives: Effects of *trans* fatty acids and stearic acid versus linoleic acid on serum lipids and lipoproteins in humans. *J Lipid Res* 33:399–410.
- Zock PL, Katan MB. 1998. Linoleic acid intake and cancer risk: A review and meta-analysis. *Am J Clin Nutr* 68:142–153.
- Zurier RB, Rossetti RG, Jacobson EW, DeMarco DM, Liu NY, Temming JE, White BM, Laposata M. 1996. Gamma-linolenic acid treatment of rheumatoid arthritis. A randomized, placebo-controlled trial. *Arthritis Rheum* 39:1808–1817.

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*Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* (ISBN 0-309-08537-3), Chapter 5, pp. 240–264.

- Abbott WG, Howard BV, Christin L, Freymond D, Lillioja S, Boyce VL, Anderson TE, Bogardus C, Ravussin E. 1988. Short-term energy balance: Relationship with protein, carbohydrate, and fat balances. *Am J Physiol* 255:E332–E337.
- Acheson K, Jéquier E, Wahren J. 1983. Influence of beta-adrenergic blockade on glucose-induced thermogenesis in man. *J Clin Invest* 72:981–986.
- Albu J, Shur M, Curi M, Murphy L, Heymsfield SB, Pi-Sunyer FX. 1997. Resting metabolic rate in obese, premenopausal black women. *Am J Clin Nutr* 66:531–538.
- Allen JC, Keller RP, Archer P, Neville MC. 1991. Studies in human lactation: Milk composition and daily secretion rates of macronutrients in the first year of lactation. *Am J Clin Nutr* 54:69–80.
- Amatruda JM, Richeson F, Welle SL, Brodows RG, Lockwood DH. 1988. The safety and efficacy of a controlled low-energy ('very-low-calorie') diet in the treatment of non-insulin-dependent diabetes and obesity. *Arch Intern Med* 148:873–877.
- Amatruda JM, Statt MC, Welle SL. 1993. Total and resting energy expenditure in obese women reduced to ideal body weight. *J Clin Invest* 92:1236–1242.
- Anderson DM, Williams FH, Merkatz RB, Schulman PK, Kerr DS, Pittard WB. 1983. Length of gestation and nutritional composition of human milk. *Am J Clin Nutr* 37:810–814.
- Anderson GH, Atkinson SA, Bryan MH. 1981. Energy and macronutrient content of human milk during early lactation from mothers giving birth prematurely and at term. *Am J Clin Nutr* 34:258–265.
- Armstrong DW. 1998. Metabolic and endocrine responses to cold air in women differing in aerobic capacity. *Med Sci Sport Exerc* 30:880–884.
- Ashworth A. 1969. Metabolic rates during recovery from protein–calorie malnutrition: The need for a new concept of specific dynamic action. *Nature* 223:407–409.
- Assel B, Rossi K, Kalhan S. 1993. Glucose metabolism during fasting through human pregnancy: Comparison of tracer method with respiratory calorimetry. *Am J Physiol* 265:E351–E356.
- Astrup A, Buemann B, Western P, Toubro S, Raben A, Christensen NJ. 1994. Obesity as an adaptation to a high-fat diet: Evidence from a cross-sectional study. *Am J Clin Nutr* 59:350–355.
- Astrup A, Toubro S, Dalgaard LT, Urhammer SA, Sorensen TI, Pedersen O. 1999. Impact of the v/v 55 polymorphism of the uncoupling protein 2 gene on 24-h energy expenditure and substrate oxidation. *Int J Obes Relat Metab Disord* 23:1030–1034.
- Bahr R, Ingnes I, Vaage O, Sejersted OM, Newsholme EA. 1987. Effect of duration of exercise on excess postexercise  $O_2$  consumption. *J Appl Physiol* 62:485–490.
- Bailey DA, McCulloch RG. 1990. Bone tissue and physical activity. *Can J Sport Sci* 15:229–239.
- Ballantyne D, Devine BL, Fife R. 1978. Interrelation of age, obesity, cigarette smoking, and blood pressure in hypertensive patients. *Br Med J* 1:880–881.

- Ballor DL, Keesey RE. 1991. A meta-analysis of the factors affecting exercise-induced changes in body mass, fat mass and fat-free mass in males and females. *Int J Obes* 15:717–726.
- Bandini LG, Schoeller DA, Cyr HN, Dietz WH. 1990a. Validity of reported energy intake in obese and nonobese adolescents. *Am J Clin Nutr* 52:421–451.
- Bandini LG, Schoeller DA, Dietz WH. 1990b. Energy expenditure in obese and nonobese adolescents. *Pediatr Res* 27:198–203.
- Barlow SE, Dietz WH. 1998. Obesity evaluation and treatment: Expert Committee recommendations. *Pediatrics* 102:E29.
- Bathalon GP, Tucker KL, Hays NP, Vinken AG, Greenberg AS, McCrory MA, Roberts SB. 2000. Psychological measures of eating behavior and the accuracy of 3 common dietary assessment methods in healthy postmenopausal women. *Am J Clin Nutr* 71:739–745.
- Baumgartner RN, Roche AF, Himes JH. 1986. Incremental growth tables: Supplementary to previously published charts. *Am J Clin Nutr* 43:711–722.
- Bellizzi MC, Dietz WH. 1999. Workshop on childhood obesity: Summary of the discussion. *Am J Clin Nutr* 70:173S–175S.
- Benedict FG, Cathcart EP. 1913. *Muscular Work. A Metabolic Study with Special Reference to the Efficiency of the Human Body as a Machine*. Washington, DC: Carnegie Institution. Pp. 163–176.
- Benedict FG, Talbot FB. 1914. *The Gaseous Metabolism of Infants, with Special Reference to its Relation of Pulse-Rate and Muscular Activity*. Washington, DC: Carnegie Institution.
- Benedict FG, Talbot FB. 1921. *Metabolism and Growth from Birth to Puberty*. Washington, DC: Carnegie Institution.
- Bielinski R, Schutz Y, Jequier E. 1985. Energy metabolism during the postexercise recovery in man. *Am J Clin Nutr* 42:69–82.
- Bingham SA, Day NE. 1997. Using biochemical markers to assess the validity of prospective dietary assessment methods and the effect of energy adjustment. *Am J Clin Nutr* 65:1130S–1137S.
- Bingham SA, Goldberg GR, Coward WA, Prentice AM, Cummings JH. 1989. The effect of exercise and improved physical fitness on basal metabolic rate. *Br J Nutr* 61:155–173.
- Bingham SA, Gill C, Welch A, Day K, Cassidy A, Khaw KT, Sneyd MJ, Key TJ, Roe L, Day NE. 1994. Comparison of dietary assessment methods in nutritional epidemiology: Weighed records v. 24 h recalls, food-frequency questionnaires and estimated-diet records. *Br J Nutr* 72:619–643.
- Bisdee JT, James WP, Shaw MA. 1989. Changes in energy expenditure during the menstrual cycle. *Br J Nutr* 61:187–199.
- Bitar A, Fellmann N, Vernet J, Coudert J, Vermorel M. 1999. Variations and determinants of energy expenditure as measured by whole-body indirect calorimetry during puberty and adolescence. *Am J Clin Nutr* 69:1209–1216.
- Blaak EE, Westerterp KR, Bar-Or O, Wouters LJ, Saris WH. 1992. Total energy expenditure and spontaneous activity in relation to training in obese boys. *Am J Clin Nutr* 55:777–782.
- Black AE. 1999. Small eaters or under-reporters? In: Guy-Grand B, Ailhaud G, eds. *Progress in Obesity Research 8*. London: John Libbey. Pp. 223–228.
- Black AE, Prentice AM, Goldberg GR, Jebb SA, Bingham SA, Livingstone MB, Coward WA. 1993. Measurements of total energy expenditure provide insights into the validity of dietary measurements of energy intake. *J Am Diet Assoc* 93:572–579.

- Black AE, Coward WA, Prentice AM. 1996. Human energy expenditure in affluent societies: An analysis of 574 doubly-labelled water measurements. *Eur J Clin Nutr* 50:72–92.
- Blaza S, Garrow JS. 1983. Thermogenic response to temperature, exercise and food stimuli in lean and obese women, studied by 24 h direct calorimetry. *Br J Nutr* 49:171–180.
- Bloesch D, Schutz Y, Breitenstein E, Jequier E, Felber JP. 1988. Thermogenic response to an oral glucose load in man: Comparison between young and elderly subjects. *J Am Coll Nutr* 7:471–483.
- Bogardus C, Lillioja S, Ravussin E, Abbott W, Zawadzki JK, Young A, Knowler WC, Jacobowitz R, Moll PP. 1986. Familial dependence of the resting metabolic rate. *N Engl J Med* 315:96–100.
- Bouchard C, Perusse L. 1993. Genetics of obesity. *Annu Rev Nutr* 13:337–354.
- Bouchard C, Tremblay A, Nadeau A, Despres JP, Theriault G, Boulay MR, Lortie G, Leblanc C, Fournier G. 1989. Genetic effect in resting and exercise metabolic rates. *Metabolism* 38:364–370.
- Bouchard C, Tremblay A, Despres JP, Nadeau A, Lupien PJ, Theriault G, Dussault J, Moorjani S, Pinault S, Fournier G. 1990. The response to long-term overfeeding in identical twins. *N Engl J Med* 322:1477–1482.
- Bratteby LE, Sandhagen B, Lotborn M, Samuelson G. 1997. Daily energy expenditure and physical activity assessed by an activity diary in 374 randomly selected 15-year-old adolescents. *Eur J Clin Nutr* 51:592–600.
- Brennan PJ, Simpson JM, Blacket RB, McGilchrist CA. 1980. The effects of body weight on serum cholesterol, serum triglycerides, serum urate and systolic blood pressure. *Aust N Z J Med* 10:15–20.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Nutrition Examination Survey: Underreporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Bronstein MN, Mak RP, King JC. 1995. The thermic effect of food in normal-weight and overweight pregnant women. *Br J Nutr* 74:261–275.
- Brooks GA, Butterfield GE, Wolfe RR, Groves BM, Mazzeo RS, Sutton JR, Wolfel EE, Reeves JT. 1991. Increased dependence on blood glucose after acclimatization to 4,300 m. *J Appl Physiol* 70:919–927.
- Brooks GA, Wolfel EE, Groves BM, Bender PR, Butterfield GE, Cymerman A, Mazzeo RS, Sutton JR, Wolfe RR, Reeves JT. 1992. Muscle accounts for glucose disposal but not lactate appearance during exercise after acclimatization to 4,300 m. *J Appl Physiol* 72:2435–2445.
- Brooks GA, Fahey TD, White TP, Baldwin KM. 2000. *Exercise Physiology: Human Bioenergetics and Its Applications*, 3rd ed. Mountain View, CA: Mayfield Publishing.
- Brown CD, Higgins M, Donato KA, Rohde FC, Garrison R, Obarzanek E, Ernst ND, Horan M. 2000. Body mass index and the prevalence of hypertension and dyslipidemia. *Obes Res* 8:605–619.
- Buemann B, Astrup A, Christensen NJ, Madsen J. 1992. Effect of moderate cold exposure on 24-h energy expenditure: Similar response in postobese and nonobese women. *Am J Physiol* 263:E1040–1045.
- Buenen GP, Malina RM, Renson R, Simons J, Ostyn M, Lefevre J. 1992. Physical activity and growth, maturation and performance: A longitudinal study. *Med Sci Sports Exerc* 24(5):576–585.

- Burstein R, Coward AW, Askew WE, Carmel K, Irving C, Shpilberg O, Moran D, Pikarsky A, Ginot G, Sawyer M, Golan R, Epstein Y. 1996. Energy expenditure variations in soldiers performing military activities under cold and hot climate conditions. *Mil Med* 161:750–754.
- Butte NF. 1990. Basal metabolism of infants. In: Schürch B, Scrimshaw NS, eds. *Activity, Energy Expenditure and Energy Requirements of Infants and Children*. Switzerland: Nestlé Foundation. Pp. 117–137.
- Butte NF. 2000. Fat intake of children in relation to energy requirements. *Am J Clin Nutr* 72:1246S–1252S.
- Butte NF, Calloway DH. 1981. Evaluation of lactational performance in Navajo women. *Am J Clin Nutr* 34:2210–2215.
- Butte NF, Hopkinson JM. 1998. Body composition changes during lactation are highly variable among women. *J Nutr* 128:381S–385S.
- Butte NF, Garza C, O'Brian Smith E, Nichols BL. 1984a. Human milk intake and growth in exclusively breast-fed infants. *J Pediatr* 104:187–195.
- Butte NF, Garza C, Stuff JE, Smith EO, Nichols BL. 1984b. Effect of maternal diet and body composition on lactational performance. *Am J Clin Nutr* 39:296–306.
- Butte NF, Wong WW, Garza C. 1989. Energy cost of growth during infancy. *Proc Nutr Soc* 48:303–312.
- Butte NF, Wong WW, Ferlic L, Smith EO, Klein PD, Garza C. 1990. Energy expenditure and deposition of breast-fed and formula-fed infants during early infancy. *Pediatr Res* 28:631–640.
- Butte NF, Hopkinson JM, Mehta N, Moon JK, Smith EO. 1999. Adjustments in energy expenditure and substrate utilization during late pregnancy and lactation. *Am J Clin Nutr* 69:299–307.
- Butte NF, Hopkinson JM, Wong WW, Smith EO, Ellis KJ. 2000a. Body composition during the first two years of life: An updated reference. *Pediatr Res* 47:578–585.
- Butte NF, Wong WW, Hopkinson JM, Heinz CJ, Mehta NR, Smith EO. 2000b. Energy requirements derived from total energy expenditure and energy deposition during the first 2 y of life. *Am J Clin Nutr* 72:1558–1569.
- Butte NF, Wong WW, Hopkinson JM. 2001. Energy requirements of lactating women derived from doubly labeled water and milk energy output. *J Nutr* 131:53–58.
- Butterfield GE, Gates J, Fleming S, Brooks GA, Sutton JR, Reeves JT. 1992. Increased energy intake minimizes weight loss in men at high altitude. *J Appl Physiol* 72:1741–1748.
- Carman WJ, Sowers M, Hawthorne VM, Weissfeld LA. 1994. Obesity as a risk factor for osteoarthritis of the hand and wrist: A prospective study. *Am J Epidemiol* 139:119–129.
- Carpenter WH, Poehlman ET, O'Connell M, Goran MI. 1995. Influence of body composition and resting metabolic rate on variation in total energy expenditure: A meta-analysis. *Am J Clin Nutr* 61:4–10.
- Carpenter WH, Fonong T, Toth MJ, Ades PA, Calles-Escandon J, Walston JD, Poehlman ET. 1998. Total daily energy expenditure in free-living older African-Americans and Caucasians. *Am J Physiol* 274:E96–E101.
- Cartee GD, Douen AG, Ramlal T, Klip A, Holloszy JO. 1991. Stimulation of glucose transport in skeletal muscle by hypoxia. *J Appl Physiol* 70:1593–1600.
- Chan JM, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. 1994. Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. *Diabetes Care* 17:961–969.

- Chu SY, Lee NC, Wingo PA, Senie RT, Greenberg RS, Peterson HB. 1991. The relationship between body mass and breast cancer among women enrolled in the Cancer and Steroid Hormone Study. *J Clin Epidemiol* 44:1197–1206.
- Cicuttini FM, Baker JR, Spector TD. 1996. The association of obesity with osteoarthritis of the hand and knee in women: A twin study. *J Rheumatol* 23:1221–1226.
- Clagett DD, Hathaway ML. 1941. Basal metabolism of normal infants from three to fifteen months of age. *Am J Dis Child* 62:967–980.
- Clarke WR, Schrott HG, Leaverton PE, Connor WE, Lauer RM. 1978. Tracking of blood lipids and blood pressures in school age children: the Muscatine study. *Circulation* 58:626–634.
- Colditz GA, Willett SC, Stampfer MJ, Manson JE, Hennekens CH, Arky RA, Speizer FE. 1990. Weight as a risk factor for clinical diabetes in women. *Am J Epidemiol* 132:501–513.
- Colditz GA, Willett WC, Rotnitzky A, Manson JE. 1995. Weight gain as a risk factor for clinical diabetes mellitus in women. *Ann Intern Med* 122:481–486.
- Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. 2000. Establishing a standard definition for child overweight and obesity worldwide: International survey. *Br Med J* 320:1–6.
- Consolazio CF, Johnson RE, Pecora LJ. 1963. *Physiological Measurements of Metabolic Functions in Man*. New York: McGraw-Hill. Pp. 414–436.
- Coward WA, Prentice AM, Murgatroyd PR, Davies HL, Cole TJ, Sawyer M, Goldberg GR, Halliday D, MacNamara JP. 1984. Measurement of CO<sub>2</sub> and water production rates in man using <sup>2</sup>H, <sup>18</sup>O-labelled H<sub>2</sub>O: Comparisons between calorimeter and isotope values. In: Van Es AJ, ed. *Human Energy Metabolism: Physical Activity and Energy Expenditure Measurements in Epidemiological Research Based upon Direct and Indirect Calorimetry*. Den Haag: CIP-gegevens Koninklijke Bibliotheek. Pp. 126–128.
- Criqui MH, Mebane I, Wallace RB, Heiss G, Holdbrook MJ. 1982. Multivariate correlates of adult blood pressures in nine North American populations: The Lipid Research Clinics Prevalence Study. *Prev Med* 11:391–402.
- Dauncey MJ. 1981. Influence of mild cold on 24 h energy expenditure, resting metabolism and diet-induced thermogenesis. *Br J Nutr* 45:257–267.
- Davies PS, Ewing G, Lucas A. 1989. Energy expenditure in early infancy. *Br J Nutr* 62:621–629.
- Davies PS, Ewing G, Coward WA, Lucas A. 1990. Energy metabolism in breast and formula fed infants. In: Atkinson SA, Hanson LA, Chandra RK, eds. *Breast-Feeding, Nutrition, Infection and Infant Growth in Developed and Emerging Countries*. St. John's, Newfoundland: Arts Biomedical. P. 521.
- Davies PS, Day JM, Lucas A. 1991. Energy expenditure in early infancy and later body fatness. *Int J Obes* 15:727–731.
- Davies PS, Wells JC, Fieldhouse CA, Day JM, Lucas A. 1995. Parental body composition and infant energy expenditure. *Am J Clin Nutr* 61:1026–1029.
- Davies PS, Wells JC, Hinds A, Day JM, Laidlaw A. 1997. Total energy expenditure in 9 month and 12 month infants. *Eur J Clin Nutr* 51:249–252.
- de Bruin NC, Degenhart HJ, Gal S, Westerterp KR, Stijnen T, Visser HK. 1998. Energy utilization and growth in breast-fed and formula-fed infants measured prospectively during the first year of life. *Am J Clin Nutr* 67:885–896.
- de Castro JM, Orozco S. 1990. Moderate alcohol intake and spontaneous eating patterns of humans: Evidence of unregulated supplementation. *Am J Clin Nutr* 52:246–253.

- de Groot LC, Boekholt HA, Spaaij CJ, van Raaij JM, Drijvers JJ, van der Heijden LJ, van der Heide D, Hautvast JG. 1994. Energy balances of healthy Dutch women before and during pregnancy: Limited scope for metabolic adaptations in pregnancy. *Am J Clin Nutr* 59:827–832.
- Deheeger M, Rolland-Cachera MF, Fontvieille AM. 1997. Physical activity and body composition in 10 year old French children: linkages with nutritional intake? *Int J Obes Relat Metab Disord* 21:372–379.
- Denne SC, Kalhan SC. 1987. Leucine metabolism in human newborns. *Am J Physiol* 253:E608–E615.
- Denne SC, Patel D, Kalhan SC. 1991. Leucine kinetics and fuel utilization during a brief fast in human pregnancy. *Metabolism* 40:1249–1256.
- DePue JD, Clark MM, Ruggiero L, Medeiros ML, Pera V. 1995. Maintenance of weight loss: A needs assessment. *Obes Res* 3:241–248.
- Despres JP, Nadeau A, Tremblay A, Ferland M, Moorjani S, Lupien PJ, Thériault G, Pinault S, Bouchard C. 1989. Role of deep abdominal fat in the association between regional adipose tissue distribution and glucose tolerance in obese women. *Diabetes* 38:304–309.
- Dewey KG, Finley DA, Lonnerdal B. 1984. Breast milk volume and composition during late lactation (7–20 months). *J Pediatr Gastroenterol Nutr* 3:713–720.
- Dewey KG, Beaton G, Fjeld C, Lonnerdal B, Reeds P. 1996. Protein requirements of infants and children. *Eur J Clin Nutr* 50:S119–S150.
- Dhuper S, Warren MP, Brooks-Gunn J, Fox R. 1990. Effects of hormonal status on bone density in adolescent girls. *J Clin Endocrinol Metab* 71:1083–1088.
- Dionne I, Despres JP, Bouchard C, Tremblay A. 1999. Gender difference in the effect of body composition on energy metabolism. *Int J Obes Relat Metab Disord* 23:312–319.
- Doar JWH, Wilde, Thompson ME, Stewell PFJ. 1975. Influence of treatment with diet alone on oral glucose-tolerance test and plasma sugar and insulin levels in patients with maturity-onset diabetes mellitus. *Lancet* 1:1263–1266.
- Dunn AL, Marcus BH, Kampert JB, Garcia ME, Kohl HW, Blair SN. 1999. Comparison of lifestyle and structured interventions to increase physical activity and cardiorespiratory fitness: A randomized trial. *J Am Med Assoc* 281:327–334.
- Durnin JV. 1990. Low energy expenditures in free-living populations. *Eur J Clin Nutr* 44:95–102.
- Durnin JV. 1996. Energy requirements: General principles. *Eur J Clin Nutr* 50: S2–S10.
- Durnin JV, McKillop FM, Grant S, Fitzgerald G. 1987. Energy requirements of pregnancy in Scotland. *Lancet* 2:897–900.
- Edholm OG, Adam JM, Healey MJ, Wolff HS, Goldsmith R, Best TW. 1970. Food intake and energy expenditure of army recruits. *Br J Nutr* 24:1091–1107.
- Elia M. 1991. Energy equivalents of CO<sub>2</sub> and their importance in assessing energy expenditure when using tracer techniques. *Am J Physiol* 260:E75–E88.
- Eliakim A, Barstow TJ, Brasel JA, Ajie H, Lee WN, Renslo R, Berman N, Cooper DM. 1996. Effect of exercise training on energy expenditure, muscle volume, and maximal oxygen uptake in female adolescents. *J Pediatr* 129:537–543.
- Ellis KJ. 1997. Body composition of a young, multiethnic, male population. *Am J Clin Nutr* 66:1323–1331.
- Ellis KJ, Abrams SA, Wong WW. 1997. Body composition of a young, multiethnic female population. *Am J Clin Nutr* 65:724–731.
- EPA (Environmental Protection Agency). 1991. *Building Air Quality: A Guide for Building Owners and Facility Managers*. Washington, DC: U.S. Government Printing Office.

- FAO/WHO/UNU (Food and Agriculture Organization/World Health Organization/United Nations University). 1985. *Energy and Protein Requirements*. Report of a Joint FAO/WHO/UNU Expert Consultation. Technical Report Series No. 724. Geneva: WHO.
- Felson DT, Anderson JJ, Naimark A, Walker AM, Meenan RF. 1988. Obesity and knee osteoarthritis. The Framingham Study. *Ann Intern Med* 109:18–24.
- Ferraro R, Lillioja S, Fontvieille AM, Rising R, Bogardus C, Ravussin E. 1992. Lower sedentary metabolic rate in women compared with men. *J Clin Invest* 90:780–784.
- Ferris AM, Dotts MA, Clark RM, Ezrin M, Jensen RG. 1988. Macronutrients in human milk at 2, 12, and 16 weeks postpartum. *J Am Diet Assoc* 88:694–697.
- Firouzbakhsh S, Mathis RK, Dorchester WL, Oseas RS, Groncy PK, Grant KE, Finklestein JZ. 1993. Measured resting energy expenditure in children. *J Pediatr Gastroenterol Nutr* 16:136–142.
- Fjeld CR, Schoeller DA, Brown KH. 1989. Body composition of children recovering from severe protein-energy malnutrition at two rates of catch-up growth. *Am J Clin Nutr* 50:1266–1275.
- Flatt JP. 1978. The biochemistry of energy expenditure. In: Bray GA, ed. *Recent Advances in Obesity Research II*. London: Newman Publishing. Pp. 211–228.
- Fletcher GF, Balady GJ, Amsterdam EA, Chaitman B, Eckel R, Fleg J, Froelicher VF, Leon AS, Piña IL, Rodney R, Simons-Morton DG, Williams MA, Bazzarre T. 2001. Exercise standards for testing and training: A statement for healthcare professionals from the American Heart Association. *Circulation* 104:1694–1740.
- Fomon SJ, Haschke F, Ziegler EE, Nelson SE. 1982. Body composition of reference children from birth to age 10 years. *Am J Clin Nutr* 35:1169–1175.
- Fontvieille AM, Dwyer J, Ravussin E. 1992. Resting metabolic rate and body composition of Pima Indian and Caucasian children. *Int J Obes Relat Metab Disord* 16:535–542.
- Forbes GB. 1987. *Human Body Composition. Growth, Aging, Nutrition, and Activity*. New York: Springer-Verlag.
- Ford ES, Williamson DF, Liu S. 1997. Weight change and diabetes incidence: Findings from a national cohort of US adults. *Am J Epidemiol* 146:214–222.
- Forman JN, Miller WC, Szymanski LM, Fernhall B. 1998. Differences in resting metabolic rates of inactive obese African-American and Caucasian women. *Int J Obes Relat Metab Disord* 22:215–221.
- Forsum E, Sadurskis A, Wager J. 1988. Resting metabolic rate and body composition of healthy Swedish women during pregnancy. *Am J Clin Nutr* 47:942–947.
- Forsum E, Kabir N, Sadurskis A, Westerterp K. 1992. Total energy expenditure of healthy Swedish women during pregnancy and lactation. *Am J Clin Nutr* 56:334–342.
- Foster GD, Wadden TA, Vogt RA. 1997. Resting energy expenditure in obese African American and Caucasian women. *Obes Res* 5:1–8.
- Foster GD, Wadden TA, Swain RM, Anderson DA, Vogt RA. 1999. Changes in resting energy expenditure after weight loss in obese African American and white women. *Am J Clin Nutr* 69:13–17.
- Frigerio C, Schutz Y, Whitehead R, Jequier E. 1991. A new procedure to assess the energy requirements of lactation in Gambian women. *Am J Clin Nutr* 54:526–533.
- Fukagawa NK, Bandini LG, Young JB. 1990. Effect of age on body composition and resting metabolic rate. *Am J Physiol* 259:E233–E238.
- Fukagawa NK, Bandini LG, Lim PH, Roinegard F, Lee MA, Young JB. 1991. Protein-induced changes in energy expenditure in young and old individuals. *Am J Physiol* 260:E345–E352.

- Gaesser GA, Brooks GA. 1984. Metabolic bases of excess post-exercise oxygen consumption: A review. *Med Sci Sports Exerc* 16:29–43.
- Garby L, Kurzer MS, Lammert O, Nielsen E. 1987. Energy expenditure during sleep in men and women: Evaporative and sensible heat losses. *Hum Nutr Clin Nutr* 41:225–233.
- Garby L, Lammert O, Nielsen E. 1990. Changes in energy expenditure of light physical activity during a 10 day period at 34°C environmental temperature. *Eur J Clin Nutr* 44:241–244.
- Geithner CA, Woynarowska B, Malina RM. 1998. The adolescent spurt and sexual maturation in girls active and nonactive in sport. *Ann Hum Biol* 25(5):415–423.
- Gibson RS, Vanderkooy PD, MacDonald AC, Goldman A, Ryan BA, Berry M. 1989. A growth-limiting, mild zinc-deficiency syndrome in some Southern Ontario boys with low height percentiles. *Am J Clin Nutr* 49:1266–1276.
- Gilliam TB, Freedson. 1980. Effects of a 12-week school physical fitness program on peak VO<sub>2</sub>, body composition and blood lipids in 7 to 9 year old children. *Int J Sports Med* 1:73–78.
- Giovannucci E, Ascherio A, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. 1995. Physical activity, obesity, and risk for colon cancer and adenoma in men. *Ann Intern Med* 122:327–334.
- Giovannucci E, Colditz GA, Stampfer MJ, Willett WC. 1996. Physical activity, obesity, and risk of colorectal adenoma in women (United States). *Cancer Causes Control* 7:253–263.
- Golay A, Schutz Y, Meyer HU, Thiebaud D, Curchod B, Maeder E, Felber JP, Jequier E. 1982. Glucose-induced thermogenesis in nondiabetic and diabetic obese subjects. *Diabetes* 31:1023–1028.
- Goldberg GR, Black AE, Jebb SA, Cole TJ, Murgatroyd PR, Coward WA, Prentice AM. 1991a. Critical evaluation of energy intake data using fundamental principles of energy physiology: 1. Derivation of cut-off limits to identify under-recording. *Eur J Clin Nutr* 45:569–581.
- Goldberg GR, Prentice AM, Coward WA, Davies HL, Murgatroyd PR, Sawyer MB, Ashford J, Black AE. 1991b. Longitudinal assessment of the components of energy balance in well-nourished lactating women. *Am J Clin Nutr* 54:788–798.
- Goldberg GR, Prentice AM, Coward WA, Davies HL, Murgatroyd PR, Wensing C, Black AE, Harding M, Sawyer M. 1993. Longitudinal assessment of energy expenditure in pregnancy by the doubly labeled water method. *Am J Clin Nutr* 57:494–505.
- Goran MI, Poehlman ET. 1992. Endurance training does not enhance total energy expenditure in healthy elderly persons. *Am J Physiol* 263:E950–E957.
- Goran MI, Calles-Escandon J, Poehlman ET, O'Connell M, Danforth E. 1994a. Effects of increased energy intake and/or physical activity on energy expenditure in young healthy men. *J Appl Physiol* 77:366–372.
- Goran MI, Kaskoun M, Johnson R. 1994b. Determinants of resting energy expenditure in young children. *J Pediatr* 125:362–367.
- Goran MI, Carpenter WH, McGloin A, Johnson R, Hardin JM, Weinsier RL. 1995a. Energy expenditure in children of lean and obese parents. *Am J Physiol* 268:E917–E924.
- Goran MI, Kaskoun M, Johnson R, Martinez C, Kelly B, Hood V. 1995b. Energy expenditure and body fat distribution in Mohawk children. *Pediatrics* 95:89–95.

- Goran MI, Gower BA, Nagy TR, Johnson RK. 1998a. Developmental changes in energy expenditure and physical activity in children: Evidence for a decline in physical activity in girls before puberty. *Pediatrics* 101:887–891.
- Goran MI, Nagy TR, Gower BA, Mazariegos M, Solomons N, Hood V, Johnson R. 1998b. Influence of sex, seasonality, ethnicity, and geographic location on the components of total energy expenditure in young children: Implications for energy requirements. *Am J Clin Nutr* 68:675–682.
- Goran MI, Shewchuk R, Gower BA, Nagy TR, Carpenter WH, Johnson RK. 1998c. Longitudinal changes in fatness in white children: No effect of childhood energy expenditure. *Am J Clin Nutr* 67:309–316.
- Griffiths M, Payne PR. 1976. Energy expenditure in small children of obese and non-obese parents. *Nature* 260:698–700.
- Grund A, Vollbrecht H, Frandsen W, Krause H, Siewers M, Rieckert H, Müller MJ. 2000. No effect of gender on different components of daily energy expenditure in free living prepubertal children. *Int J Obes Relat Metab Disord* 24:299–305.
- Grund A, Krause H, Kraus M, Siewers M, Rieckert H, Müller MJ. 2001. Association between different attributes of physical activity and fat mass in untrained, endurance- and resistance-trained men. *Eur J Appl Physiol* 84:310–320.
- Grundy SM, Mok HYI, Zech L, Steinberg D, Berman M. 1979. Transport of very low density lipoprotein triglycerides in varying degrees of obesity and hypertriglyceridemia. *J Clin Invest* 63:1274–1283.
- Guillermo-Tuazon MA, Barba CV, van Raaij JM, Hautvast JG. 1992. Energy intake, energy expenditure, and body composition of poor rural Philippine women throughout the first 6 mo of lactation. *Am J Clin Nutr* 56:874–880.
- Gutin B, Barbeau P, Owens S, Lemmon CR, Bauman M, Allison J, Kang HS, Litaker MS. 2002. Effects of exercise intensity on cardiovascular fitness, total body composition, and visceral adiposity of obese adolescents. *Am J Clin Nutr* 75:818–826.
- Guo S, Roche AF, Fomon SJ, Nelson SE, Chumlea WC, Rogers RR, Baumgartner RN, Ziegler EE, Siervogel RM. 1991. Reference data on gains in weight and length during the first two years of life. *J Pediatr* 119:355–362.
- Hadden DR, Montgomery DAD, Skelly RJ, Trimble ER, Weaver JA, Wilson EA, Buchanan KD. 1975. Maturity onset diabetes mellitus: response to intensive dietary management. *Br Med J* 2:276–278.
- Haffner SM, Mitchell BD, Hazuda HP, Stern MP. 1991. Greater influence of central distribution of adipose tissue on incidence of non-insulin-dependent diabetes in women than men. *Am J Clin Nutr* 53:1312–1317.
- Haggarty P, McNeill G, Abu Manneh MK, Davidson L, Milne E, Duncan G, Ashton J. 1994. The influence of exercise on the energy requirements of adult males in the UK. *Br J Nutr* 72:799–813.
- Harris JA, Benedict FG. 1919. *A Biometric Study of Basal Metabolism in Man*. Washington, DC: Carnegie Institution.
- Hart DJ, Spector TD. 1993. The relationship of obesity, fat distribution and osteoarthritis in women in the general population: The Chingford Study. *J Rheumatol* 20:331–335.
- Hartman WM, Stroud M, Sweet DM, Saxton J. 1993. Long-term maintenance of weight loss following supplemented fasting. *Int J Eat Disord* 14:87–93.
- Haschke F. 1989. Body composition during adolescence. In: *Body Composition Measurements in Infants and Children: Report of the 98th Ross Conference on Pediatric Research*. Columbus, OH: Ross Laboratories. Pp. 76–83.

- Hay WW. 1994. Placental supply of energy and protein substrates to the fetus. *Acta Paediatr Suppl* 405:13–19.
- Hayter JE, Henry CJ. 1993. Basal metabolic rate in human subjects migrating between tropical and temperate regions: A longitudinal study and review of previous work. *Eur J Clin Nutr* 47:724–734.
- Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. 1993. Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: The DARLING Study. *Am J Clin Nutr* 58:152–161.
- Heitmann BL, Kaprio J, Harris JR, Rissanen A, Korkeila M, Koskenvuo M. 1997. Are genetic determinants of weight gain modified by leisure-time physical activity? A prospective study of Finnish twins. *Am J Clin Nutr* 66:672–678.
- Helmrich SP, Shapiro S, Rosenberg L, Kaufman DW, Slone D, Bain C, Miettinen OS, Stolley PD, Rosenshein NB, Knapp RC, Leavitt T, Schottenfeld D, Engle RL, Levy M. 1983. Risk factors for breast cancer. *Am J Epidemiol* 117:35–45.
- Henry CJ. 2000. Mechanisms of changes in basal metabolism during aging. *Eur J Clin Nutr* 54:S77–S91.
- Herring JL, Mole PA, Meredith CN, Stern JS. 1992. Effect of suspending exercise training on resting metabolic rate in women. *Med Sci Sports Exerc* 24:59–65.
- Hessemer V, Bruck K. 1985. Influence of menstrual cycle on thermoregulatory, metabolic, and heart rate responses to exercise at night. *J Appl Physiol* 59:1911–1917.
- Heyman MB, Young VR, Fuss P, Tsay R, Joseph L, Roberts SB. 1992. Underfeeding and body weight regulation in normal-weight young men. *Am J Physiol* 263:R250–R257.
- Heymsfield SB, Gallagher D, Kotler DP, Wang Z, Allison DB, Heshka S. 2002. Body-size dependence of resting energy expenditure can be attributed to nonenergetic homogeneity of fat-free mass. *Am J Physiol* 282:E132–E138.
- Hill JO, Peters JC. 1998. Environmental contributions to the obesity epidemic. *Science* 280:1371–1374.
- Hill JR. 1964. The development of thermal stability in the newborn baby. In: Jonxis JH, Visser HK, Troelstra JA, eds. *The Adaptation of the Newborn Infant to Extra-Uterine Life*. Springfield, IL: Charles Thomas. Pp. 223–228.
- Hochberg MC, Lethbridge-Cejku M, Scott WW, Reichle R, Plato CC, Tobin JD. 1995. The association of body weight, body fatness and body fat distribution with osteoarthritis of the knee: Data from the Baltimore Longitudinal Study of Aging. *J Rheumatol* 22:488–493.
- Holden JH, Darga LL, Olson SM, Stettner DC, Ardito EA, Lucas CP. 1992. Long-term follow-up of patients attending a combination very-low calorie diet and behaviour therapy weight loss programme. *Int J Obes Relat Metab Disord* 16:605–613.
- Holliday MA. 1971. Metabolic rate and organ size during growth from infancy to maturity and during late gestation and early infancy. *Pediatrics* 47:169–179.
- Holmes FL. 1985. *Lavoisier and the Chemistry of Life*. Madison, WI: University of Wisconsin Press.
- Howe JC, Rumppler WV, Seale JL. 1993. Energy expenditure by indirect calorimetry in premenopausal women: Variation within one menstrual cycle. *J Nutr Biochem* 4:268–273.
- Huang Z, Hankinson SE, Colditz GA, Stampfer MJ, Hunter DJ, Manson JE, Hennekens CH, Rosner B, Speizer FE, Willett WC. 1997. Dual effects of weight and weight gain on breast cancer risk. *J Am Med Assoc* 278:1407–1411.

- Huang Z, Willett WC, Manson JE, Rosner B, Stampfer MJ, Speizer FE, Colditz GA. 1998. Body weight, weight change, and risk for hypertension in women. *Ann Intern Med* 128:81–88.
- Hubert HB, Feinleib M, McNamara PM, Castelli WP. 1983. Obesity as an independent risk factor for cardiovascular disease: A 26-year follow-up of participants in the Framingham Heart Study. *Circulation* 67:968–977.
- Hunt JF, White JR. 1980. Effect of ten weeks of vigorous daily exercise on serum lipids and lipoproteins in teenage males. *Med Sci Sports Exerc* 12:93.
- Hunter GR, Weinsier RL, Darnell BE, Zuckerman PA, Goran MI. 2000. Racial differences in energy expenditure and aerobic fitness in premenopausal women. *Am J Clin Nutr* 71:500–506.
- Hytten FE. 1991a. Nutrition. In: Hytten FE, Chamberlain G, eds. *Clinical Physiology in Obstetrics*. Oxford: Blackwell Scientific. Pp. 150–172.
- Hytten FE. 1991b. Weight gain in pregnancy. In: Hytten FE, Chamberlain G, eds. *Clinical Physiology in Obstetrics*. Oxford: Blackwell Scientific. Pp. 173–203.
- IDECG (International Dietary Energy Consulting Group). 1990. *The Doubly-Labelled Water Method for Measuring Energy Expenditure: A Consensus Report by the IDECG Working Group. Technical Recommendations for Use in Humans*. Vienna, Austria: NAHRES-4, International Atomic Energy Agency.
- Illingworth PJ, Jung RT, Howie PW, Leslie P, Isles TE. 1986. Diminution in energy expenditure during lactation. *Br Med J* 292:437–441.
- Illner K, Brinkmann G, Heller M, Bosy-Westphal A, Muller MJ. 2000. Metabolically active components of fat free mass and resting energy expenditure in non-obese adults. *Am J Physiol* 278:E308–E315.
- IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Washington, DC: National Academy Press.
- IOM. 1991. *Nutrition During Lactation*. Washington, DC: National Academy Press.
- Jakicic JM, Wing RR. 1998. Differences in resting energy expenditure in African-American vs. Caucasian overweight females. *Int J Obes Relat Metab Disord* 22:236–242.
- James WPT, McNeill G, Ralph A. 1990. Metabolism and nutritional adaptation to altered intakes of energy substrates. *Am J Clin Nutr* 51:264–269.
- Jensen CL, Butte NF, Wong WW, Moon JK. 1992. Determining energy expenditure in preterm infants: Comparison of  $^2\text{H}_2^{18}\text{O}$  method and indirect calorimetry. *Am J Physiol* 263:R685–R692.
- Jequier E, Tappy L. 1999. Regulation of body weight in humans. *Physiol Rev* 79:451–480.
- Jiang Z, Yan Q, Su Y, Acheson KJ, Thelin A, Piguet-Welsch C, Ritz P, Ho Z. 1998. Energy expenditure of Chinese infants in Guangdong Province, south China, determined with use of the doubly labeled water method. *Am J Clin Nutr* 67:1256–1264.
- Johnson RK. 2000. What are people really eating and why does it matter? *Nutr Today* 35:40–45.
- Johnson RK, Goran MI, Poehlman ET. 1994. Correlates of over- and under-reporting of energy intake in healthy older men and women. *Am J Clin Nutr* 59:1286–1290.
- Johnson RK, Soultanakis RP, Matthews DE. 1998. Literacy and body fatness are associated with underreporting of energy intake in U.S. low-income women using the multiple-pass 24-hour recall: A doubly labeled water study. *J Am Diet Assoc* 98:1136–1140.

- Jones PJ, Winthrop AL, Schoeller DA, Swyer PR, Smith J, Filler RM, Heim T. 1987. Validation of doubly labeled water for assessing energy expenditure in infants. *Pediatr Res* 21:242–246.
- Jones PJ, Martin LJ, Su W, Boyd NF. 1997. Canadian Recommended Nutrient Intakes underestimate true energy requirements in middle-aged women. *Can J Public Health* 88:314–319.
- Kalhan S, Rossi K, Gruca L, Burkett E, O'Brien A. 1997. Glucose turnover and gluconeogenesis in human pregnancy. *J Clin Invest* 100:1775–1781.
- Kalkhoff RK, Kisseebah AH, Kim H-J. 1978. Carbohydrate and lipid metabolism during normal pregnancy: Relationship to gestational hormone action. *Semin Perinatol* 2:291–307.
- Kannel WB, Brand N, Skinner JJ, Dawber TR, McNamara PM. 1967. The relation of adiposity to blood pressure and development of hypertension. *Ann Intern Med* 67:48–59.
- Kaplan AS, Zemel BS, Stallings VA. 1996. Differences in resting energy expenditure in prepubertal black children and white children. *J Pediatr* 129:643–647.
- Karlberg P. 1952. Determinations of standard energy metabolism (basal metabolism) in normal infants. *Acta Paediatr Scand* 41:11–151.
- Kashiwazaki H, Dejima Y, Suzuki T. 1990. Influence of upper and lower thermo-neutral room temperatures (20°C and 25°C) on fasting and post-prandial resting metabolism under different outdoor temperatures. *Eur J Clin Nutr* 44:405–413.
- Kato I, Nomura A, Stemmermann GN, Chyou P-H. 1992. Prospective study of clinical gallbladder disease and its association with obesity, physical activity, and other factors. *Dig Dis Sci* 37:784–790.
- Kempen KP, Saris WH, Westerterp KR. 1995. Energy balance during an 8-wk energy-restricted diet with and without exercise in obese women. *Am J Clin Nutr* 62:722–729.
- Kesaniemi YA, Grundy SM. 1983. Increased low density lipoprotein production associated with obesity. *Arteriosclerosis* 3:170–177.
- Keys A, Taylor H, Grande F. 1973. Basal metabolism and age of adult man. *Metabolism* 22:579–587.
- Klannemark M, Orho M, Groop L. 1998. No relationship between identified variants in the uncoupling protein 2 gene and energy expenditure. *Eur J Endocrinol* 139:217–223.
- Klausen B, Toubro S, Astrup A. 1997. Age and sex effects on energy expenditure. *Am J Clin Nutr* 65:895–907.
- Kleiber M. 1975. *The Fire of Life. An Introduction to Animal Energetics*. New York: Robert E. Krieger Publishing.
- Klein PD, James WP, Wong WW, Irving CS, Murgatroyd PR, Cabrera M, Dallosso HM, Klein ER, Nichols BL. 1984. Calorimetric validation of the doubly-labelled water method for determination of energy expenditure in man. *Hum Nutr Clin Nutr* 38C:95–106.
- Knuttgen HG, Emerson K. 1974. Physiological response to pregnancy at rest and during exercise. *J Appl Physiol* 36:549–553.
- Kopp-Hoolihan LE, Van Loan MD, Wong WW, King JC. 1999. Longitudinal assessment of energy balance in well-nourished, pregnant women. *Am J Clin Nutr* 69:697–704.
- Krebs-Smith SM, Graubard B, Kahle L, Subar A, Cleveland L, Ballard-Barbash R. 2000. Low energy reporters vs. others: A comparison of reported food intakes. *Eur J Clin Nutr* 54:281–287.

- Kuczmarski RJ, Ogden CL, Grummer-Strawn LM, Flegal KM, Guo SS, Wei R, Mei Z, Curtin LR, Roche AF, Johnson CL. 2000. CDC growth charts: United States. *Adv Data* 314:1–28.
- Kushner RF, Racette SB, Neil K, Schoeller DA. 1995. Measurement of physical activity among black and white obese women. *Obes Res* 3:261S–265S.
- Lammi-Keefe CJ, Ferris AM, Jensen RG. 1990. Changes in human milk at 0600, 1000, 1400, 1800, and 2200 h. *J Pediatr Gastroenterol Nutr* 11:83–88.
- Lanzola E, Tagliabue A, Cena H. 1990. Skin temperature and energy expenditure. *Ann Nutr Metab* 34:311–316.
- Larson DE, Ferraro RT, Robertson DS, Ravussin E. 1995. Energy metabolism in weight-stable postobese individuals. *Am J Clin Nutr* 62:735–739.
- Lean ME, Murgatroyd PR, Rothnie I, Reid IW, Harvey R. 1988. Metabolic and thyroidal responses to mild cold are abnormal in obese diabetic women. *Clin Endocrinol* 28:665–673.
- Lederman SA, Paxton A, Heymsfield SB, Wang J, Thornton J, Pierson RN. 1997. Body fat and water changes during pregnancy in women with different body weight and weight gain. *Obstet Gynecol* 90:483–488.
- Leibel RL, Rosenbaum M, Hirsch J. 1995. Changes in energy expenditure resulting from altered body weight. *N Engl J Med* 332:621–628.
- Leonard WR, Galloway VA, Ivakine E. 1997. Underestimation of daily energy expenditure with the factorial method: Implications for anthropological research. *Am J Phys Anthropol* 103:443–454.
- Leon-Velarde F, Gamboa A, Chuquiza JA, Esteba WA, Rivera-Chira M, Monge CC. 2000. Hematological parameters in high altitude residents living at 4,355, 4,660, and 5,500 meters above sea level. *High Alt Med Biol* 1:97–104.
- Levine JA, Eberhardt NL, Jensen MD. 1999. Role of nonexercise activity thermogenesis in resistance to fat gain in humans. *Science* 283:212–214.
- Levine JA, Schleusner SJ, Jensen MD. 2000. Energy expenditure of nonexercise activity. *Am J Clin Nutr* 72:1451–1454.
- Lichtman SW, Pisarska K, Berman ER, Pestone M, Dowling H, Offenbacher E, Weisel H, Heshka S, Matthews DE, Heymsfield SB. 1992. Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. *N Engl J Med* 327:1893–1898.
- Lifson N, McClintock R. 1966. Theory of use of the turnover rates of body water for measuring energy and material balance. *J Theoret Biol* 12:46–74.
- Lifson N, Gordon GB, Visscher MB, Nier AO. 1949. The fate of utilized molecular oxygen and the source of the oxygen of respiratory carbon dioxide, studied with the aid of heavy oxygen. *J Biol Chem* 180:803–811.
- Lifson N, Gordon GB, McClintock R. 1955. Measurement of total carbon dioxide production by means of  $D_2O^{18}$ . *J Appl Physiol* 7:704–710.
- Linder CW, Durant RH, Mahoney OM. 1983. The effect of physical conditioning on serum lipids and lipoproteins in white male adolescents. *Med Sci Sports Exerc* 15:232–236.
- Lindsay CA, Huston L, Amini SB, Catalano PM. 1997. Longitudinal changes in the relationship between body mass index and percent body fat in pregnancy. *Obstet Gynecol* 89:377–382.
- Lipmann F. 1941. Metabolic generation and utilization of phosphate bond energy. *Adv Enzymol* 1:99–162.

- Livesey G, Elia M. 1988. Estimation of energy expenditure, net carbohydrate utilization, and net fat oxidation and synthesis by indirect calorimetry: Evaluation of errors with special reference to the detailed composition of fuels. *Am J Clin Nutr* 47:608–628.
- Livingstone MB, Coward WA, Prentice AM, Davies PS, Strain JJ, McKenna PG, Mahoney CA, White JA, Stewart CM, Kerr MJ. 1992a. Daily energy expenditure in free-living children: Comparison of heart-rate monitoring with the doubly labeled water ( $^2\text{H}_2^{18}\text{O}$ ) method. *Am J Clin Nutr* 56:343–352.
- Livingstone MB, Prentice AM, Coward WA, Strain JJ, Black AE, Davies PS, Stewart CM, McKenna PG, Whitehead RG. 1992b. Validation of estimates of energy intake by weighed dietary record and diet history in children and adolescents. *Am J Clin Nutr* 56:29–35.
- Lovelady CA, Meredith CN, McCrory MA, Nommsen LA, Joseph LJ, Dewey KG. 1993. Energy expenditure in lactating women: A comparison of doubly labeled water and heart-rate-monitoring methods. *Am J Clin Nutr* 57:512–518.
- Lucas A, Ewing G, Roberts SB, Coward WA. 1987. How much energy does the breast fed infant consume and expend? *Br Med J* 295:75–77.
- Lundgren H, Bengtsson C, Blohme G, Lapidus L, Sjöström L. 1989. Adiposity and adipose tissue distribution in relation to incidence of diabetes in women: Results from a prospective population study in Gothenburg, Sweden. *Int J Obes* 13:413–423.
- MacMahon SW, Blacket RB, Macdonald GJ, Hall W. 1984. Obesity, alcohol consumption and blood pressure in Australian men and women. The National Heart Foundation of Australia Risk Factor Prevalence Study. *J Hypertens* 2:85–91.
- Maffei C, Schutz Y, Zoccali L, Micciolo R, Pinelli L. 1993. Meal-induced thermogenesis in lean and obese prepubertal children. *Am J Clin Nutr* 57:481–485.
- Malina RM. 1994. Physical activity: Relationship to growth, maturation, and physical fitness. In: Bouchard C, Shephard RJ, Stephens T, eds. *Physical Activity, Fitness, and Health. International Proceedings and Consensus Statement*. Champaign, IL: Human Kinetics. Pp. 918–930.
- Manson JE, Colditz GA, Stampfer MJ, Willett WC, Rosner B, Monson RR, Speizer FE, Hennekens CH. 1990. A prospective study of obesity and risk of coronary heart disease in women. *N Engl J Med* 322:882–889.
- Margaria R, Cerretelli P, Aghemo P, Sassi G. 1963. Energy cost of running *J Appl Physiol* 18:367–370.
- Mawson JT, Braun B, Rock PB, Moore LG, Mazzeo R, Butterfield GE. 2000. Women at altitude: Energy requirement at 4,300 m. *J Appl Physiol* 88:272–281.
- McCargar L, Taunton J, Birmingham CL, Paré S, Simmons D. 1993. Metabolic and anthropometric changes in female weight cyclers and controls over a 1-year period. *J Am Diet Assoc* 93:1025–1030.
- Medalie JH, Papier C, Herman JB, Goldbourt U, Tamir S, Neufeld HN, Riss E. 1974. Diabetes mellitus among 10,000 adult men. I. Five-year incidence and associated variables. *Isr J Med Sci* 10:681–697.
- Meijer GA, Westerterp KR, Saris WH, ten Hoor F. 1992. Sleeping metabolic rate in relation to body composition and the menstrual cycle. *Am J Clin Nutr* 55:637–640.
- Melanson KJ, Saltzman E, Russell R, Roberts SB. 1996. Postabsorptive and postprandial energy expenditure and substrate oxidation do not change during the menstrual cycle in young women. *J Nutr* 126:2531–2538.

- Melanson KJ, Saltzman E, Vinken AG, Russell R, Roberts SB. 1998. The effects of age on postprandial thermogenesis at four graded energetic challenges: Findings in young and older women. *J Gerontol A Biol Sci Med Sci* 53:B409–B414.
- Merrill AL, Watt BK. 1973. *Energy Value of Foods, Basis and Derivation*. Agricultural Handbook No.74. Human Nutrition Research Branch, Agricultural Research Service, United States Department of Agriculture. U.S. Government Printing Office, Washington, D.C.
- Miller WC, Koceja DM, Hamilton EJ. 1997. A meta-analysis of the past 25 years of weight loss research using diet, exercise or diet plus exercise intervention. *Int J Obes Relat Metab Disord* 21:941–947.
- Minghelli G, Schutz Y, Charbonnier A, Whitehead R, Jequier E. 1990. Twenty-four-hour energy expenditure and basal metabolic rate measured in a whole-body indirect calorimeter in Gambian men. *Am J Clin Nutr* 51:563–570.
- Moore FS. 1963. *The Body Cell Mass and Its Supporting Environment: Body Composition in Health and Disease*. Philadelphia, PA: Saunders.
- Moore LL, Nguyen USDT, Rothman KJ, Cupples LA, Ellison RC. 1995. Preschool physical activity level and change in body fatness in young children. *Am J Epidemiol* 142:982–988.
- Morgan JB, York DA. 1983. Thermic effect of feeding in relation to energy balance in elderly men. *Ann Nutr Metab* 27:71–77.
- Morio B, Ritz P, Verdier E, Montaurier C, Beaufrere B, Vermorel M. 1997. Critical evaluation of the factorial and heart-rate recording methods for the determination of energy expenditure of free-living elderly people. *Br J Nutr* 78:709–722.
- Morrison JA, Alfaro MP, Khoury P, Thornton BB, Daniels SR. 1996. Determinants of resting energy expenditure in young black girls and young white girls. *J Pediatr* 129:637–642.
- Motil KJ, Montandon CM, Garza C. 1990. Basal and postprandial metabolic rates in lactating and nonlactating women. *Am J Clin Nutr* 52:610–615.
- Murgatroyd PR, Goldberg GR, Diaz E, Prentice AM. 1990. The influence of mild cold on human energy expenditure: Is there a sex difference in the response? *Br J Nutr* 64:777.
- Must A, Strauss RS. 1999. Risks and consequences of childhood and adolescent obesity. *Int J Obes Relat Metab Disord* 23:S2–S11.
- Nagy LE, King JC. 1984. Postprandial energy expenditure and respiratory quotient during early and late pregnancy. *Am J Clin Nutr* 40:1258–1263.
- Nair KS, Halliday D, Garrow JS. 1983. Thermic response to isoenergetic protein, carbohydrate or fat meals in lean and obese subjects. *Clin Sci* 65:307–312.
- Nelson KM, Weinsier RL, Long CL, Schutz Y. 1992. Prediction of resting energy expenditure from fat-free mass and fat mass. *Am J Clin Nutr* 56:848–856.
- Neville MC. 1995. Determinants of milk volume and composition. In: Jensen RG, ed. *Handbook of Milk Composition*. San Diego, CA: Academic Press. Pp. 87–113.
- Neville MC, Keller R, Seacat J, Lutes V, Neifert M, Casey C, Allen J, Archer P. 1988. Studies in human lactation: Milk volumes in lactating women during the onset of lactation and full lactation. *Am J Clin Nutr* 48:1375–1386.
- Newman WP 3rd, Freedman DS, Voors AW, Gard PD, Srinivasan SR, Cresanta JL, Williamson GD, Webber LS, Berenson GS. 1986. Relation of serum lipoprotein levels and systolic blood pressure to early arteriosclerosis. The Bolgalusa heart study. *N Engl J Med* 314:138–144.

- NHLBI/NIDDK (National Heart, Lung, and Blood Institute/National Institute of Diabetes and Digestive and Kidney Diseases). 1998. *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. The Evidence Report*. NIH Publication No. 98-4083. Bethesda, MD: National Institutes of Health.
- Nicklas BJ, Toth MJ, Goldberg AP, Poehlman ET. 1997. Racial differences in plasma leptin concentrations in obese postmenopausal women. *J Clin Endocrinol Metab* 82:315–317.
- Nickleberry BL, Brooks GA. 1996. No effect of cycling experience on leg cycle ergometer efficiency. *Med Sci Sports Exerc* 28:1396–1401.
- Nielsen E. 1987. Acute modest changes in relative humidity do not affect energy expenditure at rest in human subjects. *Hum Nutr Clin Nutr* 41:485–488.
- NIH (National Institutes of Health). 2000. *The Practical Guide. Identification, Evaluation, and Treatment of Overweight and Obesity in Adults*. NIH Publication No. 00-4084. Bethesda, MD: National Institutes of Health.
- Nommsen LA, Lovelady CA, Heinig MJ, Lonnerdal B, Dewey KG. 1991. Determinants of energy, protein, lipid, and lactose concentrations in human milk during the first 12 mo of lactation: The DARLING Study. *Am J Clin Nutr* 53:457–465.
- NRC (National Research Council). 1989. *Recommended Dietary Allowances*, 10th ed. Washington, DC: National Academy Press.
- Ohlson L-O, Larsson B, Svärdsudd K, Welin L, Eriksson H, Wilhelmsen L, Björntorp P, Tibblin G. 1985. The influence of body fat distribution on the incidence of diabetes mellitus. 13.5 years of follow-up of the participants in the study of men born in 1913. *Diabetes* 34:1055–1058.
- Osterman J, Lin Tu, Nankin HR, Brown KA, Hornung CA. 1992. Serum cholesterol profiles during treatment of obese outpatients with a very low calorie diet. Effect of initial cholesterol levels. *Int J Obes Relat Metab Disord* 16:49–58.
- Owen OE. 1988. Regulation of energy and metabolism. In: MJ Kinney, Jeejeebhoy KN, Hill GH, Owen OE, eds. *Nutrition and Metabolism in Patient Care*. Philadelphia: W.B. Saunders. Pp. 35–59.
- Owen OE, Kayle E, Owen RS, Polansky M, Caprio S, Mozzoli MA, Kendrick ZV, Bushman MC, Boden G. 1986. A reappraisal of caloric requirements in healthy women. *Am J Clin Nutr* 44:1–19.
- Owen OE, Holup JL, D'Alessio DA, Craig ES, Polansky M, Smalley KJ, Kayle EC, Bushman MC, Owen LR, Mozzoli MA, Kendrick ZV, Boden GH. 1987. A reappraisal of the caloric requirements of men. *Am J Clin Nutr* 46:875–885.
- Owens S, Gutin B, Allison J, Riggs S, Ferguson M, Litaker M, Thompson W. 1999. Effect of physical training on total and visceral fat in obese children. *Med Sci Sports Exerc* 31:143–148.
- Pacy PJ, Cox M, Khalouha M, Elkins S, Robinson AC, Garrow JS. 1996. Does moderate aerobic activity have a stimulatory effect on 24 h resting energy expenditure: A direct calorimeter study. *Int J Food Sci Nutr* 47:299–305.
- Pahud P, Ravussin E, Jequier E. 1980. Energy expended during oxygen deficit period of submaximal exercise in man. *J Appl Physiol* 48:770–775.
- Pandolf KB, Givoni B, Goldman RF. 1977. Predicting energy expenditure with loads while standing or walking very slowly. *J Appl Physiol* 43:577–581.
- Pannemans DL, Westerterp KR. 1995. Energy expenditure, physical activity and basal metabolic rate of elderly subjects. *Br J Nutr* 73:571–581.

- Pannemans DL, Bouten CV, Westerterp KR. 1995. 24 h Energy expenditure during a standardized activity protocol in young and elderly men. *Eur J Clin Nutr* 49:49–56.
- Parizkova J. 1974. Particularities of lean body mass and fat development in growing boys as related to their motor activity. *Acta Paediatrica Belgica* 28:233S–243S.
- Passmore R, Durnin JV. 1955. Human energy expenditure. *Physiol Rev* 35:801–840.
- Penn D, Schmidt-Sommerfeld E. 1989. Lipids as an energy source for the fetus and newborn infant. In: Lebenthal E, ed. *Textbook of Gastroenterology and Nutrition in Infancy*. New York: Raven Press. Pp. 293–310.
- Piers LS, Diggavi SN, Rijkskamp J, van Raaij JM, Shetty PS, Hautvast JG. 1995a. Resting metabolic rate and thermic effect of a meal in the follicular and luteal phases of the menstrual cycle in well-nourished Indian women. *Am J Clin Nutr* 61:296–302.
- Piers LS, Diggavi SN, Thangam S, van Raaij JM, Shetty PS, Hautvast JG. 1995b. Changes in energy expenditure, anthropometry, and energy intake during the course of pregnancy and lactation in well-nourished Indian women. *Am J Clin Nutr* 61:501–513.
- Pipe NG, Smith T, Halliday D, Edmonds CJ, Williams C, Coltart TM. 1979. Changes in fat, fat-free mass and body water in human normal pregnancy. *Br J Obstet Gynaecol* 86:929–940.
- Platte P, Pirke KM, Wade SE, Trimborn P, Fichter MM. 1995. Physical activity, total energy expenditure, and food intake in grossly obese and normal weight women. *Int J Eating Disord* 17:51–57.
- Poehlman ET. 1992. Energy expenditure and requirements in aging humans. *J Nutr* 122:2057–2065.
- Poehlman ET. 1993. Regulation of energy expenditure in aging humans. *J Am Geriatr Soc* 41:552–559.
- Poehlman ET, Danforth E. 1991. Endurance training increases metabolic rate and norepinephrine appearance rate in older individuals. *Am J Physiol* 261:E233–E239.
- Poehlman ET, Melby CL, Badylak SF. 1991. Relation of age and physical exercise status on metabolic rate in younger and older healthy men. *J Gerontol* 46:B54–B58.
- Poehlman ET, Toth MJ, Gardner AW. 1995. Changes in energy balance and body composition at menopause: A controlled longitudinal study. *Ann Intern Med* 123:673–675.
- Poppitt SD, Swann D, Black AE, Prentice AM. 1998. Assessment of selective under-reporting of food intake by both obese and non-obese women in a metabolic facility. *Int J Obesity Relat Metab Disord* 22:303–311.
- Prentice AM, Black AE, Coward WA, Davies HL, Goldberg GR, Murgatroyd PR, Ashford J, Sawyer M, Whitehead RG. 1986. High levels of energy expenditure in obese women. *Br Med J* 292:983–987.
- Prentice AM, Lucas A, Vasquez-Velasquez L, Davies PS, Whitehead RG. 1988. Are current dietary guidelines for young children a prescription for overfeeding? *Lancet* 2:1066–1069.
- Prentice AM, Goldberg GR, Davies HL, Murgatroyd PR, Scott W. 1989. Energy-sparing adaptations in human pregnancy assessed by whole-body calorimetry. *Br J Nutr* 62:5–22.
- Prentice AM, Black AE, Coward WA, Cole TJ. 1996a. Energy expenditure in overweight and obese adults in affluent societies: An analysis of 319 doubly-labelled water measurements. *Eur J Clin Nutr* 50:93–97.

- Prentice AM, Spaaij CJ, Goldberg GR, Poppitt SD, van Raaij JM, Totton M, Swann D, Black AE. 1996b. Energy requirements of pregnant and lactating women. *Eur J Clin Nutr* 50:S82–S11.
- Price GM, Paul AA, Cole TJ, Wadsworth ME. 1997. Characteristics of the low-energy reporters in a longitudinal national dietary survey. *Br J Nutr* 77:833–851.
- Pryer JA, Vrijheid M, Nichols R, Kiggins M, Elliot P. 1997. Who are the ‘low energy reporters’ in the dietary and nutritional survey of British adults? *Int J Epidemiol* 26:146–154.
- Racette SB, Schoeller DA, Kushner RF, Neil KM, Herling-Iaffaldano K. 1995. Effects of aerobic exercise and dietary carbohydrate on energy expenditure and body composition during weight reduction in obese women. *Am J Clin Nutr* 61:486–494.
- Raitakari OT, Porkka KVK, Taimela S, Telama R, Rasanen L, Viikari JSA. 1994. Effects of persistent physical activity and inactivity on coronary risk factors in children and young adults. *Am J Epidemiol* 140:195–205.
- Ravussin E, Lillioja S, Anderson TE, Christin L, Bogardus C. 1986. Determinants of 24-hour energy expenditure in man: Methods and results using a respiratory chamber. *J Clin Invest* 78:1568–1578.
- Ravussin E, Lillioja S, Knowler WC, Christin L, Freymond D, Abbott WG, Boyce V, Howard BV, Bogardus C. 1988. Reduced rate of energy expenditure as a risk factor for body-weight gain. *N Engl J Med* 318:467–472.
- Ravussin E, Harper IT, Rising R, Bogardus C. 1991. Energy expenditure by doubly labeled water: Validation in lean and obese subjects. *Am J Physiol* 261:E402–E409.
- Reichman BL, Chessex P, Putet G, Verellen GJ, Smith JM, Heim T, Swyer PR. 1982. Partition of energy metabolism and energy cost of growth in the very low-birth-weight infant. *Pediatrics* 69:446–451.
- Reisin E, Abel R, Modan M, Silverberg DS, Eliahou HE, Modan B. 1978. Effect of weight loss without salt restriction on the reduction of blood pressure in overweight hypertensive patients. *N Engl J Med* 298:1–6.
- Rexrode KM, Hennekens CH, Willett WC, Colditz GA, Stampfer MJ, Rich-Edwards JW, Speizer FE, Manson JE. 1997. A prospective study of body mass index, weight change, and risk of stroke in women. *J Am Med Assoc* 277:1539–1545.
- Rexrode KM, Buring JE, Manson JE. 2001. Abdominal and total adiposity and risk of coronary heart disease in men. *Int J Obes Relat Metab Disord* 25:1047–1056.
- Rimm EB, Stampfer MJ, Giovannucci F, Ascherio A, Spiegelman D, Colditz GA, Willett WC. 1995. Body size and fat distribution as predictors of coronary heart disease among middle-aged and older US women. *Am J Epidemiol* 15:1117–1127.
- Riumallo JA, Schoeller D, Barrera G, Gattas V, Uauy R. 1989. Energy expenditure in underweight free-living adults: Impact of energy supplementation as determined by doubly labeled water and indirect calorimetry. *Am J Clin Nutr* 49:239–246.
- Roberts SB. 1996. Energy requirements of older individuals. *Eur J Clin Nutr* 50:S112–S118.
- Roberts SB, Dallal GE. 1998. Effects of age on energy balance. *Am J Clin Nutr* 68:975S–979S.
- Roberts SB, Dallal GE. 2001. The new childhood growth charts. *Nutr Rev* 59:31–36.
- Roberts SB, Young VR. 1988. Energy costs of fat and protein deposition in the human infant. *Am J Clin Nutr* 48:951–955.

- Roberts SB, Coward WA, Schlingenseipen K-H, Nohria V, Lucas A. 1986. Comparison of the doubly labeled water ( $^{2}\text{H}_2^{18}\text{O}$ ) method with indirect calorimetry and a nutrient-balance study for simultaneous determination of energy expenditure, water intake, and metabolizable energy intake in preterm infants. *Am J Clin Nutr* 44:315–322.
- Roberts SB, Savage J, Coward WA, Chew B, Lucas A. 1988. Energy expenditure and intake in infants born to lean and overweight mothers. *N Engl J Med* 318:461–466.
- Roberts SB, Young VR, Fuss P, Fiatarone MA, Richard B, Rasmussen H, Wagner D, Joseph L, Holehouse E, Evans WJ. 1990. Energy expenditure and subsequent nutrient intakes in overfed young men. *Am J Physiol* 259:R461–R469.
- Roberts SB, Heyman MB, Evans WJ, Fuss P, Tsay R, Young VR. 1991. Dietary energy requirements of young adult men, determined by using the doubly labeled water method. *Am J Clin Nutr* 54:499–505.
- Roberts SB, Young VR, Fuss P, Heyman MB, Fiatarone M, Dallal GE, Cortiella J, Evans WJ. 1992. What are the dietary energy needs of elderly adults? *Int J Obes Relat Metab Disord* 16:969–976.
- Roberts SB, Fuss P, Heyman MB, Young VR. 1995. Influence of age on energy requirements. *Am J Clin Nutr* 62:1053S–1058S.
- Rolland-Cachera MF, Deheeger M, Bellisle F, Sempe M, Guilloud-Bataille M, Patois E. 1984. Adiposity rebound in children: a simple indicator for predicting obesity. *Am J Clin Nutr* 39:129–135.
- Rolland-Cachera MF. 2001. Early adiposity rebound is not associated with energy or fat intake in infancy. *Pediatrics* 108:218–219.
- Rosenberg L, Palmer JR, Miller DR, Clarke EA, Shapiro S. 1990. A case-control study of alcoholic beverage consumption and breast cancer. *Am J Epidemiol* 131:6–14.
- Sadurskis A, Kabir N, Wager J, Forsum E. 1988. Energy metabolism, body composition, and milk production in healthy Swedish women during lactation. *Am J Clin Nutr* 48:44–49.
- Sahi T, Paffenbarger RS, Hsieh C-C, Lee I-M. 1998. Body mass index, cigarette smoking, and other characteristics as predictors of self-reported, physician-diagnosed gallbladder disease in male college alumni. *Am J Epidemiol* 147:644–651.
- Salbe AD, Fontvieille AM, Harper IT, Ravussin E. 1997. Low levels of physical activity in 5-year-old children. *J Pediatr* 131:423–429.
- Saltzman E, Roberts SB. 1995. The role of energy expenditure in energy regulation: Findings from a decade of research. *Nutr Rev* 53:209–220.
- Saris WHM, Emons HJG, Groenenboom DC, Westerterp KR. 1989. Discrepancy between FAO/WHO energy requirements and actual energy expenditure in healthy 7-11 year old children. In: Beunen G, Ghesquiere J, Reybrouck T, Claessens AL, eds. *Children and Exercise: 14th International Seminar on Pediatric Work Physiology*. Stuttgart, Germany: Ferdinand Enke Verlag Press.
- Sasaki J, Shindo M, Tanaka M, Ando M, Arakawa K. 1987. A long-term aerobic exercise program decreases the obesity index and increases high density lipoprotein cholesterol concentration in obese children. *Int J Obes* 11:339–345.
- Savage MP, Petrasits MM, Thomson WH, Berg K, Smith JL, Sady SP. 1986. Exercise training effects on serum lipids of prepubescent boys and adult men. *Med Sci Sports Exerc* 18:197–204.

- Sawaya AL, Saltzman E, Fuss P, Young VR, Roberts SB. 1995. Dietary energy requirements of young and older women determined by using the doubly labeled water method. *Am J Clin Nutr* 62:338–344.
- Schoeller DA. 1983. Energy expenditure from doubly labeled water: Some fundamental considerations in humans. *Am J Clin Nutr* 38:999–1005.
- Schoeller DA. 1995. Limitations in the assessment of dietary energy intake by self-report. *Metabolism* 44:18–22.
- Schoeller DA. 2001. The importance of clinical research: The role of thermogenesis in human obesity. *Am J Clin Nutr* 73:511–516.
- Schoeller DA, Fjeld CR. 1991. Human energy metabolism: What we have learned from the doubly labeled water method? *Annu Rev Nutr* 11:355–373.
- Schoeller DA, Webb P. 1984. Five-day comparison of the doubly labeled water method with respiratory gas exchange. *Am J Clin Nutr* 40:153–158.
- Schoeller DA, Ravussin E, Schutz Y, Acheson KJ, Baertschi P, Jequier E. 1986. Energy expenditure by doubly labeled water: Validation in humans and proposed calculation. *Am J Physiol* 250:R823–R830.
- Schofield C. 1985. An annotated bibliography of source material for basal metabolic rate data. *Hum Nutr Clin Nutr* 39C:42–91.
- Schofield WN. 1985. Predicting basal metabolic rate, new standards and review of previous work. *Hum Nutr Clin Nutr* 39C:5–41.
- Schotte DE, Stunkard AJ. 1990. The effects of weight reduction on blood pressure in 301 obese patients. *Ann Intern Med* 150:1701–1704.
- Schulz LO, Nyomba BL, Alger S, Anderson TE, Ravussin E. 1991. Effect of endurance training on sedentary energy expenditure measured in a respiratory chamber. *Am J Physiol* 260:E257–E261.
- Schulz LO, Alger S, Harper I, Wilmore JH, Ravussin E. 1992. Energy expenditure of elite female runners measured by respiratory chamber and doubly labeled water. *J Appl Physiol* 72:23–28.
- Schutz Y, Golay A, Felber JP, Jequier E. 1984. Decreased glucose-induced thermogenesis after weight loss in obese subjects: A predisposing factor for relapse obesity? *Am J Clin Nutr* 39:380–387.
- Schutz Y, Golay A, Jequier E. 1988. 24 h Energy expenditure (24-EE) in pregnant women with a standardized activity level. *Experientia* 44:A31.
- Schwartz RS, Jaeger LF, Veith RC. 1990. The thermic effect of feeding in older men: The importance of the sympathetic nervous system. *Metabolism* 39:733–737.
- Seale JL, Rumpler WV. 1997. Comparison of energy expenditure measurements by diet records, energy intake balance, doubly labeled water and room calorimetry. *Eur J Clin Nutr* 51:856–863.
- Seale JL, Rumpler WV, Conway JM, Miles CW. 1990. Comparison of doubly labeled water, intake-balance, and direct- and indirect-calorimetry methods for measuring energy expenditure in adult men. *Am J Clin Nutr* 52:66–71.
- Segal KR, Gutin B, Albu J, Pi-Sunyer FX. 1987. Thermic effects of food and exercise in lean and obese men of similar lean body mass. *Am J Physiol* 252:E110–E117.
- Segal KR, Edano A, Blando L, Pi-Sunyer FX. 1990a. Comparison of thermic effects of constant and relative caloric loads in lean and obese men. *Am J Clin Nutr* 51:14–21.
- Segal KR, Edano A, Tomas MB. 1990b. Thermic effect of a meal over 3 and 6 hours in lean and obese men. *Metabolism* 39:985–992.
- Segal KR, Chun A, Coronel P, Cruz-Noori A, Santos R. 1992. Reliability of the measurement of postprandial thermogenesis in men of three levels of body fatness. *Metabolism* 41:754–762.

- Seidell JC, Verschuren WM, Van Leer EM, Kromhout D. 1996. Overweight, underweight, and mortality: A prospective study of 48,287 men and women. *Arch Intern Med* 156:958–963.
- Shah M, Geissler CA, Miller DS. 1988. Metabolic rate during and after aerobic exercise in post-obese and lean women. *Eur J Clin Nutr* 42:455–464.
- Shetty PS, Soares MJ, James WPT. 1994. Body mass index: Its relationship to basal metabolic rates and energy requirements. *Eur J Clin Nutr* 48:S28–S38.
- Siler SQ, Neese RA, Hellerstein MK. 1999. De novo lipogenesis, lipid kinetics, and whole-body lipid balances in humans after acute alcohol consumption. *Am J Clin Nutr* 70:928–936.
- Sinclair JC. 1978. *Temperature Regulation and Energy Metabolism in the Newborn*. New York: Grune and Stratton.
- Soares MJ, Piers LS, Shetty PS, Robinson S, Jackson AA, Waterlow CJ. 1991. Basal metabolic rate, body composition and whole-body protein turnover in Indian men with differing nutritional status. *Clin Sci* 81:419–425.
- Soares MJ, Piers LS, O'Dea K, Shetty PS. 1998. No evidence for an ethnic influence on basal metabolism: An examination of data from India and Australia. *Br J Nutr* 79:333–341.
- Sohlstrom A, Forsum E. 1995. Changes in adipose tissue volume and distribution during reproduction in Swedish women as assessed by magnetic resonance imaging. *Am J Clin Nutr* 61:287–295.
- Sohlstrom A, Forsum E. 1997. Changes in total body fat during the human reproductive cycle as assessed by magnetic resonance imaging, body water dilution, and skinfold thickness: A comparison of methods. *Am J Clin Nutr* 66:1315–1322.
- Solomon SJ, Kurzer MS, Calloway DH. 1982. Menstrual cycle and basal metabolic rate in women. *Am J Clin Nutr* 36:611–616.
- Spaaij CJK, van Raaij JMA, de Groot LC, van der Heijden LJ, Boekholt HA, Hautvast JG. 1994a. Effect of lactation on resting metabolic rate and on diet- and work-induced thermogenesis. *Am J Clin Nutr* 59:42–47.
- Spaaij CJK, van Raaij JMA, van der Heijden LJ, Schouten FJM, Drijvers JJ, de Groot LC, Boekholt HA, Hautvast JG. 1994b. No substantial reduction of the thermic effect of a meal during pregnancy in well-nourished Dutch women. *Br J Nutr* 71:335–344.
- Sparks JW, Girard JR, Battaglia FC. 1980. An estimate of the caloric requirements of the human fetus. *Biol Neonate* 38:113–119.
- Stampfer MJ, Maclure KM, Colditz GA, Manson JE, Willett WC. 1992. Risk of symptomatic gallstones in women with severe obesity. *Am J Clin Nutr* 55:652–658.
- Stevens J, Cai J, Pamuk ER, Williamson DF, Thun MJ, Wood JL. 1998. The effect of age on the association between body-mass index and mortality. *N Engl J Med* 338:1–7.
- Stubbs RJ, Harbron CG, Murgatroyd PR, Prentice AM. 1995. Covert manipulation of dietary fat and energy density: Effect on substrate flux and food intake in men eating ad libitum. *Am J Clin Nutr* 62:316–329.
- Stunkard AJ, Berkowitz RI, Stallings VA, Schoeller DA. 1999. Energy intake, not energy output, is a determinant of body size in infants. *Am J Clin Nutr* 69:524–530.
- Sun M, Gower BA, Nagy TR, Trowbridge CA, Dezenberg C, Goran MI. 1998. Total, resting, and activity-related energy expenditures are similar in Caucasian and African-American children. *Am J Physiol* 274:E232–E237.

- Sun SS, Chumlea WC, Heymsfield SB, Lukaski HC, Schoeller D, Friedl K, Kuczmarski RJ, Flegal KM, Johnson CL, Hubbard VS. 2003. Development of bioelectrical impedance analysis prediction equations for body composition with the use of a multicomponent model for use in epidemiologic surveys. *Am J Clin Nutr* 77: 331–340.
- Sunnegårdh J, Bratteby LE, Hagman U, Samuelson G, Sjölin S. 1986. Physical activity in relation to energy intake and body fat in 8- and 13-year-old children in Sweden. *Acta Paediatr Scand* 75:955–963.
- Suominen H, Heikkinen E, Parkatti T, Frosberg S, Kiiskinen A. 1977. Effects of 'lifelong' physical training on functional aging in men. *Scand J Soc Med* 14:225–240.
- Suter PM, Schutz Y, Jequier E. 1992. The effect of ethanol on fat storage in healthy subjects. *N Engl J Med* 326:983–987.
- Suter PM, Hasler E, Vetter W. 1997. Effects of alcohol on energy metabolism and body weight regulation: Is alcohol a risk factor for obesity? *Nutr Rev* 55:157–171.
- Svendsen OL, Hassager C, Christiansen C. 1995. Age- and menopause-associated variations in body composition and fat distribution in healthy women as measured by dual-energy x-ray absorptiometry. *Metabolism* 44:369–373.
- Tanner JM. 1955. *Growth at Adolescence*. Springfield, IL: Charles C. Thomas.
- Thorne A, Wahren J. 1990. Diminished meal-induced thermogenesis in elderly man. *Clin Physiol* 10:427–437.
- Timmons BA, Araujo J, Thomas TR. 1985. Fat utilization enhanced by exercise in a cold environment. *Med Sci Sports Exerc* 17:673–678.
- Tomoyasu NJ, Toth MJ, Poehlman ET. 2000. Misreporting of total energy intake in older African Americans. *Int J Obes Relat Metab Disord* 24:20–26.
- Torun B, Davies PSW, Livingstone MBE, Paolisso M, Sackett R, Spurr GB. 1996. Energy requirements and dietary energy recommendations for children and adolescents 1 to 18 years old. *Eur J Clin Nutr* 50:S37–S81.
- Tounian P, Girardet J, Carlier L, Frelut ML, Veinberg F, Fontaine JL. 1993. Resting energy expenditure and food-induced thermogenesis in obese children. *J Pediatr Gastroenterol Nutr* 16:451–457.
- Tremblay A, Nadeau A, Fournier G, Bouchard C. 1988. Effect of a three-day interruption of exercise-training on resting metabolic rate and glucose-induced thermogenesis in training individuals. *Int J Obes* 12:163–168.
- Tremblay A, Nadeau A, Després JP, St-Jean L, Theriault G, Bouchard C. 1990. Long-term exercise training with constant energy intake. 2: Effect on glucose metabolism and resting energy expenditure. *Int J Obes* 14:75–84.
- Treuth MS, Adolph AL, Butte NF. 1998a. Energy expenditure in children predicted from heart rate and activity calibrated against respiration calorimetry. *Am J Physiol* 275:E12–E18.
- Treuth MS, Hunter GR, Pichon C, Figueroa-Colon R, Goran MI. 1998b. Fitness and energy expenditure after strength training in obese prepubertal girls. *Med Sci Sports Exerc* 30:1130–1136.
- Treuth MS, Butte NF, Wong W. 2000. Effects of familial predisposition to obesity on energy expenditure in multiethnic prepubertal girls. *Am J Clin Nutr* 71:893–900.
- Troiano RP, Flegal KM, Kuczmarski RJ, Campbell SM, Johnson CL. 1995. Overweight prevalence and trends for children and adolescents. The National Health and Nutrition Examination Surveys, 1963 to 1991. *Arch Pediatr Adolesc Med* 149:1085–1091.

- Troiano RP, Frongillo EA, Sobal J, Levitsky DA. 1996. The relationship between body weight and mortality: A quantitative analysis of combined information from existing studies. *Int J Obes Relat Metab Disord* 20:63–75.
- Trowbridge CA, Gower BA, Nagy TR, Hunter GR, Treuth MS, Goran MI. 1997. Maximal aerobic capacity in African-American and Caucasian prepubertal children. *Am J Physiol* 273:E809–E814.
- Tuttle WW, Horvath SM, Presson LF, Daum K. 1953. Specific dynamic action of protein in men past 60 years of age. *J Appl Physiol* 5:631–634.
- Twisk JWR. 2001. Physical activity guidelines for children and adolescents. A critical review. *Sports Med* 31:617–627.
- Tzankoff SP, Norris AH. 1977. Effect of muscle mass decrease on age-related BMR changes. *J Appl Physiol* 43:1001–1006.
- USDA/HHS (U.S. Department of Agriculture/U.S. Department of Health and Human Services). 2000. *Nutrition and Your Health: Dietary Guidelines for Americans*. Home and Garden Bulletin No. 232. Washington, DC: U.S. Government Printing Office.
- Valencia ME, McNeill G, Brockway JM, Smith JS. 1992. The effect of environmental temperature and humidity on 24 h energy expenditure in men. *Br J Nutr* 68:319–327.
- Valve R, Heikkinen S, Rissanen A, Laakso M, Uusitupa M. 1998. Synergistic effect of polymorphisms in uncoupling protein 1 and  $\beta_3$ -adrenergic receptor genes on basal metabolic rate in obese Finns. *Diabetologia* 41:357–361.
- van Baak MA. 1999. Physical activity and energy balance. *Public Health Nutr* 2:335–339.
- Van Etten LM, Westerterp KR, Verstappen FT, Boon BJ, Saris WH. 1997. Effect of an 18-wk weight-training program on energy expenditure and physical activity. *J Appl Physiol* 82:298–304.
- van Gemert WG, Westerterp KR, van Acker BA, Wagenmakers AJ, Halliday D, Greve JM, Soeters PB. 2000. Energy, substrate and protein metabolism in morbid obesity before, during and after massive weight loss. *Int J Obes Relat Metab Disord* 24:711–718.
- van Raaij JMA, Vermaat-Miedema SH, Schonk CM, Peek ME, Hautvast JG. 1987. Energy requirements of pregnancy in the Netherlands. *Lancet* 2:953–955.
- van Raaij JMA, Peek ME, Vermaat-Miedema SH, Schonk CM, Hautvast JG. 1988. New equations for estimating body fat mass in pregnancy from body density or total body water. *Am J Clin Nutr* 48:24–29.
- van Raaij JMA, Schonk CM, Vermaat-Miedema SH, Peek ME, Hautvast JG. 1989. Body fat mass and basal metabolic rate in Dutch women before, during, and after pregnancy: A reappraisal of energy cost of pregnancy. *Am J Clin Nutr* 49:765–772.
- van Raaij JMA, Schonk CM, Vermaat-Miedema SH, Peek ME, Hautvast JG. 1990. Energy cost of physical activity throughout pregnancy and the first year postpartum in Dutch women with sedentary lifestyles. *Am J Clin Nutr* 52:234–239.
- van Raaij JMA, Schonk CM, Vermaat-Miedema SH, Peek ME, Hautvast JG. 1991. Energy cost of lactation, and energy balances of well-nourished Dutch lactating women: Reappraisal of the extra energy requirements of lactation. *Am J Clin Nutr* 53:612–619.
- van Staveren WA, Deurenberg P, Burema J, de Groot LC, Hautvast JG. 1986. Seasonal variation in food intake, pattern of physical activity and change in body weight in a group of young adult Dutch women consuming self-selected diets. *Int J Obes* 10:133–145.

- Vaughan L, Zurlo F, Ravussin E. 1991. Aging and energy expenditure. *Am J Clin Nutr* 53:821–825.
- Visser M, Deurenberg P, van Staveren WA, Hautvast JG. 1995. Resting metabolic rate and diet-induced thermogenesis in young and elderly subjects: Relationship with body composition, fat distribution, and physical activity level. *Am J Clin Nutr* 61:772–778.
- Walker SP, Rimm EB, Ascherio A, Kawachi I, Stampfer MJ, Willett WC. 1996. Body size and fat distribution as predictors of stroke among US men. *Am J Epidemiol* 144:1143–1150.
- Walravens PA, Krebs NF, Hambidge KM. 1983. Linear growth of low income preschool children receiving a zinc supplement. *Am J Clin Nutr* 38:195–201.
- Warren MP, Brooks-Gunn J, Hamilton LH, Warren LF, Hamilton WG. 1986. Scoliosis and fractures in young ballet dancers. Relation to delayed menarche and secondary amenorrhea. *N Engl J Med* 314:1348–1353.
- Warwick PM, Busby R. 1990. Influence of mild cold on 24 h energy expenditure in "normally" clothed adults. *Br J Nutr* 63:481–488.
- Washburn RA, Kline G, Lackland DT, Wheeler FC. 1992. Leisure time physical activity: Are there black/white differences? *Prev Med* 21:127–135.
- Waterlow JC. 1999. The nature and significance of nutritional adaptation. *Eur J Clin Nutr* 53:S2–S5.
- Waterlow JC, James WPT, Healy MJR. 1989. Nutritional adaptation and variability. *Eur J Clin Nutr* 43:203–210.
- Webb P. 1981. Energy expenditure and fat-free mass in men and women. *Am J Clin Nutr* 34:1816–1826.
- Webber J, Macdonald IA. 2000. Signalling in body-weight homeostasis: Neuroendocrine efferent signals. *Proc Nutr Soc* 59:397–404.
- Webber LS, Cresanta JL, Voors AW, Berenson GS. 1983. Tracking of cardiovascular disease risk factor variables in school-age children. *J Chron Dis* 36:647–660.
- Weinsier RL, Schutz Y, Bracco D. 1992. Reexamination of the relationship of resting metabolic rate to fat-free mass and to the metabolically active components of fat-free mass in humans. *Am J Clin Nutr* 55:790–794.
- Weinsier RL, Hunter GR, Heini AF, Goran MI, Sell SM. 1998. The etiology of obesity: Relative contribution of metabolic factors, diet, and physical activity. *Am J Med* 105:145–150.
- Weinsier RL, Nagy TR, Hunter GR, Darnell BE, Hensrud DD, Weiss HL. 2000. Do adaptive changes in metabolic rate favor weight regain in weight-reduced individuals? An examination of the set-point theory. *Am J Clin Nutr* 72:1088–1094.
- Wells JC, Davies PS. 1995. The effect of diet and sex on sleeping metabolic rate in 12-week old infants. *Eur J Clin Nutr* 49:329–335.
- Wells JC, Cole TJ, Davies PS. 1996. Total energy expenditure and body composition in early infancy. *Arch Dis Child* 75:423–426.
- Westerterp KR, Brouns F, Saris WHM, ten Hoor F. 1988. Comparison of doubly labeled water with respirometry at low and high activity levels. *J Appl Physiol* 65:53–56.
- Westerterp KR, Lafeber HN, Sulkers EJ, Sauer PJ. 1991. Comparison of short term indirect calorimetry and doubly labeled water method for the assessment of energy expenditure in preterm infants. *Biol Neonate* 60:75–82.
- Westerterp KR, Meijer GA, Janssen EM, Saris WH, ten Hoor F. 1992. Long-term effect of physical activity on energy balance and body composition. *Br J Nutr* 68:21–30.

- Westlund K, Nicolaysen R. 1972. Ten-year mortality and morbidity related to serum cholesterol. A follow-up of 3,751 men aged 40–49. *Scand J Clin Lab Invest* 30:1–24.
- Weyer C, Snitker S, Bogardus C, Ravussin E. 1999a. Energy metabolism in African Americans: Potential risk factors for obesity. *Am J Clin Nutr* 70:13–20.
- Weyer C, Snitker S, Rising R, Bogardus C, Ravussin E. 1999b. Determinants of energy expenditure and fuel utilization in man: Effects of body composition, age, sex, ethnicity and glucose tolerance in 916 subjects. *Int J Obes Relat Metab Disord* 23:715–722.
- Whitehead RG, Paul AA, Cole TJ. 1981. A critical analysis of measured food energy intakes during infancy and early childhood in comparison with current international recommendations. *J Hum Nutr* 35:339–348.
- WHO (World Health Organization). 1998. *Obesity: Preventing and Managing the Global Epidemic. Report of a World Health Organization Consultation on Obesity*. Geneva: WHO.
- WHO Working Group. 1986. Use and interpretation of anthropometric indicators of nutritional status. *Bull World Health Organ* 64:929–941.
- Widdowson EM. 1974. Nutrition. In: Davis JA, Dobbing J, eds. *Scientific Foundations of Paediatrics*. London: William Heinemann Medical Books. Pp. 44–55.
- Willett WC, Manson JE, Stampfer MJ, Colditz GA, Rosner B, Speizer FE, Hennekens CH. 1995. Weight, weight change, and coronary heart disease in women. Risk within the ‘normal’ weight range. *J Am Med Assoc* 273:461–465.
- Willett WC, Dietz WH, Colditz GA. 1999. Guidelines for healthy weight. *N Engl J Med* 341:427–434.
- Wing RR, Marcus MD, Salata R, Epstein LH, Miaskiewicz S, Blair EH. 1991. Effects of a very-low-calorie diet on long-term glycemic control in obese Type 2 diabetic subjects. *Arch Intern Med* 151:1334–1340.
- Withers RT, Smith DA, Tucker RC, Brinkman M, Clark DG. 1998. Energy metabolism in sedentary and active 49- to 70-yr-old women. *J Appl Physiol* 84:1333–1340.
- Wong WW. 1994. Energy expenditure of female adolescents. *J Am Coll Nutr* 13:332–337.
- Wong WW, Butte NF, Ellis KJ, Hergenroeder AC, Hill RB, Stuff JE, Smith E. 1999. Pubertal African-American girls expend less energy at rest and during physical activity than Caucasian girls. *J Clin Endocrinol Metab* 84:906–911.
- Wood PD, Stefanick ML, Dreon DM, Frey-Hewitt B, Garay SC, William PT, Superko HR, Fortmann SP, Albers JJ, Vranizan KM, et al. 1988. Changes in plasma lipids and lipoproteins in overweight men during weight loss through dieting as compared with exercise. *N Engl J Med* 319(18):1173–1179.
- Wood PD, Stefanick ML, Williams PT, Haskell WL. 1991. The effects on plasma lipoproteins of a prudent weight-reducing diet, with or without exercise, in overweight men and women. *N Engl J Med* 325:461–466.
- Yanovski SZ, Reynolds JC, Boyle AJ, Yanovski JA. 1997. Resting metabolic rate in African-American and Caucasian girls. *Obes Res* 5:321–325.
- Zinker BA, Wilson RD, Wasserman DH. 1995. Interaction of decreased arterial PO<sub>2</sub> and exercise on carbohydrate metabolism in the dog. *Am J Physiol* 269:E409–E417.
- Zlotkin SH. 1996. A review of the Canadian “Nutrition Recommendations Update: Dietary Fat and Children.” *J Nutr* 126:1022S–1027S.
- Zurlo F, Ferraro RT, Fontvieille AM, Rising R, Bogardus C, Ravussin E. 1992. Spontaneous physical activity and obesity: Cross-sectional and longitudinal studies in Pima Indians. *Am J Physiol* 263:E296–E300.

## Ibid., Chapter 13, pp. 965–967.

- Bandini LG, Vu D, Must A, Cyr H, Goldberg A, Dietz WH. 1999. Comparison of high-calorie, low-nutrient-dense food consumption among obese and non-obese adolescents. *Obes Res* 7:438–443.
- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Black AE, Prentice AM, Goldberg GR, Jebb SA, Bingham SA, Livingstone MBE, Coward WA. 1993. Measurements of total energy expenditure provide insights into the validity of dietary measurements of energy intake. *J Am Diet Assoc* 93:572–579.
- Blair SN, Kohl HW, Barlow CE. 1993. Physical activity, physical fitness, and all-cause mortality in women: Do women need to be active? *J Am Coll Nutr* 12:368–371.
- Blair SN, Kohl HW, Barlow CE, Paffenbarger RS, Gibbons LW, Macera CA. 1995. Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. *J Am Med Assoc* 273:1093–1098.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Nutrition Examination Survey: Underreporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Carroll RJ, Freedman LS, Hartman AM. 1996. Use of semiquantitative food frequency questionnaires to estimate the distribution of usual intake. *Am J Epidemiol* 143:392–404.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- IOM. 2001. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Washington, DC: National Academy Press.
- Johnson RK, Goran MI, Poehlman ET. 1994. Correlates of over- and under-reporting of energy intake in healthy older men and women. *Am J Clin Nutr* 59:1286–1290.
- Johnson RK, Soultanakis RP, Matthews DE. 1998. Literacy and body fatness are associated with underreporting of energy intake in US low-income women using the multiple-pass 24-hour recall: A doubly labeled water study. *J Am Diet Assoc* 98:1136–1140.
- Kristal AR, Feng Z, Coates RJ, Oberman A, George V. 1997. Associations of race/ethnicity, education, and dietary intervention with the validity and reliability of a food frequency questionnaire: The Women's Health Trial Feasibility Study in Minority Populations. *Am J Epidemiol* 146:856–869.
- Lichtman SW, Pisarska K, Berman ER, Pestone M, Dowling H, Offenbacher E, Weisel H, Heshka S, Matthews DE, Heymsfield SB. 1992. Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. *N Engl J Med* 327:1893–1898.
- Liu K. 1994. Statistical issues related to semiquantitative food-frequency questionnaires. *Am J Clin Nutr* 59:262S–265S.

- Livingstone MB, Prentice AM, Coward WA, Strain JJ, Black AE, Davies PS, Stewart CM, McKenna PG, Whitehead RG. 1992. Validation of estimates of energy intake by weighed dietary record and diet history in children and adolescents. *Am J Clin Nutr* 56:29–35.
- Marlett JA, Cheung TF. 1997. Database and quick methods of assessing typical dietary fiber intakes using data for 228 commonly consumed foods. *J Am Diet Assoc* 97:1139–1148.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Prentice AM, Black AE, Coward WA, Davies HL, Goldberg GR, Murgatroyd PR, Ashford J, Sawyer M, Whitehead RG. 1986. High levels of energy expenditure in obese women. *Br Med J* 292:983–987.
- Pryer JA, Vrijheid M, Nichols R, Kiggins M, Elliott P. 1997. Who are the ‘low energy reporters’ in the dietary and nutritional survey of British adults? *Int J Epidemiol* 26:146–154.
- Schoeller DA. 1995. Limitations in the assessment of dietary energy by self-report. *Metabolism* 44:18–22.
- Schoeller DA, Bandini LG, Dietz WH. 1990. Inaccuracies in self-reported intake identified by comparison with the doubly labelled water method. *Can J Physiol Pharmacol* 68:941–949.
- USDA (U.S. Department of Agriculture). 2001. *USDA Nutrient Database for Standard Reference, Release 14*. Online. Nutrient Data Laboratory. Available at <http://www.nal.usda.gov/fnic/foodcomp>. Accessed April 2, 2002.
- USDA/HHS (U.S. Department of Health and Human Services). 2000. *Nutrition and Your Health: Dietary Guidelines for Americans*. Home and Garden Bulletin No. 232. Washington, DC: U.S. Government Printing Office.

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*Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* (ISBN 0-309-08537-3), Chapter 12, pp. 929–935.

- ACOG (American College of Obstetricians and Gynecologists). 1994. Exercise during pregnancy and the postpartum period. *Tech Bull* 189. Washington DC.
- ACOG (American College of Obstetricians and Gynecologists). 1995. Planning for pregnancy, birth and beyond. *Tech Bull*. Washington, DC.
- ACSM (American College of Sports Medicine). 1978. The recommended quantity and quality of exercise for developing and maintaining fitness in healthy adults. *Med Sci Sports* 10:vii–x.
- ACSM. 1980. *Guidelines for Graded Exercise Testing and Prescription*, 2nd ed. Philadelphia: Lea and Febiger.
- ACSM. 1997. Position Stand: The female athlete triad. *Med Sci Sports Exercise* 29:I-xi.
- ACSM. 2000. *ACSM's Guidelines for Exercise Testing and Prescription*, 6th ed. Philadelphia: Lippincott, Williams and Wilkins.
- ACSM, American Dietetic Association, Dietitians of Canada. 2000. Joint position statement. Nutrition and athletic performance. *Med Sci Sports Exerc* 32:2130–2145.
- AHA (American Heart Association). 1972. *Exercise Testing and Training of Apparently Healthy Individuals: A Handbook for Physicians*. New York: AHA.
- Anthony J. 1991. Psychologic aspects of exercise. *Clin Sports Med* 10:171–180.
- Bahr R, Ingnes I, Vaage O, Sejersted OM, Newsholme EA. 1987. Effect of duration of exercise on excess postexercise  $O_2$  consumption. *J Appl Physiol* 62:485–490.
- Barr SI. 1999. Effects of dehydration on exercise performance. *Can J Appl Physiol* 24:164–172.
- Benedict FG, Cathcart EP. 1913. *Muscular Work: A Metabolic Study with Special Reference to the Efficiency of the Human Body as a Machine*. Publication No. 187. Washington, DC: Carnegie Institution of Washington.
- Bengtsson B-Å, Brummer R-J, Bosaeus I. 1990. Growth hormone and body composition. *Horm Res* 33:19–24.
- Bergman B, Brooks GA. 1999. Respiratory gas-exchange ratios during graded exercise in fed and fasted trained and untrained men. *J Appl Physiol* 86:479–487.
- Bijnen FCH, Caspersen CJ, Feskens EJM, Saris WHM, Mosterd WL, Kromhout D. 1998. Physical activity and 10-year mortality from cardiovascular diseases and all causes: The Zutphen Elderly Study. *Arch Intern Med* 158:1499–1505.
- Blaak EE, Westerterp KR, Bar-Or R, Wouters LJM, Saris WHM. 1992. Total energy expenditure and spontaneous activity in relation to training in obese boys. *Am J Clin Nutr* 55:777–782.
- Blair SN, Kohl HW, Barlow CE. 1993. Physical activity, physical fitness, and all-cause mortality in women: Do women need to be active? *J Am Coll Nutr* 12:368–371.
- Blair SN, Kohl HW, Barlow CE, Paffenbarger RS, Gibbons LW, Macera CA. 1995. Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. *J Am Med Assoc* 273:1093–1098.
- Blundell JE, King NA. 1998. Effects of exercise on appetite control: Loose coupling between energy expenditure and energy intake. *Int J Obes Relat Metab Disord* 22:S22–S29.
- Borer KT. 1995. The effects of exercise on growth. *Sports Med* 26:375–397.

- Bouchard C, Shephard RJ, Stephens T. 1994. *Physical Activity, Fitness, and Health: International Proceedings and Consensus Statement*. Champaign, IL: Human Kinetics.
- Brooks GA. 1987. Amino acid and protein metabolism during exercise and recovery. *Med Sci Sports Exerc* 19:S150–S156.
- Brooks GA. 1997. Importance of the ‘crossover’ concept in exercise metabolism. *Clin Exp Pharmacol Physiol* 24:889–895.
- Brooks GA, Mercier J. 1994. Balance of carbohydrate and lipid utilization during exercise: The ‘crossover’ concept. *J Appl Physiol* 76:2253–2261.
- Brooks GA, Fahey TD, White TP, Baldwin KM. 2000. *Exercise Physiology: Human Bioenergetics and Its Applications*, 3rd ed. Mountain View, CA: Mayfield Publishing.
- Brown CH, Harrower JR, Deeter MF. 1972. The effects of cross-country running on pre-adolescent girls. *Med Sci Sports* 4:1–5.
- Campbell SE, Angus DJ, Febbraio MA. 2001. Glucose kinetics and exercise performance during phases of the menstrual cycle: Effect of glucose ingestion. *Am J Physiol* 281:E817–E825.
- CDC (Centers for Disease Control and Prevention). 2000. Youth risk behavior surveillance—United States, 1999. *Mor Mortal Wkly Rep CDC Surveill Summ* 49(SS-5):1–96.
- Chad KE, Quigley BM. 1991. Exercise intensity: Effect on postexercise O<sub>2</sub> uptake in trained and untrained women. *J Appl Physiol* 70:1713–1719.
- Chaouloff F. 1997. The serotonin hypothesis. In: Morgan WP, ed. *Physical Activity and Mental Health*. Washington, DC: Taylor and Francis. Pp. 179–198.
- Colditz GA, Coakley E. 1997. Weight, weight gain, activity, and major illnesses: The Nurses’ Health Study. *Int J Sports Med* 18:S162–S170.
- Craft LL, Landers DM. 1998. The effect of exercise on clinical depression and depression resulting from mental illness: A meta-analysis. *J Sport Exerc Psychol* 20:339–357.
- Dela F, Mikines KJ, Von Linstow M, Galbo H. 1991. Twenty-four-hour profile of plasma glucose and glucoregulatory hormones during normal living conditions in trained and untrained men. *J Clin Endocrinol Metab* 73:982–989.
- DHEW (U.S. Department of Health, Education, and Welfare). 1979. *Healthy People: The Surgeon General’s Report on Health Promotion and Disease Prevention*. DHEW (PHS) Publication No. 79-55071. Rockville, MD: Public Health Service.
- Dishman RK. 1997. The norepinephrine hypothesis. In: Morgan WP, ed. *Physical Activity and Mental Health*. Washington, DC: Taylor and Francis. Pp. 199–212.
- Eliakim A, Burke GS, Cooper DM. 1997. Fitness, fatness, and the effect of training assessed by magnetic resonance imaging and skinfold-thickness measurements in healthy adolescent females. *Am J Clin Nutr* 66:223–231.
- Epstein LH, Wing RR. 1980. Aerobic exercise and weight. *Addict Behav* 5:371–388.
- Evans WJ. 1999. Exercise training guidelines for the elderly. *Med Sci Sports Exerc* 31:12–17.
- Fletcher GF, Balady GJ, Amsterdam EA, Chaitman B, Eckel R, Fleg J, Froelicher VF, Leon AS, Piña IL, Rodney R, Simons-Morton DG, Williams MA, Bazzarre T. 2001. Exercise standards for testing and training. A statement for healthcare professionals from the American Heart Association. *Circulation* 104:1694–1740.
- Friedlander AL, Casazza GA, Horning MA, Buddinger TF, Brooks GA. 1998a. Effects of exercise intensity and training on lipid metabolism in young women. *Am J Physiol* 275:E853–E863.
- Friedlander AL, Casazza GA, Horning MA, Huie MJ, Piacentini MF, Trimmer JK, Brooks GA. 1998b. Training-induced alterations of carbohydrate metabolism in women: Women respond differently from men. *J Appl Physiol* 85:1175–1186.

- Friedlander AL, Casazza GA, Horning MA, Usaj A, Brooks GA. 1999. Endurance training increases fatty acid turnover, but not fat oxidation, in young men. *J Appl Physiol* 86:2097–2105.
- Fuchs RK, Bauer JJ, Snow CM. 2001. Jumping improves hip and lumbar spine bone mass in prepubescent children: A randomized controlled trial. *J Bone Miner Res* 16:148–156.
- Gaesser GA, Brooks GA. 1984. Metabolic bases of excess post-exercise oxygen consumption: A review. *Med Sci Sports Exerc* 16:29–43.
- Gallo L, Maciel BC, Marin-Neto JA, Martins LEB. 1989. Sympathetic and parasympathetic changes in heart rate control during dynamic exercise induced by endurance training in man. *Braz J Med Biol Res* 22:631–643.
- Graham TE, Adamo KB. 1999. Dietary carbohydrate and its effects on metabolism and substrate stores in sedentary and active individuals. *Can J Appl Physiol* 24:393–415.
- Greenleaf JE, Kozlowski S. 1982. Physiological consequences of reduced physical activity during bed rest. *Exerc Sport Sci Rev* 10:84–119.
- Grund A, Krause H, Kraus M, Siewers M, Rieckert H, Müller MJ. 2001. Association between different attributes of physical activity and fat mass in untrained, endurance- and resistance-trained men. *Eur J Appl Physiol* 84:310–320.
- Hagberg JM, Graves JE, Limacher M, Woods DR, Leggett SH, Cononie C, Gruber JJ, Pollock ML. 1989. Cardiovascular responses of 70- to 79-yr-old men and women to exercise training. *J Appl Physiol* 66:2589–2594.
- Hagerman FC, Walsh SJ, Staron RS, Hikida RS, Gilders RM, Murray TF, Toma K, Ragg KE. 2000. Effects of high-intensity resistance training on untrained older men. I. Strength, cardiovascular, and metabolic responses. *J Gerontol A Biol Sci Med Sci* 55:B336–B346.
- Haapanen N, Mielunpaio S, Vuori I, Oja P, Pasanen M. 1996. Characteristics of leisure time physical activity associated with decreased risk of premature all-cause and cardiovascular disease mortality in middle-aged men. *Am J Epidemiol* 143:870–880.
- Health Canada. 1998. *Canada's Physical Activity Guide to Healthy Active Living*. Ottawa, Canada: Health Canada, Canadian Society for Exercise Physiology.
- Helmrich SP, Ragland DR, Leung RW, Paffenbarger RS. 1991. Physical activity and reduced occurrence of non-insulin-dependent diabetes mellitus. *N Engl J Med* 325:147–152.
- HHS (U.S. Department of Health and Human Services). 1988. *The Surgeon General's Report on Nutrition and Health*. HHS (PHS) Publication No. 88-50210. Washington, DC: Public Health Service.
- HHS. 1995. *Healthy People 2000: Midcourse Review and 1995 Revisions*. Washington, DC: Public Health Service.
- HHS. 1996. *Physical Activity and Health: A Report of the Surgeon General*. Atlanta, GA: Centers for Disease Control and Prevention.
- HHS. 2000. *Healthy People 2010: Understanding and Improving Health*, 2nd ed. Washington, DC: U.S. Department of Health and Human Services.
- Hoffman P. 1997. The endorphin hypothesis. In: Morgan WP, ed. *Physical Activity and Mental Health*. Washington, DC: Taylor and Francis. Pp. 163–177.
- Hubert P, King NA, Blundell JE. 1998. Uncoupling the effects of energy expenditure and energy intake: Appetite response to short-term energy deficit induced by meal omission and physical activity. *Appetite* 31:9–19.
- Kiens B, Richter EA. 1998. Utilization of skeletal muscle triacylglycerol during postexercise recovery in humans. *Am J Physiol* 275:E332–E337.

- Kimm SYS, Glynn NW, Kriska AM, Barton BA, Kronsberg SS, Daniels SR, Crawford PB, Sabry ZI, Liu K. 2002. Decline in physical activity in black girls and white girls during adolescence. *N Engl J Med* 347:709-715.
- King DS, Dalsky GP, Staten MA, Clutter WE, Van Houten DR, Holloszy JO. 1987. Insulin action and secretion in endurance-trained and untrained humans. *J Appl Physiol* 63:2247-2252.
- King NA, Lluch A, Stubbs RJ, Blundell JE. 1997. High dose exercise does not increase hunger or energy intake in free living males. *Eur J Clin Nutr* 51: 478-483.
- Kohl HW, Powell KE, Gordon NF, Blair SN, Paffenbarger RS. 1992. Physical activity, physical fitness, and sudden cardiac death. *Epidemiol Rev* 14:37-58.
- Koplan JP. 1979. Cardiovascular deaths while running. *J Am Med Assoc* 242:2578-2579.
- Krahenbuhl GS, Williams TJ. 1992. Running economy: Changes with age during childhood and adolescence. *Med Sci Sports Exerc* 24:462-466.
- Kraus H, Hirschland RP. 1953. Muscular fitness and health. *J Health Phys Ed Rec* 24:17-19.
- Kraus WE, Houmard JA, Duscha BD, Knetzger KJ, Wharton MB, McCartney JS, Bales CW, Henes S, Samsa GP, Otvos JD, Kulkarni KR, Slentz CA. 2002. Effects of the amount and intensity of exercise on plasma lipoproteins. *N Engl J Med* 347:1483-1492.
- Landers DM, Arent SM. 2001. Physical activity and mental health. In: Singer RN, Hausenblas HA, Janelle CM, eds. *Handbook of Sport Psychology*, 2nd ed. New York: John Wiley and Sons. Pp. 740-765.
- Leon AS, Connett J, Jacobs DR, Rauramaa R. 1987. Leisure-time physical activity levels and risk of coronary heart disease and death. *JAMA* 258:2388-2395.
- Loucks AB, Verdun M, Heath EM. 1998. Low energy availability, not stress of exercise, alters LH pulsatility in exercising women. *J Appl Physiol* 84:37-46.
- Maciel BC, Gallo L, Marin-Neto JA, Lima-Filho EC, Terra-Filho J, Manco JC. 1985. Parasympathetic contribution to bradycardia induced by endurance training in man. *Cardiovasc Res* 19:642-648.
- Mahon AD, Vaccaro P. 1989. Ventilatory threshold and  $\text{Vo}_2\text{max}$  changes in children following endurance training. *Med Sci Sports Exerc* 21:425-431.
- Mahon AD, Vaccaro P. 1994. Cardiovascular adaptations in 8- to 12-year-old boys following a 14-week running program. *Can J Appl Physiol* 19:139-150.
- Manson JE, Greenland P, LaCroix AZ, Stefanick ML, Moutton CP, Oberman A, Perri MG, Sheps DS, Pettinger MB, Siscovick DS. 2002. Walking compared with vigorous exercise for the prevention of cardiovascular events in women. *N Engl J Med* 347:716-725.
- Mayer J, Marshall NB, Vitale JJ, Christensen JH, Mashayekhi MB, Stare FJ. 1954. Exercise, food intake and body weight in normal rats and genetically obese adult mice. *Am J Physiol* 177:544-548.
- Mayer J, Roy P, Mitra KP. 1956. Relation between caloric intake, body weight, and physical work: Studies in an industrial male population in West Bengal. *Am J Clin Nutr* 4:169-175.
- Mittleman MA, MacLure M, Tofler GH, Sherwood JB, Goldberg RJ, Muller JE. 1993. Triggering of acute myocardial infarction by heavy physical exertion. Protection against triggering by regular exertion. *N Engl J Med* 329:1677-1683.
- Mottola MF, Wolfe LA. 2000. The pregnant athlete. In: Drinkwater BL, ed. *Women in Sport*. Oxford: Backwell Science. Pp. 194-207.

- Mutrie N. 2000. The relationship between physical activity and clinically defined depression. In: Biddle JH, Fox KR, Boutcher SH, eds. *Physical Activity and Psychological Well-Being*. London: Routledge. Pp. 46–62.
- Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. 2002. Exercise capacity and mortality among men referred for exercise testing. *N Engl J Med* 346:793–801.
- Naghii MR. 2000. The significance of water in sport and weight control. *Nutr Health* 14:127–132.
- North TC, McCullagh P, Tran ZV. 1990. Effect of exercise on depression. *Exerc Sport Sci Rev* 18:379–415.
- Owens S, Gutin B, Allison J. 1999. Effect of physical training on total and visceral fat in obese children. *Med Sci Sports Exerc* 31:143–148.
- Paffenbarger RS, Wing AL, Hyde RT. 1978. Chronic disease in former college students. XVI. Physical activity as an index of heart attack risk in college alumni. *Am J Epidemiol* 108:161–175.
- Paffenbarger RS, Hyde RT, Wing AL, Hsieh CC. 1986. Physical activity, all-cause mortality, longevity of college alumni. *N Engl J Med* 314:605–613.
- Paffenbarger RS, Hyde RT, Wing AL, Lee I-M, Jung DL, Kampert JB. 1993. The association of changes in physical-activity level and other lifestyle characteristics with mortality among men. *N Engl J Med* 328:538–545.
- Paffenbarger RS, Kampert JB, Lee I-M, Hyde RT, Leung RW, Wing AL. 1994. Changes in physical activity and other lifeway patterns influencing longevity. *Med Sci Sports Exerc* 26:857–865.
- Paluska SA, Schwenk TL. 2000. Physical activity and mental health. Current concepts. *Sports Med* 29:167–180.
- Poehlman ET, Toth MJ, Gardner AW. 1995. Changes in energy balance and body composition at menopause: A controlled longitudinal study. *Ann Intern Med* 123:673–675.
- Puyau MR, Adolph AL, Vohra FA, Butte NF. 2002. Validation and calibration of physical activity monitors in children. *Obes Res* 10:150–157.
- Raven PB, Mitchell J. 1980. The effect of aging on the cardiovascular response to dynamic and static exercise. In: Weisfeldt ML, ed. *The Aging Heart: Its Function and Response to Stress*. New York: Raven Press. Pp. 269–296.
- Ravussin E, Lillioja S, Anderson TE, Christin L, Bogardus C. 1986. Determinants of 24-hour energy expenditure in man. Methods and results using a respiratory chamber. *J Clin Invest* 78:1568–1578.
- Rockhill B, Willett WC, Manson JE, Leitzmann MF, Stampfer MJ, Hunter DJ, Colditz GA. 2001. Physical activity and mortality: a prospective study among women. *Am J Pub Health* 91:578–583.
- Rooney BL, Schauberger, CW. 2002. Excess pregnancy weight gain and long-term obesity: One decade later. *Obstet and Gynecol* 100: 245–252.
- Salmon P. 2001. Effects of physical exercise on anxiety, depression, and sensitivity to stress: A unifying theory. *Clin Psychol Rev* 21:33–61.
- Sandvik L, Eriksson J, Thaulow E, Eriksson G, Mundal R, Rodahl K. 1993. Physical fitness as a predictor of mortality among healthy, middle-aged Norwegian men. *N Engl J Med* 328:533–537.
- Schwartz RS, Shuman WP, Larson V, Cain KC, Fellingham GW, Beard JC, Kahn SE, Stratton JR, Cerqueira MD, Abrass IB. 1991. The effect of intensive endurance exercise training on body fat distribution in young and older men. *Metabolism* 40:545–551.

- Sial S, Coggan AR, Carroll R, Goodwin J, Klein S. 1996. Fat and carbohydrate metabolism during exercise in elderly and young subjects. *Am J Physiol* 271:E983–E989.
- Siscovick DS, Weiss NS, Fletcher RH, Lasky T. 1984. The incidence of primary cardiac arrest during vigorous exercise. *N Engl J Med* 311:874–877.
- Slattery ML, Jacobs DR, Nichman MZ. 1989. Leisure time physical activity and coronary heart disease death. The US Railroad Study. *Circulation* 79:304–311.
- Suh SH, Casazza GA, Horning MA, Miller BF, Brooks GA. 2002. Luteal and follicular glucose fluxes during rest and exercise in 3-h postabsorptive women. *J Appl Physiol* 93:42–50.
- Suominen H, Heikkinen E, Parkatti T, Forsberg S, Kiiskinen A. 1977. Effects of “lifelong” physical training on functional aging in men. *Scand J Soc Med Suppl* 14:225–240.
- Tabata I, Nishimura K, Kouzaki M, Hirai Y, Ogita F, Miyachi M, Yamamoto K. 1996. Effects of moderate-intensity endurance and high-intensity intermittent training on anaerobic capacity and  $\dot{V}O_{2\text{max}}$ . *Med Sci Sports Exerc* 28:1327–1330.
- Tarnopolsky LJ, MacDougall JD, Atkinson SA, Tarnopolsky MA, Sutton JR. 1990. Gender differences in substrate for endurance exercise. *J Appl Physiol* 68:302–308.
- Thompson PD. 1982. Cardiovascular hazards of physical activity. *Exerc Sport Sci Rev* 10:208–235.
- Thrash LE, Anderson JJB. 2000. The female athlete triad: Nutrition, menstrual disturbances, and low bone mass. *Nutr Today* 35:168–174.
- Torun B. 1990. Energy cost of various physical activities in healthy children. In: Schurch B, Scrimshaw NS, eds. *Activity, Energy Expenditure and Energy Requirements of Infants and Children*. Switzerland: IDECG. Pp. 139–183.
- Treuth MS, Adolph AL, Butte NF. 1998. Energy expenditure in children predicted from heart rate and activity calibrated against respiration calorimetry. *Am J Physiol* 275:E12–E18.
- Treuth MS, Butte NF, Puyau M, Adolph A. 2000. Relations of parental obesity status to physical activity and fitness of prepubertal girls. *Pediatrics* 106:e49.
- Treuth MS, Sunehag AL, Trautwein LM, Bier DM, Haymond MW, Butte NF. (2003). Metabolic adaptation to high-fat and high-carbohydrate diets in children. *Am J Clin Nutr* 77:479–489.
- USDA/HHS (U.S. Department of Agriculture/Department of Health and Human Services). 1990. *Nutrition and Your Health: Dietary Guidelines for Americans*, 3rd ed. Home and Garden Bulletin No. 232. Washington, DC: U.S. Government Printing Office.
- USDA/HHS. 1995. *Nutrition and Your Health: Dietary Guidelines for Americans*, 4th ed. Home and Garden Bulletin No. 232. Washington, DC: U.S. Government Printing Office.
- USDA/HHS. 2000. *Nutrition and Your Health: Dietary Guidelines for Americans*, 5th ed. Home and Garden Bulletin No. 232. Washington, DC: U.S. Government Printing Office.
- Vaccaro P, Clarke DH. 1978. Cardiorespiratory alterations in 9 to 11 year old children following a season of competitive swimming. *Med Sci Sports* 10:204–207.
- van Dale D, Schoffelen PFM, ten Hoor F, Saris WHM. 1989. Effects of addition of exercise to energy restriction on 24-hour energy expenditure, sleeping metabolic rate and daily physical activity. *Eur J Clin Nutr* 43:441–451.
- Van Zant RS. 1992. Influence of diet and exercise on energy expenditure—A review. *Int J Sport Nutr* 2:1–19.

- Wei M, Macera CA, Hornung CA, Blair SN. 1997. Changes in lipids associated with change in regular exercise in free-living men. *J Clin Epidemiol* 50:1137–1142.
- Welten DC, Kemper HCG, Post GB, Van Mechelen W, Twisk J, Lips P, Teule GJ. 1994. Weight-bearing activity during youth is a more important factor for peak bone mass than calcium intake. *J Bone Miner Res* 9:1089–1096.
- West RV. 1998. The female athlete. The triad of disordered eating, amenorrhoea and osteoporosis. *Sports Med* 26:63–71.
- Wilbur J, Naftzger-Kang L, Miller AM, Chandler P, Montgomery A. 1999. Women's occupations, energy expenditure, and cardiovascular risk factors. *J Women's Health* 8:377–387.
- Willlich SN, Lewis M, Löwel H, Arntz H-R, Schubert F, Schröder R. 1993. Physical exertion as a trigger of acute myocardial infarction. *N Engl J Med* 329:1684–1690.
- World Health Organization (WHO). 2000. *Obesity: Preventing and Managing the Global Epidemic*. Geneva:WHO.
- Yen SSC, Vela P. 1968. Effects of contraceptive steroids on carbohydrate metabolism. *J Clin Endocrinol* 28:1564–1570.

Ibid., Chapter 13, pp. 965–967.

- Bandini LG, Vu D, Must A, Cyr H, Goldberg A, Dietz WH. 1999. Comparison of high-calorie, low-nutrient-dense food consumption among obese and non-obese adolescents. *Obes Res* 7:438–443.
- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Black AE, Prentice AM, Goldberg GR, Jebb SA, Bingham SA, Livingstone MBE, Coward WA. 1993. Measurements of total energy expenditure provide insights into the validity of dietary measurements of energy intake. *J Am Diet Assoc* 93:572–579.
- Blair SN, Kohl HW, Barlow CE. 1993. Physical activity, physical fitness, and all-cause mortality in women: Do women need to be active? *J Am Coll Nutr* 12:368–371.
- Blair SN, Kohl HW, Barlow CE, Paffenbarger RS, Gibbons LW, Macera CA. 1995. Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. *J Am Med Assoc* 273:1093–1098.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Nutrition Examination Survey: Underreporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Carroll RJ, Freedman LS, Hartman AM. 1996. Use of semiquantitative food frequency questionnaires to estimate the distribution of usual intake. *Am J Epidemiol* 143:392–404.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- IOM. 2001. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Washington, DC: National Academy Press.

- Johnson RK, Goran MI, Poehlman ET. 1994. Correlates of over- and under-reporting of energy intake in healthy older men and women. *Am J Clin Nutr* 59:1286–1290.
- Johnson RK, Soultanakis RP, Matthews DE. 1998. Literacy and body fatness are associated with underreporting of energy intake in US low-income women using the multiple-pass 24-hour recall: A doubly labeled water study. *J Am Diet Assoc* 98:1136–1140.
- Kristal AR, Feng Z, Coates RJ, Oberman A, George V. 1997. Associations of race/ethnicity, education, and dietary intervention with the validity and reliability of a food frequency questionnaire: The Women's Health Trial Feasibility Study in Minority Populations. *Am J Epidemiol* 146:856–869.
- Lichtman SW, Pisarska K, Berman ER, Pestone M, Dowling H, Offenbacher E, Weisel H, Heshka S, Matthews DE, Heymsfield SB. 1992. Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. *N Engl J Med* 327:1893–1898.
- Liu K. 1994. Statistical issues related to semiquantitative food-frequency questionnaires. *Am J Clin Nutr* 59:262S–265S.
- Livingstone MB, Prentice AM, Coward WA, Strain JJ, Black AE, Davies PS, Stewart CM, McKenna PG, Whitehead RG. 1992. Validation of estimates of energy intake by weighed dietary record and diet history in children and adolescents. *Am J Clin Nutr* 56:29–35.
- Marlett JA, Cheung TF. 1997. Database and quick methods of assessing typical dietary fiber intakes using data for 228 commonly consumed foods. *J Am Diet Assoc* 97:1139–1148.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Prentice AM, Black AE, Coward WA, Davies HL, Goldberg GR, Murgatroyd PR, Ashford J, Sawyer M, Whitehead RG. 1986. High levels of energy expenditure in obese women. *Br Med J* 292:983–987.
- Pryer JA, Vrijheid M, Nichols R, Kiggins M, Elliott P. 1997. Who are the 'low energy reporters' in the dietary and nutritional survey of British adults? *Int J Epidemiol* 26:146–154.
- Schoeller DA. 1995. Limitations in the assessment of dietary energy by self-report. *Metabolism* 44:18–22.
- Schoeller DA, Bandini LG, Dietz WH. 1990. Inaccuracies in self-reported intake identified by comparison with the doubly labelled water method. *Can J Physiol Pharmacol* 68:941–949.
- USDA (U.S. Department of Agriculture). 2001. *USDA Nutrient Database for Standard Reference, Release 14*. Online. Nutrient Data Laboratory. Available at <http://www.nal.usda.gov/fnic/foodcomp>. Accessed April 2, 2002.
- USDA/HHS (U.S. Department of Health and Human Services). 2000. *Nutrition and Your Health: Dietary Guidelines for Americans*. Home and Garden Bulletin No. 232. Washington, DC: U.S. Government Printing Office.

## DIETARY CARBOHYDRATES: SUGARS AND STARCHES

*Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*  
 (ISBN 0-309-08537-3), Chapter 6, pp. 324–338.

- Albrink MJ, Ullrich IH. 1986. Interaction of dietary sucrose and fiber on serum lipids in healthy young men fed high carbohydrate diets. *Am J Clin Nutr* 43:419–428.
- Allen JC, Keller RP, Archer P, Neville MC. 1991. Studies in human lactation: Milk composition and daily secretion rates of macronutrients in the first year of lactation. *Am J Clin Nutr* 54:69–80.
- Amiel SA, Caprio S, Sherwin RS, Plewe G, Haymond MW, Tamborlane WV. 1991. Insulin resistance of puberty: A defect restricted to peripheral glucose metabolism. *J Clin Endocrinol Metab* 72:277–282.
- Anderson DM, Williams FH, Merkatz RB, Schulman PK, Kerr DS, Pittard WB. 1983. Length of gestation and nutritional composition of human milk. *Am J Clin Nutr* 37:810–814.
- Anderson GH, Atkinson SA, Bryan MH. 1981. Energy and macronutrient content of human milk during early lactation from mothers giving birth prematurely and at term. *Am J Clin Nutr* 34:258–265.
- Archer SL, Liu K, Dyer AR, Ruth KJ, Jacobs DR, Van Horn L, Hilner JE, Savage PJ. 1998. Relationship between changes in dietary sucrose and high density lipoprotein cholesterol: The CARDIA Study. *Ann Epidemiol* 8:433–438.
- Aronow WS, Ahn C. 1998. Risk factors for new coronary events in older African-American men and women. *Am J Cardiol* 82:902–904.
- Arslanian S, Kalhan S. 1992. Effects of growth hormone releasing hormone on insulin action and insulin secretion in a hypopituitary patient evaluated by the clamp technique. *Acta Endocrinol* 127:93–96.
- Assel B, Rossi K, Kalhan S. 1993. Glucose metabolism during fasting through human pregnancy: Comparison of tracer method with respiratory calorimetry. *Am J Physiol* 265:E351–E356.
- Azar GJ, Bloom WL. 1963. Similarities of carbohydrate deficiency and fasting. II. Ketones, nonesterified fatty acids, and nitrogen excretion. *Arch Intern Med* 112:338–343.
- Bell JD, Margen S, Calloway DH. 1969. Ketosis, weight loss, uric acid, and nitrogen balance in obese women fed single nutrients at low caloric levels. *Metabolism* 18:193–208.
- Benito R, Obrador A, Stiggebout A, Bosch FX, Mulet M, Muñoz N, Kaldor J. 1990. A population-based case-control study of colorectal cancer in Majorca. I. Dietary factors. *Int J Cancer* 45:69–76.
- Bier DM, Leake RD, Haymond MW, Arnold KJ, Gruenke LD, Sperling MA, Kipnis DM. 1977. Measurement of “true” glucose production rates in infancy and childhood with 6,6-dideuterooglucose. *Diabetes* 26:1016–1023.
- Bloom WL, Azar GJ. 1963. Similarities of carbohydrate deficiency and fasting. I. Weight loss, electrolyte excretion, and fatigue. *Arch Intern Med* 112:333–337.
- Bolton-Smith C, Woodward M. 1994a. Coronary heart disease: Prevalence and dietary sugars in Scotland. *J Epidemiol Community Health* 48:119–122.
- Bolton-Smith C, Woodward M. 1994b. Dietary composition and fat to sugar ratios in relation to obesity. *Int J Obes Relat Metab Disord* 18:820–828.

- Bolton-Smith C, Woodward M, Smith WCS, Tunstall-Pedoe H. 1991. Dietary and non-dietary predictors of serum total and HDL-cholesterol in men and women: Results from the Scottish Heart Health Study. *Int J Epidemiol* 20:95–104.
- Bossetti BM, Kocher LM, Moranz JF, Falko JM. 1984. The effects of physiologic amounts of simple sugars on lipoprotein, glucose, and insulin levels in normal subjects. *Diabetes Care* 7:309–312.
- Boushey CJ, Beresford SA, Omenn GS, Motulsky AG. 1995. A quantitative assessment of plasma homocysteine as a risk factor for vascular disease: Probable benefits of increasing folic acid intakes. *J Am Med Assoc* 274:1049–1057.
- Bowman SA. 1999. Diets of individuals based on energy intakes from added sugars. *Fam Econ Nutr Rev* 12:31–38.
- Brand JC, Colagiuri S, Crossman S, Allen A, Roberts DCK, Truswell AS. 1991. Low-glycemic index foods improve long-term glycemic control in NIDDM. *Diabetes Care* 14:95–101.
- Brito MN, Brito NA, Migliorini RH. 1992. Thermogenic capacity of brown adipose tissue is reduced in rats fed a high protein, carbohydrate-free diet. *J Nutr* 122:2081–2086.
- Britten P, Basiotis PP, Davis CA, Anand R. 2000. Is intake of added sugars associated with diet quality? Online. *Nutrition Insights* No 21. USDA Center for Nutrition Policy and Promotion. Available at <http://www.usda.gov/cnpp/insights.htm>. Accessed June 8, 2001.
- Brooks GA, Mercier J. 1994. Balance of carbohydrate and lipid utilization during exercise: The “crossover” concept. *J Appl Physiol* 76:2253–2261.
- Brosnan JT. 1999. Comments on metabolic needs for glucose and the role of gluconeogenesis. *Eur J Clin Nutr* 53:S107–S111.
- Bruning PF, Bonfrèr JMG, van Noord PAH, Hart AAM, de Jong-Bakker M, Nooijen WJ. 1992. Insulin resistance and breast-cancer risk. *Int J Cancer* 52:511–516.
- Burley VJ. 1997. Sugar consumption and cancers of the digestive tract. *Eur J Cancer Prev* 6:422–434.
- Burley VJ. 1998. Sugar consumption and human cancer in sites other than the digestive tract. *Eur J Cancer Prev* 7:253–277.
- Burt RL, Davidson IWF. 1974. Insulin half-life and utilization in normal pregnancy. *Obstet Gynecol* 43:161–170.
- Buyken AE, Toeller M, Heitkamp G, Karamanos B, Rottiers R, Muggeo M, Fuller JH. 2001. Glycemic index in the diet of European outpatients with type 1 diabetes: Relations to glycated hemoglobin and serum lipids. *Am J Clin Nutr* 73:574–581.
- Cahill GF. 1970. Starvation in man. *N Engl J Med* 282:668–675.
- Cahill GF, Owen OE, Morgan AP. 1968. The consumption of fuels during prolonged starvation. *Adv Enzyme Reg* 6:143–150.
- Cahill GF, Aoki TT, Ruderman NB. 1973. Ketosis. *Trans Am Clin Climatol Assoc* 84:184–202.
- Calloway DH. 1971. Dietary components that yield energy. *Environ Biol Med* 1:175–186.
- Carlson MG, Snead WL, Campbell PJ. 1994. Fuel and energy metabolism in fasting humans. *Am J Clin Nutr* 60:29–36.
- Chandramouli V, Ekberg K, Schumann WC, Kalhan SC, Wahren J, Landau BR. 1997. Quantifying gluconeogenesis during fasting. *Am J Physiol* 273:E1209–E1215.
- Chew I, Brand JC, Thornburn AW, Truswell AS. 1988. Application of glycemic index to mixed meals. *Am J Clin Nutr* 47:53–56.

- Chryssanthopoulos C, Hennessy LCM, Williams C. 1994. The influence of pre-exercise glucose ingestion on endurance running capacity. *Br J Sports Med* 28:105–109.
- Chugani HT. 1993. Positron emission tomography scanning: Applications in newborns. *Clin Perinatol* 20:395–409.
- Chugani HT, Phelps ME. 1986. Maturational changes in cerebral function in infants determined by <sup>18</sup>FDG positron emission tomography. *Science* 231:840–843.
- Chugani HT, Phelps ME, Mazziotta JC. 1987. Positron emission tomography study of human brain functional development. *Ann Neurol* 22:487–497.
- Cohen JC, Schall R. 1988. Reassessing the effects of simple carbohydrates on the serum triglyceride responses to fat meals. *Am J Clin Nutr* 48:1031–1034.
- Colditz GA, Manson JE, Stampfer MJ, Rosner B, Willett WC, Speizer FE. 1992. Diet and risk of clinical diabetes in women. *Am J Clin Nutr* 55:1018–1023.
- Collier GR, Wolever TMS, Wong GS, Josse RG. 1986. Prediction of glycemic response to mixed meals in noninsulin-dependent diabetic subjects. *Am J Clin Nutr* 44:349–352.
- Collier GR, Giudici S, Kalmusky J, Wolever TMS, Helman G, Wesson V, Ehrlich RM, Jenkins DJA. 1988. Low glycaemic index starchy foods improve glucose control and lower serum cholesterol in diabetic children. *Diabetes Nutr Metab* 1:11–19.
- Condon JR, Nassim JR, Millard FJC, Hilbe A, Stainthorpe EM. 1970. Calcium and phosphorus metabolism in relation to lactose tolerance. *Lancet* 1:1027–1029.
- Coppa GV, Gabrielli O, Pierani P, Catassi C, Carlucci A, Giorgi PL. 1993. Changes in carbohydrate composition in human milk over 4 months of lactation. *Pediatrics* 91:637–641.
- Cott A. 1977. Treatment of learning disabilities. In: Williams RJ, Kalita DK, eds. *A Physician's Handbook on Orthomolecular Medicine*. New York: Pergamon Press. Pp. 90–94.
- Coulston AM, Hollenbeck CB, Liu GC, Williams RA, Starich GH, Mazzaferri EL, Reaven GM. 1984. Effect of source of dietary carbohydrate on plasma glucose, insulin, and gastric inhibitory polypeptide responses to test meals in subjects with noninsulin-dependent diabetes mellitus. *Am J Clin Nutr* 40:965–970.
- Cousins L, Rigg L, Hollingsworth D, Brink G, Aurand J, Yen SSC. 1980. The 24-hour excursion and diurnal rhythm of glucose, insulin, and C-peptide in normal pregnancy. *Am J Obstet Gynecol* 136:483–488.
- Cowett RM, Susa JB, Kahn CB, Giletti B, Oh W, Schwartz R. 1983. Glucose kinetics in nondiabetic and diabetic women during the third trimester of pregnancy. *Am J Obstet Gynecol* 146:773–780.
- Crapo PA, Kolterman OG. 1984. The metabolic effects of 2-week fructose feeding in normal subjects. *Am J Clin Nutr* 39:525–534.
- Décombaz J, Sartori D, Arnaud M-J, Thélin A-L, Schürch P, Howald H. 1985. Oxidation and metabolic effects of fructose or glucose ingested before exercise. *Int J Sports Med* 6:282–286.
- DeFronzo RA, Bonadonna RC, Ferrannini E. 1992. Pathogenesis of NIDDM. A balanced overview. *Diabetes Care* 15:318–368.
- Dekaban AS, Sadowsky D. 1978. Changes in brain weights during the span of human life: Relation of brain weights to body heights and body weights. *Ann Neurol* 4:345–356.
- DeMarco HM, Sucher KP, Cisar CJ, Butterfield GE. 1999. Pre-exercise carbohydrate meals: Application of glycemic index. *Med Sci Sports Exer* 31:164–170.

- Denne SC, Kalhan SC. 1986. Glucose carbon recycling and oxidation in human newborns. *Am J Physiol* 251:E71–E77.
- De Stefani E, Deneo-Pellegrini H, Mendilaharsu M, Ronco A, Carzoglio JC. 1998. Dietary sugar and lung cancer: A case-control study in Uruguay. *Nutr Cancer* 31:132–137.
- Dewey KG, Lönnerdal B. 1983. Milk and nutrient intake of breast-fed infants from 1 to 6 months: Relation to growth and fatness. *J Pediatr Gastroenterol Nutr* 2:497–506.
- Dewey KG, Finley DA, Lönnerdal B. 1984. Breast milk volume and composition during late lactation (7–20 months). *J Pediatr Gastroenterol Nutr* 3:713–720.
- Díez-Sampedro A, Eskandari S, Wright EM, Hirayama BA. 2001. Na<sup>+</sup>-to-sugar stoichiometry of SGLT3. *Am J Physiol Renal Physiol* 280:F278–F282.
- Dobbing J, Sands J. 1973. Quantitative growth and development of human brain. *Arch Dis Child* 48:757–767.
- Dreon DM, Frey-Hewitt B, Ellsworth N, Williams PT, Terry RB, Wood PD. 1988. Dietary fat:carbohydrate ratio and obesity in middle-aged men. *Am J Clin Nutr* 47:995–1000.
- Du Bois EF. 1928. The control of protein in the diet. *J Am Diet Assoc* 4:53–76.
- Dunnigan MG, Fyfe T, McKiddie MT, Crosbie SM. 1970. The effects of isocaloric exchange of dietary starch and sucrose on glucose tolerance, plasma insulin and serum lipids in man. *Clin Sci* 38:1–9.
- Edmond J, Austad N, Robbins RA, Bergstrom JD. 1985. Ketone body metabolism in the neonate: Development and effect of diet. *Fed Proc* 44:2359–2364.
- Egger J, Carter CM, Graham PJ, Gumley D, Soothill JF. 1985. Controlled trial of oligoantigenic treatment in the hyperkinetic syndrome. *Lancet* 1:540–545.
- Ercan N, Gannon MC, Nuttall FQ. 1994. Effect of added fat on the plasma glucose and insulin response to ingested potato given in various combinations as two meals in normal individuals. *Diabetes Care* 17:1453–1459.
- Ernst N, Fisher M, Smith W, Gordon T, Rifkind BM, Little JA, Mishkel MA, Williams OD. 1980. The association of plasma high-density lipoprotein cholesterol with dietary intake and alcohol consumption. The Lipid Research Clinics Program Prevalence Study. *Circulation* 62:IV41–IV52.
- FAO/WHO (Food and Agriculture Organization/World Health Organization). 1998. *Carbohydrates in Human Nutrition*. Rome: FAO.
- Farris RP, Nicklas TA, Myers L, Berenson GS. 1998. Nutrient intake and food group consumption of 10-year-olds by sugar intake level: The Bogalusa Heart Study. *J Am Coll Nutr* 17:579–585.
- Febbraio MA, Keenan J, Angus DJ, Campbell SE, Garnham AP. 2000. Preexercise carbohydrate ingestion, glucose kinetics, and muscle glycogen use: Effect of the glycemic index. *J Appl Physiol* 89:1845–1851.
- Fehily AM, Phillips KM, Yarnell JWG. 1984. Diet, smoking, social class, and body mass index in the Caerphilly Heart Disease Study. *Am J Clin Nutr* 40:827–833.
- Felig P. 1973. The glucose-alanine cycle. *Metabolism* 22:179–207.
- Ferris AM, Dotts MA, Clark RM, Ezrin M, Jensen RG. 1988. Macronutrients in human milk at 2, 12, and 16 weeks postpartum. *J Am Diet Assoc* 88:694–697.
- Fitzsimons D, Dwyer JT, Palmer C, Boyd LD. 1998. Nutrition and oral health guidelines for pregnant women, infants, and children. *J Am Diet Assoc* 98:182–189.
- Fomon SJ, Thomas LN, Filer LJ, Anderson TA, Nelson SE. 1976. Influence of fat and carbohydrate content of diet on food intake and growth of male infants. *Acta Paediatr Scand* 65:136–144.

- Fontvieille AM, Acosta M, Rizkalla SW, Bornet F, David P, Letanoux M, Tchobroutsky G, Slama G. 1988. A moderate switch from high to low glycaemic-index foods for 3 weeks improves the metabolic control of type I (IDDM) diabetic subjects. *Diabetes Nutr Metab* 1:139–143.
- Fontvieille AM, Rizkalla SW, Penfornis A, Acosta M, Bornet FRJ, Slama G. 1992. The use of low glycaemic index foods improves metabolic control of diabetic patients over five weeks. *Diabet Med* 9:444–450.
- Ford ES, Liu S. 2001. Glycemic index and serum high-density lipoprotein cholesterol concentration among US adults. *Arch Intern Med* 161:572–576.
- Forshee RA, Storey ML. 2001. The role of added sugars in the diet quality of children and adolescents. *J Am Coll Nutr* 20:32–43.
- Forsum E, Kabir N, Sadurskis A, Westerterp K. 1992. Total energy expenditure of healthy Swedish women during pregnancy and lactation. *Am J Clin Nutr* 56:334–342.
- Foster-Powell K, Brand Miller J. 1995. International tables of glycemic index. *Am J Clin Nutr* 62:871S–890S.
- Franceschi S, Dal Maso L, Augustin L, Negri E, Parpinel M, Boyle P, Jenkins DJA, La Vecchia C. 2001. Dietary glycemic load and colorectal cancer risk. *Ann Oncol* 12:173–178.
- Frost G, Wilding J, Beecham J. 1994. Dietary advice based on the glycaemic index improves dietary profile and metabolic control in type 2 diabetic patients. *Diabet Med* 11:397–401.
- Frost G, Leeds A, Trew G, Margara R, Dornhorst A. 1998. Insulin sensitivity in women at risk of coronary heart disease and the effect of a low glycemic diet. *Metabolism* 47:1245–1251.
- Frost G, Leeds AA, Doré CJ, Madeiros S, Brading S, Dornhorst A. 1999. Glycaemic index as a determinant of serum HDL-cholesterol concentration. *Lancet* 353:1045–1048.
- Gamble JL. 1946. Physiological information gained from studies on the life raft ration. *Harvey Lect* 42:247–273.
- Gannon MC, Nuttall FQ. 1987. Factors affecting interpretation of postprandial glucose and insulin areas. *Diabetes Care* 10:759–763.
- Gannon MC, Nuttall FQ. 1999. Protein and diabetes. In: Franz MJ, Bantle JP, eds. *American Diabetes Association Guide to Medical Nutrition Therapy for Diabetes*. Alexandria, VA: American Diabetes Association. Pp. 107–125.
- Gannon MC, Niewoehner CB, Nuttall FQ. 1985. Effect of insulin administration on cardiac glycogen synthase and synthase phosphatase activity in rats fed diets high in protein, fat or carbohydrate. *J Nutr* 115:243–251.
- Gannon MC, Nuttall FQ, Westphal SA, Seaquist ER. 1993. The effect of fat and carbohydrate on plasma glucose, insulin, C-peptide, and triglycerides in normal male subjects. *J Am Coll Nutr* 12:36–41.
- Gibbons A. 1998. Solving the brain's energy crisis. *Science* 280:1345–1347.
- Gibney M, Sigman-Grant M, Stanton JL, Keast DR. 1995. Consumption of sugars. *Am J Clin Nutr* 62:178S–194S.
- Gibson SA. 1993. Consumption and sources of sugars in the diets of British schoolchildren: Are high-sugar diets nutritionally inferior? *J Hum Nutr Diet* 6:355–371.
- Gibson SA. 1996a. Are diets high in non-milk extrinsic sugars conducive to obesity? An analysis from the Dietary and Nutritional Survey of British Adults. *J Hum Nutr Diet* 9:283–292.

- Gibson SA. 1996b. Are high-fat, high-sugar foods and diets conducive to obesity? *Int J Food Sci Nutr* 47:405–415.
- Gibson SA. 1997. Non-milk extrinsic sugars in the diets of pre-school children: Association with intakes of micronutrients, energy, fat and NSP. *Br J Nutr* 78:367–378.
- Giovannucci E, Willett WC. 1994. Dietary factors and risk of colon cancer. *Ann Med* 26:443–452.
- Giovannucci E, Rimm EB, Wolk A, Ascherio A, Stampfer MJ, Colditz GA, Willett WC. 1998. Calcium and fructose intake in relation to risk of prostate cancer. *Cancer Res* 58:442–447.
- Gleeson M, Maughan RJ, Greenhaff PL. 1986. Comparison of the effects of pre-exercise feeding of glucose, glycerol and placebo on endurance and fuel homeostasis in man. *Eur J Appl Physiol* 55:645–653.
- Glinsmann WH, Irausquin H, Park YK. 1986. Evaluation of health aspects of sugars contained in carbohydrate sweeteners. Report of Sugars Task Force. *J Nutr* 116:S1–S216.
- Goldberg GR, Prentice AM, Coward WA, Davies HL, Murgatroyd PR, Wensing C, Black AE, Harding M, Sawyer M. 1993. Longitudinal assessment of energy expenditure in pregnancy by the doubly labeled water method. *Am J Clin Nutr* 57:494–505.
- Gottstein U, Held K. 1979. Effects of aging on cerebral circulation and metabolism in man. *Acta Neurologica Scand* 60:54–55.
- Groop LC, Eriksson JG. 1992. The etiology and pathogenesis of non-insulin-dependent diabetes. *Ann Med* 24:483–489.
- Gulliford MC, Bicknell EJ, Scarpello JH. 1989. Differential effect of protein and fat ingestion on blood glucose responses to high- and low-glycemic-index carbohydrates in noninsulin-dependent diabetic subjects. *Am J Clin Nutr* 50:773–777.
- Guss JL, Kissileff HR, Pi-Sunyer FX. 1994. Effects of glucose and fructose solutions on food intake and gastric emptying in nonobese women. *Am J Physiol* 267:R1537–R1544.
- Guthrie JF, Morton JF. 2000. Food sources of added sweeteners in the diets of Americans. *J Am Diet Assoc* 100:43–48, 51.
- Haffner SM, Fong D, Hazuda HP, Pugh JA, Patterson JK. 1988a. Hyperinsulinemia, upper body adiposity, and cardiovascular risk factors in non-diabetics. *Metabolism* 37:338–345.
- Haffner SM, Stern MP, Hazuda HP, Mitchell BD, Patterson JK. 1988b. Increased insulin concentrations in nondiabetic offspring of diabetic parents. *N Engl J Med* 319:1297–1301.
- Haffner SM, Stern MP, Mitchell BD, Hazuda HP, Patterson JK. 1990. Incidence of type II diabetes in Mexican Americans predicted by fasting insulin and glucose levels, obesity, and body-fat distribution. *Diabetes* 39:283–288.
- Hallfrisch J. 1990. Metabolic effects of dietary fructose. *FASEB J* 4:2652–2660.
- Hallfrisch J, Reiser S, Prather ES. 1983. Blood lipid distribution of hyperinsulinemic men consuming three levels of fructose. *Am J Clin Nutr* 37:740–748.
- Hanson PG, Johnson RE, Zaharko DS. 1965. Correlation between ketone body and free fatty acid concentrations in the plasma during early starvation in man. *Metabolism* 14:1037–1040.
- Hargreaves M, Costill DL, Fink WJ, King DS, Fielding RA. 1987. Effect of pre-exercise carbohydrate feedings on endurance cycling performance. *Med Sci Sports Exerc* 19:33–36.

- Harnack L, Stang J, Story M. 1999. Soft drink consumption among US children and adolescents: Nutritional consequences. *J Am Diet Assoc* 99:436–441.
- Hatazawa J, Brooks RA, Di Chiro G, Bacharach SL. 1987. Glucose utilization rate versus brain size in humans. *Neurology* 37:583–588.
- Hay WW. 1994. Placental supply of energy and protein substrates to the fetus. *Acta Paediatr Suppl* 405:13–19.
- Hayford JT, Danney MM, Wiebe D, Roberts S, Thompson RG. 1979. Triglyceride integrated concentrations: Effect of variation of source and amount of dietary carbohydrate. *Am J Clin Nutr* 32:1670–1678.
- Heinbecker P. 1928. Studies on the metabolism of Eskimos. *J Biol Chem* 80:461–475.
- Hellerstein MK. 1999. De novo lipogenesis in humans: Metabolic and regulatory aspects. *Eur J Clin Nutr* 53:S53–S65.
- Holbrook WP, Árnadóttir IB, Takazoe E, Birkhed D, Frostell G. 1995. Longitudinal study of caries, cariogenic bacteria and diet in children just before and after starting school. *Eur J Oral Sci* 103:42–45.
- Hollenbeck CB, Coulston AM, Reaven GM. 1986. Glycemic effects of carbohydrates: A different perspective. *Diabetes Care* 9:641–647.
- Holt SH, Brand Miller J. 1995. Increased insulin responses to ingested foods are associated with lessened satiety. *Appetite* 24:43–54.
- Holt SHA, Brand Miller JC, Petocz P. 1997. An insulin index of foods: The insulin demand generated by 1000-kJ portions of common foods. *Am J Clin Nutr* 66:1264–1276.
- Homko CJ, Sivan E, Reece EA, Boden G. 1999. Fuel metabolism during pregnancy. *Semin Reprod Endocrinol* 17:119–125.
- Hoover HC, Grant JP, Gorschboth C, Ketcham AS. 1975. Nitrogen-sparing intravenous fluids in postoperative patients. *N Engl J Med* 293:172–175.
- Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, Willett WC. 2001. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. *N Engl J Med* 345:790–797.
- Hultman E, Harris RC, Spriet LL. 1999. Diet in work and exercise performance. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th ed. Baltimore, MD: Williams and Wilkins. Pp. 761–782.
- Indar-Brown K, Norenberg C, Madar Z. 1992. Glycemic and insulinemic responses after ingestion of ethnic foods by NIDDM and healthy subjects. *Am J Clin Nutr* 55:89–95.
- IOM (Institute of Medicine). 1991. *Nutrition During Lactation*. Washington, DC: National Academy Press.
- Janney NW. 1915. The metabolic relationship of the proteins to glucose. *J Biol Chem* 20:321–350.
- Järvi AE, Karlström BE, Granfeldt YE, Björk IME, Vessby BOH, Asp N-GL. 1995. The influence of food structure on postprandial metabolism in patients with non-insulin-dependent diabetes mellitus. *Am J Clin Nutr* 61:837–842.
- Järvi AE, Karlström BE, Granfeldt YE, Björck IE, Asp N-GL, Vessby BOH. 1999. Improved glycemic control and lipid profile and normalized fibrinolytic activity on a low-glycemic index diet in type 2 diabetic patients. *Diabetes Care* 22:10–18.
- Jenkins DJA, Wolever TMS, Taylor RH, Barker H, Fielden H, Baldwin JM, Bowling AC, Newman HC, Jenkins AL, Goff DV. 1981. Glycemic index of foods: A physiological basis for carbohydrate exchange. *Am J Clin Nutr* 34:362–366.
- Jenkins DJA, Wolever TMS, Kalmusky J, Giudici S, Giordano C, Wong GS, Bird JN, Patten R, Hall M, Buckley G, Little JA. 1985. Low glycemic index carbohydrate foods in the management of hyperlipidemia. *Am J Clin Nutr* 42:604–617.

- Jenkins DJA, Wolever TMS, Collier GR, Ocana A, Rao AV, Buckley G, Lam Y, Mayer A, Thompson LU. 1987a. Metabolic effects of a low-glycemic-index diet. *Am J Clin Nutr* 46:968–975.
- Jenkins DJA, Wolever TMS, Kalmusky J, Guidici S, Girodano C, Patten R, Wong GS, Bird J, Hall M, Buckley G, Csima A, Little JA. 1987b. Low-glycemic index diet in hyperlipidemia: Use of traditional starchy foods. *Am J Clin Nutr* 46:66–71.
- Jenkins DJA, Wolever TMS, Buckley G, Lam KY, Giudici S, Kalmusky J, Jenkins AL, Patten RL, Bird J, Wong GS, Josse RG. 1988a. Low-glycemic-index starchy food in the diabetic diet. *Am J Clin Nutr* 48:248–254.
- Jenkins DJA, Wolever TMS, Jenkins AL. 1988b. Starchy foods and glycemic index. *Diabetes Care* 11:149–159.
- Jenkins DJA, Jenkins AL, Wolever TM, Vuksan V, Brighenti F, Testolin G. 1990. Fiber and physiological and potentially therapeutic effects of slowing carbohydrate absorption. *Adv Exp Med Biol* 270:129–134.
- Johnson RK. 2000. What are people really eating and why does it matter? *Nutr Today* 35:40–46.
- Kahn SE, Prigeon RL, Schwartz RS, Fujimoto WY, Knopp RH, Brunzell JD, Porte D. 2001. Obesity, body fat distribution, insulin sensitivity and islet  $\beta$ -cell function as explanations for metabolic diversity. *J Nutr* 131:354S–360S.
- Kalhan SC, Kiliç İ. 1999. Carbohydrate as nutrient in the infant and child: Range of acceptable intake. *Eur J Clin Nutr* 53:S94–S100.
- Kalhan SC, D'Angelo LJ, Savin SM, Adam PAJ. 1979. Glucose production in pregnant women at term gestation. Sources of glucose for human fetus. *J Clin Invest* 63:388–394.
- Kalhan SC, Oliven A, King KC, Lucero C. 1986. Role of glucose in the regulation of endogenous glucose production in the human newborn. *Pediatr Res* 20:49–52.
- Kalhan S, Rossi K, Gruca L, Burkett E, O'Brien A. 1997. Glucose turnover and gluconeogenesis in human pregnancy. *J Clin Invest* 100:1775–1781.
- Kalsbeek H, Verrips GH. 1994. Consumption of sweet snacks and caries experience of primary school children. *Caries Res* 28:477–483.
- Kant AK. 2000. Consumption of energy-dense, nutrient-poor foods by adult Americans: Nutritional and health implications. The Third National Health and Nutrition Examination Survey, 1988–1994. *Am J Clin Nutr* 72:929–936.
- Kaufmann NA, Poznanski R, Blondheim SH, Stein Y. 1966. Effect of fructose, glucose, sucrose and starch on serum lipids in carbohydrate induced hypertriglyceridemia and in normal subjects. *Israel J Med Sci* 2:715–726.
- Kazer RR. 1995. Insulin resistance, insulin-like growth factor I and breast cancer: A hypothesis. *Int J Cancer* 62:403–406.
- Kennedy C, Sokoloff L. 1957. An adaptation of the nitrous oxide method to the study of the cerebral circulation in children: Normal values for cerebral blood flow and cerebral metabolic rate in childhood. *J Clin Invest* 36:1130–1137.
- Kety SS. 1957. The general metabolism of the brain in vivo. In: Richter D, ed. *Metabolism of the Nervous System*. London: Pergamon Press. Pp. 221–237.
- Kiens B, Richter EA. 1996. Types of carbohydrate in an ordinary diet affect insulin action and muscle substrates in humans. *Am J Clin Nutr* 63:47–53.
- King KC, Tserng K-Y, Kalhan SC. 1982. Regulation of glucose production in newborn infants of diabetic mothers. *Pediatr Res* 16:608–612.
- Knopp RH, Saudek CD, Arky RA, O'Sullivan JB. 1973. Two phases of adipose tissue metabolism in pregnancy: Maternal adaptations for fetal growth. *Endocrinology* 92:984–988.

- Kopp-Hoolihan LE, van Loan MD, Wong WW, King JC. 1999. Longitudinal assessment of energy balance in well-nourished, pregnant women. *Am J Clin Nutr* 69:697–704.
- Krebs-Smith SM, Graubard BI, Kahle LL, Subar AF, Cleveland LE, Ballard-Barbash R. 2000. Low energy reporters vs. others: A comparison of reported food intakes. *Eur J Clin Nutr* 54:281–287.
- Krezowski PA, Nuttall FQ, Gannon MC, Bartosh NH. 1986. The effect of protein ingestion on the metabolic response to oral glucose in normal individuals. *Am J Clin Nutr* 44:847–856.
- Kushi LK, Lew RA, Stare FJ, Ellison CR, el Lozy M, Bourke G, Daly L, Graham I, Hickey N, Mulcahy R, Kevaney J. 1985. Diet and 20-year mortality from coronary heart disease. The Ireland–Boston Diet–Heart Study. *N Engl J Med* 312:811–888.
- Laine DC, Thomas W, Levitt MD, Bantle JP. 1987. Comparison of predictive capabilities of diabetic exchange lists and glycemic index of foods. *Diabetes Care* 10:387–394.
- Lammi-Keefe CJ, Ferris AM, Jensen RG. 1990. Changes in human milk at 0600, 1000, 1400, 1800, and 2200 h. *J Pediatr Gastroenterol Nutr* 11:83–88.
- Landau BR, Wahren J, Chandramouli V, Schumann WC, Ekberg K, Kalhan SC. 1996. Contributions of gluconeogenesis to glucose production in the fasted state. *J Clin Invest* 98:378–385.
- Leenders KL, Perani D, Lammertsma AA, Heather JD, Buckingham P, Healy MJR, Gibbs JM, Wise RJS, Hatazawa J, Herold S, Beaney RP, Brooks DJ, Spinks T, Rhodes C, Frackowiak RSJ, Jones T. 1990. Cerebral blood flow, blood volume and oxygen utilization. Normal values and effect of age. *Brain* 113:27–47.
- Levin RJ. 1999. Carbohydrates. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th ed. Baltimore, MD: Williams and Wilkins. Pp. 49–65.
- Lewis CJ, Park YK, Dexter PB, Yetley EA. 1992. Nutrient intakes and body weights of persons consuming high and moderate levels of added sugars. *J Am Diet Assoc* 92:708–713.
- Liljeberg HGM, Åkerberg AKE, Björck IME. 1999. Effect of the glycemic index and content of indigestible carbohydrates of cereal-based breakfast meals on glucose tolerance at lunch in healthy subjects. *Am J Clin Nutr* 69:647–655.
- Lingstrom P, van Houte J, Kashket S. 2000. Food starches and dental caries. *Crit Rev Oral Biol Med* 11:366–380.
- Liu K, Stamler J, Trevisan M, Moss D. 1982. Dietary lipids, sugar, fiber, and mortality from coronary heart disease. Bivariate analysis of international data. *Arteriosclerosis* 2:221–227.
- Liu S, Willett WC, Stampfer MJ, Hu FB, Franz M, Sampson L, Hennekens CH, Manson JE. 2000. A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. *Am J Clin Nutr* 71:1455–1461.
- Liu S, Manson JE, Stampfer MJ, Holmes MD, Hu FB, Hankinson SE, Willett WC. 2001. Dietary glycemic load assessed by food-frequency questionnaire in relation to plasma high-density-lipoprotein cholesterol and fasting plasma triacylglycerols in postmenopausal women. *Am J Clin Nutr* 73:560–566.
- Ludwig DS, Majzoub JA, Al-Zahrani A, Dallal GE, Blanco I, Roberts SB. 1999. High glycemic index foods, overeating, and obesity. *Pediatrics* 103:E26.

- Ludwig DS, Peterson KE, Gortmaker SL. 2001. Relation between consumption of sugar-sweetened drinks and childhood obesity: A prospective, observational analysis. *Lancet* 357:505–508.
- Luscombe ND, Noakes M, Clifton PM. 1999. Diets high and low in glycemic index versus high monounsaturated fat diets: Effects on glucose and lipid metabolism in NIDDM. *Eur J Clin Nutr* 53:473–478.
- Mackrell DJ, Sokal JE. 1969. Antagonism between the effects of insulin and glucagon on the isolated liver. *Diabetes* 18:724–732.
- Macquart-Moulin G, Riboli E, Cornée J, Charnay B, Berthezène P, Day N. 1986. Case-control study on colorectal cancer and diet in Marseilles. *Int J Cancer* 38:183–191.
- Macquart-Moulin G, Riboli E, Cornée J, Kaaks R, Berthezène P. 1987. Colorectal polyps and diet: A case-control study in Marseilles. *Int J Cancer* 40:179–188.
- Mann JI, Truswell AS. 1972. Effects of isocaloric exchange of dietary sucrose and starch on fasting serum lipids, postprandial insulin secretion and alimentary lipaemia in human subjects. *Br J Nutr* 27:395–405.
- Mann JI, Watermeyer GS, Manning EB, Randles J, Truswell AS. 1973. Effects on serum lipids of different dietary fats associated with a high sucrose diet. *Clin Sci* 44:601–604.
- Marckmann P, Raben A, Astrup A. 2000. Ad libitum intake of low-fat diets rich in either starchy foods or sucrose: Effects on blood lipids, factor VII coagulant activity, and fibrinogen. *Metabolism* 49:731–735.
- Martin BC, Warram JH, Krolewski AS, Bergman RN, Soeldner JS, Kahn CR. 1992. Role of glucose and insulin resistance in development of type 2 diabetes mellitus: Results of a 25-year follow-up study. *Lancet* 340:925–929.
- Mascarenhas AK. 1998. Oral hygiene as a risk indicator of enamel and dentin caries. *Community Dent Oral Epidemiol* 26:331–339.
- Mattes RD. 1996. Dietary compensation by humans for supplemental energy provided as ethanol or carbohydrate in fluids. *Physiol Behav* 59:179–187.
- Maxwell JD, McKiddie MT, Ferguson A, Buchanan KD. 1970. Plasma insulin response to oral carbohydrate in patients with glucose and lactose malabsorption. *Gut* 11:962–965.
- McDonagh MS, Whiting PF, Wilson PM, Sutton AJ, Chestnutt I, Cooper J, Misso K, Bradley M, Treasure E, Kleijnen J. 2000. Systemic review of water fluoridation. *Br Med J* 321:855–859.
- McGee DL, Reed DM, Yano K, Kagan A, Tillotson J. 1984. Ten-year incidence of coronary heart disease in the Honolulu Heart Program. Relationship to nutrient intake. *Am J Epidemiol* 119:667–676.
- Mehta S, Kalsi HK, Nain CK, Menkes JH. 1977. Energy metabolism of brain in human protein-calorie malnutrition. *Pediatr Res* 11:290–293.
- Meyer KA, Kushi LH, Jacobs DR, Slavin J, Sellers TA, Folsom AR. 2000. Carbohydrates, dietary fiber, and incident of type 2 diabetes in older women. *Am J Clin Nutr* 71:921–930.
- Miller AB, Howe GR, Jain M, Craib KJP, Harrison L. 1983. Food items and food groups as risk factors in a case-control study of diet and colorectal cancer. *Int J Cancer* 32:155–161.
- Miller SL, Wolfe RR. 1999. Physical exercise as a modulator of adaptation to low and high carbohydrate and low and high fat intakes. *Eur J Clin Nutr* 53:S112–S119.

- Miller WC, Lindeman AK, Wallace J, Niederpruem M. 1990. Diet composition, energy intake, and exercise in relation to body fat in men and women. *Am J Clin Nutr* 52:426–430.
- Miller WC, Niederpruem MG, Wallace JP, Lindman AK. 1994. Dietary fat, sugar, and fiber predict body fat content. *J Am Diet Assoc* 94:612–615.
- Morris KL, Zemel MB. 1999. Glycemic index, cardiovascular disease, and obesity. *Nutr Rev* 57:273–276.
- Neville MC, Keller RP, Seacat J, Casey CE, Allen JC, Archer P. 1984. Studies on human lactation. I. Within-feed and between-breast variation in selected components of human milk. *Am J Clin Nutr* 40:635–646.
- Newburg DS, Neubauer SH. 1995. Carbohydrates in milks: Analysis, quantities, and significance. In: Jensen RG, ed. *Handbook of Milk Composition*. New York: Academic Press. Pp. 273–349.
- Nicklas TA, Myers L, Farris RP, Srinivasan SR, Berenson GS. 1996. Nutritional quality of a high carbohydrate diet as consumed by children: The Bogalusa Heart Study. *J Nutr* 126:1382–1388.
- Nommsen LA, Lovelady CA, Heinig MJ, Lönnnerdal B, Dewey KG. 1991. Determinants of energy, protein, lipid, and lactose concentrations in human milk during the first 12 mo of lactation: The DARLING Study. *Am J Clin Nutr* 53:457–465.
- Nordli DR, Koenigsberger D, Schroeder J, deVivo DC. 1992. Ketogenic diets. In: Resor SR, Kutt H, eds. *The Medical Treatment of Epilepsy*. New York: Marcel Dekker. Pp. 455–472.
- Nuttall FQ, Gannon MC. 1981. Sucrose and disease. *Diabetes Care* 4:305–310.
- Nuttall FQ, Mooradian AD, Gannon MC, Billington C, Krezowski P. 1984. Effect of protein ingestion on the glucose and insulin response to a standardized oral glucose load. *Diabetes Care* 7:465–470.
- Nuttall FQ, Gannon MC, Burmeister LA, Lane JT, Pyzdrowski KL. 1992. The metabolic response to various doses of fructose in type II diabetic subjects. *Metabolism* 41:510–517.
- Okano G, Takeda H, Morita I, Katoh M, Mu Z, Miyake S. 1988. Effect of pre-exercise fructose ingestion on endurance performance in fed men. *Med Sci Sports Exerc* 20:105–109.
- Owen OE, Morgan AP, Kemp HG, Sullivan JM, Herrera MG, Cahill GF. 1967. Brain metabolism during fasting. *J Clin Invest* 46:1589–1595.
- Owen OE, Smalley KJ, D'Alessio DA, Mozzoli MA, Dawson EK. 1998. Protein, fat, and carbohydrate requirements during starvation: Anaplerosis and cataplerosis. *Am J Clin Nutr* 68:12–34.
- Papas AS, Joshi A, Palmer CA, Giunta JL, Dwyer JT. 1995. Relationship of diet to root caries. *Am J Clin Nutr* 61:423S–429S.
- Park YK, Yetley EA. 1993. Intakes and food sources of fructose in the United States. *Am J Clin Nutr* 58:737S–747S.
- Parks EJ, Hellerstein MK. 2000. Carbohydrate-induced hypertriacylglycerolemia: Historical perspective and review of biological mechanisms. *Am J Clin Nutr* 71:412–433.
- Patel D, Kalhan S. 1992. Glycerol metabolism and triglyceride-fatty acid cycling in the human newborn: Effect of maternal diabetes and intrauterine growth retardation. *Pediatr Res* 31:52–58.
- Patel MS, Johnson CA, Rajan R, Owen OE. 1975. The metabolism of ketone bodies in developing human brain: Development of ketone-body-utilizing enzymes and ketone bodies as precursors for lipid synthesis. *J Neurochem* 25:905–908.

- Phelps RL, Metzger BE, Freinkel N. 1981. Carbohydrate metabolism in pregnancy. XVII. Diurnal profiles of plasma glucose, insulin, free fatty acids, triglycerides, cholesterol, and individual amino acids in late normal pregnancy. *Am J Obstet Gynecol* 140:730–736.
- Raguso CA, Pereira P, Young VR. 1999. A tracer investigation of obligatory oxidative amino acid losses in healthy, young adults. *Am J Clin Nutr* 70:474–483.
- Rath R, Mašek J, Kujalová V, Slabochová Z. 1974. Effect of a high sugar intake on some metabolic and regulatory indicators in young men. *Nahrung* 18:343–353.
- Reaven GM. 1999. Insulin resistance: A chicken that has come to roost. *Ann NY Acad Sci* 892:45–57.
- Reinmuth OM, Scheinberg P, Bourne B. 1965. Total cerebral blood flow and metabolism. *Arch Neurol* 12:49–66.
- Reiser S, Hallfrisch J. 1987. *Metabolic Effects of Dietary Fructose*. Boca Raton, FL: CRC Press.
- Reiser S, Hallfrisch J, Michaelis OE, Lazar FL, Martin RE, Prather ES. 1979a. Isocaloric exchange of dietary starch and sucrose in humans. I. Effects on levels of fasting blood lipids. *Am J Clin Nutr* 32:1659–1669.
- Reiser S, Handler HB, Gardner LB, Hallfrisch JG, Michaelis OE, Prather ES. 1979b. Isocaloric exchange of dietary starch and sucrose in humans. II. Effect on fasting blood insulin, glucose, and glucagon and on insulin and glucose response to a sucrose load. *Am J Clin Nutr* 32:2206–2216.
- Reiser S, Powell AS, Scholfield DJ, Panda P, Ellwood KC, Canary JJ. 1989. Blood lipids, lipoproteins, apoproteins, and uric acid in men fed diets containing fructose or high-amylose cornstarch. *Am J Clin Nutr* 49:832–839.
- Renner R, Elcombe AM. 1964. Factors affecting the utilization of “carbohydrate-free” diets by the chick. II. Level of glycerol. *J Nutr* 84:327–330.
- Ritz P, Krempf M, Cloarec D, Champ M, Charbonnel B. 1991. Comparative continuous-indirect-calorimetry study of two carbohydrates with different glycemic indices. *Am J Clin Nutr* 54:855–859.
- Robert JJ, Cummins JC, Wolfe RR, Durkot M, Matthews DE, Zhao XH, Bier DM, Young VR. 1982. Quantitative aspects of glucose production and metabolism in healthy elderly subjects. *Diabetes* 31:203–211.
- Roberts SB. 2000a. A review of age-related changes in energy regulation and suggested mechanisms. *Mech Ageing Dev* 116:157–167.
- Roberts SB. 2000b. High-glycemic index foods, hunger, and obesity: Is there a connection? *Nutr Rev* 58:163–169.
- Roche HM. 1999. Dietary carbohydrates and triacylglycerol metabolism. *Proc Nutr Soc* 58:201–207.
- Rodin J. 1991. Effects of pure sugar vs. mixed starch fructose loads on food intake. *Appetite* 17:213–219.
- Rossetti L, Giaccari A, DeFronzo RA. 1990. Glucose toxicity. *Diabetes Care* 13:610–630.
- Rudolf MCJ, Sherwin RS. 1983. Maternal ketosis and its effects on the fetus. *Clin Endocrinol Metab* 12:413–428.
- Ryan EA, O’Sullivan MJ, Skyler JS. 1985. Insulin action during pregnancy. Studies with the euglycemic clamp technique. *Diabetes* 34:380–389.
- Salmerón J, Ascherio A, Rimm EB, Colditz GA, Spiegelman D, Jenkins DJ, Stampfer MJ, Wing AL, Willett WC. 1997a. Dietary fiber, glycemic load, and risk of NIDDM in men. *Diabetes Care* 20:545–550.
- Salmerón J, Manson JE, Stampfer MJ, Colditz GA, Wing AL, Willett WC. 1997b. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. *J Am Med Assoc* 277:472–477.

- Sapir DG, Owen OE, Cheng JT, Ginsberg R, Boden G, Walker WG. 1972. The effect of carbohydrates on ammonium and ketoacid excretion during starvation. *J Clin Invest* 51:2093–2102.
- Saris WH, Astrup A, Prentice AM, Zunft HJ, Formiguera X, Verboeket-van de Venne WP, Raben A, Poppitt SD, Seppelt B, Johnston S, Vasilaras TH, Keogh GF. 2000. Randomized controlled trial of changes in dietary carbohydrate/fat ratio and simple vs. complex carbohydrates on body weight and blood lipids: The CARMEN study. *Int J Obes Relat Metab Disord* 24:1310–1318.
- Sawaya AL, Fuss PJ, Dallal GE, Tsay R, McCrory MA, Young V, Roberts SB. 2001. Meal palatability, substrate oxidation and blood glucose in young and older men. *Physiol Behav* 72:5–12.
- Scheinberg P, Stead EA. 1949. The cerebral blood flow in male subjects as measured by the nitrous oxide technique. Normal values for blood flow, oxygen utilization, glucose utilization, and peripheral resistance, with observations on the effect of tilting and anxiety. *J Clin Invest* 28:1163–1171.
- Settergren G, Lindblad BS, Persson B. 1976. Cerebral blood flow and exchange of oxygen, glucose, ketone bodies, lactate, pyruvate and amino acids in infants. *Acta Paediatr Scand* 65:343–353.
- Settergren G, Lindblad BS, Persson B. 1980. Cerebral blood flow and exchange of oxygen, glucose, ketone bodies, lactate, pyruvate and amino acids in anesthetized children. *Acta Paediatr Scand* 69:457–465.
- Shannon WR. 1922. Neuropathologic manifestations in infants and children as a result of anaphylactic reaction to foods contained in their diet. *Am J Dis Child* 24:89–94.
- Shaw JH. 1987. Causes and control of dental caries. *N Engl J Med* 317:996–1004.
- Slattery ML, Benson J, Berry TD, Duncan D, Edwards SL, Caan BJ, Potter JD. 1997. Dietary sugar and colon cancer. *Cancer Epidemiol Biomarkers Prev* 6:677–685.
- Smith JB, Niven BE, Mann JI. 1996. The effect of reduced extrinsic sucrose intake on plasma triglyceride levels. *Eur J Clin Nutr* 50:498–504.
- Sokoloff L. 1973. Metabolism of ketone bodies by the brain. *Annu Rev Med* 24:271–280.
- Sokoloff L, Fitzgerald GG, Kaufman EE. 1977. Cerebral nutrition and energy metabolism. In: Wurtman RJ, Wurtman JJ, eds. *Nutrition and the Brain*. New York: Raven Press. Pp. 87–139.
- Sparks JW, Girard JR, Battaglia FC. 1980. An estimate of the caloric requirements of the human fetus. *Biol Neonate* 38:113–119.
- Sparks MJ, Selig SS, Febbraio MA. 1998. Pre-exercise carbohydrate ingestion: Effect of the glycemic index on endurance exercise performance. *Med Sci Sports Exerc* 30:844–849.
- Speer F. 1954. The allergenic tension-fatigue syndrome. *Pediatr Clin North Am* 1:1029–1037.
- Spieth LE, Harnish JD, Lenders CM, Raezer LB, Pereira MA, Hangen SJ, Ludwig DS. 2000. A low-glycemic index diet in the treatment of pediatric obesity. *Arch Pediatr Adolesc Med* 154:947–951.
- Spitzer L, Rodin J. 1987. Effects of fructose and glucose preloads on subsequent food intake. *Appetite* 8:135–145.
- Streja DA, Steiner G, Marliss EB, Vranic M. 1977. Turnover and recycling of glucose in man during prolonged fasting. *Metabolism* 26:1089–1098.
- Sunehag AL, Haymond MW, Schanler RJ, Reeds PJ, Bier DM. 1999. Gluconeogenesis in very low birth weight infants receiving total parenteral nutrition. *Diabetes* 48:791–800.

- Surwit RS, Feinglos MN, McCaskill CC, Clay SL, Babyak MA, Brownlow BS, Plaisted CS, Lin P-H. 1997. Metabolic and behavioral effects of a high-sucrose diet during weight loss. *Am J Clin Nutr* 65:908–915.
- Swanson JE, Laine DC, Thomas W, Bantle JP. 1992. Metabolic effects of dietary fructose in healthy subjects. *Am J Clin Nutr* 55:851–856.
- Swink TD, Vining EPG, Freeman JM. 1997. The ketogenic diet: 1997. *Adv Pediatr* 44:297–329.
- Thomas DE, Brotherhood JR, Brand JC. 1991. Carbohydrate feeding before exercise: Effect of glycemic index. *Int J Sports Med* 12:180–186.
- Tillotson JL, Grandits GA, Bartsch GE, Stamler J. 1997. Relation of dietary carbohydrates to blood lipids in the special intervention and usual care groups in the Multiple Risk Factor Intervention Trial. *Am J Clin Nutr* 65:314S–326S.
- Troiano RP, Briefel RR, Carroll MD, Bialostosky K. 2000. Energy and fat intakes of children and adolescents in the United States: Data from the National Health and Nutrition Examination Surveys. *Am J Clin Nutr* 72:1343S–1353S.
- Tuyns AJ, Kaaks R, Haelterman M. 1988. Colorectal cancer and the consumption of foods: A case-control study in Belgium. *Nutr Cancer* 11:189–204.
- USDA (U.S. Department of Agriculture). 1996. *The Food Guide Pyramid*. Home and Garden Bulletin No. 252. Washington, DC: U.S. Government Printing Office.
- USDA/HHS (U.S. Department of Agriculture/U.S. Department of Health and Human Services). 2000. *Nutrition and Your Health: Dietary Guidelines for Americans*. Home and Garden Bulletin No. 232. Washington, DC: U.S. Government Printing Office.
- van Dam RM, Visscher AWJ, Feskens EJM, Verhoef P, Kromhout D. 2000. Dietary glycemic index in relation to metabolic risk factors and incidence of coronary heart disease: The Zutphen Elderly Study. *Eur J Clin Nutr* 54:726–731.
- Vining EPG. 1999. Clinical efficacy of the ketogenic diet. *Epilepsy Res* 37:181–190.
- Walker ARP, Cleaton-Jones PE. 1992. Sugar intake and dental caries. *Br Dent J* 172:7.
- Warram JH, Martin BC, Krolewski AS, Soeldner JS, Kahn CR. 1990. Slow glucose removal rate and hyperinsulinemia precede the development of type II diabetes in the offspring of diabetic parents. *Ann Intern Med* 113:909–915.
- Welsh S, Davis C, Shaw A. 1992. Development of the Food Guide Pyramid. *Nutr Today* 27:12–23.
- Westphal SA, Gannon MC, Nuttal FQ. 1990. Metabolic response to glucose ingested with various amounts of protein. *Am J Clin Nutr* 52:267–272.
- White JW, Wolraich M. 1995. Effect of sugar on behavior and mental performance. *Am J Clin Nutr* 62:242S–249S.
- Wolever TMS. 1990. Relationship between dietary fiber content and composition in foods and the glycemic index. *Am J Clin Nutr* 51:72–75.
- Wolever TMS, Jenkins DJA. 1986. The use of the glycemic index in predicting the blood glucose response to mixed meals. *Am J Clin Nutr* 43:167–172.
- Wolever TMS, Nuttal FQ, Lee R, Wong GS, Josse RG, Csima A, Jenkins DJA. 1985. Prediction of the relative blood glucose response of mixed meals using the white bread glycemic index. *Diabetes Care* 8:418–428.
- Wolever TMS, Jenkins DJA, Josse RG, Wong GS, Lee R. 1987. The glycemic index: Similarity of values derived in insulin-dependent and non-insulin-dependent diabetic patients. *J Am Coll Nutr* 6:295–305.
- Wolever TMS, Jenkins DJA, Ocana AM, Rao VA, Collier GR. 1988. Second-meal effect: Low-glycemic-index foods eaten at dinner improve subsequent breakfast glycemic response. *Am J Clin Nutr* 48:1041–1047.

- Wolever TMS, Jenkins DJA, Vuksan V, Josse RG, Wong GS, Jenkins AL. 1990. Glycemic index of foods in individual subjects. *Diabetes Care* 13:126–132.
- Wolever TMS, Jenkins DJA, Jenkins AL, Josse RG. 1991. The glycemic index: Methodology and clinical implications. *Am J Clin Nutr* 54:846–854.
- Wolever TMS, Jenkins DJA, Vuksan V, Jenkins AL, Buckley GC, Wong GS, Josse RG. 1992a. Beneficial effect of a low glycaemic index diet in type 2 diabetes. *Diabet Med* 9:451–458.
- Wolever TMS, Jenkins DJA, Vuksan V, Jenkins AL, Wong GS, Josse RG. 1992b. Beneficial effect of low-glycemic index diet in overweight NIDDM subjects. *Diabetes Care* 15:562–564.
- Wolraich ML, Wilson DB, White JW. 1995. The effect of sugar on behavior or cognition in children. A meta-analysis. *J Am Med Assoc* 274:1617–1621.
- World Cancer Research Fund/American Institute for Cancer Research. 1997. *Food, Nutrition and the Prevention of Cancer: A Global Perspective*. Washington, DC: American Institute for Cancer Research.
- Yamaura H, Ito M, Kubota K, Matsuzawa T. 1980. Brain atrophy during aging: A quantitative study with computed tomography. *J Gerontol* 35:492–498.
- Yudkin J, Eisa O, Kang SS, Meraji S, Bruckdorfer KR. 1986. Dietary sucrose affects plasma HDL cholesterol concentration in young men. *Ann Nutr Metab* 30:261–266.
- Ziegler EE, Fomon SJ. 1983. Lactose enhances mineral absorption in infancy. *J Pediatr Gastroenterol Nutr* 2:288–294.

Ibid., Chapter 13, pp. 965–967.

- Bandini LG, Vu D, Must A, Cyr H, Goldberg A, Dietz WH. 1999. Comparison of high-calorie, low-nutrient-dense food consumption among obese and non-obese adolescents. *Obes Res* 7:438–443.
- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Black AE, Prentice AM, Goldberg GR, Jebb SA, Bingham SA, Livingstone MBE, Coward WA. 1993. Measurements of total energy expenditure provide insights into the validity of dietary measurements of energy intake. *J Am Diet Assoc* 93:572–579.
- Blair SN, Kohl HW, Barlow CE. 1993. Physical activity, physical fitness, and all-cause mortality in women: Do women need to be active? *J Am Coll Nutr* 12:368–371.
- Blair SN, Kohl HW, Barlow CE, Paffenbarger RS, Gibbons LW, Macera CA. 1995. Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. *J Am Med Assoc* 273:1093–1098.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Nutrition Examination Survey: Underreporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Carroll RJ, Freedman LS, Hartman AM. 1996. Use of semiquantitative food frequency questionnaires to estimate the distribution of usual intake. *Am J Epidemiol* 143:392–404.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.

- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- IOM. 2001. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Washington, DC: National Academy Press.
- Johnson RK, Goran MI, Poehlman ET. 1994. Correlates of over- and under-reporting of energy intake in healthy older men and women. *Am J Clin Nutr* 59:1286–1290.
- Johnson RK, Soultanakis RP, Matthews DE. 1998. Literacy and body fatness are associated with underreporting of energy intake in US low-income women using the multiple-pass 24-hour recall: A doubly labeled water study. *J Am Diet Assoc* 98:1136–1140.
- Kristal AR, Feng Z, Coates RJ, Oberman A, George V. 1997. Associations of race/ethnicity, education, and dietary intervention with the validity and reliability of a food frequency questionnaire: The Women's Health Trial Feasibility Study in Minority Populations. *Am J Epidemiol* 146:856–869.
- Lichtman SW, Pisarska K, Berman ER, Pestone M, Dowling H, Offenbacher E, Weisel H, Heshka S, Matthews DE, Heymsfield SB. 1992. Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. *N Engl J Med* 327:1893–1898.
- Liu K. 1994. Statistical issues related to semiquantitative food-frequency questionnaires. *Am J Clin Nutr* 59:262S–265S.
- Livingstone MB, Prentice AM, Coward WA, Strain JJ, Black AE, Davies PS, Stewart CM, McKenna PG, Whitehead RG. 1992. Validation of estimates of energy intake by weighed dietary record and diet history in children and adolescents. *Am J Clin Nutr* 56:29–35.
- Marlett JA, Cheung TF. 1997. Database and quick methods of assessing typical dietary fiber intakes using data for 228 commonly consumed foods. *J Am Diet Assoc* 97:1139–1148.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Prentice AM, Black AE, Coward WA, Davies HL, Goldberg GR, Murgatroyd PR, Ashford J, Sawyer M, Whitehead RG. 1986. High levels of energy expenditure in obese women. *Br Med J* 292:983–987.
- Pryer JA, Vrijheid M, Nichols R, Kiggins M, Elliott P. 1997. Who are the 'low energy reporters' in the dietary and nutritional survey of British adults? *Int J Epidemiol* 26:146–154.
- Schoeller DA. 1995. Limitations in the assessment of dietary energy by self-report. *Metabolism* 44:18–22.
- Schoeller DA, Bandini LG, Dietz WH. 1990. Inaccuracies in self-reported intake identified by comparison with the doubly labelled water method. *Can J Physiol Pharmacol* 68:941–949.

- USDA (U.S. Department of Agriculture). 2001. *USDA Nutrient Database for Standard Reference, Release 14*. Online. Nutrient Data Laboratory. Available at <http://www.nal.usda.gov/fnic/foodcomp>. Accessed April 2, 2002.
- USDA/HHS (U.S. Department of Health and Human Services). 2000. *Nutrition and Your Health: Dietary Guidelines for Americans*. Home and Garden Bulletin No. 232. Washington, DC: U.S. Government Printing Office.

## FIBER

*Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* (ISBN 0-309-08537-3), Chapter 7, pp. 400–421.

- AAP (American Academy of Pediatrics). 1981. Plant fiber intake in the pediatric diet. *Pediatrics* 67:572–575.
- AAP. 1993. Carbohydrate and dietary fiber. In: Barness LA, ed. *Pediatric Nutrition Handbook*, 3rd ed. Elk Grove Village, IL: AAP. Pp. 100–106.
- Abraham ZD, Mehta T. 1988. Three-week psyllium-husk supplementation: Effect on plasma cholesterol concentrations, fecal steroid excretion, and carbohydrate absorption in men. *Am J Clin Nutr* 47:67–74.
- Achour L, Flourié B, Briet F, Pellier P, Marteau P, Rambaud J-C. 1994. Gastrointestinal effects and energy value of polydextrose in healthy nonobese men. *Am J Clin Nutr* 59:1362–1368.
- AHA (American Heart Association). 1983. AHA committee report. Diet in the healthy child. Task Force Committee of the Nutrition Committee and the Cardiovascular Disease in the Young Council of the American Heart Association. *Circulation* 67:1411A–1414A.
- Alberts DS, Einspahr J, Rees-McGee S, Ramanujam P, Buller MK, Clark L, Ritenbaugh C, Atwood J, Pethigal P, Earnest D, Villar H, Phelps J, Lipkin M, Wargovich M, Meyskens FL. 1990. Effects of dietary wheat-bran fiber on rectal epithelial cell proliferation in patients with resection for colorectal cancers. *J Natl Cancer Inst* 82:1280–1285.
- Alberts DS, Einspahr J, Ritenbaugh C, Aickin M, Rees-McGee S, Atwood J, Emerson S, Mason-Liddil N, Bettinger L, Patel J, Bellaprapalu S, Ramanujam PS, Phelps J, Clark L. 1997. The effect of wheat-bran fiber and calcium supplementation on rectal mucosal proliferation rates in patients with resected adenomatous colorectal polyps. *Cancer Epidemiol Biomarkers Prev* 6:161–169.
- Alberts DS, Martínez ME, Roe DJ, Guillén-Rodríguez JM, Marshall JR, van Leeuwen JB, Reid ME, Ritenbaugh C, Vargas PA, Bhattacharyya AB, Earnest DL, Sampliner RE. 2000. Lack of effect of a high-fiber cereal supplement on the recurrence of colorectal adenomas. *N Engl J Med* 342:1156–1162.
- Aldoori WH, Giovannucci EL, Rimm EB, Wing AL, Trichopoulos DV, Willett WC. 1994. A prospective study of diet and the risk of symptomatic diverticular disease in men. *Am J Clin Nutr* 60:757–764.
- Aldoori WH, Giovannucci EL, Rimm EB, Ascherio A, Stampfer MJ, Colditz GA, Wing AL, Trichopoulos DV, Willett WC. 1995. Prospective study of physical activity and the risk of symptomatic diverticular disease in men. *Gut* 36:276–282.
- Aldoori WH, Giovannucci EL, Stampfer MJ, Rimm EB, Wing AL, Willett WC. 1997. Prospective study of diet and the risk of duodenal ulcer in men. *Am J Epidemiol* 145:42–50.
- Aldoori WH, Giovannucci EL, Rockett HRH, Sampson L, Rimm EB, Willett WC. 1998. A prospective study of dietary fiber types and symptomatic diverticular disease in men. *J Nutr* 128:714–719.
- Alles MS, Hautvast JG, Nagengast FM, Hartemink R, Van Laere KM, Jansen JB. 1996. Fate of fructo-oligosaccharides in the human intestine. *Br J Nutr* 76:211–221.
- AMA (American Medical Association) Council on Scientific Affairs. 1989. Dietary fiber and health. *J Am Med Assoc* 262:542–546.

- Anderson JW, Gustafson NJ. 1988. Hypocholesterolemic effects of oat and bean products. *Am J Clin Nutr* 48:749–753.
- Anderson JW, Tietyen-Clark J. 1986. Dietary fiber: Hyperlipidemia, hypertension, and coronary heart disease. *Am J Gastroenterol* 81:907–919.
- Anderson JW, Story L, Sieling B, Chen W-JL. 1984a. Hypocholesterolemic effects of high-fibre diets rich in water-soluble plant fibres. *J Can Diet Assoc* 45:140–148.
- Anderson JW, Story L, Sieling B, Chen W-JL, Petro MS, Story J. 1984b. Hypocholesterolemic effects of oat-bran or bean intake for hypercholesterolemic men. *Am J Clin Nutr* 40:1146–1155.
- Anderson JW, Gustafson NJ, Bryant CA, Tietyen-Clark J. 1987. Dietary fiber and diabetes: A comprehensive review and practical application. *J Am Diet Assoc* 87:1189–1197.
- Anderson JW, Zettwoch N, Feldman T, Tietyen-Clark J, Oeltgen P, Bishop CW. 1988. Cholesterol-lowering effects of psyllium hydrophilic mucilloid for hypercholesterolemic men. *Arch Intern Med* 148:292–296.
- Anderson JW, Gilinsky NH, Deakins DA, Smith SF, O'Neal DS, Dillon DW, Oeltgen PR. 1991. Lipid responses of hypercholesterolemic men to oat-bran and wheat-bran intake. *Am J Clin Nutr* 54:678–683.
- Anderson JW, Garrity TF, Wood CL, Whitis SE, Smith BM, Oeltgen PR. 1992a. Prospective, randomized, controlled comparison of the effects of low-fat and low-fat plus high-fiber diets on serum lipid concentrations. *Am J Clin Nutr* 56:887–894.
- Anderson JW, Riddell-Mason S, Gustafson NJ, Smith SF, Mackey M. 1992b. Cholesterol-lowering effects of psyllium-enriched cereal as an adjunct to a prudent diet in the treatment of mild to moderate hypercholesterolemia. *Am J Clin Nutr* 56:93–98.
- Anderson JW, Allgood LD, Turner J, Oeltgen PR, Daggy BP. 1999. Effects of psyllium on glucose and serum lipid responses in men with type 2 diabetes and hypercholesterolemia. *Am J Clin Nutr* 70:466–473.
- Anderson JW, Allgood LD, Lawrence A, Altringer LA, Jerdack GR, Hengehold DA, Morel JG. 2000a. Cholesterol-lowering effects of psyllium intake adjunctive to diet therapy in men and women with hypercholesterolemia: Meta-analysis of 8 controlled trials. *Am J Clin Nutr* 71:472–479.
- Anderson JW, Davidson MH, Blonde L, Brown WV, Howard JW, Ginsberg H, Allgood LD, Weingand KW. 2000b. Long-term cholesterol-lowering effects of psyllium as an adjunct to diet therapy in the treatment of hypercholesterolemia. *Am J Clin Nutr* 71:1433–1438.
- Andersson S-O, Wolk A, Bergström R, Giovannucci E, Lindgren C, Baron J, Adami H-O. 1996. Energy, nutrient intake and prostate cancer risk: A population-based case-control study in Sweden. *Int J Cancer* 68:716–722.
- Anti M, Pignataro G, Armuzzi A, Valenti A, Iascone E, Marmo R, Lamazza A, Pretaroli AR, Pace V, Leo P, Castelli A, Gasbarrini G. 1998. Water supplementation enhances the effect of high-fiber diet on stool frequency and laxative consumption in adult patients with functional constipation. *Hepatogastroenterology* 45:727–732.
- Appleby PN, Thorogood M, Mann JI, Key TJ. 1998. Low body mass index in non-meat eaters: The possible roles of animal fat, dietary fibre and alcohol. *Int J Obes Relat Metab Disord* 22:454–460.

- Aro A, Uusitupa M, Voutilainen E, Hersio K, Korhonen T, Siitonen O. 1981. Improved diabetic control and hypocholesterolaemic effect induced by long-term dietary supplementation with guar gum in type-2 (insulin-independent) diabetes. *Diabetologia* 21:29–33.
- Aro A, Uusitupa M, Voutilainen E, Korhonen T. 1984. Effects of guar gum in male subjects with hypercholesterolemia. *Am J Clin Nutr* 39:911–916.
- Ascherio A, Rimm EB, Giovannucci EL, Colditz GA, Rosner B, Willett WC, Sacks F, Stampfer MJ. 1992. A prospective study of nutritional factors and hypertension among US men. *Circulation* 86:1475–1484.
- Ashraf W, Park F, Lof J, Quigley EM. 1995. Effects of psyllium therapy on stool characteristics, colon transit and anorectal function in chronic idiopathic constipation. *Aliment Pharmacol Ther* 9:639–647.
- Astrup A, Vrist E, Quaade F. 1990. Dietary fibre added to very low calorie diet reduces hunger and alleviates constipation. *Int J Obes* 14:105–112.
- Bagga D, Ashley JM, Geffrey SP, Wang HJ, Barnard RJ, Korenman S, Heber D. 1995. Effects of a very low fat, high fiber diet on serum hormones and menstrual function. Implications for breast cancer prevention. *Cancer* 76:2491–2496.
- Baghurst PA, Rohan TE. 1994. High-fiber diets and reduced risk of breast cancer. *Int J Cancer* 56:173–176.
- Barbone F, Austin H, Partridge EE. 1993. Diet and endometrial cancer: A case-control study. *Am J Epidemiol* 137:393–403.
- Baron JA, Schori A, Crow B, Carter R, Mann JI. 1986. A randomized controlled trial of low carbohydrate and low fat/high fiber diets for weight loss. *Am J Public Health* 76:1293–1296.
- Bartram P, Gerlach S, Scheppach W, Keller F, Kasper H. 1992. Effect of a single oat bran cereal breakfast on serum cholesterol, lipoproteins, and apolipoproteins in patients with hyperlipoproteinemia type IIa. *J Parenter Enteral Nutr* 16:533–537.
- Beer MU, Arrigoni E, Amado R. 1995. Effects of oat gum on blood cholesterol levels in healthy young men. *Eur J Clin Nutr* 49:517–522.
- Behall KM. 1990. Effect of soluble fibers on plasma lipids, glucose tolerance and mineral balance. *Adv Exp Med Biol* 270:7–16.
- Behall KM, Howe JC. 1996. Resistant starch as energy. *J Am Coll Nutr* 15:248–254.
- Behall KM, Scholfield DJ, Lee K, Powell AS, Moser PB. 1987. Mineral balance in adult men: Effect of four refined fibers. *Am J Clin Nutr* 46:307–314.
- Bell LP, Hectorn KJ, Reynolds H, Hunninghake DB. 1990. Cholesterol-lowering effects of soluble-fiber cereals as part of a prudent diet for patients with mild to moderate hypercholesterolemia. *Am J Clin Nutr* 52:1020–1026.
- Benini L, Castellani G, Brighenti F, Heaton KW, Brentegani MT, Casiraghi MC, Sembenini C, Pellegrini N, Fioretta A, Minniti G. 1995. Gastric emptying of a solid meal is accelerated by the removal of dietary fibre naturally present in food. *Gut* 36:825–830.
- Bergmann JF, Chassany O, Petit A, Triki R, Caulin C, Segrestaa JM. 1992. Correlation between echographic gastric emptying and appetite: Influence of psyllium. *Gut* 33:1042–1043.
- Berman JI, Schultz MJ. 1980. Bulk laxative ileus. *J Am Geriatr Soc* 28:224–226.
- Berta JL, Coste T, Rautureau J, Guilloud-Bataille M, Pequignot G. 1985. Diet and rectocolonic cancers. Results of a case-control study. *Gastroenterol Clin Biol* 9:348–353.

- Bidoli E, Franceschi S, Talamini R, Barra S, La Vecchia C. 1992. Food consumption and cancer of the colon and rectum in north-eastern Italy. *Int J Cancer* 50:223–229.
- Birkett AM, Jones GP, de Silva AM, Young GP, Muir JG. 1997. Dietary intake and faecal excretion of carbohydrate by Australians: Importance of achieving stool weights greater than 150 g to improve faecal markers relevant to colon cancer risk. *Eur J Clin Nutr* 51:625–632.
- Birketvedt GS, Aaseth J, Florholmen JR, Ryttig K. 2000. Long term effect of fibre supplement and reduced energy intake on body weight and blood lipids in overweight subjects. *Acta Medica (Hradec Králové)* 43:129–132.
- Blackburn NA, Holgate AM, Read NW. 1984. Does guar gum improve post-prandial hyperglycaemia in humans by reducing small intestinal contact area? *Br J Nutr* 52:197–204.
- Blake DE, Hamblett CJ, Frost PG, Judd PA, Ellis PR. 1997. Wheat bread supplemented with depolymerized guar gum reduces the plasma cholesterol concentration in hypercholesterolemic human subjects. *Am J Clin Nutr* 65:107–113.
- Blundell JE, Burley VJ. 1987. Satiation, satiety and the action of fibre on food intake. *Int J Obesity* 11:9–25.
- Bolin TD, Stanton RA. 1998. Flatus emission patterns and fibre intake. *Eur J Surg* 582:115–118.
- Bolton-Smith C, Woodward M, Tunstall-Pedoe H. 1992. The Scottish Heart Health Study. Dietary intake by food frequency questionnaire and odds ratios for coronary heart disease risk. II. The antioxidant vitamins and fibre. *Eur J Clin Nutr* 46:85–93.
- Bonithon-Kopp C, Kronborg O, Giacosa A, Räth U, Faivre J. 2000. Calcium and fibre supplementation in prevention of colorectal adenoma recurrence: A randomised intervention trial. *Lancet* 356:1300–1306.
- Bosaeus I, Carlsson NG, Sandberg AS, Andersson H. 1986. Effect of wheat bran and pectin on bile acid and cholesterol excretion in ileostomy patients. *Hum Nutr Clin Nutr* 40:429–440.
- Bosello O, Cominacini L, Zocca I, Garbin U, Ferrari F, Davoli A. 1984. Effects of guar gum on plasma lipoproteins and apolipoproteins C-II and C-III in patients affected with familial combined hyperlipoproteinemia. *Am J Clin Nutr* 40:1165–1174.
- Bouhnik Y, Flourié B, Riottot M, Bisetti N, Gailing M-F, Guibert A, Bornet F, Rambaud J-C. 1996. Effects of fructo-oligosaccharides ingestion on fecal bifidobacteria and selected metabolic indexes of colon carcinogenesis in healthy humans. *Nutr Cancer* 26:21–29.
- Bouhnik Y, Vahedi K, Achour L, Attar A, Salfati J, Pochart P, Marteau P, Flourié B, Bornet F, Rambaud J-C. 1999. Short-chain fructo-oligosaccharide administration dose-dependently increases fecal bifidobacteria in healthy humans. *J Nutr* 129:113–116.
- Boyle P, Zaridze DG, Smans M. 1985. Descriptive epidemiology of colorectal cancer. *Int J Cancer* 36:9–18.
- Braaten JT, Wood PJ, Scott FW, Riedel KD, Poste LM, Collins MW. 1991. Oat gum lowers glucose and insulin after an oral glucose load. *Am J Clin Nutr* 53:1425–1430.
- Braaten JT, Scott FW, Wood PJ, Riedel KD, Wolynetz MS, Brûlé D, Collins MW. 1994a. High  $\beta$ -glucan oat bran and oat gum reduce postprandial blood glucose and insulin in subjects with and without type 2 diabetes. *Diabetic Med* 11:312–318.

- Braaten JT, Wood PJ, Scott FW, Wolynetz MS, Lowe MK, Bradley-White P, Collins MW. 1994b. Oat beta-glucan reduces blood cholesterol concentration in hypercholesterolemic subjects. *Eur J Clin Nutr* 48:465–474.
- Briet F, Achour L, Flourié B, Beaugerie L, Pellier P, Franchisseur C, Bornet F, Rambaud JC. 1995. Symptomatic response to varying levels of fructo-oligosaccharides consumed occasionally or regularly. *Eur J Clin Nutr* 49:501–507.
- Brightenti F, Casiraghi MC, Canzi E, Ferrari A. 1999. Effect of consumption of a ready-to-eat breakfast cereal containing inulin on the intestinal milieu and blood lipids in healthy male volunteers. *Eur J Clin Nutr* 53:726–733.
- Brodrrib AJM. 1977. Treatment of symptomatic diverticular disease with a high-fibre diet. *Lancet* 1:664–666.
- Brown IL, McNaught KJ, Moloney E. 1995. Hi-maize: New directions in starch technology and nutrition. *Food Aust* 47:273–279.
- Brown L, Rosner B, Willett W, Sacks FM. 1999. Cholesterol-lowering effects of dietary fiber: A meta-analysis. *Am J Clin Nutr* 69:30–42.
- Brune M, Rossander-Hulten L, Hallberg L, Gleerup A, Sandberg AS. 1992. Iron absorption from bread in humans: Inhibiting effects of cereal fiber, phytate and inositol phosphates with different numbers of phosphate groups. *J Nutr* 122:442–449.
- Buddington RK, Williams CH, Chen S-C, Witherly SA. 1996. Dietary supplementation of neosugar alters the fecal flora and decreases activities of some reductive enzymes in human subjects. *Am J Clin Nutr* 63:709–716.
- Burdock GA, Flamm WG. 1999. A review of the studies of the safety of polydextrose in food. *Food Chem Toxicol* 37:233–264.
- Burkitt DP, Walker ARP, Painter NS. 1972. Effect of dietary fibre on stools and transit-times, and its role in the causation of disease. *Lancet* 2:1408–1412.
- Burley VJ, Paul AW, Blundell JE. 1993. Sustained post-ingestive action of dietary fibre: Effects of a sugar-beet-fibre-supplemented breakfast on satiety. *J Hum Nutr Diet* 6:43–50.
- Burr ML, Sweetnam PM. 1982. Vegetarianism, dietary fiber, and mortality. *Am J Clin Nutr* 36:873–877.
- Burr ML, Fehily AM, Gilbert JF, Rogers S, Holliday RM, Sweetnam PM, Elwood PC, Deadman NM. 1989. Effects of changes in fat, fish, and fibre intakes on death and myocardial reinfarction: Diet and Reinfarction Trial (DART). *Lancet* 2:757–761.
- Burton R, Manninen V. 1982. Influence of psyllium-based fibre preparation on faecal and serum parameters. *Acta Med Scand Suppl* 668:91–94.
- Busse WW, Schoenwetter WF. 1975. Asthma from psyllium in laxative manufacture. *Ann Intern Med* 83:361–362.
- Cameron KJ, Nyulasi IB, Collier GR, Brown DJ. 1996. Assessment of the effect of increased dietary fibre intake on bowel function in patients with spinal cord injury. *Spinal Cord* 34:277–283.
- Caygill CPJ, Charlett A, Hill MJ. 1998. Relationship between the intake of high-fibre foods and energy and the risk of cancer of the large bowel and breast. *Eur J Cancer Prev* 7:S11–S17.
- Cerda JJ, Robbins FL, Burgin CW, Baumgartner TG, Rice RW. 1988. The effects of grapefruit pectin on patients at risk for coronary heart disease without altering diet or lifestyle. *Clin Cardiol* 11:589–594.
- Chandalia M, Garg A, Lutjohann D, von Bergmann K, Grundy SM, Brinkley LJ. 2000. Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus. *N Engl J Med* 342:1392–1398.

- Chandra R, Barron JL. 2002. Anaphylactic reaction to intravenous sinistrin (Inutest). *Ann Clin Biochem* 39:76.
- Chen H-L, Haack VS, Janecky CW, Vollendorf NW, Marlett JA. 1998. Mechanisms by which wheat bran and oat bran increase stool weight in humans. *Am J Clin Nutr* 68:711–719.
- Chen WJL, Anderson JW. 1986. Hypocholesterolemic effects of soluble fibers. In: Vahouny GV, Kritchevsky D, eds. *Dietary Fiber: Basic and Clinical Aspects*. New York: Plenum Press. Pp. 275–286.
- Chiang MT, Yao HT, Chen HC. 2000. Effect of dietary chitosans with different viscosity on plasma lipids and lipid peroxidation in rats fed on a diet enriched with cholesterol. *Biosci Biotechnol Biochem* 64:965–971.
- Clausen MR, Jorgensen J, Mortensen PB. 1998. Comparison of diarrhea induced by ingestion of fructooligosaccharide Idexx and disaccharide lactulose (role of osmolarity versus fermentation of malabsorbed carbohydrate). *Dig Dis Sci* 43:2696–2707.
- Clevenger MA, Turnbill D, Inoue H, Enomoto M, Allen JA, Henderson LM, Jones E. 1988. Toxicological evaluation of neosugar: Genotoxicity, carcinogenicity, and chronic toxicity. *J Am Coll Toxicol* 7:643–662.
- Colditz GA, Manson JE, Stampfer MJ, Rosner B, Willett WC, Speizer FE. 1992. Diet and risk of clinical diabetes in women. *Am J Clin Nutr* 55:1018–1023.
- Coudray C, Bellanger J, Castiglia-Delavaud C, Remesy C, Vermorel M, Rayssignquier Y. 1997. Effect of soluble or partly soluble dietary fibres supplementation on absorption and balance of calcium, magnesium, iron and zinc in healthy young men. *Eur J Clin Nutr* 51:375–380.
- Cummings JH. 1984. Microbial digestion of complex carbohydrates in man. *Proc Nutr Soc* 43:35–44.
- Cummings JH. 1993. The effect of dietary fiber on fecal weight and composition. In: Spiller GA, ed. *CRC Handbook of Dietary Fiber in Human Nutrition*, 2nd ed. Boca Raton, FL: CRC Press. Pp. 263–349.
- Cummings JH. 2000. Nutritional management of diseases of the gut. In: Garrow JS, James WPT, Ralph A, eds. *Human Nutrition and Dietetics*, 10th ed. Edinburgh: Churchill Livingston. Pp. 547–573.
- Cummings JH, Branch WJ. 1986. Fermentation and the production of short-chain fatty acids in the human large intestine. In: Vahouny GV, Kritchevsky D, eds. *Dietary Fiber: Basic and Clinical Aspects*. New York: Plenum Press. Pp. 131–149.
- Cummings JH, Englyst HN. 1987. Fermentation in the human large intestine and the available substrates. *Am J Clin Nutr* 45:1243–1255.
- Cummings JH, Southgate DAT, Branch W, Houston H, Jenkins DJA, James WPT. 1978. Colonic responses to dietary fibre from carrot, cabbage, apple, bran, and guar gum. *Lancet* 1:5–9.
- Cummings JH, Bingham SA, Heaton KW, Eastwood MA. 1992. Fecal weight, colon cancer risk, and dietary intake of nonstarch polysaccharides (dietary fiber). *Gastroenterology* 103:1783–1789.
- Cummings JH, Beatty ER, Kingman SM, Bingham SA, Englyst HN. 1996. Digestion and physiological properties of resistant starch in the human large bowel. *Br J Nutr* 75:733–747.
- Dales LG, Friedman GD, Ury HK, Grossman S, Williams SR. 1979. A case-control study of relationships of diet and other traits to colorectal cancer in American blacks. *Am J Epidemiol* 109:132–144.
- Danielsson A, Ek B, Nyhlin H, Steen L. 1979. Effect of long term treatment with hydrophilic colloid on serum lipids. *Acta Hepatogastroenterol (Stuttg)* 26:148–153.

- Davidson MH, Maki KC. 1999. Effects of dietary inulin on serum lipids. *J Nutr* 129:1474S–1477S.
- Davidson MH, Dugan LD, Burns JH, Bova J, Story K, Drennan KB. 1991. The hypocholesterolemic effects of  $\beta$ -glucan in oatmeal and oat bran. A dose-controlled study. *J Am Med Assoc* 265:1833–1839.
- Davidson MH, Maki KC, Kong JC, Dugan LD, Torri SA, Hall HA, Drennan KB, Anderson SM, Fulgoni VL, Saldanha LG, Olson BH. 1998. Long-term effects of consuming foods containing psyllium seed husk on serum lipids in subjects with hypercholesterolemia. *Am J Clin Nutr* 67:367–376.
- de Deckere EA, Kloots WJ, van Amelsvoort JM. 1993. Resistant starch decreases serum total cholesterol and triacylglycerol concentrations in rats. *J Nutr* 123:2142–2151.
- Delargy HJ, Burley VJ, O'Sullivan KR, Fletcher RJ, Blundell JE. 1995. Effects of different soluble:insoluble fibre ratios at breakfast on 24-h pattern of dietary intake and satiety. *Eur J Clin Nutr* 49:754–766.
- de Roos N, Heijnen M-L, de Graaf C, Woestenenk G, Hobbel E. 1995. Resistant starch has little effect on appetite, food intake and insulin secretion of healthy young men. *Eur J Clin Nutr* 49:532–541.
- De Stefani E, Correa P, Ronco A, Mendilaharsu M, Guidobono M, Deneo-Pellegrini H. 1997. Dietary fiber and risk of breast cancer: A case-control study in Uruguay. *Nutr Cancer* 28:14–19.
- Dettmar PW, Sykes J. 1998. A multi-centre, general practice comparison of ispaghula husk with lactulose and other laxatives in the treatment of simple constipation. *Curr Med Res Opin* 14:227–233.
- Djoussé L, Ellison RC, Zhang Y, Arnett DK, Sholinsky P, Borecki I. 1998. Relation between dietary fiber consumption and fibrinogen and plasminogen activator inhibitor type 1: The National Heart, Lung, and Blood Institute Family Heart Study. *Am J Clin Nutr* 68:568–575.
- Drake CL, Moses ES, Tandberg D. 1991. Systemic anaphylaxis after ingestion of a psyllium-containing breakfast cereal. *Am J Emerg Med* 9:449–451.
- Duncan KH, Bacon JA, Weinsier RL. 1983. The effects of high and low energy density diets on satiety, energy intake, and eating time of obese and nonobese subjects. *Am J Clin Nutr* 37:763–767.
- Durrington PN, Manning AP, Bolton CH, Hartog M. 1976. Effect of pectin on serum lipids and lipoproteins, whole-gut transit-time, and stool weight. *Lancet* 2:394–396.
- Dutta SK, Hlasko J. 1985. Dietary fiber in pancreatic disease: Effect of high fiber diet on fat malabsorption in pancreatic insufficiency and in vitro study of the interaction of dietary fiber with pancreatic enzymes. *Am J Clin Nutr* 41:517–525.
- Dwyer J. 1980. Diets for children and adolescents that meet the dietary goals. *Am J Dis Child* 134:1073–1080.
- Eliasson K, Ryttig KR, Hylander B, Rossner S. 1992. A dietary fibre supplement in the treatment of mild hypertension. A randomized, double-blind, placebo-controlled trial. *J Hypertens* 10:195–199.
- Ellis PR, Kamalanathan T, Dawoud FM, Strange RN, Coulgate TP. 1988. Evaluation of guar biscuits for use in the management of diabetes: Tests of physiological effects and palatability in non-diabetic volunteers. *Eur J Clin Nutr* 42:425–435.
- Englyst HN, Cummings JH. 1986. Digestion of the carbohydrates of banana (*Musa paradisiaca sapientum*) in the human small intestine. *Am J Clin Nutr* 44:42–50.
- Englyst HN, Cummings JH. 1987. Digestion of polysaccharides of potato in the small intestine of man. *Am J Clin Nutr* 45:423–431.

- Englyst HN, Kingman SM, Cummings JH. 1992. Classification and measurement of nutritionally important starch fractions. *Eur J Clin Nutr* 46:S33–S50.
- Everson GT, Daggy BP, McKinley C, Story JA. 1992. Effects of psyllium hydrophilic mucilloid on LDL-cholesterol and bile acid synthesis in hypercholesterolemic men. *J Lipid Res* 33:1183–1192.
- FDA (U.S. Food and Drug Administration). 1987. Nutrition labeling of food; calorie content. *Fed Regis* 52:28590–28691.
- Feskens EJM, Loeber JG, Kromhout D. 1994. Diet and physical activity as determinants of hyperinsulinemia: The Zutphen Elderly Study. *Am J Epidemiol* 140:350–360.
- Findlay JM, Smith AN, Mitchell WD, Anderson AJB, Eastwood MA. 1974. Effects of unprocessed bran on colon function in normal subjects and in diverticular disease. *Lancet* 1:146–149.
- Franceschi S, Favero A, Decarli A, Negri E, La Vecchia C, Ferraroni M, Russo A, Salvini S, Amadori D, Conti E, Montella M, Giacosa A. 1996. Intake of macronutrients and risk of breast cancer. *Lancet* 347:1351–1356.
- Fraser GE, Sabaté J, Beeson WL, Strahan TM. 1992. A possible protective effect of nut consumption on risk of coronary heart disease. The Adventist Health Study. *Arch Intern Med* 152:1416–1424.
- Frati-Munari AC, Benitez-Pinto W, Raul Ariza-Andracá C, Casarrubias M. 1998. Lowering glycemic index of food by acarbose and Plantago psyllium mucilage. *Arch Med Res* 29:137–141.
- Freudenheim JL, Graham S, Horvath PJ, Marshall JR, Haughey BP, Wilkinson G. 1990. Risks associated with source of fiber and fiber components in cancer of the colon and rectum. *Cancer Res* 50:3295–3300.
- Freudenheim JL, Marshall JR, Vena JE, Laughlin R, Brasure JR, Swanson MK, Nemoto T, Graham S. 1996. Premenopausal breast cancer risk and intake of vegetables, fruits, and related nutrients. *J Natl Cancer Inst* 88:340–348.
- Fuchs CS, Giovannucci EL, Colditz GA, Hunter DJ, Stampfer MJ, Rosner B, Speizer FE, Willett WC. 1999. Dietary fiber and the risk of colorectal cancer and adenoma in women. *N Engl J Med* 340:169–176.
- Fuessl HS, Williams G, Adrian TE, Bloom SR. 1987. Guar sprinkled on food: Effect on glycaemic control, plasma lipids and gut hormones in non-insulin dependent diabetic patients. *Diabetic Med* 4:463–468.
- Gabbe SG, Cohen AW, Herman GO, Schwartz S. 1982. Effect of dietary fiber on the oral glucose tolerance test in pregnancy. *Am J Obstet Gynecol* 143:514–517.
- Gallaher CM, Munion J, Hesslink R, Wise J, Gallaher DD. 2000. Cholesterol reduction by glucomannan and chitosan is mediated by changes in cholesterol absorption and bile acid and fat excretion in rats. *J Nutr* 130:2753–2759.
- Gay-Crosier F, Schreiber G, Hauser C. 2000. Anaphylaxis from inulin in vegetables and processed food. *N Engl J Med* 342:1372.
- Gear JSS, Ware A, Fursdon P, Mann JI, Nolan DJ, Brodribb AJM, Vessey MP. 1979. Symptomless diverticular disease and intake of dietary fibre. *Lancet* 1:511–514.
- Gerber M. 1998. Fibre and breast cancer. *Eur J Cancer Prev* 7:S63–S67.
- Gerhardsson de Verdier M, Hagman U, Steineck G, Rieger Å, Norell SE. 1990. Diet, body mass and colorectal cancer: A case-referent study in Stockholm. *Int J Cancer* 46:832–838.
- Gibson GR, Beatty ER, Wang X, Cummings JH. 1995. Selective stimulation of bifidobacteria in the human colon by oligofructose and inulin. *Gastroenterology* 108:975–982.

- Giovannucci E, Willett WC. 1994. Dietary factors and risk of colon cancer. *Ann Med* 26:443–452.
- Giovannucci E, Stampfer MJ, Colditz G, Rimm EB, Willett WC. 1992. Relationship of diet to risk of colorectal adenoma in men. *J Natl Cancer Inst* 84:91–98.
- Giovannucci E, Rimm EB, Stampfer MJ, Colditz GA, Ascherio A, Willett WC. 1994. Intake of fat, meat, and fiber in relation to risk of colon cancer in men. *Cancer Res* 54:2390–2397.
- Golay A, Koellreutter B, Bloise D, Assal JP, Wursch P. 1992. The effect of muesli or cornflakes at breakfast on carbohydrate metabolism in type 2 diabetic patients. *Diabetes Res Clin Pract* 15:135–141.
- Gold LA, McCourt JP, Merimee TJ. 1980. Pectin: An examination in normal subjects. *Diabetes Care* 3:50–52.
- Goldin BR, Adlercreutz H, Gorbach SL, Warram JH, Dwyer JT, Swenson L, Woods MN. 1982. Estrogen excretion patterns and plasma levels in vegetarian and omnivorous women. *N Engl J Med* 307:1542–1547.
- Goodman MT, Wilkens LR, Hankin JH, Lyu L-C, Wu AH, Kolonel LN. 1997. Association of soy and fiber consumption with the risk of endometrial cancer. *Am J Epidemiol* 146:294–306.
- Gorbach SL, Goldin BR. 1987. Diet and the excretion and enterohepatic cycling of estrogens. *Prev Med* 16:525–529.
- Goulder TJ, Alberti KGMM, Jenkins DA. 1978. Effect of added fiber on the glucose and metabolic response to a mixed meal in normal and diabetic subjects. *Diabetes Care* 1:351–355.
- Graham S, Hellmann R, Marshall J, Freudenheim J, Vena J, Swanson M, Zielezny M, Nemoto T, Stubbe N, Raimondo T. 1991. Nutritional epidemiology of postmenopausal breast cancer in western New York. *Am J Epidemiol* 134:552–566.
- Graham S, Zielezny M, Marshall J, Priore R, Freudenheim J, Brasure J, Haughey B, Nasca P, Zdeb M. 1992. Diet in the epidemiology of postmenopausal breast cancer in the New York State Cohort. *Am J Epidemiol* 136:1327–1337.
- Grizard D, Barthomeuf C. 1999. Non-digestible oligosaccharides used as prebiotic agents: Mode of production and beneficial effects on animal and human health. *Reprod Nutr Dev* 39:563–588.
- Groop P-H, Aro A, Stenman S, Groop L. 1993. Long-term effects of guar gum in subjects with non-insulin-dependent diabetes mellitus. *Am J Clin Nutr* 58:513–518.
- Grossman SP. 1986. The role of glucose, insulin and glucagon in the regulation of food intake and body weight. *Neurosci Biobehav Rev* 10:295–315.
- Guerciolini R, Radu-Radulescu L, Boldrin M, Dallas J, Moore R. 2001. Comparative evaluation of fecal fat excretion induced by orlistat and chitosan. *Obes Res* 9:364–367.
- Haenszel W, Kurihara M. 1968. Studies of Japanese migrants. I. Mortality from cancer and other diseases among Japanese in the United States. *J Natl Cancer Inst* 40:43–68.
- Hallfrisch J, Powell A, Carafelli C, Reiser S, Prather ES. 1987. Mineral balances of men and women consuming high fiber diets with complex or simple carbohydrate. *J Nutr* 117:48–55.
- Hallfrisch J, Tobin JD, Muller DC, Andres R. 1988. Fiber intake, age, and other coronary risk factors in men of the Baltimore Longitudinal Study (1959–1975). *J Gerontol Med Sci* 43:M64–M68.

- Hallfrisch J, Scholfield DJ, Behall KM. 1995. Diets containing soluble oat extracts improve glucose and insulin responses of moderately hypercholesterolemic men and women. *Am J Clin Nutr* 61:379–384.
- Harris PJ, Ferguson LR. 1993. Dietary fibre: Its composition and role in protection against colorectal cancer. *Mutat Res* 290:97–110.
- Harris PJ, Triggs CM, Roberton AM, Watson ME, Ferguson LR. 1996. The adsorption of heterocyclic aromatic amines by model dietary fibres with contrasting compositions. *Chem Biol Interact* 100:13–25.
- Haseman JK, Arnold J, Eustis SL. 1990. Tumor incidences in Fischer 344 rats: NTP historical data. In: GA Boorman, ed. *Pathology of the Fischer Rat*. San Diego, CA: Academic Press. Pp. 557–564.
- Health and Welfare Canada. 1985. *Report of the Expert Advisory Committee on Dietary Fibre*. Ottawa: Supply and Services Canada.
- Health Canada. 1988. *Guideline Concerning the Safety and Physiological Effects of Novel Fibre Sources and Food Products Containing Them*. Ottawa: Food Directorate, Health Protection Branch, Health Canada.
- Health Canada. 1997. Appendix 2. Guideline for planning and statistical review of clinical laxation studies for dietary fibre. In: *Guideline Concerning the Safety and Physiological Effects of Novel Fibre Sources and Food Products Containing Them*. Ottawa: Food Directorate, Health Protection Branch, Health Canada.
- Heaton KW. 1973. Food fibre as an obstacle to energy intake. *Lancet* 2:1418–1421.
- Heijnen M-LA, van Amelsvoort JMM, Deurenberg P, Beynen AC. 1996. Neither raw nor retrograded resistant starch lowers fasting serum cholesterol concentrations in healthy normolipidemic subjects. *Am J Clin Nutr* 64:312–318.
- Heijnen M-LA, van Amelsvoort JMM, Deurenberg P, Beynen AC. 1998. Limited effect of consumption of uncooked ( $RS_2$ ) or retrograded ( $RS_3$ ) resistant starch on putative risk factors for colon cancer in healthy men. *Am J Clin Nutr* 67:322–331.
- Heilbrun LK, Nomura A, Hankin JH, Stemmermann GN. 1989. Diet and colorectal cancer with special reference to fiber intake. *Int J Cancer* 44:1–6.
- Henquin JC. 1988. *Reproduction Toxicity: Study on the Influence of Fructooligosaccharides on the Development of Foetal and Postnatal Rat*. Raffinerie Tirlemontoise Internal Report. Photocopy.
- Hill MJ. 1997. Cereals, cereal fibre and colorectal cancer risk: A review of the epidemiological literature. *Eur J Cancer Prev* 6:219–225.
- Hillman LC, Peters SG, Fisher CA, Pomare EW. 1983. Differing effects of pectin, cellulose and lignin on stool pH, transit time and weight. *Br J Nutr* 50:189–195.
- Hillman LC, Peters SG, Fisher CA, Pomare EW. 1985. The effects of the fiber components pectin, cellulose and lignin on serum cholesterol levels. *Am J Clin Nutr* 42:207–213.
- Ho SC, Tai ES, Eng PHK, Tan CE, Fok ACK. 2001. In the absence of dietary surveillance, chitosan does not reduce plasma lipids or obesity in hypercholesterolaemic obese Asian subjects. *Singapore Med J* 42:6–10.
- Hoff G, Moen IE, Trygg K, Frølich W, Sauar J, Vatn M, Gjone E, Larsen S. 1986. Epidemiology of polyps in the rectum and sigmoid colon. Evaluation of nutritional factors. *Scand J Gastroenterol* 21:199–204.
- Holman RR, Steemson J, Darling P, Turner RC. 1987. No glycemic benefit from guar administration in NIDDM. *Diabetes Care* 10:68–71.
- Holt S, Brand J, Soveny C, Hansky J. 1992. Relationship of satiety to postprandial glycaemic, insulin and cholecystokinin responses. *Appetite* 18:129–141.

- Howe GR, Benito E, Castelletto R, Cornée J, Estéve J, Gallagher RP, Iscovich JM, Deng-ao J, Kaaks R, Kune GA, Kune S, L'Abbé KA, Lee HP, Lee M, Miller AB, Peters RK, Potter JD, Riboli E, Slattery ML, Trichopoulos D, Tuyns A, Tzonou A, Whittemore AS, Wu-Williams AH, Shu Z. 1992. Dietary intake of fiber and decreased risk of cancers of the colon and rectum: Evidence from the combined analysis of 13 case-control studies. *J Natl Cancer Inst* 84:1887–1896.
- Humble CG, Malarcher AM, Tyroler HA. 1993. Dietary fiber and coronary heart disease in middle-aged hypercholesterolemic men. *Am J Prev Med* 9:197–202.
- Hunt R, Fedorak R, Frohlich J, McLennan C, Pavilani A. 1993. Therapeutic role of dietary fibre. *Can Fam Physician* 39:897–910.
- Hylla S, Gostner A, Dusel G, Anger H, Bartram H-P, Christl SU, Kasper H, Scheppach W. 1998. Effects of resistant starch on the colon in healthy volunteers: Possible implications for cancer prevention. *Am J Clin Nutr* 67:136–142.
- Ingram DM. 1981. Trends in diet and breast cancer mortality in England and Wales 1928–1977. *Nutr Cancer* 3:75–80.
- IOM (Institute of Medicine). 1991. *Nutrition During Lactation*. Washington, DC: National Academy Press.
- IOM. 2001. *Dietary Reference Intakes: Proposed Definition of Dietary Fiber*. Washington, DC: National Academy Press.
- Iscovich JM, L'Abbé KA, Castelletto R, Calzona A, Bernedo A, Chopita NA, Jmelnitsky AC, Kaldor J, Howe GR. 1992. Colon cancer in Argentina. II: Risk from fibre, fat and nutrients. *Int J Cancer* 51:858–861.
- Ito N, Hasegawa R, Sano M, Tamano S, Esumi H, Takayama S, Sugimura T. 1991. A new colon and mammary carcinogen in cooked food, 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP). *Carcinogenesis* 12:1503–1506.
- Jackson KG, Taylor GRJ, Clohessy AM, Williams CM. 1999. The effect of the daily intake of inulin fasting lipid, insulin and glucose concentrations in middle-aged men and women. *Br J Nutr* 82:23–30.
- Jacobs DR, Meyer KA, Kushi LH, Folsom AR. 1998. Whole-grain intake may reduce the risk of ischemic heart disease death in postmenopausal women: The Iowa Women's Health Study. *Am J Clin Nutr* 68:248–257.
- Jacobs LR. 1986. Relationship between dietary fiber and cancer: Metabolic, physiologic, and cellular mechanisms. *Proc Soc Exp Biol Med* 183:299–310.
- Jain M, Cook GM, Davis FG, Grace MG, Howe GR, Miller AB. 1980. A case-control study of diet and colo-rectal cancer. *Int J Cancer* 26:757–768.
- James JM, Cooke SK, Barnett A, Sampson HA. 1991. Anaphylactic reactions to a psyllium-containing cereal. *J Allergy Clin Immunol* 88:402–408.
- Jenkins DJA, Newton C, Leeds AR, Cummings JH. 1975. Effect of pectin, guar gum, and wheat fibre on serum cholesterol. *Lancet* 1:1116–1117.
- Jenkins DJA, Wolever TMS, Leeds AR, Gassull MA, Haisman P, Dilawari J, Goff DV, Metz GL, Alberti KGMM. 1978. Dietary fibres, fibre analogues, and glucose tolerance: Importance of viscosity. *Br Med J* 1:1392–1394.
- Jenkins DJA, Wolever TMS, Collier GR, Ocana A, Rao AV, Buckley G, Lam Y, Mayer A, Thompson LU. 1987. Metabolic effects of a low-glycemic-index diet. *Am J Clin Nutr* 46:968–975.
- Jenkins DJA, Vuksan V, Kendall CWC, Würsch P, Jeffcoat R, Waring S, Mehling CC, Vidgen E, Augustin LSA, Wong E. 1998. Physiological effects of resistant starches on fecal bulk, short chain fatty acids, blood lipids and glycemic index. *J Am Coll Nutr* 17:609–616.

- Jenkins DJA, Kendall CWC, Vuksan V, Vidgen E, Parler T, Faulkner D, Mehling CC, Garsetti M, Testolin G, Cunnane SC, Ryan MA, Corey PN. 2002. Soluble fiber intake at a dose approved by the US Food and Drug Administration for a health claim of health benefits: Serum lipid risk factors for cardiovascular disease assessed in a randomized controlled crossover trial. *Am J Clin Nutr* 75:834–839.
- Jennings CD, Boleyn K, Bridges SR, Wood PJ, Anderson JW. 1988. A comparison of the lipid-lowering and intestinal morphological effects of cholestyramine, chitosan, and oat gum in rats. *Proc Soc Exp Biol Med* 189:13–20.
- Jie Z, Bang-Yao L, Ming-Jie X, Hai-Wei L, Zu-Kang Z, Ting-Song W, Craig SAS. 2000. Studies on the effects of polydextrose intake on physiologic function in Chinese people. *Am J Clin Nutr* 72:1503–1509.
- Judd PA, Truswell AS. 1981. The effect of rolled oats on blood lipids and fecal steroid excretion in man. *Am J Clin Nutr* 34:2061–2067.
- Kang JY, Doe WF. 1979. Unprocessed bran causing intestinal obstruction. *Br Med J* 1:1249–1250.
- Kato I, Akhmedkhanov A, Koenig K, Toniolo PG, Shore RE, Riboli E. 1997. Prospective study of diet and female colorectal cancer: The New York University Women's Health Study. *Nutr Cancer* 28:276–281.
- Kay RM, Truswell AS. 1977. Effect of citrus pectin on blood lipids and fecal steroid excretion in man. *Am J Clin Nutr* 30:171–175.
- Kelsay JL, Behall KM, Prather ES. 1978. Effect of fiber from fruits and vegetables on metabolic responses of human subjects. I. Bowel transit time, number of defecations, fecal weight, urinary excretions of energy and nitrogen and apparent digestibilities of energy, nitrogen, and fat. *Am J Clin Nutr* 31:1149–1153.
- Key TJA, Thorogood M, Appleby PN, Burr ML. 1996. Dietary habits and mortality in 11,000 vegetarians and health conscious people: Results of a 17 year follow up. *Br Med J* 313:775–779.
- Khaw K, Barrett-Connor E. 1987. Dietary fiber and reduced ischemic heart disease mortality rates in men and women: A 12-year prospective study. *Am J Epidemiol* 126:1093–1102.
- Kirby RW, Anderson JW, Sieling B, Rees ED, Chen W-JL, Miller RE, Kay RM. 1981. Oat-bran intake selectively lowers serum low-density lipoprotein cholesterol concentrations of hypercholesterolemic men. *Am J Clin Nutr* 34:824–829.
- Kleessen B, Sykura B, Zunft HJ, Blaut M. 1997. Effects of inulin and lactose on fecal microflora, microbial activity, and bowel habit in elderly constipated persons. *Am J Clin Nutr* 65:1397–1402.
- Klurfeld DM. 1992. Dietary fiber-mediated mechanisms in carcinogenesis. *Cancer Res* 52:2055S–2059S.
- Knekt P, Steineck G, Järvinen R, Hakulinen T, Aromaa A. 1994. Intake of fried meat and risk of cancer: A follow-up study in Finland. *Int J Cancer* 59:756–760.
- Knox TA, Kassarjian Z, Dawson-Hughes B, Golner BB, Dallal GE, Arora S, Russell RM. 1991. Calcium absorption in elderly subjects on high- and low-fiber diets: Effect of gastric acidity. *Am J Clin Nutr* 53:1480–1486.
- Kochen MM, Wegscheider K, Abholz HH. 1985. Prophylaxis of constipation by wheat bran: A randomized study in hospitalized patients. *Digestion* 31:220–224.
- Krishnamachar S, Mickelsen O. 1987. The influence of different carbohydrate sources on blood glucose levels and satiety: Effect of physical activity on blood glucose response. *Hum Nutr Food Sci Nutr* 41F:29–39.

- Kromhout D, Bosscheriet EB, de Lezenne Coulander C. 1982. Dietary fibre and 10-year mortality from coronary heart disease, cancer, and all causes. The Zutphen Study. *Lancet* 2:518–522.
- Krotkiewski M. 1987. Effect of guar gum on the arterial blood pressure. *Acta Med Scand* 222:43–49.
- Kushi LH, Lew RA, Stare FJ, Ellison CR, el Lozy M, Bourke G, Daly L, Graham I, Hickey N, Mulcahy R, Kevaney J. 1985. Diet and 20-year mortality from coronary heart disease. The Ireland-Boston Diet-Heart Study. *N Engl J Med* 312:811–818.
- Lagier F, Cartier A, Somer J, Dolovich J, Malo JL. 1990. Occupational asthma caused by guar gum. *J Allergy Clin Immunol* 85:785–790.
- Landin K, Holm G, Tengborn L, Smith U. 1992. Guar gum improves insulin sensitivity, blood lipids, blood pressure, and fibrinolysis in healthy men. *Am J Clin Nutr* 56:1061–1065.
- Lantner RR, Espiritu BR, Zumerchik P, Tobin MC. 1990. Anaphylaxis following ingestion of a psyllium-containing cereal. *J Am Med Assoc* 264:2534–2536.
- Lanza E. 1990. National Cancer Institute Satellite Symposium on Fiber and Colon Cancer. In: Kritchevsky D, Bonfield C, Anderson JW, eds. *Dietary Fiber: Chemistry, Physiology, and Health Effects*. New York: Plenum Press. Pp. 383–387.
- Larson DE, Hunter GR, Williams MJ, Kekes-Szabo T, Nyikos I, Goran MI. 1996. Dietary fat in relation to body fat and intraabdominal adipose tissue: A cross-sectional analysis. *Am J Clin Nutr* 64:677–684.
- Leathwood P, Pollet P. 1988. Effects of slow release carbohydrates in the form of bean flakes on the evolution of hunger and satiety in man. *Appetite* 10:1–11.
- Lee HP, Gourley L, Duffy SW, Estève J, Lee J, Day NE. 1991. Dietary effects on breast-cancer risk in Singapore. *Lancet* 337:1197–1200.
- Lei KY, Davis MW, Fang MM, Young LC. 1980. Effect of pectin on zinc, copper and iron balances in humans. *Nutr Rep Int* 22:459–466.
- Lev R. 1990. Malignant potential of adenomatous polyps. In: *Adenomatous Polyps of the Colon: Pathobiological and Clinical Features*. New York: Springer-Verlag. Pp. 53–89.
- Levin EG, Miller VT, Muesing RA, Stoy DB, Balm TK, LaRosa JC. 1990. Comparison of psyllium hydrophilic mucilloid and cellulose as adjuncts to a prudent diet in the treatment of mild to moderate hypercholesterolemia. *Arch Intern Med* 150:1822–1827.
- Levine AS, Billington CJ. 1994. Dietary fiber: Does it affect food intake and body weight? In: Fernstrom JD, Miller GD, eds. *Appetite and Body Weight Regulation: Sugar, Fat, and Macronutrient Substitutes*. Boca Raton, FL: CRC Press. Pp. 191–200.
- Librenti MC, Cocchi M, Orsi E, Pozza G, Micossi P. 1992. Effect of soya and cellulose fibers on postprandial glycemic response in type II diabetic patients. *Diabetes Care* 15:111–113.
- Lichtenstein AH, Ausman LM, Jalbert SM, Vilella-Bach M, Jauhiainen M, McGladdery S, Erkkila AT, Ehnholm C, Frohlich J, Schaefer EJ. 2002. Efficacy of a Therapeutic Lifestyle Change/Step 2 diet in moderately hypercholesterolemic middle-aged and elderly female and male subjects. *J Lipid Res* 43:264–273.
- Lipid Research Clinics Program. 1984. The Lipid Research Clinics Coronary Primary Prevention Trial results. II. The relationship of reduction in incidence of coronary heart disease to cholesterol lowering. *J Am Med Assoc* 251:365–374.

- Little J, Logan RFA, Hawtin PG, Hardcastle JD, Turner ID. 1993. Colorectal adenomas and diet: A case-control study of subjects participating in the Nottingham Faecal Occult Blood Screening Programme. *Br J Cancer* 67:177–184.
- Livesey G. 1990. Energy values of unavailable carbohydrate and diets: An inquiry and analysis. *Am J Clin Nutr* 51:617–637.
- Loening-Baucke V. 1993. Chronic constipation in children. *Gastroenterology* 105:1557–1564.
- Lovegrove JA, Clohessy A, Milon H, Williams CM. 2000. Modest doses of  $\beta$ -glucan do not reduce concentrations of potentially atherogenic lipoproteins. *Am J Clin Nutr* 72:49–55.
- Low AG. 1990. Nutritional regulation of gastric secretion, digestion and emptying. *Nutr Res Rev* 3:229–252.
- LSRO (Life Sciences Research Office). 1987. *Physiological Effects and Health Consequences of Dietary Fiber*. Bethesda, MD: LSRO.
- Lubin F, Wax Y, Modan B. 1986. Role of fat, animal protein, and dietary fiber in breast cancer etiology: A case-control study. *J Natl Cancer Inst* 77:605–612.
- Luo J, Rizkalla SW, Alamowitch C, Boussairi A, Blayo A, Barry J-L, Laffitte A, Guyon F, Bornet FRJ, Slama G. 1996. Chronic consumption of short-chain fructooligosaccharides by healthy subjects decreased basal hepatic glucose production but had no effect on insulin-stimulated glucose metabolism. *Am J Clin Nutr* 63:939–945.
- Lupton JR. 1995. Butyrate and colonic cytokinetics: Differences between in vitro and in vivo studies. *Eur J Cancer Prev* 4:373–378.
- Lupton JR, Morin JL, Robinson MC. 1993. Barley bran flour accelerates gastrointestinal transit time. *J Am Diet Assoc* 93:881–885.
- Lyon JL, Mahoney AW, West DW, Gardner JW, Smith KR, Sorenson AW, Stanish W. 1987. Energy intake: Its relationship to colon cancer risk. *J Natl Cancer Inst* 78:853–861.
- Macfarlane GT, Englyst HN. 1986. Starch utilization by the human large intestinal microflora. *J Appl Bacteriol* 60:195–201.
- MacLennan R, Macrae F, Bain C, Battistutta D, Chapuis P, Gratten H, Lambert J, Newland RC, Ngu M, Russell A, Ward M, Wahlqvist ML. 1995. Randomized trial of intake of fat, fiber, and beta carotene to prevent colorectal adenomas. *J Natl Cancer Inst* 87:1760–1766.
- MacMahon M, Carless J. 1998. Ispaghula husk in the treatment of hypercholesterolemia: A double-blind controlled study. *J Cardiovasc Risk* 5:167–172.
- Macquart-Moulin G, Riboli E, Cornée J, Charnay B, Berthezène P, Day N. 1986. Case-control study on colorectal cancer and diet in Marseilles. *Int J Cancer* 38:183–191.
- Macquart-Moulin G, Riboli E, Cornée J, Kaaks R, Berthezène P. 1987. Colorectal polyps and diet: A case-control study in Marseilles. *Int J Cancer* 40:179–188.
- Manousos O, Day NE, Tzonou A, Papadimitriou C, Kapetanakis A, Polychronopoulou-Trichopoulou A, Trichopoulos D. 1985. Diet and other factors in the aetiology of diverticulosis: An epidemiological study in Greece. *Gut* 26:544–549.
- Marlett JA. 1992. Content and composition of dietary fiber in 117 frequently consumed foods. *J Am Diet Assoc* 92:175–186.
- Marlett JA, Longacre MJ. 1996. Comparison of in vitro and in vivo measures of resistant starch in selected grain products. *Cereal Chem* 73:63–68.
- Mathur KS, Khan MA, Sharma RD. 1968. Hypocholesterolaemic effect of Bengal gram: A long-term study in man. *Br Med J* 1:30–31.

- McBurney MI. 1991. Potential water-holding capacity and short-chain fatty acid production from purified fiber sources in a fecal incubation system. *Nutrition* 7:421–424.
- McBurney MI, Thompson LU. 1990. Fermentative characteristics of cereal brans and vegetable fibers. *Nutr Cancer* 13:271–280.
- McCann SE, Freudenheim JL, Marshall JR, Brasuer JR, Swanson MK, Graham S. 2000. Diet in the epidemiology of endometrial cancer in western New York (United States). *Cancer Causes Control* 11:965–974.
- McCann SE, Moysich KB, Mettlin C. 2001. Intakes of selected nutrients and food groups and risk of ovarian cancer. *Nutr Cancer* 39:19–28.
- McClung HJ, Boyne LJ, Linsheid T, Heitlinger LA, Murray RD, Fyda J, Li BUK. 1993. Is combination therapy for encopresis nutritionally safe? *Pediatrics* 91:591–594.
- McClung HJ, Boyne L, Heitlinger L. 1995. Constipation and dietary fiber intake in children. *Pediatrics* 96:999–1001.
- McKeown-Eyssen GE, Bright-See E, Bruce WR, Jazmaji V. 1994. A randomized trial of a low fat high fibre diet in the recurrence of colorectal polyps. *J Clin Epidemiol* 47:525–536.
- McRorie JW, Daggy BP, Morel JG, Diersing PS, Miner PB, Robinson M. 1998. Psyllium is superior to docusate sodium for treatment of chronic constipation. *Aliment Pharmacol Ther* 12:491–497.
- McRorie J, Kesler J, Bishop L, Filloon T, Allgood G, Sutton M, Hunt T, Laurent A, Rudolph C. 2000. Effects of wheat bran and Olestra on objective measures of stool and subjective reports of GI symptoms. *Am J Gastroenterol* 95:1244–1252.
- Mennen LI, Witteman JCM, den Breeijen JH, Schouten EG, de Jong PTVM, Hofman A, Grobbee DE. 1997. The association of dietary fat and fiber with coagulation factor VII in the elderly: The Rotterdam Study. *Am J Clin Nutr* 65:732–736.
- Meyer KA, Kushi LH, Jacobs DR, Slavin J, Sellers TA, Folsom AR. 2000. Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. *Am J Clin Nutr* 71:921–930.
- Miller AB, Howe GR, Jain M, Craib KJP, Harrison L. 1983. Food items and food groups as risk factors in a case-control study of diet and colo-rectal cancer. *Int J Cancer* 32:155–161.
- Miller WC, Niederpruem MG, Wallace JP, Lindeman AK. 1994. Dietary fat, sugar, and fiber predict body fat content. *J Am Diet Assoc* 94:612–615.
- Modan B, Barell V, Lubin F, Modan M, Greenberg RA, Graham S. 1975. Low-fiber intake as an etiologic factor in cancer of the colon. *J Natl Cancer Inst* 55:15–18.
- Morais MB, Vítolo MR, Aguirre ANC, Fagundes-Neto U. 1999. Measurement of low dietary fiber intake as a risk factor for chronic constipation in children. *J Pediatr Gastroenterol Nutr* 29:132–135.
- Morales M, Llopis A. 1992. Breast cancer and diet in Spain. *J Environ Pathol Toxicol Oncol* 11:157–167.
- Morris JN, Marr JW, Clayton DG. 1977. Diet and heart: A postscript. *Br Med J* 2:1307–1314.
- Moshfegh AJ, Friday JE, Goldman JP, Ahuja JKC. 1999. Presence of inulin and oligofructose in the diets of Americans. *J Nutr* 129:1407S–1411S.
- National Cholesterol Education Program. 1991. *Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents*. NIH Publication No. 91-2732. Bethesda, MD: National Heart, Lung, and Blood Institute.

- Neugut AI, Garbowski GC, Lee WC, Murray T, Nieves JW, Forde KA, Treat MR, Waye JD, Fenoglio-Preiser C. 1993. Dietary risk factors for the incidence and recurrence of colorectal adenomatous polyps. A case-control study. *Ann Intern Med* 11:91–95.
- Niemi MK, Keinänen-Kiukaanniemi SM, Salmela PI. 1988. Long-term effects of guar gum and microcrystalline cellulose on glycaemic control and serum lipids in type 2 diabetes. *Eur J Clin Pharmacol* 34:427–429.
- Niho N, Tamura T, Toyoda K, Uneyama C, Shibutani M, Hirose M. 1999. A 13-week subchronic toxicity study of chitin in F344 rats. *Kokuritsu Iyakuhin Shokuhin Eisei Kenkyusho Hokoku* 117:129–134.
- Nishimune T, Sumimoto T, Konishi Y, Yakushiji T, Komachi Y, Mitsuhashi Y, Nakayama I, Okazaki K, Tsuda T, Ichihashi A, Adachi T, Imanaka M, Kirigaya T, Ushio H, Kasuga Y, Saeki K, Yamamoto Y, Ichikawa T, Nakahara S, Oda S. 1993. Dietary fiber intake of Japanese younger generations and the recommended daily allowance. *J Nutr Sci Vitaminol (Tokyo)* 39:263–278.
- Noble JA, Grannis FW. 1984. Acute esophageal obstruction by a psyllium-based bulk laxative. *Chest* 86:800.
- NRC (National Research Council). 1989. *Diet and Health: Implications for Reducing Chronic Disease Risk*. Washington, DC: National Academy Press.
- Obarzanek E, Sacks FM, Vollmer WM, Bray GA, Miller ER, Lin P-H, Karanja NM, Most-Windhauser MM, Moore TJ, Swain JF, Bales CW, Proschan MA. 2001. Effects on blood lipids of a blood pressure-lowering diet: The Dietary Approaches to Stop Hypertension (DASH) Trial. *Am J Clin Nutr* 74:80–89.
- O'Brien KO, Allen LH, Quatromoni P, Siu-Calderra M-L, Vieira NE, Perez A, Holick MF, Yerger AL. 1993. High fiber diets slow bone turnover in young men but have no effect on efficiency of intestinal calcium absorption. *J Nutr* 123:2122–2128.
- Ohkuma K, Wakabayashi S. 2001. Fibersol-2: A soluble, non-digestible, starch-derived dietary fibre. In: McCleary BV, Prosky L, eds. *Advanced Dietary Fibre Technology*. Oxford: Blackwell Science. Pp. 510–523.
- Ohno Y, Yoshida O, Oishi K, Okada K, Yamabe H, Schroeder FH. 1988. Dietary β-carotene and cancer of the prostate: A case-control study in Kyoto, Japan. *Cancer Res* 48:1331–1336.
- Olesen M, Gudmand-Høyer E. 2000. Efficacy, safety, and tolerability of fructooligosaccharides in the treatment of irritable bowel syndrome. *Am J Clin Nutr* 72:1570–1575.
- Olson BH, Anderson SM, Becker MP, Anderson JW, Hunninghake DB, Jenkins DJA, LaRose JC, Rippe JM, Roberts DCK, Stoy DB, Summerbell CD, Truswell AS, Wolever TMS, Morris DH, Fulgoni VL. 1997. Psyllium-enriched cereals lower blood total cholesterol and LDL cholesterol, but not HDL cholesterol, in hypercholesterolemic adults: Results of a meta-analysis. *J Nutr* 127:1973–1980.
- Pastors JG, Blaisdell PW, Balm TK, Asplin CM, Pohl SL. 1991. Psyllium fiber reduces rise in postprandial glucose and insulin concentrations in patients with non-insulin-diabetes mellitus. *Am J Clin Nutr* 53:1431–1435.
- Patrick PG, Gohman SM, Marx SC, DeLegge MH, Greenberg NA. 1998. Effect of supplements of partially hydrolyzed guar gum on the occurrence of constipation and use of laxative agents. *J Am Diet Assoc* 98:912–914.
- Pedersen A, Sandstrom B, Van Amelsvoort JM. 1997. The effect of ingestion of inulin on blood lipids and gastrointestinal symptoms in healthy females. *Br J Nutr* 78:215–222.

- Penagini R, Velio P, Vigorelli R, Bozzani A, Castagnone D, Ranzi T, Bianchi PA. 1986. The effect of dietary guar on serum cholesterol, intestinal transit, and fecal output in man. *Am J Gastroenterol* 81:123–125.
- Petrakis NL, King EB. 1981. Cytological abnormalities in nipple aspirates of breast fluid from women with severe constipation. *Lancet* 2:1203–1204.
- Phillips J, Muir JG, Birkett A, Lu ZX, Jones GP, O'Dea K, Young GP. 1995. Effect of resistant starch on fecal bulk and fermentation-dependent events in humans. *Am J Clin Nutr* 62:121–130.
- Pick ME, Hawrysh ZJ, Gee MI, Toth E, Garg ML, Hardin RT. 1996. Oat bran concentrate bread products improve long-term control of diabetes: A pilot study. *J Am Diet Assoc* 96:1254–1261.
- Pietinen P, Rimm EB, Korhonen P, Hartman AM, Willett WC, Albanes D, Virtamo J. 1996. Intake of dietary fiber and risk of coronary heart disease in a cohort of Finnish men. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. *Circulation* 94:2720–2727.
- Pietinen P, Malila N, Virtanen M, Hartman TJ, Tangrea JA, Albanes D, Virtamo J. 1999. Diet and risk of colorectal cancer in a cohort of Finnish men. *Cancer Causes Control* 10:387–396.
- Pittler MH, Abbot NC, Harkness EF, Ernst E. 1999. Randomized, double-blind trial of chitosan for body weight reduction. *Eur J Clin Nutr* 53:379–381.
- Platz EA, Giovannucci E, Rimm EB, Rockett HRH, Stampfer MJ, Colditz GA, Willett WC. 1997. Dietary fiber and distal colorectal adenoma in men. *Cancer Epidemiol Biomarkers Prev* 6:661–670.
- Prior A, Whorwell PJ. 1987. Double blind study of ispagula in irritable bowel syndrome. *Gut* 28:1510–1513.
- Raben A, Tagliabue A, Christensen NJ, Madsen J, Holst JJ, Astrup A. 1994. Resistant starch: The effect on postprandial glycemia, hormonal response, and satiety. *Am J Clin Nutr* 60:544–551.
- Ranhotra GS, Gelroth JA, Leinen SD. 1997. Hypolipidemic effect of resistant starch in hamsters is not dose dependent. *Nutr Res* 17:317–323.
- Razdan A, Pettersson D. 1994. Effect of chitin and chitosan on nutrient digestibility and plasma lipid concentrations in broiler chickens. *Br J Nutr* 72:277–288.
- Razdan A, Pettersson D. 1996. Hypolipidaemic, gastrointestinal and related responses of broiler chickens to chitosans of different viscosity. *Br J Nutr* 76:387–397.
- Razdan A, Pettersson D, Pettersson J. 1997. Broiler chicken body weights, feed intakes, plasma lipid and small-intestinal bile acid concentrations in response to feeding of chitosan and pectin. *Br J Nutr* 78:283–291.
- Rigaud D, Ryttig KR, Angel LA, Apfelbaum M. 1990. Overweight treated with energy restriction and a dietary fibre supplement: A 6-month randomized, double-blind, placebo-controlled trial. *Int J Obes* 14:763–769.
- Rigaud D, Paycha F, Meulemans A, Merrouche M, Mignon M. 1998. Effect of psyllium on gastric emptying, hunger feeling and food intake in normal volunteers: A double blind study. *Eur J Clin Nutr* 52:239–245.
- Rimm EB, Ascherio A, Giovannucci E, Spiegelman D, Stampfer MJ, Willett WC. 1996. Vegetable, fruit, and cereal fiber intake and risk of coronary heart disease among men. *J Am Med Assoc* 275:447–451.
- Ripsin CM, Keenan JM, Jacobs DR, Elmer PJ, Welch RR, Van Horn L, Liu K, Turnbull WH, Thye FW, Kestin M, Hegsted M, Davidson DM, Davidson MH, Dugan LD, Demark-Wahnefried W, Beling S. 1992. Oat products and lipid lowering. A meta-analysis. *J Am Med Assoc* 267:3317–3325.

- Risch HA, Jain M, Marrett LD, Howe GR. 1994. Dietary fat intake and risk of epithelial ovarian cancer. *J Natl Cancer Inst* 86:1409–1415.
- Ritz P, Krempf M, Cloarec D, Champ M, Charbonnel B. 1991. Comparative continuous-indirect-calorimetry study of two carbohydrates with different glycemic indices. *Am J Clin Nutr* 54:855–859.
- Rivellese A, Riccardi G, Giacco A, Pacioni D, Genovese S, Mattioli PL, Mancini M. 1980. Effect of dietary fibre on glucose control and serum lipoproteins in diabetic patients. *Lancet* 2:447–450.
- Roberfroid M. 1993. Dietary fiber, inulin, and oligofructose: A review comparing their physiological effects. *Crit Rev Food Sci Nutr* 33:103–148.
- Roberts PL, Veidenheimer MC. 1990. Diverticular disease of the colon. In: Bayless TM, ed. *Current Therapy in Gastroenterology and Liver Disease—3*. Toronto: Decker Mosby. Pp. 416–419.
- Roediger WEW. 1980. The colonic epithelium in ulcerative colitis: An energy-deficiency disease? *Lancet* 2:712–715.
- Roediger WEW. 1982. Utilization of nutrients by isolated epithelial cells of the rat colon. *Gastroenterology* 83:424–429.
- Roediger WE, Duncan A, Kapaniris O, Millard S. 1993. Reducing sulfur compounds of the colon impair colonocyte nutrition: Implications for ulcerative colitis. *Gastroenterology* 104:802–809.
- Rohan TE, McMichael AJ, Baghurst PA. 1988. A population-based case-control study of diet and breast cancer in Australia. *Am J Epidemiol* 128:478–489.
- Rohan TE, Howe GR, Friedenreich CM, Jain M, Miller AB. 1993. Dietary fiber, vitamins A, C, and E, and risk of breast cancer: A cohort study. *Cancer Causes Control* 4:29–37.
- Rohan TE, Howe GR, Burch JD, Jain M. 1995. Dietary factors and risk of prostate cancer: A case-control study in Ontario, Canada. *Cancer Causes Control* 6:145–154.
- Roma E, Adamidis D, Nikolara R, Constantopoulos A, Messaritakis J. 1999. Diet and chronic constipation in children: The role of fiber. *J Pediatr Gastroenterol Nutr* 28:169–174.
- Ronco A, De Stefani E, Boffetta P, Deneo-Pellegrini H, Mendilaharsu M, Leborgne F. 1999. Vegetables, fruits, and related nutrients and risk of breast cancer: A case-control study in Uruguay. *Nutr Cancer* 35:111–119.
- Rose DP. 1990. Dietary fiber and breast cancer. *Nutr Cancer* 13:1–8.
- Rose DP. 1992. Dietary fiber, phytoestrogens, and breast cancer. *Nutrition* 8:47–51.
- Rose DP, Goldman M, Connolly JM, Strong LE. 1991. High-fiber diet reduces serum estrogen concentrations in premenopausal women. *Am J Clin Nutr* 54:520–525.
- Rössner S, von Zweigbergk D, Öhlin A, Ryttig K. 1987. Weight reduction with dietary fibre supplements. Results of two double-blind randomized studies. *Acta Med Scand* 222:83–88.
- Ryttig KR, Tellnes G, Haegh L, Boe E, Fagerthun H. 1989. A dietary fibre supplement and weight maintenance after weight reduction: A randomized, double-blind, placebo-controlled long-term trial. *Int J Obes* 13:165–171.
- Saku K, Yoshinaga K, Okura Y, Ying H, Harada R, Arakawa K. 1991. Effects of polydextrose on serum lipids, lipoproteins, and apolipoproteins in healthy subjects. *Clin Ther* 13:254–258.
- Salmerón J, Ascherio A, Rimm EB, Colditz GA, Spiegelman D, Jenkins DJ, Stampfer MJ, Wing AL, Willett WC. 1997a. Dietary fiber, glycemic load, and risk of NIDDM in men. *Diabetes Care* 20:545–550.

- Salmerón J, Manson JE, Stampfer MJ, Colditz GA, Wing AL, Willett WC. 1997b. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. *J Am Med Assoc* 277:472–477.
- Sandberg AS, Ahderinne R, Andersson H, Hallgren B, Hulten L. 1983. The effect of citrus pectin on the absorption of nutrients in the small intestine. *Hum Nutr Clin Nutr* 37:171–183.
- Sandstead HH. 1992. Fiber, phytates, and mineral nutrition. *Nutr Rev* 50:30–31.
- Schatzkin A, Lanza E, Corle D, Lance P, Iber F, Caan B, Shike M, Weissfeld J, Burt R, Cooper MR, Kikendall JW, Cahill J. 2000. Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas. *N Engl J Med* 342:1149–1155.
- Sepple CP, Read NW. 1989. Gastrointestinal correlates of the development of hunger in man. *Appetite* 13:183–191.
- Shetty PS, Kurpad AV. 1986. Increasing starch intake in the human diet increases fecal bulking. *Am J Clin Nutr* 43:210–212.
- Shultz TD, Howie BJ. 1986. In vitro binding of steroid hormones by natural and purified fibers. *Nutr Cancer* 8:141–147.
- Silvester KR, Englyst HN, Cummings JH. 1995. Ileal recovery of starch from whole diets containing resistant starch measured in vitro and fermentation of ileal effluent. *Am J Clin Nutr* 62:403–411.
- Simpson HCR, Simpson RW, Lousley S, Carter RD, Geekie M, Hockaday TDR, Mann JI. 1981. A high carbohydrate leguminous fibre diet improves all aspects of diabetic control. *Lancet* 1:1–15.
- Simpson KM, Morris ER, Cook JD. 1981. The inhibitory effect of bran on iron absorption in man. *Am J Clin Nutr* 34:1469–1478.
- Slavin JL. 1987. Dietary fiber: Classification, chemical analyses, and food sources. *J Am Diet Assoc* 87:1164–1171.
- Slavin JL, Marlett JA. 1980. Influence of refined cellulose on human bowel function and calcium and magnesium retention. *Am J Clin Nutr* 33:1932–1939.
- Slavin J, Jacobs D, Marquart L. 1997. Whole-grain consumption and chronic disease: Protective mechanisms. *Nutr Cancer* 27:14–21.
- Sleet R, Brightwell J. 1990. *FS-Teratology Study in Rats*. Raffinerie Tirlemontoise Internal Report. Photocopy.
- Smith T, Brown JC, Livesey G. 1998. Energy balance and thermogenesis in rats consuming nonstarch polysaccharides of various fermentabilities. *Am J Clin Nutr* 68:802–819.
- Spencer H, Norris C, Derler J, Osis D. 1991. Effect of oat bran muffins on calcium absorption and calcium, phosphorus, magnesium and zinc balance in men. *J Nutr* 121:1976–1983.
- Steinmetz KA, Kushi LH, Bostick RM, Folsom AR, Potter JD. 1994. Vegetables, fruit, and colon cancer in the Iowa Women's Health Study. *Am J Epidemiol* 139:1–15.
- Stephen AM, Haddad AC, Phillips SF. 1983. Passage of carbohydrate into the colon. Direct measurements in humans. *Gastroenterology* 85:589–595.
- Stevens J, Levitsky DA, VanSoest PJ, Robertson JB, Kalkwarf HJ, Roe DA. 1987. Effect of psyllium gum and wheat bran on spontaneous energy intake. *Am J Clin Nutr* 46:812–817.
- Stone-Dorshow T, Levitt MD. 1987. Gaseous response to ingestion of a poorly absorbed fructo-oligosaccharide sweetener. *Am J Clin Nutr* 46:61–65.
- Strobel S, Ferguson A, Anderson DM. 1982. Immunogenicity of foods and food additives—In vivo testing of gums arabic, karaya, and tragacanth. *Toxicol Lett* 14:247–252.

- Sugano M, Fujikawa T, Hiratsuji Y, Nakashima K, Fukuda N, Hasegawa Y. 1980. A novel use of chitosan as a hypocholesterolemic agent in rats. *Am J Clin Nutr* 33:787–793.
- Sundell IB, Ranby M. 1993. Oat husk fiber decreases plasminogen activator inhibitor type 1 activity. *Haemostasis* 23:45–50.
- Taioli E, Nicolosi A, Wynder EL. 1991. Dietary habits and breast cancer: A comparative study of United States and Italian data. *Nutr Cancer* 16:259–265.
- Thompson LU. 1994. Antioxidants and hormone-mediated health benefits of whole grains. *Crit Rev Food Sci Nutr* 34:473–497.
- Thun MJ, Calle EE, Namboodiri MM, Flanders WD, Coates RJ, Byers T, Boffetta P, Garfinkel L, Heath CW. 1992. Risk factors for fatal colon cancer in a large prospective study. *J Natl Cancer Inst* 84:1491–1500.
- Todd S, Woodward M, Tunstall-Pedoe H, Bolton-Smith C. 1999. Dietary antioxidant vitamins and fiber in the etiology of cardiovascular disease and all-causes mortality: Results from the Scottish Heart Health Study. *Am J Epidemiol* 150:1073–1080.
- Tokunaga K, Matsuoka A. 1999. Effects of a Food for Specified Health Use (FOSHU) which contains indigestible dextrin as an effective ingredient on glucose and lipid metabolism. *J Jpn Diabetes Soc* 42:61–65.
- Tomlin J, Read NW. 1988. A comparative study of the effects on colon function caused by feeding ispaghula husk and polydextrose. *Aliment Pharmacol Ther* 2:513–519.
- Tomlin J, Read NW. 1990. The effect of resistant starch on colon function in humans. *Br J Nutr* 64:589–595.
- Tomlin J, Lewis C, Read NW. 1991. Investigation of normal flatus production in healthy volunteers. *Gut* 32:665–669.
- Tremblay A, Lavallée N, Alméras N, Allard L, Després J-P, Bouchard C. 1991. Nutritional determinants of the increase in energy intake associated with a high-fat diet. *Am J Clin Nutr* 53:1134–1137.
- Trock B, Lanza E, Greenwald P. 1990. Dietary fiber, vegetables, and colon cancer: Critical review and meta-analyses of the epidemiologic evidence. *J Natl Cancer Inst* 82:650–661.
- Truswell AS. 1992. Glycaemic index of foods. *Eur J Clin Nutr* 46:S91–S101.
- Tuohy KM, Kolida S, Lustenberger AM, Gibson GR. 2001. The prebiotic effects of biscuits containing partially hydrolysed guar gum and fructo-oligosaccharides—A human volunteer study. *Br J Nutr* 86:341–348.
- Tuyns AJ, Haelterman M, Kaaks R. 1987. Colorectal cancer and the intake of nutrients: Oligosaccharides are a risk factor, fats are not. A case-control study in Belgium. *Nutr Cancer* 10:181–196.
- Tzonou A, Hsieh C-C, Polychronopoulou A, Kaprinis G, Toupadaki N, Trichopoulou A, Karakatsani A, Trichopoulos D. 1993. Diet and ovarian cancer: A case-control study in Greece. *Int J Cancer* 55:411–414.
- USDA/HHS (U.S. Department of Agriculture/U.S. Department of Health and Human Services). 2000. *Nutrition and Your Health: Dietary Guidelines for Americans*. Home and Garden Bulletin No. 232. Washington, DC: U.S. Government Printing Office.
- van Dokkum W, Wezendonk B, Srikumar TS, van den Heuvel EGHM. 1999. Effect of nondigestible oligosaccharides on large-bowel functions, blood lipid concentrations and glucose absorption in young healthy male subjects. *Eur J Clin Nutr* 53:1–7.

- Van Horn LV, Liu K, Parker D, Emidy L, Liao Y, Pan WH, Giumetti D, Hewitt J, Stamler J. 1986. Serum lipid response to oat product intake with a fat-modified diet. *J Am Diet Assoc* 86:759–764.
- van Munster IP, Nagengast FM. 1993. The role of carbohydrate fermentation in colon cancer prevention. *Scand J Gastroenterol* 200:80–86.
- van Munster IP, de Boer HM, Jansen MC, de Haan AF, Katan MB, van Amelsvoort JM, Nagengast FM. 1994. Effect of resistant starch on breath-hydrogen and methane excretion in healthy volunteers. *Am J Clin Nutr* 59:626–630.
- van't Veer P, Kolb CM, Verhoef P, Kok FJ, Schouten EG, Hermus RJ, Sturmans F. 1990. Dietary fiber, beta-carotene and breast cancer: Results from a case-control study. *Int J Cancer* 45:825–828.
- Verhoeven DTH, Assen N, Goldbohm RA, Dorant E, van't Veer P, Sturmans F, Hermus RJ, van den Brandt PA. 1997. Vitamins C and E, retinol, beta-carotene and dietary fibre in relation to breast cancer risk: A prospective cohort study. *Br J Cancer* 75:149–155.
- Visek WJ. 1978. Diet and cell growth modulation by ammonia. *Am J Clin Nutr* 31:S216–S220.
- Wakabayashi S, Ueda Y, Matsuoka A. 1993. Effects of indigestible dextrin on blood glucose and insulin levels after various sugar loads in rats. *J Jpn Soc Nutr Food Sci* 46:131–137.
- Wakabayashi S, Kishimoto Y, Matsuoka A. 1995. Effects of indigestible dextrin on glucose tolerance in rats. *J Endocrinol* 144:533–538.
- Watters DAK, Smith AN. 1990. Strength of the colon wall in diverticular disease. *Br J Surg* 77:257–259.
- Weaver GA, Krause JA, Miller TL, Wolin MJ. 1988. Short chain fatty acid distributions of enema samples from a sigmoidoscopy population: An association of high acetate and low butyrate ratios with adenomatous polyps and colon cancer. *Gut* 29:1539–1543.
- West DW, Slattery ML, Robison LM, Schuman KL, Ford MH, Mahoney AW, Lyon JL, Sorensen AW. 1989. Dietary intake and colon cancer: Sex- and anatomic site-specific associations. *Am J Epidemiol* 130:883–894.
- Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Speizer FE. 1990. Relation of meat, fat, and fiber intake to the risk of colon cancer in a prospective study among women. *N Engl J Med* 323:1664–1672.
- Willett WC, Hunter DJ, Stampfer MJ, Colditz G, Manson JE, Spiegelman D, Rosner B, Hennekens CH, Speizer FE. 1992. Dietary fat and fiber in relation to risk of breast cancer. An 8-year follow-up. *J Am Med Assoc* 268:2037–2044.
- Williams CH, Witherly SA, Buddington RK. 1994. Influence of dietary neosugar on selected bacterial groups of the human faecal microbiota. *Microb Ecol Health Dis* 7:91–97.
- Williams CL, Bollella M. 1995. Is a high-fiber diet safe for children? *Pediatrics* 96:1014–1019.
- Williams CL, Bollella M, Wynder EL. 1995. A new recommendation for dietary fiber in childhood. *Pediatrics* 96:985–988.
- Wisker E, Nagel R, Tanudjaja TK, Feldheim W. 1991. Calcium, magnesium, zinc, and iron balances in young women: Effects of a low-phytate barley-fiber concentrate. *Am J Clin Nutr* 54:553–559.
- Witte JS, Ursin G, Siemiatycki J, Thompson WD, Paganini-Hill A, Haile RW. 1997. Diet and premenopausal bilateral breast cancer: A case-control study. *Breast Cancer Res Treat* 42:243–251.

- Wolever TMS. 1995. In vitro and in vivo models for predicting the effect of dietary fiber and starchy foods on carbohydrate metabolism. In: Kritchevsky D, Bonfield C, eds. *Dietary Fiber in Health and Disease*. St. Paul, MN: Eagan Press. Pp. 360–377.
- Wolever TMS, Jenkins DJA. 1993. Effect of dietary fiber and foods on carbohydrate metabolism. In: Spiller G, ed. *CRC Handbook of Dietary Fiber in Human Nutrition*. Boca Raton, FL: CRC Press. Pp. 111–162.
- Wolk A, Manson JE, Stampfer MJ, Colditz GA, Hu FB, Speizer FE, Hennekens CH, Willett WC. 1999. Long-term intake of dietary fiber and decreased risk of coronary heart disease among women. *J Am Med Assoc* 281:1998–2004.
- Wood PJ, Braaten JT, Scott FW, Riedel KD, Wolynetz MS, Collins MW. 1994. Effect of dose and modification of viscous properties of oat gum on plasma glucose and insulin following an oral glucose load. *Br J Nutr* 72:731–743.
- Woods MN, Gorbach SL, Longcope C, Goldin BR, Dwyer JT, Morrill-LaBrode A. 1989. Low-fat, high-fiber diet and serum estrone sulfate in premenopausal women. *Am J Clin Nutr* 49:1179–1183.
- Woods MN, Barnett JB, Spiegelman D, Trail N, Hertzmark E, Longcope C, Gorbach SL. 1996. Hormone levels during dietary changes in premenopausal African-American women. *J Natl Cancer Inst* 88:1369–1374.
- Wuolijoki E, Hirvelä T, Ylitalo P. 1999. Decrease in serum LDL cholesterol with microcrystalline chitosan. *Methods Find Exp Clin Pharmacol* 21:357–361.
- Wynder EL, Berenson GS. 1984. Preventive strategies for reducing hyperlipidemia in childhood. *Prev Med* 13:327–329.
- Yamashita K, Kawai K, Itakura M. 1984. Effects of fructo-oligosaccharides on blood glucose and serum lipids in diabetic subjects. *Nutr Res* 4:961–966.
- Younes H, Levrat MA, Demigne C, Remesy C. 1995. Resistant starch is more effective than cholestyramine as a lipid-lowering agent in the rat. *Lipids* 30:847–853.
- Yu H, Harris RE, Gao Y-T, Gao R, Wynder RL. 1991. Comparative epidemiology of cancers of the colon, rectum, prostate and breast in Shanghai, China versus the United States. *Int J Epidemiol* 20:76–81.
- Yuan J-M, Wang Q-S, Ross RK, Henderson BE, Yu MC. 1995. Diet and breast cancer in Shanghai and Tianjin, China. *Br J Cancer* 71:1353–1358.
- Zacour AC, Silva ME, Cecon PR, Bambirra EA, Vieira EC. 1992. Effect of dietary chitin on cholesterol absorption and metabolism in rats. *J Nutr Sci Vitaminol (Tokyo)* 38:609–613.

Ibid., Chapter 13, pp. 965–967.

- Bandini LG, Vu D, Must A, Cyr H, Goldberg A, Dietz WH. 1999. Comparison of high-calorie, low-nutrient-dense food consumption among obese and non-obese adolescents. *Obes Res* 7:438–443.
- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Black AE, Prentice AM, Goldberg GR, Jebb SA, Bingham SA, Livingstone MBE, Coward WA. 1993. Measurements of total energy expenditure provide insights into the validity of dietary measurements of energy intake. *J Am Diet Assoc* 93:572–579.
- Blair SN, Kohl HW, Barlow CE. 1993. Physical activity, physical fitness, and all-cause mortality in women: Do women need to be active? *J Am Coll Nutr* 12:368–371.

- Blair SN, Kohl HW, Barlow CE, Paffenbarger RS, Gibbons LW, Macera CA. 1995. Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. *J Am Med Assoc* 273:1093–1098.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Nutrition Examination Survey: Underreporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Carroll RJ, Freedman LS, Hartman AM. 1996. Use of semiquantitative food frequency questionnaires to estimate the distribution of usual intake. *Am J Epidemiol* 143:392–404.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment.* Washington, DC: National Academy Press.
- IOM. 2001. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc.* Washington, DC: National Academy Press.
- Johnson RK, Goran MI, Poehlman ET. 1994. Correlates of over- and under-reporting of energy intake in healthy older men and women. *Am J Clin Nutr* 59:1286–1290.
- Johnson RK, Soultanakis RP, Matthews DE. 1998. Literacy and body fatness are associated with underreporting of energy intake in US low-income women using the multiple-pass 24-hour recall: A doubly labeled water study. *J Am Diet Assoc* 98:1136–1140.
- Kristal AR, Feng Z, Coates RJ, Oberman A, George V. 1997. Associations of race/ethnicity, education, and dietary intervention with the validity and reliability of a food frequency questionnaire: The Women's Health Trial Feasibility Study in Minority Populations. *Am J Epidemiol* 146:856–869.
- Lichtman SW, Pisarska K, Berman ER, Pestone M, Dowling H, Offenbacher E, Weisel H, Heshka S, Matthews DE, Heymsfield SB. 1992. Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. *N Engl J Med* 327:1893–1898.
- Liu K. 1994. Statistical issues related to semiquantitative food-frequency questionnaires. *Am J Clin Nutr* 59:262S–265S.
- Livingstone MB, Prentice AM, Coward WA, Strain JJ, Black AE, Davies PS, Stewart CM, McKenna PG, Whitehead RG. 1992. Validation of estimates of energy intake by weighed dietary record and diet history in children and adolescents. *Am J Clin Nutr* 56:29–35.
- Marlett JA, Cheung TF. 1997. Database and quick methods of assessing typical dietary fiber intakes using data for 228 commonly consumed foods. *J Am Diet Assoc* 97:1139–1148.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys.* Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.

- Prentice AM, Black AE, Coward WA, Davies HL, Goldberg GR, Murgatroyd PR, Ashford J, Sawyer M, Whitehead RG. 1986. High levels of energy expenditure in obese women. *Br Med J* 292:983–987.
- Pryer JA, Vrijheid M, Nichols R, Kiggins M, Elliott P. 1997. Who are the ‘low energy reporters’ in the dietary and nutritional survey of British adults? *Int J Epidemiol* 26:146–154.
- Schoeller DA. 1995. Limitations in the assessment of dietary energy by self-report. *Metabolism* 44:18–22.
- Schoeller DA, Bandini LG, Dietz WH. 1990. Inaccuracies in self-reported intake identified by comparison with the doubly labelled water method. *Can J Physiol Pharmacol* 68:941–949.
- USDA (U.S. Department of Agriculture). 2001. *USDA Nutrient Database for Standard Reference, Release 14*. Online. Nutrient Data Laboratory. Available at <http://www.nal.usda.gov/fnic/foodcomp>. Accessed April 2, 2002.
- USDA/HHS (U.S. Department of Health and Human Services). 2000. *Nutrition and Your Health: Dietary Guidelines for Americans*. Home and Garden Bulletin No. 232. Washington, DC: U.S. Government Printing Office.

## DIETARY FAT: TOTAL FAT AND FATTY ACIDS

*Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* (ISBN 0-309-08537-3), Chapter 8, pp. 515–541.

- Abedin L, Lien EL, Vingrys AJ, Sinclair AJ. 1999. The effects of dietary  $\alpha$ -linolenic acid compared with docosahexaenoic acid on brain, retina, liver, and heart in the guinea pig. *Lipids* 34:475–482.
- Adlof RO, Duval S, Emken EA. 2000. Biosynthesis of conjugated linoleic acid in humans. *Lipids* 35:131–135.
- Aggett PJ, Haschke F, Heine W, Hernell O, Koletzko B, Launiala K, Rey J, Rubino A, Schöch G, Senterre J, Tormo R. 1991. Comment on the content and composition of lipids in infant formulas. *Acta Paediatr Scand* 80:887–896.
- Agner E, Hansen PF. 1983. Fasting serum cholesterol and triglycerides in a ten-year prospective study in old age. *Acta Med Scand* 214:33–41.
- Agostoni C, Trojan S, Bellù R, Riva E, Giovannini M. 1995. Neurodevelopment quotient of healthy term infants at 4 months and feeding practice: The role of long-chain polyunsaturated fatty acids. *Pediatr Res* 38:262–266.
- Agostoni C, Trojan S, Bellù R, Riva E, Buzzese MG, Giovannini M. 1997. Developmental quotient at 24 months and fatty acid composition of diet in early infancy: A follow up study. *Arch Dis Child* 76:421–424.
- Allison DB, Egan SK, Barraj LM, Caughman C, Infante M, Heimbach JT. 1999. Estimated intakes of *trans* fatty and other fatty acids in the US population. *J Am Diet Assoc* 99:166–174.
- Almendingen K, Jordal O, Kierulf P, Sandstad B, Pedersen JI. 1995. Effects of partially hydrogenated fish oil, partially hydrogenated soybean oil, and butter on serum lipoproteins and Lp[a] in men. *J Lipid Res* 36:1370–1384.
- Almendingen K, Seljeflot I, Sandstad B, Pedersen JI. 1996. Effects of partially hydrogenated fish oil, partially hydrogenated soybean oil, and butter on hemostatic variables in men. *Arterioscler Thromb Vasc Biol* 16:375–380.
- Anderson DM, Williams FH, Merkatz RB, Schulman PK, Kerr DS, Pittard WB. 1983. Length of gestation and nutritional composition of human milk. *Am J Clin Nutr* 37:810–814.
- Anderson GJ, Connor WE. 1989. On the demonstration of  $\omega$ -3 essential-fatty-acid deficiency in humans. *Am J Clin Nutr* 49:585–587.
- Anderson GJ, Connor WE, Corliss JD. 1990. Docosahexaenoic acid is the preferred dietary  $n$ -3 fatty acid for the development of the brain and retina. *Pediatr Res* 27:89–97.
- Anderson RE, Benolken RM, Dudley PA, Landis DJ, Wheeler TG. 1974. Polyunsaturated fatty acids of photoreceptor membranes. *Exp Eye Res* 18:205–213.
- Ando K, Nagata K, Beppu M, Kikugawa T, Kawabata T, Hasegawa K, Suzuki M. 1998. Effect of  $n$ -3 fatty acid supplementation on lipid peroxidation and protein aggregation in rat erythrocyte membranes. *Lipids* 33:505–512.
- Aro A, Salminen I. 1998. Difference between animal and vegetable *trans* fatty acids. *Am J Clin Nutr* 68:918–919.
- Aro A, Jauhainen M, Partanen R, Salminen I, Mutanen M. 1997. Stearic acid, *trans* fatty acids, and dairy fat: Effects on serum and lipoprotein lipids, apolipoproteins, lipoprotein(a), and lipid transfer proteins in healthy subjects. *Am J Clin Nutr* 65:1419–1426.

- Aro A, Amaral E, Kesteloot H, Rimestad A, Thamm M, van Poppel G. 1998a. *Trans* fatty acids in French fries, soups, and snacks from 14 European countries: The TRANSFAIR Study. *J Food Comp Anal* 11:170–177.
- Aro A, Antoine JM, Pizzoferrato L, Reykdal O, van Poppel G. 1998b. *Trans* fatty acids in dairy and meat products from 14 European countries: The TRANSFAIR Study. *J Food Comp Anal* 11:150–160.
- Aro A, Van Amelsvoort J, Becker W, van Erp-Baart M-A, Kafatos A, Leth T, van Poppel G. 1998c. *Trans* fatty acids in dietary fats and oils from 14 European countries: The TRANSFAIR Study. *J Food Comp Anal* 11:137–149.
- Arora S, Kassarjian Z, Krasinski SD, Croffey B, Kaplan MM, Russell RM. 1989. Effect of age on tests of intestinal and hepatic function in healthy humans. *Gastroenterology* 96:1560–1565.
- ARS (Agricultural Research Service). 2001. *USDA Nutrient Database for Standard Reference, Release 14*. Online. U.S. Department of Agriculture. Available at <http://www.nal.usda.gov/fnic/foodcomp/Data/SR14/sr14.html>. Accessed November 13, 2001.
- Ascherio A, Hennekens CH, Buring JE, Master C, Stampfer MJ, Willett WC. 1994. *Trans*-fatty acids intake and risk of myocardial infarction. *Circulation* 89:94–101.
- Ascherio A, Rimm EB, Giovannucci EL, Spiegelman D, Stampfer M, Willett WC. 1996. Dietary fat and risk of coronary heart disease in men: Cohort follow up study in the United States. *Br Med J* 313:84–90.
- Ascherio A, Katan MB, Zock PL, Stampfer MJ, Willett WC. 1999. Trans fatty acids and coronary heart disease. *N Engl J Med* 340:1994–1998.
- Astrup A, Buemann B, Christensen NJ, Toustrup S. 1994. Failure to increase lipid oxidation in response to increasing dietary fat content in formerly obese women. *Am J Physiol* 266:E592–E599.
- Auestad N, Montalto MB, Hall RT, Fitzgerald KM, Wheeler RE, Connor WE, Neuringer M, Connor SL, Taylor JA, Hartmann EE. 1997. Visual acuity, erythrocyte fatty acid composition, and growth in term infants fed formulas with long chain polyunsaturated fatty acids for one year. *Pediatr Res* 41:1–10.
- Auestad N, Halter R, Hall RT, Blatter M, Bogle ML, Burks W, Erickson JR, Fitzgerald KM, Dobson V, Innis SM, Singer LT, Montalto MB, Jacobs JR, Qiu W, Bornstein MH. 2001. Growth and development in term infants fed long-chain polyunsaturated fatty acids: A double-masked, randomized, parallel, prospective, multivariate study. *Pediatrics* 108:372–381.
- Bang HO, Dyerberg J. 1980. The bleeding tendency in Greenland Eskimos. *Dan Med Bull* 27:202–205.
- Bang HO, Dyerberg J, Sinclair HM. 1980. The composition of the Eskimo food in north western Greenland. *Am J Clin Nutr* 33:2657–2661.
- Barr LH, Dunn GD, Brennan MF. 1981. Essential fatty acid deficiency during total parenteral nutrition. *Ann Surg* 193:304–311.
- Bartoš V, Groh J. 1969. The effect of repeated stimulation of the pancreas on the pancreatic secretion in young and aged men. *Gerontol Clin* 11:56–62.
- Benolken RM, Anderson RE, Wheeler TG. 1973. Membrane fatty acids associated with the electrical response in visual excitation. *Science* 182:1253–1254.
- Berge RK, Madsen L, Vaagenes H, Tronstad KJ, Göttlicher M, Rustan AC. 1999. In contrast with docosahexaenoic acid, eicosapentaenoic acid and hypolipidaemic derivatives decrease hepatic synthesis and secretion of triacylglycerol by decreased diacylglycerol acyltransferase activity and stimulation of fatty acid oxidation. *Biochem J* 343:191–197.

- Bessesen DH, Rupp CL, Eckel RH. 1995. Trafficking of dietary fat in lean rats. *Obes Res* 3:191–203.
- Birch EE, Hoffman DR, Uauy R, Birch DG, Prestidge C. 1998. Visual acuity and the essentiality of docosahexaenoic acid and arachidonic acid in the diet of term infants. *Pediatr Res* 44:201–209.
- Birch EE, Garfield S, Hoffman DR, Uauy R, Birch DG. 2000. A randomized controlled trial of early dietary supply of long-chain polyunsaturated fatty acids and mental development in term infants. *Dev Med Child Neurol* 42:174–181.
- Bistrian BR, Bothe A, Blackburn GL, DeFriez AI. 1981. Low plasma cortisol and hematologic abnormalities associated with essential fatty acid deficiency in man. *J Parenter Enteral Nutr* 5:141–144.
- Bitman J, Wood DL, Hamosh M, Hamosh P, Mehta NR. 1983. Comparison of the lipid composition of breast milk from mothers of term and preterm infants. *Am J Clin Nutr* 38:300–312.
- Bjerve KS. 1989. n-3 Fatty acid deficiency in man. *J Intern Med* 225:171–175.
- Bjerve KS, Mostad IL, Thoresen L. 1987a. Alpha-linolenic acid deficiency in patients on long-term gastric-tube feeding: Estimation of linolenic acid and long-chain unsaturated n-3 fatty acid requirement in man. *Am J Clin Nutr* 45:66–77.
- Bjerve KS, Thoresen L, Mostad IL, Alme K. 1987b. Alpha-linolenic acid deficiency in man: Effect of essential fatty acids on fatty acid composition. *Adv Prostaglandin Thromboxane Leukot Res* 17:862–865.
- Bjerve KS, Thoresen L, Børsting S. 1988. Linseed and cod liver oil induce rapid growth in a 7-year-old girl with n-3 fatty acid deficiency. *J Parenter Enteral Nutr* 12:521–525.
- Bjerve KS, Fischer S, Wammer F, Egeland T. 1989. α-Linolenic acid and long-chain ω-3 fatty acid supplementation in three patients with ω-3 fatty acid deficiency: Effect on lymphocyte function, plasma and red cell lipids, and prostanoid formation. *Am J Clin Nutr* 49:290–300.
- Blok WL, Deslypere JP, Demacker PNM, van der Ven-Jongekrijg J, Hectors MPC, van der Meer JWM, Katan MB. 1997. Pro- and anti-inflammatory cytokines in healthy volunteers fed various doses of fish oil for 1 year. *Eur J Clin Invest* 27:1003–1008.
- Blonk MC, Bilo HJG, Nauta JJP, Popp-Snijders C, Mulder C, Donker AJM. 1990. Dose-response effects of fish-oil supplementation in healthy volunteers. *Am J Clin Nutr* 52:120–127.
- Boissonneault GA, Johnston PV. 1983. Essential fatty acid deficiency, prostaglandin synthesis and humoral immunity in Lewis rats. *J Nutr* 113:1187–1194.
- Bonanome A, Grundy SM. 1988. Effect of dietary stearic acid on plasma cholesterol and lipoprotein levels. *N Engl J Med* 318:1244–1248.
- Bonanome A, Grundy SM. 1989. Intestinal absorption of stearic acid after consumption of high fat meals in humans. *J Nutr* 119:1556–1560.
- Boulton TJC, Magarey AM. 1995. Effects of differences in dietary fat on growth, energy and nutrient intake from infancy to eight years of age. *Acta Paediatr* 84:146–150.
- Bourre JM, Francois M, Youyou A, Dumont O, Piciotti M, Pascal G, Durand G. 1989. The effects of dietary α-linolenic acid on the composition of nerve membranes, enzymatic activity, amplitude of electrophysiological parameters, resistance to poisons and performance of learning tasks in rats. *J Nutr* 119:1880–1892.

- Bourre J-M, Dumont O, Durand G. 1996. Does an increase in dietary linoleic acid modify tissue concentrations of cervonic acid and consequently alter alpha-linolenic requirements? Minimal requirement of linoleic acid in adult rats. *Biochem Mol Biol Int* 39:607–619.
- Brauer PM, Slavin JL, Marlett JA. 1981. Apparent digestibility of neutral detergent fiber in elderly and young adults. *Am J Clin Nutr* 34:1061–1070.
- Brenner RR. 1974. The oxidative desaturation of unsaturated fatty acids in animals. *Mol Cell Biochem* 3:41–52.
- Brossard N, Croset M, Pachiaudi C, Riou JP, Tayot JL, Lagarde M. 1996. Retroconversion and metabolism of [<sup>13</sup>C]22:6n-3 in humans and rats after intake of a single dose of [<sup>13</sup>C]22:6n-3-triacylglycerols. *Am J Clin Nutr* 64:577–586.
- Bruckner G, Shimp J, Goswami S, Mai J, Kinsella JE. 1982. Dietary trilinoelaidate: Effects on metabolic parameters related to EFA metabolism in rats. *J Nutr* 112:126–135.
- Bunker CH, Ukoli FA, Okoro FI, Olomu AB, Kriska AM, Huston SL, Markovic N, Kuller LH. 1996. Correlates of serum lipids in a lean black population. *Atherosclerosis* 123:215–225.
- Burr GO, Burr MM. 1929. A new deficiency disease produced by the rigid exclusion of fat from the diet. *J Biol Chem* 82:345–367.
- Butte NF. 2000. Fat intake of children in relation to energy requirements. *Am J Clin Nutr* 72:1246S–1252S.
- Butte NF, Garza C, Smith EO, Nichols BL. 1984. Human milk intake and growth in exclusively breast-fed infants. *J Pediatr* 104:187–195.
- Byard RW, Makrides M, Need M, Neumann MA, Gibson RA. 1995. Sudden infant death syndrome: Effect of breast and formula feeding on frontal cortex and brainstem lipid composition. *J Paediatr Child Health* 31:14–16.
- Calles-Escandon J, Goran MI, O'Connell M, Nair KS, Danforth E. 1996. Exercise increases fat oxidation at rest unrelated to changes in energy balance or lipolysis. *Am J Physiol* 270:E1009–E1014.
- Carlson SE, Rhodes PG, Ferguson MG. 1986. Docosahexaenoic acid status of preterm infants at birth and following feeding with human milk or formula. *Am J Clin Nutr* 44:798–804.
- Carlson SE, Cooke RJ, Werkman SH, Tolley EA. 1992. First year growth of preterm infants fed standard compared to marine oil n-3 supplemented formula. *Lipids* 27:901–907.
- Carlson SE, Werkman SH, Peeples JM, Cooke RJ, Tolley EA. 1993. Arachidonic acid status correlates with first year growth in preterm infants. *Proc Natl Acad Sci USA* 90:1073–1077.
- Carlson SE, Ford AJ, Werkman SH, Peeples JM, Koo WWK. 1996a. Visual acuity and fatty acid status of term infants fed human milk and formulas with and without docosahexaenoate and arachidonate from egg yolk lecithin. *Pediatr Res* 39:882–888.
- Carlson SE, Werkman SH, Tolley EA. 1996b. Effect of long-chain n-3 fatty acid supplementation on visual acuity and growth of preterm infants with and without bronchopulmonary dysplasia. *Am J Clin Nutr* 63:687–697.
- Carnielli VP, Luijendijk IHT, Van Goudoever JB, Sulkers EJ, Boerlage AA, Degenhart HJ, Sauer PJJ. 1996a. Structural position and amount of palmitic acid in infant formulas: Effects on fat, fatty acid, and mineral balance. *J Pediatr Gastroenterol Nutr* 23:553–560.

- Carnielli VP, Wattimena DJL, Luijendijk IHT, Boerlage A, Degenhart HJ, Sauer PJ. 1996b. The very low birth weight premature infant is capable of synthesizing arachidonic and docosahexaenoic acids from linoleic and linolenic acids. *Pediatr Res* 40:169–174.
- Castuma JC, Brenner RR, Kunau W. 1977. Specificity of  $\Delta 6$  desaturase—Effect of chain length and number of double bonds. *Adv Exp Med Biol* 83:127–134.
- Caughey GE, Mantzioris E, Gibson RA, Cleland LG, James MJ. 1996. The effect on human tumor necrosis factor  $\alpha$  and interleukin 1 $\beta$  production of diets enriched in *n*-3 fatty acids from vegetable oil or fish oil. *Am J Clin Nutr* 63:116–122.
- CDC (Centers for Disease Control and Prevention). 1994. Daily dietary fat and total food-energy intakes—Third National Health and Nutrition Examination Survey, Phase 1, 1988–91. *Morb Mortal Wkly Rep* 43:116–117, 123–125.
- Chambaz J, Ravel D, Manier M-C, Pepin D, Mulliez N, Bereziat G. 1985. Essential fatty acids interconversion in the human fetal liver. *Biol Neonate* 47:136–140.
- Chang HR, Dulloo AG, Vladoianu IR, Piguet PF, Arsenijevic D, Girardier L, Pechère JC. 1992. Fish oil decreases natural resistance of mice to infection with *Salmonella typhimurium*. *Metabolism* 41:1–2.
- Chappell JE, Clandinin MT, Kearney-Volpe C. 1985. Trans fatty acids in human milk lipids: Influence of maternal diet and weight loss. *Am J Clin Nutr* 42:49–56.
- Chen Q, Nilsson Å. 1993. Desaturation and chain elongation of *n*-3 and *n*-6 polyunsaturated fatty acids in the human CaCo-2 cell line. *Biochim Biophys Acta* 1166:193–201.
- Chen ZY, Pelletier G, Hollywood R, Ratnayake WMN. 1995a. *Trans* fatty acid isomers in Canadian human milk. *Lipids* 30:15–21.
- Chen ZY, Ratnayake WMN, Fortier L, Ross R, Cunnane SC. 1995b. Similar distribution of *trans* fatty acid isomers in partially hydrogenated vegetable oils and adipose tissue of Canadians. *Can J Physiol Pharmacol* 73:718–723.
- Chin SF, Liu W, Storkson JM, Ha YL, Pariza MW. 1992. Dietary sources of conjugated dienoic isomers of linoleic acid, a newly recognized class of anti-carcinogens. *J Food Comp Anal* 5:185–197.
- Chin SF, Storkson JM, Liu W, Albright KJ, Pariza MW. 1994. Conjugated linoleic acid (9,11- and 10,12-octadecadienoic acid) is produced in conventional but not germ-free rats fed linoleic acid. *J Nutr* 124:694–701.
- Chisholm A, Mann J, Sutherland W, Duncan A, Skeaff M, Frampton C. 1996. Effect on lipoprotein profile of replacing butter with margarine in a low fat diet: Randomised crossover study with hypercholesterolaemic subjects. *Br Med J* 312:931–934.
- Cho HP, Nakamura MT, Clarke SD. 1999. Cloning, expression, and nutritional requirements of the mammalian  $\Delta 6$  desaturase. *J Biol Chem* 274:471–477.
- Clark KJ, Makrides M, Neumann MA, Gibson RA. 1992. Determination of the optimal ratio of linoleic acid to  $\alpha$ -linolenic acid in infant formulas. *J Pediatr* 120:S151–S158.
- Clarke JTR, Cullen-Dean G, Regelink E, Chan L, Rose V. 1990. Increased incidence of epistaxis in adolescents with familial hypercholesterolemia treated with fish oil. *J Pediatr* 116:139–141.
- Clarke R, Frost C, Collins R, Appleby P, Peto R. 1997. Dietary lipids and blood cholesterol: Quantitative meta-analysis of metabolic ward studies. *Br Med J* 314:112–117.
- Clouet P, Niot I, Bézard J. 1989. Pathway of  $\alpha$ -linolenic acid through the mitochondrial outer membrane in the rat liver and influence on the rate of oxidation. Comparison with linoleic and oleic acids. *Biochem J* 263:867–873.

- Cobiac L, Clifton PM, Abbey M, Belling GB, Nestel PJ. 1991. Lipid, lipoprotein, and hemostatic effects of fish vs. fish-oil *n*-3 fatty acids in mildly hyperlipidemic males. *Am J Clin Nutr* 53:1210–1216.
- Cohen SA, Hendricks KM, Eastham EJ, Mathis RK, Walker WA. 1979. Chronic nonspecific diarrhea. A complication of dietary fat restriction. *Am J Dis Child* 133:490–492.
- Colditz GA, Manson JE, Stampfer MJ, Rosner B, Willett WC, Speizer FE. 1992. Diet and risk of clinical diabetes in women. *Am J Clin Nutr* 55:1018–1023.
- Collins FD, Sinclair AJ, Royle JP, Coats DA, Maynard AT, Leonard RF. 1971. Plasma lipids in human linoleic acid deficiency. *Nutr Metab* 13:150–167.
- Connor WE, Lowensohn R, Hatcher L. 1996. Increased docosahexaenoic acid levels in human newborn infants by administration of sardines and fish oil during pregnancy. *Lipids* 31:S183–S187.
- Conquer JA, Holub BJ. 1996. Supplementation with an algae source of docosahexaenoic acid increases (*n*-3) fatty acid status and alters selected risk factors for heart disease in vegetarian subjects. *J Nutr* 126:3032–3039.
- Conti S, Farchi G, Menotti A. 1983. Coronary risk factors and excess mortality from all causes and specific causes. *Int J Epidemiol* 12:301–307.
- Cook HW. 1981. The influence of *trans*-acids on desaturation and elongation of fatty acids in developing brain. *Lipids* 16:920–926.
- Cooling J, Blundell J. 1998. Differences in energy expenditure and substrate oxidation between habitual high fat and low fat consumers (phenotypes). *Int J Obes Relat Metab* 22:612–618.
- Cooper AL, Gibbons L, Horan MA, Little RA, Rothwell NJ. 1993. Effect of dietary fish oil supplementation on fever and cytokine production in human volunteers. *Clin Nutr* 12:321–328.
- Corazza GR, Frazzoni M, Gatto MR, Gasbarrini G. 1986. Ageing and small-bowel mucosa: A morphometric study. *Gerontology* 32:60–65.
- Corti MC, Guralnik JM, Salive ME, Harris T, Ferrucci L, Glynn RJ, Havlik RJ. 1997. Clarifying the direct relation between total cholesterol levels and death from coronary heart disease in older persons. *Ann Intern Med* 126:753–760.
- Costa MB, Ferreira SRG, Franco LJ, Gimeno SGA, Iunes M, Japanese-Brazilian Diabetes Study Group. 2000. Dietary patterns in a high-risk population for glucose intolerance. *J Epidemiol* 10:111–117.
- Craig-Schmidt MC. 2001. Isomeric fatty acids: Evaluating status and implications for maternal and child health. *Lipids* 36:997–1006.
- Cuchel M, Schwab US, Jones PJH, Vogel S, Lammi-Keefe C, Li Z, Ordovas J, McNamara JR, Schaefer EJ, Lichtenstein AH. 1996. Impact of hydrogenated fat consumption on endogenous cholesterol synthesis and susceptibility of low-density lipoprotein to oxidation in moderately hypercholesterolemic individuals. *Metabolism* 45:241–247.
- Cunnane SC, Ross R, Bannister JL, Jenkins DJA. 2001.  $\beta$ -Oxidation of linoleate in obese men undergoing weight loss. *Am J Clin Nutr* 73:709–714.
- Cuthbertson WFJ. 1976. Essential fatty acid requirements in infancy. *Am J Clin Nutr* 29:559–568.
- De Caterina R, Giannessi D, Mazzone A, Berini W, Lazzerini G, Maffei S, Cerri M, Salvatore L, Weksler B. 1990. Vascular prostacyclin is increased in patients ingesting  $\omega$ -3 polyunsaturated fatty acids before coronary artery bypass graft surgery. *Circulation* 82:428–438.
- Decsi T, Koletzko B. 1995. Do trans fatty acids impair linoleic acid metabolism in children? *Ann Nutr Metab* 39:36–41.

- de la Presa Owens S, Innis SM. 1999. Docosahexaenoic and arachidonic acid prevent a decrease in dopaminergic and serotonergic neurotransmitters in frontal cortex caused by a linoleic and  $\alpha$ -linolenic acid deficient diet in formula-fed piglets. *J Nutr* 129:2088–2093.
- Denke MA. 1994. Effects of cocoa butter on serum lipids in humans: Historical highlights. *Am J Clin Nutr* 60:1014S–1016S.
- Denke MA. 1995. Serum lipid concentrations in humans. *Am J Clin Nutr* 62:693S–700S.
- De Stefani E, Deneo-Pellegrini H, Mendilaharsu M, Carzoglio JC, Ronco A. 1997. Dietary fat and lung cancer: A case-control study in Uruguay. *Cancer Causes Control* 8:913–921.
- Dewey KG, Lönnerdal B. 1983. Milk and nutrient intake of breast-fed infants from 1 to 6 months: Relation to growth and fatness. *J Pediatr Gastroenterol Nutr* 2:497–506.
- Dewey KG, Finley DA, Lönnerdal B. 1984. Breast milk volume and composition during late lactation. *J Pediatr Gastroenterol Nutr* 3:713–720.
- Dolecek TA, Grandits G. 1991. Dietary polyunsaturated fatty acids and mortality in the Multiple Risk Factor Intervention Trial (MRFIT). *World Rev Nutr Diet* 66:205–216.
- Doucet E, Alméras N, White MD, Després J-P, Bouchard C, Tremblay A. 1998. Dietary fat composition and human adiposity. *Eur J Clin Nutr* 52:2–6.
- Dyerberg J, Bang HO. 1979. Haemostatic function and platelet polyunsaturated fatty acids in Eskimos. *Lancet* 2:433–435.
- Dyerberg J, Bang HO, Stoffersen E, Moncada S, Vane JR. 1978. Eicosapentaenoic acid and prevention of thrombosis and atherosclerosis? *Lancet* 2:117–119.
- Eisenstein AB. 1982. Nutritional and metabolic effects of alcohol. *J Am Diet Assoc* 81:247–251.
- Elias SL, Innis SM. 2001. Infant plasma *trans*, *n*-6, and *n*-3 fatty acids and conjugated linoleic acids are related to maternal plasma fatty acids, length of gestation, and birth weight and length. *Am J Clin Nutr* 73:807–814.
- Elias SL, Innis SM. 2002. Bakery foods are the major dietary source of *trans*-fatty acids among pregnant women with diets providing 30 percent energy from fat. *J Am Diet Assoc* 102:46–51.
- Emken EA. 1979. Utilization and effects of isomeric fatty acids in humans. In: Emken EA, Dutton HJ, eds. *Geometrical and Positional Fatty Acid Isomers*. Champaign, IL: American Oil Chemists' Society. Pp. 99–129.
- Emken EA. 1984. Nutrition and biochemistry of *trans* and positional fatty acid isomers in hydrogenated oils. *Annu Rev Nutr* 4:339–376.
- Emken EA. 1994. Metabolism of dietary stearic acid relative to other fatty acids in human subjects. *Am J Clin Nutr* 60:1023S–1028S.
- Emken EA. 1995. Physicochemical properties, intake, and metabolism. *Am J Clin Nutr* 62:659S–669S.
- Emken EA, Adloff RO, Gulley RM. 1994. Dietary linoleic acid influences desaturation and acylation of deuterium-labeled linoleic and linolenic acids in young adult males. *Biochim Biophys Acta* 1213:277–288.
- Emken EA, Adloff RO, Duval SM, Nelson GJ. 1998. Effect of dietary arachidonic acid on metabolism of deuterated linoleic acid by adult male subjects. *Lipids* 33:471–480.
- Emken EA, Adloff RO, Duval SM, Nelson GJ. 1999. Effect of dietary docosahexaenoic acid on desaturation and uptake *in vivo* of isotope-labeled oleic, linoleic, and linolenic acids by male subjects. *Lipids* 34:785–791.

- Endres S, Ghorbani R, Kelley VE, Georgilis K, Lonnemann G, van der Meer JWM, Cannon JG, Rogers TS, Klempner MS, Weber PC, Schaefer EJ, Wolff SM, Dinarello CA. 1989. The effect of dietary supplementation with *n*-3 polyunsaturated fatty acids on the synthesis of interleukin-1 and tumor necrosis factor by mononuclear cells. *N Engl J Med* 320:265–271.
- Endres S, Meydani SN, Ghorbani R, Schindler R, Dinarello CA. 1993. Dietary supplementation with *n*-3 fatty acids suppresses interleukin-2 production and mononuclear cell proliferation. *J Leukoc Biol* 54:599–603.
- Enig MG, Atal S, Keeney M, Sampugna J. 1990. Isomeric *trans* fatty acids in the U.S. diet. *J Am Coll Nutr* 5:471–486.
- Ens JG, Ma DW, Cole KS, Field CJ, Clandinin MT. 2001. An assessment of *c*9, *t*11 linoleic acid intake in a small group of young Canadians. *Nutr Res* 21:955–960.
- Ezaki O, Takahashi M, Shigematsu T, Shimamura K, Kimura J, Ezaki H, Gotoh T. 1999. Long-term effects of dietary  $\alpha$ -linolenic acid from perilla oil on serum fatty acids composition and on the risk factors of coronary heart disease in Japanese elderly subjects. *J Nutr Sci Vitaminol* 45:759–772.
- Falase AO, Cole TO, Osuntokun BO. 1973. Myocardial infarction in Nigerians. *Trop Geogr Med* 25:147–150.
- FAO/WHO (Food and Agricultural Organization/World Health Organization). 1994. General conclusions and recommendations of the consultation. In: *Fats and Oils in Human Nutrition*. Rome: FAO. Pp. 3–7.
- Farquharson J. 1994. Infant cerebral cortex and dietary fatty acids. *Eur J Clin Nutr* 48:S24–S26.
- Farquharson J, Cockburn F, Patrick WA, Jamieson EC, Logan RW. 1992. Infant cerebral cortex phospholipid fatty-acid composition and diet. *Lancet* 340:810–813.
- Farquharson J, Jamieson EC, Abbasi KA, Patrick WJA, Logan RW, Cockburn F. 1995. Effect of diet on the fatty acid composition of the major phospholipids of infant cerebral cortex. *Arch Dis Child* 72:198–203.
- Fasching P, Ratheiser K, Schneeweiss B, Rohac M, Nowotny P, Waldhausl W. 1996. No effect of short-term dietary supplementation of saturated and poly- and monounsaturated fatty acids on insulin secretion and sensitivity in healthy men. *Ann Nutr Metab* 40:116–122.
- Fellner V, Sauer FD, Kramer JKG. 1999. Effect of ionophores on conjugated linoleic acid in ruminal cultures and in the milk of dairy cows. In: Yurawecz MP, Mossoba MM, Kramer JKG, Pariza MW, Nelson CJ, eds. *Advances in Conjugated Linoleic Acid Research*, Vol. 1. Champaign, IL: AOCS Press. Pp. 209–214.
- Ferris AM, Dotts MA, Clark RM, Ezrin M, Jensen RG. 1988. Macronutrients in human milk at 2, 12, and 16 weeks postpartum. *J Am Diet Assoc* 88:694–697.
- Feskens EJM, Virtanen SM, Räsänen L, Tuomilehto J, Stengard J, Pekkanen J, Nissinen A, Kromhout D. 1995. Dietary factors determining diabetes and impaired glucose tolerance: A 20-year follow-up of the Finnish and Dutch cohorts of the Seven Countries Study. *Diabetes Care* 18:1104–1112.
- Finley DA, Lönnedal B, Dewey KG, Grivetti LE. 1985. Breast milk composition: Fat content and fatty acid composition in vegetarians and non-vegetarians. *Am J Clin Nutr* 41:787–800.
- Fischer DR, Morgan KJ, Zabik ME. 1985. Cholesterol, saturated fatty acids, polyunsaturated fatty acids, sodium, and potassium intakes of the United States population. *J Am Coll Nutr* 4:207–224.
- Fleming CR, Smith LM, Hodges RE. 1976. Essential fatty acid deficiency in adults receiving total parenteral nutrition. *Am J Clin Nutr* 29:976–983.

- Fomon SJ, Thomas LN, Filer LJ, Anderson TA, Nelson SE. 1976. Influence of fat and carbohydrate content of diet on food intake and growth of male infants. *Acta Paediatr Scand* 65:136–144.
- Frank JW, Reed DM, Grove JS, Benfante R. 1992. Will lowering population levels of serum cholesterol affect total mortality? Expectations from the Honolulu Heart Program. *J Clin Epidemiol* 45:333–346.
- Freese R, Mutanen M. 1997.  $\alpha$ -Linolenic acid and marine long-chain *n*-3 fatty acids differ only slightly in their effects on hemostatic factors in healthy subjects. *Am J Clin Nutr* 66:591–598.
- Friday KE, Childs MT, Tsunehara CH, Fujimoto WY, Bierman EL, Ensinck JW. 1989. Elevated plasma glucose and lowered triglyceride levels from omega-3 fatty acid supplementation in type II diabetes. *Diabetes Care* 12:276–281.
- Fritzsche KL, Shahbazian LM, Feng C, Berg JN. 1997. Dietary fish oil reduces survival and impairs bacterial clearance in C3H/Hen mice challenged with *Listeria monocytogenes*. *Clin Sci* 92:95–101.
- Gallai V, Sarchielli P, Trequattrini A, Franceschini M, Floridi A, Firenze C, Alberti A, Di Benedetto D, Stragliotto E. 1995. Cytokine secretion and eicosanoid production in the peripheral blood mononuclear cells of MS patients undergoing dietary supplementation with *n*-3 polyunsaturated fatty acids. *J Neuroimmunol* 56:143–153.
- Ganji V, Betts N. 1995. Fat, cholesterol, fiber and sodium intakes of US population: Evaluation of diets reported in 1987–88 Nationwide Food Consumption Survey. *Eur J Clin Nutr* 49:915–920.
- Garland M, Sacks FM, Colditz GA, Rimm EB, Sampson LA, Willett WC, Hunter DJ. 1998. The relation between dietary intake and adipose tissue composition of selected fatty acids in US women. *Am J Clin Nutr* 67:25–30.
- Gazzaniga JM, Burns TL. 1993. Relationship between diet composition and body fatness, with adjustment for resting energy expenditure and physical activity, in preadolescent children. *Am J Clin Nutr* 58:21–28.
- Ghebremeskel K, Min Y, Crawford MA, Nam J-H, Kim A, Koo J-N, Suzuki H. 2000. Blood fatty acid composition of pregnant and nonpregnant Korean women: Red cells may act as a reservoir of arachidonic acid and docosahexaenoic acid for utilization by the developing fetus. *Lipids* 35:567–574.
- Gibson RA, Kneebone GM. 1981. Fatty acid composition of human colostrum and mature breast milk. *Am J Clin Nutr* 34:252–257.
- Gibson RA, Neumann MA, Makrides M. 1997. Effect of increasing breast milk docosahexaenoic acid on plasma and erythrocyte phospholipid fatty acids and neural indices of exclusively breast fed infants. *Eur J Clin Nutr* 51:578–584.
- Gillman MW, Cupples LA, Gagnon D, Millen BE, Ellison RC, Castelli WP. 1997. Margarine intake and subsequent coronary heart disease in men. *Epidemiology* 8:144–149.
- Giovannucci E, Rimm EB, Colditz GA, Stampfer MJ, Ascherio A, Chute CC, Willett WC. 1993. A prospective study of dietary fat and risk of prostate cancer. *J Natl Cancer Inst* 85:1571–1579.
- Glauber H, Wallace P, Griver K, Brechtel G. 1988. Adverse metabolic effect of omega-3 fatty acids in non-insulin-dependent diabetes mellitus. *Ann Intern Med* 108:663–668.
- Goedecke JH, Christie C, Wilson G, Dennis SC, Noakes TD, Hopkins WG, Lambert EV. 1999. Metabolic adaptations to a high-fat diet in endurance cyclists. *Metabolism* 48:1509–1517.

- Goldbourt U, Yaari S, Medalie JH. 1993. Factors predictive of long-term coronary heart disease mortality among 10,059 male Israeli civil servants and municipal employees. A 23-year mortality follow-up in the Israeli Ischemic Heart Disease Study. *Cardiology* 82:100–121.
- González CA, Pera G, Quirós JR, Lasheras C, Tormo MJ, Rodriguez M, Navarro C, Martínez C, Dorronsoro M, Chirlaque MD, Beguiristain JM, Barricarte A, Amiano P, Agudo A. 2000. Types of fat intake and body mass index in a Mediterranean country. *Public Health Nutr* 3:329–336.
- Goodgame JT, Lowry SF, Brennan MF. 1978. Essential fatty acid deficiency in total parenteral nutrition: Time course of development and suggestions for therapy. *Surgery* 84:271–277.
- Goodnight SH, Harris WS, Connor WE. 1981. The effects of dietary  $\omega$ 3 fatty acids on platelet composition and function in man: A prospective, controlled study. *Blood* 58:880–885.
- Gore SM. 1999. Statistical considerations in infant nutrition trials. *Lipids* 34:185–197.
- Greiner RCS, Winter J, Nathanielsz PW, Brenna JT. 1997. Brain docosahexaenoate accretion in fetal baboons: Bioequivalence of dietary  $\alpha$ -linolenic and docosahexaenoic acids. *Pediatr Res* 42:826–834.
- Griinari JM, Bauman DE. 1999. Biosynthesis of conjugated linoleic acid and its incorporation into meat and milk ruminants. In: Yurawecz MP, Mossoba MM, Kramer JKG, Pariza MW, Nelson GJ, eds. *Advances in Conjugated Linoleic Acid Research*, Vol. 1. Champaign, IL: AOCS Press. Pp. 180–200.
- Griinari JM, Corl BA, Lacy SH, Chouinard PY, Nurmela KVV, Bauman DE. 2000. Conjugated linoleic acid is synthesized endogenously in lactating cows by  $\Delta^9$ -desaturase. *J Nutr* 130:2285–2291.
- Ha YL, Grimm NK, Pariza MW. 1989. Newly recognized anticarcinogenic fatty acids: Identification and quantification in natural and processed cheeses. *J Agric Food Chem* 37:75–81.
- Haheim LL, Holme I, Hjermann I, Leren P. 1993. The predictability of risk factors with respect to incidence and mortality of myocardial infarction and total mortality. A 12-year follow-up of the Oslo Study, Norway. *J Intern Med* 234:17–24.
- Halvorsen B, Almendingen K, Nenseter MS, Pedersen JI, Christiansen EN. 1996. Effects of partially hydrogenated fish oil, partially hydrogenated soybean oil and butter on the susceptibility of low density lipoprotein to oxidative modification in men. *Eur J Clin Nutr* 50:364–370.
- Hansen AE, Haggard ME, Boelsche AN, Adam DJD, Wiese HF. 1958. Essential fatty acids in infant nutrition. III. Clinical manifestations of linoleic acid deficiency. *J Nutr* 66:565–576.
- Hansen AE, Wiese HF, Boelsche AN, Haggard ME, Adam DJD, Davis H. 1963. Role of linoleic acid in infant nutrition. Clinical and chemical study of 428 infants fed on milk mixtures varying in kind and amount of fat. *Pediatrics* 31:171–192.
- Hansen HS, Jensen B. 1985. Essential function of linoleic acid esterified in acylglucosylceramide and acylceramide in maintaining the epidermal water permeability barrier. Evidence from feeding studies with oleate, linoleate, arachidonate, columbinate and  $\alpha$ -linolenate. *Biochim Biophys Acta* 834:357–363.
- Harris WS, Connor WE, Lindsey S. 1984. Will dietary  $\omega$ -3 fatty acids change the composition of human milk? *Am J Clin Nutr* 40:780–785.
- Hegsted DM, McGandy RB, Myers ML, Stare FJ. 1965. Quantitative effects of dietary fat on serum cholesterol in man. *Am J Clin Nutr* 17:281–295.
- Hegsted DM, Ausman LM, Johnson JA, Dallal GE. 1993. Dietary fat and serum lipids: An evaluation of the experimental data. *Am J Clin Nutr* 57:875–883.

- Heitmann BL, Lissner L, Sørensen TIA, Bengtsson C. 1995. Dietary fat intake and weight gain in women genetically predisposed for obesity. *Am J Clin Nutr* 61:1213–1217.
- Helge JW. 2000. Adaptation to a fat-rich diet. Effects on endurance performance in humans. *Sports Med* 30:347–357.
- Henderson RA, Jensen RG, Lammi-Keefe CJ, Ferris AM, Dardick KR. 1992. Effect of fish oil on the fatty acid composition of human milk and maternal and infant erythrocytes. *Lipids* 27:863–869.
- Hill JO, Schlundt DG, Sbrocco T, Sharp T, Pope-Cordle J, Stetson B, Kaler M, Heim C. 1989. Evaluation of an alternating-calorie diet with and without exercise in the treatment of obesity. *Am J Clin Nutr* 50:248–254.
- Hill JO, Peters JC, Reed GW, Schlundt DG, Sharp T, Greene HL. 1991. Nutrient balance in humans: Effects of diet composition. *Am J Clin Nutr* 54:10–17.
- Holman RT. 1960. The ratio of trienoic:tetraenoic acids in tissue lipids as a measure of essential fatty acid requirement. *J Nutr* 70:405–410.
- Holman RT, Smythe L, Johnson S. 1979. Effect of sex and age on fatty acid composition of human serum lipids. *Am J Clin Nutr* 32:2390–2399.
- Holman RT, Johnson SB, Hatch TF. 1982. A case of human linolenic acid deficiency involving neurological abnormalities. *Am J Clin Nutr* 35:617–623.
- Holman RT, Johnson SB, Ogburn PL. 1991. Deficiency of essential fatty acids and membrane fluidity during pregnancy and lactation. *Proc Natl Acad Sci USA* 88:4835–4839.
- Holmes MD, Hunter DJ, Colditz GA, Stampfer MJ, Hankinson SE, Speizer FE, Rosner B, Willett WC. 1999. Association of dietary intake of fat and fatty acids with risk of breast cancer. *J Am Med Assoc* 281:914–920.
- Hu FB, Stampfer MJ, Manson JE, Rimm E, Colditz GA, Rosner BA, Hennekens CH, Willett WC. 1997. Dietary fat intake and the risk of coronary heart disease in women. *N Engl J Med* 337:1491–1499.
- Hu FB, Stampfer MJ, Manson JE, Ascherio A, Colditz GA, Speizer FE, Hennekens CH, Willett WC. 1999a. Dietary saturated fats and their food sources in relation to the risk of coronary heart disease in women. *Am J Clin Nutr* 70:1001–1008.
- Hu FB, Stampfer MJ, Manson JE, Rimm EB, Wolk A, Colditz GA, Hennekens CH, Willett WC. 1999b. Dietary intake of α-linolenic acid and risk of fatal ischemic heart disease among women. *Am J Clin Nutr* 69:890–897.
- Hu FB, Stampfer MJ, Rimm E, Ascherio A, Rosner BA, Spiegelman D, Willett WC. 1999c. Dietary fat and coronary heart disease: A comparison of approaches for adjusting for total energy intake and modeling repeated dietary measurements. *Am J Epidemiol* 149:531–540.
- Hu FB, van Dam RM, Liu S. 2001. Diet and risk of type II diabetes: The role of types of fat and carbohydrate. *Diabetologia* 44:805–817.
- Hudgins LC, Hirsch J, Emken EA. 1991. Correlation of isomeric fatty acids in human adipose tissue with clinical risk factors for cardiovascular disease. *Am J Clin Nutr* 53:474–482.
- Hughes DA, Pinder AC, Piper Z, Johnson IT, Lund EK. 1996. Fish oil supplementation inhibits the expression of major histocompatibility complex class II molecules and adhesion molecules on human monocytes. *Am J Clin Nutr* 63:267–272.
- Hursting SD, Thornquist M, Henderson MM. 1990. Types of dietary fat and the incidence of cancer at five sites. *Prev Med* 19:242–253.
- Hwang DH, Chanmugam P, Anding R. 1982. Effects of dietary 9-trans,12-trans linoleate on arachidonic acid metabolism in rat platelets. *Lipids* 17:307–313.

- Innis SM. 1991. Essential fatty acids in growth and development. *Prog Lipid Res* 30:39–103.
- Innis SM, King DJ. 1999. *Trans* fatty acids in human milk are inversely associated with concentrations of essential *all-cis n-6* and *n-3* fatty acids and determine *trans*, but not *n-6* and *n-3*, fatty acids in plasma lipids of breast-fed infants. *Am J Clin Nutr* 70:383–390.
- Innis SM, Kuhnlein HV. 1988. Long-chain *n-3* fatty acids in breast milk of Inuit women consuming traditional foods. *Early Hum Dev* 18:185–189.
- Innis SM, Auestad N, Siegman JS. 1996. Blood lipid docosahexaenoic and arachidonic acid in term gestation infants fed formulas with high docosahexaenoic acid, low eicosapentaenoic acid fish oil. *Lipids* 31:617–625.
- Innis SM, Green TJ, Halsey TK. 1999. Variability in the *trans* fatty acid content of foods within a food category: Implications for estimation of dietary *trans* fatty acid intakes. *J Am Coll Nutr* 18:255–260.
- Iso H, Rexrode KM, Stampfer MJ, Manson JE, Colditz GA, Speizer FE, Hennekens CH, Willett WC. 2001. Intake of fish and omega-3 fatty acids and risk of stroke in women. *J Am Med Assoc* 285:304–312.
- ISSFAL (International Society for the Study of Fatty Acids and Lipids). 1994. *Recommendations for the Essential Fatty Acid Requirement for Infant Formulas*. Online. Available at <http://www.issfal.org.uk/infantnutr.htm>. Accessed July 2, 2001.
- Jamieson EC, Abbasi KA, Cockburn F, Farquharson J, Logan RW, Patrick WA. 1994. Effect of diet on term infant cerebral cortex fatty acid composition. *World Rev Nutr Diet* 75:139–141.
- Jamieson EC, Farquharson J, Logan RW, Howatson AG, Patrick WJA, Weaver LT, Cockburn F. 1999. Infant cerebral gray and white matter fatty acids in relation to age and diet. *Lipids* 34:1065–1071.
- Jensen C, Buist NRM, Wilson T. 1986. Absorption of individual fatty acids from long chain or medium chain triglycerides in very small infants. *Am J Clin Nutr* 43:745–751.
- Jensen CL, Prager TC, Fraley JK, Chen H, Anderson RE, Heird WC. 1997. Effect of dietary linoleic/alpha-linolenic acid ratio on growth and visual function of term infants. *J Pediatr* 131:200–209.
- Jensen RG. 1999. Lipids in human milk. *Lipids* 34:1243–1271.
- Jeppesen PB, Høy C-E, Mortensen PB. 1998. Essential fatty acid deficiency in patients receiving home parenteral nutrition. *Am J Clin Nutr* 68:126–133.
- Jeppesen PB, Hoy CE, Mortensen PB. 2000. Deficiencies of essential fatty acids, vitamin A and E and changes in plasma lipoproteins in patients with reduced fat absorption or intestinal failure. *Eur J Clin Nutr* 54:632–642.
- Jéquier E. 1999. Response to and range of acceptable fat intake in adults. *Eur J Clin Nutr* 53:S84–S93.
- Jones PJH, Kubow S. 1999. Lipids, sterols, and their metabolites. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th ed. Baltimore, MD: Williams and Wilkins. Pp. 67–94.
- Jones PJH, Pencharz PB, Clandinin MT. 1985. Whole body oxidation of dietary fatty acids: Implications for energy utilization. *Am J Clin Nutr* 42:769–777.
- Jonnalagadda SS, Egan SK, Heimbach JT, Harris SS, Kris-Etherton PM. 1995. Fatty acid consumption pattern of Americans: 1987–1988 USDA Nationwide Food Consumption Survey. *Nutr Res* 15:1767–1781.

- Jørgensen MG, Hølmer G, Lund P, Hernell O, Michaelsen KM. 1998. Effect of formula supplemented with docosahexaenoic acid and  $\gamma$ -linolenic acid on fatty acid status and visual acuity in term infants. *J Pediatr Gastroenterol Nutr* 26:412–421.
- Jousilahti P, Vartiainen E, Pekkanen J, Tuomilehto J, Sundvall J, Puska P. 1998. Serum cholesterol distribution and coronary heart disease risk. Observations and predictions among middle-aged population in eastern Finland. *Circulation* 97:1087–1094.
- Judd JT, Clevidence BA, Muesing RA, Witten J, Sunkin ME, Podczasny JJ. 1994. Dietary *trans* fatty acids: Effects on plasma lipids and lipoproteins of healthy men and women. *Am J Clin Nutr* 59:861–868.
- Judd JT, Baer DJ, Clevidence BA, Muesing RA, Chen SC, Weststrate JA, Meijer GW, Witten J, Lichtenstein AH, Vilella-Bach M, Schaefer EJ. 1998. Effects of margarine compared with those of butter on blood lipid profiles related to cardiovascular disease risk factors in normolipemic adults fed controlled diets. *Am J Clin Nutr* 68:768–777.
- Judd JT, Baer DJ, Clevidence BA, Kris-Etherton P, Muesing RA, Iwane M. 2002. Dietary *cis* and *trans* monounsaturated and saturated FA and plasma lipids and lipoproteins in men. *Lipids* 37:123–131.
- Jump DB, Clarke SD. 1999. Regulation of gene expression by dietary fat. *Annu Rev Nutr* 19:63–90.
- Kagan A, McGee DL, Yano K, Rhoads GG, Nomura A. 1981. Serum cholesterol and mortality in a Japanese-American population: The Honolulu Heart Program. *Am J Epidemiol* 114:11–20.
- Kasim SE, Stern B, Khilnani S, McLin P, Baciorowski S, Jen K-LC. 1988. Effects of omega-3 fish oils on lipid metabolism, glycemic control, and blood pressure in type II diabetic patients. *J Clin Endocrinol Metab* 67:1–5.
- Kelley DS, Branch LB, Love JE, Taylor PC, Rivera YM, Iacono JM. 1991. Dietary  $\alpha$ -linolenic acid and immunocompetence in humans. *Am J Clin Nutr* 53:40–46.
- Kelley DS, Taylor PC, Nelson GJ, Mackey BE. 1998. Dietary docosahexaenoic acid and immunocompetence in young healthy men. *Lipids* 33:559–566.
- Kelley DS, Taylor PC, Nelson GJ, Schmidt PC, Ferretti A, Erickson KL, Yu R, Chandra RK, Mackey BE. 1999. Docosahexaenoic acid ingestion inhibits natural killer cell activity and production of inflammatory mediators in young healthy men. *Lipids* 34:317–324.
- Kelly FD, Sinclair AJ, Mann NJ, Turner AH, Abedin L, Li D. 2001. A stearic acid-rich diet improves thrombogenic and atherogenic risk factor profiles in healthy males. *Eur J Clin Nutr* 55:88–96.
- Keys A, Anderson JT, Grande F. 1965. Serum cholesterol response to changes in the diet. IV. Particular saturated fatty acids in the diet. *Metabolism* 14:776–787.
- Keys A, Aravanis C, Blackburn H, Buzina R, Djordevic' BS, Dontas AS, Fidanza F, Karvonen MJ, Kimura N, Menotti A, Mohac'ek I, Nedeljkovic' S, Puddu V, Punyar S, Taylor HL, van Buchem FSP. 1980. *Seven Countries. A Multivariate Analysis of Death and Coronary Heart Disease*. Cambridge, MA: Harvard University Press.
- Kinsella JE, Lokesh B, Stone RA. 1990. Dietary *n*-3 polyunsaturated fatty acids and amelioration of cardiovascular disease: Possible mechanisms. *Am J Clin Nutr* 52:1–28.
- Klag MJ, Ford DE, Mead LA, He J, Whelton PK, Liang KY, Levine DM. 1993. Serum cholesterol in young men and subsequent cardiovascular disease. *N Engl J Med* 328:313–318.

- Kliewer SA, Sundseth SS, Jones SA, Brown PJ, Wisely GB, Koble CS, Devchand P, Wahli W, Willson TM, Lenhard JM, Lehmann JM. 1997. Fatty acids and eicosanoids regulate gene expression through direct interactions with peroxisome proliferator-activated receptors  $\alpha$  and  $\gamma$ . *Proc Natl Acad USA* 94:4318–4323.
- Kneebone GM, Kneebone R, Gibson R. 1985. Fatty acid composition of breast milk from three racial groups from Penang, Malaysia. *Am J Clin Nutr* 41:765–769.
- Kohlmeier L, Simonsen N, van't Veer P, Strain JJ, Martin-Moreno JM, Margolin B, Huttunen JK, Fernández-Crehuet Navajas J, Martin BC, Thamm M, Kardinaal AFM, Kok FJ. 1997. Adipose tissue *trans* fatty acids and breast cancer in the European Community Multicenter Study on Antioxidants, Myocardial Infarction, and Breast Cancer. *Cancer Epidemiol Biomarkers Prev* 6:705–710.
- Koletzko B. 1992. *Trans* fatty acids may impair biosynthesis of long-chain polyunsaturates and growth in man. *Acta Paediatr* 81:302–306.
- Kris-Etherton PM, Derr J, Mitchell DC, Mustad VA, Russell ME, McDonnell ET, Salabsky D, Pearson TA. 1993. The role of fatty acid saturation on plasma lipids, lipoproteins, and apolipoproteins: I. Effects of whole food diets high in cocoa butter, olive oil, soybean oil, dairy butter, and milk chocolate on the plasma lipids of young men. *Metabolism* 42:121–129.
- Kris-Etherton PM, Taylor DS, Yu-Poth S, Huth P, Moriarty K, Fishell V, Hargrove RL, Zhao G, Etherton TD. 2000. Polyunsaturated fatty acids in the food chain in the United States. *Am J Clin Nutr* 71:179S–188S.
- Kristensen MØ. 1983. Increased incidence of bleeding intracranial aneurysms in Greenlandic Eskimos. *Acta Neurochir* 67:37–43.
- Kritchevsky D. 1982. Trans fatty acid effects in experimental atherosclerosis. *Fed Proc* 41:2813–2817.
- Kritchevsky D, Tepper SA, Wright S, Tso P, Czarnecki SK. 2000. Influence of conjugated linoleic acid (CLA) on establishment and progression of atherosclerosis in rabbits. *J Am Coll Nutr* 19:472S–477S.
- Kromann N, Green A. 1980. Epidemiological studies in the Upernivik district, Greenland. Incidence of some chronic diseases 1950–1974. *Acta Med Scand* 208:401–406.
- Kromhout D, de Lezenne Coulander C. 1984. Diet, prevalence and 10-year mortality from coronary heart disease in 871 middle-aged men. *Am J Epidemiol* 119:733–741.
- Kromhout D, Bosscheriet EB, de Lezenne Coulander C. 1985. The inverse relation between fish consumption and 20-year mortality from coronary heart disease. *N Engl J Med* 312:1205–1209.
- Kromhout D, Menotti A, Bloomberg B, Aravanis C, Blackburn H, Buzina R, Dontas AS, Fidanza F, Giampaoli S, Jansen A, Karvonen M, Katan M, Nissinen A, Nedeljkovic S, Pekkanen J, Pekkarinen M, Punstar S, Räsänen L, Simic B, Toshima H. 1995. Dietary saturated and *trans* fatty acids and cholesterol and 25-year mortality from coronary heart disease: The Seven Countries Study. *Prev Med* 24:308–315.
- Lagström H, Seppänen R, Jokinen E, Niinikoski H, Rönnemaa T, Viikari J, Simell O. 1999. Influence of dietary fat on the nutrient intake and growth of children from 1 to 5 y of age: The Special Turku Coronary Risk Factor Intervention Project. *Am J Clin Nutr* 69:516–523.
- Lands WEM, Hamazaki T, Yamazaki K, Okuyama H, Sakai K, Goto Y, Hubbard VS. 1990. Changing dietary patterns. *Am J Clin Nutr* 51:991–993.

- Lands WEM, Libelt B, Morris A, Kramer NC, Prewitt TE, Bowen P, Schmeisser D, Davidson MH, Burns JH. 1992. Maintenance of lower proportions of (*n*-6) eicosanoid precursors in phospholipids of human plasma in response to added dietary (*n*-3) fatty acids. *Biochim Biophys Acta* 1180:147–162.
- Lapinleimu H, Viikari J, Jokinen E, Salo P, Routi T, Leino A, Rönnemaa R, Seppänen R, Välimäki I, Simell O. 1995. Prospective randomised trial in 1062 infants of diet low in saturated fat and cholesterol. *Lancet* 345:471–476.
- Larson DE, Hunter GR, Williams MJ, Kekes-Szabo T, Nyikos I, Goran MI. 1996. Dietary fat in relation to body fat and intraabdominal adipose tissue: A cross-sectional analysis. *Am J Clin Nutr* 64:677–684.
- Latruffe N, Vamecq J. 1997. Peroxisome proliferators and peroxisome proliferator activated receptors (PPARs) as regulators of lipid metabolism. *Biochimie* 79:81–94.
- Lee TH, Hoover RL, Williams JD, Sperling RI, Ravalese JD, Spur BW, Robinson DR, Corey EJ, Lewis RA, Austen KF. 1985. Effect of dietary enrichment with eicosapentaenoic and docosahexaenoic acids on in vitro neutrophil and monocyte leukotriene generation and neutrophil function. *N Engl J Med* 312:1217–1224.
- Leibel RL, Hirsch J, Appel BE, Checani GC. 1992. Energy intake required to maintain body weight is not affected by wide variation in diet composition. *Am J Clin Nutr* 55:350–355.
- Leibovitz BE, Hu ML, Tappel AL. 1990. Lipid peroxidation in rat tissue slices: Effect of dietary vitamin E, corn oil-lard and mehaden oil. *Lipids* 25:125–129.
- Lemaitre RN, King IB, Patterson RE, Psaty BM, Kestin M, Heckbert SR. 1998. Assessment of *trans*-fatty acid intake with a food frequency questionnaire and validation with adipose tissue levels of *trans*-fatty acids. *Am J Epidemiol* 148:1085–1093.
- Levinson PD, Iosiphidis AH, Saritelli AL, Herbert PN, Steiner M. 1990. Effects of *n*-3 fatty acids in essential hypertension. *Am J Hypertens* 3:754–760.
- Lichtenstein AH, Ausman LM, Carrasco W, Jenner JL, Ordovas JM, Schaefer EJ. 1993. Hydrogenation impairs the hypolipidemic effect of corn oil in humans. Hydrogenation, *trans* fatty acids, and plasma lipids. *Arterioscler Thromb* 13:154–161.
- Lichtenstein AH, Ausman LM, Jalbert SM, Schaefer EJ. 1999. Effects of different forms of dietary hydrogenated fats on serum lipoprotein cholesterol levels. *N Engl J Med* 340:1933–1940.
- Lippi G, Guidi G. 1999. Biochemical risk factors and patient's outcome: The case of lipoprotein(a). *Clin Chim Acta* 280:59–71.
- Litin L, Sacks F. 1993. *Trans*-fatty-acid content of common foods. *N Engl J Med* 329:1969–1970.
- London SJ, Sacks FM, Caesar J, Stampfer MJ, Siguel E, Willett WC. 1991. Fatty acid composition of subcutaneous adipose tissue and diet in postmenopausal US women. *Am J Clin Nutr* 54:340–345.
- Lorenz R, Spengler U, Fischer S, Duhm J, Weber PC. 1983. Platelet function, thromboxane formation and blood pressure control during supplementation of the Western diet with cod liver oil. *Circulation* 67:504–511.
- Louheranta AM, Turpeinen AK, Schwab US, Vidgren HM, Parviainen MT, Uusitupa MJ. 1998. A high-steric acid diet does not impair glucose tolerance and insulin sensitivity in healthy women. *Metabolism* 47:529–534.

- Louheranta AM, Turpeinen AK, Vidgren HM, Schwab US, Uusitupa MJ. 1999. A high-trans fatty acid diet and insulin sensitivity in young healthy women. *Metabolism* 48:870–875.
- LSRO (Life Sciences Research Office). 1998. Fat. In: Raiten DJ, Talbot JM, Waters JH, eds. *Assessment of Nutrient Requirements for Infant Formulas*. Bethesda, MD: LSRO. Pp. 19–46.
- Lucas A, Quinlan P, Abrams S, Ryan S, Meah S, Lucas PJ. 1997. Randomised controlled trial of a synthetic triglyceride milk formula for preterm infants. *Arch Dis Child* 77:F178–F184.
- Lucas A, Stafford M, Morley R, Abbott R, Stephenson T, MacFadyen U, Elias-Jones A, Clements H. 1999. Efficacy and safety of long-chain polyunsaturated fatty acid supplementation of infant-formula milk: A randomised trial. *Lancet* 354:1948–1954.
- Ludwig DS, Pereira MA, Kroenke CH, Hilner JE, Van Horn L, Slattery ML, Jacobs DR. 1999. Dietary fiber, weight gain, and cardiovascular disease risk factors in young adults. *J Am Med Assoc* 282:1539–1546.
- Ma DWL, Wierzbicki AA, Field CJ, Clandinin MT. 1999. Conjugated linoleic acid in Canadian dairy and beef products. *J Agric Food Chem* 47:1956–1960.
- MacDonald HB. 2000. Conjugated linoleic acid and disease prevention: A review of current knowledge. *J Am Coll Nutr* 19:111S–118S.
- Makrides M, Neumann MA, Byard RW, Simmer K, Gibson RA. 1994. Fatty acid composition of brain, retina, and erythrocytes in breast- and formula-fed infants. *Am J Clin Nutr* 60:189–194.
- Makrides M, Neumann M, Simmer K, Pater J, Gibson R. 1995. Are long-chain polyunsaturated fatty acids essential nutrients in infancy? *Lancet* 345:1463–1468.
- Makrides M, Neumann MA, Gibson RA. 1996. Is dietary docosahexaenoic acid essential for term infants? *Lipids* 31:115–119.
- Makrides M, Neumann MA, Jeffrey B, Lien EL, Gibson RA. 2000a. A randomized trial of different ratios of linoleic to α-linolenic acid in the diet of term infants: Effects on visual function and growth. *Am J Clin Nutr* 71:120–129.
- Makrides M, Neumann MA, Simmer K, Gibson RA. 2000b. A critical appraisal of the role of dietary long-chain polyunsaturated fatty acids on neural indices of term infants: A randomized controlled trial. *Pediatrics* 105:32–38.
- Marshall JA, Bessesen DH, Hamman RF. 1997. High saturated fat and low starch and fibre are associated with hyperinsulinemia in a non-diabetic population: The San Luis Valley Diabetes Study. *Diabetologia* 40:430–438.
- Martin MJ, Hulley SB, Browner WS, Kuller LH, Wentworth D. 1986. Serum cholesterol, blood pressure, and mortality: Implications from a cohort of 361,662 men. *Lancet* 2:933–936.
- Martinez M. 1992. Tissue levels of polyunsaturated fatty acids during early human development. *J Pediatr* 120:S129–S138.
- Martinez M, Ballabriga A, Gil-Gibernau JJ. 1988. Lipids of the developing human retina: I. Total fatty acids, plasmalogens, and fatty acid composition of ethanolamine and choline phosphoglycerides. *J Neurosci Res* 20:484–490.
- Mascioli EA, Smith MF, Trerice MS, Meng HC, Blackburn GL. 1979. Effect of total parenteral nutrition with cycling on essential fatty acid deficiency. *J Parenter Enteral Nutr* 3:171–173.
- Mascioli EA, Lopes SM, Champagne C, Driscoll DF. 1996. Essential fatty acid deficiency and home total parenteral nutrition patients. *Nutrition* 12:245–249.

- McGee DL, Reed DM, Yano K, Kagan A, Tillotson J. 1984. Ten-year incidence of coronary heart disease in the Honolulu Heart Program. Relationship to nutrient intake. *Am J Epidemiol* 119:667–676.
- Meng HC. 1983. A case of human linolenic acid deficiency involving neurological abnormalities. *Am J Clin Nutr* 37:157–159.
- Mensink RP, Hornstra G. 1995. The proportion of *trans* monounsaturated fatty acids in serum triacylglycerols or platelet phospholipids as an objective indicator of their short-term intake in healthy men. *Br J Nutr* 73:605–612.
- Mensink RP, Katan MB. 1990. Effect of dietary *trans* fatty acids on high-density and low-density lipoprotein cholesterol levels in healthy subjects. *N Engl J Med* 323:439–445.
- Mensink RP, Katan MB. 1992. Effect of dietary fatty acids on serum lipids and lipoproteins. A meta-analysis of 27 trials. *Arterioscler Thromb* 12:911–919.
- Mensink RP, de Louw MHJ, Katan MB. 1991. Effects of dietary *trans* fatty acids on blood pressure in normotensive subjects. *Eur J Clin Nutr* 45:375–382.
- Mensink RP, Zock PL, Katan MB, Hornstra G. 1992. Effect of dietary *cis* and *trans* fatty acids on serum lipoprotein[a] levels in humans. *J Lipid Res* 33:1493–1501.
- Mensink RP, Temme EH, Hornstra G. 1994. Dietary saturated and *trans* fatty acids and lipoprotein metabolism. *Ann Med* 26:461–464.
- Meydani SN, Endres S, Woods MM, Goldin BR, Soo C, Morrill-Labrode A, Dinarello CA, Gorbach SL. 1991. Oral (*n*-3) fatty acid supplementation suppresses cytokine production and lymphocyte proliferation: Comparison between young and older women. *J Nutr* 121:547–555.
- Meydani SN, Lichtenstein AH, Cornwall S, Meydani M, Goldin BR, Rasmussen H, Dinarello CA, Schaefer EJ. 1993. Immunologic effects of National Cholesterol Education Panel Step-2 Diets with and without fish-derived *n*-3 fatty acid enrichment. *J Clin Invest* 92:105–113.
- Michels K, Sacks F. 1995. Trans fatty acids in European margarines. *N Engl J Med* 332:541–542.
- Miller WC, Niederpruem MG, Wallace JP, Lindeman AK. 1994. Dietary fat, sugar, and fiber predict body fat content. *J Am Diet Assoc* 94:612–615.
- Mohrhauer H, Holman RT. 1963. The effect of dose level of essential fatty acids upon fatty acid composition of the rat liver. *J Lipid Res* 4:151–159.
- Mølvig J, Pociot F, Worsaae H, Wogensen LD, Baek L, Christensen P, Mandrup-Poulsen T, Andersen K, Madsen P, Dyerberg J, Nerup J. 1991. Dietary supplementation with  $\omega$ -3-polyunsaturated fatty acids decreases mononuclear cell proliferation and interleukin-1 $\beta$  content but not monokine secretion in healthy and insulin-dependent diabetic individuals. *Scand J Immunol* 34:399–410.
- Moore SA, Yoder E, Murphy S, Dutton GR, Spector AA. 1991. Astrocytes, not neurons, produce docosahexaenoic acid (22: $\omega$ -3) and arachidonic acid (20: $\omega$ -6). *J Neurochem* 56:518–524.
- Morley R. 1998. Nutrition and cognitive development. *Nutrition* 14:752–754.
- Mortensen JZ, Schmidt EB, Nielsen AH, Dyerberg J. 1983. The effect of *n*-6 and *n*-3 fatty acids on hemostasis, blood lipids and blood pressure. *Thromb Haemostas* 50:543–546.
- Müller H, Jordal O, Seljeflot I, Kierulf P, Kirkhus B, Ledsaak O, Pedersen JI. 1998. Effect on plasma lipids and lipoproteins of replacing partially hydrogenated fish oil with vegetable fat in margarine. *Br J Nutr* 80:243–251.
- Murgatroyd PR, Van De Ven MLHM, Goldberg GR, Prentice AM. 1996. Alcohol and the regulation of energy balance: Overnight effects on diet-induced thermogenesis and fuel storage. *Br J Nutr* 75:33–45.

- Murgatroyd PR, Goldberg GR, Leahy FE, Gilsenan MB, Prentice AM. 1999. Effects of inactivity and diet composition on human energy balance. *Int J Obes Relat Metab Disord* 23:1269–1275.
- Mustad VA, Etherton TD, Cooper AD, Mastro AM, Pearson TA, Jonnalagadda SS, Kris-Etherton PM. 1997. Reducing saturated fat intake is associated with increased levels of LDL receptors on mononuclear cells in healthy men and women. *J Lipid Res* 38:459–468.
- Mutanen M, Aro A. 1997. Coagulation and fibrinolysis factors in healthy subjects consuming high stearic or *trans* fatty acid diets. *Thromb Haemost* 77:99–104.
- Neaton JD, Wentworth D. 1992. Serum cholesterol, blood pressure, cigarette smoking, and death from coronary heart disease. Overall findings and differences by age for 316,099 white men. *Arch Intern Med* 152:56–64.
- Nelson GJ, Schmidt PC, Corash L. 1991. The effect of a salmon diet on blood clotting, platelet aggregation and fatty acids in normal adult men. *Lipids* 26:87–96.
- Nelson GJ, Schmidt PC, Bartolini GL, Kelley DS, Kyle D. 1997. The effect of dietary docosahexaenoic acid on plasma lipoproteins and tissue fatty acid composition in humans. *Lipids* 32:1137–1146.
- Nestel PJ, Noakes M, Belling GB, McArthur R, Clifton PM, Abbey M. 1992a. Plasma cholesterol-lowering potential of edible-oil blends suitable for commercial use. *Am J Clin Nutr* 55:46–50.
- Nestel PJ, Noakes M, Belling B, McArthur R, Clifton P, Janus E, Abbey M. 1992b. Plasma lipoprotein lipid and Lp[a] changes with substitution of elaidic acid for oleic acid in the diet. *J Lipid Res* 33:1029–1036.
- Nestel P, Clifton P, Noakes M. 1994. Effects of increasing dietary palmitoleic acid compared with palmitic and oleic acids on plasma lipids of hypercholesterolemic men. *J Lipid Res* 35:656–662.
- Neuringer M, Connor WE, Van Petten C, Barstad L. 1984. Dietary omega-3 fatty acid deficiency and visual loss in infant rhesus monkeys. *J Clin Invest* 73:272–276.
- Neuringer M, Connor WE, Lin DS, Barstad L, Luck S. 1986. Biochemical and functional effects of prenatal and postnatal ω3 fatty acid deficiency on retina and brain in rhesus monkeys. *Proc Natl Acad Sci USA* 83:4021–4025.
- Nielsen LB. 1999. Atherogeneity of lipoprotein(a) and oxidized low density lipoprotein: Insight from *in vivo* studies of arterial wall influx, degradation and efflux. *Atherosclerosis* 143:229–243.
- Niinikoski H, Lapinleimu H, Viikari J, Rönnemaa T, Jokinen E, Seppänen R, Terho P, Tuominen J, Välimäki I, Simell O. 1997a. Growth until 3 years of age in a prospective, randomized trial of a diet with reduced saturated fat and cholesterol. *Pediatrics* 99:687–694.
- Niinikoski H, Viikari J, Rönnemaa T, Helenius H, Jokinen E, Lapinleimu H, Routi T, Lagström H, Seppänen R, Välimäki I, Simell O. 1997b. Regulation of growth of 7- to 36-month-old children by energy and fat intake in the prospective, randomized STRIP baby trial. *Pediatrics* 100:810–816.
- Noakes M, Clifton PM. 1998. Oil blends containing partially hydrogenated or interesterified fats: Differential effects on plasma lipids. *Am J Clin Nutr* 68:242–247.
- Noble RC, Moore JH, Harfoot CG. 1974. Observations on the pattern of biohydrogenation of esterified and unesterified linoleic acid in the rumen. *Br J Nutr* 31:99–108.

- Nommsen LA, Lovelady CA, Heinig MJ, Lönnnerdal B, Dewey KG. 1991. Determinants of energy, protein, lipid, and lactose concentrations in human milk during the first 12 mo of lactation: The DARLING Study. *Am J Clin Nutr* 53:457–465.
- Obarzanek E, Hunsberger SA, Van Horn L, Hartmuller VV, Barton BA, Stevens VJ, Kwiterovich PO, Franklin FA, Kimm SYS, Lasser NL, Simons-Morton DG, Lauer RM. 1997. Safety of a fat-reduced diet: The Dietary Intervention Study in Children (DISC). *Pediatrics* 100:51–59.
- Olsen SF, Hansen HS, Jensen B, Sørensen TIA. 1989. Pregnancy duration and the ratio of long-chain n-3 fatty acids to arachidonic acid in erythrocytes from Faroese women. *J Intern Med* 225:185–189.
- Olsen SF, Sørensen JD, Secher NJ, Hedegaard M, Henriksen TB, Hansen HS, Grant A. 1992. Randomised controlled trial of effect of fish-oil supplementation on pregnancy duration. *Lancet* 339:1003–1007.
- O'Neill JA, Caldwell MD, Meng HC. 1977. Essential fatty acid deficiency in surgical patients. *Ann Surg* 185:535–542.
- Ou J, Tu H, Luk A, DeBose-Boyd RA, Bashmakov Y, Goldstein JL, Brown MS. 2001. Unsaturated fatty acids inhibit transcription of the sterol regulatory element-binding protein-1c (SREBP-1c) gene by antagonizing ligand-dependent activation of the LXR. *Proc Natl Acad Sci USA* 98:6027–6032.
- Pan DA, Lillioja S, Kriketos AD, Milner MR, Baur LA, Bogardus C, Jenkins AB, Storlien LH. 1997. Skeletal muscle triglyceride levels are inversely related to insulin action. *Diabetes* 46:983–988.
- Pariza MW, Park Y, Cook ME. 2001. The biologically active isomers of conjugated linoleic acid. *Prog Lipid Res* 40:283–298.
- Parker DR, Weiss ST, Troisi R, Cassano PA, Vokonas PS, Landsberg L. 1993. Relationship of dietary saturated fatty acids and body habitus to serum insulin concentrations: The Normative Aging Study. *Am J Clin Nutr* 58:129–136.
- Paulsrud JR, Pensler L, Whitten CF, Stewart S, Holman RT. 1972. Essential fatty acid deficiency in infants induced by fat-free intravenous feeding. *Am J Clin Nutr* 25:897–904.
- Pedersen HS, Mulvad G, Seidelin KN, Malcom GT, Boudreau DA. 1999. n-3 Fatty acids as a risk factor for haemorrhagic stroke. *Lancet* 353:812–813.
- Pietinen P, Ascherio A, Korhonen P, Hartman AM, Willett WC, Albanes D, Virtamo J. 1997. Intake of fatty acids and risk of coronary heart disease in a cohort of Finnish men. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. *Am J Epidemiol* 145:876–887.
- Ponder DL, Innis SM, Benson JD, Siegman JS. 1992. Docosahexaenoic acid status of term infants fed breast milk or infant formula containing soy oil or corn oil. *Pediatr Res* 32:683–688.
- Putnam JC, Carlson SE, DeVoe PW, Barness LA. 1982. The effect of variations in dietary fatty acids on the fatty acid composition of erythrocyte phosphatidylcholine and phosphatidylethanolamine in human infants. *Am J Clin Nutr* 36:106–114.
- Raben A, Andersen HB, Christensen NJ, Madsen J, Holst JJ, Astrup A. 1994. Evidence for an abnormal postprandial response to a high-fat meal in women predisposed to obesity. *Am J Physiol* 267:E549–E559.
- Ratnayake WMN, Hollywood R, O'Grady E, Pelletier G. 1993. Fatty acids in some common food items in Canada. *J Am Coll Nutr* 12:651–660.

- Ratnayake WM, Chardigny JM, Wolff RL, Bayard CC, Sebedio JL, Martine L. 1997. Essential fatty acids and their *trans* geometrical isomers in powdered and liquid infant formulas sold in Canada. *J Pediatr Gastroenterol* 25:400–407.
- Rhee SK, Kayani AJ, Ciszek A, Brenna JT. 1997. Desaturation and interconversion of dietary stearic and palmitic acids in human plasma and lipoproteins. *Am J Clin Nutr* 65:451–458.
- Richardson TJ, Sgoutas D. 1975. Essential fatty acid deficiency in four adult patients during total parenteral nutrition. *Am J Clin Nutr* 28:258–263.
- Riella MC, Broviac JW, Wells M, Scribner BH. 1975. Essential fatty acid deficiency in human adults during total parenteral nutrition. *Ann Intern Med* 83:786–789.
- Ritzenthaler KL, McGuire MK, Falen R, Shultz TD, Dasgupta N, McGuire MA. 2001. Estimation of conjugated linoleic acid intake by written dietary assessment methodologies underestimates actual intake evaluated by food duplicate methodology. *J Nutr* 131:1548–1554.
- Roche HM, Zampelas A, Jackson KG, Williams CM, Gibney MJ. 1998. The effect of test meal monounsaturated fatty acid:saturated fatty acid ratio on postprandial lipid metabolism. *Br J Nutr* 79:419–424.
- Roden M, Price TB, Perseghin G, Petersen KF, Rothman DL, Cline GW, Shulman GI. 1996. Mechanism of free fatty acid-induced insulin resistance in humans. *J Clin Invest* 97:2859–2865.
- Rodriguez A, Sarda P, Nessmann C, Boulot P, Poisson J-P, Leger CL, Descomps B. 1998. Fatty acid desaturase activities and polyunsaturated fatty acid composition in human fetal liver between the seventeenth and thirty-sixth gestational weeks. *Am J Obstet Gynecol* 179:1063–1070.
- Rogers S, James KS, Butland BK, Etherington MD, O'Brien JR, Jones JG. 1987. Effects of a fish oil supplement on serum lipids, blood pressure, bleeding time, haemostatic and rheological variables. A double blind randomised controlled trial in healthy volunteers. *Atherosclerosis* 63:137–143.
- Rosenthal MD, Doloresco MA. 1984. The effects of *trans* fatty acids on fatty acyl Δ5 desaturation by human skin fibroblasts. *Lipids* 19:869–874.
- Rudel LL, Haines J, Sawyer JK, Shah R, Wilson MS, Carr TP. 1997. Hepatic origin of cholesterol oleate in coronary artery atherosclerosis in African green monkeys. *J Clin Invest* 100:74–83.
- Russell RM. 1992. Changes in gastrointestinal function attributed to aging. *Am J Clin Nutr* 55:1203S–1207S.
- Ruttenberg H, Davidson LM, Little NA, Klurfeld DM, Kritchevsky D. 1983. Influence of *trans* unsaturated fats on experimental atherosclerosis in rabbits. *J Nutr* 113:835–844.
- Ryan AS, Montaldo MB, Groh-Wargo S, Mimouni F, Sentipal-Walerius J, Doyle J, Siegman JS, Thomas AJ. 1999. Effect of DHA-containing formula on growth of preterm infants to 59 weeks postmenstrual age. *Am J Hum Biol* 11:457–467.
- Rywic SL, Manolio TA, Pajak A, Piotrowski W, Davids CE, Broda GB, Kawalec E. 1999. Association of lipids and lipoprotein level with total mortality and mortality caused by cardiovascular and cancer diseases (Poland and United States collaborative study on cardiovascular epidemiology). *Am J Cardiol* 84:540–548.
- Salem N, Wegher B, Mena P, Uauy R. 1996. Arachidonic and docosahexaenoic acids are biosynthesized from their 18-carbon precursors in human infants. *Proc Natl Acad Sci USA* 93:49–54.
- Salem N, Litman B, Kim H-Y, Gawrisch K. 2001. Mechanisms of action of docosahexaenoic acid in the nervous system. *Lipids* 36:945–959.

- Salmerón J, Hu FB, Manson JE, Stampfer MJ, Colditz GA, Rimm EB, Willett WC. 2001. Dietary fat intake and risk of type 2 diabetes in women. *Am J Clin Nutr* 73:1019–1026.
- Sanders TAB, Reddy S. 1992. The influence of a vegetarian diet on the fatty acid composition of human milk and the essential fatty acid status of the infant. *J Pediatr* 120:S71–S77.
- Sanders TAB, Vickers M, Haines AP. 1981. Effect of blood lipids and haemostasis of a supplement of cod-liver oil, rich in eicosapentaenoic and docosahexaenoic acids, in healthy young men. *Clin Sci* 61:317–324.
- Sanders TAB, de Grassi T, Miller GJ, Morrissey JH. 2000. Influence of fatty acid chain length and *cis/trans* isomerization on postprandial lipemia and factor VII in healthy subjects (postprandial lipids and factor VII). *Atherosclerosis* 149:413–420.
- Sanjurjo P, Matorras R, Ingunza N, Alonso M, Rodriguez-Alarcón J, Perteagudo L. 1993. Cross-sectional study of percentual changes in total plasmatic fatty acids during pregnancy. *Horm Metab Res* 25:590–592.
- Santora JE, Palmquist DL, Roehrig KL. 2000. *Trans*-vaccenic acid is desaturated to conjugated linoleic acid in mice. *J Nutr* 130:208–215.
- Sauerwald TU, Hachey DL, Jensen CL, Chen H, Anderson RE, Heird WC. 1996. Effect of dietary  $\alpha$ -linolenic acid intake on incorporation of docosahexaenoic and arachidonic acids into plasma phospholipids of term infants. *Lipids* 31:S131–S135.
- Sauerwald TU, Hachey DL, Jensen CL, Chen H, Anderson RE, Heird WC. 1997. Intermediates in endogenous synthesis of C22:6 $\omega$ 3 and C20:4 $\omega$ 6 by term and preterm infants. *Pediatr Res* 41:183–187.
- Schakel SF, Buzzard IM, Gebhardt SE. 1997. Procedures for estimating nutrient values for food composition databases. *J Food Comp Anal* 10:102–114.
- Schmidt DE, Allred JB, Kien CL. 1999. Fractional oxidation of chylomicron-derived oleate is greater than that of palmitate in healthy adults fed frequent small meals. *J Lipid Res* 40:2322–2332.
- Schmidt EB, Pedersen JO, Ekelund S, Grunnet N, Jersild C, Dyerberg J. 1989. Cod liver oil inhibits neutrophil and monocyte chemotaxis in healthy males. *Atherosclerosis* 77:53–57.
- Schmidt EB, Varming K, Ernst E, Madsen P, Dyerberg J. 1990. Dose-response studies on the effect of *n*-3 polyunsaturated fatty acids on lipids and haemostasis. *Thromb Haemost* 63:1–5.
- Schmidt EB, Lervang H-H, Varming K, Madsen P, Dyerberg J. 1992. Long-term supplementation with *n*-3 fatty acids. I: Effect on blood lipids, haemostasis and blood pressure. *Scand J Clin Lab Invest* 52:221–228.
- Schutz Y. 2000. Role of substrate utilization and thermogenesis on body-weight control with particular reference to alcohol. *Proc Nutr Soc* 59:511–517.
- Scott DT, Janowsky JS, Carroll RE, Taylor JA, Auestad N, Montaldo MB. 1998. Formula supplementation with long-chain polyunsaturated fatty acids: Are there developmental benefits? *Pediatrics* 102:E59.
- Seppänen-Laakso T, Vanhanen H, Laakso I, Kohtamäki H, Viikari J. 1993. Replacement of margarine on bread by rapeseed and olive oils: Effects on plasma fatty acid composition and serum cholesterol. *Ann Nutr Metab* 37:161–174.
- Sessler AM, Ntambi JM. 1998. Polyunsaturated fatty acid regulation of gene expression. *J Nutr* 128:923–926.
- Sevak L, McKeigue PM, Marmot MG. 1994. Relationship of hyperinsulinemia to dietary intake in South Asian and European men. *Am J Clin Nutr* 59:1069–1074.

- Shea S, Basch CE, Stein AD, Contento IR, Irigoyen M, Zybert P. 1993. Is there a relationship between dietary fat and stature or growth in children three to five years of age? *Pediatrics* 92:579–586.
- Shekelle RB, Missell L, Paul O, Shyrock AM, Stamler J. 1985. Fish consumption and mortality from coronary heart disease. *N Engl J Med* 313:820.
- Sherwood NE, Jeffery RW, French SA, Hannan PJ, Murray DM. 2000. Predictors of weight gain in the Pound of Prevention Study. *Int J Obes Relat Metab Disord* 24:395–403.
- Shetty PS, Prentice AM, Goldberg GR, Murgatroyd PR, McKenna APM, Stubbs RJ, Volschenk PA. 1994. Alterations in fuel selection and voluntary food intake in response to isoenergetic manipulation of glycogen stores in humans. *Am J Clin Nutr* 60:534–543.
- Shimp JL, Bruckner G, Kinsella JE. 1982. The effects of dietary trilinoelaidin on fatty acid and acyl desaturases in rat liver. *J Nutr* 112:722–735.
- Shintani TT, Beckham S, Brown AC, O'Connor HK. 2001. The Hawaii Diet: Ad libitum high carbohydrate, low fat multi-cultural diet for the reduction of chronic disease risk factors: Obesity, hypertension, hypercholesterolemia, and hyperglycemia. *Hawaii Med J* 60:69–73.
- Siguel EN, Lerman RH. 1993. Trans-fatty acid patterns in patients with angiographically documented coronary artery disease. *Am J Cardiol* 71:916–920.
- Siguel EN, Blumberg JB, Caesar J. 1986. Monitoring the optimal infusion of intravenous lipids. *Arch Pathol Lab Med* 110:792–797.
- Sinclair AJ. 1975. Incorporation of radioactive polyunsaturated fatty acids into liver and brain of developing rat. *Lipids* 10:175–184.
- Sinclair AJ, Murphy KJ, Li D. 2000. Marine lipids: Overview “news insights and lipid composition of Lyprinol™” *Allerg Immunol (Paris)* 32:261–271.
- Slattery ML, Potter JD, Duncan DM, Berry TD. 1997. Dietary fats and colon cancer: Assessment of risk associated with specific fatty acids. *Int J Cancer* 73:670–677.
- Smith P, Arnesen H, Opstad T, Dahl KH, Eritsland J. 1989. Influence of highly concentrated n-3 fatty acids on serum lipids and hemostatic variables in survivors of myocardial infarction receiving either oral anticoagulants or matching placebo. *Thromb Res* 53:467–474.
- Song JH, Miyazawa T. 2001. Enhanced level of n-3 fatty acid in membrane phospholipids induces lipid peroxidation in rats fed dietary docosahexaenoic acid oil. *Atherosclerosis* 155:9–18.
- Sørensen NS, Marckmann P, Høy C-E, van Duyvenvoorde W, Princen HMG. 1998. Effect of fish-oil-enriched margarine on plasma lipids, low-density-lipoprotein particle composition, size, and susceptibility to oxidation. *Am J Clin Nutr* 68:235–241.
- Sorkin JD, Andres R, Muller DC, Baldwin HL, Fleg JL. 1992. Cholesterol as a risk factor for coronary heart disease in elderly men. The Baltimore Longitudinal Study of Aging. *Ann Epidemiol* 2:59–67.
- Spady DK, Woolett LA, Dietschy JM. 1993. Regulation of plasma LDL-cholesterol levels by dietary cholesterol and fatty acids. *Annu Rev Nutr* 13:355–361.
- Sperling RI, Benincaso AI, Knoell CT, Larkin JK, Austen KF, Robinson DR. 1993. Dietary ω-3 polyunsaturated fatty acids inhibit phosphoinositide formation and chemotaxis in neutrophils. *J Clin Invest* 91:651–660.
- Sprecher H. 1992. Interconversions between 20- and 22-carbon n-3 and n-6 fatty acids via 4-desaturase independent pathways. In: Sinclair AJ, Gibson R, eds. *Essential Fatty Acids and Eicosanoids: Invited Papers from the Third International Congress*. Champaign, IL: American Oil Chemists' Society. Pp. 18–22.

- Sprecher H, Luthria DL, Mohammed BS, Baykousheva SP. 1995. Reevaluation of the pathways for the biosynthesis of polyunsaturated fatty acids. *J Lipid Res* 36:2471–2477.
- Stacpoole PW, Alig J, Ammon L, Crockett SE. 1989. Dose-response effects of dietary marine oil on carbohydrate and lipid metabolism in normal subjects and patients with hypertriglyceridemia. *Metabolism* 38:946–956.
- Stamler J, Wentworth D, Neaton JD. 1986. Is relationship between serum cholesterol and risk of premature death from coronary heart disease continuous and graded? Findings in 356,222 primary screenees of the Multiple Risk Factor Intervention Trial (MRFIT). *J Am Med Assoc* 256:2823–2828.
- Sugano M, Ikeda I. 1996. Metabolic interactions between essential and *trans*-fatty acids. *Curr Opin Lipidol* 7:38–42.
- Sundram K, Ismail A, Hayes KC, Jeyamalar R, Pathmanathan R. 1997. *Trans* (elaidic) fatty acids adversely affect the lipoprotein profile relative to specific saturated fatty acids in humans. *J Nutr* 127:514S–520S.
- Suter PM, Schutz Y, Jequier E. 1992. The effect of ethanol on fat storage in healthy subjects. *N Engl J Med* 326:983–987.
- Tavani A, Negri E, D'Avanzo B, La Vecchia C. 1997. Margarine intake and risk of nonfatal acute myocardial infarction in Italian women. *Eur J Clin Nutr* 51:30–32.
- Thompson PJ, Misso NLA, Passarelli M, Phillips MJ. 1991. The effect of eicosapentaenoic acid consumption on human neutrophil chemiluminescence. *Lipids* 26:1223–1226.
- Thomsen C, Rasmussen O, Lousen T, Holst JJ, Fenselau S, Schrezenmeir J, Hermansen K. 1999. Differential effects of saturated and monounsaturated fatty acids on postprandial lipemia and incretin responses in healthy subjects. *Am J Clin Nutr* 69:1135–1143.
- Thorngren M, Gustafson A. 1981. Effects of 11-week increase in dietary eicosapentaenoic acid on bleeding time, lipids, and platelet aggregation. *Lancet* 2:1190–1193.
- Tomarelli RM, Meyer BJ, Weaber JR, Bernhart FW. 1968. Effect of positional distribution on the absorption of the fatty acids of human milk and infant formulas. *J Nutr* 95:583–590.
- Troiano RP, Briefel RR, Carroll MD, Bialostosky K. 2000. Energy and fat intakes of children and adolescents in the United States: Data from the National Health and Nutrition Examination Surveys. *Am J Clin Nutr* 72:1343S–1353S.
- Troisi R, Willett WC, Weiss ST. 1992. *Trans*-fatty acid intake in relation to serum lipid concentrations in adult men. *Am J Clin Nutr* 56:1019–1024.
- Turpeinen AM, Wübert J, Aro A, Lorenz R, Mutanen M. 1998. Similar effects of diets rich in stearic acid or *trans*-fatty acids on platelet function and endothelial prostacyclin production in humans. *Arterioscler Thromb Vasc Biol* 18:316–322.
- Tuyns AJ, Kaaks R, Haelterman M. 1988. Colorectal cancer and the consumption of foods: A case-control study in Belgium. *Nutr Cancer* 11:189–204.
- Uauy R, Mena P, Wegher B, Nieto S, Salem N. 2000a. Long chain polyunsaturated fatty acid formation in neonates: Effect of gestational age and intrauterine growth. *Pediatr Res* 47:127–135.
- Uauy R, Mize CE, Castillo-Duran C. 2000b. Fat intake during childhood: Metabolic responses and effects on growth. *Am J Clin Nutr* 72:1354S–1360S.
- Umegaki K, Hashimoto M, Yamasaki H, Fujii Y, Yoshimura M, Sugisawa A, Shinozuka K. 2001. Docosahexaenoic acid supplementation-increased oxidative damage in bone marrow DNA in aged rats and its relation to antioxidant vitamins. *Free Radic Res* 34:427–435.

- USDA (U.S. Department of Agriculture). 1996. *The Food Guide Pyramid*. Home and Garden Bulletin No. 252. Washington, DC: U.S. Government Printing Office.
- USDA/HHS (U.S. Department of Health and Human Services). 2000. *Nutrition and Your Health: Dietary Guidelines for Americans*, 5th ed. Home and Garden Bulletin No. 232. Washington, DC: U.S. Government Printing Office.
- Valenzuela A, Morgado N. 1999. Trans fatty acid isomers in human health and in the food industry. *Biol Res* 32:273–287.
- van Dam RM, Huang Z, Giovannucci E, Rimm EB, Hunter DJ, Colditz GA, Stampfer MJ, Willett WC. 2000. Diet and basal cell carcinoma of the skin in a prospective cohort of men. *Am J Clin Nutr* 71:135–141.
- van den Brandt PA, van't Veer P, Goldbohm RA, Dorant E, Volovics A, Hermus RJJ, Sturmans F. 1993. A prospective cohort study on dietary fat and the risk of postmenopausal breast cancer. *Cancer Res* 53:75–82.
- van Erp-baart M-A, Couet C, Cuadrado C, Kafatos A, Stanley J, van Poppel G. 1998. Trans fatty acids in bakery products from 14 European countries: The TRANSFAIR Study. *J Food Comp Anal* 11:161–169.
- van Houwelingen AC, Hornstra G. 1994. Trans fatty acids in early human development. *World Rev Nutr Diet* 75:175–178.
- van Houwelingen AC, Sørensen JD, Hornstra G, Simonis MMG, Boris J, Olsen SF, Secher NJ. 1995. Essential fatty acid status in neonates after fish-oil supplementation during late pregnancy. *Br J Nutr* 74:723–731.
- van Poppel G, van Erp-baart M-A, Leth T, Gevers E, Van Amelsvoort J, Lanzmann-Petithory D, Kafatos A, Aro A. 1998. Trans fatty acids in foods in Europe: The TRANSFAIR Study. *J Food Comp Anal* 11:112–136.
- Veierød MB, Laake P, Thelle DS. 1997. Dietary fat intake and risk of lung cancer: A prospective study of 51,452 Norwegian men and women. *Eur J Cancer Prev* 6:540–549.
- Velie E, Kulldorff M, Schairer C, Block G, Albanes D, Schatzkin A. 2000. Dietary fat, fat subtypes, and breast cancer in postmenopausal women: A prospective cohort study. *J Natl Cancer Inst* 92:833–839.
- Verhulst A, Janssen G, Parmentier G, Eyssen H. 1987. Isomerization of polyunsaturated long chain fatty acids by propionibacteria. *Syst Appl Microbiol* 9:12–15.
- Vermunt SHF, Mensink RP, Simonis MMG, Hornstra G. 2000. Effects of dietary α-linolenic acid on the conversion and oxidation of  $^{13}\text{C}$ -α-linolenic acid. *Lipids* 35:137–142.
- Vessby B, Uusitupa M, Hermansen K, Riccardi G, Rivellese AA, Tapsell LC, Nälsén C, Berglund L, Louheranta A, Rasmussen BM, Calvert GD, Maffetone A, Pedersen E, Gustafsson I-B, Storlien LH. 2001. Substituting dietary saturated for monounsaturated fat impairs insulin sensitivity in healthy men and women: The KANWU study. *Diabetologia* 44:312–319.
- Vidgren HM, Ågren JJ, Schwab U, Rissanen T, Hänninen O, Uusitupa MIJ. 1997. Incorporation of n-3 fatty acids into plasma lipid fractions, and erythrocyte membranes and platelets during dietary supplementation with fish, fish oil, and docosahexaenoic acid-rich oil among healthy young men. *Lipids* 32:697–705.
- Vidgren HM, Louheranta AM, Ågren JJ, Schwab US, Uusitupa MIJ. 1998. Divergent incorporation of dietary trans fatty acids in different serum lipid fractions. *Lipids* 33:955–962.
- Virella G, Fourspring K, Hyman B, Haskill-Stroud R, Long L, Virella I, La Via M, Gross AJ, Lopes-Virella M. 1991. Immunosuppressive effects of fish oil in normal human volunteers: Correlation with the in vitro effects of eicosapentanoic acid on human lymphocytes. *Clin Immunol Immunopathol* 61:161–176.

- Virtanen SM, Feskens EJM, Räsänen L, Fidanza F, Tuomilehto J, Giampaoli S, Nissinen A, Kromhout D. 2000. Comparison of diets of diabetic and non-diabetic elderly men in Finland, The Netherlands and Italy. *Eur J Clin Nutr* 54:181–186.
- Vobecky JS, Vobecky J, Normand L. 1995. Risk and benefit of low fat intake in childhood. *Ann Nutr Metab* 39:124–133.
- Vogel RA, Corretti MC, Plotnick GD. 2000. The postprandial effect of components of the Mediterranean diet on endothelial function. *J Am Coll Cardiol* 36:1455–1460.
- Voss A, Reinhart M, Sankarappa S, Sprecher H. 1991. The metabolism of 7,10,13,16,19-docosapentaenoic acid to 4,7,10,13,16,19-docosahexaenoic acid in rat liver is independent of a 4-desaturase. *J Biol Chem* 266:19995–20000.
- Ward KD, Sparrow D, Vokonas PS, Willett WC, Landsberg L, Weiss ST. 1994. The relationships of abdominal obesity, hyperinsulinemia and saturated fat intake to serum lipid levels: The Normative Aging Study. *Int J Obes Relat Metab Disord* 18:137–144.
- Watts GF, Jackson P, Burke V, Lewis B. 1996. Dietary fatty acids and progression of coronary artery disease in men. *Am J Clin Nutr* 64:202–209.
- Weijenberg MP, Feskens EJM, Kromhout D. 1996. Total and high density lipoprotein cholesterol as risk factors for coronary heart disease in elderly men during 5 years of follow-up. The Zutphen Elderly Study. *Am J Epidemiol* 143:151–158.
- Wene JD, Connor WE, DenBesten L. 1975. The development of essential fatty acid deficiency in healthy men fed fat-free diets intravenously and orally. *J Clin Invest* 56:127–134.
- West DB, York B. 1998. Dietary fat, genetic predisposition, and obesity: Lessons from animal models. *Am J Clin Nutr* 67:505S–512S.
- Wetzel MG, Li J, Alvarez RA, Anderson RE, O'Brien PJ. 1991. Metabolism of linolenic acid and docosahexaenoic acid in rat retinas and rod outer segments. *Exp Eye Res* 53:437–446.
- Wheeler TG, Benolken RM, Anderson RE. 1975. Visual membranes: Specificity of fatty acid precursors for the electrical response to illumination. *Science* 188:1312–1314.
- Wild SH, Fortmann SP, Marcovina SM. 1997. A prospective case-control study of lipoprotein(a) levels and apo(a) size and risk of coronary heart disease in Stanford Five-City Project participants. *Arterioscler Thromb Vasc Biol* 17:239–245.
- Willatts P, Forsyth JS, DiModugno MK, Varma S, Colvin M. 1998. Effect of long-chain polyunsaturated fatty acids in infant formula on problem solving at 10 months of age. *Lancet* 352:688–691.
- Willett WC, Stampfer MJ, Mason JE, Colditz GA, Speizer FE, Rosner BA, Sampson LA, Hennekens CH. 1993. Intake of *trans* fatty acids and risk of coronary heart disease among women. *Lancet* 341:581–585.
- Wojenski CM, Silver MJ, Walker J. 1991. Eicosapentaenoic acid ethyl ester as an antithrombotic agent: Comparison to an extract of fish oil. *Biochim Biophys Acta* 1081:33–38.
- Wong KH, Deitel M. 1981. Studies with a safflower oil emulsion in total parenteral nutrition. *Can Med Assoc J* 125:1328–1334.
- Wong S, Nestel PJ. 1987. Eicosapentaenoic acid inhibits the secretion of triacylglycerol and of apoprotein B and the binding of LDL in Hep G2 cells. *Atherosclerosis* 64:139–146.

- Wood R, Kubena K, O'Brien B, Tseng S, Martin G. 1993a. Effect of butter, mono- and polyunsaturated fatty acid-enriched butter, *trans* fatty acid margarine, and zero *trans* fatty acid margarine on serum lipids and lipoproteins in healthy men. *J Lipid Res* 34:1–11.
- Wood R, Kubena K, Tseng S, Martin G, Crook R. 1993b. Effect of palm oil, margarine, butter, and sunflower oil on the serum lipids and lipoproteins of normocholesterolemic middle-aged men. *J Nutr Biochem* 4:286–297.
- Yamashita N, Maruyama M, Yamazaki K, Hamazaki T, Yano S. 1991. Effect of eicosapentaenoic and docosahexaenoic acid on natural killer cell activity in human peripheral blood lymphocytes. *Clin Immunol Immunopathol* 59:335–345.
- Yao CH, Slattery ML, Jacobs DR, Folsom AR, Nelson ET. 1991. Anthropometric predictors of coronary heart disease and total mortality: Findings from the US Railroad Study. *Am J Epidemiol* 134:1278–1289.
- Yaqoob P, Pala HS, Cortina-Borja M, Newsholme EA, Calder PC. 2000. Encapsulated fish oil enriched in  $\alpha$ -tocopherol alters plasma phospholipid and mononuclear cell fatty acid compositions but not mononuclear cell functions. *Eur J Clin Invest* 30:260–274.
- Yasuda S, Watanabe S, Kobayashi T, Hata N, Misawa Y, Utsumi H, Okuyama H. 1999. Dietary docosahexaenoic acid enhances ferric nitrilotriacetate-induced oxidative damage in mice but not when additional alpha-tocopherol is supplemented. *Free Radic Res* 30:199–205.
- Yu S, Derr J, Etherton TD, Kris-Etherton PM. 1995. Plasma cholesterol-predictive equations demonstrate that stearic acid is neutral and monounsaturated fatty acids are hypocholesterolemic. *Am J Clin Nutr* 61:1129–1139.
- Zambon S, Friday KE, Childs MT, Fujimoto WY, Bierman EL, Ensinck JW. 1992. Effect of glyburide and  $\omega$ 3 fatty acid dietary supplements on glucose and lipid metabolism in patients with non-insulin-dependent diabetes mellitus. *Am J Clin Nutr* 56:447–454.
- Zevenbergen JL, Houtsmuller UMT, Gottenbos JJ. 1988. Linoleic acid requirement of rats fed *trans* fatty acids. *Lipids* 23:178–186.
- Zock PL, Katan MB. 1992. Hydrogenation alternatives: Effects of *trans* fatty acids and stearic acid versus linoleic acid on serum lipids and lipoproteins in humans. *J Lipid Res* 33:399–410.
- Zock PL, Mensink RP. 1996. Dietary *trans*-fatty acids and serum lipoproteins in humans. *Curr Opin Lipidol* 7:34–37.
- Zock PL, Blijlevens RAMT, de Vries JHM, Katan MB. 1993. Effects of stearic acid and *trans* fatty acids versus linoleic acid on blood pressure in normotensive women and men. *Eur J Clin Nutr* 47:437–444.
- Zock PL, Katan MB, Mensink RP. 1995. Dietary *trans* fatty acids and lipoprotein cholesterol. *Am J Clin Nutr* 61:617.
- Zucker ML, Bilyeu DS, Helmkamp GM, Harris WS, Dujovne CA. 1988. Effects of dietary fish oil on platelet function and plasma lipids in hyperlipoproteinemic and normal subjects. *Atherosclerosis* 73:13–22.

Ibid., Chapter 13, pp. 965–967.

Bandini LG, Vu D, Must A, Cyr H, Goldberg A, Dietz WH. 1999. Comparison of high-calorie, low-nutrient-dense food consumption among obese and non-obese adolescents. *Obes Res* 7:438–443.

- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Black AE, Prentice AM, Goldberg GR, Jebb SA, Bingham SA, Livingstone MBE, Coward WA. 1993. Measurements of total energy expenditure provide insights into the validity of dietary measurements of energy intake. *J Am Diet Assoc* 93:572–579.
- Blair SN, Kohl HW, Barlow CE. 1993. Physical activity, physical fitness, and all-cause mortality in women: Do women need to be active? *J Am Coll Nutr* 12:368–371.
- Blair SN, Kohl HW, Barlow CE, Paffenbarger RS, Gibbons LW, Macera CA. 1995. Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. *J Am Med Assoc* 273:1093–1098.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Nutrition Examination Survey: Underreporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Carroll RJ, Freedman LS, Hartman AM. 1996. Use of semiquantitative food frequency questionnaires to estimate the distribution of usual intake. *Am J Epidemiol* 143:392–404.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- IOM. 2001. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Washington, DC: National Academy Press.
- Johnson RK, Goran MI, Poehlman ET. 1994. Correlates of over- and under-reporting of energy intake in healthy older men and women. *Am J Clin Nutr* 59:1286–1290.
- Johnson RK, Soultanakis RP, Matthews DE. 1998. Literacy and body fatness are associated with underreporting of energy intake in US low-income women using the multiple-pass 24-hour recall: A doubly labeled water study. *J Am Diet Assoc* 98:1136–1140.
- Kristal AR, Feng Z, Coates RJ, Oberman A, George V. 1997. Associations of race/ethnicity, education, and dietary intervention with the validity and reliability of a food frequency questionnaire: The Women's Health Trial Feasibility Study in Minority Populations. *Am J Epidemiol* 146:856–869.
- Lichtman SW, Pisarska K, Berman ER, Pestone M, Dowling H, Offenbacher E, Weisel H, Heshka S, Matthews DE, Heymsfield SB. 1992. Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. *N Engl J Med* 327:1893–1898.
- Liu K. 1994. Statistical issues related to semiquantitative food-frequency questionnaires. *Am J Clin Nutr* 59:262S–265S.
- Livingstone MB, Prentice AM, Coward WA, Strain JJ, Black AE, Davies PS, Stewart CM, McKenna PG, Whitehead RG. 1992. Validation of estimates of energy intake by weighed dietary record and diet history in children and adolescents. *Am J Clin Nutr* 56:29–35.
- Marlett JA, Cheung TF. 1997. Database and quick methods of assessing typical dietary fiber intakes using data for 228 commonly consumed foods. *J Am Diet Assoc* 97:1139–1148.

- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Prentice AM, Black AE, Coward WA, Davies HL, Goldberg GR, Murgatroyd PR, Ashford J, Sawyer M, Whitehead RG. 1986. High levels of energy expenditure in obese women. *Br Med J* 292:983–987.
- Pryer JA, Vrijheid M, Nichols R, Kiggins M, Elliott P. 1997. Who are the ‘low energy reporters’ in the dietary and nutritional survey of British adults? *Int J Epidemiol* 26:146–154.
- Schoeller DA. 1995. Limitations in the assessment of dietary energy by self-report. *Metabolism* 44:18–22.
- Schoeller DA, Bandini LG, Dietz WH. 1990. Inaccuracies in self-reported intake identified by comparison with the doubly labelled water method. *Can J Physiol Pharmacol* 68:941–949.
- USDA (U.S. Department of Agriculture). 2001. *USDA Nutrient Database for Standard Reference, Release 14*. Online. Nutrient Data Laboratory. Available at <http://www.nal.usda.gov/fnic/foodcomp>. Accessed April 2, 2002.
- USDA/HHS (U.S. Department of Health and Human Services). 2000. *Nutrition and Your Health: Dietary Guidelines for Americans*. Home and Garden Bulletin No. 232. Washington, DC: U.S. Government Printing Office.

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*Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* (ISBN 0-309-08537-3), Chapter 9, pp. 578–588.

- Alavanja MCR, Brown CC, Swanson C, Brownson RC. 1993. Saturated fat intake and lung cancer risk among nonsmoking women in Missouri. *J Natl Cancer Inst* 85:1906–1916.
- Andersen GE, Lifschitz C, Friis-Hansen B. 1979. Dietary habits and serum lipids during first 4 years of life. A study of 95 Danish children. *Acta Paediatr Scand* 68:165–170.
- Anderson JT, Grande F, Keys A. 1976. Independence of the effects of cholesterol and degree of saturation of the fat in the diet on serum cholesterol in man. *Am J Clin Nutr* 29:1184–1189.
- Andersson S-O, Wolk A, Bergström R, Giovannucci E, Lindgren C, Baron J, Adami H-O. 1996. Energy, nutrient intake and prostate cancer risk: A population-based case-control study in Sweden. *Int J Cancer* 68:716–722.
- Applebaum-Bowden D, Haffner SM, Hartsook E, Luk KH, Albers JJ, Hazzard WR. 1984. Down-regulation of the low-density lipoprotein receptor by dietary cholesterol. *Am J Clin Nutr* 39:360–367.
- Ascherio A, Rimm EB, Giovannucci EL, Spiegelman D, Stampfer M, Willett WC. 1996. Dietary fat and risk of coronary heart disease in men: Cohort follow up study in the United States. *Br Med J* 313:84–90.
- Bayley TM, Alasmi M, Thorkelson T, Krug-Wispe S, Jones PJH, Bulani JL, Tsang RC. 1998. Influence of formula versus breast milk on cholesterol synthesis rates in four-month-old infants. *Pediatr Res* 44:60–67.
- Berge KE, Tian H, Graf GA, Yu L, Grishin NV, Schultz J, Kwiterovich P, Shan B, Barnes R, Hobbs HH. 2000. Accumulation of dietary cholesterol in sitosterolemia caused by mutations in adjacent ABC transporters. *Science* 290:1771–1775.
- Beveridge JMR, Connell WF, Mayer GA, Haust HL. 1960. The response of man to dietary cholesterol. *J Nutr* 71:61–65.
- Beynen AC, Katan MB. 1985a. Effect of egg yolk feeding on the concentration and composition of serum lipoproteins in man. *Atherosclerosis* 54:157–166.
- Beynen AC, Katan MB. 1985b. Reproducibility of the variations between humans in the response of serum cholesterol to cessation of egg consumption. *Atherosclerosis* 57:19–31.
- Bitman J, Wood L, Hamosh M, Hamosh P, Mehta NR. 1983. Comparison of the lipid composition of breast milk from mothers of term and preterm infants. *Am J Clin Nutr* 38:300–312.
- Bocan TMA. 1998. Animal models of atherosclerosis and interpretation of drug intervention studies. *Curr Pharm Des* 4:37–52.
- Bronsgeest-Schout DC, Hautvast JGAJ, Hermus RJJ. 1979a. Dependence of the effects of dietary cholesterol and experimental conditions on serum lipids in man. I. Effects of dietary cholesterol in a linoleic acid-rich diet. *Am J Clin Nutr* 33:2183–2187.
- Bronsgeest-Schout DC, Hermus RJJ, Dallinga-Thie GM, Hautvast JGAJ. 1979b. Dependence of the effects of dietary cholesterol and experimental conditions on serum lipids in man. II. Effects of dietary cholesterol in a linoleic acid-poor diet. *Am J Clin Nutr* 33:2188–2192.

- Brown MS, Goldstein JL. 1999. A proteolytic pathway that controls the cholesterol content of membranes, cells, and blood. *Proc Natl Acad Sci USA* 96:11041–11048.
- Byers TE, Graham S, Haughey BP, Marshall JR, Swanson MK. 1987. Diet and lung cancer risk: Findings from the Western New York Diet Study. *Am J Epidemiol* 125:351–363.
- Clark RM, Ferris AM, Fey M, Brown PB, Hundrieser KE, Jensen RG. 1982. Changes in the lipids of human milk from 2 to 16 weeks postpartum. *J Pediatr Gastroenterol Nutr* 1:311–315.
- Clarke R, Frost C, Collins R, Appleby P, Peto R. 1997. Dietary lipids and blood cholesterol: Quantitative meta-analysis of metabolic ward studies. *Br Med J* 314:112–117.
- Clifton PM, Kestin M, Abbey M, Drysdale M, Nestel PJ. 1990. Relationship between sensitivity to dietary fat and dietary cholesterol. *Arteriosclerosis* 10:394–401.
- Clifton PM, Abbey M, Noakes M, Beltrame S, Rumbelow N, Nestel PJ. 1995. Body fat distribution is a determinant of the high-density lipoprotein response to dietary fat and cholesterol in women. *Arterioscler Thromb Vasc Biol* 15:1070–1078.
- Connor WE, Hodges RE, Bleiler RE. 1961a. Effect of dietary cholesterol upon serum lipids in man. *J Lab Clin Med* 57:331–342.
- Connor WE, Hodges RE, Bleiler RE. 1961b. The serum lipids in men receiving high cholesterol and cholesterol-free diets. *J Clin Invest* 40:894–901.
- Connor WE, Stone DB, Hodges RE. 1964. The interrelated effects of dietary cholesterol and fat upon human serum lipid levels. *J Clin Invest* 43:1691–1696.
- Cruz MLA, Wong WW, Mimouni F, Hachey DL, Setchell KDR, Klein PD, Tsang RC. 1994. Effects of infant nutrition on cholesterol synthesis rates. *Pediatr Res* 35:135–140.
- Darmady JM, Fosbrooke AS, Lloyd JK. 1972. Prospective study of serum cholesterol levels during first year of life. *Br Med J* 2:685–688.
- Di Buono M, Jones PJH, Beaumier L, Wykes LJ. 2000. Comparison of deuterium incorporation and mass isotopomer distribution analysis for measurement of human cholesterol biosynthesis. *J Lipid Res* 41:1516–1523.
- Dietschy JM, Turley SD, Spady DK. 1993. Role of liver in the maintenance of cholesterol and low density lipoprotein homeostasis in different animal species, including humans. *J Lipid Res* 34:1637–1659.
- Dreon DM, Krauss RM. 1997. Diet-gene interactions in human lipoprotein metabolism. *J Am Coll Nutr* 16:313–324.
- Edington J, Geekie M, Carter R, Benfield L, Fisher K, Ball M, Mann J. 1987. Effect of dietary cholesterol on plasma cholesterol concentration in subjects following reduced fat, high fibre diet. *Br Med J* 294:333–336.
- Edmond J, Korsak RA, Morrow JW, Torok-Both G, Catlin DH. 1991. Dietary cholesterol and the origin of cholesterol in the brain of developing rats. *J Nutr* 121:1323–1330.
- Erickson BA, Coots RH, Mattson FH, Kligman AM. 1964. The effect of partial hydrogenation of dietary fats, of the ratio of polyunsaturated to saturated fatty acids, and of dietary cholesterol upon plasma lipids in man. *J Clin Invest* 43:2017–2025.
- Esrey KL, Joseph L, Grover SA. 1996. Relationship between dietary intake and coronary heart disease mortality: Lipid research clinics prevalence follow-up study. *J Clin Epidemiol* 49:211–216.

## ONLINE REFERENCES

## 731

- Fall CHD, Barker DJP, Osmond C, Winter PD, Clark PMS, Hales CN. 1992. Relation of infant feeding to adult serum cholesterol concentration and death from ischaemic heart disease. *Br Med J* 304:801–805.
- FASEB (Federation of American Societies for Experimental Biology). 1995. *Third Report on Nutrition Monitoring in the United States*. Washington, DC: U.S. Government Printing Office.
- Fielding CJ, Havel RJ, Todd KM, Yeo KE, Schloetter MC, Weinberg V, Frost PH. 1995. Effects of dietary cholesterol and fat saturation on plasma lipoproteins in an ethnically diverse population of healthy young men. *J Clin Invest* 95:611–618.
- Flynn MA, Nolph GB, Flynn TC, Kahrs R, Krause G. 1979. Effect of dietary egg on human serum cholesterol and triglycerides. *Am J Clin Nutr* 32:1051–1057.
- Franceschi S, Favero A, Decarli A, Negri E, La Vecchia C, Ferraroni M, Russo A, Salvini S, Amadori D, Conti E, Montella M, Giacosa A. 1996. Intake of macronutrients and risk of breast cancer. *Lancet* 347:1351–1356.
- Friedman G, Goldberg SJ. 1975. Concurrent and subsequent serum cholesterol of breast- and formula-fed infants. *Am J Clin Nutr* 28:42–45.
- Ginsberg HN, Karmally W, Siddiqui M, Holleran S, Tall AR, Rumsey SC, Deckelbaum RJ, Blaner WS, Ramakrishnan R. 1994. A dose-response study of the effects of dietary cholesterol on fasting and postprandial lipid and lipoprotein metabolism in healthy young men. *Arterioscler Thromb* 14:576–586.
- Ginsberg HN, Karmally W, Siddiqui M, Holleran S, Tall AR, Blaner WS, Ramakrishnan R. 1995. Increases in dietary cholesterol are associated with modest increases in both LDL and HDL cholesterol in healthy young women. *Arterioscler Thromb Vasc Biol* 15:169–178.
- Giovannucci E, Rimm EB, Stampfer MJ, Colditz GA, Ascherio A, Willett WC. 1994. Intake of fat, meat, and fiber in relation to risk of colon cancer in men. *Cancer Res* 54:2390–2397.
- Glueck CJ, Tsang R, Balistreri W, Fallat R. 1972. Plasma and dietary cholesterol in infancy: Effects of early low or moderate dietary cholesterol intake on subsequent response to increased dietary cholesterol. *Metabolism* 21:1181–1192.
- Goodman MT, Kolonel LN, Yoshizawa CN, Hankin JH. 1988. The effect of dietary cholesterol and fat on the risk of lung cancer in Hawaii. *Am J Epidemiol* 128:1241–1255.
- Haave NC, Innis SM. 2001. Cholesterol synthesis and accretion within various tissues of the fetal and neonatal rat. *Metabolism* 50:12–18.
- Hahn P, Koldovský O. 1966. *Utilization of Nutrients During Postnatal Development*. New York: Pergamon Press.
- Hamosh M. 1988. Does infant nutrition affect adiposity and cholesterol levels in the adult? *J Pediatr Gastroenterol Nutr* 7:10–16.
- Hauser H, Dyer JH, Nandy A, Vega MA, Werder M, Bieliauskaitė E, Weber FE, Compani S, Gemperli A, Boffelli D, Wehrli E, Schulthess G, Phillips MC. 1998. Identification of a receptor mediating absorption of dietary cholesterol in the intestine. *Biochemistry* 37:17843–17850.
- Hegsted DM. 1986. Serum-cholesterol response to dietary cholesterol: A re-evaluation. *Am J Clin Nutr* 44:299–305.
- Hegsted DM, McGandy RB, Myers ML, Stare FJ. 1965. Quantitative effects of dietary fat on serum cholesterol in man. *Am J Clin Nutr* 17:281–295.
- Hegsted DM, Ausman LM, Johnson JA, Dallal GE. 1993. Dietary fat and serum lipids: An evaluation of the experimental data. *Am J Clin Nutr* 57:875–883.
- Heilbrun LK, Nomura AMY, Stemmermann GN. 1984. Dietary cholesterol and lung cancer risk among Japanese men in Hawaii. *Am J Clin Nutr* 39:375–379.

- Hinds MW, Kolonel LN, Lee J, Hankin JH. 1983. Dietary cholesterol and lung cancer risk among men in Hawaii. *Am J Clin Nutr* 37:192–193.
- Hirohata T, Nomura AMY, Hankin JH, Kolonel LN, Lee J. 1987. An epidemiological study on the association between diet and breast cancer. *J Natl Cancer Inst* 78:595–600.
- Hodgson PA, Ellefson RD, Elveback LR, Harris LE, Nelson RA, Weidman WH. 1976. Comparison of serum cholesterol in children fed high, moderate, or low cholesterol milk diets during neonatal period. *Metabolism* 25:739–746.
- Hopkins PN. 1992. Effects of dietary cholesterol on serum cholesterol: A meta-analysis and review. *Am J Clin Nutr* 55:1060–1070.
- Howell WH, McNamara DJ, Tosca MA, Smith BT, Gaines JA. 1997. Plasma lipid and lipoprotein responses to dietary fat and cholesterol: A meta-analysis. *Am J Clin Nutr* 65:1747–1764.
- Hu FB, Stampfer MJ, Manson JE, Rimm E, Colditz GA, Rosner BA, Hennekens CH, Willett WC. 1997. Dietary fat intake and the risk of coronary heart disease in women. *N Engl J Med* 337:1491–1499.
- Hu FB, Stampfer MJ, Rimm EB, Manson JE, Ascherio A, Colditz GA, Rosner BA, Spiegelman D, Speizer FE, Sacks FM, Hennekens CH, Willett WC. 1999. A prospective study of egg consumption and risk of cardiovascular disease in men and women. *J Am Med Assoc* 281:1387–1394.
- Huisman M, van Beusekom CM, Lanting CI, Nijeboer HJ, Muskiet FAJ, Boersma ER. 1996. Triglycerides, fatty acids, sterols, mono- and disaccharides and sugar alcohols in human milk and current types of infant formula milk. *Eur J Clin Nutr* 50:255–260.
- Huttunen JK, Saarinen UM, Kostiainen E, Siimes MA. 1983. Fat composition of the infant diet does not influence subsequent serum lipid levels in man. *Atherosclerosis* 46:87–94.
- Jain M, Burch JD, Howe GR, Risch HA, Miller AB. 1990. Dietary factors and risk of lung cancer: Results from a case-control study, Toronto, 1981–1985. *Int J Cancer* 45:287–293.
- Jensen RG, Lammi-Keefe CJ, Ferris AM, Jackson MB, Couch SC, Capacchione CM, Ahn HS, Murtaugh M. 1995. Human milk total lipid and cholesterol are dependent on interval of sampling during 24 hours. *J Pediatr Gastroenterol Nutr* 20:91–94.
- Johnson C, Greenland P. 1990. Effects of exercise, dietary cholesterol, and dietary fat on blood lipids. *Arch Intern Med* 150:137–141.
- Jones DY, Schatzkin A, Green SB, Block G, Brinton LA, Ziegler RG, Hoover R, Taylor PR. 1987. Dietary fat and breast cancer in the National Health and Nutrition Examination Survey. I. Epidemiologic follow-up study. *J Natl Cancer Inst* 79:465–471.
- Jurevics HA, Morell P. 1994. Sources of cholesterol for kidney and nerve during development. *J Lipid Res* 35:112–120.
- Katan MB, Beynen AC, De Vries JHM, Nobels A. 1986. Existence of consistent hypo- and hyperresponders to dietary cholesterol in man. *Am J Epidemiol* 123:221–234.
- Katan MB, Berns MAM, Glatz JFC, Knuiman JT, Nobels A, de Vries JHM. 1988. Congruence of individual responsiveness to dietary cholesterol and to saturated fat in humans. *J Lipid Res* 29:883–892.
- Kern F. 1994. Effects of dietary cholesterol on cholesterol and bile acid homeostasis in patients with cholesterol gallstones. *J Clin Invest* 93:1186–1194.

- Kesäniemi YA, Ehnholm C, Miettinen TA. 1987. Intestinal cholesterol absorption efficiency in man is related to apoprotein E phenotype. *J Clin Invest* 80:578–581.
- Kestin M, Clifton PM, Rouse IL, Nestel PJ. 1989. Effect of dietary cholesterol in normolipidemic subjects is not modified by nature and amount of dietary fat. *Am J Clin Nutr* 50:528–532.
- Key TJA, Silcocks PB, Davey GK, Appleby PN, Bishop DT. 1997. A case-control study of diet and prostate cancer. *Br J Cancer* 76:678–687.
- Keys A, Anderson JT, Grande F. 1965. Serum cholesterol response to changes in the diet. II. The effect of cholesterol in the diet. *Metabolism* 14:759–765.
- Kita T, Brown MS, Bilheimer DW, Goldstein JL. 1982. Delayed clearance of very low density and intermediate density lipoproteins with enhanced conversion to low density lipoprotein in WHHL rabbits. *Proc Natl Acad Sci USA* 79:5693–5697.
- Kolaček S, Kapetanović T, Zimolo A, Lužar V. 1993. Early determinants of cardiovascular risk factors in adults. A. Plasma lipids. *Acta Paediatr* 82:699–704.
- Kolonel LN, Yoshizawa CN, Hankin JH. 1988. Diet and prostatic cancer: A case-control study in Hawaii. *Am J Epidemiol* 127:999–1012.
- Knekt P, Seppänen R, Järvinen R, Virtamo J, Hyvönen L, Pukkala E, Teppo L. 1991. Dietary cholesterol, fatty acids, and the risk of lung cancer among men. *Nutr Cancer* 16:267–275.
- Kris-Etherton PM, Layman DK, York PV, Frantz ID. 1979. The influence of early nutrition on the serum cholesterol of the adult rat. *J Nutr* 109:1244–1257.
- Kritchevsky SB, Kritchevsky D. 2000. Egg consumption and coronary heart disease: An epidemiologic overview. *J Am Coll Nutr* 19:549S–555S.
- Kromhout D, de Lezenne Coulander C. 1984. Diet, prevalence and 10-year mortality from coronary heart disease in 871 middle-aged men. The Zutphen Study. *Am J Epidemiol* 119:733–741.
- Kromhout D, Menotti A, Bloomberg B, Aravanis C, Blackburn H, Buzina R, Dontas AS, Fidanza F, Giampaoli S, Jansen A, Karvonen M, Katan M, Nissinen A, Nedeljkovic S, Pekkanen J, Pekkarinen M, Punstar S, Räsänen L, Simic B, Toshima H. 1995. Dietary saturated and *trans* fatty acids and cholesterol and 25-year mortality from coronary heart disease: The Seven Countries Study. *Prev Med* 24:308–315.
- Kummerow FA, Kim Y, Hull J, Pollard J, Ilinov P, Dorossiev DL, Valek J. 1977. The influence of egg consumption on the serum cholesterol level in human subjects. *Am J Clin Nutr* 30:664–673.
- Kushi LH, Lew RA, Stare FJ, Ellison CR, el Lozy M, Bourke G, Daly L, Graham I, Hickey N, Mulcahy R, Kevaney J. 1985. Diet and 20-year mortality from coronary heart disease. The Ireland-Boston Diet-Heart Study. *N Engl J Med* 312:811–818.
- Lammi-Keefe CJ, Ferris AM, Jensen RG. 1990. Changes in human milk at 0600, 1000, 1400, 1800, and 2200 h. *J Pediatr Gastroenterol Nutr* 11:83–88.
- Leeson CPM, Kattenhorn M, Deanfield JE, Lucas A. 2001. Duration of breast feeding and arterial distensibility in early adult life: Population based study. *Br Med J* 322:643–647.
- Le Marchand L, Wilkens LR, Hankin JH, Kolonel LN, Lyu L-C. 1997. A case-control study of diet and colorectal cancer in a multiethnic population in Hawaii (United States): Lipids and foods of animal origin. *Cancer Causes Control* 8:637–648.
- Lewis DS, Mott GE, McMahan CA, Masoro EJ, Carey KD, McGill HC. 1988. Deferred effects of preweaning diet on atherosclerosis in adolescent baboons. *Arteriosclerosis* 8:274–280.

- Lin DS, Connor WE. 1980. The long term effects of dietary cholesterol upon the plasma lipids, lipoproteins, cholesterol adsorption, and the sterol balance in man: The demonstration of feedback inhibition of cholesterol biosynthesis and increased bile acid excretion. *J Lipid Res* 21:1042–1052.
- Ling WH, Jones PJH. 1995. Dietary phytosterols: A review of metabolism, benefits, and side effects. *Life Sci* 57:195–206.
- Lütjohann D, Björkhem I, Ose L. 1996. Phytosterolaemia in a Norwegian family: Diagnosis and characterization of the first Scandinavian case. *Scand J Clin Lab Invest* 56:229–240.
- Mahley RW, Innerarity TL, Bersot TP, Lipson A, Margolis S. 1978. Alterations in human high-density lipoproteins, with or without increased plasma-cholesterol, induced by diets high in cholesterol. *Lancet* 2:807–809.
- Mann JI, Appleby PN, Key TJ, Thorogood M. 1997. Dietary determinants of ischaemic heart disease in health conscious individuals. *Heart* 78:450–455.
- Maranhão RC, Quintão ECR. 1983. Long term steroid metabolism balance studies in subjects on cholesterol-free and cholesterol-rich diets: Comparison between normal and hypercholesterolemic individuals. *J Lipid Res* 24:167–173.
- Mattson FH, Erickson BA, Kligman AM. 1972. Effect of dietary cholesterol on serum cholesterol in man. *Am J Clin Nutr* 25:589–594.
- McCombs RJ, Marcadis DE, Ellis J, Weinberg RB. 1994. Attenuated hypercholesterolemic response to a high-cholesterol diet in subjects heterozygous for the apolipoprotein A-IV-2 allele. *N Engl J Med* 331:706–710.
- McGee DL, Reed DM, Yano K, Kagan A, Tillotson J. 1984. Ten-year incidence of coronary heart disease in the Honolulu Heart Program. Relationship to nutrient intake. *Am J Epidemiol* 119:667–676.
- McGee D, Reed D, Stemmerman G, Rhoads G, Yano K, Feinleib M. 1985. The relationship of dietary fat and cholesterol to mortality in 10 years: The Honolulu Heart Program. *Int J Epidemiol* 14:97–105.
- McMurry MP, Connor WE, Goplerud CP. 1981. The effects of dietary cholesterol upon the hypercholesterolemia of pregnancy. *Metabolism* 30:869–879.
- McMurry MP, Connor WE, Cerqueira MT. 1982. Dietary cholesterol and the plasma lipids and lipoproteins in the Tarahumara Indians: A people habituated to a low cholesterol diet after weaning. *Am J Clin Nutr* 35:741–744.
- McMurry MP, Connor WE, Lin DS, Cerqueira MT, Connor SL. 1985. The absorption of cholesterol and the sterol balance in the Tarahumara Indians of Mexico fed cholesterol-free and high cholesterol diets. *Am J Clin Nutr* 41:1289–1298.
- McNamara DJ. 2000. Dietary cholesterol and atherosclerosis. *Biochim Biophys Acta* 1529:310–320.
- McNamara DJ, Kolb R, Parker TS, Batwin H, Samuel P, Brown CD, Ahrens EH. 1987. Heterogeneity of cholesterol homeostasis in man. Response to changes in dietary fat quality and cholesterol quantity. *J Clin Invest* 79:1729–1739.
- Mellies MJ, Burton K, Larsen R, Fixler D, Glueck CJ. 1979. Cholesterol, phytosterols, and polyunsaturated/saturated fatty acid ratios during the first 12 months of lactation. *Am J Clin Nutr* 32:2383–2389.
- Miettinen TA, Gylling H. 1999. Regulation of cholesterol metabolism by dietary plant sterols. *Curr Opin Lipidol* 10:9–14.
- Mistry P, Miller NE, Laker M, Hazzard WR, Lewis B. 1981. Individual variation in the effects of dietary cholesterol on plasma lipoproteins and cellular cholesterol homeostasis in man. Studies of low density lipoprotein receptor activity and 3-hydroxy-3-methylglutaryl coenzyme A reductase activity in blood mononuclear cells. *J Clin Invest* 67:493–502.

- Mize CE, Uauy R, Kramer R, Benser M, Allen S, Grundy SM. 1995. Lipoprotein-cholesterol responses in healthy infants fed defined diets from ages 1 to 12 months: Comparison of diets predominant in oleic acid versus linoleic acid, with parallel observations in infants fed a human milk-based diet. *J Lipid Res* 36:1178–1187.
- Mott GE, Jackson EM, McMahan CA, McGill HC. 1990. Cholesterol metabolism in adult baboons is influenced by infant diet. *J Nutr* 120:243–251.
- Mott GE, Jackson EM, DeLallo L, Lewis DS, McMahan CA. 1995. Differences in cholesterol metabolism in juvenile baboons are programmed by breast-versus formula-feeding. *J Lipid Res* 36:299–307.
- National Diet-Heart Study Research Group. 1968. Faribault second study. National Diet-Heart Study final report. *Circulation* 37:I260–I274.
- Neaton JD, Wentworth D. 1992. Serum cholesterol, blood pressure, cigarette smoking, and death from coronary heart disease. Overall findings and differences by age for 316,099 white men. Multiple Risk Factor Intervention Trial Research Group. *Arch Intern Med* 152:56–64.
- Nestel PJ, Poyser A. 1976. Changes in cholesterol synthesis and excretion when cholesterol intake is increased. *Metabolism* 25:1591–1599.
- Nestel P, Tada N, Billington T, Huff M, Fidge N. 1982. Changes in very low density lipoproteins with cholesterol loading in man. *Metabolism* 31:398–405.
- Oh SY, Miller LT. 1985. Effect of dietary egg on variability of plasma cholesterol levels and lipoprotein cholesterol. *Am J Clin Nutr* 42:421–431.
- Packard CJ, McKinney L, Carr K, Shepherd J. 1983. Cholesterol feeding increases low density lipoprotein synthesis. *J Clin Invest* 72:45–51.
- Picciano MF, Guthrie HA, Sheehe DM. 1978. The cholesterol content of human milk. A variable constituent among women and within the same women. *Clin Pediatr* 17:359–362.
- Pietinen P, Ascherio A, Korhonen P, Hartman AM, Willett WC, Albanes D, Virtamo J. 1997. Intake of fatty acids and risk of coronary heart disease in a cohort of Finnish men. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. *Am J Epidemiol* 145:876–887.
- Pietinen P, Malila N, Virtanen M, Hartman TJ, Tangrea JA, Albanes D, Virtamo J. 1999. Diet and risk of colorectal cancer in a cohort of Finnish men. *Cancer Causes Control* 10:387–396.
- Porter MW, Yamanaka W, Carlson SD, Flynn MA. 1977. Effect of dietary egg on serum cholesterol and triglyceride of human males. *Am J Clin Nutr* 30:490–495.
- Posner BM, Cobb JL, Belanger AJ, Cupples LA, D'Agostino RB, Stokes J. 1991. Dietary lipid predictors of coronary heart disease in men. The Framingham Study. *Arch Intern Med* 151:1181–1187.
- Quintão E, Grundy SM, Ahrens EH. 1971. Effects of dietary cholesterol on the regulation of total body cholesterol in man. *J Lipid Res* 12:233–247.
- Quintão ECR, Brumer S, Stechhahn K. 1977. Tissue storage and control of cholesterol metabolism in man on high cholesterol diets. *Atherosclerosis* 26:297–310.
- Ravelli ACJ, van der Meulen JHP, Osmond C, Barker DJP, Bleker OP. 2000. Infant feeding and adult glucose tolerance, lipid profile, blood pressure, and obesity. *Arch Dis Child* 82:248–252.
- Reiser R, Sideman Z. 1972. Control of serum cholesterol homeostasis by cholesterol in the milk of the suckling rat. *J Nutr* 102:1009–1016.
- Reiser R, O'Brien BC, Henderson GR, Moore RW. 1979. Studies on a possible function for cholesterol in milk. *Nutr Rept Int* 30:835–849.

- Repa JJ, Mangelsdorf DJ. 2000. The role of orphan nuclear receptors in the regulation of cholesterol homeostasis. *Annu Rev Cell Dev Biol* 16:459–481.
- Repa JJ, Turley SD, Lobaccaro J-MA, Medina J, Li L, Lustig K, Shan B, Heyman RA, Dietschy JM, Mangelsdorf DJ. 2000. Regulation of absorption and ABC1-mediated efflux of cholesterol by RXR heterodimers. *Science* 289:1524–1529.
- Roberts SL, McMurry MP, Connor WE. 1981. Does egg feeding (i.e., dietary cholesterol) affect plasma cholesterol levels in humans? The results of a double-blind study. *Am J Clin Nutr* 34:2092–2099.
- Romano G, Tilly-Kiesi MK, Patti L, Taskinen M-R, Pacioni D, Cassader M, Riccardi G, Rivellese AA. 1998. Effects of dietary cholesterol on plasma lipoproteins and their subclasses in IDDM patients. *Diabetologia* 41:193–200.
- Ros E. 2000. Intestinal absorption of triglyceride and cholesterol. Dietary and pharmacological inhibition to reduce cardiovascular risk. *Atherosclerosis* 151:357–379.
- Rudel LL. 1997. Genetic factors influence the atherogenic response of lipoproteins to dietary fat and cholesterol in nonhuman primates. *J Am Coll Nutr* 16:306–312.
- Salen G, Ahrens EH, Grundy SM. 1970. Metabolism of  $\beta$ -sitosterol in man. *J Clin Invest* 49:952–967.
- Salen G, Shefer S, Nguyen L, Ness GC, Tint GS, Shore V. 1992. Sitosterolemia. *J Lipid Res* 33:945–955.
- Sandler RS, Lyles CM, Peipins LA, McAuliffe CA, Woosley JT, Kupper LL. 1993. Diet and risk of colorectal adenomas: Macronutrients, cholesterol, and fiber. *J Natl Cancer Inst* 85:884–891.
- Schonfeld G, Patsch W, Rudel LL, Nelson C, Epstein M, Olson RE. 1982. Effects of dietary cholesterol and fatty acids on plasma lipoproteins. *J Clin Invest* 69:1072–1080.
- Sehayek E, Nath C, Heinemann T, McGee M, Seidman CE, Samuel P, Breslow JL. 1998. U-shape relationship between change in dietary cholesterol absorption and plasma lipoprotein responsiveness and evidence for extreme interindividual variation in dietary cholesterol absorption in humans. *J Lipid Res* 39:2415–2422.
- Sehayek E, Shefer S, Nguyen LB, Ono JG, Merkel M, Breslow JL. 2000. Apolipoprotein E regulates dietary cholesterol absorption and biliary cholesterol excretion: Studies in C57BL/6 apolipoprotein E knockout mice. *Proc Natl Acad Sci USA* 97:3433–3437.
- Shekelle RB, Rossof AH, Stamler J. 1991. Dietary cholesterol and incidence of lung cancer: The Western Electric Study. *Am J Epidemiol* 134:480–484.
- Slater G, Mead J, Dhopeshwarkar G, Robinson S, Alfin-Slater RB. 1976. Plasma cholesterol and triglycerides in men with added eggs in the diet. *Nutr Rep Int* 14:249–260.
- Sorkin JD, Andres R, Muller DC, Baldwin HL, Fleg JL. 1992. Cholesterol as a risk factor for coronary heart disease in elderly men. The Baltimore Longitudinal Study of Aging. *Ann Epidemiol* 2:59–67.
- Stamler J, Shekelle R. 1988. Dietary cholesterol and human coronary heart disease. The epidemiologic evidence. *Arch Pathol Lab Med* 112:1032–1040.
- Stamler J, Wentworth D, Neaton JD. 1986. Is relationship between serum cholesterol and risk of premature death from coronary heart disease continuous and graded? Findings in 356,222 primary screenees of the Multiple Risk Factor Intervention Trial (MRFIT). *J Am Med Assoc* 256:2823–2828.

- Staprans I, Pan X-M, Rapp JH, Grunfeld C, Feingold KR. 2000. Oxidized cholesterol in the diet accelerates the development of atherosclerosis in LDL receptor- and apolipoprotein E-deficient mice. *Arterioscler Thromb Vasc Biol* 20:708–714.
- Steiner A, Howard EJ, Akgun S. 1962. Importance of dietary cholesterol in man. *J Am Med Assoc* 181:186–190.
- Sundram K, Hayes KC, Siru OH. 1994. Dietary palmitic acid results in lower serum cholesterol than does a lauric-myristic acid combination in normolipemic humans. *Am J Clin Nutr* 59:841–846.
- Sutherland WHF, Ball MJ, Walker H. 1997. The effect of increased egg consumption on plasma cholestryl ester transfer activity in healthy subjects. *Eur J Clin Nutr* 51:172–176.
- Swanson CA, Brown CC, Sinha R, Kulldorff M, Brownson RC, Alavanja MCR. 1997. Dietary fats and lung cancer risk among women: The Missouri Women's Health Study (United States). *Cancer Causes Control* 8:883–893.
- Tell GS, Evans GW, Folsom AR, Shimakawa T, Carpenter MA, Heiss G. 1994. Dietary fat intake and carotid artery wall thickness: The Atherosclerosis Risk in Communities (ARIC) Study. *Am J Epidemiol* 139:979–989.
- Toeller M, Buyken AE, Heitkamp G, Scherbaum WA, Krans HMJ, Fuller JH. 1999. Associations of fat and cholesterol intake with serum lipid levels and cardiovascular disease: The EURODIAB IDDM Complications Study. *Exp Clin Endocrinol Diabetes* 107:512–521.
- Tzonou A, Kalandidi A, Trichopoulou A, Hsieh C-C, Toupadaki N, Willett W, Trichopoulos D. 1993. Diet and coronary heart disease: A case-control study in Athens, Greece. *Epidemiology* 4:511–516.
- van de Bovenkamp P, Kosmeijer-Schuil TG, Katan MB. 1988. Quantification of oxysterols in Dutch foods: Egg products and mixed diets. *Lipids* 23:1079–1085.
- van den Brandt PA, van't Veer P, Goldbohm RA, Dorant E, Volovics A, Hermus RJ, Sturmans F. 1993. A prospective cohort study on dietary fat and the risk of postmenopausal breast cancer. *Cancer Res* 53:75–82.
- Vine DF, Mamo JCL, Beilin LJ, Mori TA, Croft KD. 1998. Dietary oxysterols are incorporated in plasma triglyceride-rich lipoproteins, increase their susceptibility to oxidation and increase aortic cholesterol concentration of rabbits. *J Lipid Res* 39:1995–2004.
- Vlajinac HD, Marinkovic JM, Ilic MD, Kocev NI. 1997. Diet and prostate cancer: A case-control study. *Eur J Cancer* 33:101–107.
- Watts GF, Jackson P, Mandalia S, Brunt JNH, Lewis ES, Coltart DJ, Lewis B. 1994. Nutrient intake and progression of coronary artery disease. *Am J Cardiol* 73:328–332.
- Weggemans RM, Zock PL, Meyboom S, Funke H, Katan MB. 2000. Apolipoprotein A4-1/2 polymorphism and response of serum lipids to dietary cholesterol in humans. *J Lipid Res* 41:1623–1628.
- Weggemans RM, Zock PL, Katan MB. 2001. Dietary cholesterol from eggs increases the ratio of total cholesterol to high-density lipoprotein cholesterol in humans: A meta-analysis. *Am J Clin Nutr* 73:885–891.
- Weijenberg MP, Feskens EJM, Kromhout D. 1996. Total and high density lipoprotein cholesterol as risk factors for coronary heart disease in elderly men during 5 years of follow-up. The Zutphen Elderly Study. *Am J Epidemiol* 143:151–158.
- Weinberg RB, Geissinger BW, Kasala K, Hockey KJ, Terry JG, Easter L, Crouse JR. 2000. Effect of apolipoprotein A-IV genotype and dietary fat on cholesterol absorption in humans. *J Lipid Res* 41:2035–2041.

- Wells VM, Bronte-Stewart B. 1963. Egg yolk and serum-cholesterol levels: Importance of dietary cholesterol intake. *Br Med J* 1:577–581.
- Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Hennekens CH, Speizer FE. 1987. Dietary fat and the risk of breast cancer. *N Engl J Med* 316:22–28.
- Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Speizer FE. 1990. Relation of meat, fat, and fiber intake to the risk of colon cancer in a prospective study among women. *N Engl J Med* 323:1664–1672.
- Wong WW, Hachey DL, Insull W, Opekuon AR, Klein PD. 1993. Effect of dietary cholesterol on cholesterol synthesis in breast-fed and formula-fed infants. *J Lipid Res* 34:1403–1411.
- Wu Y, Zheng W, Sellers TA, Kushi LH, Bostick RM, Potter JD. 1994. Dietary cholesterol, fat, and lung cancer incidence among older women: The Iowa Women's Health Study (United States). *Cancer Causes Control* 5:395–400.
- Zanni EE, Zannis VI, Blum CB, Herbert PN, Breslow JL. 1987. Effect of egg cholesterol and dietary fats on plasma lipids, lipoproteins, and apoproteins of normal women consuming natural diets. *J Lipid Res* 28:518–527.

Ibid., Chapter 13, pp. 965–967.

- Bandini LG, Vu D, Must A, Cyr H, Goldberg A, Dietz WH. 1999. Comparison of high-calorie, low-nutrient-dense food consumption among obese and non-obese adolescents. *Obes Res* 7:438–443.
- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Black AE, Prentice AM, Goldberg GR, Jebb SA, Bingham SA, Livingstone MBE, Coward WA. 1993. Measurements of total energy expenditure provide insights into the validity of dietary measurements of energy intake. *J Am Diet Assoc* 93:572–579.
- Blair SN, Kohl HW, Barlow CE. 1993. Physical activity, physical fitness, and all-cause mortality in women: Do women need to be active? *J Am Coll Nutr* 12:368–371.
- Blair SN, Kohl HW, Barlow CE, Paffenbarger RS, Gibbons LW, Macera CA. 1995. Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. *J Am Med Assoc* 273:1093–1098.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Nutrition Examination Survey: Underreporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Carroll RJ, Freedman LS, Hartman AM. 1996. Use of semiquantitative food frequency questionnaires to estimate the distribution of usual intake. *Am J Epidemiol* 143:392–404.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- IOM. 2001. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Washington, DC: National Academy Press.

- Johnson RK, Goran MI, Poehlman ET. 1994. Correlates of over- and under-reporting of energy intake in healthy older men and women. *Am J Clin Nutr* 59:1286–1290.
- Johnson RK, Soultanakis RP, Matthews DE. 1998. Literacy and body fatness are associated with underreporting of energy intake in US low-income women using the multiple-pass 24-hour recall: A doubly labeled water study. *J Am Diet Assoc* 98:1136–1140.
- Kristal AR, Feng Z, Coates RJ, Oberman A, George V. 1997. Associations of race/ethnicity, education, and dietary intervention with the validity and reliability of a food frequency questionnaire: The Women's Health Trial Feasibility Study in Minority Populations. *Am J Epidemiol* 146:856–869.
- Lichtman SW, Pisarska K, Berman ER, Pestone M, Dowling H, Offenbacher E, Weisel H, Heshka S, Matthews DE, Heymsfield SB. 1992. Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. *N Engl J Med* 327:1893–1898.
- Liu K. 1994. Statistical issues related to semiquantitative food-frequency questionnaires. *Am J Clin Nutr* 59:262S–265S.
- Livingstone MB, Prentice AM, Coward WA, Strain JJ, Black AE, Davies PS, Stewart CM, McKenna PG, Whitehead RG. 1992. Validation of estimates of energy intake by weighed dietary record and diet history in children and adolescents. *Am J Clin Nutr* 56:29–35.
- Marlett JA, Cheung TF. 1997. Database and quick methods of assessing typical dietary fiber intakes using data for 228 commonly consumed foods. *J Am Diet Assoc* 97:1139–1148.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Prentice AM, Black AE, Coward WA, Davies HL, Goldberg GR, Murgatroyd PR, Ashford J, Sawyer M, Whitehead RG. 1986. High levels of energy expenditure in obese women. *Br Med J* 292:983–987.
- Pryer JA, Vrijheid M, Nichols R, Kiggins M, Elliott P. 1997. Who are the 'low energy reporters' in the dietary and nutritional survey of British adults? *Int J Epidemiol* 26:146–154.
- Schoeller DA. 1995. Limitations in the assessment of dietary energy by self-report. *Metabolism* 44:18–22.
- Schoeller DA, Bandini LG, Dietz WH. 1990. Inaccuracies in self-reported intake identified by comparison with the doubly labelled water method. *Can J Physiol Pharmacol* 68:941–949.
- USDA (U.S. Department of Agriculture). 2001. *USDA Nutrient Database for Standard Reference, Release 14*. Online. Nutrient Data Laboratory. Available at <http://www.nal.usda.gov/fnic/foodcomp>. Accessed April 2, 2002.
- USDA/HHS (U.S. Department of Health and Human Services). 2000. *Nutrition and Your Health: Dietary Guidelines for Americans*. Home and Garden Bulletin No. 232. Washington, DC: U.S. Government Printing Office.

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*Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* (ISBN 0-309-08537-3), Chapter 10, pp. 738–768.

- Abumrad NN, Robinson RP, Gooch BR, Lacy WW. 1982. The effect of leucine infusion on substrate flux across the human forearm. *J Surg Res* 32:453–463.
- Agharanya JC, Alonso R, Wurtman RJ. 1981. Changes in catecholamine excretion after short-term tyrosine ingestion in normally fed human subjects. *Am J Clin Nutr* 34:82–87.
- Ahlborg B, Ekelund LG, Nilsson CG. 1968. Effect of potassium-magnesium-aspartate on the capacity for prolonged exercise in man. *Acta Physiol Scand* 74:238–245.
- Al-Damluji S, Ross G, Touzel R, Perrett D, White A, Besser GM. 1988. Modulation of the actions of tyrosine by  $\alpha$ -2-adrenoceptor blockade. *Br J Pharmacol* 95:405–412.
- Alexander D, Ball MJ, Mann J. 1994. Nutrient intake and haematological status of vegetarians and age-sex matched omnivores. *Eur J Clin Nutr* 48:538–546.
- Allen DH, Delohery J, Baker G. 1987. Monosodium L-glutamate-induced asthma. *J Allergy Clin Immunol* 80:530–537.
- Allen JC, Keller RP, Archer P, Neville MC. 1991. Studies in human lactation: Milk composition and daily secretion rates of macronutrients in the first year of lactation. *Am J Clin Nutr* 54:69–80.
- Allison SP. 1992. The uses and limitations of nutritional support. *Clin Nutr* 11:319–330.
- Allison SP. 1995. Cost-effectiveness of nutritional support in the elderly. *Proc Nutr Soc* 54:693–699.
- Alonso R, Gibson CJ, Wurtman RJ, Agharanya JC, Prieto L. 1982. Elevation of urinary catecholamines and their metabolites following tyrosine administration in humans. *Biol Psychiatry* 17:781–790.
- Ambos M, Leavitt NR, Marmorek L, Wolschina SB. 1968. Sin Cib-Syn: Accent on glutamate. *N Engl J Med* 279:105.
- Amen RJ, Yoshimura NN. 1981. The pharmacology of branched-chain amino acids. *Nutr Pharmacol* 4:73–116.
- Anantharaman K. 1979. In utero and dietary administration of monosodium L-glutamate to mice: Reproductive performance and development in a multigeneration study. In: Filer LJ, ed. *Glutamic Acid: Advances in Biochemistry and Physiology*. Pp. 231–253.
- Anderson DM, Williams FH, Merkatz RB, Schulman PK, Kerr DS, Pittard WB. 1983. Length of gestation and nutritional composition of human milk. *Am J Clin Nutr* 37:810–814.
- Anderson GH, Johnston JL. 1983. Nutrient control of brain neurotransmitter synthesis and function. *Can J Physiol Pharmacol* 61:271–281.
- Anderson GH, Atkinson SA, Bryan MH. 1981. Energy and macronutrient content of human milk during early lactation from mothers giving birth prematurely and at term. *Am J Clin Nutr* 34:258–265.
- Anderson SA, Tews JK, Harper AE. 1990. Dietary branched-chain amino acids and protein selection by rats. *J Nutr* 120:52–63.

- ARS (Agricultural Research Service). 2001. *USDA Nutrient Database for Standard Reference, Release 14*. Online. U.S. Department of Agriculture. Available at <http://www.nal.usda.gov/fnic/foodcomp/Data/SR14/sr14.html>. Accessed July 3, 2002.
- Artom C, Fishman WH, Morehead RP. 1945. The relative toxicity of L- and D-serine in rats. *Proc Soc Exp Biol Med* 60:284–287.
- Ashley DV, Anderson GH. 1975. Correlation between the plasma tryptophan to neutral amino acid ratio and protein intake in the self-selecting weanling rat. *J Nutr* 105:1412–1421.
- Atkinson SA, Anderson GH, Bryan MH. 1980. Human milk: comparison of the nitrogen composition in milk from mothers of premature and full-term infants. *Am J Clin Nutr* 33:811–814.
- Ball MJ, Bartlett MA. 1999. Dietary intake and iron status of Australian vegetarian women. *Am J Clin Nutr* 70:353–358.
- Barbul A. 1986. Arginine: Biochemistry, physiology, and therapeutic implications. *J Parenter Enteral Nutr* 10:227–238.
- Barbul A, Wasserkrug HL, Sisto DA, Seifter E, Rettura G, Levenson SM, Efron G. 1980. Thymic stimulatory actions of arginine. *J Parenter Enteral Nutr* 4:446–449.
- Barbul A, Sisto DA, Wasserkrug HL, Efron G. 1981. Arginine stimulates lymphocyte immune response in healthy human beings. *Surgery* 90:244–251.
- Barbul A, Lazarou SA, Efron DT, Wasserkrug HL, Efron G. 1990. Arginine enhances wound healing and lymphocyte immune responses in humans. *Surgery* 108:331–337.
- Barr SI, Broughton TM. 2000. Relative weight, weight loss efforts and nutrient intakes among health-conscious vegetarian, past vegetarian and nonvegetarian women ages 18 to 50. *J Am Coll Nutr* 19:781–788.
- Basile-Filho A, Beaumier L, El-Khoury AE, Yu Y, Kenneway M, Gleason RE, Young VR. 1998. Twenty-four-hour L-[1-<sup>13</sup>C]tyrosine and L-[3,3-<sup>2</sup>H<sub>2</sub>]phenylalanine oral tracer studies at generous, intermediate, and low phenylalanine intakes to estimate aromatic amino acid requirements in adults. *Am J Clin Nutr* 67:640–659.
- Batshaw ML, Wachtel RC, Thomas GH, Starrett A, Brusilow SW. 1984. Arginine-responsive asymptomatic hyperammonemia in the premature infant. *J Pediatr* 105:86–91.
- Baxter CF, Baldwin RA, Davis JL, Flood JF. 1985. High proline levels in the brains of mice as related to specific learning deficits. *Pharmacol Biochem Behav* 22:1053–1059.
- Bazzano G, D'Elia JA, Olson RE. 1970. Monosodium glutamate: Feeding of large amounts in man and gerbils. *Science* 169:1208–1209.
- Benabe JE, Martinez-Maldonado M. 1998. The impact of malnutrition on kidney function. *Mineral Electrolyte Metab* 24:20–26.
- Benedict CR, Anderson GH, Sole MJ. 1983. The influence of oral tyrosine and tryptophan feeding on plasma catecholamines in man. *Am J Clin Nutr* 38:429–435.
- Benevenga NJ, Steele RD. 1984. Adverse effects of excessive consumption of amino acids. *Annu Rev Nutr* 4:157–181.
- Benevenga NJ, Yeh M-H, Lalich JJ. 1976. Growth depression and tissue reaction to the consumption of excess dietary methionine and S-methyl-L-cysteine. *J Nutr* 106:1714–1720.
- Bergner H, Schwandt H, Kruger U. 1990. Determination of a prececal N-absorption from natural feed by <sup>15</sup>N-labeled laboratory rats using the isotope dilution method. *Arch Tierernahr* 40:569–582.

- Bernacchi AS, DeFerreyra EC, DeCastro CR, Castro JA. 1993. Ultrastructural alterations in testes from rats treated with cysteine. *Biomed Environ Sci* 6:172–178.
- Berry HK, Butcher RE, Elliot LA, Brunner RL. 1974. The effect of monosodium glutamate on the early biochemical and behavioral development of the rat. *Dev Psychobiol* 7:165–173.
- Birt DF, Julius AD, Hasegawa R, St. John M, Cohen S. 1987. Effect of L-tryptophan excess and vitamin B<sub>6</sub> deficiency on rat urinary bladder cancer promotion. *Cancer Res* 47:1244–1250.
- Bistrian BR. 1990. Recent advances in parenteral and enteral nutrition: A personal perspective. *J Parenteral Enteral Nutr* 14:329–334.
- Blauvelt A, Falanga V. 1991. Idiopathic and L-tryptophan-associated eosinophilic fasciitis before and after L-tryptophan contamination. *Arch Dermatol* 127:1159–1166.
- Block KP. 1989. Interactions among leucine, isoleucine, and valine with special reference to the branched-chain amino acid antagonism. In: Friedman M, ed. *Absorption and Utilization of Amino Acids*, Vol. 1. Boca Raton, FL: CRC Press. Pp. 229–244.
- Blumenkrantz MJ, Shapiro DJ, Swendseid ME, Kopple JD. 1975. Histidine supplementation for treatment of anaemia of uraemia. *Br Med J* 2:530–533.
- Borgonha S, Regan MM, Oh SH, Condon M, Young VR. 2002. Threonine requirement of healthy adults, derived with a 24-h indicator amino acid balance technique. *Am J Clin Nutr* 75:698–704.
- Brattstrom LE, Hardebo JE, Hultberg BL. 1984. Moderate homocysteinemia—A possible risk factor for arteriosclerotic cerebrovascular disease. *Stroke* 15:1012–1016.
- Brattstrom L, Israelsson B, Norrvig B, Bergqvist D, Thorne J, Hultberg B, Hamfelt A. 1990. Impaired homocysteine metabolism in early-onset cerebral and peripheral occlusive arterial disease. *Atherosclerosis* 81:51–60.
- Bross R, Ball RO, Pencharz PB. 1998. Development of a minimally invasive protocol for the determination of phenylalanine and lysine kinetics in humans during the fed state. *J Nutr* 128:1913–1919.
- Bross R, Ball RO, Clarke JTR, Pencharz PB. 2000. Tyrosine requirements in children with classical PKU determined by indicator amino acid oxidation. *Am J Physiol* 278:E195–E201.
- Brunton JA, Ball RO, Pencharz PB. 1998. Determination of amino acid requirements by indicator amino acid oxidation: Applications in health and disease. *Curr Opin Clin Nutr Metab Care* 1:449–453.
- Brunton JA, Bertolo RF, Pencharz PB, Ball RO. 1999. Proline ameliorates arginine deficiency during enteral but not parenteral feeding in neonatal piglets. *Am J Physiol* 277:E223–E231.
- Brusilow SW, Horwitz AL. 1989. Urea cycle enzymes. In: Scriver CR, Beaudet AL, Sly WS, Valle D, eds. *The Metabolic Basis of Inherited Disease*, 6th ed. New York: McGraw-Hill. Pp. 629–663.
- Brusilow SW, Danney M, Waber LJ, Batshaw M, Burton B, Levitsky L, Roth K, McKeethren C, Ward J. 1984. Treatment of episodic hyperammonemia in children with inborn errors of urea synthesis. *N Engl J Med* 310:1630–1634.
- Burke BS, Harding WV, Stuart HC. 1943. Nutrition studies during pregnancy. IV. Relation of protein content of mother's diet during pregnancy to birth length, birth weight, and condition of infant at birth. *J Pediatr* 23:506–515.
- Bushinsky DA, Gennari FJ. 1978. Life-threatening hyperkalemia induced by arginine. *Ann Intern Med* 89:632–634.

- Butte NF, Garza C, Johnson CA, O'Brian Smith E, Nichols BL. 1984a. Longitudinal changes in milk composition of mothers delivering preterm and term infants. *Early Hum Dev* 9:153–162.
- Butte NF, Garza C, O'Brian Smith E, Nichols BL. 1984b. Human milk intake and growth in exclusively breast-fed infants. *J Pediatr* 104:187–195.
- Butte NF, Hopkinson JM, Wong WW, Smith EO, Ellis KJ. 2000. Body composition during the first 2 years of life: An updated reference. *Pediatr Res* 47:578–585.
- Calabrese V, Rausa N, Antico A, Mangiameli S, Rizza V. 1997. Cysteine-induced enhancement of lipid peroxidation in substantia nigra: Comparative effect with exogenous administration of reduced glutathione. *Drugs Exp Clin Res* 23:25–31.
- Calloway DH. 1974. Nitrogen balance during pregnancy. In: Winnick M, ed. *Nutrition and Fetal Development*, Vol. 2. New York: John Wiley and Sons. Pp. 79–94.
- Calloway DH, Margen S. 1971. Variation in endogenous nitrogen excretion and dietary nitrogen utilization as determinants of human protein requirement. *J Nutr* 101:205–216.
- Calloway DH, Odell AC, Margen S. 1971. Sweat and miscellaneous nitrogen losses in human balance studies. *J Nutr* 101:775–786.
- Campbell WW, Evans WJ. 1996. Protein requirements of elderly people. *Eur J Clin Nutr* 50:S180–S185.
- Campbell WW, Crim MC, Dallal GE, Young VR, Evans WJ. 1994. Increased protein requirements in elderly people: New data and retrospective reassessments. *Am J Clin Nutr* 60:501–509.
- Campbell WW, Crim MC, Young VR, Joseph LJ, Evans WJ. 1995. Effects of resistance training and dietary protein intake on protein metabolism in older adults. *Am J Physiol* 268:E1143–E1153.
- Campbell WW, Trappe TA, Wolfe RR, Evans WJ. 2001. The recommended dietary allowance for protein may not be adequate for older people to maintain skeletal muscle. *J Gerontol A Biol Sci Med Sci* 56:M373–M380.
- Carlson HE, Miglietta JT, Roginsky MS, Stegink LD. 1989. Stimulation of pituitary hormone secretion by neurotransmitter amino acids in humans. *Metabolism* 38:1179–1182.
- Carmichael S, Abrams B, Selvin S. 1997. The pattern of maternal weight gain in women with good pregnancy outcomes. *Am J Public Health* 87:1984–1988.
- Castaneda C, Charnley JM, Evans WJ, Crim MC. 1995a. Elderly women accommodate to a low-protein diet with losses of body cell mass, muscle function, and immune response. *Am J Clin Nutr* 62:30–39.
- Castaneda C, Dolnikowski GG, Dallal GE, Evans WJ, Crim MC. 1995b. Protein turnover and energy metabolism of elderly women fed a low-protein diet. *Am J Clin Nutr* 62:40–48.
- Celander DR, George MJ. 1963. Dietary interrelationships of ethionine and methionine in the weanling rat. *Biochem J* 87:143–146.
- Chambers BJ, Klein NW, Nosel PG, Khairallah LH, Romanow JS. 1995. Methionine overcomes neural tube defects in rat embryos cultured on sera from laminin-immunized monkeys. *J Nutr* 125:1587–1599.
- Chatot CL, Klein NW, Clapper ML, Resor SR, Singer WD, Russman BS, Holmes GL, Mattson RH, Cramer JA. 1984. Human serum teratogenicity studied by rat embryo culture: Epilepsy, anticonvulsant drugs, and nutrition. *Epilepsia* 25:205–216.

- Chen MK, Salloum RM, Austgen TR, Bland JB, Bland KI, Copeland EM, Souba WW. 1991. Tumor regulation of hepatic glutamine metabolism. *J Parenter Enteral Nutr* 15:159–164.
- Chen MK, Espat NJ, Bland KI, Copeland EM, Souba WW. 1993. Influence of progressive tumor growth on glutamine metabolism in skeletal muscle and kidney. *Ann Surg* 217:655–667.
- Cheng AH, Gomez A, Bergan JG, Lee TC, Monckeberg F, Chichester CO. 1978. Comparative nitrogen balance study between young and aged adults using three levels of protein intake from a combination wheat-soy-milk mixture. *Am J Clin Nutr* 31:12–22.
- Chien PFW, Smith K, Watt PW, Scrimgeour CM, Taylor DJ, Rennie MJ. 1993. Protein turnover in the human fetus studied at term using stable isotope tracer amino acids. *Am J Physiol* 265:E31–E35.
- Chipponi JX, Bleier JC, Santi MT, Rudman D. 1982. Deficiencies of essential and conditionally essential nutrients. *Am J Clin Nutr* 35:1112–1116.
- Cho ES, Anderson HL, Wixom RL, Hanson KC, Krause GF. 1984. Long-term effects of low histidine intake on men. *J Nutr* 114:369–384.
- Christman AA. 1971. Determination of anserine, carnosine, and other histidine compounds in muscle extractives. *Anal Biochem* 39:181–187.
- Chung TK, Gelberg HB, Dorner JL, Baker DH. 1991. Safety of L-tryptophan for pigs. *J Anim Sci* 69:2955–2960.
- Ciechanover A, DiGiuseppe JA, Bercovich B, Orian A, Richter JD, Schwartz AL, Brodeur GM. 1991. Degradation of nuclear oncoproteins by the ubiquitin system in vitro. *Proc Natl Acad Sci USA* 88:139–143.
- Clarke JTR, Bier DM. 1982. The conversion of phenylalanine to tyrosine in man. Direct measurement by continuous intravenous tracer infusions of L-[ring-<sup>2</sup>H<sub>5</sub>] phenylalanine and L-[1-<sup>13</sup>C] tyrosine in the postabsorptive state. *Metabolism* 31:999–1005.
- Clarke R, Daly L, Robinson K, Naughten E, Cahalane S, Fowler B, Graham I. 1991. Hyperhomocysteinemia: An independent risk factor for vascular disease. *N Engl J Med* 324:1149–1155.
- Coelho CN, Klein NW. 1990. Methionine and neural tube closure in cultured rat embryos: Morphological and biochemical analyses. *Teratology* 42:437–451.
- Cohlan SQ, Stone SM. 1961. Effects of dietary and intraperitoneal excess of L-lysine and L-leucine on rat pregnancy and offspring. *J Nutr* 74:93–95.
- Colquhoun A, Newsholme EA. 1997. Aspects of glutamine metabolism in human tumour cells. *Biochem Mol Biol Int* 41:583–596.
- Connor H, Newton DJ, Preston FE, Woods HF. 1978. Oral methionine loading as a cause of acute serum folate deficiency: Its relevance to parental nutrition. *Postgrad Med J* 54:318–320.
- Cordain L, Miller JB, Eaton SB, Mann N, Holt SH, Speth JD. 2000. Plant-animal subsistence ratios and macronutrient energy estimations in worldwide hunter-gatherer diets. *Am J Clin Nutr* 71:682–692.
- Corish CA, Kennedy NP. 2000. Protein-energy undernutrition in hospital in-patients. *Br J Nutr* 83:575–591.
- Creel DJ, Wang JM, Wong KC. 1987. Transient blindness associated with transurethral resection of the prostate. *Arch Ophthalmol* 105:1537–1539.
- Cuche JL, Prinseau J, Selz F, Ruget G, Tual JL, Reingeissen L, Devoisin M, Baglin A, Guedon J, Fritel D. 1985. Oral load of tyrosine or L-dopa and plasma levels of free and sulfoconjugated catecholamines in healthy men. *Hypertension* 7:81–89.

- Cuervo AM, Dice JF. 1998. Lysosomes, a meeting point of proteins, chaperones, and proteases. *J Mol Med* 76:6–12.
- Danner DJ, Elsas LF. 1989. Disorders of branched chain amino acid and keto acid metabolism. In: Scriver CR, Beaudet AL, Sly WS, Valle D, eds. *The Metabolic Basis of Inherited Disease*, 6th ed., Vol. I. New York: McGraw-Hill. Pp. 671–692.
- Danner DJ, Lemmon SK, Besharse JC, Elsas LJ. 1979. Purification and characterization of branched chain alpha-ketoacid dehydrogenase from bovine liver mitochondria. *J Biol Chem* 254:5522–5526.
- Darling PB, Grunow J, Rafii M, Brookes S, Ball RO Pencharz PB. 2000. Threonine dehydrogenase is a minor degradative pathway of threonine catabolism in human adults. *Am J Physiol* 278:E877–E884.
- Darragh AJ, Hodgkinson SM. 2000. Quantifying the digestibility of dietary protein. *J Nutr* 130:1850S–1856S.
- Darragh AJ, Moughan PJ. 1998. The amino acid composition of human milk corrected for amino acid digestibility. *Br J Nutr* 80:25–34.
- Das TK, Waterlow JC. 1974. The rate of adaptation of urea cycle enzymes, amino-transferases and glutamic dehydrogenase to changes in dietary protein intake. *Br J Nutr* 32:353–373.
- David JC. 1976. Evidence for the possible formation of a toxic tyrosine metabolite by the liver microsomal drug metabolizing system. *Naunyn Schmiedebergs Arch Pharmacol* 292:79–86.
- David JC, Dairman W, Udenfriend S. 1974. Decarboxylation to tyramine: A major route of tyrosine metabolism in mammals. *Proc Natl Acad Sci USA* 71:1771–1775.
- Davis TA, Nguyen HV, Garcia-Bravo R, Fiorotto ML, Jackson EM, Lewis DS, Lee DR, Reeds PJ. 1994. Amino acid composition of human milk is not unique. *J Nutr* 124:1126–1132.
- De Aloysio D, Mantuano R, Mauloni M, Nicoletti G. 1982. The clinical use of arginine aspartate in male infertility. *Acta Eur Fertil* 13:133–167.
- de Blaauw I, Deutz NEP, Von Meyenfeldt MF. 1996. In vivo amino acid metabolism of gut and liver during short and prolonged starvation. *Am J Physiol* 270:G298–G306.
- de Haan A, van Doorn JE, Westra HG. 1985. Effects of potassium + magnesium aspartate on muscle metabolism and force development during short intensive static exercise. *Int J Sports Med* 6:44–49.
- Dekker J, Aelmans PH, Strous GJ. 1991. The oligomeric structure of rat and human gastric mucins. *Biochem J* 277:423–427.
- de Lange CFM, Sauer WC, Mosenthin R, Souffrant WB. 1989. The effect of feeding different protein-free diets on the recovery and amino acid composition of endogenous protein collected from the distal ileum and feces in pigs. *J Anim Sci* 67:746–754.
- de Vreese M, Frik R, Roos N, Hagemeister H. 2000. Protein-bound D-amino acids, and to a lesser extent lysinoalanine, decrease true ileal protein digestibility in minipigs as determined with <sup>15</sup>N-labeling. *J Nutr* 130:2026–2031.
- Dewey KG, Lönnerdal B. 1983. Milk and nutrient intake of breast-fed infants from 1 to 6 months: Relation to growth and fatness. *J Pediatr Gastroenterol Nutr* 2:497–506.
- Dewey KG, Finley DA, Lönnerdal B. 1984. Breast milk volume and composition during late lactation (7–20 months). *J Pediatr Gastroenterol Nutr* 3:713–720.
- Dewey KG, Beaton G, Fjeld C, Lönnerdal B, Reeds P. 1996. Protein requirements of infants and children. *Eur J Clin Nutr* 50:S119–S150.

- DHEW (U.S. Department of Health, Education and Welfare). 1978. *Bioassay of L-Tryptophan for Possible Carcinogenicity*. National Cancer Institute Technical Report Series No. 71. Washington, DC: U.S. Government Printing Office.
- Di Buono M, Wykes LJ, Ball RO, Pencharz PB. 2001. Total sulfur amino acid requirement in young men determined by indicator amino acid oxidation with L-[1-<sup>13</sup>C] phenylalanine. *Am J Clin Nutr* 74:756–760.
- Diem K. 1962. *Documenta Geigy Scientific Tables*, 6th ed. Ardsley, NY: Geigy Pharmaceuticals. Pp.528.
- DiGiovanna JJ, Blank H. 1984. Failure of lysine in frequently recurrent herpes simplex infection. Treatment and prophylaxis. *Arch Dermatol* 120:48–51.
- DiGiovanna JJ, Blank H. 1985. Failure of lysine? *Arch Dermatol* 121:21.
- Drago F, Continella G, Alloro MC, Auditore S, Pennisi G. 1984. Behavioral effects of arginine in male rats. *Pharmacol Res Commun* 16:899–907.
- Dubois S, Dougherty C, Duquette M-P, Hanley JA, Moutquin J-M. 1991. Twin pregnancy: The impact of the Higgins Nutrition Intervention Program on maternal and neonatal outcomes. *Am J Clin Nutr* 53:1397–1403.
- Dubois S, Coulombe C, Pencharz P, Pinsonneault O, Duquette M-P. 1997. Ability of the Higgins Nutrition Intervention Program to improve adolescent pregnancy outcome. *J Am Diet Assoc* 97:871–878.
- Dubow E, Maher A, Gish D, Erk V. 1958. Lysine tolerance in infants. *J Pediatr* 52:30–37.
- Duffy B, Gunn T, Collinge J, Pencharz PB. 1981. The effect of varying protein quality and energy intake on the nitrogen metabolism of parenterally fed very low birthweight (<1600 g) infants. *Pediatr Res* 15:1040–1044.
- Dutra-Filho CS, Wanmacher CM, Pires RF, Gus G, Kalil AM, Wajner M. 1989. Reduced locomotor activity of rats made histidinemic by injection of histidine. *J Nutr* 119:1223–1227.
- Ebert AG. 1979a. The dietary administration of L-monosodium glutamate, DL-monosodium glutamate, and L-glutamic acid to rats. *Toxicol Lett* 3:71–78.
- Ebert AG. 1979b. The dietary administration of monosodium glutamate or glutamic acid to C-57 black mice for 2 years. *Toxicol Lett* 3:65–70.
- Edmonds MS, Baker DH. 1987. Amino acid excesses for young pigs: Effects of excess methionine, tryptophan, threonine or leucine. *J Anim Sci* 64:1664–1671.
- Edmonds MS, Gonyou HW, Baker DH. 1987. Effect of excess levels of methionine, tryptophan, arginine, lysine or threonine on growth and dietary choice in the pig. *J Anim Sci* 65:179–185.
- Egana JI, Fuentes A, Uauy R. 1984. Protein needs of Chilean pre-school children fed milk and soy protein isolate diets. In: Rand WM, Uauy R, Scrimshaw NS, eds. *Protein-Energy Requirement Studies in Developing Countries: Results of International Research*. Tokyo, Japan: United Nations University Press. Pp. 249–257.
- Egana JI, Uauy R, Cassorla X, Barrera G, Yanez E. 1992. Sweet lupin protein quality in young men. *J Nutr* 122:2341–2347.
- Ehlers K, Drews E, Nau H. 1994. The amino acid methionine reduces the valproic acid-induced spina bifida rate in the mouse. *Teratology* 50:28A.
- Elia M, Livesey G. 1983. Effects of ingested steak and infused leucine on forelimb metabolism in man and the fate of the carbon skeletons and amino groups of branched-chain amino acids. *Clin Sci* 64:517–526.
- El-Khoury AE, Fukagawa NK, Sanchez M, Tsay RH, Gleason RE, Chapman TE, Young VR. 1994a. The 24-h pattern and rate of leucine oxidation, with particular reference to tracer estimates of leucine requirements in healthy adults. *Am J Clin Nutr* 59:1012–1020.

- El-Khoury AE, Fukagawa NK, Sanchez M, Tsay RH, Gleason RE, Chapman TE, Young VR. 1994b. Validation of the tracer-balance concept with reference to leucine: 24-h intravenous tracer studies with L-[1-<sup>13</sup>C]leucine and [<sup>15</sup>N-<sup>15</sup>N]urea. *Am J Clin Nutr* 59:1000–1011.
- El-Khoury AE, Forslund A, Olsson R, Branth S, Sjodin A, Andersson A, Atkinson A, Selvaraj A, Hambraeus L, Young VR. 1997. Moderate exercise at energy balance does not affect 24-h leucine oxidation or nitrogen retention in healthy men. *Am J Physiol* 273:E394–E407.
- El-Khoury AE, Pereira PC, Borgonha S, Basile-Filho A, Beaumier L, Wang SY, Metges CC, Ajami AM, Young VR. 2000. Twenty-four-hour oral tracer studies with L-[1-<sup>13</sup>C]lysine at a low ( $15 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ ) and intermediate ( $29 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ ) lysine intake in healthy adults. *Am J Clin Nutr* 72:122–130.
- Ellis KJ, Shypailo RJ, Abrams SA, Wong WW. 2000. The reference child and adolescent models of body composition. A contemporary comparison. *Ann NY Acad Sci* 904:374–382.
- Emerson K, Poindexter EL, Kothari M. 1975. Changes in total body composition during normal and diabetic pregnancy: Relation to oxygen consumption. *Obstet Gynecol* 45:505–511.
- Eriksson LS, Hagenfeldt L, Felig P, Wahren J. 1983. Leucine uptake by splanchnic and leg tissues in man: Relative independence of insulin levels. *Clin Sci* 65:491–498.
- Fahr MJ, Kornbluth J, Blossom S, Schaeffer R, Klimberg VS. 1994. Harry M. Vars Research Award. Glutamine enhances immunoregulation of tumor growth. *J Parenter Enteral Nutr* 18:471–476.
- FAO (Food and Agriculture Organization). 2000. *The State of Food and Agriculture 2000*. Rome: FAO.
- FAO/Agrostat. 1991. *Computerized information series No. 1. Food balance sheets*. Rome: FAO.
- FAO/WHO (World Health Organization). 1965. *Protein Requirements*. Report of a Joint FAO/WHO Expert Group. Technical Report Series No. 37. Rome: FAO.
- FAO/WHO. 1973. *Energy and Protein Requirements*. Report of a Joint FAO/WHO Ad Hoc Expert Committee. Technical Report Series No. 522. Geneva, Switzerland: WHO.
- FAO/WHO. 1991. *Protein Quality Evaluation*. FAO Food and Nutrition Paper 51. Rome: FAO.
- FAO/WHO/UNU (United Nations University). 1985. *Energy and Protein Requirements*. Report of a Joint FAO/WHO/UNU Expert Consultation. Technical Report Series No. 724. Geneva, Switzerland: WHO.
- Fawcett LB, Pugarelli JE, Brent RL. 2000. Effects of supplemental methionine on antiserum-induced dysmorphology in rat embryos cultured in vitro. *Teratology* 61:332–341.
- Fee BA, Weil WB. 1963. Body composition of infants of diabetic mothers by direct analysis. *Ann NY Acad Sci* 110:869.
- Fernstrom JD, Larin F, Wurtman RJ. 1973. Correlations between brain tryptophan and plasma neutral amino acid levels following food consumption in rats. *Life Sci* 13:517–524.
- Fernstrom JD, Cameron JL, Fernstrom MH, McConaha C, Weltzin TE, Kaye WH. 1996. Short-term neuroendocrine effects of a large oral dose of monosodium glutamate in fasting male subjects. *J Clin Endocrinol Metab* 81:184–191.

- Ferrari DA, Gilles PA, Klein NW, Nadler D, Weeks BS, Lammi-Keefe CJ, Hillman RE, Carey SW, Ying Y-K, Maier D, Olsen P, Wemple DW, Greenstein R, Muechler EK, Miller RK, Mariona FG. 1994. Rat embryo development on human sera is related to numbers of previous spontaneous abortions and nutritional factors. *Am J Obstet Gynecol* 170:228–236.
- Filer LJ, Stegink LD. 1988. Effect of aspartame on plasma phenylalanine concentration in humans. In: Wurtman RJ, Ritter-Walker E, eds. *Dietary Phenylalanine and Brain Function*. Boston: Birkhauser. Pp. 18–40.
- Finkelstein MW, Daabees TT, Stegink LD, Applebaum AE. 1983. Correlation of aspartate dose, plasma dicarboxylic amino acid concentration, and neuronal necrosis in infant mice. *Toxicology* 29:109–119.
- Finkelstein MW, Daabees TT, Stegink LD, Applebaum AE. 1988. Aspartate-induced neuronal necrosis in infant mice: Protective effect of carbohydrate and insulin. *J Toxicol Environ Health* 23:395–406.
- Fisher H, Brush MK, Griminger P, Sostman ER. 1967. Nitrogen retention in adult man: A possible factor in protein requirements. *Am J Clin Nutr* 20:927–934.
- Fomon S. 1991. Requirements and recommended dietary intakes of protein during infancy. *Pediatr Res* 30:391–395.
- Forbes GB. 1987. *Human Body Composition: Growth, Aging, Nutrition, and Activity*. New York: Springer-Verlag.
- Forslund AH, Hamraeus L, Olsson RM, El-Khoury AE, Yu YM, Young VR. 1998. The 24-h whole body leucine and urea kinetics at normal and high protein intakes with exercise in healthy adults. *Am J Physiol* 275:E310–E320.
- Forsum E, Sadurskis A, Wager J. 1988. Resting metabolic rate and body composition of healthy Swedish women during pregnancy. *Am J Clin Nutr* 47:942–947.
- Fregly MJ, Rowland NE, Sumners C. 1989. Effect of chronic dietary treatment with L-tryptophan on spontaneous salt appetite of rats. *Pharmacol Biochem Behav* 33:401–406.
- Frexes-Steed M, Warner ML, Bulus N, Flakoll P, Abumrad NN. 1990. Role of insulin and branched-chain amino acids in regulating protein metabolism during fasting. *Am J Physiol* 258:E907–E917.
- Frey GH. 1976. Use of aspartame by apparently healthy children and adolescents. *J Toxicol Environ Health* 2:401–415.
- Frisancho AR, Matos J, Flegel P. 1983. Maternal nutritional status and adolescent pregnancy outcome. *Am J Clin Nutr* 38:739–746.
- Fuller MF, Garlick PJ. 1994. Human amino acid requirements: Can the controversy be resolved? *Annu Rev Nutr* 14:217–241.
- Fuller MF, Reeds PJ. 1998. Nitrogen cycling in the gut. *Annu Rev Nutr* 18:385–411.
- Funk DN, Worthington-Roberts B, Fantel A. 1991. Impact of supplemental lysine or tryptophan on pregnancy course and outcome in rats. *Nutr Res* 11:501–512.
- Furst P. 1989. Amino acid metabolism in uremia. *J Am Coll Nutr* 8:310–323.
- Garlick PJ, Reeds PJ. 1993. Proteins. In: Garrow JS, James WPT, Ralph A, eds. *Human Nutrition and Dietetics*. Edinburgh: Churchill Livingstone. Pp. 56–76.
- Garlick PJ, McNurlan MA, Patlak CS. 1999. Adaptation of protein metabolism in relation to limits to high dietary protein intake. *Eur J Clin Nutr* 53:S34–S43.
- Garza C, Scrimshaw NS, Young VR. 1976. Human protein requirements: The effect of variations in energy intake within the maintenance range. *Am J Clin Nutr* 29:280–287.
- Garza C, Scrimshaw NS, Young VR. 1977a. Human protein requirements: A long-term metabolic nitrogen balance study in young men to evaluate the 1973 FAO/WHO safe level of egg protein intake. *J Nutr* 107:335–352.

- Garza C, Scrimshaw NS, Young VR. 1977b. Human protein requirements: Evaluation of the 1973 FAO/WHO safe level of protein intake for young men at high energy intakes. *Br J Nutr* 37:403–420.
- Garza C, Scrimshaw NS, Young VR. 1978. Human protein requirements: Interrelationships between energy intake and nitrogen balance in young men consuming the 1973 FAO/WHO safe level of egg protein, with added non-essential amino acids. *J Nutr* 108:90–96.
- Gaspar J, Laires A, Va S, Pereira S, Mariano A, Quina M, Rueff J. 1996. Mutagenic activity of glycine upon nitrosation in the presence of chloride and human gastric juice: A possible role in gastric carcinogenesis. *Teratog Carcinog Mutagen* 16:275–286.
- Gattas V, Barrera GA, Riumallo JS, Uauy R. 1990. Protein-energy requirements of prepubertal school-age boys determined by using the nitrogen-balance response to a mixed-protein diet. *Am J Clin Nutr* 52:1037–1042.
- Gattas V, Barrera GA, Riumallo JS, Uauy R. 1992. Protein-energy requirements of boys 12–14 y old determined by using the nitrogen-balance response to a mixed-protein diet. *Am J Clin Nutr* 56:499–503.
- Gaudichon C, Mahe S, Benamouzig R, Luengo C, Fouillet H, Dare S, Van Oycke M, Ferriere F, Rautureau J, Tome D. 1999. Net postprandial utilization of [<sup>15</sup>N]-labeled milk protein nitrogen is influenced by diet composition in humans. *J Nutr* 129:890–895.
- Gausserès N, Mahé S, Benamouzig R, Luengo C, Ferriere F, Rautureau J, Tomé D. 1997. [<sup>15</sup>N]-Labeled pea flour protein nitrogen exhibits good ileal digestibility and postprandial retention in humans. *J Nutr* 127:1160–1165.
- Geha RS, Beiser A, Ren C, Patterson R, Greenberger P, Grammer LC, Ditto AM, Harris KE, Shaughnessy MA, Yarnold PR, Corren J, Saxon A. 2000. Multicenter, double blind, placebo-controlled, multiple-challenge evaluation of reported reactions to monosodium glutamate. *J Allergy Clin Immunol* 106:973–980.
- Gelieber AA, Hashim SA, Van Itallie TB. 1981. Oral L-histidine fails to reduce taste and smell acuity but induces anorexia and urinary zinc excretion. *Am J Clin Nutr* 34:119–120.
- Genuth SM. 1973. Effects of oral alanine administration in fasting obese subjects. *Metabolism* 22:927–937.
- Genuth SM, Castro J. 1974. Effect of oral alanine on blood beta-hydroxybutyrate and plasma glucose, insulin, free fatty acids, and growth hormone in normal and diabetic subjects. *Metabolism* 23:375–386.
- Gerard JM, Luisiri A. 1997. A fatal overdose of arginine hydrochloride. *Clin Toxicol* 35:621–625.
- Germano P, Cohen SG, Hahn B, Metcalfe DD. 1991. An evaluation of clinical reactions to monosodium glutamate (MSG) in asthmatics, using a blinded placebo-controlled challenge. *J Allergy Clin Immunol* 87:177.
- Gersovitz M, Motil K, Munro HN, Scrimshaw NS, Young VR. 1982. Human protein requirements: Assessment of the adequacy of the current Recommended Dietary Allowance for dietary protein in elderly men and women. *Am J Clin Nutr* 35:6–14.
- Gipson IK, Burns RP, Wolfe-Lande JD. 1975. Crystals in corneal epithelial lesions of tyrosine-fed rats. *Invest Ophthalmol* 14:937–941.
- Glaeser BS, Melamed E, Growdon JH, Wurtman RJ. 1979. Evaluation of plasma tyrosine after a single oral dose of L-tyrosine. *Life Sci* 25:265–271.
- Glatt H. 1989. Mutagenicity spectra in *Salmonella typhimurium* strains of glutathione, L-cysteine and active oxygen species. *Mutagenesis* 4:221–227.

- Glatt H. 1990. Endogenous mutagens derived from amino acids. *Mutat Res* 238:235–243.
- Glyn JR, Lipton JM. 1981. Effects of central administration of alanine on body temperature of the rabbit: Comparisons with the effects of serine, glycine and taurine. *Brain Res Bull* 6:467–472.
- Goldberg AL, Rock KL. 1992. Proteolysis, proteasomes and antigen presentation. *Nature* 357:375–379.
- Greenwood MH, Lader MH, Kantamneni BD, Curzon G. 1975. The acute effects of oral (−)-tryptophan in human subjects. *Br J Clin Pharmacol* 2:165–172.
- Griffith RS, Norins AL, Kagan C. 1978. A multicentered study of lysine therapy in herpes simplex infection. *Dermatologica* 156:257–267.
- Griffith RS, Walsh DE, Myrmel KH, Thompson RW, Behforooz A. 1987. Success of L-lysine therapy in frequently recurrent herpes simplex infection. Treatment and prophylaxis. *Dermatologica* 175:183–190.
- Grossie VB, Nishioka K, Ajani JA, Ota DM. 1992. Substituting ornithine for arginine in total parenteral nutrition eliminates enhanced tumor growth. *J Surg Oncol* 50:161–167.
- Growdon JH, Melamed E, Logue M, Hefti F, Wurtman RJ. 1982. Effects of oral L-tyrosine administration on CSF tyrosine and homovanillic acid levels in patients with Parkinson's disease. *Life Sci* 30:827–832.
- Growdon JH, Nader TM, Schoenfeld J, Wurtman RJ. 1991. L-threonine in the treatment of spasticity. *Clin Neuropharmacol* 14:403–412.
- Haddad EH, Berk LS, Kettering JD, Hubbard RW, Peters WR. 1999. Dietary intake and biochemical, hematologic, and immune status of vegans compared with nonvegetarians. *Am J Clin Nutr* 70:586S–593S.
- Hagenfeldt L, Eriksson S, Wahren J. 1980. Influence of leucine on arterial concentrations and regional exchange of amino acids in healthy subjects. *Clin Sci* 59:173–181.
- Hahn RG. 1988. Serum amino acid patterns and toxicity symptoms following the absorption of irrigant containing glycine in transurethral prostatic surgery. *Acta Anaesthesiol Scand* 32:493–501.
- Hamilton B, Moriarty M. 1929. Comparison of growth in infancy. *Am J Dis Child* 37:1169.
- Hansen RD, Raja C, Allen BJ. 2000. Total body protein in chronic diseases and in aging. *Ann NY Acad Sci* 904:345–352.
- Hara S, Shibuya T, Nakakawaji K, Kyu M, Nakamura Y, Hoshikawa H, Takeuchi T, Iwao T, Ino H. 1962. Observations of pharmacological actions and toxicity of sodium glutamate, with comparisons between natural and synthetic products. *J Tokyo Med Coll* 20:69–100.
- Harper AE. 1983. Dispensable and indispensable amino acid interrelationships. In: Blackburn GL, Grant JP, Young VR, eds. *Amino Acids. Metabolism and Medical Applications*. Boston: John Wright-PSG. Pp. 105–121.
- Harper AE, Becker RV, Stucki WP. 1966. Some effects of excessive intakes of indispensable amino acids. *Proc Soc Exp Biol Med* 121:695–699.
- Harper AE, Benevenga NJ, Wohlhueter RM. 1970. Effects of ingestion of disproportionate amounts of amino acids. *Physiol Rev* 50:428–558.
- Harper AE, Miller RH, Block KP. 1984. Branched-chain amino acid metabolism. *Annu Rev Nutr* 4:409–454.
- Harvey PW, Hunsaker HA, Allen KG. 1981. Dietary L-histidine-induced hypercholesterolemia and hypocupremia in the rat. *J Nutr* 111:639–647.

- Hayasaka S, Saito T, Nakajima H, Takahashi O, Mizuno K, Tada K. 1985. Clinical trials of vitamin B<sub>6</sub> and proline supplementation for gyrate atrophy of the choroid and retina. *Br J Ophthalmol* 69:283–290.
- Hays PM, Smeltzer JS. 1986. Multiple gestation. *Clin Obstet Gynecol* 29:264–285.
- Health and Welfare Canada. 1990. *Report of the Expert Advisory Committee on Amino Acids*. Minister of Supply and Services Canada: Ottawa, Canada.
- Hediger ML, Scholl TO, Ances IG, Belsky DH, Salmon RW. 1990. Rate and amount of weight gain during adolescent pregnancy: Associations with maternal weight-for-height and birth weight. *Am J Clin Nutr* 52:793–799.
- Hegsted DM. 1963. Variation in requirements of nutrients: amino acids. *Fed Proc* 22:1420–1430.
- Hegsted DM. 1976. Balance studies. *J Nutr* 106:307–311.
- Hegsted DM. 1978. Assessment of nitrogen requirements. *Am J Clin Nutr* 31:1669–1677.
- Heine WE, Klein PD, Reeds PJ. 1991. The importance of  $\alpha$ -lactalbumin in infant nutrition. *J Nutr* 121:277–283.
- Heinig MJ, Nommsen LA, Peerson JM, Lönnerdal B, Dewey KG. 1993. Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: The DARLING Study. *Am J Clin Nutr* 58:152–161.
- Heird WC, Driscoll JM, Schullinger JN, Grebin B, Winters RW. 1972. Intravenous alimentation in pediatric patients. *J Pediatr* 80:351–372.
- Hellekson KL. 2001. NIH consensus statement on phenylketonuria. *Am Fam Physician* 63:1430–1432.
- Henkin RI, Patten BM, Re PK, Bronzert DA. 1975. A syndrome of acute zinc loss. Cerebellar dysfunction, mental changes, anorexia, and taste and smell dysfunction. *Arch Neurol* 32:745–751.
- Hershko A, Ciechanover A. 1998. The ubiquitin system. *Ann Rev Biochem* 67:425–479.
- Hevia P, Kari FW, Ulman EA, Visek WJ. 1980a. Serum and liver lipids in growing rats fed casein with L-lysine. *J Nutr* 110:1224–1230.
- Hevia P, Ulman EA, Kari FW, Visek WJ. 1980b. Serum lipids of rats fed excess L-lysine and different carbohydrates. *J Nutr* 110:1231–1239.
- Hibbs JR, Mittleman B, Hill P, Medsger TA. 1992. L-Tryptophan-associated eosinophilic fasciitis prior to the 1989 eosinophilia-myalgia syndrome outbreak. *Arthritis Rheum* 35:299–303.
- Higgins AC. 1976. Nutritional status and the outcome of pregnancy. *J Can Diet Assoc* 37:17–35.
- Hill GL. 1992. Body composition research: Implications for the practice of clinical nutrition. *J Parenteral Enteral Nutr* 16:197–218.
- Himwich WA, Petersen IM, Graves JP. 1954. Ingested sodium glutamate and plasma levels of glutamic acid. *J Appl Physiol* 1:196–199.
- Hitomi-Ohmura E, Amano N, Aoyama Y, Yoshida A. 1992. The effect of a histidine-excess diet on cholesterol synthesis and degradation in rats. *Lipids* 27:755–760.
- Hood DA, Terjung RL. 1990. Amino acid metabolism during exercise and following endurance training. *Sports Med* 9:23–35.
- Hoorn AJ. 1989. Dimethylglycine and chemically related amines tested for mutagenicity under potential nitrosation conditions. *Mutat Res* 222:343–350.
- Hornsby-Lewis L, Shike M, Brown P, Klang M, Pearlstone D, Brennan MF. 1994. L-Glutamine supplementation in home total parenteral nutrition patients: Stability, safety, and effects on intestinal absorption. *J Parenteral Enteral Nutr* 18:268–273.

- Howat PM, Korslund MK, Abernathy RP, Ritchy SJ. 1975. Sweat losses by and nitrogen balance of preadolescent girls consuming three levels of dietary protein. *Am J Clin Nutr* 28:879–882.
- Hrboticky N, Leiter LA, Anderson GH. 1985. Effects of L-tryptophan on short term food intake in lean men. *Nutr Res* 5:595–607.
- Huang P-C, Lin CP, Hsu JY. 1980. Protein requirements of normal infants at the age of 1 year: Maintenance nitrogen requirement and obligatory nitrogen losses. *J Nutr* 110:1727–1735.
- Hurson M, Regan MC, Kirk SJ, Wasserkrug HL, Barbul A. 1995. Metabolic effects of arginine in a healthy elderly population. *J Parenteral Enteral Nutr* 19:227–230.
- Hutson SM, Harper AE. 1981. Blood and tissue branched-chain amino and  $\alpha$ -keto acid concentrations: Effect of diet, starvation, and disease. *Am J Clin Nutr* 34:173–183.
- Hytten FE, Leitch I. 1971. *The Physiology of Human Pregnancy*, 2nd ed. Oxford: Blackwell.
- Ikezaki S, Nishikawa A, Furukawa F, Imazawa T, Enami T, Mitsui M, Takahashi M. 1994. 13-Week subchronic toxicity study of L-histidine monohydrochloride in F344 rats. *Eisei Shikenjo Hokoku* 112:57–63.
- Ikezaki S, Nishikawa A, Furukawa F, Enami T, Mitsui M, Tanakamaru Z, Kim HC, Lee IS, Imazawa T, Takahashi M. 1996. Long-term toxicity/carcinogenicity study of L-histidine monohydrochloride in F344 rats. *Food Chem Toxicol* 34:687–691.
- Inoue G, Fujita Y, Niijima Y. 1973. Studies on protein requirements of young men fed egg protein and rice protein with excess and maintenance energy intakes. *J Nutr* 103:1673–1687.
- Intengan CL. 1984. Protein requirements of Filipino children 22–29 months old consuming local diets. In: Rand WM, Uauy R, Scrimshaw NS, eds. *Protein-Energy Requirement Studies in Developing Countries: Results of International Research*. Tokyo, Japan: United Nations University Press.
- Intengan CL, Roxas BV, Loyola A, Carlos E. 1981. Protein requirements of Filipino children 20 to 29 months old consuming local diets. In: Torun B, Young VR, Rand WM, eds. *Protein-Energy Requirements of Developing Countries: Evaluation of New Data*. Tokyo, Japan: United Nations University Press. Pp. 172–181.
- Inubushi T, Shikiji M, Endo K, Kakegawa H, Kishino Y, Katunuma N. 1996. Hormonal and dietary regulation of lysosomal cysteine proteinases in liver under gluconeogenesis conditions. *Biol Chem* 377:539–542.
- Iob V, Swanson WW. 1934. Mineral growth of the human fetus. *Am J Dis Child* 47:302.
- IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Washington, DC: National Academy Press.
- IOM. 1991. *Nutrition During Lactation*. Washington, DC: National Academy Press.
- Ip CC, Harper AE. 1973. Effects of dietary protein content and glucagon administration on tyrosine metabolism and tyrosine toxicity in the rat. *J Nutr* 103:1594–1607.
- Isidori A, Lo Monaco A, Cappa M. 1981. A study of growth hormone release in man after oral administration of amino acids. *Curr Med Res Opin* 7:475–481.
- Istfan N, Murray E, Janghorbani M, Young VR. 1983. An evaluation of the nutritional value of a soy protein concentrate in young adult men using the short-term N-balance method. *J Nutr* 113:2516–2523.

- Iwata S, Ichimura M, Matsuzawa Y, Takasaki Y, Sasaoka M. 1979. Behavioural studies in rats treated with monosodium L-glutamate during the early stages of life. *Toxicol Lett* 4:345–357.
- Jackson AA. 1989. Optimizing amino acid and protein supply and utilization in the newborn. *Proc Nutr Soc* 48:293–301.
- Jackson AA. 1991. The glycine story. *Eur J Clin Nutr* 45:59–65.
- Janas LM, Picciano MF, Hatch TF. 1985. Indices of protein metabolism in term infants fed human milk, whey-predominant formula, or cow's milk formula. *Pediatrics* 75:775–784.
- Janas LM, Picciano MF, Hatch TF. 1987. Indices of protein metabolism in term infants fed either human milk or formulas with reduced protein concentration and various whey/casein ratios. *J Pediatrics* 10:838–848.
- Janelle KC, Barr SI. 1995. Nutrient intakes and eating behavior scores of vegetarian and nonvegetarian women. *J Am Diet Assoc* 95:180–186, 189.
- Järvenpää AL, Räihä NCR, Rassin DK, Gaull GE. 1982a Milk protein quantity and quality in the term infant. I. Metabolic responses and effect on growth. *Pediatrics* 70:214–220.
- Järvenpää AL, Räihä NCR, Rassin DK, Gaull GE. 1982b. Milk protein quantity and quality in the term infant. II. Effects on acidic and neutral amino acids. *Pediatrics* 70:221–230.
- JECFA (Joint FAO/WHO Expert Committee on Food Additives). 1988. *Toxicological Evaluation of Certain Food Additives*. WHO Food Additive Series No. 22. Geneva: WHO/FAO.
- Jefferson LS, Kimball S. 2001. Amino acid regulation of gene expression. *J Nutr* 131:2460S–2466S.
- Jelliffe DB. 1966. The assessment of the nutritional status of the community. WHO Monograph Series No. 53. Geneva: WHO.
- Jiang ZM, Cao JD, Zhu XG, Zhao WX, Yu JC, Ma EL, Wang XR, Zhu MW, Shu H, Liu YW. 1999. The impact of alanyl-glutamine on clinical safety, nitrogen balance, intestinal permeability, and clinical outcome in postoperative patients: A randomized, double-blind, controlled study in 120 patients. *J Parenter Enteral Nutr* 23:S62–S66.
- Jones EM, Baumann CA, Reynolds MS. 1956. Nitrogen balances of women maintained on various levels of lysine. *J Nutr* 60:549–562.
- Jungas RL, Halperin ML, Brosnan JT. 1992. Quantitative analysis of amino acid oxidation and related gluconeogenesis in humans. *Physiol Rev* 72:419–448.
- Kakizoe T, Nishio Y, Honma Y, Niijima T, Sugimura T. 1983. L-Isoleucine and L-leucine are promoters of bladder cancer in rats. *Princess Takamatsu Symp* 14:373–380.
- Kalhan SC. 2000. Protein metabolism in pregnancy. *Am J Clin Nutr* 71:1249S–1255S.
- Kalhan SC, Devapatla S. 1999. Pregnancy, insulin resistance and nitrogen accretion. *Curr Opin Clin Nutr Metab Care* 2:359–363.
- Kalhan SC, Rossi KQ, Gruca LL, Super DM, Savin SM. 1998. Relation between transamination of branched-chain amino acid and urea synthesis: Evidence from human pregnancy. *Am J Physiol* 275:E423–E431.
- Kamin H, Handler P. 1951. Effect of infusion of single amino acids upon excretion of other amino acids. *Am J Physiol* 164:654–661.
- Kampel D, Kupferschmidt R, Lubec G. 1990. Toxicity of D-proline. In: Lubec G, Rosenthal GA, eds. *Amino Acids: Chemistry, Biology, and Medicine*. ESCOM: Leiden, The Netherlands. Pp. 1164–1171.

- Karlsen RL, Pedersen OO. 1982. A morphological study of the acute toxicity of L-cysteine on the retina of young rats. *Exp Eye Res* 34:65–69.
- Katagiri M, Nakamura K. 2002. Animals are dependent on preformed  $\alpha$ -amino nitrogen as an essential nutrient. *Life* 53:125–129.
- Kawabe M, Takesada Y, Tamano S, Hagiwara A, Ito N, Shirai T. 1996. Subchronic toxicity study of L-isoleucine in F344 rats. *J Toxicol Environ Health* 47:499–508.
- Kenney RA. 1986. The Chinese Restaurant Syndrome: An anecdote revisited. *Food Chem Toxicol* 24:351–354.
- Kenney RA, Tidball CS. 1972. Human susceptibility to oral monosodium L-glutamate. *Am J Clin Nutr* 25:140–146.
- Khatri IA, Forstner GG, Forstner F. 1998. Susceptibility of the cysteine-rich N-terminal and C-terminal ends of rat intestinal mucin Muc 2 to proteolytic cleavage. *Biochem J* 331:323–330.
- Kim KI, McMillan I, Bayley HS. 1983. Determination of amino acid requirements of young pigs using an indicator amino acid. *Br J Nutr* 50:369–382.
- King JC. 1975. Protein metabolism during pregnancy. *Clin Perinatol* 2:243–254.
- King JC, Calloway DH, Margen S. 1973. Nitrogen retention, total body  $^{40}\text{K}$  and weight gain in teenage pregnant girls. *J Nutr* 103:772–785.
- Kirschner M. 1999. Intracellular proteolysis. *Trends Cell Biol* 9:M42–M45.
- Klavins JV, Kinney TD, Kaufman N. 1963. Body iron levels and hematologic findings during excess methionine feeding. *J Nutr* 79:101–104.
- Klein DG. 1990. Physiologic response to traumatic shock. *AACN Clin Issues Crit Care Nurs* 1:505–521.
- Klimberg VS, McClellan J. 1996. Glutamine, cancer, and its therapy. *Am J Surg* 172:418–424.
- Klimberg VS, Souba WW, Salloum RM, Plumley DA, Cohen FS, Dolson DJ, Bland KI, Copeland EM. 1990. Glutamine-enriched diets support muscle glutamine metabolism without stimulating tumor growth. *J Surg Res* 48:319–323.
- Knopp RH, Brandt K, Arky RA. 1976. Effects of aspartame in young persons during weight reduction. *J Toxicol Environ Health* 2:417–428.
- Knox WE, Horowitz ML, Friedell GH. 1969. The proportionality of glutaminase content to growth rate and morphology of rat neoplasms. *Cancer Res* 29:669–680.
- Kopple JD. 1987. Uses and limitations of the balance technique. *J Parenter Enteral Nutr* 11:79S–85S.
- Kopple JD, Swendseid ME. 1975. Evidence that histidine is an essential amino acid in normal and chronically uremic men. *J Clin Invest* 55:881–891.
- Korslund MK, Leung EY, Meiners CR, Crews MG, Taper J, Abernathy RP, Ritchey SJ. 1976. The effects of sweat nitrogen losses in evaluating protein utilization by preadolescent children. *Am J Clin Nutr* 29:600–603.
- Kovacevic Z, Morris HP. 1972. The role of glutamine in the oxidative metabolism of malignant cells. *Cancer Res* 32:326–333.
- Kriengsinyos W, Wykes LJ, Ball RO, Pencharz PB. 2002. Oral and intravenous tracer protocols of the indicator amino acid oxidation method provide the same estimate of the lysine requirement in healthy men. *J Nutr* 132:2251–2257.
- Krogh A, Krogh M. 1913. *A Study of the Diet and Metabolism of Eskimos*. Bianco Luno, Copenhagen.
- Kudo Y, Boyd CA. 1990. Transport of amino acids by the human placenta: Predicted effects thereon of maternal hyperphenylalaninaemia. *J Inherit Metab Dis* 13:617–626.

- Kurpad AV, Raj T, El-Khoury A, Beaumier L, Kuriyan R, Srivatsa A, Borgonha S, Selvaraj A, Regan MM, Young VR. 2001a. Lysine requirements of healthy adult Indian subjects, measured by an indicator amino acid balance technique. *Am J Clin Nutr* 73:900–907.
- Kurpad AV, Raj T, El-Khoury A, Kuriyan R, Maruthy K, Borgonha S, Chandakudlu D, Regan MM, Young VR. 2001b. Daily requirement for and splanchnic uptake of leucine in healthy adult Indians. *Am J Clin Nutr* 74:747–755.
- Kurpad AV, Regan MM, Raj T, El-Khoury A, Kuriyan R, Vaz M, Chandakudlu D, Venkataswamy VG, Borgonha S, Young VR. 2002a. Lysine requirements of healthy adult Indian subjects receiving long-term feeding, measured with a 24-h indicator amino acid oxidation and balance technique. *Am J Clin Nutr* 76:404–412.
- Kurpad AV, Raj T, Regan MM, Vasudevan J, Caszo B, Nazareth D, Gnanou J, Young VR. 2002b. Threonine requirements of healthy Indian adults, measured by a 24-h indicator amino acid oxidation and balance technique. *Am J Clin Nutr* 76:789–797.
- Labow BI, Souba WW. 2000. Glutamine. *World J Surg* 24:1503–1513.
- Lacey JM, Crouch JB, Benfell K, Ringer SA, Wilmore CK, Maguire D, Wilmore DW. 1996. The effects of glutamine-supplemented parenteral nutrition in premature infants. *J Parenter Enteral Nutr* 20:74–80.
- Laidlaw SA, Kopple JD. 1987. Newer concepts of the indispensable amino acids. *Am J Clin Nutr* 46:593–605.
- Lammi-Keefe CJ, Ferris AM, Jensen RG. 1990. Changes in human milk at 0600, 1000, 1400, 1800, and 2200 h. *J Pediatr Gastroenterol Nutr* 11:83–88.
- Lamperti A, Blaha G. 1976. The effects of neonatally-administered monosodium glutamate on the reproductive system of adult hamsters. *Biol Reprod* 14:362–369.
- Lamperti A, Blaha G. 1980. Further observations on the effects of neonatally administered monosodium glutamate on the reproductive axis of hamsters. *Biol Reprod* 22:687–693.
- Lazaris-Brunner G, Rafii M, Ball RO, Pencharz P. 1998. Tryptophan requirement in young adult women as determined by indicator amino acid oxidation with L-[<sup>13</sup>C]-phenylalanine. *Am J Clin Nutr* 68:303–310.
- Leathwood PD, Fernstrom JD. 1990. Effect of an oral tryptophan/carbohydrate load on tryptophan, large neutral amino acid, and serotonin and 5-hydroxyindoleacetic acid levels in monkey brain. *J Neural Transm Gen Sect* 79:25–34.
- Leiderman E, Zylberman I, Zukin SR, Cooper TB, Javitt DC. 1996. Preliminary investigation of high-dose oral glycine on serum levels and negative symptoms in schizophrenia: An open-label trial. *Biol Psychiatry* 39:213–215.
- Leiter LA, Hrboticky N, Anderson GH. 1987. Effects of L-tryptophan on food intake and selection in lean men and women. *Ann NY Acad Sci* 499:327–328.
- Lemon PWR. 1996. Is increased dietary protein necessary or beneficial for individuals with a physically active lifestyle? *Nutr Rev* 54:S169–S175.
- Lemon PW, Nagle FJ, Mullin JP, Benevenga NJ. 1982. In vivo leucine oxidation at rest and during two intensities of exercise. *J Appl Physiol* 53:947–954.
- Lemon PW, Benevenga NJ, Mullin JP, Nagle FJ. 1985. Effect of daily exercise and food intake on leucine oxidation. *Biochem Med* 33:67–76.
- Lemon PW, Tarnopolsky MA, MacDougall JD, Atkinson SA. 1992. Protein requirements and muscle mass/strength changes during intensive training in novice bodybuilders. *J Appl Physiol* 73(2):767–775.
- Lemons JA, Moye L, Hall D, Simmons M. 1982. Differences in the composition of preterm and term human milk during early lactation. *Pediatr Res* 16:113–117.

- Lenke RR, Levy HL. 1980. Maternal phenylketonuria and hyperphenylalaninemia. An international survey of the outcome of untreated and treated pregnancies. *N Engl J Med* 303:1202–1208.
- Lentner C. 1981. *Geigy Scientific Tables, 8th ed.*, Vol. 1. *Units of Measurement, Body Fluids, Composition of the Body, Nutrition*. West Caldwell, NJ: Ciba-Geigy Corporation.
- Leverton RM, Gram MR, Brodovsky E, Chaloupka M, Mitchell A, Johnson N. 1956a. The quantitative amino acid requirements of young women. II. Valine. *J Nutr* 58:83–93.
- Leverton RM, Gram MR, Chaloupka M, Brodovsky E, Mitchell A. 1956b. The quantitative amino acid requirements of young women. I. Threonine. *J Nutr* 58:59–81.
- Leverton RM, Johnson N, Ellison J, Geschwender D, Schmidt F. 1956c. The quantitative amino acid requirements of young women. IV. Phenylalanine, with and without tyrosine. *J Nutr* 58:341–353.
- Leverton RM, Johnson N, Pazur J, Ellison J. 1956d. The quantitative amino acid requirements of young women. III. Tryptophan. *J Nutr* 58:219–229.
- Levey S, Harroun JE, Smyth CJ. 1949. Serum glutamic acid levels and the occurrence of nausea and vomiting after the intravenous administration of amino acid mixtures. *J Lab Clin Med* 34:1238–1248.
- Levy HM, Montanez G, Feaver ER, Murphy EA, Dunn MS. 1954. Effect of arginine on tumor growth in rats. *Cancer Res* 14:198–200.
- Lieb CW. 1929. The effects on human beings of a twelve months' exclusive meat diet. *J Am Med Assoc* 93:20–22.
- Lieberman HR, Corkin S, Spring BJ, Wurtman RJ, Growdon JH. 1985. The effects of dietary neurotransmitter precursors on human behavior. *Am J Clin Nutr* 42:366–370.
- Lieberman HR, Caballero B, Emde GG, Bernstein JG. 1988. The effects of aspartame on human mood, performance, and plasma amino acid levels. In: Wurtman RJ, Ritter-Walker E, eds. *Dietary Phenylalanine and Brain Function*. Boston: Birkhauser. Pp. 198–200.
- Linder-Horowitz M, Knox WE, Morris HP. 1969. Glutaminase activities and growth rates of rat hepatomas. *Cancer Res* 29:1195–1199.
- Longenecker JB, Hause NL. 1959. Relationship between plasma amino acids and composition of ingested protein. *Arch Bioch Biophys* 84:46.
- Longenecker JB, Hause NL. 1961. Relationship between plasma amino acids and composition of ingested protein. II. A shortened procedure to determine plasma amino acid (PAA) ratios. *Am J Clin Nutr* 9:356–362.
- Lönnnerdal B. 1986. Effects of maternal nutrition in human lactation. In: Hamosh M, Goldman AS, eds. *Human Lactation 2: Maternal and Environmental Factors*. New York: Plenum Press. Pp. 301–323.
- Lönnnerdal B, Chen CL. 1990. Effects of formula protein level and ration on infant growth, plasma amino acids and serum trace elements I: Cow's milk formula. *Acta Paediatr Scand* 79:257–265.
- Lönnnerdal B, Woodhouse LR, Glazier C. 1987. Compartmentalization and quantitation of protein in human milk. *J Nutr* 117:1385–1395.
- LSRO (Life Sciences Research Office). 1992. *Safety of Amino Acids Used as Dietary Supplements*. Bethesda, MD: LSRO.
- Lucas DR, Newhouse JP. 1957. The toxic effect of sodium L-glutamate on the inner layers of the retina. *AMA Arch Ophthalmol* 58:193–201.
- Lucas A, Morley R, Cole TJ, Lister G, Leeson-Payne C. 1992. Breast milk and subsequent intelligence quotient in children born preterm. *Lancet* 339:261–264.

- MacGillivray I, Buchanan TJ. 1958. Total exchangeable sodium and potassium in non-pregnant women and in normal and pre-eclamptic pregnancy. *Lancet* 2:1090–1093.
- Manatt MW, Garcia PA. 1992. Nitrogen balance: Concepts and techniques. In: Nissen S, ed. *Modern Methods in Protein Nutrition and Metabolism*. San Diego: Academic Press. Pp. 9–63.
- Marchesini G, Dioguardi FS, Bianchi GP, Zoli M, Bellati G, Roffi L, Martines D, Abbiati R. 1990. Long-term oral branched-chain amino acid treatment in chronic hepatic encephalopathy. A randomized double-blind casein-controlled trial. The Italian Multicenter Study Group. *J Hepatol* 11:92–101.
- Mariotti F, Mahe S, Benamouzig R, Luengo C, Dare S, Gaudichon C, Tome D. 1999. Nutritional value of [ $^{15}\text{N}$ ]-soy protein isolate assessed from ileal digestibility and postprandial protein utilization in humans. *J Nutr* 129:1992–1997.
- Martindale LW. 1967. *Extra Pharmacopoeia*, 25th ed.. London: Pharmaceutical Press.
- Massara F, Cagliero E, Bisbocci D, Passarino G, Carta Q, Molinatti GM. 1981. The risk of pronounced hyperkalaemia after arginine infusion in the diabetic subject. *Diabete Metab* 7:149–153.
- Matsueda S, Niijima Y. 1982. The effects of excess amino acids on maintenance of pregnancy and fetal growth in rats. *J Nutr Sci Vitaminol* 28:557–573.
- Matsuwa Y, Yonetani S, Takasaki Y, Iwata S, Sekine S. 1979. Studies on reproductive endocrine function in rats treated with monosodium L-glutamate early in life. *Toxicol Lett* 4:359–371.
- Matthews DE. 1999. Proteins and amino acids. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th ed. Baltimore: Williams and Wilkins. Pp. 11–48.
- Maughan RJ, Sadler DJ. 1983. The effects of oral administration of salts of aspartic acid on the metabolic response to prolonged exhausting exercise in man. *Int J Sports Med* 4:119–123.
- Mayes PA. 1990. Oxidation of fatty acids: Ketogenesis. In: Murray RK, Granner DK, Mayes PA, Rodwell VW, eds. *Harper's Biochemistry*, 22nd ed. Norwalk, CT: Appleton and Lange. Pp. 206–217.
- McCarthy CF, Borland JL, Lynch HJ, Owen EE, Tyor MP. 1964. Defective uptake of basic amino acids and L-cystine by intestinal mucosa of patients with cystinuria. *J Clin Invest* 43:1518–1524.
- McClellan WS, Du Bois EF. 1930. Clinical calorimetry XLV. Prolonged meat diets with a study of kidney function and ketosis. *J Biol Chem* 87:651–668.
- McClellan WS, Rupp VR, Toscani V. 1930. Clinical calorimetry XLVI. Prolonged meat diets with a study of the metabolism of nitrogen, calcium and phosphorus. *J Biol Chem* 87:669–680.
- McClellan WS, Spencer HJ, Falk EA. 1931. Clinical calorimetry XLVII. Prolonged meat diets with a study of the respiratory metabolism. *J Biol Chem* 93:419–434.
- McCune MA, Perry HO, Muller SA, O'Fallon WM. 1984. Treatment of recurrent herpes simplex infections with L-lysine monohydrochloride. *Cutis* 34:366–373.
- McGilvery RW. 1983. *Biochemistry—A Functional Approach*. Philadelphia: WB Saunders. Pp. 791–793.
- McNurlan MA, Garlick PJ. 1980. Contribution of rat liver and gastrointestinal tract to whole-body protein synthesis in the rat. *Biochem J* 186:381–383.
- Meakins TS, Jackson AA. 1996. Salvage of exogenous urea nitrogen enhances nitrogen balance in normal men consuming marginally inadequate protein diets. *Clin Sci* 90:215–225.

- Meguid MM, Matthews DE, Bier DM, Meredith CN, Soeldner JS, Young VR. 1986a. Leucine kinetics at graded leucine intakes in young men. *Am J Clin Nutr* 43:770–780.
- Meguid MM, Matthews DE, Bier DM, Meredith CN, Young VR. 1986b. Valine kinetics at graded valine intakes in young men. *Am J Clin Nutr* 43:781–786.
- Melamed E, Glaeser B, Growdon JH, Wurtman RJ. 1980. Plasma tyrosine in normal humans: Effects of oral tyrosine and protein-containing meals. *J Neural Trans* 47:299–306.
- Meldrum BS. 2000. Glutamate as a neurotransmitter in the brain: Review of physiology and pathology. *J Nutr* 130:1007S–1015S.
- Meredith CN, Wen ZM, Bier DM, Matthews DE, Young VR. 1986. Lysine kinetics at graded lysine intakes in young men. *Am J Clin Nutr* 43:787–794.
- Meredith CN, Zackin MJ, Frontera WR, Evans WJ. 1989. Dietary protein requirements and body protein metabolism in endurance-trained men. *J Appl Physiol* 66:2850–2856.
- Metges CC, El-Khoury AE, Henneman L, Petzke KJ, Grant I, Bedri S, Pereira PP, Ajami AM, Fuller MF, Young VR. 1999a. Availability of intestinal microbial lysine for whole body lysine homeostasis in human subjects. *Am J Physiol* 277:E597–E607.
- Metges CC, Petzke KJ, El-Khoury AE, Henneman L, Grant I, Bedri S, Regan MM, Fuller MF, Young VR. 1999b. Incorporation of urea and ammonia nitrogen into ileal and fecal microbial proteins and plasma free amino acids in normal men and ileostomates. *Am J Clin Nutr* 70:1046–1058.
- Millward DJ. 1998. Metabolic demands for amino acids and the human dietary requirement: Millward and Rivers (1988) revisited. *J Nutr* 128:2563S–2576S.
- Millward DJ. 1999. The nutritional value of plant-based diets in relation to human amino acid and protein requirements. *Proc Nutr Soc* 58:249–260.
- Millward DJ, Roberts SB. 1996. Protein requirements of older individuals. *Nutr Rev* 9:67–87.
- Millward DJ, Price GM, Pacy PJ, Halliday D. 1990. Maintenance protein requirements: The need for conceptual re-evaluation. *Proc Nutr Soc* 49:473–487.
- Millward DJ, Fereday A, Gibson N, Pacy PJ. 1997. Aging, protein requirements, and protein turnover. *Am J Clin Nutr* 66:774–786.
- Milman N, Scheibel J, Jessen O. 1980. Lysine prophylaxis in recurrent herpes simplex labialis: A double-blind, controlled crossover study. *Acta Derm Venereol* 60:85–87.
- Mizutani AR, Parker J, Katz J, Schmidt J. 1990. Visual disturbances, serum glycine levels and transurethral resection of the prostate. *J Urol* 144:697–699.
- Moephuli SR, Klein NW, Baldwin MT, Krider HM. 1997. Effects of methionine on the cytoplasmic distribution of actin and tubulin during neural tube closure in rat embryos. *Proc Natl Acad Sci USA* 94:543–548.
- Mogensen CE, Solling K. 1977. Studies on renal tubular protein reabsorption: Partial and near complete inhibition by certain amino acids. *Scand J Clin Lab Invest* 37:477–486.
- Moldawer LL, Kawamura I, Bistrian BR, Blackburn GL. 1983. The contribution of phenylalanine to tyrosine in vivo: Studies in the post-absorptive and phenylalanine-loaded rat. *Biochem J* 210:811–817.
- Moneret-Vautrin DA. 1987. Monosodium glutamate induced asthma: A study of the potential risk in 30 asthmatics and review of the literature. *Allerg Immunol (Paris)* 19:29–35.

- Morehead RP, Fishman WH, Artom C. 1945. Renal injury in the rat following the administration of serine by stomach tube. *Am J Pathol* 21:803–815.
- Morlion BJ, Stehle P, Wachtler P, Siedhoff HP, Koller M, Konig W, Furst P, Puchstein C. 1998. Total parenteral nutrition with glutamine dipeptide after major abdominal surgery: A randomised, double-blind, controlled study. *Ann Surg* 227:302–308.
- Motil KJ, Opekun AR, Montandon CM, Berthold HK, Davis TA, Klein PD, Reeds PJ. 1994. Leucine oxidation changes rapidly after dietary protein intake is altered in adult women but lysine flux is unchanged as is lysine incorporation into VLDL-apolipoprotein B-100. *J Nutr* 124:41–51.
- Motil KJ, Davis TA, Montandon CM, Wong WW, Klein PD, Reeds PJ. 1996. Whole-body protein turnover in the fed state is reduced in response to dietary protein restriction in lactating women. *Am J Clin Nutr* 64:32–39.
- Motil KJ, Sheng H-P, Kertz BL, Montandon CM, Ellis KJ. 1998. Lean body mass of well-nourished women is preserved during lactation. *Am J Clin Nutr* 67:292–300.
- Munro, HN. 1970. Free amino acid pools and their role in regulation. In: Munro HN, ed. *Mammalian Protein Metabolism*, Vol. IV. New York: Academic Press. Chap 34.
- Muramatsu K, Odagiri H, Morishita S, Takeuchi H. 1971. Effect of excess levels of individual amino acids on growth of rats fed casein diets. *J Nutr* 101:1117–1125.
- Nakagawa I, Takahashi T, Suzuki T. 1961a. Amino acid requirements of children: Isoleucine and leucine. *J Nutr* 73:186–190.
- Nakagawa I, Takahashi T, Suzuki T. 1961b. Amino acid requirements of children: Minimal needs of lysine and methionine based on nitrogen balance method. *J Nutr* 74:401–407.
- Nakagawa I, Takahashi T, Suzuki T, Kobayashi K. 1962. Amino acid requirements of children: Minimal needs of threonine, valine and phenylalanine based on nitrogen balance method. *J Nutr* 77:61–68.
- Nakagawa I, Takahashi T, Suzuki T, Kobayashi K. 1963. Amino acid requirements of children: Minimal needs of tryptophan, arginine and histidine based on nitrogen balance method. *J Nutr* 80:305–310.
- Nakagawa I, Takahashi T, Suzuki T, Kobayashi K. 1964. Amino acid requirements of children: Nitrogen balance at the minimal level of essential amino acids. *J Nutr* 83:115–118.
- Neale RJ, Waterlow JC. 1974. The metabolism of <sup>14</sup>C-labelled essential amino acids given by intragastric or intravenous infusion to rats on normal and protein-free diets. *Br J Nutr* 32:11–25.
- Neri DF, Wiegmann D, Stanny RR, Shappell SA, McCardie A, McKay DL. 1995. The effects of tyrosine on cognitive performance during extended wakefulness. *Aviat Space Environ Med* 66:313–319.
- Neville MC, Keller RP, Seacat J, Casey CE, Allen JC, Archer P. 1984. Studies on human lactation. I. Within-feed and between-breast variation in selected components of human milk. *Am J Clin Nutr* 40:635–646.
- Newsholme EA, Blomstrand E, Hassmen P, Ekblom B. 1991. Physical and mental fatigue: Do changes in plasma amino acids play a role? *Biochem Soc Trans* 19:358–362.
- Nikoletseas MM. 1977. Obesity in exercising, hypophagic rats treated with monosodium glutamate. *Physiol Behav* 19:767–773.
- Nishio Y, Kakizoe T, Ohtani M, Sato S, Sugimura T, Fukushima S. 1986. L-isoleucine and L-leucine: Tumor promoters of bladder cancer in rats. *Science* 231:843–845.

- Nommsen LA, Lovelady CA, Heinig MJ, Lönnnerdal B, Dewey KG. 1991. Determinants of energy, protein, lipid, and lactose concentrations in human milk during the first 12 mo of lactation: The DARLING Study. *Am J Clin Nutr* 53:457–465.
- Oddy EA, Margen S. 1979. Nitrogen balance studies in humans: Long-term effect of high nitrogen intake on nitrogen accretion. *J Nutr* 109:363–377.
- Ohmura E, Aoyama Y, Yoshida A. 1986. Changes in lipids in liver and serum of rats fed a histidine-excess diet or cholesterol-supplemented diets. *Lipids* 21:748–753.
- Oishi R, Furuno K, Gomita Y, Araki Y, Saeki K. 1989. Effect of acute treatment of mice with L-histidine on the brain levels of amino acids. *Jpn J Pharmacol* 49:143–146.
- Olivo M, Kitahama K, Valatz JL, Jouvet M. 1986. Neonatal monosodium glutamate dosing alters the sleep-wake cycle of the mature rat. *Neurosci Lett* 67:186–190.
- Olney JW. 1969. Brain lesions, obesity, and other disturbances in mice treated with monosodium glutamate. *Science* 164:719–721.
- Olney JW. 1989. Glutamate, a neurotoxic transmitter. *J Child Neurol* 4:218–226.
- Olney JW. 1994. Excitotoxins in foods. *Neuro Toxicol* 15:535–544.
- Olney JW, Ho OL. 1970. Brain damage in infant mice following oral intake of glutamate, aspartate or cysteine. *Nature* 227:609–611.
- Olney JW, Cicero TJ, Meyer ER, de Gubareff T. 1976. Acute glutamate-induced elevations in serum testosterone and luteinizing hormone. *Brain Res* 112:420–424.
- Owen G, Cherry CP, Prentice DE, Worden AN. 1978a. The feeding of diets containing up to 4% monosodium glutamate to rats for 2 years. *Toxicol Lett* 1:221–226.
- Owen G, Cherry CP, Prentice DE, Worden AN. 1978b. The feeding of diets containing up to 10% monosodium glutamate to beagle dogs for 2 years. *Toxicol Lett* 1:217–219.
- Park KG, Heys SD, Blessing K, Kelly P, McNurlan MA, Eremin O, Garlick PJ. 1992. Stimulation of human breast cancers by dietary L-arginine. *Clin Sci* 82:413–417.
- Patrick J, Pencharz PB, Belmonte M, Ste-Marie M, Boland MP, Issenman RM, Van Aerde JEE, Rousseau-Harsany E. 1994. Undernutrition in children with neurodevelopmental disability. *Can Med Assoc J* 151:753–759.
- Pellett PL, Young VR. 1992. The effects of different levels of energy intake on protein metabolism and of different levels of protein intake on energy metabolism: A statistical evaluation from the published literature. In: Scrimshaw NS, Schürch B, eds. *Protein-Energy Interaction*. Lausanne, Switzerland: IDECG, Nestlé Foundation. Pp. 81–121.
- Pencharz PB. 1985. Body composition and growth. In: Walker A, ed. *Nutrition in Pediatrics. Basic Science and Clinical Application*. Boston. Little, Brown. Pp. 77–85.
- Pencharz PB, Azcue M. 1996. Use of bioelectrical impedance analysis (BIA) measurements in the clinical management of malnutrition. *Am J Clin Nutr* 64:S485–S488.
- Pencharz BP, House JD, Wykes LJ, Ball RO. 1996. What are the essential amino acids for the preterm and term infant? In: Bindels JG, Goedhart A, Visser HKA, eds. *Recent Developments in Infant Nutrition. Nutricia Symposia Vol. 9*. Dordrecht, The Netherlands: Kluwer Academic Publishers. Pp. 278–296.
- Pepplinkhuizen L, Bruinvelds J, Blom W, Moleman P. 1980. Schizophrenia-like psychosis caused by a metabolic disorder. *Lancet* 1:454–456.
- Perry TL, Hardwick DF, Dixon GH, Dolman CL, Hansen S. 1965. Hypermethioninemia: A metabolic disorder associated with cirrhosis, islet cell hyperplasia, and renal tubular degeneration. *Pediatrics* 36:236–250.
- Persaud TV. 1969. The foetal toxicity of leucine in the rat. *West Indian Med J* 18:34–39.

- Peters JC, Harper AE. 1987. Acute effects of dietary protein on food intake, tissue amino acids, and brain serotonin. *Am J Physiol* 252:R902–R914.
- Picou D, Halliday D, Garrow JS. 1966. Total body protein, collagen and non-collagen protein in infantile protein malnutrition. *Clin Sci* 30:345–351.
- Pilc A, Rogoz Z, Skuza G. 1982. Histidine-induced bizarre behaviour in rats: The possible involvement of central cholinergic system. *Neuropharmacology* 21:781–785.
- Pinals RS, Harris ED, Burnett JB, Gerber DA. 1977. Treatment of rheumatoid arthritis with L-histidine: A randomized, placebo-controlled, double-blind trial. *J Rheumatol* 4:414–419.
- Pineda O, Torun B, Viteri FE, Arroyave G. 1981. Protein quality in relation to estimates of essential amino acids requirements. In: Bodwell CE, Adkins JS, Hopkins DT, eds. *Protein Quality in Humans: Assessment and In Vitro Estimation*. Westport, CT: AVI Publishing. Pp. 29–42.
- Pinto-Scognamiglio W, Amorico L, Gatti GL. 1972. Toxicity and tolerance to monosodium glutamate studied by a conditioned avoidance test. *Farmaco* 27:19–27.
- Pipe NGJ, Smith T, Halliday D, Edmonds CJ, Williams C, Coltart TM. 1979. Changes in fat, fat-free mass and body water in human normal pregnancy. *Br J Obstet Gynaecol* 86:929–940.
- Pizzi WJ, Barnhart JE, Fanslow DJ. 1977. Monosodium glutamate administration to the newborn reduces reproductive ability in female and male mice. *Science* 196:452–454.
- Pizzi WJ, Tabor JM, Barnhart JE. 1978. Somatic, behavioral, and reproductive disturbances in mice following neonatal administration of sodium L-aspartate. *Pharmacol Biochem Behav* 9:481–485.
- Pollitt E. 2000. Developmental sequel from early nutritional deficiencies: Conclusive and probability judgements. *J Nutr* 130:350S–353S.
- Poon TK, Cameron DP. 1978. Measurement of oxygen consumption and locomotor activity in monosodium glutamate-induced obesity. *Am J Physiol* 234:E532–E534.
- Porter PB, Griffin AC. 1950. Effects of glutamic acid on maze learning and recovery from electroconvulsive shocks in albino rats. *J Comp Physiol Psychol* 43:1–15.
- Pradhan SN, Lynch JF. 1972. Behavioral changes in adult rats treated with monosodium glutamate in the neonatal stage. *Arch Int Pharmacodyn Ther* 197:301–304.
- Pratt EL, Snyderman SE, Cheung MW, Norton P, Holt LE. 1955. The threonine requirement of the normal infant. *J Nutr* 56:231–251.
- Prentice AM, Goldberg GR, Prentice A. 1994. Body mass index and lactation performance. *Eur J Clin Nutr* 48:S78–S86.
- Prosky L, O'Dell RG. 1972. Biochemical changes of brain and liver in neonatal offspring of rats fed monosodium-L-glutamate. *Experientia* 28:260–263.
- Raguso CA, Pereira P, Young VR. 1999. A tracer investigation of obligatory oxidative amino acids losses in healthy, young adults. *Am J Clin Nutr* 70:474–483.
- Räihä N, Minoli I, Moro G. 1986a. Milk protein intake in the term infant I: Metabolic responses and effects on growth. *Acta Paediatr Scand* 75:881–886.
- Räihä N, Minoli I, Moro G. 1986b. Milk protein intake in the term infant II: Effects on plasma amino acid concentrations. *Acta Paediatr Scand* 75:887–892.
- Raiten DJ, Talbot JM, Fisher KD. 1995. *Analysis of Adverse Reactions to Monosodium Glutamate (MSG)*. Bethesda, MD: Federation of American Societies for Experimental Biology.
- Ramsey BW, Farrell P, Pencharz PB. 1992. Nutritional assessment and management in cystic fibrosis: a consensus report. *Am J Clin Nutr* 55:108–116.

- Rand WM, Young VR. 1999. Statistical analysis of nitrogen balance data with reference to the lysine requirement in adults. *J Nutr* 129:1920–1926.
- Rand WM, Young VR, Scrimshaw NS. 1976. Change of urinary nitrogen excretion in response to low-protein diets in adults. *Am J Clin Nutr* 29:639–644.
- Rand WM, Scrimshaw NS, Young VR. 1981. Conventional (“long-term”) nitrogen balance studies for protein quality evaluation in adults: Rationale and limitations. In: Bodwell CE, Adkins JS, Hopkins DT, eds. *Protein Quality in Humans: Assessment and In Vitro Estimation*. Westport, CT: AVI Publishing. Pp. 61–94.
- Rand RM, Pellett PL, Young VR. 2003. Meta-analysis of nitrogen balance studies for estimating protein requirements in healthy adults. *Am J Clin Nutr* 77:109–127.
- Reeds PJ, Burrin DG. 2001. Glutamine and the bowel. *J Nutr* 131:2505S–2508S.
- Reeds PJ, Garlick PJ. 1984. Nutrition and protein turnover in man. *Adv Nutr Res* 6:93–138.
- Reeds PJ, Field CR, Jahoor F. 1994. Do the differences between the amino acid compositions of acute-phase and muscle proteins have a bearing on nitrogen loss in traumatic states? *J Nutr* 124:906–910.
- Reif-Lehrer L. 1976. Possible significance of adverse reactions to glutamate in humans. *Fed Proc* 35:2205–2211.
- Rennie MJ, Edwards RH, Krywawych S, Davies CT, Halliday D, Waterlow JC, Millward DJ. 1981. Effect of exercise on protein turnover in man. *Clin Sci (Lond)* 61:627–639.
- Reynolds JV, Thom AK, Zhang SM, Ziegler MM, Naji A, Daly JM. 1988. Arginine, protein malnutrition, and cancer. *J Surg Res* 45:513–522.
- Reynolds JV, Daly JM, Shou J, Sigal R, Ziegler MM, Naji A. 1990. Immunologic effects of arginine supplementation in tumor-bearing and non-tumor-bearing hosts. *Ann Surg* 211:202–210.
- Reynolds JV, O’Farrelly C, Feighery C, Murchan P, Leonard N, Fulton G, O’Morain C, Keane FB, Tanner WA. 1996. Impaired gut barrier function in malnourished patients. *Br J Surg* 83:1288–1291.
- Reynolds MS, Steel DL, Jones EM, Baumann CA. 1958. Nitrogen balances of women maintained on various levels of methionine and cystine. *J Nutr* 64:99–111.
- Reynolds WA, Stegink LD, Filer LJ Jr, Renn E. 1980. Aspartame administration to the infant monkey: Hypothalamic morphology and plasma amino acid levels. *Anat Rec* 198:73–85.
- Rich LF, Beard ME, Burns RP. 1973. Excess dietary tyrosine and corneal lesions. *Exp Eye Res* 17:87–97.
- Rigo J, Senterre H. 1980. Optimal threonine intake for preterm infants fed on oral or parenteral nutrition. *J Parenteral Enteral Nutr* 4:15–17.
- Roberton AM, Rabel B, Harding CA, Tasman-Jones C, Harris PJ, Lee SP. 1991. Use of the ileal conduit as a model for studying human small intestinal mucus glycoprotein secretion. *Am J Physiol* 261:G728–G734.
- Roberts S. 1996. Energy requirements of older individuals. *Eur J Clin Nutr* 50:S112–S118.
- Roberts S, Thorpe JM, Ball RO, Pencharz PB. 2001. Tyrosine requirement of healthy men receiving a fixed phenylalanine intake determined by using indicator amino acid oxidation. *Am J Clin Nutr* 73:276–282.
- Rodwell VW. 1990. Conversion of amino acids to specialized products. In: Murray RK, Mayes PA, Granner DK, Rodwell VW, eds. *Harper’s Biochemistry*, 22nd ed. Norwalk, CT: Appleton & Lange. Pp. 307–313.
- Rogan WJ, Gladen BC. 1993. Breast-feeding and cognitive development. *Early Human Dev* 31:181–193.

- Roig JC, Meetze WH, Auestad N, Jasionowski T, Veerman M, McMurray CA, Neu J. 1996. Enteral glutamine supplementation for the very low birthweight infant: Plasma amino acid concentrations. *J Nutr* 126:1115S–1120S.
- Ronnenberg AG, Gross KL, Hartman WJ, Meydani SN, Prior RL. 1991. Dietary arginine supplementation does not enhance lymphocyte proliferation or interleukin-2 production in young and aged rats. *J Nutr* 121:1270–1278.
- Rose DP, Leklem JE, Fardal L, Baron RB, Shrago E. 1977. Effect of oral alanine loads on the serum triglycerides of oral contraceptive users and normal subjects. *Am J Clin Nutr* 30:691–694.
- Rose WC. 1957. The amino acid requirements of adult man. *Nutr Abs Rev* 27:631–647.
- Rose WC, Haines WJ, Warner DT, Johnson JE. 1951. The amino acid requirements of man. II. The role of threonine and histidine. *J Biol Chem* 188:49–58.
- Rose WC, Borman A, Coon MJ, Lambert GF. 1955a. The amino acid requirements of man. X. The lysine requirement. *J Biol Chem* 214:579–587.
- Rose WC, Coon MJ, Lambert GF. 1955b. The amino acid requirements of man. VIII. The metabolic availability of the optical isomers of acetyltryptophan. *J Biol Chem* 212:201–205.
- Rose WC, Coon MJ, Lockhart HB, Lambert GF. 1955c. The amino acid requirements of man. XI. The threonine and methionine requirements. *J Biol Chem* 215:101–110.
- Rose WC, Eades CH, Coon MJ. 1955d. The amino acid requirements of man. XII. The leucine and isoleucine requirements. *J Biol Chem* 216:225–234.
- Rose WC, Leach BE, Coon MJ, Lambert GF. 1955e. The amino acid requirements of man. IX. The phenylalanine requirement. *J Biol Chem* 213:913–922.
- Rose WC, Wixom RL, Lockhart HB, Lambert GF. 1955f. The amino acid requirements of man. XV. The valine requirement; Summary and final observations. *J Biol Chem* 217:987–995.
- Rosenberg LE, Downing S, Durant JL, Segal S. 1966. Cystinuria: Biochemical evidence for three genetically distinct diseases. *J Clin Invest* 45:365–371.
- Rudman D, DiFulco TJ, Galambos JT, Smith RB, Salam AA, Warren WD. 1973. Maximal rates of excretion and synthesis of urea in normal and cirrhotic subjects. *J Clin Invest* 52:2241–2249.
- Ryan-Harshman M, Leiter LA, Anderson GH. 1987. Phenylalanine and aspartame fail to alter feeding behavior, mood and arousal in men. *Physiol Behav* 39:247–253.
- Said AK, Hegsted DM. 1970. Response of adult rats to low dietary levels of essential amino acids. *J Nutr* 100:1362–1375.
- Sauberlich HE. 1961. Studies on the toxicity and antagonism of amino acids for weanling rats. *J Nutr* 75:61–72.
- Schaafsma G. 2000. The protein digestibility-corrected amino acid score. *J Nutr* 130:1865S–1867S.
- Schainer B, Olney JW. 1974. Glutamate-type hypothalamic-pituitary syndrome in mice treated with aspartate or cysteate in infancy. *J Neural Trans* 35:207–215.
- Schaumburg HH, Byck R. 1968. Sin cib-syn: Accent on glutamate. *N Engl J Med* 279:105.
- Schaumburg HH, Byck R, Gerstl R, Mashman JH. 1969. Monosodium L-glutamate: Its pharmacology and role in the Chinese restaurant syndrome. *Science* 163:826–828.
- Schechter PJ, Prakash NJ. 1979. Failure of oral L-histidine to influence appetite or affect zinc metabolism in man: A double-blind study. *Am J Clin Nutr* 32:1011–1014.

- Scholl TO, Hediger ML, Ances IG. 1990. Maternal growth during pregnancy and decreased infant birth weight. *Am J Clin Nutr* 51:790–793.
- Scholl TO, Hediger ML, Schall JI, Khoo C-S, Fischer RL. 1994. Maternal growth during pregnancy and the competition for nutrients. *Am J Clin Nutr* 60:183–188.
- Schwartz JC, Lampart C, Rose C. 1972. Histamine formation in rat brain in vivo: Effects of histidine loads. *J Neurochem* 19:801–810.
- Schwartzstein RM, Kelleher M, Weinberger SE, Weiss JW, Drazen JM. 1987. Airways effects of monosodium glutamate in subjects with chronic stable asthma. *J Asthma* 24:167–172.
- Scrimshaw NS, Hussein MA, Murray E, Rand WM, Young VR. 1972. Protein requirements of man: Variations in obligatory urinary and fecal nitrogen losses in young men. *J Nutr* 102:1595–1604.
- Scriver CR, Kaufman S, Woo SL. 1989. The hyperphenylalaninemias. In: Scriver CR, Beaudet AL, Sly WS, Valle D, eds. *The Metabolic Basis of Inherited Disease*, 6th ed. New York: McGraw-Hill. Pp. 495–546.
- Semprini ME, Frasca MA, Mariani A. 1971. Effects of monosodium glutamate (MSG) administration on rats during the intrauterine life and the neonatal period. *Quaderni delle Nutrizione* 31:85–100.
- Sen Gupta J, Srivastava KK. 1973. Effect of potassium-magnesium aspartate on endurance work in man. *Ind J Expt Biol* 11:392–394.
- Shaw GM, Velie EM, Schaffer DM. 1997. Is dietary intake of methionine associated with a reduction in risk for neural tube defect-affected pregnancies? *Teratology* 56:295–299.
- Simon CA, Van Melle GD, Ramelet AA. 1985. Failure of lysine in frequently recurrent herpes simplex infection. *Arch Dermatol* 121:167–168.
- Simon RA. 2000. Additive-induced urticaria: Experience with monosodium glutamate (MSG). *J Nutr* 130:1063S–1066S.
- Sivam SP, Chermak T. 1992. Neonatal administration of L-cysteine does not produce long-term effects on neurotransmitter or neuropeptide systems in the rat striatum. *Res Comm Chem Pathol Pharm* 77:219–225.
- Skeie B, Kvetan V, Gil KM, Rothkopf MM, Newsholme EA, Askanazi J. 1990. Branch-chain amino acids: Their metabolism and clinical utility. *Crit Care Med* 18:549–571.
- Smith B, Prockop DJ. 1962. Central-nervous-system effects of ingestion of L-tryptophan by normal subjects. *N Engl J Med* 267:1338–1341.
- Snyderman SE, Pratt EL, Cheung MW, Norton P, Holt LE, Hansen AE, Panos TC. 1955. The phenylalanine requirement of the normal infant. *J Nutr* 56: 253–263.
- Snyderman SE, Holt LE, Smellie F, Boyer A, Westall RG. 1959a. The essential amino acid requirements of infants: Valine. *Am J Dis Child* 97:186–191.
- Snyderman SE, Norton PM, Fowler DI, Holt LE. 1959b. The essential amino acid requirements of infants: Lysine. *Am J Dis Child* 97:175–185.
- Snyderman SE, Boyer A, Phansalkar SV, Holt LE. 1961a. Essential amino acid requirements of infants. Tryptophan. *Am J Dis Child* 102:41–45.
- Snyderman SE, Roitman EL, Boyer A, Holt LE. 1961b. Essential amino acid requirements of infants. Leucine. *Am J Dis Child* 102:35–40.
- Snyderman SE, Boyer A, Roitman E, Holt LE, Prose PH. 1963. The histidine requirement of the infant. *Pediatrics* 31:786–801.
- Snyderman SE, Boyer A, Norton PM, Roitman E, Holt LE. 1964a. The essential amino acid requirements of infants. IX. Isoleucine. *Am J Clin Nutr* 15:313–321.

- Snyderman SE, Boyer A, Norton PM, Roitman E, Holt LE. 1964b. The essential amino acid requirements of infants. X. Methionine. *Am J Clin Nutr* 15:322–330.
- Sole MJ, Benedict CR, Myers MG, Leenen FH, Anderson GH. 1985. Chronic dietary tyrosine supplements do not affect mild essential hypertension. *Hypertension* 7:593–596.
- Solomon JK, Geison RL. 1978. Effect of excess dietary L-histidine on plasma cholesterol levels in weanling rats. *J Nutr* 108:936–943.
- Souba WW. 1993. Glutamine and cancer. *Ann Surg* 218:715–728.
- Speth JD. 1989. Early hominid hunting and scavenging: The role of meat as an energy source. *J Hum Evol* 18:329–343.
- Speth JD, Spielmann KA. 1983. Energy source, protein metabolism, and hunter-gatherer subsistence strategies. *J Anthropol Archaeol* 2:1–31.
- Stechmiller JK, Treloar D, Allen N. 1997. Gut dysfunction in critically ill patients: A review of the literature. *Am J Crit Care* 6:204–209.
- Steele RD, Barber TA, Lalich J, Benevenga NJ. 1979. Effects of dietary 3-methylthiopropionate on metabolism, growth and hematopoiesis in the rat. *J Nutr* 109:1739–1751.
- Stefansson V. 1944a. *Arctic Manual*. New York: Macmillan.
- Stefansson V. 1944b. Pemmican. *Military Surg* 95:89–98.
- Stegink LD. 1976. Absorption, utilization, and safety of aspartic acid. *J Toxicol Environ Health* 2:215–242.
- Stegink LD, Shepherd JA, Brummel MC, Murray LM. 1974. Toxicity of protein hydrolysate solutions: Correlation of glutamate dose and neuronal necrosis to plasma amino acid levels in young mice. *Toxicology* 2:285–299.
- Stegink LD, Filer LJ, Baker GL. 1977. Effect of aspartame and aspartate loading upon plasma and erythrocyte free amino acid levels in normal adult volunteers. *J Nutr* 107:1837–1845.
- Stegink LD, Filer LJ, Baker GL. 1980. Plasma methionine levels in normal adult subjects after oral loading with L-methionine and N-acetyl-L-methionine. *J Nutr* 110:42–49.
- Stegink LD, Filer LJ, Baker GL. 1982a. Plasma and erythrocyte amino acid levels in normal adult subjects fed a high protein meal with and without added monosodium glutamate. *J Nutr* 112:1953–1960.
- Stegink LD, Filer LJ, Baker GL. 1982b. Plasma and urinary methionine levels in one-year-old infants after oral loading with L-methionine and N-acetyl-L-methionine. *J Nutr* 112:597–603.
- Stegink LD, Filer LJ Jr, Baker GL. 1983a. Effect of carbohydrate on plasma and erythrocyte glutamate levels in humans ingesting large doses of monosodium L-glutamate in water. *Am J Clin Nutr* 37:961–968.
- Stegink LD, Filer LJ Jr, Baker GL. 1983b. Plasma amino acid concentrations in normal adults fed meals with added monosodium L-glutamate and aspartame. *J Nutr* 113:1851–1860.
- Stekol JA, Szaran J. 1962. Pathological effects of excessive methionine in the diet of growing rats. *J Nutr* 77:81–90.
- Stellar E, McElroy WD. 1948. Does glutamic acid have any effect on learning? *Science* 108:281–283.
- Stephenson LS, Lathan MC, Ottesen EA. 2000. Global malnutrition. *Parasitology* 121:S5–S22.
- Stevenson DD. 2000. Monosodium glutamate and asthma. *J Nutr* 130:1067S–1073S.

- Stokes AF, Belger A, Banich MT, Taylor H. 1991. Effects of acute aspartame and acute alcohol ingestion upon the cognitive performance of pilots. *Aviat Space Environ Med* 62:648–653.
- Stoll B, Henry J, Reeds PJ, Yu H, Jahoor F, Burrin DG. 1998. Catabolism dominates the first-pass intestinal metabolism of dietary essential amino acids in milk protein-fed piglets. *J Nutr* 128:606–614.
- Strain GW, Strain JJ, Zumoff B. 1985. L-Tryptophan does not increase weight loss in carbohydrate-craving obese subjects. *Int J Obes* 9:375–380.
- Sweetman L. 1989. Branched chain organic acidurias. In: Scriver CR, Beaudet AL, Sly WS, Valle D, eds. *The Metabolic Basis of Inherited Disease*, 6th ed. New York: McGraw-Hill. Pp. 791–819.
- Swick RW, Benevenga NJ. 1977. Labile protein reserves and protein turnover. *J Dairy Sci* 60:505–515.
- Tachibana K, Mukai K, Hiraoka I, Moriguchi S, Takama S, Kishino Y. 1985. Evaluation of the effect of arginine-enriched amino acid solution on tumor growth. *J Parenter Enteral Nutr* 9:428–434.
- Tarasoff L, Kelly MF. 1993. Monosodium L-glutamate: A double-blind study and review. *Food Chem Toxicol* 31:1019–1035.
- Tarnopolsky MA, MacDougall JD, Atkinson SA. 1988. Influence of protein intake and training status on nitrogen balance and lean body mass. *J Appl Physiol* 64:187–193.
- Tarnopolsky MA, Atkinson SA, MacDougall JD, Senor BB, Lemon PW, Schwarcz H. 1991. Whole body leucine metabolism during and after resistance exercise in fed humans. *Med Sci Sports Exerc* 23:326–333.
- Taverner MR, Hume ID, Farrell DJ. 1981. Availability to pigs of amino acids in cereal grains. 1. Endogenous levels of amino acids in ileal digesta and faeces of pigs given cereal diets. *Br J Nutr* 46:149–158.
- Terry LC, Epelbaum J, Martin JB. 1981. Monosodium glutamate: Acute and chronic effects on rhythmic growth hormone and prolactin secretion, and somatostatin in the undisturbed male rat. *Brain Res* 217:129–142.
- Thein DJ, Hurt WC. 1984. Lysine as a prophylactic agent in the treatment of recurrent herpes simplex labialis. *Oral Surg* 58:659–666.
- Thoemke F, Huether G. 1984. Breeding rats on amino acid imbalanced diets for three consecutive generations affects the concentrations of putative amino acid transmitters in the developing brain. *Int J Dev Neurosci* 2:567–574.
- Thompson GN, Halliday D. 1992. Protein turnover in pregnancy. *Eur J Clin Nutr* 46:411–417.
- Torun B, Viteri FE. 1981. Obligatory nitrogen losses and factorial calculations of protein requirements of pre-school children. In: Torun B, Young VR, Rand WM, eds. *Protein-Energy Requirements of Developing Countries: Evaluation of New Data*. Tokyo, Japan: United Nations University Press. Pp. 159–163.
- Torun B, Cabrera Santiago M, Viteri FE. 1981. Protein requirements of pre-school children: Milk and soybean protein isolate. In: Torun B, Young VR, Rand WM, eds. *Protein-Energy Requirements of Developing Countries: Evaluation of New Data*. Tokyo, Japan: United Nations University Press. Pp. 182–190.
- Uauy R, Scrimshaw NS, Young VR. 1978. Human protein requirements: Nitrogen balance response to graded levels of egg protein in elderly men and women. *Am J Clin Nutr* 31:779–785.

- Uauy R, Yanez E, Ballester D, Barrera G, Guzman E, Saitua MT, Zacaris I. 1981. Obligatory urinary and faecal nitrogen losses in young Chilean men fed two levels of dietary energy intake. In: Torun B, Young VR, Rand WM, eds. *Protein-Energy Requirements of Developing Countries: Evaluation of New Data*. Tokyo, Japan: United Nations University Press.
- van Acker BA, von Meyenfeldt MF, van der Hulst RR, Hulsewe KW, Wagenmakers AJ, Deutz NE, de Blaauw I, Dejong CH, van Kreel BK, Soeters PB. 1999. Glutamine: The pivot of our nitrogen economy? *J Parenter Enteral Nutr* 23:S45–S48.
- van der Schoor SRD, van Goudoever JB, Stoll B, Henry JF, Rosenberger JR, Burrin DG, Reeds PJ. 2001. The pattern of intestinal substrate oxidation is altered by protein restriction in pigs. *Gastroenterology* 121:1167–1175.
- van Raaij JMA, Pee MEM, Vermaat-Miedema SH, Schonk CM, Hautvast JGAJ 1988. New equations for estimating body fat mass in pregnancy from body density or total body water. *Am J Clin Nutr* 48:24–29.
- van Wouwe JP, Hoogenkamp S, Van den Hamer CJ. 1989. Histidine supplement and Zn status in Swiss random mice. *Biol Trace Elem Res* 22:35–43.
- Viau AT, Leathem JH. 1973. Excess dietary methionine and pregnancy in the rat. *J Reprod Fertil* 33:109–111.
- Vijayasarathy C, Khan-Siddiqui L, Murthy SN, Bamji MS. 1987. Rise in plasma trimethyllysine levels in humans after oral lysine load. *Am J Clin Nutr* 46:772–777.
- Villalpando S, Butte NF, Flores-Huerta S, Thotathuchery M. 1998. Qualitative analysis of human milk produced by women consuming a maize-predominant diet typical of rural Mexico. *Ann Nutr Metab* 42:23–32.
- Viteri FE, Martinez C. 1981. Integumental nitrogen losses of pre-school children with different levels and sources of dietary protein intake. In: Torun B, Young VR, Rand WM, eds. *Protein-Energy Requirements of Developing Countries: Evaluation of New Data*. Tokyo, Japan: United Nations University Press.
- Wachstein M. 1947. Nephrotoxic action of dl-serine in the rat. II. The protective action of various amino acids and some other compounds. *Arch Pathol* 43:515–526.
- Wagenmakers AJ. 1998. Muscle amino acid metabolism at rest and during exercise: Role in human physiology and metabolism. *Exerc Sport Sci Rev* 26:287–314.
- Waisman HA, Harlow HF. 1965. Experimental phenylketonuria in infant monkeys: A high phenylalanine diet produces abnormalities simulating those of the hereditary disease. *Science* 147:685–695.
- Wang JML, Creel DJ, Wong KC. 1989. Transurethral resection of the prostate, serum glycine levels, and ocular evoked potentials. *Anesthesiology* 70:36–41.
- Waterlow JC. 1969. The assessment of protein nutrition and metabolism in the whole animal, with special reference to man. In: Munro HN ed. *Mammalian Protein Metabolism*, Vol III. New York: Academic Press. Pp. 347–348.
- Waterlow JC. 1984. Protein turnover with special reference to man. *Quart J Exp Physiol* 69:409–438.
- Waterlow JC, Garlick PJ, Millward DJ. 1978. *Protein Turnover in Mammalian Tissues and in the Whole Body*. Amsterdam: North-Holland Publishing.
- Webber WA, Brown JL, Pitts RF. 1961. Interactions of amino acids in renal tubular transport. *Am J Physiol* 200:380–386.
- White TP, Brooks GA. 1981. [ $^{14}\text{C}$ ]glucose, -alanine, and -leucine oxidation in rates at rest and two intensities of running. *Am J Physiol* 240:E155–E165.

- Widdowson EM, Dickerson JWT. 1964. Chemical composition of the body. In: Comar CL, Bronner F, eds. *Mineral Metabolism: An Advanced Treatise*, Vol 2. New York: Academic Press.
- Wilcken DE, Reddy SG, Gupta VJ. 1983. Homocysteinemia, ischemic heart disease, and the carrier state for homocystinuria. *Metabolism* 32:363–370.
- Wilkin JK. 1986. Does monosodium glutamate cause flushing (or merely “glutamania”)? *J Am Acad Dermatol* 15:225–230.
- Willard MD, Gilsdorf RB, Price RA. 1980. Protein-calorie malnutrition in a community hospital. *J Am Med Assoc* 243:1720–1722.
- Williams GM, Whysner J. 1996. Epigenetic carcinogens: Evaluation and risk assessment. *Exp Toxicol Pathol* 48:189–195.
- Wilson DC, Pencharz PB. 1997. Nutritional care of the chronically ill. In: Tsang RC, Zlotkin SH, Nichols BL, Hansen JW, eds. *Nutrition During Infancy: Birth to 2 Years*. Cincinnati: Digital Educational Publishing, Inc. Pp. 37–56.
- Wilson D, Rafii M, Ball RO, Pencharz PB. 2000. Threonine requirement in young men determined by indicator amino acid oxidation with use of L-[1-<sup>13</sup>C]-phenylalanine. *Am J Clin Nutr* 71:757–764.
- Woessner KM, Simon RA, Stevenson DD. 1999. Monosodium glutamate sensitivity in asthma. *J Allergy Clin Immunol* 104:305–310.
- Woods RK, Weiner JM, Thien F, Abramson M, Walters EH. 1998. The effects of monosodium glutamate in adults with asthma who perceive themselves to be monosodium glutamate-intolerant. *J Allergy Clin Immunol* 101:762–771.
- Wurtman JJ, Wurtman RJ, Growdon JH, Henry P, Lipscomb A, Zeisel SH. 1981. Carbohydrate craving in obese people: Suppression by treatments affecting serotonergic transmission. *Int J Eating Disord* 1:2–15.
- Wynn M, Wynn A. 1979. *Prevention of Handicap and the Health of Women*. London: Routledge and Kegan Paul. Pp. 43–81.
- Yamashita K, Ashida K. 1971. Effect of excessive levels of lysine and threonine on the metabolism of these amino acids in rats. *J Nutr* 101:1607–1614.
- Yanez E, Uauy R, Ballester D, Barrera G, Chavez N, Guzman E, Saitua MT, Zacarias I. 1982. Capacity of the Chilean mixed diet to meet the protein and energy requirements of young adult males. *Br J Nutr* 47:1–10.
- Yang WH, Drouin MA, Herbert M, Mao Y, Karsh J. 1997. The monosodium glutamate symptom complex: Assessment in a double-blind, placebo-controlled, randomized study. *J Allergy Clin Immunol* 99:757–762.
- Yeatman TJ, Risley GL, Brunson ME. 1991. Depletion of dietary arginine inhibits growth of metastatic tumor. *Arch Surg* 126:1376–1382.
- Yogman MW, Zeisel SH. 1983. Diet and sleep patterns in newborn infants. *N Engl J Med* 309:1147–1149.
- Yogman MW, Zeisel SH. 1985. Nutrients, neurotransmitters and infant behavior. *Am J Clin Nutr* 42:352–360.
- Yonetani S, Ishii H, Kirimura J. 1979. Effect of dietary administration of monosodium L-glutamate on growth and reproductive functions in mice. *Oyo Yakuri (Pharmacometrics)* 17:143–152.
- Young SN. 1986. The clinical psychopharmacology of tryptophan. In: Wurtman RJ, Wurtman JJ, eds. *Nutrition and the Brain*, Vol. 7. New York: Raven Press. Pp. 49–88.
- Young SN, Gauthier S. 1981. Effect of tryptophan administration on tryptophan, 5-hydroxyindoleacetic acid and indoleacetic acid in human lumbar and cisternal cerebrospinal fluid. *J Neurol Neurosurg Psychiatry* 44:323–327.

- Young VR. 1987. 1987 McCollum Award Lecture. Kinetics of human amino acid metabolism: Nutritional implications and some lessons. *Am J Clin Nutr* 46:709–725.
- Young VR, Borgonha S. 2000. Nitrogen and amino acid requirements: The Massachusetts Institute of Technology Amino Acid Requirement Pattern. *J Nutr* 130:1841S–1849S.
- Young VR, Pellett PL. 1990. Current concepts concerning indispensable amino acid needs in adults and their implications for international nutrition planning. *Food Nutr Bull* 12:289–300.
- Young VR, Pellett PL. 1994. Plant proteins in relation to human protein and amino acid nutrition. *Am J Clin Nutr* 59:1203S–1212S.
- Young VR, Hussein MA, Scrimshaw JS. 1968. Estimate of loss of labile body nitrogen during acute protein deprivation in young adults. *Nature* 218:568–569.
- Young VR, Tontisirin K, Ozalp I, Lakshmanan F, Scrimshaw NS. 1972. Plasma amino acid response curve and amino acid requirements in young men: Valine and lysine. *J Nutr* 102:1159–1169.
- Young VR, Taylor YS, Rand WM, Scrimshaw NS. 1973. Protein requirements of man: Efficiency of egg protein utilization at maintenance and sub-maintenance levels in young men. *J Nutr* 103:1164–1174.
- Young VR, Fajardo L, Murray E, Rand WM, Scrimshaw NS. 1975a. Protein requirements of man: Comparative nitrogen balance response within the submaintenance-to-maintenance range of intakes of wheat and beef proteins. *J Nutr* 105:534–542.
- Young VR, Steffee WP, Pencharz PB, Winterer JC, Scrimshaw NS. 1975b. Total human body protein synthesis in relation to protein requirements at various ages. *Nature* 253:192–194.
- Young VR, Puig M, Queiroz E, Scrimshaw NS, Rand WM. 1984. Evaluation of the protein quality of an isolated soy protein in young men: Relative nitrogen requirements and effect of methionine supplementation. *Am J Clin Nutr* 39:16–24.
- Young VR, Gucalp C, Rand WM, Matthews DE, Bier DM. 1987. Leucine kinetics during three weeks at submaintenance-to-maintenance intakes of leucine in men: Adaptation and accommodation. *Hum Nutr Clin Nutr* 41:1–18.
- Young VR, Bier DM, Pellett PL. 1989. A theoretical basis for increasing current estimates of the amino acid requirements in adult man, with experimental support. *Am J Clin Nutr* 50:80–92.
- Young VR, Marchini JS, Cortiella J. 1990. Assessment of protein nutritional status. *J Nutr* 120:1496–1502.
- Young VR, Wagner DA, Burini R, Storch KJ. 1991. Methionine kinetics and balance at the 1985 FAO/WHO/UNU intake requirement in adult men studied with L-[<sup>2</sup>H<sub>3</sub>-methyl-1-<sup>13</sup>C]methionine as a tracer. *Am J Clin Nutr* 54:377–385.
- Young VR, El-Khoury AE, Raguso CA, Forslund AH, Hambraeus L. 2000. Rates of urea production and hydrolysis and leucine oxidation change linearly over widely varying protein intakes in healthy adults. *J Nutr* 130:761–766.
- Yuwiler A, Brammer GL, Morley JE, Raleigh MJ, Flannery JW, Geller E. 1981. Short-term and repetitive administration of oral tryptophan in normal men. Effects on blood tryptophan, serotonin, and kynurene concentrations. *Arch Gen Psychiatry* 38:619–626.
- Zanni E, Calloway DH, Zezulka AY. 1979. Protein requirements of elderly men. *J Nutr* 109:513–524.

- Zello GA, Pencharz PB, Ball RO. 1990. Phenylalanine flux, oxidation and conversion to tyrosine in humans studied with L-[1-<sup>13</sup>C]phenylalanine. *Am J Physiol* 259:E835–E843.
- Zello GA, Pencharz PB, Ball RO. 1993. Dietary lysine requirement of young adult males determined by oxidation of L-[1-<sup>13</sup>C]phenylalanine. *Am J Physiol* 264:E677–E685.
- Zello GA, Wykes LJ, Ball RO, Pencharz PB. 1995. Recent advances in methods of assessing dietary amino acid requirements for adult humans. *J Nutr* 125:2907–2915.
- Zezulka AY, Calloway DH. 1976a. Nitrogen retention in men fed isolated soybean protein supplemented with L-methionine, D-methionine, N-acetyl-L-methionine, or inorganic sulfate. *J Nutr* 106:1286–1291.
- Zezulka AY, Calloway DH. 1976b. Nitrogen retention in men fed varying levels of amino acids from soy protein with or without added L-methionine. *J Nutr* 106:212–221.
- Zhao X-H, Wen ZM, Meredith CN, Matthews DE, Bier DM, Young VR. 1986. Threonine kinetics at graded threonine intakes in young men. *Am J Clin Nutr* 43:795–802.
- Ziegler TR, Benfell K, Smith RJ, Young LS, Brown E, Ferrari-Baliviera E, Lowe DK, Wilmore DW. 1990. Safety and metabolic effects of L-glutamine administration in humans. *J Parenter Enteral Nutr* 14:137S–146S.
- Zimmerman FT, Burgemeister BB. 1959. A controlled experiment of glutamic acid therapy. *AMA Arch Neurol Psych* 81:639–648.
- Zlotkin SH. 1989. Nutrient interactions with total parenteral nutrition: Effect of histidine and cysteine intake on urinary zinc excretion. *J Pediatr* 114:859–864.

Ibid., Chapter 13, pp. 965–967.

- Bandini LG, Vu D, Must A, Cyr H, Goldberg A, Dietz WH. 1999. Comparison of high-calorie, low-nutrient-dense food consumption among obese and non-obese adolescents. *Obes Res* 7:438–443.
- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Black AE, Prentice AM, Goldberg GR, Jebb SA, Bingham SA, Livingstone MBE, Coward WA. 1993. Measurements of total energy expenditure provide insights into the validity of dietary measurements of energy intake. *J Am Diet Assoc* 93:572–579.
- Blair SN, Kohl HW, Barlow CE. 1993. Physical activity, physical fitness, and all-cause mortality in women: Do women need to be active? *J Am Coll Nutr* 12:368–371.
- Blair SN, Kohl HW, Barlow CE, Paffenbarger RS, Gibbons LW, Macera CA. 1995. Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. *J Am Med Assoc* 273:1093–1098.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Nutrition Examination Survey: Underreporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Carroll RJ, Freedman LS, Hartman AM. 1996. Use of semiquantitative food frequency questionnaires to estimate the distribution of usual intake. *Am J Epidemiol* 143:392–404.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.

- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- IOM. 2001. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Washington, DC: National Academy Press.
- Johnson RK, Goran MI, Poehlman ET. 1994. Correlates of over- and under-reporting of energy intake in healthy older men and women. *Am J Clin Nutr* 59:1286–1290.
- Johnson RK, Soultanakis RP, Matthews DE. 1998. Literacy and body fatness are associated with underreporting of energy intake in US low-income women using the multiple-pass 24-hour recall: A doubly labeled water study. *J Am Diet Assoc* 98:1136–1140.
- Kristal AR, Feng Z, Coates RJ, Oberman A, George V. 1997. Associations of race/ethnicity, education, and dietary intervention with the validity and reliability of a food frequency questionnaire: The Women's Health Trial Feasibility Study in Minority Populations. *Am J Epidemiol* 146:856–869.
- Lichtman SW, Pisarska K, Berman ER, Pestone M, Dowling H, Offenbacher E, Weisel H, Heshka S, Matthews DE, Heymsfield SB. 1992. Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. *N Engl J Med* 327:1893–1898.
- Liu K. 1994. Statistical issues related to semiquantitative food-frequency questionnaires. *Am J Clin Nutr* 59:262S–265S.
- Livingstone MB, Prentice AM, Coward WA, Strain JJ, Black AE, Davies PS, Stewart CM, McKenna PG, Whitehead RG. 1992. Validation of estimates of energy intake by weighed dietary record and diet history in children and adolescents. *Am J Clin Nutr* 56:29–35.
- Marlett JA, Cheung TF. 1997. Database and quick methods of assessing typical dietary fiber intakes using data for 228 commonly consumed foods. *J Am Diet Assoc* 97:1139–1148.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Prentice AM, Black AE, Coward WA, Davies HL, Goldberg GR, Murgatroyd PR, Ashford J, Sawyer M, Whitehead RG. 1986. High levels of energy expenditure in obese women. *Br Med J* 292:983–987.
- Pryer JA, Vrijheid M, Nichols R, Kiggins M, Elliott P. 1997. Who are the 'low energy reporters' in the dietary and nutritional survey of British adults? *Int J Epidemiol* 26:146–154.
- Schoeller DA. 1995. Limitations in the assessment of dietary energy by self-report. *Metabolism* 44:18–22.
- Schoeller DA, Bandini LG, Dietz WH. 1990. Inaccuracies in self-reported intake identified by comparison with the doubly labelled water method. *Can J Physiol Pharmacol* 68:941–949.

USDA (U.S. Department of Agriculture). 2001. *USDA Nutrient Database for Standard Reference, Release 14*. Online. Nutrient Data Laboratory. Available at <http://www.nal.usda.gov/fnic/foodcomp>. Accessed April 2, 2002.

USDA/HHS (U.S. Department of Health and Human Services). 2000. *Nutrition and Your Health: Dietary Guidelines for Americans*. Home and Garden Bulletin No. 232. Washington, DC: U.S. Government Printing Office.

## WATER

*Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate (ISBN 0-309-09158-6)*, Chapter 4, pp. 166–185.

- Adler S. 1980. Hyponatremia and rhabdomyolysis: A possible relationship. *South Med J* 73:511–513.
- Adolph EF. 1933. The metabolism and distribution of water in body and tissues. *Physiol Rev* 13:336–371.
- Adolph EF. 1943. *Physiological Regulations*. Lancaster, PA: The Jaques Cattell Press.
- Adolph EF. 1947a. Signs and symptoms of desert dehydration. In: Adolph EF, ed. *Physiology of Man in the Desert*. New York: Intersciences Publishers. Pp. 226–240.
- Adolph EF. 1947b. Urinary excretion of water and solutes. In: Adolph EF, ed. *Physiology of Man in the Desert*. New York: Intersciences Publishers. Pp. 96–109.
- Adolph EF, Wills JH. 1947. Thirst. In: Adolph EF, ed. *Physiology of Man in the Desert*. New York: Intersciences Publishers. Pp. 241–253.
- Agren J, Stromberg B, Sedin G. 1997. Evaporation rate and skin blood flow in full term infants nursed in a warm environment before and after feeding cold water. *Acta Paediatr* 86:1085–1089.
- Ahlman K, Karvonen MJ. 1961. Weight reduction by sweating in wrestlers, and its effect on physical fitness. *J Sports Med Phys Fitness* 1:58–62.
- Akasaki Y, Nagatomo I, Akasaki Y, Nomaguchi M, Akasaki Y, Matsumoto K. 1993. Water intoxication in a schizophrenic patient with rhabdomyolysis. *Jpn J Psychiatry Neurol* 47:843–846.
- Almroth S, Bidinger PD. 1990. No need for water supplementation for exclusively breast-fed infants under hot and arid conditions. *Trans R Soc Trop Med Hyg* 84:602–604.
- Altman PL. 1961. *Blood and Other Body Fluids*. Washington, DC: Federation of American Societies for Experimental Biology.
- Anand IS, Chandrashekhar Y. 1996. Fluid metabolism at high altitudes. In: Marriott BM, Carlson SJ, eds. *Nutritional Needs in Cold and in High-Altitude Environments*. Washington, DC: National Academy Press. Pp. 331–356.
- Andreoli TE, Reeves WB, Bichet DG. 2000. Endocrine control of water balance. In: Fray JCS, Goodman HM, eds. *Handbook of Physiology, Section 7, Volume III: Endocrine Regulation of Water and Electrolyte Balance*. New York: Oxford University Press. Pp. 530–569.
- Araki T, Toda Y, Matsushita K, Tsujino A. 1979. Age differences in sweating during muscular exercise. *Jpn J Phys Fitness Sports Med* 28:239–248.
- Arieff AI, Kronlund BA. 1999. Fatal child abuse by forced water intoxication. *Pediatrics* 103:1292–1295.
- Armstrong LE, Hubbard RW, Szlyk PC, Matthew WT, Sils IV. 1985. Voluntary dehydration and electrolyte losses during prolonged exercise in the heat. *Aviat Space Environ Med* 56:765–770.
- Armstrong LE, Hubbard RW, Jones BH, Daniels JT. 1986. Preparing Alberto Salazar for the heat of the 1984 Olympic marathon. *Phys Sports Med* 14:73–81.
- Armstrong LE, Maresh CM, Castellani JW, Bergeron MF, Kenefick RW, LaGasse KE, Riebe D. 1994. Urinary indices of hydration status. *Int J Sport Nutr* 4:265–279.
- Armstrong LE, Maresh CM, Gabaree CV, Hoffman JR, Kavouras SA, Kenefick RW, Castellani JW, Ahlquist LE. 1997. Thermal and circulatory responses during exercise: Effects of hypohydration, dehydration, and water intake. *J Appl Physiol*

- 82:2028–2035.
- Aufderheide S, Lax D, Goldberg SJ. 1994. Gender differences in dehydration-induced mitral valve prolapse. *Am Heart J* 129:83–86.
- Bachle L, Eckerson J, Albertson L, Ebersole K, Goodwin J, Petzel D. 2001. The effect of fluid replacement on endurance performance. *J Strength Cond Res* 15:217–224.
- Baird IM, Walters RL, Davies PS, Hill MJ, Drasar BS, Southgate DAT. 1977. The effects of two dietary fiber supplements on gastrointestinal transit, stool weight and frequency, and bacterial flora, and fecal bile acids in normal subjects. *Metabolism* 26:117–128.
- Ballauff A, Kersting M, Manz F. 1988. Do children have an adequate fluid intake? Water balance studies carried out at home. *Ann Nutr Metab* 32:332–339.
- Bar-Or O, Dotan R, Inbar O, Rotstein A, Zonder H. 1980. Voluntary hypohydration in 10 to 12 year old boys. *J Appl Physiol* 48:104–108.
- Bar-Or O, Blimkie CJR, Hay JA, MacDougall JD, Ward DS, Wilson WM. 1992. Voluntary dehydration and heat intolerance in cystic fibrosis. *Lancet* 339:696–699.
- Barr SI, Costill DL, Fink WJ. 1991. Fluid replacement during prolonged exercise: Effects of water, saline, or no fluid. *Med Sci Sports Exerc* 23:811–817.
- Bartok C, Schoeller DA, Randall-Clark R, Sullivan JC, Landry GL. 2004. The effect of dehydration on wrestling minimum weight assessment. *Med Sci Sports Exerc* 36:160–167.
- Bass DE, Henschel A. 1956. Responses of body fluid compartments to heat and cold. *Physiol Rev* 36:128–144.
- Baumgartner RN, Stauber PM, McHugh D, Koehler KM, Garry PJ. 1995. Cross-sectional age differences in body composition in persons 60+ years of age. *J Gerontol* 50A:M307–M316.
- Baylis PH, Thompson C, Burd J, Tunbridge WMG, Snodgrass CA. 1986. Recurrent pregnancy-induced polyuria and thirst due to hypothalamic diabetes insipidus: An investigation into possible mechanisms responsible for polyuria. *Clin Endocrinol* 24:459–466.
- Below PR, Mora-Rodriguez R, Gonzalez-Alonso J, Coyle EF. 1995. Fluid and carbohydrate ingestion independently improve performance during 1 h of intense exercise. *Med Sci Sports Exerc* 27:200–210.
- Bijlani RL, Sharma KN. 1980. Effect of dehydration and a few regimes of rehydration on human performance. *Indian J Physiol Pharmacol* 24:255–266.
- Bitterman WA, Farhadian H, Abu Samra C, Lerner D, Amoun H, Krapf D, Makov UE. 1991. Environmental and nutritional factors significantly associated with cancer of the urinary tract among different ethnic groups. *Urol Clin North Amer* 18:501–508.
- Blanc S, Normand S, Ritz P, Pachiaudi C, Vico L, Gharib C, Gauquelin-Koch G. 1998. Energy and water metabolism, body composition, and hormonal changes induced by 42 days of enforced inactivity and simulated weightlessness. *J Clin Endocrinol Metab* 83:4289–4297.
- Blatteis CM. 1998. Fever. In: Blatteis CM, ed. *Physiology and Pathophysiology of Temperature Regulation*. River Edge, NJ: World Scientific. Pp. 178–191.
- Blyth CS, Burt JJ. 1961. Effect of water balance on ability to perform in high ambient temperatures. *Res Q* 32:301–307.
- Borghi L, Meschi T, Amato F, Briganti A, Novarini A, Giannini A. 1996. Urinary volume, water and recurrences in idiopathic calcium nephrolithiasis: A 5-year randomized prospective study. *J Urol* 155:839–843.
- Bosco JS, Terjung RL, Greenleaf JE. 1968. Effects of progressive hypohydration on

- maximal isometric muscle strength. *J Sports Med Phys Fitness* 8:81–86.
- Bosco JS, Greenleaf JE, Bernauer EM, Card DH. 1974. Effects of acute dehydration and starvation on muscular strength and endurance. *Acta Physiol Pol* 25:411–421.
- Bouchama A, Knochel JP. 2002. Heat stroke. *N Engl J Med* 346:1978–1988.
- Boulze D, Montastruc P, Cabanac M. 1983. Water intake, pleasure and water temperature in humans. *Physiol Behav* 30:97–102.
- Braver DJ, Modan M, Chetrit A, Lusky A, Braf Z. 1987. Drinking, micturition habits, and urine concentration as potential risk factors in urinary bladder cancer. *J Natl Cancer Inst* 78:437–440.
- Brown AH. 1947a. Dehydration exhaustion. In: Adolph EF, ed. *Physiology of Man in the Desert*. New York: Intersciences Publishers. Pp. 208–225.
- Brown AH. 1947b. Water requirements of man in the desert. In: Adolph EF, ed. *Physiology of Man in the Desert*. New York: Intersciences Publishers. Pp. 115–135.
- Brown AH. 1947c. Water shortage in the desert. In: Adolph EF, ed. *Physiology of Man in the Desert*. New York: Intersciences Publishers. Pp. 136–159.
- Browne PM. 1979. Rhabdomyolysis and myoglobinuria associated with acute water intoxication. *West J Med* 130:459–461.
- Bruemmer B, White E, Vaughan TL, Cheney CL. 1997. Fluid intake and the incidence of bladder cancer among middle-aged men and women in a three-county area of western Washington. *Nutr Cancer* 29:163–168.
- Burge CM, Carey MF, Payne WR. 1993. Rowing performance, fluid balance, and metabolic function following dehydration and rehydration. *Med Sci Sports Exerc* 25:1358–1364.
- Buskirk ER, Iampietro PF, Bass DE. 1958. Work performance after dehydration: Effects of physical conditioning and heat acclimatization. *J Appl Physiol* 12:189–194.
- Butte NF, Wong WW, Patterson BW, Garza C, Klein PD. 1988. Human-milk intake measured by administration of deuterium oxide to the mother: A comparison with the test-weighing technique. *Am J Clin Nutr* 47:815–821.
- Butte NF, Wong WW, Klein PD, Garza C. 1991. Measurement of milk intake: Tracer-to-infant deuterium dilution method. *Br J Nutr* 65:3–14.
- Caldwell JE, Ahonen E, Nousiainen U. 1984. Differential effects of sauna-, diuretic-, and exercise-induced hypohydration. *J Appl Physiol* 57:1018–1023.
- Candas V, Libert J-P, Brandenberger G, Sagot J-C, Kahn J-M. 1988. Thermal and circulatory responses during prolonged exercise at different levels of hydration. *J Physiol (Paris)* 83:11–18.
- Casa DJ, Armstrong LE, Hillman SK, Montain SJ, Reiff RV, Rich BSE, Roberts WO, Stone JA. 2000. National Athletic Trainers' Association position statement: Fluid replacement for athletes. *J Athl Train* 35:212–224.
- Catalano PM, Wong WW, Drago MN, Amini SB. 1995. Estimating body composition in late gestation: A new hydration constant for body density and total body water. *Am J Physiol* 268:E153–E158.
- Charkoudian N, Halliwill JR, Morgan BJ, Eisenach JE, Joyner MJ. 2003. Influences of hydration on post-exercise cardiovascular control in humans. *J Physiol* 552:635–644.
- Chesley LC. 1978. *Hypertensive Disorders in Pregnancy*. New York: Appleton-Century-Crofts.
- Cheung SS, McLellan TM. 1998. Influence of hydration status and fluid replacement on heat tolerance while wearing NBC protective clothing. *Eur J Appl Physiol* 77:139–148.

- Cheuvront SN, Haymes EM. 2001. Thermoregulation and marathon running: Biological and environmental influences. *Sports Med* 31:743–762.
- Cheuvront SN, Haymes EM, Sawka MN. 2002. Comparison of sweat loss estimates for women during prolonged high-intensity running. *Med Sci Sports Exerc* 34: 1344–1350.
- Cheuvront SN, Carter R III, Sawka MN. 2003. Fluid balance and endurance exercise performance. *Curr Sports Med Rep* 2:202–208.
- Cian C, Koulmann N, Barraud PA, Raphel C, Jimenez C, Melin B. 2000. Influence of variations in body hydration on cognitive function: Effect of hyperhydration, heat stress, and exercise-induced dehydration. *J Psychophysiol* 14:29–36.
- Cian C, Barraud PA, Melin B, Raphel C. 2001. Effects of fluid ingestion on cognitive function after heat stress or exercise-induced dehydration. *Int J Psychophysiol* 42:243–251.
- Clark BA, Elahi D, Fish L, McAloon-Dyke M, Davis K, Minaker KL, Epstein FH. 1991. Atrial natriuretic peptide suppresses osmostimulated vasopressin release in young and elderly humans. *Am J Physiol* 261:E252–E256.
- Cohen RJ, Brown KH, Rivera LL, Dewey KG. 2000. Exclusively breastfed, low birthweight term infants do not need supplemental water. *Acta Paediatr* 89:550–552.
- Commonwealth of Massachusetts. 1988. *The Report of the Investigation of Attorney General James M. Shannon of the Class 12 Experience at the Edward W. Connally Criminal Justice Training Center, Agawam, Massachusetts*. Boston: Department of the Attorney General.
- Consolazio CF, Johnson RE, Pecora LJ. 1963. *Physiological Measurements of Metabolic Functions in Man*. New York: McGraw-Hill.
- Consolazio CF, Matoush LO, Johnson HL, Nelson RA, Krzywicki HJ. 1967. Metabolic aspects of acute starvation in normal humans (10 days). *Am J Clin Nutr* 20:672–683.
- Consolazio CF, Matoush LO, Johnson HL, Daws TA. 1968. Protein and water balances of young adults during prolonged exposure to high altitude (4,300 meters). *Amer J Clin Nutr* 21:154–161.
- Convertino VA. 1991. Blood volume: Its adaptation to endurance training. *Med Sci Sports Exerc* 23:1338–1348.
- Costi D, Calcaterra PG, Iori N, Vourna S, Nappi G, Passeri M. 1999. Importance of bioavailable calcium drinking water for the maintenance of bone mass in postmenopausal women. *J Endocrinol Invest* 22:852–856.
- Costill DL. 1977. Sweating: Its composition and effects on body fluids. *Ann NY Acad Sci* 301:160–174.
- Costill DL, Fink WJ. 1974. Plasma volume changes following exercise and thermal dehydration. *J Appl Physiol* 37:521–525.
- Costill DL, Saltin B. 1974. Factors limiting gastric emptying during rest and exercise. *J Appl Physiol* 37:679–683.
- Costill DL, Kammer WF, Fisher A. 1970. Fluid ingestion during distance running. *Arch Environ Health* 21:520–525.
- Coyle EF. 1998. Cardiovascular drift during prolonged exercise and the effects of dehydration. *Int J Sports Med* 19:S121–S124.
- Craig FN, Cummings EG. 1966. Dehydration and muscular work. *J Appl Physiol* 21:670–674.
- Crowe MJ, Forsling ML, Rolls BJ, Phillips PA, Ledingham JGG, Smith RF. 1987. Altered water excretion in healthy elderly men. *Age Ageing* 16:285–293.
- Cummings JH, Hill MJ, Jenkins DJA, Pearson JR, Wiggins HS. 1976. Changes in

- fecal composition and colonic function due to cereal fiber. *Am J Clin Nutr* 29:1468–1473.
- Curhan GC, Willett WC, Rimm EB, Stampfer MJ. 1993. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. *N Engl J Med* 328:833–838.
- Curhan GC, Willett WC, Rimm EB, Spiegelman D, Stampfer MJ. 1996. Prospective study of beverage use and the risk of kidney stones. *Am J Epidemiol* 143:240–247.
- Curhan GC, Willett WC, Speizer FE, Spiegelman D, Stampfer MJ. 1997. Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk for kidney stones in women. *Ann Intern Med* 126:497–504.
- Curhan GC, Willett WC, Speizer FE, Stampfer MJ. 1998. Beverage use and risk for kidney stones in women. *Ann Intern Med* 128:534–540.
- Davison JM, Vallotton MB, Lindheimer MD. 1981. Plasma osmolality and urinary concentration and dilution during and after pregnancy: Evidence that lateral recumbency inhibits maximal urinary concentrating ability. *Br J Obstet Gynaecol* 88:472–479.
- Davison JM, Gilmore EA, Durr JA, Robertson GL, Lindheimer MD. 1984. Altered osmotic thresholds for vasopressin secretion and thirst in human pregnancy. *Am J Physiol* 246:F105–F109.
- Davison JM, Sheills EA, Philips PR, Lindheimer MD. 1988. Serial evaluation of vasopressin release and thirst in human pregnancy. Role of human chorionic gonadotrophin on the osmoregulatory changes of gestation. *J Clin Invest* 81:798–806.
- Davison JM, Sheills EA, Barron WM, Robinson AG, Lindheimer MD. 1989. Changes in the metabolic clearance of vasopressin and in plasma vasopressinase throughout human pregnancy. *J Clin Invest* 83:1313–1318.
- Davison JM, Sheills EA, Philips PR, Barron WM, Lindheimer MD. 1993. Metabolic clearance of vasopressin and an analogue resistant to vasopressinase in human pregnancy. *Am J Physiol* 264:F348–F353.
- de Leon J, Verghese C, Tracy JI, Josiassen RC, Simpson GM. 1994. Polydipsia and water intoxication in psychiatric patients: A review of the epidemiological literature. *Biol Psychiatry* 35:408–419.
- Dontas AS, Marketos S, Papanayiotou P. 1972. Mechanisms of renal tubular defects in old age. *Postgrad Med J* 48:295–303.
- Dorfman LJ, Jarvik ME. 1970. Comparative stimulant and diuretic actions of caffeine and theobromine in man. *Clin Pharmacol Ther* 11:869–872.
- Durkot MJ, Martinez O, Brooks-McQuade D, Francesconi R. 1986. Simultaneous determination of fluid shifts during thermal stress in a small-animal model. *J Appl Physiol* 61:1031–1034.
- Durr JA, Hoggard JG, Hunt JM, Schrier RW. 1987. Diabetes insipidus in pregnancy associated with abnormally high circulating vasopressinase activity. *N Engl J Med* 316:1070–1074.
- Eckford SD, Keane DP, Lamond KE, Jackson SR, Abrams P. 1995. Hydration monitoring in the prevention of recurrent idiopathic urinary tract infections in premenopausal women. *Br J Urol* 76:90–93.
- Eddy NB, Downs AW. 1928. Tolerance and cross-tolerance in the human subject to the diuretic effect of caffeine, theobromine and theophylline. *J Pharmacol Exp Ther* 33:167–174.
- Eichna JW, Bean WB, Ashe WF. 1945. Performance in relation to environmental

- temperature. *Bull Johns Hopkins Hosp* 76:25–58.
- Ekbom B, Greenleaf CJ, Greenleaf JE, Hermansen L. 1970. Temperature regulation during exercise dehydration in man. *Acta Physiol Scand* 79:475–483.
- Embon OM, Rose GA, Rosenbaum T. 1990. Chronic dehydration stone disease. *Br J Urol* 66:357–362.
- Engell D. 1995. Effects of beverage consumption and hydration status on caloric intake. In: Institute of Medicine. *Not Eating Enough*. Washington, DC: National Academy Press. Pp. 217–237.
- Engell DB, Maller O, Sawka MN, Francesconi RN, Drolet L, Young AJ. 1987. Thirst and fluid intake following graded hypohydration levels in humans. *Physiol Behav* 40:229–236.
- Epstein M. 1985. Aging and the kidney: Clinical implications. *Am Fam Physician* 31:123–137.
- Epstein Y, Keren G, Moisseiev J, Gasko O, Yachin S. 1980. Psychomotor deterioration during exposure to heat. *Aviat Space Environ Med* 51:607–610.
- Ershow AG, Cantor KP. 1989. *Total Water and Tapwater Intake in the United States: Population-Based Estimates of Quantities and Sources*. Bethesda, MD: Life Sciences Research Office.
- Falk B. 1998. Effects of thermal stress during rest and exercise in the paediatric population. *Sports Med* 25:221–240.
- Falk B, Bar-Or O, Calvert R, MacDougall JD. 1992a. Sweat gland response to exercise in the heat among pre-, mid-, and late-pubertal boys. *Med Sci Sports Exerc* 24:313–319.
- Falk B, Bar-Or O, MacDougall JD. 1992b. Thermoregulatory responses of pre-, mid-, and late-pubertal boys to exercise in dry heat. *Med Sci Sports Exerc* 24:688–694.
- Fallowfield JL, Williams C, Booth J, Choo BH, Growns S. 1996. Effect of water ingestion on endurance capacity during prolonged running. *J Sports Sci* 14:497–502.
- Fish LC, Minaker KL, Rowe JW. 1985. Altered thirst threshold during hypertonic stress in aging men. *Gerontologist* 25:A118–A119.
- Fitzsimons JT. 1976. The physiological basis of thirst. *Kidney Int* 10:3–11.
- Floch MH, Fuchs H-M. 1978. Modification of stool content by increased bran intake. *Am J Clin Nutr* 31:S185–S189.
- Fomon SJ. 1967. Body composition of the male reference infant during the first year of life. *Pediatrics* 40:863–870.
- Forsum E, Sadurskis A, Wager J. 1988. Resting metabolic rate and body composition of healthy Swedish women during pregnancy. *Am J Clin Nutr* 47:942–947.
- Fortney SM, Nadel ER, Wenger CB, Bove JR. 1981. Effect of blood volume on sweating rate and body fluids in exercising humans. *J Appl Physiol* 51:1594–1600.
- Fortney SM, Wenger CB, Bove JR, Nadel ER. 1984. Effect of hyperosmolality on control of blood flow and sweating. *J Appl Physiol* 57:1688–1695.
- Francesconi RP, Hubbard RW, Szlyk PC, Schnakenberg D, Carlson D, Leva N, Sils I, Hubbard L, Pease V, Young J, Moore D. 1987. Urinary and hematologic indexes of hypohydration. *J Appl Physiol* 62:1271–1276.
- Freund BJ, Young AJ. 1996. Environmental influences on body fluid balance during exercise: Cold exposure. In: Buskirk ER, Puhl SM, eds. *Body Fluid Balance: Exercise and Sport*. Boca Raton, FL: CRC Press. Pp. 159–181.
- Freund BJ, Montain SJ, Young AJ, Sawka MN, DeLuca JP, Pandolf KB, Valeri CR. 1995. Glycerol hyperhydration: Hormonal, renal, and vascular fluid responses.

- J Appl Physiol* 79:2069–2077.
- Fritzsche RG, Switzer TW, Hodgkinson BJ, Lee SH, Martian JC, Coyle EF. 2000. Water and carbohydrate ingestion during prolonged exercise increase maximal neuromuscular power. *J Appl Physiol* 88:730–737.
- Fusch C, Hungerland E, Scharrer B, Moeller H. 1993. Water turnover of healthy children measured by deuterated water elimination. *Eur J Pediatr* 152:110–114.
- Fusch C, Gfrorer W, Koch C, Thomas A, Grunert A, Moeller H. 1996. Water turnover and body composition during long-term exposure to high altitude (4,900–7,600 m). *J Appl Physiol* 80:1118–1125.
- Fusch C, Gfrorer W, Dickhuth H-H, Moeller H. 1998. Physical fitness influences water turnover and body water changes during trekking. *Med Sci Sports Exerc* 30:704–708.
- Gamble JL. 1947. Physiological information gained from studies on the life raft ration. In: The Harvey Society of New York, eds. *The Harvey Lectures*. Lancaster, PA: The Sciences Press Printing Co. Pp. 247–273.
- Gardner JW. 2002. Death by water intoxication. *Mil Med* 167:432–434.
- Gardner JW, Gutmann FD. 2002. Fatal water intoxication of an Army trainee during urine drug test. *Mil Med* 167:435–437.
- Garigan TP, Ristedt DE. 1999. Death from hyponatremia as a result of acute water intoxication in an Army basic trainee. *Mil Med* 164:234–237.
- Gehi MM, Rosenthal RH, Fizette NB, Crowe LR, Webb WL. 1981. Psychiatric manifestations of hyponatremia. *Psychosomatics* 22:739–743.
- Geoffroy-Perez B, Cordier S. 2001. Fluid consumption and the risk of bladder cancer: Results of a multicenter case-control study. *Int J Cancer* 93:880–887.
- Gibbs MA, Wolfson AB, Tayal VS. 2002. Electrolyte disturbances. In: Marx JA, Hockberger RS, Walls RM, Adams J, Barkin RM, Barsan WG, Danzl DF, Gausche-Hill M, Hamilton GC, Ling LJ, Newton E, eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice*, 5th ed. St. Louis, MO: Mosby. Pp. 1724–1744.
- Gisolfi CV, Copping JR. 1974. Thermal effects of prolonged treadmill exercise in the heat. *Med Sci Sports* 6:108–113.
- Gisolfi CV, Ryan AJ. 1996. Gastrointestinal physiology during exercise. In: Buskirk ER, Puhl SM, eds. *Body Fluid Balance: Exercise and Sport*. Boca Raton, FL: CRC Press. Pp. 19–51.
- Goellner MH, Ziegler EE, Formon SJ. 1981. Urination during the first three years of life. *Nephron* 28:174–178.
- Gonzalez-Alonso J, Mora-Rodriguez R, Below PR, Coyle EF. 1997. Dehydration markedly impairs cardiovascular function in hyperthermic endurance athletes during exercise. *J Appl Physiol* 82:1229–1236.
- Gopinathan PM, Pichan G, Sharma VM. 1988. Role of dehydration in heat stress-induced variations in mental performance. *Arch Environ Health* 43:15–17.
- Goran MI, Poehlman ET, Danforth E, Sreekumaran Nair K. 1994. Comparison of body fat estimates derived from underwater weight and total body water. *Int J Obes Relat Metab Disord* 18:622–626.
- Gosselin RE. 1947. Rates of sweating in the desert. In: Adolph EF, ed. *Physiology of Man in the Desert*. New York: Intersciences Publishers. Pp. 44–76.
- Grandjean AC, Reimers KJ, Bannick KE, Haven MC. 2000. The effect of caffeinated, non-caffeinated, caloric and non-caloric beverages on hydration. *J Am Coll Nutr* 19:591–600.
- Greenleaf JE. 1992. Problem: Thirst, drinking behavior, and involuntary dehydration. *Med Sci Sports Exerc* 24:645–656.
- Greenleaf JE, Castle BL. 1971. Exercise temperature regulation in man during

- hypohydration and hyperhydration. *J Appl Physiol* 30:847–853.
- Greenleaf JE, Morimoto T. 1996. Mechanisms controlling fluid ingestion: Thirst and drinking. In: Buskirk ER, Puhl SM, eds. *Body Fluid Balance: Exercise and Sport*. Boca Raton, FL: CRC Press. Pp. 3–17.
- Greenleaf JE, Matter M Jr, Bosco JS, Douglas LG, Averkin EG. 1966. Effects of hypohydration on work performance and tolerance to  $+G_Z$  acceleration in man. *Aerospace Med* 37:34–39.
- Greenleaf JE, Bernauer EM, Juhos LT, Young HL, Morse JT, Staley RW. 1977. Effects of exercise on fluid exchange and body composition in man during 14-day bed rest. *J Appl Physiol* 43:126–132.
- Greiwe JS, Staffey KS, Melrose DR, Narve MD, Knowlton RG. 1998. Effects of dehydration on isometric muscular strength and endurance. *Med Sci Sports Exerc* 30:284–288.
- Grucza R, Szczypaczewska M, Kozlowski S. 1987. Thermoregulation in hyperhydrated men during physical exercise. *Eur J Appl Physiol* 56:603–607.
- Gudivaka R, Schoeller DA, Kushner RF, Bolt MJG. 1999. Single- and multifrequency models for bioelectrical impedance analysis of body water compartments. *J Appl Physiol* 87:1087–1096.
- Gunga HC, Maillet A, Kirsch K, Rocker L, Gharib C, Vaernes R. 1993. Water and salt turnover. *Adv Space Biol Med* 3:185–200.
- Guyton AC, Hall JE. 2000. *Textbook of Medical Physiology*, 10th ed. Philadelphia: WB Saunders.
- Habener JF, Dashe AM, Solomon DH. 1964. Response of normal subjects to prolonged high fluid intake. *J Appl Physiol* 19:134–136.
- Hackney AC, Coyne JT, Pozos R, Feith S, Seale J. 1995. Validity of urine-blood hydriational measures to assess total body water changes during mountaineering in the Sub-Arctic. *Arct Med Res* 54:69–77.
- Hamada K, Doi T, Sakura M, Matsumoto K, Yanagisawa K, Suzuki T, Kikuchi N, Okuda J, Miyazaki H, Okoshi H, Zeniya M, Asukata I. 2002. Effects of hydration on fluid balance and lower-extremity blood viscosity during long airplane flights. *J Am Med Assoc* 287:844–845.
- Hancock PA. 1981. Heat stress impairment of mental performance: A revision of tolerance limits. *Aviat Space Environ Med* 52:177–180.
- Harrison MH, Hill LC, Spaul WA, Greenleaf JE. 1986. Effect of hydration on some orthostatic and hematological responses to head-up tilt. *Eur J Appl Physiol* 55:187–194.
- Haughey BP. 1990. Ingestion of cold fluids: Related to onset of arrhythmias? *Crit Care Nurse* 10:98–110.
- Haussinger D, Lang F, Gerok W. 1994. Regulation of cell function by the cellular hydration state. *Am J Physiol* 267:E343–E355.
- He FJ, Markandu ND, Sagnella GA, MacGregor GA. 2001. Effect of salt intake on renal excretion of water in humans. *Hypertension* 38:317–320.
- Helderman JH, Vestal RE, Rowe JW, Tobin JD, Andres R, Robertson GL. 1978. The response of arginine vasopressin to intravenous ethanol and hypertonic saline in man: The impact of aging. *J Gerontol* 33:39–47.
- Heller KE, Sohn W, Burt BA, Eklund SA. 1999. Water consumption in the United States in 1994–96 and implications for water fluoridation policy. *J Public Health Dent* 59:3–11.
- Heller KE, Sohn W, Burt BA, Feigal RJ. 2000. Water consumption and nursing characteristics of infants by race and ethnicity. *J Public Health Dent* 60:140–146.
- Herbert WG, Ribisl PM. 1972. Effects of dehydration upon physical working capac-

- ity of wrestlers under competitive conditions. *Res Q* 43:416–422.
- Hirvonen T, Pietinen P, Virtanen M, Albanes D, Virtamo J. 1999. Nutrient intake and use of beverages and the risk of kidney stones among male smokers. *Am J Epidemiol* 150:187–194.
- Hooton TM. 1995. A simplified approach to urinary tract infection. *Hosp Pract* 30:23–30.
- Horber FF, Thomi F, Casez JP, Fonteille J, Jaeger P. 1992. Impact of hydration status on body composition as measured by dual energy X-ray absorptiometry in normal volunteers and patients on haemodialysis. *Br J Radiol* 65:895–900.
- Hosking DH, Erickson SB, Van Den Berg CJ, Wilson DM, Smith LH. 1983. The stone clinic effect in patients with idiopathic calcium urolithiasis. *J Urol* 130: 1115–1118.
- Houston ME, Marrin DA, Green HJ, Thomson JA. 1981. The effect of rapid weight loss on physiological functions in wrestlers. *Phys Sportsmed* 9:73–78.
- Hoyt RW, Honig A. 1996. Environmental influences on body fluid balance during exercise: Altitude. In: Buskirk ER, Puhl SM, eds. *Body Fluid Balance: Exercise and Sport*. Boca Raton, FL: CRC Press. Pp. 183–196.
- Hubbard RW, Sandick BL, Matthew WT, Francesconi RP, Sampson JB, Durkot MJ, Maller O, Engell DB. 1984. Voluntary dehydration and alliesthesia for water. *J Appl Physiol* 57:868–873.
- Hyttén FE. 1980. Weight gain in pregnancy. In: Hyttén FE, Chamberlain G, eds. *Clinical Physiology in Obstetrics*. Oxford: Blackwell Scientific. Pp. 193–230.
- Hyttén FE, Leitch I. 1971. *The Physiology of Human Pregnancy*. Oxford: Blackwell Scientific.
- IOM (Institute of Medicine). 1993. *Nutritional Needs in Hot Environments: Applications for Military Personnel in Field Operations*. Washington, DC: National Academy Press.
- IOM. 1994. *Fluid Replacement and Heat Stress*. Washington, DC: National Academy Press.
- IOM. 2001a. *Caffeine for the Sustainment of Mental Task Performance*. Washington, DC: National Academy Press.
- IOM. 2001b. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- IOM. 2002/2005. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*. Washington, DC: The National Academies Press.
- Jacobs I. 1980. The effects of thermal dehydration on performance of the Wingate Anaerobic Test. *Int J Sports Med* 1:21–24.
- Johnson RE. 1964. Water and osmotic economy on survival rations. *J Am Diet Assoc* 45:124–129.
- Jos CJ, Evenson RC, Mallya AR. 1986. Self-induced water intoxication: A comparison of 34 cases with matched controls. *J Clin Psychiatry* 47:368–370.
- Keating JP, Schears GJ, Dodge PR. 1991. Oral water intoxication in infants. An American epidemic. *Am J Dis Child* 145:985–990.
- Keith NM. 1924. Experimental dehydration: Changes in blood composition and body temperature. *Am J Physiol* 68:80–96.
- Kenney WL, Tankersley CG, Newswanger DL, Hyde DE, Puhl SM, Turner NL. 1990. Age and hypohydration independently influence the peripheral vascular response to heat stress. *J Appl Physiol* 68:1902–1908.
- Kim AH, Keltz MD, Arici A, Rosenberg M, Olive DL. 1995. Dilutional hyponatremia during hysteroscopic myomectomy with sorbitol-mannitol distention me-

- dium. *J Am Assoc Gynecol Laparosc* 2:237–242.
- Kimura T, Minai K, Matsui K, Mouri T, Sato T, Yoshinaga K, Hoshi T. 1976. Effect of various states of hydration on plasma ADH and renin in man. *J Clin Endocrinol Metab* 42:79–87.
- Knepper MA, Valtin H, Sands JM. 2000. Renal actions of vasopressin. In: Fray JCS, Goodman HM, eds. *Handbook of Physiology, Section 7, Volume III: Endocrine Regulation of Water and Electrolyte Balance*. New York: Oxford University Press. Pp. 496–529.
- Koczapski AB, Millson RC. 1989. Individual differences in serum sodium levels in schizophrenic men with self-induced water intoxication. *Am J Psychiatry* 146: 1614–1615.
- Korzets A, Ori Y, Floro S, Ish-Tov E, Chagnac A, Weinstein T, Zevin D, Gruzman C. 1996. Case report: Severe hyponatremia after water intoxication: A potential cause of rhabdomyolysis. *Am J Med Sci* 312:92–94.
- Kriemler S, Wilk B, Schurer W, Wilson WM, Bar-Or O. 1999. Preventing dehydration in children with cystic fibrosis who exercise in the heat. *Med Sci Sports Exerc* 31:774–779.
- Kristal-Boneh E, Glusman JG, Chaemovitz C, Cassuto Y. 1988. Improved thermoregulation caused by forced water intake in human desert dwellers. *Eur J Appl Physiol* 57:220–224.
- Kuno Y. 1956. *Human Perspiration*. Springfield, IL: Charles C. Thomas Publisher.
- Kushner RF, Schoeller DA. 1986. Estimation of total body water by bioelectrical impedance analysis. *Am J Clin Nutr* 44:417–424.
- Kushner RF, Schoeller DA, Fjeld CR, Danford L. 1992. Is the impedance index ( $ht^2/R$ ) significant in predicting total body water? *Am J Clin Nutr* 56:835–839.
- Ladell WSS. 1955. The effects of water and salt intake upon the performance of men working in hot and humid environments. *J Physiol* 127:11–46.
- Lane HW, Gretebeck RJ, Schoeller DA, Davis-Street J, Socki RA, Gibson EK. 1997. Comparison of ground-based and space flight energy expenditure and water turnover in middle-aged healthy male US astronauts. *Am J Clin Nutr* 65:4–12.
- Latzka WA, Sawka MN, Montain SJ, Skrinar GS, Fielding RA, Matott RP, Pandolf KB. 1997. Hyperhydration: Thermoregulatory effects during compensable exercise-heat stress. *J Appl Physiol* 83:860–866.
- Latzka WA, Sawka MN, Montain SJ, Skrinar GA, Fielding RA, Matott RP, Pandolf KB. 1998. Hyperhydration: Tolerance and cardiovascular effects during uncompensable exercise-heat stress. *J Appl Physiol* 84:1858–1864.
- Lax D, Eicher M, Goldberg SJ. 1992. Mild dehydration induces echocardiographic signs of mitral valve prolapse in healthy females with prior normal cardiac findings. *Am Heart J* 124:1533–1540.
- Ledochowski M, Kahler M, Dienstl F, Fleischhacker W, Barnes C. 1986. Water intoxication in the course of an acute schizophrenic episode. *Intensive Care Med* 12:47–48.
- Lee DHK. 1964. Terrestrial animals in dry heat: Man in the desert. In: Dill DB, Adolph EF, Wilber CG, eds. *Handbook of Physiology, Section 4: Adaptation to the Environment*. Washington, DC: American Physiological Society. Pp. 551–582.
- Leibowitz HW, Abernethy CN, Buskirk ER, Bar-Or O, Hennessy RT. 1972. The effect of heat stress on reaction time to centrally and peripherally presented stimuli. *Hum Factors* 14:155–160.
- Leiper JB, Carnie A, Maughan RJ. 1996. Water turnover rates in sedentary and exercising middle aged men. *Br J Sports Med* 30:24–26.
- Leiper JB, Pitsiladis Y, Maughan RJ. 2001. Comparison of water turnover rates in

- men undertaking prolonged cycling exercise and sedentary men. *Int J Sports Med* 22:181–185.
- Leon LR. 2002. Invited review: Cytokine regulation of fever: Studies using gene knockout mice. *J Appl Physiol* 92:2648–2655.
- Leoni GB, Pitzalis S, Podda R, Zanda M, Silvetti M, Caocci L, Cao A, Rosatelli MC. 1995. A specific cystic fibrosis mutation (T338I) associated with the phenotype of isolated hypotonic dehydration. *J Pediatr* 127:281–283.
- Levine L, Quigley MD, Cadarette BS, Sawka MN, Pandolf KB. 1990. Physiologic strain associated with wearing toxic-environment protective systems during exercise in the heat. In: Das B, ed. *Advances in Industrial Ergonomics and Safety II*. London: Taylor & Francis. Pp. 897–904.
- Lindeman RD, Lee TD Jr, Yiengst MJ, Shock NW. 1966. Influence of age, renal disease, hypertension, diuretics, and calcium on the antidiuretic responses to suboptimal infusions of vasopressin. *J Lab Clin Med* 68:206–223.
- Lindheimer MD, Davison JM. 1995. Osmoregulation, the secretion of arginine vasopressin and its metabolism during pregnancy. *Eur J Endocrinol* 132:133–143.
- Lindheimer MD, Katz AI. 1985. Fluid and electrolyte metabolism in normal and abnormal pregnancy. In: Arieff AI, DeFronzo RA, eds. *Fluid, Electrolyte, and Acid-Base Disorders*. New York: Churchill Livingstone. Pp. 1041–1086.
- Lindheimer MD, Katz AI. 2000. Renal physiology and disease in pregnancy. In: Seldin DW, Giebisch G, eds. *The Kidney: Physiology and Pathophysiology*. Philadelphia: Lippincott, Williams & Wilkins. Pp. 2597–2644.
- Lloyd LE, McDonald BE, Crampton EW. 1978. Water and its metabolism. In: *Fundamentals of Nutrition*, 2nd ed. San Francisco: WH Freeman. Pp. 22–35.
- Lubin F, Rozen P, Arieli B, Farbstein M, Knaani Y, Bat L, Farbstein H. 1997. Nutritional and lifestyle habits and water-fiber interaction in colorectal adenoma etiology. *Cancer Epidemiol Biomarkers Prev* 6:79–85.
- Luft FC, Fineberg NS, Sloan RS, Hunt JN. 1983. The effect of dietary sodium and protein on urine volume and water intake. *J Lab Clin Med* 101:605–610.
- Lyons TP, Reidesel ML, Meuli LE, Chick TW. 1990. Effects of glycerol-induced hyperhydration prior to exercise in the heat on sweating and core temperature. *Med Sci Sports Exerc* 22:477–483.
- Macias-Nunez JF, Garcia-Iglesias C, Bondia-Roman A, Rodriguez-Commes JL, Corbacho-Becerra L, Tabernero-Romo JM, De Castro del Pozo S. 1978. Renal handling of sodium in old people: A functional study. *Age Ageing* 7:178–181.
- Macias-Nunez JF, Garcia-Iglesias C, Tabernero-Romo JM, Rodriguez-Commes JL, Corbacho-Becerra L, Sanchez-Tomero JA. 1980. Renal management of sodium under indomethacin and aldosterone in the elderly. *Age Ageing* 9:165–172.
- Mack GW, Nadel ER. 1996. Body fluid balance during heat stress in humans. In: Fregly MJ, Blatteis CM, eds. *Handbook of Physiology, Section 4: Environmental Physiology*. New York: Oxford University Press. Pp. 187–214.
- Mack GW, Weseman CA, Langhans GW, Scherzer H, Gillen CM, Nadel ER. 1994. Body fluid balance in dehydrated healthy older men: Thirst and renal osmoregulation. *J Appl Physiol* 76:1615–1623.
- Maresh CM, Bergeron MF, Kenefick RW, Castellani JW, Hoffman JR, Armstrong LE. 2001. Effect of overhydration on time-trial swim performance. *J Strength Cond Res* 15:514–518.
- Martin AD, Daniel MZ, Drinkwater DT, Clarys JP. 1994. Adipose tissue density, estimated adipose lipid fraction and whole body adiposity in male cadavers. *Int J Obes Relat Metab Disord* 18:79–83.

- Math MV, Rampal PM, Faure XR, Delmont JP. 1986. Gallbladder emptying after drinking water and its possible role in prevention of gallstone formation. *Singapore Med J* 27:531–532.
- Maughan RJ, Fenn CE, Leiper JB. 1989. Effects of fluid, electrolyte and substrate ingestion on endurance capacity. *Eur J Appl Physiol* 58:481–486.
- Maughan RJ, Leiper JB, Shirreffs SM. 1996. Restoration of fluid balance after exercise-induced dehydration: Effects of food and fluid intake. *Eur J Appl Physiol Occup Physiol* 73:317–325.
- Mazariegos M, Wang Z-M, Gallagher D, Baumgartner RN, Allison DB, Wang J, Pierson RN, Heymsfield SB. 1994. Differences between young and old females in the five levels of body composition and their relevance to the two-compartment chemical model. *J Gerontol* 49:M201–M208.
- McAloon-Dyke M, David KM, Clark BA, Fish LC, Elahi D, Minaker KL. 1997. Effects of hypertonicity on water intake in the elderly: An age-related failure. *Geriatr Nephrol Urol* 7:11–16.
- McConnell GK, Burge CM, Skinner SL, Hargreaves M. 1997. Influence of ingested fluid volume on physiological responses during prolonged exercise. *Acta Physiol Scand* 160:149–156.
- McConnell GK, Stephens TJ, Canny BJ. 1999. Fluid ingestion does not influence intense 1-h exercise performance in a mild environment. *Med Sci Sports Exerc* 31:386–392.
- Meyer F, Bar-Or O, Salsberg A, Passe D. 1994. Hypohydration during exercise in children: Effect on thirst, drinking preferences, and rehydration. *Int J Sport Nutr* 4:22–35.
- Michaud DS, Spiegelman D, Clinton SK, Rimm EB, Curhan GC, Willett WC, Giovannucci EL. 1999. Fluid intake and the risk of bladder cancer in men. *N Engl J Med* 340:1390–1397.
- Miescher E, Fortney SM. 1989. Responses to dehydration and rehydration during heat exposure in young and older men. *Am J Physiol* 257:R1050–R1056.
- Miller JH, Shock NW. 1953. Age differences in the renal tubular response to antidiuretic hormone. *J Gerontol* 8:446–450.
- Miller PD, Krebs RA, Neal BJH, McIntyre DO. 1982. Hypodipsia in geriatric patients. *Am J Med* 73:354–356.
- Mitchell JB, Voss KW. 1991. The influence of volume on gastric emptying and fluid balance during prolonged exercise. *Med Sci Sports Exerc* 23:314–319.
- Mitchell JW, Nadel ER, Stolwijk JAJ. 1972. Respiratory weight losses during exercise. *J Appl Physiol* 32:474–476.
- Mittleman KD. 1996. Influence of angiotensin II blockade during exercise in the heat. *Eur J Appl Physiol Occup Physiol* 72:542–547.
- Mnatzakanian PA, Vaccaro P. 1982. Effects of 4% dehydration and rehydration on hematological profiles, urinary profiles and muscular endurance of college wrestlers. *Med Sci Sports Exerc* 14:117.
- Molnar GW. 1947. Man in the tropics compared with man in the desert. In: Adolph EF, ed. *Physiology of Man in the Desert*. New York: Intersciences Publishers. Pp. 315–325.
- Montain SJ, Coyle EF. 1992. Influence of graded dehydration on hyperthermia and cardiovascular drift during exercise. *J Appl Physiol* 73:1340–1350.
- Montain SJ, Sawka MN, Cadarette BS, Quigley MD, McKay JM. 1994. Physiological tolerance to uncompensable heat stress: Effects of exercise intensity, protective clothing, and climate. *J Appl Physiol* 77:216–222.
- Montain SJ, Latzka WA, Sawka MN. 1995. Control of thermoregulatory sweating is

- altered by hydration level and exercise intensity. *J Appl Physiol* 79:1434–1439.
- Montain SJ, Laird JE, Latzka WA, Sawka MN. 1997. Aldosterone and vasopressin responses in the heat: Hydration level and exercise intensity effects. *Med Sci Sports Exerc* 29:661–668.
- Montain SJ, Sawka MN, Latzka WA, Valeri CR. 1998a. Thermal and cardiovascular strain from hypohydration: Influence of exercise intensity. *Int J Sports Med* 19:87–91.
- Montain SJ, Smith SA, Mattot RP, Zientara GP, Jolesz FA, Sawka MN. 1998b. Hypohydration effects on skeletal muscle performance and metabolism: A  $^{31}\text{P}$ -MRS study. *J Appl Physiol* 84:1889–1894.
- Montain SJ, Sawka MN, Wenger CB. 2001. Hyponatremia associated with exercise: Risk factors and pathogenesis. *Exerc Sports Sci Rev* 29:113–117.
- Montner P, Stark DM, Riedesel ML, Murata G, Robergs R, Timms M, Chick TW. 1996. Pre-exercise glycerol hydration improves cycling endurance time. *Int J Sports Med* 17:27–33.
- Mor F, Mor-Snir I, Wysenbeek AJ. 1987. Rhabdomyolysis in self-induced water intoxication. *J Nerv Ment Dis* 175:742–743.
- Moran D, Shapiro Y, Epstein Y, Burstein R, Stroschein L, Pandolf KB. 1995. Validation and adjustment of the mathematical prediction model for human rectal temperature responses to outdoor environmental conditions. *Ergonomics* 38: 1011–1018.
- Morimoto A, Murakami N, Ono T, Watanabe T. 1986. Dehydration enhances endotoxin fever by increased production of endogenous pyrogen. *Am J Physiol* 251:R41–R47.
- Morimoto T. 1990. Thermoregulation and body fluids: Role of blood volume and central venous pressure. *Jpn J Physiol* 40:165–179.
- Moroff SV, Bass DE. 1965. Effects of overhydration on man's physiological responses to work in the heat. *J Appl Physiol* 20:267–270.
- Mudambo KSMT, Leese GP, Rennie MJ. 1997a. Dehydration in soldiers during walking/running exercise in the heat and the effects of fluid ingestion during and after exercise. *Eur J Appl Physiol* 76:517–524.
- Mudambo KSMT, Scrimgeour CM, Rennie MJ. 1997b. Adequacy of food rations in soldiers during exercise in hot, day-time conditions assessed by doubly labelled water and energy balance methods. *Eur J Appl Physiol* 76:346–351.
- Murphy DJ, Minaker KL, Fish LC, Rowe JW. 1988. Impaired osmostimulation of water ingestion delays recovery from hyperosmolarity in normal elderly. *Geron-tologist* 28:A141.
- Murray R. 1987. The effects of consuming carbohydrate-electrolyte beverages on gastric emptying and fluid absorption during and following exercise. *Sports Med* 4:322–351.
- Nadel ER, Fortney SM, Wenger CB. 1980. Effect of hydration state on circulatory and thermal regulations. *J Appl Physiol* 49:715–721.
- Nagy KA, Costa DP. 1980. Water flux in animals: Analysis of potential errors in the tritiated water method. *Am J Physiol* 238:R454–R465.
- Neufer PD, Young AJ, Sawka MN. 1989a. Gastric emptying during exercise: Effects of heat stress and hypohydration. *Eur J Appl Physiol* 58:433–439.
- Neufer PD, Young AJ, Sawka MN. 1989b. Gastric emptying during walking and running: Effects of varied exercise intensity. *Eur J Appl Physiol* 58:440–445.
- Neufer PD, Sawka MN, Young AJ, Quigley MD, Latzka WA, Levine L. 1991. Hypohydration does not impair skeletal muscle glycogen resynthesis after exercise. *J Appl Physiol* 70:1490–1494.

- Neuhäuser-Berthold M, Beine S, Verwied SC, Luhrmann PM. 1997. Coffee consumption and total body water homeostasis as measured by fluid balance and bioelectrical impedance analysis. *Ann Nutr Metab* 41:29–36.
- Newburgh LH, Woodwell Johnston M, Falcon-Lesses M. 1930. Measurement of total water exchange. *J Clin Invest* 8:161–196.
- Nielsen B. 1974. Effects of changes in plasma volume and osmolarity on thermoregulation during exercise. *Acta Physiol Scand* 90:725–730.
- Nielsen B, Hansen G, Jorgensen SO, Nielsen E. 1971. Thermoregulation in exercising man during dehydration and hyperhydration with water and saline. *Int J Biometeorol* 15:195–200.
- Nielsen B, Kubica R, Bonnesen A, Rasmussen IB, Stoklosa J, Wilk B. 1981. Physical work capacity after dehydration and hyperthermia. *Scand J Sports Sci* 3:2–10.
- Noakes TD. 2002. Hyponatremia in distance runners: Fluid and sodium balance during exercise. *Curr Sports Med Rep* 4:197–207.
- Noakes TD, Wilson G, Gray DA, Lambert MI, Dennis SC. 2001. Peak rates of diuresis in healthy humans during oral fluid overload. *S Afr Med J* 91:852–857.
- Nose H, Morimoto T, Ogura K. 1983. Distribution of water losses among fluid compartments of tissues under thermal dehydration in the rat. *Jpn J Physiol* 33:1019–1029.
- Nose H, Mack GW, Shi X, Nadel ER. 1988. Role of osmolality and plasma volume during rehydration in humans. *J Appl Physiol* 65:325–331.
- Novak LP. 1989. Changes in total body water during adolescent growth. *Hum Biol* 61:407–414.
- NRC (National Research Council). 1989. *Recommended Dietary Allowances*, 10th ed. Washington, DC: National Academy Press.
- Nurminen ML, Niitynen L, Korpela R, Vapaatalo H. 1999. Coffee, caffeine and blood pressure: A critical review. *Eur J Clin Nutr* 53:831–839.
- O'Brien C, Montain SJ. 2003. Hypohydration effect on finger skin temperature and blood flow during cold-water finger immersion. *J Appl Physiol* 94:598–603.
- O'Brien C, Freund BJ, Sawka MN, McKay J, Hesslink RL, Jones TE. 1996. Hydration assessment during cold-weather military field training exercises. *Arctic Med Res* 55:20–26.
- O'Brien C, Young AJ, Sawka MN. 1998. Hypohydration and thermoregulation in cold air. *J Appl Physiol* 84:185–189.
- O'Brien C, Baker-Fulco CJ, Young AJ, Sawka MN. 1999. Bioimpedance assessment of hypohydration. *Med Sci Sports Exerc* 31:1466–1471.
- O'Brien C, Young AJ, Sawka MN. 2002. Bioelectrical impedance to estimate changes in hydration status. *Int J Sports Med* 23:361–366.
- O'Brien KK, Montain SJ, Corr WP, Sawka MN, Knapik JJ, Craig SC. 2001. Hyponatremia associated with overhydration in U.S. Army trainees. *Mil Med* 166:405–410.
- Okuno T, Yawata T, Nose H, Morimoto T. 1988. Difference in rehydration process due to salt concentration of drinking water in rats. *J Appl Physiol* 64:2438–2443.
- Okura M, Okada K, Nagamine I, Yamaguchi H, Karisha K, Ishimoto Y, Ikuta T. 1990. Electroencephalographic changes during and after water intoxication. *Jpn J Psychiatry Neurol* 44:729–734.
- Olsson K-E, Saltin B. 1970. Variation in total body water with muscle glycogen changes in man. *Acta Physiol Scand* 80:11–18.
- Orenstein DM, Henke KG, Costill DL, Doershuk CF, Lemon PJ, Stern RC. 1983. Exercise and heat stress in cystic fibrosis patients. *Pediatr Res* 17:267–269.
- Passmore AP, Kondowe GB, Johnston GD. 1987. Renal and cardiovascular effects

- of caffeine: A dose-response study. *Clin Sci* 72:749–756.
- Phillips PA, Rolls BJ, Ledingham JGG, Forsling ML, Morton JJ, Crowe MJ, Wollner L. 1984. Reduced thirst after water deprivation in healthy elderly men. *N Engl J Med* 311:753–759.
- Pichan G, Gauttam RK, Tomar OS, Bajaj AC. 1988. Effect of primary hypohydration on physical work capacity. *Int J Biometeorol* 32:176–180.
- Pitt M. 1989. Fluid intake and urinary tract infection. *Nurs Times* 85:36–38.
- Pitts GC, Johnson RE, Consolazio FC. 1944. Work in the heat as affected by intake of water, salt and glucose. *Am J Physiol* 142:253–259.
- Pohllabeln H, Jockel K-H, Bolm-Audorff U. 1999. Non-occupational risk factors for cancer of the lower urinary tract in Germany. *Eur J Epidemiol* 15:411–419.
- Popowski LA, Oppliger RA, Lambert GP, Johnson RF, Johnson AK, Gisolf CV. 2001. Blood and urinary measures of hydration status during progressive acute dehydration. *Med Sci Sports Exerc* 33:747–753.
- Posner L, Mokrzycki MH. 1996. Transient central diabetes insipidus in the setting of underlying chronic nephrogenic diabetes insipidus associated with lithium use. *Am J Nephrol* 16:339–343.
- Pratte AL, Padilla GV, Baker VE. 1973. Alterations in cardiac activity from ingestion of ice water. *Commun Nurs Res* 6:148–155.
- Raman A, Schoeller DA, Subar AF, Troiano RP, Schatzkin A, Harris T, Bauer D, Bingham S, Everhart J, Newman AB, Tylavsky FA. 2004. Water turnover in US adults 40–79 years of age. *Am J Physiol Renal Physiol* 286:F394–F401.
- Rehrer NJ, Beckers EJ, Brouns F, Ten Hoor F, Saris WHM. 1990. Effects of dehydration on gastric emptying and gastrointestinal distress while running. *Med Sci Sports Exerc* 22:790–795.
- Remick D, Chancellor K, Pederson J, Zambraski EJ, Sawka MN, Wenger CB. 1998. Hyperthermia and dehydration-related deaths associated with intentional rapid weight loss in three collegiate wrestlers—North Carolina, Wisconsin, and Michigan, November–December 1997. *Morb Mortal Wkly Rep* 47:105–108.
- Richmond CA. 2001. Effects of hydration on febrile temperature patterns in rabbits. *Biol Res Nurs* 2:277–291.
- Rivera-Brown AM, Gutierrez R, Gutierrez JC, Frontera WR, Bar-Or O. 1999. Drink composition, voluntary drinking, and fluid balance in exercising, trained, heat-acclimatized boys. *J Appl Physiol* 86:78–84.
- Robinson TA, Hawley JA, Palmer GS, Wilson GR, Gray DA, Noakes TD, Dennis SC. 1995. Water ingestion does not improve 1-h cycling performance in moderate ambient temperatures. *Eur J Appl Physiol* 71:153–160.
- Rolls BJ, Rolls ET. 1982. *Thirst*. Cambridge: Cambridge University Press.
- Roth J, Schulze K, Simon E, Zeisberger E. 1992. Alteration of endotoxin fever and release of arginine vasopressin by dehydration in the guinea pig. *Neuroendocrinology* 56:680–686.
- Rothstein A, Towbin EJ. 1947. Blood circulation and temperature of men dehydrating in the heat. In: Adolph EF, ed. *Physiology of Man in the Desert*. New York: Intersciences Publishers. Pp. 172–196.
- Rowe JW, Shock NW, DeFronzo RA. 1976. The influence of age on the renal response to water deprivation in man. *Nephron* 17:270–278.
- Rowe JW, Minaker KL, Sparrow D, Robertson GL. 1982. Age-related failure of volume-pressure-mediated vasopressin release. *J Clin Endocrinol Metab* 54:661–664.
- Ruby BC, Shriver TC, Zderic TW, Sharkey BJ, Burks C, Tysk S. 2002. Total energy expenditure during arduous wildfire suppression. *Med Sci Sports Exerc* 34:1048–

- 1054.
- Ryan AJ, Lambert GP, Shi X, Chang RT, Summers RW, Gisolfi CV. 1998. Effect of hypohydration on gastric emptying and intestinal absorption during exercise. *J Appl Physiol* 84:1581–1588.
- Saltin B. 1964. Aerobic and anaerobic work capacity after dehydration. *J Appl Physiol* 19:1114–1118.
- Sanford RA, Wells BB. 1962. The urine. In: Davidsohn I, Wells BB, eds. *Clinical Diagnosis by Laboratory Methods*. Philadelphia: WB Saunders. Pp. 22–60.
- Sawka MN. 1988. Body fluid responses and hypohydration during exercise-heat stress. In: Pandolf KB, Sawka MN, Gonzalez RR, eds. *Human Performance Physiology and Environmental Medicine at Terrestrial Extremes*. Indianapolis, IN: Benchmark Press. Pp. 227–266.
- Sawka MN. 1992. Physiological consequences of hypohydration: Exercise performance and thermoregulation. *Med Sci Sports Exerc* 24:657–670.
- Sawka MN, Coyle EF. 1999. Influence of body water and blood volume on thermoregulation and exercise performance in the heat. In: Holloszy, ed. *Exercise and Sport Sciences Reviews*. Vol 27. Baltimore, MD: Lippincott, Williams & Wilkins. Pp. 167–218.
- Sawka MN, Montain SJ. 2001. Fluid and electrolyte balance: Effects on thermoregulation and exercise in the heat. In: Bowman BA, Russell RM, eds. *Present Knowledge in Nutrition*, 8th ed. Washington, DC: ILSI Press. Pp. 115–124.
- Sawka MN, Knowlton RG, Critz JB. 1979. Thermal and circulatory responses to repeated bouts of prolonged running. *Med Sci Sports* 11:177–180.
- Sawka MN, Hubbard RW, Francesconi RP, Horstman DH. 1983a. Effects of acute plasma volume expansion on altering exercise-heat performance. *Eur J Appl Physiol* 51:303–312.
- Sawka MN, Toner MM, Francesconi RP, Pandolf KB. 1983b. Hypohydration and exercise: Effects of heat acclimation, gender, and environment. *J Appl Physiol* 55:1147–1153.
- Sawka MN, Francesconi RP, Pimental NA, Pandolf KB. 1984a. Hydration and vascular fluid shifts during exercise in the heat. *J Appl Physiol* 56:91–96.
- Sawka MN, Francesconi RP, Young AJ, Pandolf KB. 1984b. Influence of hydration level and body fluids on exercise performance in the heat. *J Am Med Assoc* 252:1165–1169.
- Sawka MN, Young AJ, Francesconi RP, Muza SR, Pandolf KB. 1985. Thermoregulatory and blood responses during exercise at graded hypohydration levels. *J Appl Physiol* 59:1394–1401.
- Sawka MN, Gonzalez RR, Young AJ, Muza SR, Pandolf KB, Latzka WA, Dennis RC, Valeri CR. 1988. Polycythemia and hydration: Effects on thermoregulation and blood volume during exercise-heat stress. *Am J Physiol* 255:R456–R463.
- Sawka MN, Gonzalez RR, Young AJ, Dennis RC, Valeri CR, Pandolf KB. 1989a. Control of thermoregulatory sweating during exercise in the heat. *Am J Physiol* 257:R311–R316.
- Sawka MN, Young AJ, Dennis RC, Gonzalez RR, Pandolf KB, Valeri CR. 1989b. Human intravascular immunoglobulin responses to exercise-heat and hypohydration. *Aviat Space Environ Med* 60:634–638.
- Sawka MN, Young AJ, Latzka WA, Neufer PD, Quigley MD, Pandolf KB. 1992. Human tolerance to heat strain during exercise: Influence of hydration. *J Appl Physiol* 73:368–375.
- Sawka MN, Wenger CB, Pandolf KB. 1996a. Thermoregulatory responses to acute exercise-heat stress and heat acclimation. In: Fregly MJ, Blatteis CM, eds. *Hand-*

- book of Physiology. Section 4: Environmental Physiology, Volume 1.* New York: Oxford University Press. Pp. 157–185.
- Sawka MN, Young AJ, Rock PB, Lyons TP, Boushel R, Freund BJ, Muza SR, Cymerman A, Dennis RC, Pandolf KB, Valeri CR. 1996b. Altitude acclimatization and blood volume: Effects of exogenous erythrocyte volume expansion. *J Appl Physiol* 81:636–642.
- Sawka MN, Convertino VA, Eichner ER, Schnieder SM, Young AJ. 2000. Blood volume: Importance and adaptations to exercise training, environmental stresses, and trauma/sickness. *Med Sci Sports Exerc* 32:332–348.
- Sawka MN, Montain SJ, Latzka WA. 2001. Hydration effects on thermoregulation and performance in the heat. *Comp Biochem Physiol A* 128:679–690.
- Schloerb PR, Friis-Hansen BJ, Edelman IS, Solomon AK, Moore FD. 1950. The measurement of total body water in the human subject by deuterium oxide dilution. *J Clin Invest* 29:1296–1310.
- Schroeder C, Bush VE, Norcliffe LJ, Luft FC, Tank J, Jordan J, Hainsworth R. 2002. Water drinking acutely improves orthostatic tolerance in health subjects. *Circulation* 106:2806–2811.
- Scott EM, Greenwood JP, Gilby SG, Stoker JB, Mary DASG. 2001. Water ingestion increases sympathetic vasoconstrictor discharge in normal human subjects. *Clin Sci* 100:335–342.
- Senay LC Jr, Christensen ML. 1965. Changes in blood plasma during progressive dehydration. *J Appl Physiol* 20:1136–1140.
- Serfass RC, Stull GA, Alexander JF, Ewing JL Jr. 1984. The effects of rapid weight loss and attempted rehydration on strength and endurance of the handgripping muscles in college wrestlers. *Res Q Exerc Sport* 55:46–52.
- Seymour DG, Henschke PJ, Cape RDT, Campbell AJ. 1980. Acute confusional states and dementia in the elderly: The role of dehydration/volume depletion, physical illness and age. *Age Ageing* 9:137–146.
- Shannon IL, Segreto VA. 1968. *Saliva Specific Gravity*. Technical Report SAM-TR-68-88. Brooks Air Force Base, TX: United States Air Force. Pp. 1–8.
- Shannon J, White E, Shattuck AL, Potter JD. 1996. Relationship of food groups and water intake to colon cancer risk. *Cancer Epidemiol Biomarkers Prev* 5:495–502.
- Shapiro Y, Pandolf KB, Goldman RF. 1982. Predicting sweat loss response to exercise, environment and clothing. *Eur J Appl Physiol Occup Physiol* 48:83–96.
- Shapiro Y, Moran D, Epstein Y, Stroschein L, Pandolf KB. 1995. Validation and adjustment of the mathematical prediction model for human sweat rate responses to outdoor environmental conditions. *Ergonomics* 38:981–986.
- Share L, Claybaugh JR, Hatch FE Jr, Johnson JG, Lee S, Muirhead EE, Shaw P. 1972. Effects of change in posture and of sodium depletion on plasma levels of vasopressin and renin in normal human subjects. *J Clin Endocrinol Metab* 35:171–174.
- Sharma VM, Pichan G, Panwar MR. 1983. Differential effects of hot-humid and hot-dry environments on mental functions. *Int Arch Occup Environ Health* 52: 315–327.
- Sharma VM, Sridharan K, Pichan G, Panwar MR. 1986. Influence of heat-stress induced dehydration on mental functions. *Ergonomics* 29:791–799.
- Ship JA, Fischer DJ. 1997. The relationship between dehydration and parotid salivary gland function in young and older healthy adults. *J Gerontol* 52A:M310–M319.
- Ship JA, Fischer DJ. 1999. Metabolic indicators of hydration status in the predi-

- tion of parotid salivary-gland function. *Arch Oral Biol* 44:343–350.
- Shirreffs SM, Maughan RJ. 1998. Urine osmolality and conductivity as indicies of hydration status in athletes in the heat. *Med Sci Sports Exerc* 30:1598–1602.
- Shore AC, Markandu ND, Sagnella GA, Singer DRJ, Forsling ML, Buckley MG, Sugden AL, MacGregor GA. 1988. Endocrine and renal response to water loading and water restriction in normal man. *Clin Sci* 75:171–177.
- Sidi Y, Gassner S, Sandbank U, Keren G, Pinkhas J. 1984. Water intoxication, hyperpyrexia and rhabdomyolysis in a patient with psychogenic polydipsia. *NY State J Med* 84:462–464.
- Siegel AJ, Baldessarini RJ, Klepser MB, McDonald JC. 1998. Primary and drug-induced disorders of water homeostasis in psychiatric patients: Principles of diagnosis and management. *Harvard Rev Psychiatry* 6:190–200.
- Singer RN, Weiss SA. 1968. Effects of weight reduction on selected anthropometric, physcial, and performance measures of wrestlers. *Res Q* 39:361–369.
- Slattery ML, West DW, Robison LM. 1988. Fluid intake and bladder cancer in Utah. *Int J Cancer* 42:17–22.
- Slattery ML, Caan BJ, Anderson KE, Potter JD. 1999. Intake of fluids and methylxanthine-containing beverages: Association with colon cancer. *Int J Cancer* 81: 199–204.
- Sleeper FH. 1935. Investigation of polyuria in schizophrenia. *Am J Psychiatry* 91: 1019–1031.
- Snyder NA, Fiegal DW, Ariegg AI. 1987. Hypernatremia in elderly patients. A heterogeneous, morbid, and iatrogenic entity. *Ann Intern Med* 107:309–319.
- Speedy DB, Noakes TD, Boswell T, Thompson JM, Rehrer N, Boswell DR. 2001. Response to a fluid load in athletes with a history of exercise induced hyponatremia. *Med Sci Sports Exerc* 33:1434–1442.
- Sproles CB, Smith DP, Byrd RJ, Allen TE. 1976. Circulatory responses to submaximal exercise after dehydration and rehydration. *J Sports Med* 16:98–105.
- Stachenfeld NS, Mack GW, Takamata A, DiPietro L, Nadel ER. 1996. Thirst and fluid regulatory responses to hypertonicity in older adults. *Am J Physiol* 271: R757–R765.
- Stachenfeld NS, DiPietro L, Nadel ER, Mack GW. 1997. Mechanism of attenuated thirst in aging: Role of central volume receptors. *Am J Physiol* 272:R148–R157.
- Stone KA. 1999. Lithium-induced nephrogenic diabetes insipidus. *J Am Board Fam Pract* 12:43–47.
- Stookey JD. 1999. The diuretic effects of alcohol and caffeine and total water intake misclassification. *Eur J Epidemiol* 15:181–188.
- Stricker EM, Sved AF. 2000. Thirst. *Nutrition* 16:821–826.
- Strydom NB, Holdsworth LD. 1968. The effects of different levels of water deficit on physiological responses during heat stress. *Int Z Angew Physiol* 26:95–102.
- Susset J. 1993. The hazards of excessive fluid intake. *J Urol Nurs* 12:605–608.
- Svenberg T, Christofides ND, Fitzpatrick ML, Bloom SR, Welbourn RB. 1985. Oral water causes emptying of the human gallbladder through actions of vagal stimuli rather than motilin. *Scand J Gastroenterol* 20:775–778.
- Szlyk PC, Sils IV, Francesconi RP, Hubbard RW, Armstrong LE. 1989. Effects of water temperature and flavoring on voluntary dehydration in man. *Physiol Behav* 45:639–647.
- Szlyk PC, Sils IV, Francesconi RP, Hubbard RW. 1990. Patterns of human drinking: Effects of exercise, water temperature, and food consumption. *Aviat Space Environ Med* 61:43–48.

- Taivainen H, Laitinen R, Tahtela R, Kiiasmaa K, Valimaki MJ. 1995. Role of plasma vasopressin in changes of water balance accompanying acute alcohol intoxication. *Alcohol Clin Exp Res* 19:759–762.
- Tietz NW. 1995. *Clinical Guide to Laboratory Tests*, 3rd ed. Philadelphia: WB Saunders.
- Tilkian SM, Boudreau Conover M, Tilkian AG. 1995. *Clinical & Nursing Implications of Laboratory Tests*, 5th ed. St. Louis: Mosby.
- Tomiyama J, Kametani H, Kumagai Y, Adachi Y, Tohri K. 1990. Water intoxication and rhabdomyolysis. *Jpn J Med* 29:52–55.
- Torranin C, Smith DP, Byrd RJ. 1979. The effect of acute thermal dehydration and rapid rehydration on isometric and isotonic endurance. *J Sports Med* 19:1–9.
- Tuttle WW. 1943. The effect of weight loss by dehydration and the withholding of food on the physiologic responses of wrestlers. *Res Q* 14:158–166.
- U.S. Army. 1959. *Southwest Asia: Environment and its Relationship to Military Activities*. Technical Report EP-118. Natick, MA: Environmental Protection Research Division, Quartermaster Research and Engineering Command, U.S. Army.
- U.S. Army. 2003. *Heat Stress Control and Heat Casualty Management*. TB MED 507/AFPAM 48-152(I). Washington, DC: Department of the Army and Air Force.
- USDA/ARS (U.S. Department of Agriculture/Agricultural Research Service). 2002. *USDA National Nutrient Database for Standard Reference, Release 15*. Online. Available at <http://www.nal.usda.gov/fnic/foodcomp>. Accessed June 30, 2003.
- Valtin H. 2002. Drink at least eight glasses of water a day. Really? Is there scientific evidence for “8 x 8”? *Am J Physiol* 283:R993–1004.
- Van Loan MD, Boileau RA. 1996. Age, gender, and fluid balance. In: Buskirk ER, Puhl SM, eds. *Body Fluid Balance: Exercise and Sport*. Boca Raton, FL: CRC Press. Pp. 215–230.
- Van Loan MD, Kopp LE, King JC, Wong WW, Mayclin PL. 1995. Fluid changes during pregnancy: Use of bioimpedance spectroscopy. *J Appl Physiol* 78:1037–1042.
- Vio FR, Infante CB, Lara WC, Mardones-Santander F, Rosso PR. 1986. Validation of the deuterium dilution technique for the measurement of fluid intake in infants. *Hum Nutr Clin Nutr* 40C:327–332.
- Visser M, Gallagher D. 1998. Age-related change in body water and hydration in old age. In: Arnaud MJ, ed. *Hydration Throughout Life*. Montrouge, France: John Libbey Eurotext. Pp. 117–125.
- Visser M, Gallagher D, Deurenberg P, Wang J, Peirson RN Jr, Heymsfield SB. 1997. Density of fat-free body mass: Relationship with race, age, and level of body fatness. *Am J Physiol* 272:E781–E787.
- Wagner JA, Robinson S, Tzankoff SP, Marino RP. 1972. Heat tolerance and acclimatization to work in the heat in relation to age. *J Appl Physiol* 33:616–622.
- Wakefield B, Mentes J, Diggelmann L, Culp K. 2002. Monitoring hydration status in elderly veterans. *West J Nurs Res* 24:132–142.
- Walsh NP, Montague JC, Callow N, Rowlands AV. 2004. Saliva flow rate, total protein concentration and osmolality as potential markers of whole body hydration status during progressive acute dehydration in humans. *Arch Oral Biol* 49:149–154.
- Walsh RM, Noakes TD, Hawley JA, Dennis SC. 1994. Impaired high-intensity cycling performance time at low levels of dehydration. *Int J Sports Med* 15:392–398.
- Watanabe T, Hashimoto M, Wada M, Imoto T, Miyoshi M, Sadamitsu D, Maekawa T. 2000. Angiotensin-converting enzyme inhibitor inhibits dehydration-enhanced fever induced by endotoxin in rats. *Am J Physiol* 279:R1512–R1516.

- Webster S, Rutt R, Weltman A. 1990. Physiological effects of a weight loss regimen practiced by college wrestlers. *Med Sci Sports Exerc* 22:229–234.
- Weinberg AD, Pals JK, Levesque PG, Beal LF, Cunningham TJ, Minaker KL. 1994a. Dehydration and death during febrile episodes in the nursing home. *J Am Geriatr Soc* 42:968–971.
- Weinberg AD, Pals JK, McGlinchey-Berroth R, Minaker KL. 1994b. Indices of dehydration among frail nursing home patients: Highly variable but stable over time. *J Am Geriatr Soc* 42:1070–1073.
- Welch BE, Buskirk ER, Iampietro PF. 1958. Relation of climate and temperature to food and water intake in man. *Metabolism* 7:141–148.
- Wenger CB. 1972. Heat of evaporation of sweat: Thermodynamic considerations. *J Appl Physiol* 32:456–459.
- West JB. 1990. Regulation of volume and osmolality of the body fluids. In: West JB, ed. *Best and Taylor's Physiological Basis of Medical Practice*, 11th ed. Baltimore: Williams and Wilkins. Pp. 478–485.
- Wierzuchowski M. 1936. The limiting rate of assimilation of glucose introduced intravenously at constant speed in the resting dog. *J Physiol* 87:311–335.
- Wilk B, Bar-Or O. 1996. Effect of drink flavor and NaCl on voluntary drinking and hydration in boys exercising in the heat. *J Appl Physiol* 80:1112–1117.
- Wilkens LR, Kadir MM, Kolonel LN, Nomura AMY, Hankin JH. 1996. Risk factors for lower urinary tract cancer: The role of total fluid consumption, nitrates and nitrosamines, and selected foods. *Cancer Epidemiol Biomarkers Prev* 5:161–166.
- Yamamura T, Takahashi T, Kusunoki M, Kantoh M, Seino Y, Utsunomiya J. 1988. Gallbladder dynamics and plasma cholecystokinin responses after meals, oral water, or sham feeding in healthy subjects. *Am J Med Sci* 295:102–107.
- Yokozawa K, Torikoshi S, Nagano J, Ito K, Suzuki Y. 1993. Water intake and urinary volume during 20 days bed-rest in young women. *Physiologist* 36:S123–S124.
- Yonemura K, Hishida A, Miyajima H, Tawarahara K, Mizoguchi K, Nishimura Y, Ohishi K. 1987. Water intoxication due to excessive water intake: Observation of initiation stage. *Jpn J Med* 26:249–252.
- Young AJ, Muza SR, Sawka MN, Pandolf KB. 1987. Human vascular fluid responses to cold stress are not altered by cold acclimation. *Undersea Biomed Res* 14:215–228.
- Zambraski EJ. 1996. The kidney and body fluid balance during exercise. In: Buskirk ER, Puhl SM, eds. *Body Fluid Balance: Exercise and Sport*. Boca Raton, FL: CRC Press. Pp. 75–95.
- Zambraski EJ, Tipton CM, Jordon HR, Palmer WK, Tcheng TK. 1974. Iowa wrestling study: Urinary profiles of state finalists prior to competition. *Med Sci Sports* 6:129–132.
- Zellner DA, Bartoli AM, Eckard R. 1991. Influence of color on odor identification and liking ratings. *Am J Psychol* 104:547–561.

Ibid., Chapter 8, pp. 462–464.

- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.

- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- IOM. 2001. *Caffeine for the Sustainment of Mental Task Performance*. Washington, DC: National Academy Press.
- IOM. 2002/2005. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*. Washington, DC: The National Academies Press.
- IOM. 2003. *Dietary Reference Intakes: Applications in Dietary Planning*. Washington, DC: The National Academies Press.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Schoeller DA. 1995. Limitations in the assessment of dietary energy by self-report. *Metabolism* 44:18–22.
- Schoeller DA, Bandini LG, Dietz WH. 1990. Inaccuracies in self-reported intake identified by comparison with the doubly labelled water method. *Can J Physiol Pharmacol* 68:941–949.
- Taivainen H, Laitinen R, Tahtela R, Kiianmaa K, Valimaki MJ. 1995. Role of plasma vasopressin in changes of water balance accompanying acute alcohol intoxication. *Alcohol Clin Exp Res* 19:759–762.
- Vasan RS, Beiser A, Seshadri S, Larson MG, Kannel WB, D'Agostino RB, Levey D. 2002. Residual lifetime risk for developing hypertension in middle-aged women and men: The Framingham Heart Study. *J Am Med Assoc* 287:1003–1010.

## VITAMIN A

*Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*  
 (ISBN 0-309-07290-5), Chapter 4, pp. 146–161.

- AAP (American Academy of Pediatrics Committee on Infectious Diseases). 1993. Vitamin A treatment of measles. *Pediatrics* 91:1014–1015.
- Abedin Z, Hussain MA, Ahmad K. 1976. Liver reserve of vitamin A from medico-legal cases in Bangladesh. *Bangladesh Med Res Counc Bull* 2:43–51.
- Alvarez JO, Salazar-Lindo E, Kohatsu J, Miranda P, Stephensen CB. 1995. Urinary excretion of retinol in children with acute diarrhea. *Am J Clin Nutr* 61:1273–1276.
- Amedee-Manesme O, Anderson D, Olson JA. 1984. Relation of the relative dose response to liver concentrations of vitamin A in generally well-nourished surgical patients. *Am J Clin Nutr* 39:898–902.
- Amedee-Manesme O, Mourey MS, Hanck A, Therasse J. 1987. Vitamin A relative dose response test: Validation by intravenous injection in children with liver disease. *Am J Clin Nutr* 46:286–289.
- Amine EK, Corey J, Hegsted DM, Hayes KC. 1970. Comparative hematology during deficiencies of iron and vitamin A in the rat. *J Nutr* 100:1033–1040.
- Arena JM, Sarazen P, Baylin GJ. 1951. Hypervitaminosis A: Report of an unusual case with marked craniotabes. *Pediatrics* 8:788–794.
- Arroyave G, Aguilar JR, Flores M, Guzman MA. 1979. *Evaluation of Sugar Fortification with Vitamin A at the National Level*. Scientific Publication No. 384. Washington, DC: Pan American Health Organization.
- Arthur P, Kirkwood B, Ross D, Morris S, Gyapong J, Tomkins A, Addy H. 1992. Impact of vitamin A supplementation on childhood morbidity in northern Ghana. *Lancet* 339:361–362.
- Baly DL, Golub MS, Gershwin ME, Hurley LS. 1984. Studies of marginal zinc deprivation in rhesus monkeys. III. Effects on vitamin A metabolism. *Am J Clin Nutr* 40:199–207.
- Bankson DD, Ellis JK, Russell RM. 1989. Effects of a vitamin-A-free diet on tissue vitamin A concentration and dark adaptation of aging rats. *Exp Gerontol* 24:127–136.
- Barclay AJ, Foster A, Sommer A. 1987. Vitamin A supplements and mortality related to measles: A randomised clinical trial. *Br Med J* 294:294–296.
- Barreto ML, Santos LM, Assis AM, Araujo MP, Farenzena GG, Santos PA, Fiaccone RL. 1994. Effect of vitamin A supplementation on diarrhoea and acute lower-respiratory-tract infections in young children in Brazil. *Lancet* 344:228–231.
- Barua AB, Olson JA. 1989. Chemical synthesis of all-trans [ $^{11}\text{H}$ ]-retinoyl  $\beta$ -glucuronide in its metabolism in rats *in vivo*. *Biochem J* 263:403–409.
- Batchelder EL, Ebbs JC. 1943. Some observations of dark adaptation in man and their bearing on the problem of human requirement for vitamin A. *Rhode Island Agricultural Experiment Station Bulletin*, No. 645.
- Bauernfeind JC. 1972. Carotenoid vitamin A precursors and analogs in foods and feeds. *J Agric Food Chem* 20:456–473.
- Bauernfeind JC. 1980. *The Safe Use of Vitamin A*. A report of the International Vitamin A Consultative Group. Washington, DC: The Nutrition Foundation.

- Bausch J, Rietz P. 1977. Method for the assessment of vitamin A liver stores. *Acta Vitaminol Enzymol* 31:99–112.
- Beaton GH, Martorell R, Aronson KJ, Edmonston B, McCabe G, Ross AC, Harvey B. 1993. *Effectiveness of Vitamin A Supplementation in the Control of Young Child Morbidity and Mortality in Developing Countries*. Geneva: Subcommittee on Nutrition, Administrative Committee on Coordination, World Health Organization.
- Beaton GH, Milner J, McGuire V, Feather TE, Little JA. 1983. Source of variance in 24-hour dietary recall data: Implications for nutrition study design and interpretation. Carbohydrate source, vitamins and minerals. *Am J Clin Nutr* 37:986–995.
- Bendich A, Langseth L. 1989. Safety of vitamin A. *Am J Clin Nutr* 49:358–371.
- Bernhardt IB, Dorsey DJ. 1974. Hypervitaminosis A and congenital renal anomalies in a human infant. *Obstet Gynecol* 43:750–755.
- Blanchard EL, Harper HA. 1940. Measurement of vitamin A status of young adults by the dark adaptation technic. *Arch Int Med* 66:661–669.
- Blaner WS, Olson JA. 1994. Retinol and retinoic acid metabolism. In: Sporn MB, Roberts AB, Goodman DS, eds. *The Retinoids: Biology, Chemistry, and Medicine*, 2nd ed. New York: Raven Press. Pp. 229–255.
- Bloem MW, Wedel M, Egger RJ, Speek AJ, Schrijver J, Saowakontha S, Schreurs WH. 1989. Iron metabolism and vitamin A deficiency in children in northeast Thailand. *Am J Clin Nutr* 50:332–338.
- Bloem MW, Wedel M, Egger RJ, Speek AJ, Schrijver J, Saowakontha S, Schreurs WH. 1990. Mild vitamin A deficiency and risk of respiratory tract diseases and diarrhea in preschool and school children in northeastern Thailand. *Am J Epidemiol* 131:332–339.
- Blomhoff HK, Smeland EB, Erikstein B, Rasmussen AM, Skrede B, Skjonsberg C, Blomhoff R. 1992. Vitamin A is a key regulator for cell growth, cytokine production, and differentiation in normal B cells. *J Biol Chem* 267:23988–23992.
- Blomstrand RM, Werner B. 1967. Studies on the intestinal absorption of radioactive β-carotene and vitamin A in man. *Scand J Clin Lab Invest* 19:339–345.
- Boileau TW, Moore AC, Erdman JW Jr. 1999. Carotenoids and vitamin A. In: Papas AM, ed. *Antioxidant Status, Diet, Nutrition and Health*. Boca Raton, FL: CRC Press. Pp. 133–158.
- Borel P, Dubois C, Mekki N, Grolier P, Partier A, Alexandre-Gouabau MC, Lairon D, Azais-Braesco V. 1997. Dietary triglycerides, up to 40 g/meal, do not affect preformed vitamin A bioavailability in humans. *Eur J Clin Nutr* 51:717–722.
- Borel P, Mekki N, Boirie Y, Partier A, Alexandre-Gouabau MC, Grolier P, Beaufrere B, Portugal H, Lairon D, Azais-Braesco V. 1998. Comparison of the post-prandial plasma vitamin A response in young and older adults. *J Gerontol A Biol Sci Med Sci* 53:B133–B140.
- Brent RL, Hendrickx AG, Holmes LB, Miller RK. 1996. Teratogenicity of high vitamin A intake. *N Engl J Med* 334:1196–1197.
- Brubacher G, Weiser H. 1985. The vitamin A activity of beta-carotene. *Int J Vitam Nutr Res* 55:5–15.
- Bush ME, Dahms BB. 1984. Fatal hypervitaminosis A in a neonate. *Arch Pathol Lab Med* 108:838–842.
- Butera ST, Krakowka S. 1986. Assessment of lymphocyte function during vitamin A deficiency. *Am J Vet Res* 47:850–855.
- Butte NF, Calloway DH. 1981. Evaluation of lactational performance of Navajo women. *Am J Clin Nutr* 34:2210–2215.

- Canfield LM, Giuliano AR, Neilson EM, Yap HH, Graver EJ, Cui HA, Blashill BM. 1997. Beta-carotene in breast milk and serum is increased after a single beta-carotene dose. *Am J Clin Nutr* 66:52–61.
- Canfield LM, Giuliano AR, Neilson EM, Blashill BM, Graver EJ, Yap HH. 1998. Kinetics of the response of milk and serum beta-carotene to daily beta-carotene supplementation in healthy, lactating women. *Am J Clin Nutr* 67:276–283.
- Cantorna MT, Nashold FE, Hayes CE. 1995. Vitamin A deficiency results in a priming environment conducive for TH1 cell development. *Eur J Immunol* 25:1673–1679.
- Carlier C, Moulia-Pelat J-P, Ceccon J-F, Mourey MS, Fall M, N'Diaye M, Amedee-Manesme. 1991. Prevalence of malnutrition and vitamin A deficiency in the Diourbel, Fatick and Kaolack regions of Senegal: Feasibility of the method of impression cytology with transfer. *Am J Clin Nutr* 53:66–69.
- Carman JA, Smith SM, Hayes CE. 1989. Characterization of a helper T-lymphocyte defect in vitamin A deficient mice. *J Immunol* 142:388–393.
- Carman JA, Pond L, Nashold F, Wassom DL, Hayes CE. 1992. Immunity to *Trichinella spiralis* infection in vitamin A-deficient mice. *J Exp Med* 175:111–120.
- Carney EA, Russell RM. 1980. Correlation of dark adaptation test results with serum vitamin A levels in diseased adults. *J Nutr* 110:552–557.
- Carney SM, Underwood BA, Loerch JD. 1976. Effects of zinc and vitamin A deficient diets on the hepatic mobilization and urinary excretion of vitamin A in rats. *J Nutr* 106:1773–1781.
- Carpenter TO, Pettifor JM, Russell RM, Pitha J, Mobarhan S, Ossip MS, Wainer S, Anast CS. 1987. Severe hypervitaminosis A in siblings: Evidence of variable tolerance to retinol intake. *J Pediatr* 111:507–512.
- Castenmiller JJ, West CE. 1998. Bioavailability and bioconversion of carotenoids. *Ann Rev Nutr* 18:19–38.
- Castenmiller JJ, West CE, Linssen JP, Van het Hof KH, Voragen AG. 1999. The food matrix of spinach is a limiting factor in determining the bioavailability of beta-carotene and to a lesser extent of lutein in humans. *J Nutr* 129:349–355.
- Chappell JE, Francis T, Clandinin MT. 1985. Vitamin A and E content of human milk at early stages of lactation. *Early Hum Dev* 11:157–167.
- Chase HP, Kumar V, Dodds JM, Sauberlich HE, Hunter RM, Burton RS, Spalding V. 1971. Nutritional status of preschool Mexican-American migrant farm children. *Am J Dis Child* 122:316–324.
- Christian P, West KP Jr. 1998. Interactions between zinc and vitamin A: An update. *Am J Clin Nutr* 68:435S–441S.
- Christian P, Schulze K, Stoltzfus RJ, West KP Jr. 1998a. Hyporetinolemia, illness symptoms, and acute phase protein response in pregnant women with and without night blindness. *Am J Clin Nutr* 67:1237–1243.
- Christian P, West KP Jr, Khatri SK, Katz J, LeClerq S, Pradhan EK, Shrestha SR. 1998b. Vitamin A or beta-carotene supplementation reduces but does not eliminate maternal night blindness in Nepal. *J Nutr* 128:1458–1463.
- Chug-Ahuja JK, Holden JM, Forman MR, Mangels AR, Beecher GR, Lanza E. 1993. The development and application of a carotenoid database for fruits, vegetables, and selected multicomponent foods. *J Am Diet Assoc* 93:318–323.
- Chytil F. 1996. Retinoids in lung development. *FASEB J* 10:986–992.
- Cohen BE, Elin RJ. 1974. Vitamin A-induced nonspecific resistance to infection. *J Infect Dis* 129:597–600.
- Cohlan SQ. 1953. Excessive intake of vitamin A as a cause of congenital anomalies in the rat. *Science* 117:535–536.

- Cohlan SQ. 1954. Congenital anomalies in the rat produced by excessive intake of vitamin A during pregnancy. *Pediatrics* 13:556–567.
- Congdon N, Sommer A, Severns M, Humphrey J, Friedman D, Clement L, Wu LS, Natadisastra G. 1995. Pupillary and visual thresholds in young children as an index of population vitamin A status. *Am J Clin Nutr* 61:1076–1082.
- Cooper AD. 1997. Hepatic uptake of chylomicron remnants. *J Lipid Res* 38:2173–2192.
- Coutsoudis A, Broughton M, Coovadia HM. 1991. Vitamin A supplementation reduces measles morbidity in young African children: A randomized, placebo-controlled, double-blind trial. *Am J Clin Nutr* 54:890–895.
- Coutsoudis A, Kiepiela P, Coovadia HM, Broughton M. 1992. Vitamin A supplementation enhances specific IgG antibody levels and total lymphocyte numbers while improving morbidity in measles. *Pediatr Infect Dis J* 11:203–209.
- Czeizel AE, Rockenbauer M. 1998. Prevention of congenital abnormalities by vitamin A. *Int J Vitam Nutr Res* 68:219–231.
- Dawson HD, Ross AC. 1999. Chronic marginal vitamin A status effects the distribution and function of T cells and natural T cells in aging Lewis rats. *J Nutr* 129:1782–1790.
- Dawson HD, Li NQ, DeCicco KL, Nibert JA, Ross AC. 1999. Chronic marginal vitamin A status reduces natural killer cell number and function in aging Lewis rats. *J Nutr* 129:1510–1517.
- de Francisco A, Chakraborty J, Chowdhury HR, Yunus M, Baqui AH, Siddique AK, Sack RB. 1993. Acute toxicity of vitamin A given with vaccines in infancy. *Lancet* 342:526–527.
- de Pee S, West CE, Muhilal, Karyadi D, Hautvast JG. 1995. Lack of improvement in vitamin A status with increased consumption of dark-green leafy vegetables. *Lancet* 346:75–81.
- de Pee S, West CE, Permaesih D, Martuti S, Muhilal, Hautvast JG. 1998. Orange fruit is more effective than dark-green, leafy vegetables in increasing serum concentrations of retinol and beta-carotene in schoolchildren in Indonesia. *Am J Clin Nutr* 68:1058–1067.
- Deuel HJ, Greenberg SM, Straub E, Fukui T, Chatterjee A, Zechmeister L. 1949. Stereochemical configuration and provitamin A activity. VII. Neocryptoxanthin U. *Arch Biochem* 23:239–240.
- Devadas R, Premakumari S, Subramanian G. 1978. Biological availability of β-carotene from fresh and dried green leafy vegetables on preschool children. *Ind J Nutr Dietet* 15:335–340.
- Dew SE, Ong DE. 1994. Specificity of the retinol transporter of the rat small intestine brush border. *Biochemistry* 33:12340–12345.
- Dickman ED, Smith SM. 1996. Selective regulation of cardiomyocyte gene expression and cardiac morphogenesis by retinoic acid. *Dev Dyn* 206:39–48.
- Donnen P, Dramaix M, Brasseur D, Bitwe R, Vertongen F, Hennart P. 1998. Randomized placebo-controlled clinical trial of the effect of a single high dose or daily low doses of vitamin A on the morbidity of hospitalized, malnourished children. *Am J Clin Nutr* 68:1254–1260.
- Dorea JG, Olson JA. 1986. The rate of rhodopsin regeneration in the bleached eyes of zinc-deficient rats in the dark. *J Nutr* 116:121–127.
- Dorea JG, Souza JA, Galvao MO, Iunes MA. 1984. Concentration of vitamin A in the liver of foetuses and infants dying of various causes in Brasilia, Brazil. *Int J Vitam Nutr Res* 54:119–123.

- Dowling JE, Gibbons IR. 1961. In: Smelser GK, ed. *The Structure of the Eye*. New York: Academic Press.
- Dudas I, Czeizel AE. 1992. Use of 6,000 IU vitamin A during early pregnancy without teratogenic effect. *Teratology* 45:335–336.
- Duester G. 1996. Involvement of alcohol dehydrogenase, short-chain dehydrogenase/reductase, aldehyde dehydrogenase, and cytochrome P450 in the control of retinoid signaling by activation of retinoic acid synthesis. *Biochemistry* 35:12221–12227.
- Duncan JR, Hurley LS. 1978. An interaction between zinc and vitamin A in pregnant and fetal rats. *J Nutr* 108:1431–1438.
- Eaton ML. 1978. Chronic hypervitaminosis A. *Am J Hosp Pharm* 35:1099–1102.
- Eckhoff C, Nau H. 1990. Vitamin A supplementation increases levels of retinoic acid compounds in human plasma: Possible implications for teratogenesis. *Arch Toxicol* 64:502–503.
- Eckhoff C, Bailey JR, Collins MD, Slikker W Jr, Nau H. 1991. Influence of dose and pharmaceutical formulation of vitamin A on plasma levels of retinyl esters and retinol and metabolic generation of retinoic acid compounds and beta-glucuronides in the cynomolgus monkey. *Toxicol Appl Pharmacol* 111:116–127.
- Ellis JK, Russell RM, Makrauer FL, Schaefer EJ. 1986. Increased risk for vitamin A toxicity in severe hypertriglyceridemia. *Ann Intern Med* 105:877–879.
- Farrell GC, Bhathal PS, Powell LW. 1977. Abnormal liver function in chronic hypervitaminosis A. *Am J Dig Dis* 22:724–728.
- Farris WA, Erdman JW Jr. 1982. Protracted hypervitaminosis A following long-term, low-level intake. *J Am Med Assoc* 247:1317.
- Fawzi WW, Chalmers TC, Herrera MG, Mosteller F. 1993. Vitamin A supplementation and child mortality. A meta-analysis. *J Am Med Assoc* 269:898–903.
- Figueira F, Mendonca S, Rocha J, Azevedo M, Bunce GE, Reynolds JW. 1969. Absorption of vitamin A by infants receiving fat-free or fat-containing dried skim milk formulas. *Am J Clin Nutr* 22:588–593.
- Filteau SM, Morris SS, Raynes JG, Arthur P, Ross DA, Kirkwood BR, Tomkins AM, Gyapong JO. 1995. Vitamin A supplementation, morbidity, and serum acute-phase proteins in young Ghanaian children. *Am J Clin Nutr* 62:434–438.
- Flores H. 1993. Frequency distributions of serum vitamin A levels in cross-sectional surveys and in surveys before and after vitamin A supplementation. In: *A Brief Guide to Current Methods of Assessing Vitamin A Status*. A report of the International Vitamin A Consultative Group (IVACCG). Washington, DC: The Nutrition Foundation. Pp. 9–11.
- Flores H, de Araujo RC. 1984. Liver levels of retinol in unselected necropsy specimens: A prevalence survey of vitamin A deficiency in Recife, Brazil. *Am J Clin Nutr* 40:146–152.
- Freudenheim JL, Johnson NE, Smith EL. 1986. Relationships between usual nutrient intake and bone-mineral content of women 35–65 years of age: Longitudinal and cross-sectional analysis. *Am J Clin Nutr* 44:863–876.
- Friedman A, Sklan D. 1989. Impaired T lymphocyte immune response in vitamin A depleted rats and chicks. *Br J Nutr* 62:439–449.
- Furr HC, Amedee-Manesme O, Clifford AJ, Bergen HR, Jones AD, Anderson LD, Olson JA. 1989. Vitamin A concentrations in liver determined by isotope dilution assay with tetradeuterated vitamin A and by biopsy in generally healthy adult humans. *Am J Clin Nutr* 49:713–716.
- Geelen JA. 1979. Hypervitaminosis A induced teratogenesis. *CRC Crit Rev Toxicol* 6:351–375.

- Geubel AP, De Galocsy C, Alves N, Rahier J, Dive C. 1991. Liver damage caused by therapeutic vitamin A administration: Estimate of dose-related toxicity in 41 cases. *Gastroenterology* 100:1701–1709.
- Ghana VAST Study Team. 1993. Vitamin A supplementation in northern Ghana: Effects on clinic attendances, hospital admissions, and child mortality. *Lancet* 342:7–12.
- Glasziou PP, Mackerras DE. 1993. Vitamin A supplementation and infectious disease: A meta-analysis. *Br Med J* 306:366–370.
- Golner BB, Reinhold RB, Jacob RA, Sadowski JA, Russell RM. 1987. The short and long term effect of gastric partitioning surgery on serum protein levels. *J Am Coll Nutr* 6:279–285.
- Goodman DS, Blaner WS. 1984. Biosynthesis, absorption, and hepatic metabolism of retinol. In: Sporn MB, Roberts AB, Goodman DS, eds. *The Retinoids*, Vol. 2. Orlando: Academic Press. Pp. 1–39.
- Goodman DS, Huang HS, Shiratori T. 1965. Tissue distribution and metabolism of newly absorbed vitamin A in the rat. *J Lipid Res* 6:390–396.
- Goodman DS, Blomstrand R, Werner B, Huang HS, Shiratori T. 1966. The intestinal absorption and metabolism of vitamin A and β-carotene in man. *J Clin Invest* 45:1615–1623.
- Gudas LJ, Sporn MB, Roberts AB. 1994. Cellular biology and biochemistry of the retinoids. In: Sporn MB, Roberts AB, Goodman DS, eds. *The Retinoids: Biology, Chemistry, and Medicine*, 2nd ed. New York: Raven Press. Pp. 443–520.
- Hallfrisch J, Muller DC, Singh VN. 1994. Vitamin A and E intakes and plasma concentrations of retinol, beta-carotene, and alpha-tocopherol in men and women of the Baltimore Longitudinal Study of Aging. *Am J Clin Nutr* 60:176–182.
- Harrison EH. 1993. Enzymes catalyzing the hydrolysis of retinyl esters. *Biochim Biophys Acta* 1170:99–108.
- Haskell MJ, Handelman GJ, Peerson JM, Jones AD, Rabbi MA, Awal MA, Wahed MA, Mahalanabis D, Brown KH. 1997. Assessment of vitamin A status by the deuterated-retinol-dilution technique and comparison with hepatic vitamin A concentration in Bangladeshi surgical patients. *Am J Clin Nutr* 66:67–74.
- Hatchell DL, Sommer A. 1984. Detection of ocular surface abnormalities in experimental vitamin A deficiency. *Arch Ophthalmol* 102:1389–1393.
- Hathcock JN, Hattan DG, Jenkins MY, McDonald JT, Sundaresan PR, Wilkening VL. 1990. Evaluation of vitamin A toxicity. *Am J Clin Nutr* 52:183–202.
- Hatoff DE, Gertler SL, Miyai K, Parker BA, Weiss JB. 1982. Hypervitaminosis A unmasked by acute viral hepatitis. *Gastroenterology* 82:124–128.
- Hendriks HF, Verhoofstad WA, Brouwer A, de Leeuw AM, Knook DL. 1985. Perisinusoidal fat-storing cells are the main vitamin A storage sites in rat liver. *Exp Cell Res* 160:138–149.
- Hicks RJ. 1867. Night-blindness in the Confederate Army. *Richmond Med J* 3:34–38.
- Hicks VA, Gunning DB, Olson JA. 1984. Metabolism, plasma transport, and biliary excretion of radioactive vitamin A and its metabolites as a function of liver reserves of vitamin A in the rat. *J Nutr* 114:1327–1333.
- Hofmann C, Eichele G. 1994. Retinoids in development. In: Sporn MB, Roberts AB, Goodman DS, eds. *The Retinoids: Biology, Chemistry, and Medicine*, 2nd ed. New York: Raven Press. Pp. 387–441.
- Hollander D, Muralidhara KS. 1977. Vitamin A1 intestinal absorption in vivo: Influence of luminal factors on transport. *Am J Physiol* 232:E471–E477.

- Hoppner K, Phillips WE, Murray TK, Campbell JS. 1968. Survey of liver vitamin A stores of Canadians. *Can Med Assoc J* 99:983–986.
- Hoppner K, Phillips WE, Erdody P, Murray TK, Perrin DE. 1969. Vitamin A reserves of Canadians. *Can Med Assoc J* 101:84–86.
- Houtkooper LB, Ritenbaugh C, Aickin M, Lohman TG, Going SB, Weber JL, Greaves KA, Boyden TW, Pamenter RW, Hall MC. 1995. Nutrients, body composition and exercise are related to change in bone mineral density in premenopausal women. *J Nutr* 125:1229–1237.
- Hume EM, Krebs HA. 1949. *Vitamin A Requirement of Human Adults. An Experimental Study of Vitamin A Deprivation in Man*. Medical Research Council Special Report Series No. 264. London: His Majesty's Stationery Office.
- Humphrey JH, Agoestina T, Wu L, Usman A, Nurachim M, Subardja D, Hidayat S, Tielsch J, West KP Jr, Sommer A. 1996. Impact of neonatal vitamin A supplementation on infant morbidity and mortality. *J Pediatr* 128:489–496.
- Huque T. 1982. A survey of human liver reserves of retinol in London. *Br J Nutr* 47:165–172.
- Hussey GD, Klein M. 1990. A randomized, controlled trial of vitamin A in children with severe measles. *N Engl J Med* 323:160–164.
- Hutchings DE, Gaston J. 1974. The effects of vitamin A excess administered during the mid-fetal period on learning and development in rat offspring. *Dev Psychobiol* 7:225–233.
- Hutchings DE, Gibbon J, Kaufman MA. 1973. Maternal vitamin A excess during the early fetal period: Effects on learning and development in the offspring. *Dev Psychobiol* 6:445–457.
- IOM (Institute of Medicine). 2000. *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*. Washington, DC: National Academy Press.
- Jalal F, Nesheim MC, Agus Z, Sanjur D, Habicht JP. 1998. Serum retinol concentrations in children are affected by food sources of beta-carotene, fat intake, and anthelmintic drug treatment. *Am J Clin Nutr* 68:623–629.
- Jang JT, Green JB, Beard JL, Green MH. 2000. Kinetic analysis shows that iron deficiency decreases liver vitamin A mobilization in rats. *J Nutr* 130:1291–1296.
- Jayarajan P, Reddy V, Mohanram M. 1980. Effect of dietary fat on absorption of β-carotene from green leafy vegetables in children. *Indian J Med Res* 71:53–56.
- Jensen SK, Nielsen KN. 1996. Tocopherols, retinol, beta-carotene and fatty acids in fat globule membrane and fat globule core in cows' milk. *J Dairy Sci* 63:565–574.
- Johnson EJ, Qin J, Krinsky NI, Russell RM. 1997. Ingestion by men of a combined dose of β-carotene and lycopene does not affect the absorption of β-carotene but improves that of lycopene. *J Nutr* 127:1833–1837.
- Kalter H, Warkany J. 1961. Experimental production of congenital malformations in strains of inbred mice by maternal treatment with hypervitaminosis A. *Am J Pathol* 38:1–14.
- Katz DR, Drzymala M, Turton JA, Hicks RM, Hunt R, Palmer L, Malkovsky M. 1987. Regulation of accessory cell function by retinoids in murine immune responses. *Br J Exp Pathol* 68:343–350.
- Katz J, West KP Jr, Khatri SK, Thapa MD, LeClerq SC, Pradhan EK, Pokhrel RP, Sommer A. 1995. Impact of vitamin A supplementation on prevalence and incidence of xerophthalmia in Nepal. *Invest Ophthalmol Vis Sci* 36:2577–2583.

- Keenum D. 1993. Conjunctival impression cytology. In: *A Brief Guide to Current Methods of Assessing Vitamin A Status*. A report of the International Vitamin A Consultative Group (IVACG). Washington, DC: The Nutrition Foundation. Pp. 19–21.
- Keenum D, Semba RD, Wirasasmita S, Natadisastra G, Muhilal, West KP Jr, Sommer A. 1990. Assessment of vitamin A status by a disk applicator for conjunctival impression cytology. *Arch Ophthalmol* 108:1436–1441.
- Keilson B, Underwood BA, Loerch JD. 1979. Effects of retinoic acid on the mobilization of vitamin A from the liver in rats. *J Nutr* 109:787–795.
- Khoury MJ, Moore CA, Mulinare J. 1996. Vitamin A and birth defects. *Lancet* 347:322.
- Kostic D, White WS, Olson JA. 1995. Intestinal absorption, serum clearance, and interactions between lutein and beta-carotene when administered to human adults in separate or combined oral doses. *Am J Clin Nutr* 62:604–610.
- Kowalski TE, Falestiny M, Furth E, Malet PF. 1994. Vitamin A hepatotoxicity: A cautionary note regarding 25,000 IU supplements. *Am J Med* 97:523–528.
- Krasinski SD, Russell RM, Otradovec CL, Sadowski JA, Hartz SC, Jacob RA, McGandy RB. 1989. Relationship of vitamin A and vitamin E intake to fasting plasma retinol, retinol-binding protein, retinyl ester, carotene, alpha-tocopherol, and cholesterol among elderly people and young adults: Increased plasma retinyl esters among vitamin A-supplement users. *Am J Clin Nutr* 49:112–120.
- Krinsky NI, Wang X-D, Tang G, Russell RM. 1993. Mechanism of carotenoid cleavage to retinoids. *Ann NY Acad Sci* 691:167–176.
- Kusin JA, Reddy V, Sivakumar B. 1974. Vitamin E supplements and the absorption of a massive dose of vitamin A. *Am J Clin Nutr* 27:774–776.
- Lachance PA. 1997. Nutrient addition to foods: The public health impact in countries with rapidly westernizing diets. In: Bendich A, Deckelbaum RJ, eds. *Preventive Nutrition: The Comprehensive Guide for Health Professionals*. Totowa, NJ: Humana Press. Pp. 441–454.
- Lammer EJ, Chen DT, Hoar RM, Agnish ND, Benke PJ, Braun JT, Curry CJ, Fernhoff PM, Grix AW Jr, Lott IT, Richard JM, Sun SC. 1985. Retinoic acid embryopathy. *N Engl J Med* 313:837–841.
- Large S, Neal G, Glover J, Thanangkul O, Olson RE. 1980. The early changes in retinol-binding protein and prealbumin concentrations in plasma of protein-energy malnourished children after treatment with retinol and an improved diet. *Br J Nutr* 43:393–402.
- Leo MA, Lieber CS. 1982. Hepatic vitamin A depletion in alcoholic liver injury. *N Engl J Med* 307:597–601.
- Leo MA, Lieber CS. 1985. New pathway for retinol metabolism in liver microsomes. *J Biol Chem* 260:5228–5231.
- Leo MA, Lieber CS. 1999. Alcohol, vitamin A, and beta-carotene: Adverse interactions, including hepatotoxicity and carcinogenicity. *Am J Clin Nutr* 69:1071–1085.
- Lewis JM, Bodansky O, Falk KG, McGuire G. 1942. Vitamin A requirements in the rat. The relation of vitamin A intake to growth and to concentration of vitamin A in the blood plasma, liver and retina. *J Nutr* 23:351–363.
- Lieber CS, Leo MA. 1986. Interaction of alcohol and nutritional factors with hepatic fibrosis. *Prog Liver Dis* 8:253–272.

- Loerch JD, Underwood BA, Lewis KC. 1979. Response of plasma levels of vitamin A to a dose of vitamin A as an indicator of hepatic vitamin A reserves in rat. *J Nutr* 109:778–786.
- Looker AC, Johnson CL, Woteki CE, Yetley EA, Underwood BA. 1988. Ethnic and racial differences in serum vitamin A levels of children aged 4–11 years. *Am J Clin Nutr* 47:247–252.
- Loyd-Puryear MA, Mahoney J, Humphrey JH, Mahoney F, Siren N, Moorman C, West KP Jr. 1991. Vitamin A deficiency in Micronesia: A statewide survey in Chuuk. *Nutr Res* 11:1101–1110.
- Lynch SR. 1997. Interaction of iron with other nutrients. *Nutr Rev* 55:102–110.
- Mahalanabis D, Simpson TW, Chakraborty ML, Ganguli C, Bhattacharjee AK, Mukherjee KL. 1979. Malabsorption of water miscible vitamin A in children with giardiasis and ascariasis. *Am J Clin Nutr* 32:313–318.
- Mahoney CP, Margolis MT, Knauss TA, Labbe RF. 1980. Chronic vitamin A intoxication in infants fed chicken liver. *Pediatrics* 65:893–897.
- Martinez-Frias ML, Salvador J. 1990. Epidemiological aspects of prenatal exposure to high doses of vitamin A in Spain. *Eur J Epidemiol* 6:118–123.
- Mastroiacovo P, Mazzzone T, Addis A, Elephant E, Carlier P, Vial T, Garbis H, Robert E, Bonati M, Ornoy A, Finardi A, Schaffer C, Caramelli L, Rodriguez-Pinilla E, Clementi M. 1999. High vitamin A intake in early pregnancy and major malformations: A multicenter prospective controlled study. *Teratology* 59:7–11.
- Maxwell JD, Murray D, Ferguson A, Calder E. 1968. Ascaris lumbricoides infection associated with jejunal mucosal abnormalities. *Scott Med J* 13:280–281.
- McCaffery P, Drager UC. 1995. Retinoic acid synthesizing enzymes in the embryonic and adult vertebrate. In: Weiner H, Holmes RS, Wermuth B, eds. *Enzymology and Molecular Biology of Carbonyl Metabolism* 5. New York: Plenum Press. Pp. 173–183.
- Melhus H, Michaelsson K, Kindmark A, Bergstrom R, Holmberg L, Mallmin H, Wolk A, Ljunghall S. 1998. Excessive dietary intake of vitamin A is associated with reduced bone mineral density and increased risk for hip fracture. *Ann Intern Med* 129:770–778.
- Micozzi MS, Brown ED, Edwards BK, Bieri JG, Taylor PR, Khachik F, Beecher GR, Smith JC. 1992. Plasma carotenoid response to chronic intake of selected foods and β-carotene supplements in men. *Am J Clin Nutr* 55:1120–1125.
- Mills JL, Simpson JL, Cunningham GC, Conley MR, Rhoads GG. 1997. Vitamin A and birth defects. *Am J Obstet Gynecol* 177:31–36.
- Minuk GY, Kelly JK, Hwang WS. 1988. Vitamin A hepatotoxicity in multiple family members. *Hepatology* 8:272–275.
- Mitchell GV, Young M, Seward CR. 1973. Vitamin A and carotene levels of a selected population in metropolitan Washington, D.C. *Am J Clin Nutr* 26:992–997.
- Mobarhan S, Russell RM, Underwood BA, Wallingford J, Mathieson RD, Al-Midan H. 1981. Evaluation of the relative dose response test for vitamin A nutriture in cirrhotics. *Am J Clin Nutr* 34:2264–2270.
- Mobarhan S, Seitz HK, Russell RM, Mehta R, Hupert J, Friedman H, Layden TJ, Meydani M, Langenberg P. 1991. Age-related effects of chronic ethanol intake on vitamin A status in Fisher 344 rats. *J Nutr* 121:510–517.
- Money DF. 1978. Vitamin E, selenium, iron, and vitamin A content of livers from Sudden Infant Death Syndrome cases and control children: Interrelationships and possible significance. *NZ J Sci* 21:41–45.

- Montreewasuwat N, Olson JA. 1979. Serum and liver concentrations of vitamin A in Thai fetuses as a function of gestational age. *Am J Clin Nutr* 32:601–606.
- Morrison SA, Russell RM, Carney EA, Oaks EV. 1978. Zinc deficiency: A cause of abnormal dark adaptation in cirrhotics. *Am J Clin Nutr* 31:276–281.
- Morriß-Kay GM, Sokolova N. 1996. Embryonic development and pattern formation. *FASEB J* 10:961–968.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance Data, Vital and Health Statistics of the National Center for Health Statistics, Number 174. Hyattsville, MD: National Center for Health Statistics.
- Muhilal, Permeisih D, Idjradinata YR, Muherdiyantiningsih, Karyadi D. 1988. Vitamin A-fortified monosodium glutamate and health, growth, and survival of children: A controlled field trial. *Am J Clin Nutr* 48:1271–1276.
- Munoz EC, Rosado JL, Lopez P, Furr HC, Allen LH. 2000. Iron and zinc supplementation improves indicators of vitamin A status of Mexican preschoolers. *Am J Clin Nutr* 71:789–794.
- Napoli JL, Race KR. 1988. Biogenesis of retinoic acid from β-carotene: Differences between the metabolism of β-carotene and retinal. *J Biol Chem* 263:17372–17377.
- Napoli JL, Boerman MH, Chai X, Zhai Y, Fiorella PD. 1995. Enzymes and binding proteins affecting retinoic acid concentrations. *J Steroid Biochem Mol Biol* 53:497–502.
- Natadisastra G, Wittpenn JR, West KP Jr, Muhilal, Sommer A. 1987. Impression cytology for detection of vitamin A deficiency. *Arch Ophthalmol* 105:1224–1228.
- Nauss KM, Newberne PM. 1985. Local and regional immune function of vitamin A-deficient rats with ocular herpes simplex virus (HSV) infections. *J Nutr* 115:1316–1324.
- Naz JF, Edwards WM. 1952. Hypervitaminosis A: A case report. *N Engl J Med* 246:87–89.
- Nierenberg DW, Dain BJ, Mott LA, Baron JA, Greenberg ER. 1997. Effects of 4 y of oral supplementation with beta-carotene on serum concentrations of retinol, tocopherol, and five carotenoids. *Am J Clin Nutr* 66:315–319.
- Novotny JA, Dueker SR, Zech LA, Clifford AJ. 1995. Compartmental analysis of the dynamics of β-carotene metabolism in an adult volunteer. *J Lipid Res* 36:1825–1838.
- NRC (National Research Council). 1980. *Recommended Dietary Allowances*, 9th ed. Washington, DC: National Academy Press.
- NRC. 1986. *Nutrient Adequacy: Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC. 1989. *Recommended Dietary Allowances*, 10th ed. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1986. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Olson JA. 1972. The prevention of childhood blindness by the administration of massive doses of vitamin A. *Isr J Med Sci* 8:1199–1206.
- Olson JA. 1979. Liver vitamin A reserves of neonates, preschool children and adults dying of various causes in Salvador, Brazil. *Arch Latinoam Nutr* 29:521–545.
- Olson JA. 1982. New approaches to methods for the assessment of nutritional status of the individual. *Am J Clin Nutr* 35:1166–1168.

- Olson JA. 1983. Adverse effects of large doses of vitamin A and retinoids. *Semin Oncol* 10:290–293.
- Olson JA. 1987. Recommended dietary intakes (RDI) of vitamin A in humans. *Am J Clin Nutr* 45:704–716.
- Olson JA. 1991. Vitamin A. In: Machlin LJ, ed. *Handbook of Vitamins*, 2nd ed. New York: Marcel Dekker. Pp. 1–57.
- Olson JA, Hayaishi O. 1965. The enzymatic cleavage of  $\beta$ -carotene into vitamin A by soluble enzymes of rat liver and intestine. *Proc Nat Acad Sci USA* 54:1364–1370.
- Olson JA, Gunning D, Tilton R. 1979. The distribution of vitamin A in human liver. *Am J Clin Nutr* 32:2500–2507.
- Oren R, Ilan Y. 1992. Reversible hepatic injury induced by long-term vitamin A ingestion. *Am J Med* 93:703–704.
- Panfili G, Manzi P, Pizzoferrato L. 1998. Influence of thermal and other manufacturing stresses on retinol isomerization in milk and dairy products. *J Dairy Res* 65:253–260.
- Papiz MZ, Sawyer L, Eliopoulos EE, North AC, Findlay JB, Sivaprasadarao R, Jones TA, Newcomer ME, Kraulis PJ. 1986. The structure of beta-lactoglobulin and its similarity to plasma retinol-binding protein. *Nature* 324:383–385.
- Parker RS, Swanson JE, You CS, Edwards AJ, Huang T. 1999. Bioavailability of carotenoids in human subjects. *Proc Nutr Soc* 58:155–162.
- Pasatiempo AM, Kinoshita M, Taylor CE, Ross AC. 1990. Antibody production in vitamin A-depleted rats is impaired after immunization with bacterial polysaccharide or protein antigens. *FASEB J* 4:2518–2527.
- Patton S, Kelly JJ, Keenan TW. 1980. Carotene in bovine milk fat globules: Observations on origin and high content in tissue mitochondria. *Lipids* 15:33–38.
- Persson B, Tunell R, Ekengren K. 1965. Chronic vitamin A intoxication during the first half year of life. *Acta Paediatr Scand* 54:49–60.
- Persson B, Krook M, Jornvall H. 1995. Short-chain dehydrogenases/reductases. In: Weiner H, Holmes RS, Wermuth B, eds. *Enzymology and Molecular Biology of Carbonyl Metabolism* 5. New York: Plenum Press. Pp. 383–395.
- Pilch SM. 1987. Analysis of vitamin A data from the health and nutrition examination surveys. *J Nutr* 117:636–640.
- Pinnock CB, Alderman CP. 1992. The potential for teratogenicity of vitamin A and its congeners. *Med J Aust* 157:804–809.
- Rahmathullah L, Underwood BA, Thulasiraj RD, Milton RC, Ramaswamy K, Rahmathullah R, Babu G. 1990. Reduced mortality among children in southern India receiving a small weekly dose of vitamin A. *N Engl J Med* 323:929–935.
- Raica N Jr, Scott J, Lowry L, Sauberlich HE. 1972. Vitamin A concentration in human tissues collected from five areas in the United States. *Am J Clin Nutr* 25:291–296.
- Reddy V. 1985. *Vitamin A Requirements of Preschool Children*. Joint FAO/WHO Expert Group on Requirement for Vitamin A, Iron, Folate and Vitamin B12, Doc. No. 6. Geneva: World Health Organization.
- Reddy V, Srikantia SG. 1966. Serum vitamin A in kwashiorkor. *Am J Clin Nutr* 18:105–109.
- Rock CL, Lovalvo JL, Emenhiser C, Ruffin MT, Flatt SW, Schwartz SJ. 1998. Bioavailability of  $\beta$ -carotene is lower in raw than in processed carrots and spinach in women. *J Nutr* 128:913–916.
- Roels OA, Trout M, Dujacquier R. 1958. Carotene balances on boys in Ruanda where vitamin A deficiency is prevalent. *J Nutr* 65:115–127.

- Roels OA, Djaeni S, Trout ME, Lauw TG, Heath A, Poey SH, Tarwotjo MS, Suhadi B. 1963. The effect of protein and fat supplements on vitamin A deficient children. *Am J Clin Nutr* 12:380–387.
- Rohde CM, Manatt M, Clagett-Dame M, DeLuca HF. 1999. Vitamin A antagonizes the action of vitamin D in rats. *J Nutr* 129:2246–2250.
- Rosales FJ, Ritter SJ, Zolfaghari R, Smith JE, Ross AC. 1996. Effects of acute inflammation on plasma retinol, retinol-binding protein, and its mRNA in the liver and kidneys of vitamin A-sufficient rats. *J Lipid Res* 37:962–971.
- Rosales FJ, Jang JT, Pinero DJ, Erikson KM, Beard JL, Ross AC. 1999. Iron deficiency in young rats alters the distribution of vitamin A between plasma and liver and between hepatic retinol and retinyl esters. *J Nutr* 129:1223–1228.
- Ross AC. 1996. Vitamin A deficiency and retinoid repletion regulate the antibody response to bacterial antigens and the maintenance of natural killer cells. *Clin Immunol Immunopathol* 80:S63–S72.
- Ross AC. 1999. Vitamin A and retinoids. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th ed. Baltimore, MD: Williams & Wilkins. Pp. 305–328.
- Rothman KJ, Moore LL, Singer MR, Nguyen UDT, Mannino S, Milunsky B. 1995. Teratogenicity of high vitamin A intake. *N Engl J Med* 333:1369–1373.
- Saari JC. 1994. Retinoids in photosensitive systems. In: Sporn MB, Roberts AB, Goodman DS, eds. *The Retinoids: Biology, Chemistry, and Medicine*, 2nd ed. New York: Raven Press. Pp. 351–385.
- Salazar-Lindo E, Salazar M, Alvarez JO. 1993. Association of diarrhea and low serum retinol in Peruvian children. *Am J Clin Nutr* 58:110–113.
- Sanchez AM, Congdon NG, Sommer A, Rahmathullah L, Venkataswamy PG, Chandravathi PS, Clement L. 1997. Pupillary threshold as an index of population vitamin A status among children in India. *Am J Clin Nutr* 65:61–66.
- Sato M, Lieber CS. 1981. Hepatic vitamin A depletion after chronic ethanol consumption in baboons and rats. *J Nutr* 111:2015–2023.
- Sauberlich HE, Hodges HE, Wallace DL, Kolder H, Canham JE, Hood J, Raica N, Lowry LK. 1974. Vitamin A metabolism and requirements in the human studied with the use of labeled retinol. *Vitam Horm* 32:251–275.
- Schindler R, Friedrich DH, Kramer M, Wacker HH, Feldheim W. 1988. Size and composition of liver vitamin A reserves of human beings who died of various causes. *Int J Vitam Nutr Res* 58:146–154.
- Semba RD, Muhilal, Scott AL, Natadisastra G, Wirasasmita S, Mele L, Ridwan E, West KP Jr, Sommer A. 1992. Depressed immune response to tetanus in children with vitamin A deficiency. *J Nutr* 122:101–107.
- Semba RD, Bulterys M, Munyeshuli V, Gatsinzi T, Saah A, Chao A, Dushimimana A. 1996. Vitamin A deficiency and T-cell subpopulations in children with meningococcal disease. *J Trop Pediatr* 42:287–290.
- Shankar AH, Genton B, Semba RD, Baisor M, Paino J, Tamja S, Adiguma T, Wu L, Rare L, Tielsch JM, Alpers MP, West KP Jr. 1999. Effect of vitamin A supplementation on morbidity due to *Plasmodium falciparum* in young children in Papua, New Guinea: A randomised trial. *Lancet* 354:203–209.
- Shaw GM, Wasserman CR, Block G, Lammer EJ. 1996. High maternal vitamin A intake and risk of anomalies of structures with a cranial neural crest cell contribution. *Lancet* 347:899–900.
- Shingwekar AG, Mohanram M, Reddy V. 1979. Effect of zinc supplementation on plasma levels of vitamin A and retinol-binding protein in malnourished children. *Clin Chim Acta* 93:97–100.

- Siegel NJ, Spackman TJ. 1972. Chronic hypervitaminosis A with intracranial hypertension and low cerebrospinal fluid concentration of protein. Two illustrative cases. *Clin Pediatr* 11:580–584.
- Sivakumar B, Reddy V. 1972. Absorption of labelled vitamin A in children during infection. *Br J Nutr* 27:299–304.
- Sivakumar B, Reddy V. 1975. Absorption of vitamin A in children with ascariasis. *J Trop Med Hyg* 78:114–115.
- Smith FR, Goodman DS. 1976. Vitamin A transport in human vitamin A toxicity. *N Engl J Med* 294:805–808.
- Smith JE, Brown ED, Smith JC Jr. 1974. The effect of zinc deficiency on the metabolism of retinol-binding protein in the rat. *J Lab Clin Med* 84:692–697.
- Smith SM, Levy NL, Hayes CE. 1987. Impaired immunity in vitamin A-deficient mice. *J Nutr* 117:857–865.
- Solomons NW, Morrow FD, Vasquez A, Bulux J, Guerrero AM, Russell RM. 1990. Test-retest reproducibility of the relative dose response for vitamin A status in Guatemalan adults: Issues of diagnostic sensitivity. *J Nutr* 120:738–744.
- Sommer A. 1982. *Nutritional Blindness. Xerophthalmia and Keratomalacia*. New York: Oxford University Press.
- Sommer A, West KP Jr. 1996. *Vitamin A Deficiency: Health, Survival, and Vision*. New York: Oxford University Press.
- Sommer A, Tarwotjo I, Hussaini G, Susanto D. 1983. Increased mortality in children with mild vitamin A deficiency. *Lancet* 2:585–588.
- Sommer A, Katz J, Tarwotjo I. 1984. Increased risk of respiratory disease and diarrhea in children with pre-existing mild vitamin A deficiency. *Am J Clin Nutr* 40:1090–1095.
- Sommer A, Tarwotjo I, Djunaedi E, West KP Jr, Loeden AA, Tilden R, Mele L. 1986. Impact of vitamin A supplementation on childhood mortality: A randomized controlled community trial. *Lancet* 1:1169–1173.
- Sporn MB, Roberts AB, Goodman DS. 1984. *The Retinoids*. Orlando: Academic Press.
- Staab DB, Hodges RE, Metcalf WK, Smith JL. 1984. Relationship between vitamin A and iron in the liver. *J Nutr* 114:840–844.
- Stauber PM, Sherry B, VanderJagt DJ, Bhagavan HN, Garry PJ. 1991. A longitudinal study of the relationship between vitamin A supplementation and plasma retinol, retinyl esters, and liver enzyme activities in a healthy elderly population. *Am J Clin Nutr* 54:878–883.
- Stephensen CB, Blount SR, Schoeb TR, Park JY. 1993. Vitamin A deficiency impairs some aspects of the host response to influenza A virus infection in BALB/c mice. *J Nutr* 123:823–833.
- Stephensen CB, Alvarez JO, Kohatsu J, Hardmeier R, Kennedy JI, Gammon RB. 1994. Vitamin A is excreted in the urine during acute infection. *Am J Clin Nutr* 60:388–392.
- Stewart BE, Young RS. 1989. Pupillary response: An index of visual threshold. *Appl Optics* 28:1122–1127.
- Suharno D, West CE, Muhilal, Karyadi D, Hautvast JG. 1993. Supplementation with vitamin A and iron for nutritional anaemia in pregnant women in West Java, Indonesia. *Lancet* 342:1325–1328.
- Suthutvoravoot S, Olson JA. 1974. Plasma and liver concentration of vitamin A in a normal population of urban Thai. *Am J Clin Nutr* 27:883–891.
- Takyi EE. 1999. Children's consumption of dark green, leafy vegetables with added fat enhances serum retinol. *J Nutr* 129:1549–1554.

## ONLINE REFERENCES

## 807

- Tang G, Qin J, Dolnikowski GG, Russell RM. 2000. Vitamin A equivalence of  $\beta$ -carotene in a woman as determined by a stable isotope reference method. *Eur J Nutr* 39:7–11.
- Tanumihardjo SA. 1993. The modified relative dose-response assay. In: *A Brief Guide to Current Methods of Assessing Vitamin A Status*. A report of the International Vitamin A Consultative Group (IVACCG). Washington, DC: The Nutrition Foundation. Pp. 14–15.
- Tanumihardjo SA, Olson JA. 1991. The reproducibility of the modified relative dose response (MRDR) assay in healthy individuals over time and its comparison with conjunctival impression cytology (CIC). *Eur J Clin Nutr* 45:407–411.
- Terhune MW, Sandstead HH. 1972. Decreased RNA polymerase activity in mammalian zinc deficiency. *Science* 177:68–69.
- Thatcher AJ, Lee CM, Erdman JW Jr. 1998. Tissue stores of  $\beta$ -carotene are not conserved for later use as a source of vitamin A during compromised vitamin A status in Mongolian gerbils (*Meriones unguiculatus*). *J Nutr* 128:1179–1185.
- Tomlinson JE, Hemken RW, Mitchell GE, Tucker RE. 1976. Mammary transfer of vitamin A alcohol and ester in lactating dairy cows. *J Dairy Sci* 59:607–613.
- Torronen R, Lehmusaho M, Hakkinen S, Hanninen O, Mykkonen H. 1996. Serum  $\beta$ -carotene response to supplementation with raw carrots, carrot juice or purified  $\beta$ -carotene in healthy non-smoking women. *Nutr Res* 16:565–575.
- Trechsel U, Evequoz V, Fleisch H. 1985. Stimulation of interleukin 1 and 3 production by retinoic acid in vitro. *Biochem J* 230:339–344.
- Underwood BA. 1984. Vitamin A in animal and human nutrition. In: Sporn MB, Roberts AB, Goodman DS, eds. *The Retinoids*, Vol. 1. New York: Academic Press. Pp. 281–392.
- Underwood BA. 1994. Hypovitaminosis A: International programmatic issues. *J Nutr* 124:1467S–1472S.
- Underwood BA, Siegel H, Weisell RC, Dolinski M. 1970. Liver stores of vitamin A in a normal population dying suddenly or rapidly from unnatural causes in New York City. *Am J Clin Nutr* 23:1037–1042.
- Van den Berg H, van Vliet T. 1998. Effect of simultaneous, single oral doses of  $\beta$ -carotene with lutein or lycopene on the  $\beta$ -carotene and retinyl ester responses in the triacylglycerol-rich lipoprotein fraction of men. *Am J Clin Nutr* 68:82–89.
- Van het Hof KH, Gartner C, West CE, Tijburg LB. 1998. Potential of vegetable processing to increase the delivery of carotenoids to man. *Int J Vitam Nutr Res* 68:366–370.
- Van het Hof KH, Brouwer IA, West CE, Haddeman E, Steegers-Theunissen RP, van Dusseldorp M, Weststrate JA, Ekes TK, Hautvast JG. 1999. Bioavailability of lutein from vegetables is five times higher than that of  $\beta$ -carotene. *Am J Clin Nutr* 70:261–268.
- Von Lennep E, El Khazen N, De Pierreux G, Amy JJ, Rodesch F, Van Regemorter N. 1985. A case of partial sirenomelia and possible vitamin A teratogenesis. *Prenat Diagn* 5:35–40.
- Wagner KH. 1940. Die experimentelle avitaminose a bei menschen. *Ztsch Physiol Chem* 264:153–188.
- Wallingford JC, Underwood BA. 1987. Vitamin A status needed to maintain vitamin A concentrations in nonhepatic tissues of the pregnant rat. *J Nutr* 117:1410–1415.
- Wang XD. 1999. Chronic alcohol intake interferes with retinoid metabolism and signaling. *Nutr Rev* 57:51–59.

- Watkins M, Moore C, Mulinare J. 1996. Teratogenicity of high vitamin A intake. *N Engl J Med* 334:1196–1197.
- Weber FL Jr, Mitchell GE Jr, Powell DE, Reiser BJ, Banwell JG. 1982. Reversible hepatotoxicity associated with hepatic vitamin A accumulation in a protein-deficient patient. *Gastroenterology* 82:118–123.
- Wendling O, Chambon P, Mark M. 1999. Retinoid X receptors are essential for early mouse development and placentogenesis. *Proc Natl Acad Sci USA* 96:547–551.
- Werler MM, Lammer EJ, Mitchell AA. 1996. Teratogenicity of high vitamin A intake. *N Engl J Med* 334:1195–1196.
- West KP Jr, Pokhrel RP, Katz J, LeClerq SC, Khatry SK, Shrestha SR, Pradhan EK, Tielsch JM, Pandey MR, Sommer A. 1991. Efficacy of vitamin A in reducing preschool child mortality in Nepal. *Lancet* 338:67–71.
- West KP Jr, Katz J, Khatry SK, LeClerq SC, Pradhan EK, Shrestha SR, Conner PB, Dali SM, Christian P, Pokhrel RP, Sommer A. 1999. Double blind, cluster randomized trial of low dose supplementation with vitamin A or beta carotene on mortality related to pregnancy in Nepal. *Br Med J* 318:570–575.
- WHO (World Health Organization). 1950. *Expert Committee on Biological Standardisation*. Technical Report Series, No. 3. Geneva: WHO.
- WHO. 1966. *WHO Expert Committee on Biological Standardization Eighteenth Report*. Technical Report Series, No. 329. Geneva: WHO.
- WHO. 1982. *Control of Vitamin A Deficiency and Xerophthalmia*. Technical Report Series No. 672. Geneva: WHO.
- WHO. 1995. *Global Prevalence of Vitamin A Deficiency*. Micronutrient Deficiency Information System Working Paper, No. 2. Geneva: WHO.
- WHO. 1997. *Vitamin A Supplements: A Guide to Their Use in the Treatment of Vitamin A Deficiency and Xerophthalmia*. Geneva: WHO.
- Wiedermann U, Hanson LA, Kahu H, Dahlgren UI. 1993. Aberrant T-cell function in vitro and impaired T-cell dependent antibody response in vivo in vitamin A-deficient rats. *Immunology* 80:581–586.
- Wilson JG, Roth CB, Warkany J. 1953. An analysis of the syndrome of malformations induced by maternal vitamin A deficiency. Effects of restoration of vitamin A at various times during gestation. *Am J Anat* 92:189–217.
- Wittpenn JR, Tseng SC, Sommer A. 1986. Detection of early xerophthalmia by impression cytology. *Arch Ophthalmol* 104:237–239.
- Wolde-Gebriel Z, West CE, Gebru H, Tadesse AS, Fisseha T, Gabre P, Aboye C, Ayana G, Hautvast JG. 1993. Interrelationship between vitamin A, iodine and iron status in schoolchildren in Shoa Region, central Ethiopia. *Br J Nutr* 70:593–607.
- Woodard WK, Miller LJ, Legant O. 1961. Acute and chronic hypervitaminosis in a 4-month-old infant. *J Pediatr* 59:260–264.
- Zafrani ES, Bernauau D, Feldmann G. 1984. Peliosis-like ultrastructural changes of the hepatic sinusoids in human chronic hypervitaminosis A: Report of three cases. *Hum Pathol* 15:1166–1170.
- Zahar M, Smith DE, Martin F. 1995. Vitamin A distribution among fat globule core, fat globule membrane, and serum fraction in milk. *J Dairy Sci* 78:498–505.
- Zhao Z, Ross AC. 1995. Retinoic acid repletion restores the number of leukocytes and their subsets and stimulates natural cytotoxicity in vitamin A-deficient rats. *J Nutr* 125:2064–2073.

Zhao Z, Murasko DM, Ross AC. 1994. The role of vitamin A in natural killer cell cytotoxicity, number and activation in the rat. *Nat Immun* 13:29–41.

Ibid., Chapter 14, pp. 578–579.

- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Examination Survey: Under-reporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Gibson RS, Ferguson EL. 1998. Assessment of dietary zinc in a population. *Am J Clin Nutr* 68:430S–434S.
- Hallberg L, Hulthen L. 2000. Prediction of dietary iron absorption: An algorithm for calculating absorption and bioavailability of dietary iron. *Am J Clin Nutr* 71:1147–1160.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1980. *Recommended Dietary Allowances*, 9th ed. Washington, DC: National Academy Press.
- NRC. 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC. 1989. *Recommended Dietary Allowances*, 10th ed. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Schoeller DA. 1999. Recent advances from application of doubly labeled water to measurement of human energy expenditure. *J Nutr* 129:1765–1768.
- USDA (U.S. Department of Agriculture). 1999. *USDA Nutrient Database for Standard Reference*, Release 13. [Online.] Available: <http://www.nal.usda.gov/fnic/foodcomp> [accessed February 2000].
- WHO (World Health Organization). 1996. Zinc. In: *Trace Elements in Human Nutrition and Health*. Geneva: WHO. Pp. 72–104.

VITAMIN B<sub>6</sub>

*Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline* (ISBN 0-309-06411-2), Chapter 7, pp. 188–195.

- Andon MB, Reynolds RD, Moser-Veillon PB, Howard MP. 1989. Dietary intake of total and glycosylated vitamin B<sub>6</sub> and the vitamin B<sub>6</sub> nutritional status of un-supplemented lactating women and their infants. *Am J Clin Nutr* 50:1050–1058.
- Baer RL. 1984. Cutaneous skin changes probably due to pyridoxine abuse. *J Am Acad Dermatol* 10:527–528.
- Baker EM, Canham JE, Nunes WT, Sauberlich HE, McDowell ME. 1964. Vitamin B<sub>6</sub> requirement for adult men. *Am J Clin Nutr* 15:59–66.
- Barnard HC, de Kock JJ, Vermaak WJ, Potgieter GM. 1987. A new perspective in the assessment of vitamin B<sub>6</sub> nutritional status during pregnancy in humans. *J Nutr* 117:1303–1306.
- Berger A, Schaumburg HH. 1984. More on neuropathy from pyridoxine abuse. *N Engl J Med* 311:986–987.
- Bernstein AL, Lobitz CS. 1988. A clinical and electrophysiologic study of the treatment of painful diabetic neuropathies with pyridoxine. In: Leklem JE, Reynolds RD, eds. *Clinical and Physiological Applications of Vitamin B<sub>6</sub>. Current Topics in Nutrition and Disease*. New York: Alan R. Liss. Pp. 415–423.
- Bessey OA, Adam DJ, Hansen AE. 1957. Intake of vitamin B<sub>6</sub> and infantile convulsions: A first approximation of requirements of pyridoxine in infants. *Pediatrics* 20:33–44.
- Bhagavan HN. 1985. Interaction between vitamin B<sub>6</sub> and drugs. In: Reynolds RD, Leklem JE, eds. *Vitamin B<sub>6</sub>: Its Role in Health and Disease*. New York: Liss. Pp. 401–415.
- Bhagavan HN, Coleman M, Coursin DB. 1975. The effect of pyridoxine hydrochloride on blood serotonin and pyridoxal phosphate contents in hyperactive children. *Pediatrics* 55:437–441.
- Borschel MW. 1995. Vitamin B<sub>6</sub> in infancy: Requirements and current feeding practices. In: Raiten DJ, ed. *Vitamin B<sub>6</sub> Metabolism in Pregnancy, Lactation and Infancy*. Boca Raton, FL: CRC Press. Pp. 109–124.
- Borschel MW, Kirksey A, Hanneman RE. 1986. Effects of vitamin B<sub>6</sub> intake on nutriture and growth of young infants. *Am J Clin Nutr* 43:7–15.
- Brattstrom LE, Israelsson B, Norrvig B, Bergkvist D, Thorne J, Hultberg B, Hamfelt A. 1990. Impaired homocysteine metabolism in early-onset cerebral and peripheral occlusive arterial disease. Effects of pyridoxine and folic acid treatment. *Atherosclerosis* 81:51–60.
- Bredesen E, Parry GJ. 1984. Pyridoxine neuropathy. *Neurology* 34:136.
- Brophy MH, Siiteri PK. 1975. Pyridoxal phosphate and hypertensive disorders of pregnancy. *Am J Obstet Gynecol* 121:1075–1079.
- Brown RR, Rose DP, Leklem JE, Linkswiler H, Anand R. 1975. Urinary 4-pyridoxic acid, plasma pyridoxal phosphate, and erythrocyte aminotransferase levels in oral contraceptive users receiving controlled intakes of vitamin B<sub>6</sub>. *Am J Clin Nutr* 28:10–19.

- Brush MG, Bennett T, Hansen K. 1988. Pyridoxine in the treatment of premenstrual syndrome: A retrospective survey in 630 patients. *Br J Clin Pract* 42:448–452.
- Brussaard JH, Lowik MR, van den Berg H, Brants HA, Bemelmans W. 1997a. Dietary and other determinants of vitamin B<sub>6</sub> parameters. *Eur J Clin Nutr* 51:S39–S45.
- Brussaard JH, Lowik MR, van den Berg H, Brants HA, Kistemaker C. 1997b. Micronutrient status, with special reference to vitamin B<sub>6</sub>. *Eur J Clin Nutr* 51:S32–S38.
- Canham JE, Nunes WT, Eberlin EW. 1964. Electroencephalographic and central nervous system manifestations of vitamin B<sub>6</sub> deficiency and induced vitamin B<sub>6</sub> dependency in normal human adults. In: *Proceedings of the Sixth International Congress on Nutrition*. Edinburgh: E & S Livingstone.
- Cleary RE, Lumeng L, Li TK. 1975. Maternal and fetal plasma levels of pyridoxal phosphate at term: Adequacy of vitamin B<sub>6</sub> supplementation during pregnancy. *Am J Obstet Gynecol* 121:25–28.
- Coburn SP. 1990. Location and turnover of vitamin B<sub>6</sub> pools and vitamin B<sub>6</sub> requirements of humans. *Ann NY Acad Sci* 585:76–85.
- Coburn SP, Mahuren JD, Szadkowska Z, Schaltenbrand WE, Townsend DW. 1987. Kinetics of vitamin B<sub>6</sub> metabolism examined in miniature swine by continuous administration of labelled pyridoxine. In: Canolty NL, Caine TP, eds. *Proceedings of the 1985 Conference on Mathematical Models in Experimental Nutrition*. Athens: University of Georgia. Pp. 99–111.
- Coburn SP, Lewis DL, Fink WJ, Mahuren JD, Schaltenbrand WE, Costill DL. 1988a. Human vitamin B<sub>6</sub> pools estimated through muscle biopsies. *Am J Clin Nutr* 48:291–294.
- Coburn SP, Mahuren JD, Kennedy MS, Schaltenbrand WE, Sampson DA, O'Connor DK, Snyder DL, Wostmann BS. 1988b. B<sub>6</sub> vitamin content of rat tissues measured by isotope tracer and chromatographic methods. *Biofactors* 1:307–312.
- Cohen M, Bendich A. 1986. Safety of pyridoxine—A review of human and animal studies. *Toxicol Lett* 34:129–139.
- Contractor SF, Shane B. 1968. Estimation of vitamin B<sub>6</sub> compounds in human blood and urine. *Clin Chim Acta* 21:71–77.
- Contractor SF, Shane B. 1970. Blood and urine levels of vitamin B<sub>6</sub> in the mother and fetus before and after loading of the mother with vitamin B<sub>6</sub>. *Am J Obstet Gynecol* 107:635–640.
- Contractor SF, Shane B. 1971. Metabolism of [<sup>14</sup>C] pyridoxol in the pregnant rat. *Biochim Biophys Acta* 230:127–136.
- Coursin DB. 1954. Convulsive seizures in infants with pyridoxine-deficient diet. *JAMA* 154:406–408.
- Crozier PG, Cordain L, Sampson DA. 1994. Exercise-induced changes in plasma vitamin B-6 concentrations do not vary with exercise intensity. *Am J Clin Nutr* 60:552–558.
- Dakshinamurti K, ed. 1990. Vitamin B<sub>6</sub>. *Ann NY Acad Sci* 585:1–570.
- Dakshinamurti K, Stephens MC. 1969. Pyridoxine deficiency in the neonatal rat. *J Neurochem* 6:1515–1522.
- Dakshinamurti K, Sharma SK, Sundaram M. 1991. Domoic acid induced seizure activity in rats. *Neurosci Lett* 127:193–197.

- Dakshinamurti K, Sharma SK, Sundaram M, Watanabe T. 1993. Hippocampal changes in developing postnatal mice following intrauterine exposure to domoic acid. *J Neurosci* 13:4486–4495.
- Dalton K. 1985. Pyridoxine overdose in premenstrual syndrome. *Lancet* 1168–1169.
- Dalton K, Dalton MJT. 1987. Characteristics of pyridoxine overdose neuropathy syndrome. *Acta Neurol Scand* 76:8–11.
- Del Tredici AM, Bernstein AL, Chinn K. 1985. Carpal tunnel syndrome and vitamin B<sub>6</sub> therapy. In: Reynolds RD, Leklem JE, eds. *Vitamin B<sub>6</sub>: Its Role in Health and Disease. Current Topics in Nutrition and Disease*. New York: Alan R. Liss. Pp. 459–462.
- De Zegher F, Przyrembel H, Chalmers RA, Wolff ED, Huijmans JG. 1985. Successful treatment of infantile type I primary hyperoxaluria complicated by pyridoxine toxicity. *Lancet* 17:392–393.
- Donaldson GL, Bury RG. 1982. Multiple congenital abnormalities in a newborn boy associated with maternal use of fluphenazine enanthate and other drugs during pregnancy. *Acta Paediatr Scand* 71:335–338.
- Dorsey CW. 1949. The use of pyridoxine and suprarenal cortex combined in the treatment of the nausea and vomiting of pregnancy. *Am J Obstet Gynecol* 58:1073–1078.
- Dreon DM, Butterfield GE. 1986. Vitamin B<sub>6</sub> utilization in active and inactive young men. *Am J Clin Nutr* 43:816–824.
- Driskell JA, Moak SW. 1986. Plasma pyridoxal phosphate concentrations and coenzyme stimulation of erythrocyte alanine aminotransferase activities of white and black adolescent girls. *Am J Clin Nutr* 43:599–603.
- Driskell JA, Clark AJ, Bazzarre TL, Chopin LF, McCoy H, Kenney MA, Moak SW. 1985. Vitamin B<sub>6</sub> status of southern adolescent girls. *J Am Diet Assoc* 85:46–49.
- Driskell JA, Clark AJ, Moak SW. 1987. Longitudinal assessment of vitamin B<sub>6</sub> status in Southern adolescent girls. *J Am Diet Assoc* 87:307–310.
- Driskell JA, McChrisley B, Reynolds LK, Moak SW. 1989. Plasma pyridoxal 5'-phosphate concentrations in obese and nonobese black women residing near Petersburg, VA. *Am J Clin Nutr* 50:37–40.
- Ellis JM. 1987. Treatment of carpal tunnel syndrome with vitamin. *South Med J* 80:882–884.
- Ellis J, Folkers K, Watanabe T, Kaji M, Saji S, Caldwell JW, Temple CA, Wood FS. 1979. Clinical results of a cross-over treatment with pyridoxine and placebo of the carpal tunnel syndrome. *Am J Clin Nutr* 32:2040–2046.
- Fogelholm M. 1992. Micronutrient status in females during a 24-week fitness-type exercise program. *Ann Nutr Metab* 36:209–218.
- Fonda ML, Trauss C, Guempel UM. 1991. The binding of pyridoxal 5'-phosphate to human serum albumin. *Arch Biochem Biophys* 288:79–86.
- Foukas MD. 1973. An antilactogenic effect of pyridoxine. *J Obstet Gynaecol Br Commonw* 80:718–720.
- Friedman MA, Resnick JS, Baer RL. 1986. Subepidermal vesicular dermatosis and sensory peripheral neuropathy caused by pyridoxine abuse. *J Am Acad Dermatol* 14:915–917.
- Fries ME, Chrisley BM, Driskell JA. 1981. Vitamin B<sub>6</sub> status of a group of preschool children. *Am J Clin Nutr* 34:2706–2710.
- Gardner LI, Welsh-Sloan J, Cady RB. 1985. Phocomelia in infant whose mother took large doses of pyridoxine during pregnancy. *Lancet* 1:636.
- Gaynor R, Dempsey WB. 1972. Vitamin B<sub>6</sub> enzymes in normal and pre-eclamptic human placentae. *Clin Chim Acta* 37:411–416.

- Grabow JD, Linkswiler H. 1969. Electroencephalographic and nerve-conduction studies in experimental vitamin B<sub>6</sub> deficiency in adults. *Am J Clin Nutr* 22:1429–1434.
- Gregory JF 3rd. 1997. Bioavailability of vitamin B<sub>6</sub>. *Eur J Clin Nutr* 51:S43–S48.
- Guilarte TR. 1993. Vitamin B<sub>6</sub> and cognitive development: Recent research findings from human and animal studies. *Nutr Rev* 51:193–198.
- Hamfelt A, Tuvemo T. 1972. Pyridoxal phosphate and folic acid concentration in blood and erythrocyte aspartate aminotransferase activity during pregnancy. *Clin Chim Acta* 41:287–298.
- Hamm MW, Mehansho H, Henderson LM. 1979. Transport and metabolism of pyridoxamine and pyridoxamine phosphate in the small intestine of the rat. *J Nutr* 109:1552–1559.
- Hansen CM, Leklem JE, Miller LT. 1996a. Vitamin B-6 status indicators decrease in women consuming a diet high in pyridoxine glucoside. *J Nutr* 126:2512–2518.
- Hansen CM, Leklem JE, Miller LT. 1996b. Vitamin B-6 status of women with a constant intake of vitamin B-6 changes with three levels of dietary protein. *J Nutr* 126:1891–1901.
- Hansen CM, Leklem JE, Miller LT. 1997. Changes in vitamin B-6 status indicators of women fed a constant protein diet with varying levels of vitamin B-6. *Am J Clin Nutr* 66:1379–1387.
- Hart BF, McConnell WT. 1943. Vitamin B factors in toxic psychosis of pregnancy and the puerperium. *Am J Obstet Gynecol* 46:304.
- Hawkins WW, Barsky J. 1948. An experiment on human vitamin B<sub>6</sub> deprivation. *Science* 108:284–286.
- Heiskanen K, Salmenperä L, Perheentupa J, Siimes MA. 1994. Infant vitamin B-6 status changes with age and with formula feeding. *Am J Clin Nutr* 60:907–910.
- Heiskanen K, Kallio M, Salmenperä L, Siimes MA, Ruokonen I, Perheentupa J. 1995. Vitamin B-6 status during childhood: Tracking from 2 months to 11 years of age. *J Nutr* 125:2985–2992.
- Hendrickx AG, Cukierski M, Prahalada S, Janos Booher S, Nyland T. 1985. Evaluation of bendectin embryotoxicity nonhuman primates: II. Double-blind study term cynomolgus monkeys. *Teratology* 32:191–194.
- Huang Y-C, Chen W, Evans MA, Mitchell ME, Shultz TD. 1998. Vitamin B<sub>6</sub> requirement and status assessment of young women fed a high-protein diet with various levels of vitamin B-6. *Am J Clin Nutr* 67:208–220.
- Hultberg B, Andersson A, Sterner G. 1993. Plasma homocysteine in renal failure. *Clin Nephrol* 40:230–235.
- Hunt AD Jr, Stokes J Jr, McCrory WW, Stroud HH. 1954. Pyridoxine dependency: Report of a case of intractable convulsions in an infant controlled by pyridoxine. *Pediatrics* 13:140–145.
- Johansson S, Lindstedt S, Register U, Wadstrom L. 1966. Studies on the metabolism of labeled pyridoxine in man. *Am J Clin Nutr* 18:185–196.
- Kang-Yoon SA, Kirksey A, Giacoia GP, West KD. 1995. Vitamin B<sub>6</sub> adequacy in neonatal nutrition: Associations with preterm delivery, type of feeding, and vitamin B-6 supplementation. *Am J Clin Nutr* 62:932–942.
- Khera KS. 1975. Teratogenicity study in rats given high doses pyridoxine (vitamin B<sub>6</sub>) during organogenesis. *Experientia* 31:469–470.
- Kirksey A, Roepke JL. 1981. Vitamin B<sub>6</sub> nutriture of mothers of three breast-fed neonates with central nervous system disorders. *Fed Proc* 40:864.
- Kirksey A, Keaton K, Abernathy RP, Greger JL. 1978. Vitamin B<sub>6</sub> nutritional status of a group of female adolescents. *Am J Clin Nutr* 31:946–954.

- Kretsch MJ, Sauberlich HE, Newbrun E. 1991. Electroencephalographic changes and periodontal status during short-term vitamin B-6 depletion of young, non-pregnant women. *Am J Clin Nutr* 53:1266–1274.
- Kretsch MJ, Sauberlich HE, Skala JH, Johnson HL. 1995. Vitamin B-6 requirement and status assessment: Young women fed a depletion diet followed by a plant- or animal-protein diet with graded amounts of vitamin B-6. *Am J Clin Nutr* 61:1091–1101.
- Leklem JE. 1990. Vitamin B-6: A status report. *J Nutr* 120:1503–1507.
- Leklem JE. 1991. Vitamin B<sub>6</sub>. In: Machlin LJ ed. *Handbook of Vitamins*, 2nd edition. New York: Marcel Dekker. Pp. 341–392.
- Leklem JE. 1994. Vitamin B<sub>6</sub>. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*. Philadelphia: Lea & Febiger. Pp. 383–394.
- Leklem JE, Shultz TD. 1983. Increased plasma pyridoxal 5'-phosphate and vitamin B-6 in male adolescents after 4500-meter run. *Am J Clin Nutr* 38:541–548.
- Lindberg AS, Leklem JE, Miller LT. 1983. The effect of wheat bran on the bioavailability of vitamin B-6 in young men. *J Nutr* 113:2578–2586.
- Linkswiler HM. 1978. Vitamin B<sub>6</sub> requirements of men. In: *Human Vitamin B<sub>6</sub> Requirements: Proceedings of a Workshop*. Washington, DC: National Academy of Sciences. Pp. 279–290.
- Lui A, Lumeng L, Aronoff GR, Li T-K. 1985. Relationship between body store of vitamin B<sub>6</sub> and plasma pyridoxal-P clearance: Metabolic balance studies in humans. *J Lab Clin Med* 106:491–497.
- Lumeng L, Li TK. 1974. Vitamin B<sub>6</sub> metabolism in chronic alcohol abuse. Pyridoxal phosphate levels in plasma and the effects of acetaldehyde on pyridoxal phosphate synthesis and degradation in human erythrocytes. *J Clin Invest* 53:693–704.
- Lumeng L, Cleary RE, Li TK. 1974. Effect of oral contraceptives on the plasma concentration of pyridoxal phosphate. *Am J Clin Nutr* 27:326–333.
- Lumeng L, Cleary RE, Wagner R, Pao-Lo Y, Li TK. 1976. Adequacy of vitamin B<sub>6</sub> supplementation during pregnancy: A prospective study. *Am J Clin Nutr* 29:1376–1383.
- Lumeng L, Ryan MP, Li TK. 1978. Validation of the diagnostic value of plasma pyridoxal 5'-phosphate measurements in vitamin B<sub>6</sub> nutrition of the rat. *J Nutr* 108:545–553.
- Manore MM, Leklem JE. 1988. Effect of carbohydrate and vitamin B<sub>6</sub> on fuel substrates during exercise in women. *Med Sci Sports Exerc* 20:233–241.
- Manore MN, Leklem JE, Walter MC. 1987. Vitamin B<sub>6</sub> metabolism as affected by exercise in trained and untrained women fed diets differing in carbohydrate and vitamin B<sub>6</sub> content. *Am J Clin Nutr* 46:995–1004.
- Marcus RG. 1975. Suppression of lactation with high doses of pyridoxine. *S Afr Med J* 49:2155–2156.
- Merrill AH Jr, Henderson JM, Wang E, McDonald BW, Millikan WJ. 1984. Metabolism of vitamin B-6 by human liver. *J Nutr* 114:1664–1674.
- Meydani SN, Ribaya-Mercado JD, Russell RM, Sahyoun N, Morrow FD, Gershoff SN. 1991. Vitamin B-6 deficiency impairs interleukin 2 production and lymphocyte proliferation in elderly adults. *Am J Clin Nutr* 53:1275–1280.
- Miller LT, Linkswiler H. 1967. Effect of protein intake on the development of abnormal tryptophan metabolism by men during vitamin B<sub>6</sub> depletion. *J Nutr* 93:53–59.

- Miller LT, Johnson A, Benson EM, Woodring MJ. 1975. Effect of oral contraceptives and pyridoxine on the metabolism of vitamin B<sub>6</sub> and on plasma tryptophan and α-amino nitrogen. *Am J Clin Nutr* 28:846–853.
- Miller LT, Leklem JE, Shultz TD. 1985. The effect of dietary protein on the metabolism of vitamin B<sub>6</sub> in humans. *J Nutr* 115:1663–1672.
- Mitwalli A, Blair G, Oreopoulos DG. 1984. Safety of intermediate doses of pyridoxine. *Can Med Assoc J* 131:14.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance Data, Vital and Health Statistics of the National Center for Health Statistics, No. 174. Hyattsville, MD: National Center for Health Statistics.
- Mueller JF, Vilten RW. 1950. Pyridoxine deficiency in human beings induced by desoxypyridoxine. *J Clin Invest* 29:193–201.
- Nakano H, Gregory JF 3rd. 1997. Pyridoxine and pyridoxine-5'-beta-D-glucoside exert different effects on tissue B-6 vitamins but similar effects of beta-glucosidase activity in rats. *J Nutr* 125:2751–2762.
- Pannemans DL, van den Berg H, Westerterp KR. 1994. The influence of protein intake on vitamin B<sub>6</sub> metabolism differs in young and elderly humans. *J Nutr* 124:1207–1214.
- Parry GJ, Bredesen DE. 1985. Sensory neuropathy with low-dose pyridoxine. *Neurology* 35:1466–1468.
- Phillips WE, Mills JH, Charbonneau SM, Tryphonas L, Hatina GV, Zawidzka Z, Bryce FR, Munro IC. 1978. Subacute toxicity of pyridoxine hydrochloride in the beagle dog. *Toxicol Appl Pharmacol* 44:323–333.
- Philpot J, Muntoni F, Skellett S, Dubowitz V. 1995. Congenital symmetrical weakness of the upper limbs resembling brachial plexus palsy: A possible sequel of drug toxicity in the first trimester of pregnancy. *Neuromuscul Disord* 5:67–69.
- Raica N Jr, Sauberlich HE. 1964. Blood cell transaminase activity in human vitamin B<sub>6</sub> deficiency. *Am J Clin Nutr* 15:67–72.
- Ribaya-Mercado JD, Russell RM, Sahyoun N, Morrow FD, Gershoff SN. 1991. Vitamin B-6 requirements of elderly men and women. *J Nutr* 121:1062–1074.
- Riggs KM, Spiro A, Tucker K, Rush D. 1996. Relations of vitamin B-12, vitamin B-6, folate, and homocysteine to cognitive performance in the Normative Aging Study. *Am J Clin Nutr* 63:306–314.
- Rimm EB, Willett WC, Hu FB, Sampson L, Colditz GA, Manson JE, Hennekens C, Stampfer MJ. 1998. Folate and vitamin B<sub>6</sub> from diet and supplements in relation to risk of coronary heart disease among women. *J Am Med Assoc* 279:359–364.
- Robinson K, Mayer EL, Miller DP, Green R, van Lente F, Gupta A, Kottke-Marchant K, Savon SR, Selhub J, Nissen SE, Kutner M, Topol EJ, Jacobsen DW. 1995. Hyperhomocysteinemia and low pyridoxal phosphate. Common and independent reversible risk factors for coronary artery disease. *Circulation* 92:2825–2830.
- Rose CS, Gyorgy P, Butler M, Andres R, Norris AH, Shock NW, Tobin J, Brin M, Spiegel H. 1976. Age differences in vitamin B<sub>6</sub> status of 617 men. *Am J Clin Nutr* 29:847–853.
- Rose DP. 1978. Oral Contraceptives and Vitamin B<sub>6</sub>. In: *Human Vitamin B<sub>6</sub> Requirements: Proceedings of a Workshop*. Washington, DC: National Academy Press. Pp. 193–201.
- Sauberlich HE. 1964. Human requirements for vitamin B<sub>6</sub>. *Vitam Horm* 22:807–823.

- Sauberlich HE, Canham JE, Baker EM, Raica N Jr, Herman YF. 1972. Biochemical assessment of the nutritional status of vitamin B<sub>6</sub> in the human. *Am J Clin Nutr* 25:629–642.
- Scaglione D, Vecchione A. 1982. Pyridoxine for the suppression of lactation—a clinical trial on 1592 cases. *Acta Vitaminol Enzymol* 4:207–214.
- Schaeppi U, Krinke G. 1985. Differential vulnerability of three rapidly conducting somatosensory pathways in the dog with vitamin B<sub>6</sub> neuropathy. *Agents Actions* 16:567–579.
- Schaumburg HH, Berger A. 1988. Pyridoxine neurotoxicity. In: *Clinical and Physiological Applications of Vitamin B<sub>6</sub>*. New York: Alan R. Liss. Pp. 403–414.
- Schaumburg H, Kaplan J, Windebank A, Vick N, Rasmus S, Pleasure D, Brown MJ. 1983. Sensory neuropathy from pyridoxine abuse. *N Engl J Med* 309:445–448.
- Schumacher MF, Williams MA, Lyman RL. 1965. Effect of high intakes of thiamine, riboflavin and pyridoxine on reproduction in rats and vitamin requirements of the offspring. *J Nutr* 86:343–349.
- Schuster K, Bailey LB, Mahan CS. 1981. Vitamin B<sub>6</sub> status of low-income adolescent and adult pregnant women and the condition of their infants at birth. *Am J Clin Nutr* 34:1731–1735.
- Selhub J, Jacques PF, Wilson PWF, Rush D, Rosenberg IH. 1993. Vitamin status and intake as primary determinants of homocysteinemia in an elderly population. *J Am Med Assoc* 270:2693–2698.
- Selhub J, Jacques PF, Bostom AG, D'Agostino RB, Wilson PW, Belanger AJ, O'Leary DH, Wolf PA, Schaefer EJ, Rosenberg IH. 1995. Association between plasma homocysteine concentrations and extracranial carotid-artery stenosis. *N Engl J Med* 332:286–291.
- Shane B. 1978. Vitamin B<sub>6</sub> and blood. In: *Human Vitamin B<sub>6</sub> Requirements: Proceedings of a Workshop*. Washington, DC: National Academy Press. Pp. 111–128.
- Shane B, Contractor SF. 1975. Assessment of vitamin B<sub>6</sub> status. Studies on pregnant women and oral contraceptive agent users. *Am J Clin Nutr* 28:739–747.
- Shane B, Contractor SF. 1980. Vitamin B<sub>6</sub> status and metabolism in pregnancy. In: Tryfatiates GP, ed. *Vitamin B<sub>6</sub> Metabolism and Role in Growth*. Westport, CT: Food & Nutrition Press. Pp. 137–171.
- Sharma SK, Dakshinamurti K. 1992. Seizure activity in pyridoxine-deficient adult rats. *Epilepsia* 33:235–247.
- Sharma SK, Bolster B, Dakshinamurti K. 1994. Picrotoxin and pentylenetetrazole induced seizure activity in pyridoxine-deficient rats. *J Neurol Sci* 121:1–9.
- Shultz TD, Leklem JE. 1981. Urinary 4-pyridoxic acid, urinary vitamin B<sub>6</sub>, and plasma pyridoxal phosphate as measures of vitamin B<sub>6</sub> status and dietary intake in adults. In: Leklem JE, Reynolds RD, eds. *Methods in Vitamin B<sub>6</sub> Nutrition*. New York: Plenum Press. Pp. 389–392.
- Snell EE. 1958. Some aspects of the metabolism of vitamin B<sub>6</sub>. In: *Fourth International Congress of Biochemistry-Vitamin Metabolism*, Vol. 11. New York: Pergamon. Pp. 250–265.
- Snyderman SE, Holt LE, Carretero R, Jacobs K. 1953. Pyridoxine deficiency in the human infant. *Am J Clin Nutr* 1:200.
- Stephens MC, Havlicek V, Dakshinamurti K. 1971. Pyridoxine deficiency and development of the central nervous system in the rat. *J Neurochem* 18:2407–2416.
- Subbarao K, Kakkar PV. 1979. Thrombin induced surface changes of human platelets. *Biochem Biophys Res Commun* 88:470–476.
- Tarr JB, Tamura T, Stokstad EL. 1981. Availability of vitamin B<sub>6</sub> and pantothenate in an average American diet in man. *Am J Clin Nutr* 34:1328–1337.

- Tolis G, Laliberte R, Guyda H, Naftolin F. 1977. Ineffectiveness of pyridoxine (B<sub>6</sub>) to alter secretion of growth hormone and prolactin and absence of therapeutic effects on galactorrhea-amenorrhea syndromes. *J Clin Endocrinol Metab* 44:1197–1199.
- Ubbink JB, Vermaak WJ, Delpot R, van der Merwe A, Becker PJ, Potgieter H. 1995. Effective homocysteine metabolism may protect South African blacks against coronary heart disease. *Am J Clin Nutr* 62:802–808.
- Ubbink JB, van der Merwe A, Delpot R, Allen RH, Stabler SP, Riezler R, Vermaak WJ. 1996. The effect of a subnormal vitamin B<sub>6</sub> status on homocysteine metabolism. *J Clin Invest* 98:177–184.
- Unna K, Antopol W. 1940. Toxicity of vitamin B<sub>6</sub>. *Proc Soc Exp Biol Med* 43:116–118.
- van der Beek EJ, van Dokkum W, Wedel M, Schrijver J, van den Berg H. 1994. Thiamin, riboflavin and vitamin B<sub>6</sub>: Impact of restricted intake on physical performance in man. *J Am Coll Nutr* 13:629–640.
- Weinstein BB, Wohl Z, Mitchell GJ, Sustendal GF. 1944. Oral administration of pyridoxine hydrochloride in the treatment of nausea and vomiting of pregnancy. *Am J Obstet Gynecol* 47:389–394.
- Weir MR, Keniston RC, Enriquez JI Sr, McNamee GA. 1991. Depression of vitamin B<sub>6</sub> levels due to dopamine. *Vet Hum Toxicol* 33:118–121.
- West KD, Kirksey A. 1976. Influence of vitamin B<sub>6</sub> intake on the content of the vitamin in human milk. *Am J Clin Nutr* 29:961–969.
- Willis RS, Winn WW, Morris AT, Newsome AA, Massey WE. 1942. Clinical observations in treatment of nausea and vomiting in pregnancy with vitamin B1 and B6. A preliminary report. *Am J Obstet Gynecol* 44:265–271.
- Wozenski JR, Leklem JE, Miller LT. 1980. The metabolism of small doses of vitamin B<sub>6</sub> in men. *J Nutr* 110:275–285.
- Yess N, Price JM, Brown RR, Swan PB, Linkswiler H. 1964. Vitamin B<sub>6</sub> depletion in man: Urinary excretion of tryptophan metabolites. *J Nutr* 84:229–236.

Ibid., Chapter 13, p. 436.

- Beaton GH. 1994. Criteria of an adequate diet. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*, 8th ed. Philadelphia: Lea & Febiger. Pp. 1491–1505.
- Hegsted DM. 1972. Problems in the use and interpretation of the Recommended Dietary Allowances. *Ecol Food Nutr* 1:255–265.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- USDA (U.S. Department of Agriculture). 1992. *The Food Guide Pyramid*. Home and Garden Bulletin Number 252. Washington, DC: US Government Printing Office.
- WHO (World Health Organization). 1996. *Trace Elements in Human Nutrition and Health*. Prepared in collaboration with the Food and Agriculture Organization of the United Nations and the International Atomic Energy Agency. Geneva: WHO.

VITAMIN B<sub>12</sub>

*Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline* (ISBN 0-309-06411-2), Chapter 9, pp. 348–356.

- Adams JF. 1962. The measurement of the total assayable vitamin B<sub>12</sub> in the body. In: Heinrich HC, ed. *Vitamin B<sub>12</sub> und Intrinsic Faktor*. Stuttgart, Germany: Ferdinand Enke. Pp. 397–403.
- Adams JF. 1970. Correlation of serum and urine vitamin B<sub>12</sub>. *Br Med J* 1:138–139.
- Adams JF, Tankel HI, MacEwan F. 1970. Estimation of the total body vitamin B<sub>12</sub> in the live subject. *Clin Sci* 39:107–113.
- Adams JF, Ross SK, Mervyn RL, Boddy K, King P. 1971. Absorption of cyanocobalamin, coenzyme B<sub>12</sub>, methylcobalamin, and hydroxocobalamin at different dose levels. *Scand J Gastroenterol* 6:249–252.
- Adams JF, Boddy K, Douglas AS. 1972. Interrelation of serum vitamin B<sub>12</sub>, total body vitamin B<sub>12</sub>, peripheral blood morphology and the nature of erythropoiesis. *Br J Haematol* 23:297–305.
- Allen RH, Stabler SP, Lindenbaum J. 1993. Serum betaine, N,N-dimethylglycine and N-methylglycine levels in patients with cobalamin and folate deficiency and related inborn errors of metabolism. *Metabolism* 42:1448–1460.
- Amin S, Spinks T, Ranicar A, Short MD, Hoffbrand AV. 1980. Long-term clearance of [57Co]cyanocobalamin in vegans and pernicious anaemia. *Clin Sci* 58:101–103.
- Andrews GR, Haneman B, Arnold BJ, Booth JC, Taylor K. 1967. Atrophic gastritis in the aged. *Australas Ann Med* 16:230–235.
- Areekul S, Oumarum K, Dougbarn J. 1977. Determination of vitamin B<sub>12</sub> and vitamin B<sub>12</sub>-binding protein in human and cow's milk. *Mod Med Asia* 13:17–23.
- Baker SJ, Mathan VI. 1981. Evidence regarding the minimal daily requirement of dietary vitamin B<sub>12</sub>. *Am J Clin Nutr* 34:2423–2433.
- Baker SJ, Jacob E, Rajan KT, Swaminathan SP. 1962. Vitamin B<sub>12</sub> deficiency in pregnancy and the puerperium. *Br Med J* 1:1658–1661.
- Bastrup-Madsen P, Helleberg-Rasmussen I, Norregaard S, Halver B, Hansen T. 1983. Long term therapy of pernicious anaemia with the depot cobalamin preparation Betolvex®. *Scand J Haematol* 31:57–62.
- Beck WS. 1991. Neuropsychiatric consequences of cobalamin deficiency. *Adv Intern Med* 36:33–56.
- Bellou A, Aimone-Gastin I, De Korwin JD, Bronowicki JP, Moneret-Vautrin A, Nicolas JP, Bigard MA, Gueant JL. 1996. Cobalamin deficiency with megaloblastic anaemia in one patient under long-term omeprazole therapy. *J Intern Med* 240:161–164.
- Berlin H, Berlin R, Brante G. 1968. Oral treatment of pernicious anemia with high doses of vitamin B<sub>12</sub> without intrinsic factor. *Acta Med Scand* 184:247–258.
- Berlin H, Berlin R, Brante G. 1969. Treatment with high oral doses of vitamin B<sub>12</sub>. Five years experience. *Lakartidningen* 66:153–158.
- Best WR, White WF, Robbins KC, Landmann WA, Steelman SL. 1956. Studies on urinary excretion of vitamin B<sub>12</sub>Co<sup>60</sup> in pernicious anemia for determining effective dosage of intrinsic factor concentrates. *Blood* 11:338–351.

- Black AK, Allen LH, Pelto GH, de Mata M, Chávez A. 1994. Iron, vitamin B-12 and folate status in Mexico: Associated factors in men and women and during pregnancy and lactation. *J Nutr* 124:1179–1188.
- Boddy K, Adams JF. 1968. Excretion of cobalamins and coenzyme B<sub>12</sub> following massive parenteral doses. *Am J Clin Nutr* 21:657–664.
- Boddy K, Adams JF. 1972. The long-term relationship between serum vitamin B<sub>12</sub> and total body vitamin B<sub>12</sub>. *Am J Clin Nutr* 25:395–400.
- Bozian RC, Ferguson JL, Heyssel RM, Meneely GR, Darby WJ. 1963. Evidence concerning the human requirement for vitamin B<sub>12</sub>. Use of the whole body counter for determination of absorption of vitamin B<sub>12</sub>. *Am J Clin Nutr* 12:117–129.
- Carmel R. 1988. Pernicious anemia. The expected findings of very low serum cobalamin levels, anemia, and macrocytosis are often lacking. *Arch Intern Med* 148:1712–1714.
- Carmel R. 1992. Reassessment of the relative prevalences of antibodies to gastric parietal cell and to intrinsic factor in patients with pernicious anaemia: Influence of patient age and race. *Clin Exp Immunol* 89:74–77.
- Carmel R. 1996. Prevalence of undiagnosed pernicious anemia in the elderly. *Arch Intern Med* 156:1097–1100.
- Carmel R, Sinow RM, Karnaze DS. 1987. Atypical cobalamin deficiency. Subtle biochemical evidence of deficiency is commonly demonstrable in patients without megaloblastic anemia and is often associated with protein-bound cobalamin malabsorption. *J Lab Clin Med* 109:454–463.
- Carmel R, Sinow RM, Siegel ME, Samloff IM. 1988. Food cobalamin malabsorption occurs frequently in patients with unexplained low serum cobalamin levels. *Arch Intern Med* 148:1715–1719.
- Carmel R, Green R, Jacobsen DW, Qian GD. 1996. Neutrophil nuclear segmentation in mild cobalamin deficiency: Relation to metabolic tests of cobalamin status and observations on ethnic differences in neutrophil segmentation. *Am J Clin Pathol* 106:57–63.
- Casterline JE, Allen LH, Ruel MT. 1997. Vitamin B-12 deficiency is very prevalent in lactating Guatemalan women and their infants at three months postpartum. *J Nutr* 127:1966–1972.
- Chanarin I. 1969. *The Megaloblastic Anaemias*, 1st ed. Oxford: Blackwell Scientific.
- Chanarin I. 1979. *The Megaloblastic Anaemias*, 2nd ed. Oxford: Blackwell Scientific.
- Chanarin I. 1990. *The Megaloblastic Anaemias*, 3rd ed. Boston: Blackwell Scientific.
- Dagnelie PC, van Staveren WA, Hautvast JG. 1991. Stunting and nutrient deficiencies in children on alternative diets. *Acta Paediatr Scand Suppl* 374:111–118.
- Darby WJ, Bridgforth EB, Le Brocqquy J, Clark SL, De Oliviera JD, Kevany J, McGanity WJ, Perez C. 1958. Vitamin B<sub>12</sub> requirement of adult man. *Am J Med* 25: 726–732.
- Day PL, Payne LD, Dinning JS. 1950. Procarcinogenic effect of vitamin B<sub>12</sub> on *p*-dimethylaminoazobenzene-fed rats. *Proc Soc Exp Biol Med* 74:854–857.
- Doi K, Matsuura M, Kawara A, Tanaka T, Baba S. 1983. Influence of dietary fiber (konjac mannan) on absorption of vitamin B<sub>12</sub> and vitamin E. *Tohoku J Exp Med* 141:677–681.
- Donangelo CM, Trugo NM, Koury JC, Barreto Silva MI, Freitas LA, Feldheim W, Barth C. 1989. Iron, zinc, folate and vitamin B<sub>12</sub> nutritional status and milk composition of low-income Brazilian mothers. *Eur J Clin Nutr* 43:253–266.
- Doscherholmen A, Hagen PS. 1957. A dual mechanism of vitamin B<sub>12</sub> plasma absorption. *J Clin Invest* 36:1551–1557.

- Doscherholmen A, McMahon J, Ripley D. 1975. Vitamin B<sub>12</sub> absorption from eggs. *Proc Soc Exp Biol Med* 149:987–990.
- Doscherholmen A, McMahon J, Ripley D. 1978. Vitamin B<sub>12</sub> assimilation from chicken meat. *Am J Clin Nutr* 31:825–830.
- Doscherholmen A, McMahon J, Economou P. 1981. Vitamin B<sub>12</sub> absorption from fish. *Proc Soc Exp Biol Med* 167:480–484.
- Doscherholmen A, Silvis S, McMahon J. 1983. Dual isotope Schilling test for measuring absorption of food-bound and free vitamin B<sub>12</sub> simultaneously. *Am J Clin Pathol* 80:490–495.
- Draper A, Lewis J, Malhotra N, Wheeler E. 1993. The energy and nutrient intakes of different types of vegetarian: A case for supplements? *Br J Nutr* 69:3–19.
- Dugois P, Amblard P, Imbert R, Bignicourt B. 1969. Acne caused by vitamin B<sub>12</sub>. *Lyon Med* 221:1165–1167.
- Dupre A, Albarel N, Bonafe JL, Christol B, Lassere J. 1979. Vitamin B<sub>12</sub>-induced acnes. *Cutis* 24:210–211.
- El Kholy S, Gueant JL, Bressler L, Djalali M, Boissel P, Gerard P, Nicolas JP. 1991. Portal and biliary phases of enterohepatic circulation of corrinoids in humans. *Gastroenterology* 101:1399–1408.
- Fernandes-Costa F, Metz J. 1982. Levels of transcobalamins I, II, and III during pregnancy and in cord blood. *Am J Clin Nutr* 35:87–94.
- Fernandes-Costa F, van Tonder S, Metz J. 1985. A sex difference in serum cobalamin and transcobalamin levels. *Am J Clin Nutr* 41:784–786.
- Ford JE, Hutner SH. 1955. Role of vitamin B<sub>12</sub> in the metabolism of micro-organisms. *Vitam Horm* 13:101–136.
- Foulds WS. 1968. Hydroxocobalamin in the treatment of Leber's hereditary optic atrophy. *Lancet* 1:896–897.
- Foulds WS. 1969a. Cyanide induced optic neuropathy. *Ophthalmologica* 158:350–358.
- Foulds WS. 1969b. The optic neuropathy of pernicious anemia. *Arch Ophthalmol* 82:427–432.
- Foulds WS. 1970. The investigation and therapy of the toxic amblyopias. *Trans Ophthalmol Soc UK* 90:739–763.
- Fréry N, Huel G, Leroy M, Moreau T, Savard R, Blot P, Lellouch J. 1992. Vitamin B<sub>12</sub> among parturients and their newborns and its relationship with birth-weight. *Eur J Obstet Gynecol Reprod Biol* 45:155–163.
- Gambon RC, Lentze MJ, Rossi E. 1986. Megaloblastic anaemia in one of monozygous twins breast fed by their vegetarian mother. *Eur J Pediatr* 145:570–571.
- Garry PJ, Goodwin JS, Hunt WC. 1984. Folate and vitamin B<sub>12</sub> status in a healthy elderly population. *J Am Geriatr Soc* 32:719–726.
- Georgadze GE. 1960. Effect of vitamin B<sub>1</sub> and B<sub>12</sub> on induction of malignant growths in hamsters. *Vopr Onkol* 6:54–58.
- Grasbeck T, Nyberg W, Reizenstein P. 1958. Biliary and fecal vitamin B<sub>12</sub> excretion in man. An isotope study. *Proc Soc Exp Biol Med* 97:780–784.
- Green R, Kinsella LJ. 1995. Current concepts in the diagnosis of cobalamin deficiency. *Neurology* 45:1435–1440.
- Green R, Jacobsen DW, Van Tonder SV, Kew MC, Metz J. 1982. Absorption of biliary cobalamin in baboons following total gastrectomy. *J Lab Clin Med* 100:771–777.
- Gueant JL, Champigneulle B, Gaucher P, Nicolas JP. 1990. Malabsorption of vitamin B<sub>12</sub> in pancreatic insufficiency of the adult and of the child. *Pancreas* 5:559–567.

- Hall CA, Finkler AE. 1966. Function of transcobalamin II: A B<sub>12</sub> binding protein in human plasma. *Proc Soc Exp Biol Med* 123:55–58.
- Hansen HA, Weinfeld A. 1962. Metabolic effects and diagnostic value of small doses of folic acid and B<sub>12</sub> in megaloblastic anemias. *Acta Med Scand* 172:427–443.
- Healton EB, Savage DG, Brust JC, Garrett TJ, Lindenbaum J. 1991. Neurologic aspects of cobalamin deficiency. *Medicine (Baltimore)* 70:229–245.
- Heinrich HC. 1964. Metabolic basis of the diagnosis and therapy of vitamin B<sub>12</sub> deficiency. *Semin Hematol* 1:199–249.
- Hellegers A, Okuda K, Nesbitt RE Jr, Smith DW, Chow BF. 1957. Vitamin B<sub>12</sub> absorption in pregnancy and in the newborn. *Am J Clin Nutr* 5:327–331.
- Herbert V, Jacob E, Wong KT, Scott J, Pfeffer RD. 1978. Low serum vitamin B<sub>12</sub> levels in patients receiving ascorbic acid in megadoses: Studies concerning the effect of ascorbate on radioisotope vitamin B<sub>12</sub> assay. *Am J Clin Nutr* 31:253–258.
- Herzlich B, Herbert V. 1988. Depletion of serum holotranscobalamin II. An early sign of negative vitamin B<sub>12</sub> balance. *Lab Invest* 58:332–337.
- Heyssel RM, Bozian RC, Darby WJ, Bell MC. 1966. Vitamin B<sub>12</sub> turnover in man. The assimilation of vitamin B<sub>12</sub> from natural foodstuff by man and estimates of minimal daily requirements. *Am J Clin Nutr* 18:176–184.
- Hoey H, Linnell JC, Oberholzer VG, Laurance BM. 1982. Vitamin B<sub>12</sub> deficiency in a breastfed infant of a mother with pernicious anaemia. *JR Soc Med* 75:656–658.
- Houston GA, Files JC, Morrison FS. 1985. Race, age, and pernicious anemia. *South Med J* 78:69–70.
- Hsing AW, Hansson LE, McLaughlin JK, Nyren O, Blot WJ, Ekbom A, Faumeni JF. 1993. Pernicious anemia and subsequent cancer: A population-based cohort study. *Cancer* 71:745–750.
- Hurwitz A, Brady DA, Schaal SE, Samloff IM, Dedon J, Ruhl CE. 1997. Gastric acidity in older adults. *J Am Med Assoc* 278:659–662.
- Isaacs R, Friedman A. 1938. Standards for maximum reticulocyte percentage after intramuscular liver therapy in pernicious anemia. *Am J Med Sci* 196:718–719.
- Isaacs R, Bethell FH, Riddle MC, Friedman A. 1938. Standards for red blood cell increase after liver and stomach therapy in pernicious anemia. *JAMA* 111:2291.
- Jadhav M, Webb JK, Vaishnava S, Baker SJ. 1962. Vitamin B<sub>12</sub> deficiency in Indian infants. *Lancet* 1962:903–907.
- Jathar VS, Inamdar-Deshmukh AB, Rege DV, Satoskar RS. 1975. Vitamin B<sub>12</sub> and vegetarianism in India. *Acta Haematol* 53:90–97.
- Johnsen R, Bernersen B, Straume B, Forde OH, Bostad L, Burhol PG. 1991. Prevalences of endoscopic and histological findings in subjects with and without dyspepsia. *Br Med J* 302:749–752.
- Johnson PR Jr, Roloff JS. 1982. Vitamin B<sub>12</sub> deficiency in an infant strictly breast-fed by a mother with latent pernicious anemia. *J Pediatr* 100:917–919.
- Jones BP, Broomhead AF, Kwan YL, Grace CS. 1987. Incidence and clinical significance of protein-bound vitamin B<sub>12</sub> malabsorption. *Eur J Haematol* 38:131–136.
- Joosten E, Pelemans W, Devos P, Lesaffre E, Goossens W, Criel A, Verhaeghe R. 1993. Cobalamin absorption and serum homocysteine and methylmalonic acid in elderly subjects with low serum cobalamin. *Eur J Haematol* 51:25–30.

- Joosten E, Lesaffre E, Riezler R. 1996. Are different reference intervals for methylmalonic acid and total homocysteine necessary in elderly people? *Eur J Haematol* 57:222–226.
- Kalnev VR, Rachkus I, Kanopkaite SI. 1977. Influence of methylcobalamin and cyanocobalamin on the neoplastic process in rats. *Prikl Biochim Mikrobiol* 13:677.
- Kano Y, Sakamoto S, Miura Y, Takaku F. 1985. Disorders of cobalamin metabolism. *Crit Rev Oncol Hematol* 3:1–34.
- Karnaze DS, Carmel R. 1990. Neurologic and evoked potential abnormalities in subtle cobalamin deficiency states, including deficiency without anemia and with normal absorption of free cobalamin. *Arch Neurol* 47:1008–1012.
- Kato N, Narita Y, Kamohara S. 1959. Liver vitamin B<sub>12</sub> levels in chronic liver diseases. *J Vitam* 5:134–140.
- Krasinski SD, Russell RM, Samloff IM, Jacob RA, Dallal GE, McGandy RB, Hartz SC. 1986. Fundic atrophic gastritis in an elderly population: Effect on hemoglobin and several serum nutritional indicators. *J Am Geriatr Soc* 34:800–806.
- Kuhne T, Bubl R, Baumgartner R. 1991. Maternal vegan diet causing a serious infantile neurological disorder due to vitamin B<sub>12</sub> deficiency. *Eur J Pediatr* 150:205–208.
- Lindenbaum J, Heaton EB, Savage DG, Brust JC, Garrett TJ, Podell ER, Marcell PD, Stabler SP, Allen RH. 1988. Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis. *N Engl J Med* 318:1720–1728.
- Lindenbaum J, Savage DG, Stabler SP, Allen RH. 1990. Diagnosis of cobalamin deficiency: 2. Relative sensitivities of serum cobalamin, methylmalonic acid, and total homocysteine concentrations. *Am J Hematol* 34:99–107.
- Lindenbaum J, Rosenberg IH, Wilson PW, Stabler SP, Allen RH. 1994. Prevalence of cobalamin deficiency in the Framingham elderly population. *Am J Clin Nutr* 60:2–11.
- Linnell JC, Smith AD, Smith CL, Wilson J, Matthews DM. 1968. Effects of smoking on metabolism and excretion of vitamin B<sub>12</sub>. *Br Med J* 2:215–216.
- Loria A, Vaz-Pinto A, Arroyo P, Ramirez-Mateos C, Sanchez-Medal L. 1977. Nutritional anemia. 6. Fetal hepatic storage of metabolites in the second half of pregnancy. *J Pediatr* 91:569–573.
- Low-Bear TS, McCarthy CF, Austad WI, Brzechwa-Ajdukiewicz A, Read AE. 1968. Serum vitamin B<sub>12</sub> levels and vitamin B<sub>12</sub> binding capacity in pregnant and non-pregnant Europeans and West Indians. *Br Med J* 4:160–161.
- Luhby AL, Cooperman JM, Donnenfeld AM, Herrero JM, Teller DN, Wenig JB. 1958. Observations on transfer of vitamin B<sub>12</sub> from mother to fetus and newborn. *Am J Dis Child* 96:532–533.
- Mangiarotti G, Canavese C, Salomone M, Thea A, Pacitti A, Gaido M, Calitri V, Pelizza D, Canavero W, Vercellone A. 1986. Hypervitaminosis B<sub>12</sub> in maintenance hemodialysis patients receiving massive supplementation of vitamin B<sub>12</sub>. *Int J Artif Organs* 9:417–420.
- Martin DC, Francis J, Protetch J, Huff J. 1992. Time dependency of cognitive recovery with cobalamin replacement: Report of a pilot study. *J Am Geriatr Soc* 40:168–172.
- McEvoy AW, Fenwick JD, Boddy K, James OF. 1982. Vitamin B<sub>12</sub> absorption from the gut does not decline with age in normal elderly humans. *Age Ageing* 11:180–183.

- Metz J, Hart D, Harpending HC. 1971. Iron, folate, and vitamin B<sub>12</sub> nutrition in a hunter-gatherer people: A study of the Kung Bushmen. *Am J Clin Nutr* 24:229–242.
- Miller DR, Specker BL, Ho L, Norman EJ. 1991. Vitamin B-12 status in a macrobiotic community. *Am J Clin Nutr* 53:524–529.
- Miller A, Furlong D, Burrows BA, Slingerland DW. 1992. Bound vitamin B<sub>12</sub> absorption in patients with low serum B<sub>12</sub> levels. *Am J Hematol* 40:63–166.
- Moelby L, Rasmussen K, Jensen MK, Pedersen KO. 1990. The relationship between clinically confirmed cobalamin deficiency and serum methylmalonic acid. *J Intern Med* 228:373–378.
- Mollin DL, Ross GI. 1952. The vitamin B<sub>12</sub> concentrations of serum and urine of normals and of patients with megaloblastic anaemias and other diseases. *J Clin Pathol* 5:129–139.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance Data, Vital and Health Statistics of the National Center for Health Statistics, No. 174. Hyattsville, MD: National Center for Health Statistics.
- Muir M, Landon M. 1985. Endogenous origin of microbiologically-inactive cobalamins (cobalamin analogues) in the human fetus. *Br J Haematol* 61:303–306.
- Narayanan MN, Dawson DW, Lewis MJ. 1991. Dietary deficiency of vitamin B<sub>12</sub> is associated with low serum cobalamin levels in non-vegetarians. *Eur J Haematol* 47:115–118.
- Naurath HJ, Joosten E, Riezler R, Stabler SP, Allen RH, Lindenbaum J. 1995. Effects of vitamin B<sub>12</sub>, folate, and vitamin B<sub>6</sub> supplements in elderly people with normal serum vitamin concentrations. *Lancet* 346:85–89.
- Nilsson-Ehle H, Jagenburg R, Landahl S, Lindstedt G, Swolin B, Westin J. 1986. Cyanocobalamin absorption in the elderly: Results for healthy subjects and for subjects with low serum cobalamin concentration. *Clin Chem* 32:1368–1371.
- Norman EJ, Morrison JA. 1993. Screening elderly populations for cobalamin (vitamin B<sub>12</sub>) deficiency using the urinary methylmalonic acid assay by gas chromatography mass spectrometry. *Am J Med* 94:589–594.
- Ostryanova AD. 1971. Effect of vitamin B<sub>12</sub> on the induction of tumors in mouse skin. *Patol Fiziol Eksperim Terapiya* 15:48–53.
- Pennypacker LC, Allen RH, Kelly JP, Matthews LM, Grigsby J, Kaye K, Lindenbaum J, Stabler SP. 1992. High prevalence of cobalamin deficiency in elderly outpatients. *J Am Geriatr Soc* 40:1197–1204.
- Puissant A, Vanbremeersch F, Monfort J, Lamberton J-N. 1967. A new iatrogenic dermatosis: Acne caused by vitamin B<sub>12</sub>. *Bull Soc Fr Dermatol Syphiligr* 74:813–815.
- Quinn K, Basu TK. 1996. Folate and vitamin B<sub>12</sub> status of the elderly. *Eur J Clin Nutr* 50:340–342.
- Rautio AL, Torronen R, Hanninen O, Mykkanen H. 1995. Vitamin B-12 status of long-term adherents of a strict uncooked vegan diet (“living food diet”) is compromised. *J Nutr* 125:2511–2515.
- Reizenstein P. 1959. Excretion of non-labeled vitamin B<sub>12</sub> in man. *Acta Med Scand* 165:313–320.
- Reizenstein P, Ek G, Matthews CM. 1966. Vitamin B<sub>12</sub> kinetics in man. Implications on total-body B<sub>12</sub> determinations, human requirements, and normal and pathological cellular B<sub>12</sub> uptake. *Phys Med Biol* 11:295–306.

- Robertson JA, Gallagher ND. 1983. Increased intestinal uptake of cobalamin in pregnancy does not require synthesis of new receptors. *Biochim Biophys Acta* 757:145–150.
- Rogers AE. 1975. Variable effects of a lipotrope-deficient, high-fat diet on chemical carcinogens in rats. *Cancer Res* 35:2469–2474.
- Rosenberg LE, Fenton WA. 1989. Disorders of propionate and methylmalonate metabolism. In: Scriver CR, Beaudet AL, Sly WS, Valle D, eds. *The Metabolic Basis of Inherited Disease*, 6th ed. New York: McGraw-Hill. Pp. 821–844.
- Rosner F, Schreiber ZA. 1972. Serum vitamin B<sub>12</sub> and vitamin B<sub>12</sub> binding capacity in chronic myelogenous leukemia and other disorders. *Am J Med Sci* 263:473–480.
- Russell RM. 1992. Vitamin B<sub>12</sub>. In: Hartz SC, Russell RM, Rosenberg IH, eds. *Nutrition in the Elderly. The Boston Nutritional Status Survey*. London: Smith-Gordon. Pp. 141–145.
- Sahyoun NR, Otradovec CL, Hartz SC, Jacob RA, Peters H, Russell RM, McGandy RB. 1988. Dietary intakes and biochemical indicators of nutritional status in an elderly, institutionalized population. *Am J Clin Nutr* 47:524–533.
- Savage D, Gangaidzo I, Lindenbaum J. 1994a. Vitamin B<sub>12</sub> deficiency is the primary cause of megaloblastic anemia in Zimbabwe. *Br J Haematol* 86:844–850.
- Savage DG, Lindenbaum J, Stabler SP, Allen RH. 1994b. Sensitivity of serum methylmalonic acid and total homocysteine determinations for diagnosing cobalamin and folate deficiencies. *Am J Med* 96:239–246.
- Scarlett JD, Read H, O'Dea K. 1992. Protein-bound cobalamin absorption declines in the elderly. *Am J Hematol* 39:79–83.
- Schilling RF. 1953. Intrinsic factor studies II. The effect of gastric juice on the urinary excretion of radioactivity after the oral administration of radioactive vitamin B<sub>12</sub>. *J Lab Clin Med* 42:860–866.
- Schneede J, Dagnelie PC, van Staveren WA, Vollset SE, Refsum H, Ueland PM. 1994. Methylmalonic acid and homocysteine in plasma as indicators of functional cobalamin deficiency in infants on macrobiotic diets. *Pediatr Res* 36:194–201.
- Scott JM. 1997. Bioavailability of vitamin B<sub>12</sub>. *Eur J Clin Nutr* 51 Suppl 1:S49–S53.
- Scott JM, Bloomfield FJ, Stebbins R, Herbert V. 1974. Studies on derivation of transcobalamin 3 from granulocytes. Enhancement by lithium and elimination by fluoride of in vitro increments in vitamin B<sub>12</sub>-binding capacity. *J Clin Invest* 53:228–239.
- Seetharam B, Alpers DH. 1982. Absorption and transport of cobalamin (vitamin B<sub>12</sub>). *Annu Rev Nutr* 2:343–369.
- Shapiro J, Alberts HW, Welch P, Metz J. 1965. Folate and vitamin B<sub>12</sub> deficiency associated with lactation. *Br J Haematol* 11:498–504.
- Sherertz EF. 1991. Acneiform eruption due to “megadose” vitamins B<sub>6</sub> and B<sub>12</sub>. *Cutis* 48:119–120.
- Sklar R. 1986. Nutritional vitamin B<sub>12</sub> deficiency in a breast-fed infant of a vegan-diet mother. *Clin Pediatr* 25:219–221.
- Specker BL, Miller D, Norman EJ, Greene H, Hayes KC. 1988. Increased urinary methylmalonic acid excretion in breast-fed infants of vegetarian mothers and identification of an acceptable dietary source of vitamin B<sub>12</sub>. *Am J Clin Nutr* 47:89–92.

- Specker BL, Black A, Allen L, Morrow F. 1990. Vitamin B-12: Low milk concentrations are related to low serum concentrations in vegetarian women and to methylmalonic aciduria in their infants. *Am J Clin Nutr* 52:1073–1076.
- Srikantia SG, Reddy V. 1967. Megaloblastic anaemia of infancy and vitamin B<sub>12</sub>. *Br J Haematol* 13:949–953.
- Stabler SP, Marcell PD, Podell ER, Allen RH, Savage DG, Lindenbaum J. 1988. Elevation of total homocysteine in the serum of patients with cobalamin or folate deficiency detected by capillary gas chromatography-mass spectrometry. *J Clin Invest* 81:466–474.
- Stabler SP, Lindenbaum J, Allen RH. 1996. The use of homocysteine and other metabolites in the specific diagnosis of vitamin B-12 deficiency. *J Nutr* 126:1266S–1272S.
- Stahlberg KG, Radner S, Norden A. 1967. Liver B<sub>12</sub> in subjects with and without vitamin B<sub>12</sub> deficiency. A quantitative and qualitative study. *Scand J Haematol* 4:312–330.
- Stewart JS, Roberts PD, Hoffbrand AV. 1970. Response of dietary vitamin B<sub>12</sub> deficiency to physiological oral doses of cyanocobalamin. *Lancet* 2:542–545.
- Sullivan LW, Herbert V. 1965. Studies on the minimum daily requirement for vitamin B<sub>12</sub>. Hematopoietic responses to 0.1 microgram of cyanocobalamin or coenzyme B<sub>12</sub> and comparison of their relative potency. *N Engl J Med* 272:340–346.
- Suter PM, Golner BB, Goldin BR, Morrow FD, Russell RM. 1991. Reversal of protein-bound vitamin B<sub>12</sub> malabsorption with antibiotics in atrophic gastritis. *Gastroenterology* 101:1039–1045.
- Teo NH, Scott JM, Neale G, Weir DG. 1980. Effect of bile on vitamin B<sub>12</sub> absorption. *Br Med J* 281:831–833.
- Termanini B, Gibril F, Sutliff VE, Yu F, Venzon DJ, Jensen RT. 1998. Effect of long-term gastric acid suppressive therapy on serum vitamin B<sub>12</sub> levels in patients with Zollinger-Ellison syndrome. *Am J Med* 104:422–430.
- Toh B-H, van Driel IR, Gleeson PA. 1997. Pernicious anemia. *N Engl J Med* 337:1441–1448.
- Trugo NM, Sardinha F. 1994. Cobalamin and cobalamin-binding capacity in human milk. *Nutr Res* 14:22–33.
- Tudhope GR, Swan HT, Spray GH. 1967. Patient variation in pernicious anaemia, as shown in a clinical trial of cyanocobalamin, hydroxocobalamin and cyanocobalamin-zinc tannate. *Br J Haematol* 13:216–228.
- USDA (U.S. Department of Agriculture). 1997. USDA, ARS Nutrient Data Laboratory. [WWW document]. URL <http://www.nal.usda.gov/fnic/foodcomp/>.
- van Asselt DZ, van den Broek WJ, Lamers CB, Corstens FH, Hoefnagels WH. 1996. Free and protein-bound cobalamin absorption in healthy middle-aged and older subjects. *J Am Geriatr Soc* 44:949–953.
- Vaz Pinto A, Torras V, Sandoval JF, Dillman E, Mateos CR, Cordova MS. 1975. Folic acid and vitamin B<sub>12</sub> determination in fetal liver. *Am J Clin Nutr* 28:1085–1086.
- Vu T, Amin J, Ramos M, Flener V, Vanyo L, Tisman G. 1993. New assay for the rapid determination of plasma holotranscobalamin II levels: Preliminary evaluation in cancer patients. *Am J Hematol* 42:202–211.
- WHO (World Health Organization). 1970. *Requirements of Ascorbic Acid, Vitamin D, Vitamin B<sub>12</sub>, Folate, and Iron*. Report of a Joint FAO/WHO Expert Group. Technical Report Series No. 452. Geneva: WHO.

- Will JJ, Mueller JF, Brodine C, Kiely CE, Friedman B, Hawkins VR, Dutra J, Vilter RN. 1959. Folic acid and vitamin B<sub>12</sub> in pernicious anemia. Studies on patients treated with these substances over a ten-year period. *J Lab Clin Med* 53:22–38.
- Wilson J, Matthews DM. 1966. Metabolic inter-relationships between cyanide, thiocyanate and vitamin B<sub>12</sub> in smokers and non-smokers. *Clin Sci* 31:1–7.
- Winawer SJ, Streiff RR, Zamcheck N. 1967. Gastric and hematological abnormalities in a vegan with nutritional vitamin B<sub>12</sub> deficiency: Effect of oral vitamin B<sub>12</sub>. *Gastroenterology* 53:130–135.

Ibid., Chapter 13, p. 436.

- Beaton GH. 1994. Criteria of an adequate diet. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*, 8th ed. Philadelphia: Lea & Febiger. Pp. 1491–1505.
- Hegsted DM. 1972. Problems in the use and interpretation of the Recommended Dietary Allowances. *Ecol Food Nutr* 1:255–265.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- USDA (U.S. Department of Agriculture). 1992. *The Food Guide Pyramid*. Home and Garden Bulletin Number 252. Washington, DC: US Government Printing Office.
- WHO (World Health Organization). 1996. *Trace Elements in Human Nutrition and Health*. Prepared in collaboration with the Food and Agriculture Organization of the United Nations and the International Atomic Energy Agency. Geneva: WHO.

## BIOTIN

*Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline* (ISBN 0-309-06411-2), Chapter 11, pp. 386–389.

- Allred JB, Roman-Lopez CR. 1988. Enzymatically inactive forms of acetyl-CoA carboxylase in rat liver mitochondria. *Biochem J* 251:881–885.
- Allred JB, Roman-Lopez CR, Jurin RR, McCune SA. 1989. Mitochondrial storage forms of acetyl-CoA carboxylase: Mobilization/activation accounts for increased activity of the enzyme in liver of genetically obese Zucker rats. *J Nutr* 119:478–483.
- Baugh CM, Malone JH, Butterworth CE Jr. 1968. Human biotin deficiency. A case history of biotin deficiency induced by raw egg consumption in a cirrhotic patient. *Am J Clin Nutr* 21:173–182.
- Bhagavan HN. 1969. Biotin content of blood during gestation. *Int Z Vitaminforsch* 39:235–237.
- Boas MA. 1927. The effect of desiccation upon the nutritive properties of egg white. *Biochem J* 21:712–724.
- Bonjour J-P. 1991. Biotin. In: Machlin LJ, ed. *Handbook of Vitamins*. New York: Marcel Dekker. Pp. 393–427.
- Bowers-Komro DM, McCormick DB. 1985. Biotin uptake by isolated rat liver hepatocytes. *Ann NY Acad Sci* 447:350–358.
- Bull NL, Buss DH. 1982. Biotin, pantothenic acid and vitamin E in the British household food supply. *Hum Nutr Appl Nutr* 36:190–196.
- Carlson GL, Williams N, Barber D, Shaffer JL, Wales S, Isherwood D, Shenkin A, Irving MH. 1995. Biotin deficiency complicating long-term total parenteral nutrition in an adult patient. *Clin Nutr* 14:186–190.
- Chauhan J, Dakshinamurti K. 1988. Role of human serum biotinidase as biotin-binding protein. *Biochem J* 256:265–270.
- Colamaria V, Burlina AB, Gaburro D, Pajno-Ferrara F, Saudubray JM, Merino RG, Dalla Bernardina B. 1989. Biotin-responsive infantile encephalopathy: EEG-polygraphic study of a case. *Epilepsia* 30:573–578.
- Dakshinamurti K. 1994. Biotin. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*. Philadelphia: Lea & Febiger. Pp. 426–431.
- Dostalova L. 1984. Vitamin status during puerperium and lactation. *Ann Nutr Metab* 28:385–408.
- Gillis J, Murphy FR, Boxall LB, Pencharz PB. 1982. Biotin deficiency in a child on long-term TPN. *J Parenter Enteral Nutr* 6:308–310.
- Guilarte TR. 1985. Measurement of biotin levels in human plasma using a radio-metric-microbiological assay. *Nutr Rep Int* 31:1155–1163.
- Hirano M, Honma K, Daimatsu T, Hayakawa K, Oizumi J, Zaima K, Kanke Y. 1992. Longitudinal variations of biotin content in human milk. *Int J Vitam Nutr Res* 62:281–282.
- Hoppner K, Lampi B, Smith DC. 1978. An appraisal of the daily intakes of vitamin B<sub>12</sub>, pantothenic acid and biotin from a composite Canadian diet. *Can Inst Food Sci Technol J* 11:71–74.
- Hu Z-Q, Henderson GI, Mock DM, Schenker S. 1994. Biotin uptake by basolateral membrane vesicles of human placenta: Normal characteristics and role of ethanol. *Proc Soc Exp Biol Med* 206:404–408.

- Innis SM, Allardyce DB. 1983. Possible biotin deficiency in adults receiving long-term total parenteral nutrition. *Am J Clin Nutr* 37:185–187.
- Karl PI, Fisher SE. 1992. Biotin transport in microvillous membrane vesicles, cultured trophoblasts and isolated perfused human placenta. *Am J Physiol* 262:C302–C308.
- Khalidi N, Wesley JR, Thoene JG, Whitehouse WM Jr, Baker WL. 1984. Biotin deficiency in a patient with short bowel syndrome during home parenteral nutrition. *J Parenter Enteral Nutr* 8:311–314.
- Kien CL, Kohler E, Goodman SI, Berlow S, Hong R, Horowitz SP, Baker H. 1981. Biotin-responsive in vivo carboxylase deficiency in two siblings with secretory diarrhea receiving total parenteral nutrition. *J Pediatr* 99:546–550.
- Kopinski JS, Leibholz J, Bryden WL. 1989a. Biotin studies in pigs. 3. Biotin absorption and synthesis. *Br J Nutr* 62:767–772.
- Kopinski JS, Leibholz J, Bryden WL. 1989b. Biotin studies in pigs. 4. Biotin availability in feedstuffs for pigs and chickens. *Br J Nutr* 62:773–780.
- Koutsikos D, Fourtounas C, Kapetanaki A, Agroyannis B, Tzanatos H, Rammos G, Kopelias I, Bosiolis B, Bovoleti O, Darema M, Sallum G. 1996. Oral glucose tolerance test after high-dose i.v. biotin administration in normoglycemic hemodialysis patients. *Ren Fail* 18:131–137.
- Kramer TR, Briske-Anderson M, Johnson SB, Holman RT. 1984. Effects of biotin deficiency on polyunsaturated fatty acid metabolism in rats. *J Nutr* 114:2047–2052.
- Lagier P, Bimar P, Seriat-Gautier S, Dejode JM, Brun T, Bimar J. 1987. Zinc and biotin deficiency during prolonged parenteral nutrition in infants. *Presse Med* 16:1795–1797.
- Lewis J, Buss DH. 1988. Trace nutrients: Minerals and vitamins in the British household food supply. *Br J Nutr* 60:413–424.
- Liu YY, Shigematsu Y, Bykov I, Nakai A, Kikawa Y, Fukui T, Sudo M. 1994. Abnormal fatty acid composition of lymphocytes of biotin-deficient rats. *J Nutr Sci Vitaminol* 40:283–288.
- Livaniou E, Evangelatos GP, Ithakissios DS, Yatzidis H, Koutsicos DC. 1987. Serum biotin levels in patients undergoing chronic hemodialysis. *Nephron* 46:331–332.
- Matsusue S, Kashihara S, Takeda H, Koisumi S. 1985. Biotin deficiency during total parenteral nutrition: Its clinical manifestation and plasma nonesterified fatty acid level. *J Parenter Enteral Nutr* 9:760–763.
- McCormick DB. 1976. Biotin. In: Hegsted M, ed. *Present Knowledge in Nutrition*. Washington, DC: The Nutrition Foundation. Pp. 217–225.
- McCormick DB, Wright LD. 1971. The metabolism of biotin and analogues. In: Florkin M, Stotz EH, eds. *Comprehensive Biochemistry*, Vol. 21. Amsterdam: Elsevier. Pp. 81–110.
- Mock DM. 1996. Biotin. In: Ziegler EE, Filer LJ Jr, eds. *Present Knowledge in Nutrition*, 7th ed. Washington, DC: ILSI Nutrition Foundation. Pp. 220–235.
- Mock DM, Dyken ME. 1997. Biotin catabolism is accelerated in adults receiving long-term therapy with anticonvulsants. *Neurology* 49:1444–1447.
- Mock DM, Heird GM. 1997. Urinary biotin analogs increase in humans during chronic supplementation: The analogs are biotin metabolites. *Am J Physiol* 272:E83–E85.
- Mock DM, Malik MI. 1992. Distribution of biotin in human plasma: Most of the biotin is not bound to protein. *Am J Clin Nutr* 56:427–432.

- Mock DM, Stadler DD. 1997. Conflicting indicators of biotin status from a cross-sectional study of normal pregnancy. *J Am Coll Nutr* 16:252–257.
- Mock DM, Delorimer AA, Lieberman WM, Sweetman L, Baker H. 1981. Biotin deficiency: An unusual complication of parenteral alimentation. *N Engl J Med* 304:820–823.
- Mock DM, Baswell DL, Baker H, Holman RT, Sweetman L. 1985. Biotin deficiency complicating parenteral alimentation: Diagnosis, metabolic repercussions, and treatment. *J Pediatr* 106:762–769.
- Mock DM, Johnson SB, Holman RT. 1988a. Effects of biotin deficiency on serum fatty acid composition: Evidence for abnormalities in humans. *J Nutr* 118:342–348.
- Mock DM, Mock NI, Johnson SB, Holman RT. 1988b. Effects of biotin deficiency on plasma and tissue fatty acid composition: Evidence for abnormalities in rats. *Pediatr Res* 24:396–403.
- Mock DM, Mock NI, Langbehn SE. 1992. Biotin in human milk: Methods, location, and chemical form. *J Nutr* 122:535–545.
- Mock DM, Mock NI, Stratton SL. 1997a. The concentrations of biotin metabolites in human milk. *J Pediatr* 131:456–458.
- Mock DM, Stadler DD, Stratton SL, Mock NI. 1997b. Biotin status assessed longitudinally in pregnant women. *J Nutr* 127:710–716.
- Mock NI, Malik MI, Stumbo PJ, Bishop WP, Mock DM. 1997. Increased urinary excretion of 3-hydroxyisovaleric acid and decreased urinary excretion of biotin are sensitive early indicators of decreased status in experimental biotin deficiency. *Am J Clin Nutr* 65:951–958.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance Data, Vital and Health Statistics of the National Center for Health Statistics, No. 174. Hyattsville, MD: National Center for Health Statistics.
- Murphy SP, Calloway DH. 1986. Nutrient intake of women in NHANES II, emphasizing trace minerals, fiber, and phytate. *J Am Diet Assoc* 86:1366–1372.
- NRC (National Research Council). 1989. *Recommended Dietary Allowances*, 10th ed. Washington, DC: National Academy Press.
- Oppel TW. 1948. Studies of biotin metabolism in man: 4. Studies of the mechanism of absorption of biotin and the effect of biotin administration on a few cases of seborrhea and other conditions. *Am J Med Sci* 215:76–83.
- Paul AA, Southgate DAT. 1978. *McCance and Widdowson's The Composition of Foods*. London: Her Majesty's Stationery Office.
- Paul PK, Duttagupta PN. 1975. The effect of an acute dose of biotin at the pre-implantation stage and its relation with female sex steroids in the rat. *J Nutr Sci Vitaminol (Tokyo)* 21:89–101.
- Paul PK, Duttagupta PN. 1976. The effect of an acute dose of biotin at a post-implantation stage and its relation with female sex steroids in the rat. *J Nutr Sci Vitaminol (Tokyo)* 22:181–186.
- Ramaekers VT, Brab M, Rau G, Heimann G. 1993. Recovery from neurological deficits following biotin treatment in a biotinidase Km variant. *Neuropediatrics* 24:98–102.
- Roth KS, Yang W, Allan L, Saunders M, Gravel RA, Dakshinamurti K. 1982. Prenatal administration of biotin in biotin responsive multiple carboxylase deficiency. *Pediatr Res* 16:126–129.

- Salmenpera L, Perheentupa J, Pispa JP, Siimes MA. 1985. Biotin concentrations in maternal plasma and milk during prolonged lactation. *Int J Vitam Nutr Res* 55:281–285.
- Schenker S, Hu Z, Johnson RF, Yang Y, Frosto T, Elliott BD, Henderson GI, Mock DM. 1993. Human placental biotin transport: Normal characteristics and effect of ethanol. *Alcohol Clin Exp Res* 17:566–575.
- Shriver BJ, Roman-Shriver C, Allred JB. 1993. Depletion and repletion of biotinyl enzymes in liver of biotin-deficient rats: Evidence of a biotin storage system. *J Nutr* 123:1140–1149.
- Sorrell MF, Frank O, Thompson AD, Aquino H, Baker H. 1971. Absorption of vitamins from the large intestine in vivo. *Nutr Rep Int* 3:143–148.
- Wolf B, Heard GS, McVoy JR, Raetz HM. 1984. Biotinidase deficiency: The possible role of biotinidase in the processing of dietary protein-bound biotin. *J Inherit Metab Dis* 7:121–122.
- Wolf B, Grier RE, McVoy JR, Heard GS. 1985. Biotinidase deficiency: A novel vitamin recycling defect. *J Inherit Metab Dis* 8:53–58.
- Yatzidis H, Koutsicos D, Agroyannis B, Papastefanidis C, Francos-Plemenos M, Delatola Z. 1984. Biotin in the management of uremic neurologic disorders. *Nephron* 36:183–186.
- Zempleni J, McCormick DB, Mock DM. 1997. Identification of biotin sulfone, bis-norbiotin methyl ketone, and tetranorbiotin-1-sulfoxide in human urine. *Am J Clin Nutr* 65:508–511.

Ibid., Chapter 13, p. 436.

- Beaton GH. 1994. Criteria of an adequate diet. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*, 8th ed. Philadelphia: Lea & Febiger. Pp. 1491–1505.
- Hegsted DM. 1972. Problems in the use and interpretation of the Recommended Dietary Allowances. *Ecol Food Nutr* 1:255–265.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- USDA (U.S. Department of Agriculture). 1992. *The Food Guide Pyramid*. Home and Garden Bulletin Number 252. Washington, DC: US Government Printing Office.
- WHO (World Health Organization). 1996. *Trace Elements in Human Nutrition and Health*. Prepared in collaboration with the Food and Agriculture Organization of the United Nations and the International Atomic Energy Agency. Geneva: WHO.

## VITAMIN C

*Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*  
(ISBN 0-309-06949-1), Chapter 5, pp. 167–185.

- Afroz M, Bhothinard B, Etzkorn JR, Horenstein S, McGarry JD. 1975. Vitamins C and B<sub>12</sub>. *J Am Med Assoc* 232:246.
- Alexy U, Kersting M, Sichert-Hellert W, Manz F, Schöch G. 1999. Vitamin intake of 3- to 36-month-old German infants and children—Results of the DONALD study. *Int J Vitam Nutr Res* 69:285–291.
- Allen JC, Keller RP, Archer P, Neville MC. 1991. Studies in human lactation: Milk composition and daily secretion rates of macronutrients in the first year of lactation. *Am J Clin Nutr* 54:69–80.
- Alvares O. 1997. Ascorbic acid and periodontal disease. In: Packer L, Fuchs J, eds. *Vitamin C in Health and Disease*. New York: Marcel Dekker. Pp. 505–516.
- Ames BN, Gold LS, Willett WC. 1995. The causes and prevention of cancer. *Proc Natl Acad Sci USA* 92:5258–5265.
- Anderson D, Phillips BJ, Yu T, Edwards AJ, Ayesh R, Butterworth KR. 1997. The effects of vitamin C supplementation on biomarkers of oxygen radical generated damage in human volunteers with “low” or “high” cholesterol levels. *Environ Mol Mutagen* 30:161–174.
- Anderson DM, Pittard WB. 1985. Vitamin E and C concentrations in human milk with maternal megadosing. A case report. *J Am Diet Assoc* 85:715–717.
- Anderson R, Lukey PT. 1987. A biological role for ascorbate in the selective neutralization of extracellular phagocyte-derived oxidants. *Ann NY Acad Sci* 498: 229–247.
- Anderson R, Oosthuizen R, Maritz R, Theron A, Van Rensburg AJ. 1980. The effects of increasing weekly doses of ascorbate on certain cellular and humoral immune function in normal volunteers. *Am J Clin Nutr* 33:71–76.
- Asami S, Manabe H, Miyake J, Tsurudome Y, Hirano T, Yamaguchi R, Itoh H, Kasai H. 1997. Cigarette smoking induces an increase in oxidative DNA damage, 8-hydroxydeoxyguanosine, in a central site in the human lung. *Carcinogenesis* 18:1763–1766.
- Auer BL, Auer D, Rodgers AL. 1998. Relative hyperoxaluria, crystalluria and haematuria after megadose ingestion of vitamin C. *Eur J Clin Invest* 28:695–700.
- Bacon BR, Olynik JK, Brunt EM, Britton RS, Wolff RK. 1999. HFE genotype in patients with hemochromatosis and other liver diseases. *Ann Int Med* 130:953–962.
- Baer DM, Tekawa IS, Hurley LB. 1994. Iron stores are not associated with acute myocardial infarction. *Circulation* 89:2915–2918.
- Baker EM, Sauberlich HE, Wolfskill SJ, Wallace WT, Dean EE. 1962. Tracer studies of vitamin C utilization in men: Metabolism of D-glucuronolactone-6-C<sup>14</sup>, D-glucuronic-6-C<sup>14</sup> acid and L-ascorbic-1-C<sup>14</sup> acid. *Proc Soc Exp Biol Med* 109:737–741.
- Baker EM, Hodges RE, Hood J, Sauberlich HE, March SC. 1969. Metabolism of ascorbic-1-C<sup>14</sup> acid in experimental human scurvy. *Am J Clin Nutr* 22:549–558.
- Baker EM, Hodges RE, Hood J, Sauberlich HE, March SC, Canham JE. 1971. Metabolism of <sup>14</sup>C- and <sup>3</sup>H-labeled L-ascorbic acid in human scurvy. *Am J Clin Nutr* 24:444–454.

- Ballin A, Brown EJ, Koren G, Zipursky A. 1988. Vitamin C-induced erythrocyte damage in premature infants. *J Pediatr* 113:114–120.
- Bandera EV, Freudenheim JL, Marshall JR, Zielezny M, Priore RL, Brasure J, Baptiste M, Graham S. 1997. Diet and alcohol consumption and lung cancer risk in the New York State Cohort. *Cancer Causes Control* 8:828–840.
- Barrett B, Gunter E, Jenkins J, Wang M. 1991. Ascorbic acid concentration in amniotic fluid in late pregnancy. *Biol Neonate* 60:333–335.
- Bates CJ, Prentice AM, Prentice A, Paul AA, Whitehead RG. 1982. Seasonal variations in ascorbic acid status and breast milk ascorbic acid levels in rural Gambian women in relation to dietary intake. *Trans Royal Soc Trop Med Hyg* 76:341–347.
- Belcher JD, Balla J, Balla G, Jacobs DR Jr, Gross M, Jacob HS, Vercellotti GM. 1993. Vitamin E, LDL, and endothelium. Brief oral vitamin supplementation prevents oxidized LDL-mediated vascular injury in vitro. *Arterioscler Thromb* 13: 1779–1789.
- Bendich A, Cohen M. 1990. Ascorbic acid safety: Analysis of factors affecting iron absorption. *Toxicol Lett* 51:189–201.
- Berger L, Gerson CD, Yu TF. 1977. The effect of ascorbic acid on uric acid excretion with a commentary on the renal handling of ascorbic acid. *Am J Med* 62:71–76.
- Berger TM, Polidori MC, Dabbagh A, Evans PJ, Halliwell B, Morrow JD, Roberts LJ II, Frei B. 1997. Antioxidant activity of vitamin C in iron-overloaded human plasma. *J Biol Chem* 272:15656–15660.
- Berliner JA, Heinecke JW. 1996. The role of oxidized lipoproteins in atherogenesis. *Free Radic Biol Med* 20:707–727.
- Bermudez E, Stone K, Carter KM, Pryor WA. 1994. Environmental tobacco smoke is just as damaging to DNA as mainstream smoke. *Environ Hlth Perspect* 102:870–874.
- Beutler E. 1991. Glucose-6-phosphate dehydrogenase deficiency. *N Engl J Med* 324:169–174.
- Blanchard J. 1991a. Depletion and repletion kinetics of vitamin C in humans. *J Nutr* 121:170–176.
- Blanchard J. 1991b. Effects of gender on vitamin C pharmacokinetics in man. *J Am Coll Nutr* 10:453–459.
- Blanchard J, Conrad KA, Watson RR, Garry PJ, Crawley JD. 1989. Comparison of plasma, mononuclear and polymorphonuclear leucocyte vitamin C levels in young and elderly women during depletion and supplementation. *Eur J Clin Nutr* 43:97–106.
- Blanchard J, Conrad KA, Garry PJ. 1990a. Effects of age and intake on vitamin C disposition in females. *Eur J Clin Nutr* 44:447–460.
- Blanchard J, Conrad KA, Mead RA, Garry PJ. 1990b. Vitamin C disposition in young and elderly men. *Am J Clin Nutr* 51:837–845.
- Blanchard J, Tozer TN, Rowland M. 1997. Pharmacokinetic perspectives on megadoses of ascorbic acid. *Am J Clin Nutr* 66:1165–1171.
- Block G. 1991. Vitamin C and cancer prevention: The epidemiologic evidence. *Am J Clin Nutr* 53:270S–282S.
- Blot WJ, Li J-Y, Taylor PR, Guo W, Dawsey S, Wang G-Q, Yang CS, Zheng S-F, Gail M, Li G-Y, Yu Y, Liu B-Q, Tangrea J, Sun Y-H, Liu F, Fraumeni JF Jr, Zhang Y-H, Li B. 1993. Nutrition intervention trials in Linxian, China: Supplementation with specific vitamin/mineral combinations, cancer incidence, and dis-

- ease-specific mortality in the general population. *J Natl Cancer Inst* 85: 1483–1492.
- Bors W, Michel C, Schikora S. 1995. Interaction of flavonoids with ascorbate and determination of their univalent redox potentials: A pulse radiolysis study. *Free Radic Biol Med* 19:45–52.
- Bostick RM, Potter JD, McKenzie DR, Sellers TA, Kushi LH, Steinmetz KA, Folsom AR. 1993. Reduced risk of colon cancer with high intake of vitamin E: The Iowa Women's Health Study. *Cancer Res* 53:4230–4237.
- Britton JR, Pavord ID, Richards KA, Knox AJ, Wisniewski AF, Lewis SA, Tattersfield AE, Weiss ST. 1995. Dietary antioxidant vitamin intake and lung function in the general population. *Am J Respir Crit Care Med* 151:1383–1387.
- Bucca C, Rolla G, Farina JC. 1992. Effect of vitamin C on transient increase of bronchial responsiveness in conditions affecting the airways. *Ann NY Acad Sci* 669:175–187.
- Bueno de Mesquita HB, Maisonneuve P, Runia S, Moerman CJ. 1991. Intake of foods and nutrients and cancer of the exocrine pancreas: A population-based case-control study in The Netherlands. *Int J Cancer* 48:540–549.
- Buettner GR. 1993. The pecking order of free radicals and antioxidants: Lipid peroxidation, alpha-tocopherol, and ascorbate. *Arch Biochem Biophys* 300:535–543.
- Buettner GR, Jurkiewicz BA. 1996. Catalytic metals, ascorbate and free radicals: Combinations to avoid. *Radiat Res* 145:532–541.
- Burr ML, Elwood PC, Hole DJ, Hurley RJ, Hughes RE. 1974. Plasma and leukocyte ascorbic acid levels in the elderly. *Am J Clin Nutr* 27:144–151.
- Bussey HJ, DeCosse JJ, Deschner EE, Evers AA, Lesser ML, Morson BC, Ritchie SM, Thomson JP, Wadsworth J. 1982. A randomized trial of ascorbic acid in polyposis coli. *Cancer* 50:1434–1439.
- Butte NF, Garza C, Smith EO, Nichols BL. 1984. Human milk intake and growth in exclusively breast-fed infants. *J Pediatr* 104:187–195.
- Byerley LO, Kirksey A. 1985. Effects of different levels of vitamin C intake on the vitamin C concentration in human milk and the vitamin C intakes of breast-fed infants. *Am J Clin Nutr* 41:665–671.
- Byun J, Mueller DM, Fabjan JS, Heinecke JW. 1999. Nitrogen dioxide radical generated by the myeloperoxidase-hydrogen peroxide-nitrite system promotes lipid peroxidation of low density lipoprotein. *FEBS Lett* 455:243–246.
- Cadenas S, Rojas C, Méndez J, Herrero A, Barja G. 1996. Vitamin E decreases urine lipid peroxidation products in young healthy human volunteers under normal conditions. *Pharmacol Toxicol* 79:247–253.
- Cahill RJ, O'Sullivan KR, Mathias PM, Beattie S, Hamilton H, O'Morain C. 1993. Effects of vitamin antioxidant supplementation on cell kinetics of patients with adenomatous polyps. *Gut* 34:963–967.
- Cameron E, Campbell A. 1974. The orthomolecular treatment of cancer. II. Clinical trial of high-dose ascorbic acid supplements in advanced human cancer. *Chem Biol Interact* 9:285–315.
- Campbell GD Jr, Steinberg MH, Bower JD. 1975. Ascorbic acid-induced hemolysis in G-6-PD deficiency. *Ann Intern Med* 82:810.
- Carr AC, Frei B. 1999. Toward a new recommended dietary allowance for vitamin C based on antioxidant and health effects in humans. *Am J Clin Nutr* 69:1086–1087.

- Casanueva E, Polo E, Tejero E, Meza C. 1993. Premature rupture of amniotic membranes as functional assessment of vitamin C status during pregnancy. *Ann NY Acad Sci* 678:369–370.
- Chalmers TC. 1975. Effects of ascorbic acid on the common cold. An evaluation of the evidence. *Am J Med* 58:532–536.
- Chazan JA, Mistilis SP. 1963. The pathophysiology of scurvy. *Am J Med* 34:350–358.
- Cheng L, Cohen M, Bhagavan HN. 1985. Vitamin C and the elderly. In: Watson RR, ed. *CRC Handbook of Nutrition in the Aged*. Boca Raton, FL: CRC Press. Pp. 157–185.
- Choi JL, Rose RC. 1989. Transport and metabolism of ascorbic acid in human placenta. *Am J Physiol* 257:C110–C113.
- Cochrane WA. 1965. Overnutrition in prenatal and neonatal life: A problem? *Can Med Assoc J* 93:893–899.
- Cohen HA, Neuman I, Nahum H. 1997. Blocking effect of vitamin C in exercise-induced asthma. *Arch Pediatr Adolesc Med* 151:367–370.
- Cook JD, Watson SS, Simpson KM, Lipschitz DA, Skikne BS. 1984. The effect of high ascorbic acid supplementation on body iron stores. *Blood* 64:721–726.
- Cooke MS, Evans MD, Podmore ID, Herbert KE, Mistry N, Mistry P, Hickenbotham PT, Hussieni A, Griffiths HR, Lunec J. 1998. Novel repair action of vitamin C upon in vivo oxidative DNA damage. *FEBS Lett* 439:363–367.
- Coulehan JL, Eberhard S, Kapner L, Taylor F, Rogers K, Garry P. 1976. Vitamin C and acute illness in Navajo school children. *N Engl J Med* 295:973–977.
- Cross CE, Halliwell B. 1993. Nutrition and human disease: How much extra vitamin C might smokers need? *Lancet* 341:1091.
- Cross CE, Forte T, Stocker R, Louie S, Yamamoto Y, Ames BN, Frei B. 1990. Oxidative stress and abnormal cholesterol metabolism in patients with adult respiratory distress syndrome. *J Lab Clin Med* 115:396–404.
- Crott JW, Fenech M. 1999. Effect of vitamin C supplementation on chromosome damage, apoptosis and necrosis ex vivo. *Carcinogenesis* 20:1035–1041.
- Curhan GC, Willett WC, Rimm EB, Stampfer MJ. 1996. A prospective study of the intake of vitamins C and B<sub>6</sub>, and the risk of kidney stones in men. *J Urol* 155:1847–1851.
- Curhan GC, Willett WC, Speizer FE, Stampfer MJ. 1999. Intake of vitamins B<sub>6</sub> and C and the risk of kidney stones in women. *J Am Soc Nephrol* 10:840–845.
- Dabrowski K. 1990. Gastro-intestinal circulation of ascorbic acid. *Comp Biochem Physiol* 95A:481–486.
- Dallongeville J, Marécaux N, Fruchart J-C, Amouyel P. 1998. Cigarette smoking is associated with unhealthy patterns of nutrient intake: A meta-analysis. *J Nutr* 128:1450–1457.
- Davies HE, Davies JE, Hughes RE, Jones E. 1984. Studies on the absorption of L-xyloascorbic acid (vitamin C) in young and elderly subjects. *Hum Nutr Clin Nutr* 38C:463–471.
- Davies HE, Gruffudd S, Hughes RE, Jones E. 1987. Ascorbic acid and carnitine in man. *Nutr Report Int* 36:941–948.
- DeCosse JJ, Adams MB, Kuzma JF, LoGerfo P, Condon RE. 1975. Effect of ascorbic acid on rectal polyps of patients with familial polyposis. *Surgery* 78:608–612.
- Delafuente JC, Prendergast JM, Modigh A. 1986. Immunologic modulation by vitamin C in the elderly. *Int J Immunopharmacol* 8:205–211.
- Delamere NA. 1996. Ascorbic acid and the eye. *Subcell Biochem* 25:313–329.
- Devaraj S, Jialal I. 1996. Oxidized low-density lipoprotein and atherosclerosis. *Int J Clin Lab Res* 26:178–184.

- Dewey KG, Finley DA, Lonnerdal B. 1984. Breast milk volume and composition during late lactation (7–20 months). *J Pediatr Gastroenterol Nutr* 3:713–720.
- Drake IM, Davies MJ, Mapstone NP, Dixon MF, Schorah CJ, White KLM, Chalmers DM, Axon ATR. 1996. Ascorbic acid may protect against human gastric cancer by scavenging mucosal oxygen radicals. *Carcinogenesis* 17:559–562.
- Duthie SJ, Ma A, Ross MA, Collins AR. 1996. Antioxidant supplementation decreases oxidative DNA damage in human lymphocytes. *Cancer Res* 56:1291–1295.
- Dyke GW, Craven JL, Hall R, Garner RC. 1994a. Effect of vitamin C supplementation on gastric mucosal DNA damage. *Carcinogenesis* 15:291–295.
- Dyke GW, Craven JL, Hall R, Garner RC. 1994b. Effect of vitamin C upon gastric mucosal  $O^6$ -alkyltransferase activity and on gastric vitamin C levels. *Cancer Lett* 86:159–165.
- Eichholzer M, Stahelin HB, Gey KF. 1992. Inverse correlation between essential antioxidants in plasma and subsequent risk to develop cancer, ischemic heart disease and stroke respectively: 12-year follow-up of the Prospective Basel Study. *Exp Suppl* 62:398–410.
- Ekvall S, Chen IW, Bozian R. 1981. The effect of supplemental ascorbic acid on serum vitamin B<sub>12</sub> levels in myelomenigocele patients. *Am J Clin Nutr* 34:1356–1361.
- Elneihoum AM, Falke P, Hedblad B, Lindgarde F, Ohlsson K. 1997. Leukocyte activation in atherosclerosis: Correlation with risk factors. *Atherosclerosis* 131:79–84.
- Englard S, Seifter S. 1986. The biochemical functions of ascorbic acid. *Annu Rev Nutr* 6:365–406.
- Enstrom JE, Kanim LE, Breslow L. 1986. The relationship between vitamin C intake, general health practices, and mortality in Alameda County, California. *Am J Pub Hlth* 76:1124–1130.
- Enstrom JE, Kanim LE, Klein MA. 1992. Vitamin C intake and mortality among a sample of the United States population. *Epidemiology* 3:194–202.
- Erdman JW Jr, Klein BP. 1982. The influence of harvesting, processing, and cooking on vitamin C in foods. In: Seib PA, Tolbert BM, eds. *Ascorbic Acid: Chemistry, Metabolism and Uses*. Washington, DC: American Chemical Society. Pp. 499–532.
- Evans RM, Currie L, Campbell A. 1982. The distribution of ascorbic acid between various cellular components of blood in normal individuals, and its relation to the plasma concentration. *Br J Nutr* 47:473–482.
- FDA (Food and Drug Administration). 1985. Nutrient requirements for infant formulas. *Fed Regis* 50:45106–45108.
- Fellstrom B, Danielson BG, Karlstrom B, Lithell H, Ljunghall S, Vessby B. 1989. Dietary habits in renal stone patients compared with healthy subjects. *Br J Urol* 63:575–580.
- Fishbaine B, Butterfield G. 1984. Ascorbic acid status of running and sedentary men. *Int J Vitam Nutr Res* 54:273.
- Fituri N, Allawi N, Bentley M, Costello J. 1983. Urinary and plasma oxalate during ingestion of pure ascorbic acid: A re-evaluation. *Eur Urol* 9:312–315.
- Flodin NW. 1988. *Pharmacology of Micronutrients*. New York: Alan R. Liss. Pp. 201–244.
- Fontham ET. 1994. Vitamin C, vitamin C-rich foods, and cancer: Epidemiologic studies. In: Frei B, ed. *Natural Antioxidants in Human Health and Disease*. San Diego: Academic Press. Pp. 157–197.

- Fontham ET, Pickle LW, Haenszel W, Correa P, Lin YP, Falk RT. 1988. Dietary vitamins A and C and lung cancer risk in Louisiana. *Cancer* 62:2267–2273.
- Fraga CG, Motchnik PA, Shigenaga MK, Helbock HJ, Jacob RA, Ames BN. 1991. Ascorbic acid protects against endogenous oxidative DNA damage in human sperm. *Proc Natl Acad Sci USA* 88:11003–11006.
- Frei B, Stocker R, Ames BN. 1988. Antioxidant defenses and lipid peroxidation in human blood plasma. *Proc Natl Acad Sci USA* 85:9748–9752.
- Frei B, England L, Ames BN. 1989. Ascorbate is an outstanding antioxidant in human blood plasma. *Proc Natl Acad Sci USA* 86:6377–6381.
- Frei B, Forte TM, Ames BN, Cross CE. 1991. Gas phase oxidants of cigarette smoke induce lipid peroxidation and changes in lipoprotein properties in human blood plasma. Protective effects of ascorbic acid. *Biochem J* 277:133–138.
- Freudenheim JL, Graham S, Marshall JR, Haughey BP, Wilkinson G. 1990. A case-control study of diet and rectal cancer in western New York. *Am J Epidemiol* 131:612–624.
- Fuller CJ, Grundy SM, Norkus EP, Jialal I. 1996. Effect of ascorbate supplementation on low density lipoprotein oxidation in smokers. *Atherosclerosis* 119:139–150.
- Gale CR, Martyn CN, Winter PD, Cooper C. 1995. Vitamin C and risk of death from stroke and coronary heart disease in cohort of elderly people. *Br Med J* 310:1563–1566.
- Garry PJ, Goodwin JS, Hunt WC, Gilbert BA. 1982. Nutritional status in a healthy elderly population: Vitamin C. *Am J Clin Nutr* 36:332–339.
- Garry PJ, Vanderjagt DJ, Hunt WC. 1987. Ascorbic acid intakes and plasma levels in healthy elderly. *Ann NY Acad Sci* 498:90–99.
- George DR, De Francesca BA. 1989. Human milk in comparison to cow milk. In: Lebenthal E, ed. *Textbook of Gastroenterology and Nutrition in Infancy and Childhood*, 2nd edition. New York: Raven Press. Pp. 242–243.
- Gey KF. 1995. Ten-year retrospective on the antioxidant hypothesis of arteriosclerosis: Threshold plasma levels of antioxidant micronutrients related to minimum cardiovascular risk. *Nutr Biochem* 6:206–236.
- Gey KF. 1998. Vitamins E plus C and interacting conutrients required for optimal health. A critical and constructive review of epidemiology and supplementation data regarding cardiovascular disease and cancer. *Biofactors* 7:113–174.
- Gey KF, Stahelin HB, Eichholzer M. 1993. Poor plasma status of carotene and vitamin C is associated with higher mortality from ischemic heart disease and stroke: Basel Prospective Study. *Clin Invest* 71:3–6.
- Ghadirian P, Boyle P, Simard A, Baillargeon J, Maisonneuve P, Perret C. 1991. Reported family aggregation of pancreatic cancer within a population-based case-control study in the francophone community in Montreal, Canada. *Int J Pancreatol* 10:183–196.
- Giunta JL. 1983. Dental erosion resulting from chewable vitamin C tablets. *J Am Dent Assoc* 107:253–256.
- Gogel HK, Tandberg D, Strickland RG. 1989. Substances that interfere with guaiac card tests: Implications for gastric aspirate testing. *Am J Emerg Med* 7:474–480.
- Goldsmith GA. 1961. Human requirements for vitamin C and its use in clinical medicine. *Ann NY Acad Sci* 92:230–245.
- Gosiewska A, Mahmoodian F, Peterkofsky B. 1996. Gene expression of iron-related proteins during iron deficiency caused by scurvy in guinea pigs. *Arch Biochem Biophys* 325:295–303.

- Graham S, Zielezny M, Marshall J, Priore R, Freudenheim J, Brasure J, Haughey B, Nasca P, Zdeb M. 1992. Diet in the epidemiology of postmenopausal breast cancer in the New York State Cohort. *Am J Epidemiol* 136:1327–1337.
- Green MHL, Lowe JE, Waugh APW, Aldridge KE, Cole J, Arlett CF. 1994. Effect of diet and vitamin C on DNA strand breakage in freshly-isolated human white blood cells. *Mutat Res* 316:91–102.
- Greenberg ER, Baron JA, Tosteson TD, Freeman DH, Beck GJ, Bond JH, Colacchio TA, Coller JA, Frankl HD, Haile RW, Mandel JS, Nierenberg DW, Rothstein R, Snover DC, Stevens MM, Summers RW, van Stolk RU. 1994. A clinical trial of antioxidant vitamins to prevent colorectal adenoma. *N Engl J Med* 331:141–147.
- Gutteridge JMC. 1991. Plasma ascorbate levels and inhibition of the antioxidant activity of caeruloplasmin. *Clin Sci* 81:413–417.
- Hallberg L. 1985. The role of vitamin C in improving the critical iron balance situation in women. *Int J Vitam Nutr Res* 27:177–187.
- Halliwell B. 1998. Can oxidative DNA damage be used as a biomarker of cancer risk in humans? *Free Radic Res* 29:469–486.
- Halliwell B, Whiteman M. 1997. Antioxidant and prooxidant properties of vitamin C. In: Packer L, Fuchs J, eds. *Vitamin C in Health and Disease*. New York: Marcel Dekker. Pp. 59–73.
- Halliwell B, Wasil M, Grootveld M. 1987. Biologically significant scavenging of the myeloperoxidase-derived oxidant hypochlorous acid by ascorbic acid. *FEBS Lett* 213:15–17.
- Halpner AD, Handelman GJ, Belmont CA, Harris JM, Blumberg JB. 1998. Protection by vitamin C of oxidant-induced loss of vitamin E in rat hepatocytes. *J Nutr Biochem* 9:355–359.
- Hankinson SE, Stampfer MJ, Seddon JM, Colditz GA, Rosner B, Speizer FE, Willett WC. 1992. Nutrient intake and cataract extraction in women: A prospective study. *Br Med J* 305:335–339.
- Harats D, Ben-Naim M, Dabach Y, Hollander G, Havivi E, Stein O, Stein Y. 1990. Effect of vitamin C and E supplementation on susceptibility of plasma lipoproteins to peroxidation induced by acute smoking. *Atherosclerosis* 85:47–54.
- Harats D, Chevion S, Nahir M, Norman Y, Sagee O, Berry EM. 1998. Citrus fruit supplementation reduces lipoprotein oxidation in young men ingesting a diet high in saturated fat: Presumptive evidence for an interaction between vitamins C and E in vivo. *Am J Clin Nutr* 67:240–245.
- Harris ED, Percival SS. 1991. A role for ascorbic acid in copper transport. *Am J Clin Nutr* 54:1193S–1197S.
- Hartz SC, Russell RM, Rosenberg IH. 1992. *Nutrition in the Elderly. The Boston Nutritional Status Survey*. London: Smith-Gordon. P. 38.
- Haslam RH, Dalby JT, Rademaker AW. 1984. Effects of megavitamin therapy on children with attention deficit disorders. *Pediatrics* 74:103–111.
- Hatch GE. 1995. Asthma, inhaled oxidants, and dietary antioxidants. *Am J Clin Nutr* 61:625S–630S.
- Hatch M, Mulgrew S, Bourke E, Keogh B, Costello J. 1980. Effect of megadoses of ascorbic acid on serum and urinary oxalate. *Eur Urol* 6:166–169.
- Hazell LJ, Arnold L, Flowers D, Waeg G, Malle E, Stocker R. 1996. Presence of hypochlorite-modified proteins in human atherosclerotic lesions. *J Clin Invest* 97:1535–1544.

- Heinecke JW. 1997. Pathways for oxidation of low density lipoprotein by myeloperoxidase: Tyrosyl radical, reactive aldehydes, hypochlorous acid and molecular chlorine. *BioFactors* 6:145–155.
- Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. 1993. Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: The DARLING Study. *Am J Clin Nutr* 58:152–161.
- Heitzer T, Just H, Munzel T. 1996. Antioxidant vitamin C improves endothelial dysfunction in chronic smokers. *Circulation* 94:6–9.
- Heller R, Munscher-Paulig F, Grabner R, Till U. 1999. L-Ascorbic acid potentiates nitric oxide synthesis in endothelial cells. *J Biol Chem* 274:8254–8260.
- Hemila H. 1996. Vitamin C, the placebo effect, and the common cold: A case study of how preconceptions influence the analysis of results. *J Clin Epidemiol* 49: 1079–1084.
- Hemila H. 1997. Vitamin C intake and susceptibility to the common cold. *Br J Nutr* 77:59–72.
- Hemila H, Herman ZS. 1995. Vitamin C and the common cold: A retrospective analysis of Chalmers' review. *J Am Coll Nutr* 14:116–123.
- Henning SM, Zhang JZ, McKee RW, Swendseid ME, Jacob RA. 1991. Glutathione blood levels and other oxidant defense indices in men fed diets low in vitamin C. *J Nutr* 121:1969–1975.
- Herbert V. 1978. Risk of oxalate stones from large doses of vitamin C. *N Engl J Med* 298:856.
- Herbert V. 1995. Vitamin C supplements and disease—Counterpoint. *J Am Coll Nutr* 14:112–113.
- Herbert V, Jacob E. 1974. Destruction of vitamin B<sub>12</sub> by ascorbic acid. *J Am Med Assoc* 230:241–242.
- Hevia P, Omaye ST, Jacob RA. 1990. Urinary hydroxyproline excretion and vitamin C status in healthy young men. *Am J Clin Nutr* 51:644–648.
- Hinds MW, Kolonel LN, Hankin JH, Lee J. 1984. Dietary vitamin A, carotene, vitamin C and risk of lung cancer in Hawaii. *Am J Epidemiol* 119:227–237.
- Hoffer A. 1971. Ascorbic acid and toxicity. *N Engl J Med* 285:635–636.
- Hoffer A. 1973. Vitamin C and infertility. *Lancet* 2:1146.
- Hofstad B, Almendingen K, Vatn M, Andersen S, Owen R, Larsen S, Osnes M. 1998. Growth and recurrence of colorectal polyps: A double-blind 3-year intervention with calcium and antioxidants. *Digestion* 59:148–156.
- Hogenkamp HP. 1980. The interaction between vitamin B<sub>12</sub> and vitamin C. *Am J Clin Nutr* 33:1–3.
- Hornig B, Arakawa N, Kohler C, Drexler H. 1998. Vitamin C improves endothelial function of conduit arteries in patients with chronic heart failure. *Circulation* 97:363–368.
- Hornig D. 1975. Distribution of ascorbic acid, metabolites and analogues in man and animals. *Ann NY Acad Sci* 258:103–118.
- Hornig DH, Moser U. 1981. The safety of high vitamin C intakes in man. In: Counsell JN, Hornig DH, eds. Vitamin C (Ascorbic Acid). London: Applied Science. Pp. 225–248.
- Horrobin DF. 1996. Ascorbic acid and prostaglandin synthesis. *Subcell Biochem* 25:109–115.

- Howe GR, Hirohata T, Hislop TG, Iscovich JM, Yuan JM, Katsouyanni K, Lubin F, Marubini E, Modan B, Rohan T. 1990. Dietary factors and risk of breast cancer: Combined analysis of 12 case-control studies. *J Natl Cancer Inst* 82:561–569.
- Howe GR, Ghadirian P, Bueno de Mesquita HB, Zatonski WA, Baghurst PA, Miller AB, Simard A, Baillargeon J, de Waard F, Przewozniak K. 1992. A collaborative case-control study of nutrient intake and pancreatic cancer within the search programme. *Int J Cancer* 51:365–372.
- Hoyt CJ. 1980. Diarrhea from vitamin C. *J Am Med Assoc* 244:1674.
- Hughes C, Dutton S, Truswell AS. 1981. High intakes of ascorbic acid and urinary oxalate. *J Hum Nutr* 35:274–280.
- Hunt JR, Gallagher SK, Johnson LK. 1994. Effect of ascorbic acid on apparent iron absorption by women with low iron stores. *Am J Clin Nutr* 59:1381–1385.
- Hunter DJ, Manson JE, Colditz GA, Stampfer MJ, Rosner B, Hennekens CH, Speizer FE, Willett WC. 1993. A prospective study of the intake of vitamins C, E, and A and the risk of breast cancer. *N Engl J Med* 329:234–240.
- IOM (Institute of Medicine). 1991. *Nutrition During Lactation*. Washington, DC: National Academy Press. P. 179.
- Itoh R, Yamada K, Oka J, Echizen H, Murakami K. 1989. Sex as a factor in levels of serum ascorbic acid in a healthy elderly population. *Int J Vitam Nutr Res* 59:365–372.
- Jacob RA. 1995. The integrated antioxidant system. *Nutr Res* 15:755–766.
- Jacob RA. 1999. Vitamin C. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th edition. Baltimore, MD: Williams & Wilkins. Pp. 467–483.
- Jacob RA, Pianalto FS. 1997. Urinary carnitine excretion increases during experimental vitamin C depletion of healthy men. *J Nutr Biochem* 8:265–269.
- Jacob RA, Skala JH, Omaye ST. 1987a. Biochemical indices of human vitamin C status. *Am J Clin Nutr* 46:818–826.
- Jacob RA, Skala JH, Omaye ST, Turnlund JR. 1987b. Effect of varying ascorbic acid intakes on copper absorption and ceruloplasmin levels of young men. *J Nutr* 117:2109–2115.
- Jacob RA, Otradovec CL, Russell RM, Munro HN, Hartz SC, McGandy RB, Morrow FD, Sadowski JA. 1988. Vitamin C status and nutrient interactions in a healthy elderly population. *Am J Clin Nutr* 48:1436–1442.
- Jacob RA, Kelley DS, Pianalto FS, Swendseid ME, Henning SM, Zhang JZ, Ames BN, Fraga CG, Peters JH. 1991. Immunocompetence and oxidant defense during ascorbate depletion of healthy men. *Am J Clin Nutr* 54:1302S–1309S.
- Jacob RA, Pianalto FS, Agee RE. 1992. Cellular ascorbate depletion in healthy men. *J Nutr* 122:1111–1118.
- Jacob RA, Kutnink MA, Csallany AS, Daroszewska M, Burton GW. 1996. Vitamin C nutriture has little short-term effect on vitamin E concentrations in healthy women. *J Nutr* 126:2268–2277.
- Jacques PF, Chylack LT Jr. 1991. Epidemiologic evidence of a role for the antioxidant vitamins and carotenoids in cataract prevention. *Am J Clin Nutr* 53:352S–355S.
- Jacques PF, Taylor A, Hankinson SE, Willett WC, Mahnken B, Lee Y, Vaid K, Lahav M. 1997. Long-term vitamin C supplement use and prevalence of early age-related lens opacities. *Am J Clin Nutr* 66:911–916.

- Jaffe RM, Kasten B, Young DS, MacLowry JD. 1975. False-negative stool occult blood tests caused by ingestion of ascorbic acid (vitamin C). *Ann Intern Med* 83:824–826.
- Jama JW, Launer LJ, Witteman JC, den Breeijen JH, Breteler MM, Grobbee DE, Hofman A. 1996. Dietary antioxidants and cognitive function in a population-based sample of older persons. The Rotterdam Study. *Am J Epidemiol* 144:275–280.
- Jariwalla RJ, Harakeh S. 1996. Antiviral and immunomodulatory activities of ascorbic acid. *Subcell Biochem* 25:213–231.
- Jarvinen R, Knekt P, Seppanen R, Teppo L. 1997. Diet and breast cancer risk in a cohort of Finnish women. *Cancer Lett* 114:251–253.
- Jendryczko A, Tomala J. 1995. The total free radical trapping ability of blood plasma in eclampsia. *Zentralbl Gynakol* 117:126–129.
- Jha P, Flather M, Lonn E, Farkouh M, Yusuf S. 1995. The antioxidant vitamins and cardiovascular disease. A critical review of epidemiologic and clinical trial data. *Ann Intern Med* 123:860–872.
- Jialal I, Devaraj S. 1996. The role of oxidized low density lipoprotein in atherogenesis. *J Nutr* 126:1053S–1057S.
- Jialal I, Grundy SM. 1991. Preservation of the endogenous antioxidants in low density lipoprotein by ascorbate but not probucol during oxidative modification. *J Clin Invest* 87:597–601.
- Jialal I, Vega GL, Grundy SM. 1990. Physiologic levels of ascorbate inhibit the oxidative modification of low density lipoprotein. *Atherosclerosis* 82:185–191.
- Johnston CS. 1991. Complement component C1q unaltered by ascorbate supplementation in healthy men and women. *J Nutr Biochem* 2:499–501.
- Johnston CS. 1999. Biomarkers for establishing a tolerable upper intake level for vitamin C. *Nutr Rev* 57:71–77.
- Johnston CS, Luo B. 1994. Comparison of the absorption and excretion of three commercially available sources of vitamin C. *J Am Diet Assoc* 94:779–781.
- Johnston CS, Thompson LL. 1998. Vitamin C status of an outpatient population. *J Am Coll Nutr* 17:366–370.
- Johnston CS, Martin LJ, Cai X. 1992. Antihistamine effect of supplemental ascorbic acid and neutrophil chemotaxis. *J Am Coll Nutr* 11:172–176.
- Johnston CS, Meyer CG, Srilakshmi JC. 1993. Vitamin C elevates red blood cell glutathione in healthy adults. *Am J Clin Nutr* 58:103–105.
- Johnston CS, Solomon E, Corte C. 1996. Vitamin C depletion is associated with alterations in blood histamine and plasma free carnitine in adults. *J Am Coll Nutr* 15:586–591.
- Kallner A, Hartmann D, Hornig D. 1979. Steady-state turnover and body pool of ascorbic acid in man. *Am J Clin Nutr* 32:530–539.
- Kallner AB, Hartmann D, Hornig DH. 1981. On the requirements of ascorbic acid in man: Steady-state turnover and body pool in smokers. *Am J Clin Nutr* 34:1347–1355.
- Karra MV, Udupi SA, Kirksey A, Roepke JL. 1986. Changes in specific nutrients in breast milk during extended lactation. *Am J Clin Nutr* 43:495–503.
- Katsuki H. 1996. Vitamin C and nervous tissue: In vivo and in vitro aspects. *Subcell Biochem* 25:293–311.
- Keith RE. 1994. Vitamins and physical activity. In: Wolinsky I, Hickson JF, eds. *Nutrition in Exercise and Sport*, 2nd edition. Boca Raton, FL: CRC Press. Pp. 159–183.

- Kelly FJ, Mudway I, Blomberg A, Frew A, Sandstrom T. 1999. Altered lung antioxidant status in patients with mild asthma. *Lancet* 354:482–483.
- Kennes B, Dumont I, Brohee D, Hubert C, Neve P. 1983. Effect of vitamin C supplements on cell-mediated immunity in old people. *Gerontology* 29:305–310.
- Knek P, Jarvinen R, Seppanen R, Rissanen A, Aromaa A, Heinonen OP, Albanes D, Heinonen M, Pukkala E, Teppo L. 1991. Dietary antioxidants and the risk of lung cancer. *Am J Epidemiol* 134:471–479.
- Knek P, Reunanan A, Jarvinen R, Seppanen R, Heliovaara M, Aromaa A. 1994. Antioxidant vitamin intake and coronary mortality in a longitudinal population study. *Am J Epidemiol* 139:1180–1189.
- Kritchevsky SB, Shimakawa T, Tell G, Dennis B, Carpenter M, Eckfeldt JH, Peacher-Ryan H, Heiss G. 1995. Dietary antioxidants and carotid artery wall thickness. The ARIC Study. *Circulation* 92:2142–2150.
- Kushi LH, Fee RM, Sellers TA, Zheng W, Folsom AR. 1996a. Intake of vitamins A, C, and E and postmenopausal breast cancer. The Iowa Women's Health Study. *Am J Epidemiol* 144:165–174.
- Kushi LH, Folsom AR, Prineas RJ, Mink PJ, Wu Y, Bostick RM. 1996b. Dietary antioxidant vitamins and death from coronary heart disease in postmenopausal women. *N Engl J Med* 334:1156–1162.
- Lamden MP, Chrystowski GA. 1954. Urinary oxalate excretion by man following ascorbic acid ingestion. *Proc Soc Exp Biol Med* 85:190–192.
- Laudicina DC, Marnett LJ. 1990. Enhancement of hydroperoxide-dependent lipid peroxidation in rat liver microsomes by ascorbic acid. *Arch Biochem Biophys* 278:73–80.
- Leaf CD, Vecchio AJ, Roe DA, Hotchkiss JH. 1987. Influence of ascorbic acid dose on N-nitrosoproline formation in humans. *Carcinogenesis* 8:791–795.
- Leggott PJ, Robertson PB, Rothman DL, Murray PA, Jacob RA. 1986. The effect of controlled ascorbic acid depletion and supplementation on periodontal health. *J Periodontol* 57:480–485.
- Leggott PJ, Robertson PB, Jacob RA, Zambon JJ, Walsh M, Armitage GC. 1991. Effects of ascorbic acid depletion and supplementation on periodontal health and subgingival microflora in humans. *J Dent Res* 70:1531–1536.
- Lehr HA, Weyrich AS, Saetzler RK, Jurek A, Arfors KE, Zimmerman GA, Prescott SM, McIntyre TM. 1997. Vitamin C blocks inflammatory platelet-activating factor mimetics created by cigarette smoking. *J Clin Invest* 99:2358–2364.
- Le Marchand L, Yoshizawa CN, Kolonel LN, Hankin JH, Goodman MT. 1989. Vegetable consumption and lung cancer risk: A population-based case-control study in Hawaii. *J Natl Cancer Inst* 81:1158–1164.
- Lenton KJ, Therriault H, Fulop T, Payette H, Wagner JR. 1999. Glutathione and ascorbate are negatively correlated with oxidative DNA damage in human lymphocytes. *Carcinogenesis* 20:607–613.
- Leske MC, Chylack LT Jr, Wu SY. 1991. The Lens Opacities Case-Control Study. Risk factors for cataract. *Arch Ophthalmol* 109:244–251.
- Levine GN, Frei B, Koulouris SN, Gerhard MD, Keaney JF Jr, Vita JA. 1996. Ascorbic acid reverses endothelial vasomotor dysfunction in patients with coronary artery disease. *Circulation* 93:1107–1113.
- Levine M, Dhariwal KR, Wang Y, Park JB, Welch RW. 1994. Ascorbic acid in neutrophils. In: Frei B, ed. *Natural Antioxidants in Health and Disease*. San Diego: Academic Press. Pp. 469–488.

- Levine M, Conry-Cantilena C, Wang Y, Welch RW, Washko PW, Dhariwal KR, Park JB, Lazarev A, Graumlich JF, King J, Cantilena LR. 1996a. Vitamin C pharmacokinetics in healthy volunteers: Evidence for a recommended dietary allowance. *Proc Natl Acad Sci USA* 93:3704–3709.
- Levine M, Rumsey S, Wang Y, Park J, Kwon O, Xu W, Amano N. 1996b. Vitamin C. In: Ziegler EE, Filer LJ Jr, eds. *Present Knowledge in Nutrition*, 7th edition. Washington, DC: ILSI Press. Pp. 146–159.
- Levy R, Shriker O, Porath A, Riesenbergs K, Schlaeffer F. 1996. Vitamin C for the treatment of recurrent furunculosis in patients with impaired neutrophil functions. *J Infect Dis* 173:1502–1505.
- Loft S, Vistisen K, Ewertz M, Tjonneland A, Overvad K, Poulsen HE. 1992. Oxidative DNA damage estimated by 8-hydroxydeoxyguanosine excretion in humans: Influence of smoking, gender and body mass index. *Carcinogenesis* 13: 2241–2247.
- Losonczi KG, Harris TB, Havlik RJ. 1996. Vitamin E and vitamin C supplement use and risk of all-cause and coronary heart disease mortality in older persons: The Established Populations for Epidemiologic Studies of the Elderly. *Am J Clin Nutr* 64:190–196.
- Løvstad RA. 1997. A study on ascorbate inhibition of ceruloplasmin ferroxidase activity. *BioMetals* 10:123–126.
- LSRO/FASEB (Life Sciences Research Office/ Federation of American Societies for Experimental Biology). 1989. *Nutrition Monitoring in the United States: An Update Report on Nutrition Monitoring*. Prepared for the U.S. Department of Agriculture and the U.S. Department of Health and Human Services. DHHS Publication No. (PHS) 89-1255. Washington, DC: U.S. Government Printing Office.
- Ludvigsson J, Hansson LO, Tibbling G. 1977. Vitamin C as a preventive medicine against common colds in children. *Scand J Infect Dis* 9:91–98.
- Ludvigsson J, Hansson LO, Stendahl O. 1979. The effect of large doses of vitamin C on leukocyte function and some laboratory parameters. *Int J Vitam Nutr Res* 49:160–165.
- Lunec J, Blake DR. 1985. The determination of dehydroascorbic acid and ascorbic acid in the serum and synovial fluid of patients with rheumatoid arthritis. *Free Radic Res Commun* 1:31–39.
- Lykkesfeldt J, Loft S, Nielsen JB, Poulsen HE. 1997. Ascorbic acid and dehydroascorbic acid as biomarkers of oxidative stress caused by smoking. *Am J Clin Nutr* 65:959–963.
- Lykkesfeldt J, Christen S, Wallock LM, Change HH, Jacob RA, Ames BN. 2000. Ascorbate is depleted by smoking and repleted by moderate supplementation: A study in male smokers and nonsmokers with matched dietary antioxidant intakes. *Am J Clin Nutr* 71:530–536.
- Mangels AR, Block G, Frey CM, Patterson BH, Taylor PR, Norkus EP, Levander OA. 1993. The bioavailability to humans of ascorbic acid from oranges, orange juice and cooked broccoli is similar to that of synthetic ascorbic acid. *J Nutr* 123:1054–1061.
- Mannick EE, Bravo LE, Zarama G, Realpe JL, Zhang XJ, Ruiz B, Fontham ETH, Mera R, Miller MJS, Correa P. 1996. Inducible nitric oxide synthase, nitrotyrosine, and apoptosis in *Helicobacter pylori* gastritis: Effect of antibiotics and antioxidants. *Cancer Res* 56:3238–3243.

- Marangon K, Herbeth B, Artur Y, Esterbauer H, Siest G. 1997. Low and very low density lipoprotein composition and resistance to copper-induced oxidation are not notably modified in smokers. *Clin Chim Acta* 265:1–12.
- Marangon K, Herbeth B, Lecomte E, Paul-Dauphin A, Grolier P, Chancerelle Y, Artur Y. 1998. Diet, antioxidant status, and smoking habits in French men. *Am J Clin Nutr* 67: 231–239.
- May JM, Cobb CE, Mendiratta S, Hill KE, Burk RF. 1998. Reduction of the ascorbyl free radical to ascorbate by thioredoxin reductase. *J Biol Chem* 273:23039–23045.
- May JM, Mendiratta S, Qu ZC, Loggins E. 1999. Vitamin C recycling and function in human monocytic U-937 cells. *Free Radic Biol Med* 26:1513–1523.
- McKeown-Eyssen G, Holloway C, Jazmaji V, Bright-See E, Dion P, Bruce WR. 1988. A randomized trial of vitamins C and E in the prevention of recurrence of colorectal polyps. *Cancer Res* 48:4701–4705.
- McLaran CJ, Bett JHN, Nye JA, Halliday JW. 1982. Congestive cardiomyopathy and haemochromatosis—Rapid progression possibly accelerated by excessive ingestion of ascorbic acid. *Aust NZ J Med* 12:187–188.
- Melethil S, Mason WD, Chang C-J. 1986. Dose-dependent absorption and excretion of vitamin C in humans. *Int J Pharmaceut* 31:83–89.
- Mentzer WC, Collier E. 1975. Hydrops fetalis associated with erythrocyte G-6-PD deficiency and maternal ingestion of fava beans and ascorbic acid. *J Pediatr* 86:565–567.
- Metz J, Hundertmark U, Pevny I. 1980. Vitamin C allergy of the delayed type. *Contact Dermatitis* 6:172–174.
- Millar J. 1995. The nitric oxide/ascorbate cycle: How neurones may control their own oxygen supply. *Med Hypoth* 45:21–26.
- Miller JZ, Nance WE, Norton JA, Wolen RL, Griffith RS, Rose RJ. 1977. Therapeutic effect of vitamin C. A co-twin control study. *J Am Med Assoc* 237:248–251.
- Mirvish SS. 1994. Experimental evidence for inhibition of *N*-nitroso compound formation as a factor in the negative correlation between vitamin C consumption and the incidence of certain cancers. *Cancer Res* 54:1948S–1951S.
- Mitch WE, Johnson MW, Kirshenbaum JM, Lopez RE. 1981. Effect of large oral doses of ascorbic acid on uric acid excretion by normal subjects. *Clin Pharmacol Ther* 29:318–321.
- Montaldo MB, Benson JD, Martinez GA. 1985. Nutrient intakes of formula-fed infants and infants fed cow's milk. *Pediatrics* 75:343–351.
- Morrow JD, Frei B, Longmire AW, Gaziano JM, Lynch SM, Shyr Y, Strauss WE, Oates JA, Roberts LJ II. 1995. Increase in circulating products of lipid peroxidation ( $F_2$ -isoprostanes) in smokers. *N Engl J Med* 332:1198–1203.
- Morse EH, Clark RP, Keyser DE, Merrow SB, Bee DE. 1975. Comparison of the nutritional status of pregnant adolescents with adult pregnant women. I. Biochemical findings. *Am J Clin Nutr* 28:1000–1013.
- Moser U. 1987. Uptake of ascorbic acid by leukocytes. *Ann NY Acad Sci* 498:200–215.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance Data, Vital and Health Statistics of the National Center for Health Statistics. Number 174. Hyattsville, MD: National Center for Health Statistics. Pp. 1–19.

- Motoyama T, Kawano H, Kugiyama K, Hirashima O, Ohgushi M, Yoshimura M, Ogawa H, Yasue H. 1997. Endothelium-dependent vasodilation in the brachial artery is impaired in smokers: Effect of vitamin C. *Am J Physiol* 273:H1644–H1650.
- Mudway IS, Krishna MT, Frew AJ, MacLeod D, Sandstrom T, Holgate ST, Kelly FJ. 1999. Compromised concentrations of ascorbate in fluid lining the respiratory tract in human subjects after exposure to ozone. *Occup Environ Med* 56:473–481.
- Mulholland CW, Strain JJ, Trinick TR. 1996. Serum antioxidant potential, and lipoprotein oxidation in female smokers following vitamin C supplementation. *Int J Food Sci Nutr* 47:227–231.
- Naidoo D, Lux O. 1998. The effect of vitamin C and E supplementation on lipid and urate oxidation products in plasma. *Nutr Res* 18:953–961.
- Ness AR, Khaw KT, Bingham S, Day NE. 1996. Vitamin C status and respiratory function. *Eur J Clin Nutr* 50:573–579.
- Newmark HL, Scheiner MS, Marcus M, Prabhudesai M. 1976. Stability of vitamin B<sub>12</sub> in the presence of ascorbic acid. *Am J Clin Nutr* 29:645–649.
- Newton HM, Schorah CJ, Habibzadeh N, Morgan DB, Hullin RP. 1985. The cause and correction of low blood vitamin C concentrations in the elderly. *Am J Clin Nutr* 42:656–659.
- NRC (National Research Council). 1989. *Recommended Dietary Allowances*, 10th edition. Washington, DC: National Academy Press.
- Nyssonen K, Parviainen MT, Salonen R, Tuomilehto J, Salonen JT. 1997a. Vitamin C deficiency and risk of myocardial infarction: Prospective population study of men from eastern Finland. *Br Med J* 314:634–638.
- Nyssonen K, Poulsen HE, Hayn M, Agerbo P, Porkkala-Sarataho E, Kaikkonen J, Salonen R, Salonen JT. 1997b. Effect of supplementation of smoking men with plain or slow release ascorbic acid on lipoprotein oxidation. *Eur J Clin Nutr* 51:154–163.
- Ocke MC, Bueno-de-Mesquita HB, Feskens EJ, van Staveren WA, Kromhout D. 1997. Repeated measurements of vegetables, fruits, beta-carotene, and vitamins C and E in relation to lung cancer. *Am J Epidemiol* 145:358–365.
- Omaye ST, Skala JH, Jacob RA. 1986. Plasma ascorbic acid in adult males: Effects of depletion and supplementation. *Am J Clin Nutr* 44:257–264.
- Omaye ST, Schaus EE, Kutnink MA, Hawkes WC. 1987. Measurement of vitamin C in blood components by high-performance liquid chromatography. Implication in assessing vitamin C status. *Ann NY Acad Sci* 498:389–401.
- Ono K. 1986. Secondary hyperoxalemia caused by vitamin C supplementation in regular hemodialysis patients. *Clin Nephrol* 26:239–243.
- Oreopoulos DG, Lindeman RD, VanderJagt DJ, Tzamaloukas AH, Bhagavan HN, Garry PJ. 1993. Renal excretion of ascorbic acid: Effect of age and sex. *J Am Coll Nutr* 12:537–542.
- Ortega RM, Lopez-Sobaler AM, Quintas ME, Martinez RM, Andres P. 1998. The influence of smoking on vitamin C status during the third trimester of pregnancy and on vitamin C levels in maternal milk. *J Am Coll Nutr* 17:379–384.
- O'Toole P, Lombard M. 1996. Vitamin C and gastric cancer: Supplements for some or fruit for all? *Gut* 39:345–347.
- Panayiotidis M, Collins AR. 1997. Ex vivo assessment of lymphocyte antioxidant status using the comet assay. *Free Rad Res* 27:533–537.

- Pandey DK, Shekelle R, Selwyn BJ, Tangney C, Stamler J. 1995. Dietary vitamin C and beta-carotene and risk of death in middle-aged men. The Western Electric Study. *Am J Epidemiol* 142:1269–1278.
- Panush RS, Delafuente JC, Katz P, Johnson J. 1982. Modulation of certain immunologic responses by vitamin C. III. Potentiation of in vitro and in vivo lymphocyte responses. *Int J Vitam Nutr Res Suppl* 23:35–47.
- Park JB, Levine M. 1996. Purification, cloning and expression of dehydroascorbic acid-reducing activity from human neutrophils: Identification as glutaredoxin. *Biochem J* 315:931–938.
- Parkkinen J, Vaaranen O, Vahtera E. 1996. Plasma ascorbate protects coagulation factors against photooxidation. *Thromb Haemost* 75:292–297.
- Pelletier O. 1977. Vitamin C and tobacco. *Int J Vitam Nutr Res Suppl* 16:147–170.
- Perrig WJ, Perrig P, Stahelin HB. 1997. The relation between antioxidants and memory performance in the old and very old. *J Am Geriatr Soc* 45:718–724.
- Peters EM, Goetzsche JM, Grobbelaar B, Noakes TD. 1993. Vitamin C supplementation reduces the incidence of postrace symptoms of upper-respiratory-tract infection in ultramarathon runners. *Am J Clin Nutr* 57:170–174.
- Pfeffer F, Valdes-Ramos R, Avila-Rosas H, Meza C, Casanueva E. 1996. Iron, zinc and vitamin C nutritional status is not related to weight gain in pregnant women. *Nutr Res* 16:555–564.
- Phull PS, Price AB, White KL, Schorah CJ, Jacyna MR. 1999. Gastroduodenal mucosal vitamin-C levels in *Helicobacter pylori* infection. *Scand J Gastroenterol* 34:361–366.
- Pirkle JL, Flegal KM, Bernert JT, Brody DJ, Etzel RA, Maurer KR. 1996. Exposure of the US population to environmental tobacco smoke: The Third National Health and Nutrition Examination Survey, 1988 to 1991. *J Am Med Assoc* 275:1233–1240.
- Podmore ID, Griffiths HR, Herbert KE, Mistry N, Mistry P, Lunec J. 1998. Vitamin C exhibits pro-oxidant properties. *Nature* 392:559.
- Pohl H, Reidy JA. 1989. Vitamin C intake influences the bleomycin-induced chromosome damage assay: Implications for detection of cancer susceptibility and chromosome breakage syndromes. *Mutat Res* 224:247–252.
- Powers HJ, Loban A, Silvers K, Gibson AT. 1995. Vitamin C at concentrations observed in premature babies inhibits the ferroxidase activity of caeruloplasmin. *Free Radic Res* 22:57–65.
- Prieme H, Loft S, Nyssonnen K, Salonen JT, Poulsen HE. 1997. No effect of supplementation with vitamin E, ascorbic acid, or coenzyme Q<sub>10</sub> on oxidative DNA damage estimated by 8-hydroxy-7,8-dihydro-2'-deoxyguanosine excretion in smokers. *Am J Clin Nutr* 65:503–507.
- Pryor WA. 1992. Biological effects of cigarette smoke, wood smoke, and the smoke from plastics: The use of electron spin resonance. *Free Radic Biol Med* 13:659–676.
- Pryor WA. 1997. Cigarette smoke radicals and the role of free radicals in chemical carcinogenicity. *Environ Hlth Perspect* 105:875–882.
- Pryor WA, Prier DG, Church DF. 1983. Electron-spin resonance study of mainstream and sidestream cigarette smoke: Nature of the free radicals in gas-phase smoke and in cigarette tar. *Environ Hlth Perspect* 47:345–355.
- Rajalakshmi R, Deodhar AD, Ramakrishnan CV. 1965. Vitamin C secretion during lactation. *Acta Paediatr Scand* 54:375–382.
- Rebouche CJ. 1995. Renal handling of carnitine in experimental vitamin C deficiency. *Metabolism* 44:1639–1643.

- Rees DC, Kelsey H, Richards JDM. 1993. Acute haemolysis induced by high dose ascorbic acid in glucose-6-phosphate dehydrogenase deficiency. *Br Med J* 306: 841–842.
- Rehman A, Collis CS, Yang M, Kelly M, Diplock AT, Halliwell B, Rice-Evans C. 1998. The effects of iron and vitamin C co-supplementation on oxidative damage to DNA in healthy volunteers. *Biochem Biophys Res Commun* 246:293–298.
- Reilly M, Delanty N, Lawson JA, Fitzgerald GA. 1996. Modulation of oxidant stress in vivo in chronic cigarette smokers. *Circulation* 94:19–25.
- Rhead WJ, Schrauzer GN. 1971. Risks of long-term ascorbic acid overdosage. *Nutr Rev* 29:262–263.
- Rifici VA, Khachadurian AK. 1993. Dietary supplementation with vitamins C and E inhibits in vitro oxidation of lipoproteins. *J Am Coll Nutr* 12:631–637.
- Rimm EB, Stampfer MJ, Ascherio A, Giovannucci E, Colditz GA, Willett WC. 1993. Vitamin E consumption and the risk of coronary heart disease in men. *N Engl J Med* 328:1450–1456.
- Rivers JM. 1987. Safety of high-level vitamin C ingestion. *Ann NY Acad Sci* 498:445–454.
- Robertson JM, Donner AP, Trevithick JR. 1989. Vitamin E intake and risk of cataracts in humans. *Ann NY Acad Sci* 570:372–382.
- Rokitzki L, Hinkel S, Klemp C, Cufi D, Keul J. 1994. Dietary, serum and urine ascorbic acid status in male athletes. *Int J Sports Med* 15:435–440.
- Rokkas T, Papatheodorou G, Karameris A, Mavrogeorgis A, Kalogeropoulos N, Giannikos N. 1995. *Helicobacter pylori* infection and gastric juice vitamin C levels. Impact of eradication. *Dig Dis Sci* 40:615–621.
- Romney SL, Duttagupta C, Basu J, Palan PR, Karp S, Slagle NS, Dwyer A, Wassertheil-Smoller S, Wylie-Rosett J. 1985. Plasma vitamin C and uterine cervical dysplasia. *Am J Obstet Gynecol* 151:976–980.
- Ronchetti IP, Quaglino D Jr, Bergamini G. 1996. Ascorbic acid and connective tissue. *Subcell Biochem* 25:249–264.
- Rose RC, Richer SP, Bode AM. 1998. Ocular oxidants and antioxidant protection. *Proc Soc Exp Biol Med* 217:397–407.
- Rumsey SC, Levine M. 1998. Absorption, transport, and disposition of ascorbic acid in humans. *J Nutr Biochem* 9:116–130.
- Russell AL. 1967. Epidemiology of periodontal disease. *Int Dent J* 17:282–296.
- Sahyoun NR, Jacques PF, Russell RM. 1996. Carotenoids, vitamins C and E, and mortality in an elderly population. *Am J Epidemiol* 144:501–511.
- Salmenpera L. 1984. Vitamin C nutrition during prolonged lactation: Optimal in infants while marginal in some mothers. *Am J Clin Nutr* 40:1050–1056.
- Salonen JT, Salonen R, Nyssonnen K, Korpela H. 1992. Iron sufficiency is associated with hypertension and excess risk of myocardial infarction: The Kuopio Ischemic Heart Disease Risk Factor Study (KIHD). *Circulation* 85:864–876.
- Samman S, Brown AJ, Beltran C, Singh S. 1997. The effect of ascorbic acid on plasma lipids and oxidisability of LDL in male smokers. *Eur J Clin Nutr* 51:472–477.
- Sasaki A, Kondo K, Sakamoto Y, Kurata H, Itakura H, Ikeda Y. 1997. Smoking cessation increases the resistance of low-density lipoprotein to oxidation. *Atherosclerosis* 130:109–111.
- Satarug S, Haswell-Elkins MR, Tsuda M, Mairiang P, Sithithaworn P, Mairiang E, Esumi H, Sukprasert S, Yongvanit P, Elkins DB. 1996. Thiocyanate-independent nitrosation in humans with carcinogenic parasite infection. *Carcinogenesis* 17:1075–1081.

- Sauberlich HE. 1994. Pharmacology of vitamin C. *Annu Rev Nutr* 14:371–391.
- Scaccini C, Jialal I. 1994. LDL Modification by activated polymorphonuclear leukocytes: A cellular model of mild oxidative stress. *Free Radic Biol Med* 16:49–55.
- Schechtman G, Byrd JC, Hoffmann R. 1991. Ascorbic acid requirements for smokers: Analysis of a population survey. *Am J Clin Nutr* 53:1466–1470.
- Schmidt KH, Hagmaier V, Hornig DH, Vuilleumier JP, Rutishauser G. 1981. Urinary oxalate excretion after large intakes of ascorbic acid in man. *Am J Clin Nutr* 34:305–311.
- Schrauzer GN, Rhead WJ. 1973. Ascorbic acid abuse: Effects on long-term ingestion of excessive amounts on blood levels and urinary excretion. *Int J Vitam Nutr Res* 43:201–211.
- Schrauzer GN, Ishmael D, Kiefer GW. 1975. Some aspects of current vitamin C usage: Diminished high-altitude resistance following overdosage. *Ann NY Acad Sci* 258:377–381.
- Schwartz J, Weiss ST. 1994. Relationship between dietary vitamin C intake and pulmonary function in the First National Health and Nutrition Examination Survey (NHANES I). *Am J Clin Nutr* 59:110–114.
- Schwarz KB, Cox J, Sharma S, Witter F, Clement L, Sehnert SS, Risby TH. 1995. Cigarette smoking is pro-oxidant in pregnant women regardless of antioxidant nutrient intake. *J Nutr Environ Med* 5:225–234.
- Sharpe PC, MacAuley D, McCrum EE, Stott G, Evans AE, Mulholland C, Boreham CA, Duly E, Trinick TR. 1994. Ascorbate and exercise in the Northern Ireland population. *Int J Vitam Nutr Res* 64:277–282.
- Shekelle RB, Lepper M, Liu S, Maliza C, Raynor WJ, Rossof AH. 1981. Dietary vitamin A and risk of cancer in the Western Electric Study. *Lancet* 2:1185–1190.
- Shilohri PG, Bhat KS. 1977. Effect of mega doses of vitamin C on bactericidal activity of leukocytes. *Am J Clin Nutr* 30:1077–1081.
- Siegel C, Barker B, Kunstadter M. 1982. Conditioned oral scurvy due to megavitamin C withdrawal. *J Periodontol* 53:453–455.
- Sies H, Stahl W. 1995. Vitamins E and C, beta-carotene, and other carotenoids as antioxidants. *Am J Clin Nutr* 62:1315S–1321S.
- Simon JA. 1992. Vitamin C and cardiovascular disease: A review. *J Am Coll Nutr* 11:107–125.
- Simon JA, Hudes ES, Browner WS. 1998. Serum ascorbic acid and cardiovascular disease prevalence in US adults. *Epidemiology* 9:316–321.
- Singh RB, Ghosh S, Niaz MA, Singh R, Beegum R, Chibo H, Shoumin Z, Postiglione A. 1995. Dietary intake, plasma levels of antioxidant vitamins, and oxidative stress in relation to coronary artery disease in elderly subjects. *Am J Cardiol* 76:1233–1238.
- Sinha R, Block G, Taylor PR. 1993. Problems with estimating vitamin C intakes. *Am J Clin Nutr* 57:547–550.
- Skaper SD, Fabris M, Ferrari V, Carbonare MD, Leon A. 1997. Quercetin protects cutaneous tissue-associated cell types including sensory neurons from oxidative stress induced by glutathione depletion: Cooperative effects of ascorbic acid. *Free Radic Biol Med* 22:669–678.
- Sneed SM, Zane C, Thomas MR. 1981. The effects of ascorbic acid, vitamin B<sub>6</sub>, vitamin B<sub>12</sub>, and folic acid supplementation on the breast milk and maternal nutritional status of low socioeconomic lactating women. *Am J Clin Nutr* 34:1338–1346.

- Solzbach U, Hornig B, Jeserich M, Just H. 1997. Vitamin C improves endothelial dysfunction of epicardial coronary arteries in hypertensive patients. *Circulation* 96:1513–1519.
- Specker BL, Beck A, Kalkwarf H., Ho M. 1997. Randomized trial of varying mineral intake on total body bone mineral accretion during the first year of life. *Pediatrics* 99:e12.
- Stein HB, Hasan A, Fox IH. 1976. Ascorbic acid-induced uricosuria. *Ann Intern Med* 84:385–388.
- Taddei S, Virdis A, Ghiadoni L, Magagna A, Salvetti A. 1998. Vitamin C improves endothelium-dependent vasodilation by restoring nitric oxide activity in essential hypertension. *Circulation* 97:2222–2229.
- Thomas MR, Kawamoto J, Snead SM, Eakin R. 1979. The effects of vitamin C, vitamin B<sub>6</sub>, and vitamin B<sub>12</sub> supplementation on the breast milk and maternal status of well-nourished women. *Am J Clin Nutr* 32:1679–1685.
- Thomas MR, Snead SM, Wei C, Nail PA, Wilson M, Sprinkle EE. 1980. The effects of vitamin C, vitamin B<sub>6</sub>, vitamin B<sub>12</sub>, folic acid, riboflavin, and thiamin on the breast milk and maternal status of well-nourished women at 6 months postpartum. *Am J Clin Nutr* 33:2151–2156.
- Timimi FK, Ting HH, Haley EA, Roddy MA, Ganz P, Creager MA. 1998. Vitamin C improves endothelium-dependent vasodilation in patients with insulin-dependent diabetes mellitus. *J Am Coll Cardiol* 31:552–557.
- Ting HH, Timimi FK, Boles KS, Creager SJ, Ganz P, Creager MA. 1996. Vitamin C improves endothelium-dependent vasodilation in patients with non-insulin-dependent diabetes mellitus. *J Clin Invest* 97:22–28.
- Ting HH, Timimi FK, Haley EA, Roddy MA, Ganz P, Creager MA. 1997. Vitamin C improves endothelium-dependent vasodilation in forearm resistance vessels of humans with hypercholesterolemia. *Circulation* 95:2617–2622.
- Tiselius HG, Almgard LE. 1977. The diurnal urinary excretion of oxalate and the effect of pyridoxine and ascorbate on oxalate excretion. *Eur Urol* 3:41–46.
- Tlaskal P, Novakova V. 1990. Vitamins C and E in neonates and their mothers. *Cesk Pediatr* 45:339–343.
- Tribble DL, Giuliano LJ, Fortmann SP. 1993. Reduced plasma ascorbic acid concentrations in nonsmokers regularly exposed to environmental tobacco smoke. *Am J Clin Nutr* 58:886–890.
- Tsao CS. 1997. An overview of ascorbic acid chemistry and biochemistry. In: Packer L, Fuchs J, eds. *Vitamin C in Health and Disease*. New York: Marcel Dekker. Pp. 25–58.
- Tsao CS, Leung PY. 1988. Urinary ascorbic acid levels following the withdrawal of large doses of ascorbic acid in guinea pigs. *J Nutr* 118:895–900.
- Tsao CS, Salimi SL. 1984. Effect of large intake of ascorbic acid on urinary and plasma oxalic acid levels. *Int J Vitam Nutr Res* 54:245–249.
- Udipi SA, Kirksey A, West K, Giacoia G. 1985. Vitamin B<sub>6</sub>, vitamin C and folacin levels in milk from mothers of term and preterm infants during the neonatal period. *Am J Clin Nutr* 42:522–530.
- Urivetzky M, Kessaris D, Smith AD. 1992. Ascorbic acid overdosing: A risk factor for calcium oxalate nephrolithiasis. *J Urol* 147:1215–1218.
- Valkonen M, Kuusi T. 1998. Passive smoking induces atherogenic changes in low-density lipoprotein. *Circulation* 97:2012–2016.
- VanderJagt DJ, Garry PJ, Bhagavan HN. 1987. Ascorbic acid intake and plasma levels in healthy elderly people. *Am J Clin Nutr* 46:290–294.
- Van Eekelen M. 1953. Occurrence of vitamin C in foods. *Proc Nutr Soc* 12:228–232.

- Vitale S, West S, Hallfrisch J, Alston C, Wang F, Moorman C, Muller D, Singh V, Taylor HR. 1993. Plasma antioxidants and risk of cortical and nuclear cataract. *Epidemiology* 4:195–203.
- Vogel RI, Lamster IB, Wechsler SA, Macedo B, Hartley LJ, Macedo JA. 1986. The effects of megadoses of ascorbic acid on PMN chemotaxis and experimental gingivitis. *J Periodontol* 57:472–479.
- Wandzilak TR, D'Andre SD, Davis PA, Williams HE. 1994. Effect of high dose vitamin C on urinary oxalate levels. *J Urol* 151:834–837.
- Wang Y, Russo TA, Kwon O, Chanock S, Rumsey SC, Levine M. 1997. Ascorbate recycling in human neutrophils: Induction by bacteria. *Proc Natl Acad Sci USA* 94:13816–13819.
- Waring AJ, Drake IM, Schorah CJ, White KL, Lynch DA, Axon AT, Dixon MF. 1996. Ascorbic acid and total vitamin C concentrations in plasma, gastric juice, and gastrointestinal mucosa: Effects of gastritis and oral supplementation. *Gut* 38:171–176.
- Wassertheil-Smoller S, Romney SL, Wylie-Rosett J, Slagle S, Miller G, Lucido D, Duttagupta C, Palan PR. 1981. Dietary vitamin C and uterine cervical dysplasia. *Am J Epidemiol* 114:714–724.
- Weber C, Wolfgang E, Weber K, Weber PC. 1996. Increased adhesiveness of isolated monocytes to endothelium is prevented by vitamin C intake in smokers. *Circulation* 93:1488–1492.
- Wen Y, Cooke T Feely, J. 1997. The effect of pharmacological supplementation with vitamin C on low-density lipoprotein oxidation. *Br J Clin Pharmacol* 44:94–97.
- Witt EH, Reznick AZ, Viguie CA, Starke-Reed P, Packer L. 1992. Exercise, oxidative damage and effects of antioxidant manipulation. *J Nutr* 122:766–773.
- Witztum JL, Steinberg D. 1991. Role of oxidized low density lipoprotein in atherosclerosis. *J Clin Invest* 88:1785–1792.
- Woolfe SN, Kenney EB, Hume WR, Carranza FA Jr. 1984. Relationship of ascorbic acid levels of blood and gingival tissue with response to periodontal therapy. *J Clin Periodontol* 11:159–165.
- Yong LC, Brown CC, Schatzkin A, Dresser CM, Slesinski MJ, Cox CS, Taylor PR. 1997. Intake of vitamins E, C, and A and risk of lung cancer. The NHANES I Epidemiologic Followup Study. *Am J Epidemiol* 146:231–243.
- Young JC, Kenyon EM, Calabrese EJ. 1990. Inhibition of beta-glucuronidase in human urine by ascorbic acid. *Hum Exp Toxicol* 9:165–170.
- Zatonski W, Przewozniak K, Howe GR, Maisonneuve P, Walker AM, Boyle P. 1991. Nutritional factors and pancreatic cancer: A case-control study from southwest Poland. *Int J Cancer* 48:390–394.

Ibid., Chapter 9, 399–400.

- AIN (American Institute of Nutrition). 1990. Nomenclature policy: Generic descriptors and trivial names for vitamins and related compounds. *J Nutr* 120:12–19.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the third National Health and Nutrition Examination Survey: Underreporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.

- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- Horwitt MK. 1976. Vitamin E: A reexamination. *Am J Clin Nutr* 29:569–578.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances be Revised?* Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1997. *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride.* Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1998. *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline.* Washington, DC: National Academy Press.
- IUPAC-IUB Commission on Biochemical Nomenclature. 1974. Nomenclature of tocopherols and related compounds. Recommendations 1973. *Eur J Biochem* 46:217–219.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1980. *Drinking Water and Health*, Volume 3. Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys.* Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Swanson CA, Patterson BH, Levander OA, Veillon C, Taylor PR, Helzlsouer K, McAdam PA, Zech LA. 1991. Human [<sup>74</sup>Se]selenomethionine metabolism: A kinetic model. *Am J Clin Nutr* 54:917–926.
- Thomson CD, Robinson MF. 1986. Urinary and fecal excretions and absorption of a large supplement of selenium: Superiority of selenate over selenite. *Am J Clin Nutr* 44:659–663.
- USDA (U.S. Department of Agriculture). 1999. USDA Nutrient Database for Standard Reference, Release, [Online]. Available: <http://www.nal.usda.gov/fnic/foodcomp>.
- Weiser H, Vecchi M, Schlachter M. 1986. Stereoisomers of alpha-tocopherol acetate. IV. USP units and alpha-tocopherol equivalents of all-rac-, 2-ambo- and RRR-alpha-tocopherol evaluated by simultaneous determination of resorption-gestation, myopath and liver storage capacity in rats. *Int J Vitam Nutr Res* 56:45–56.
- Williams AW, Erdman JW Jr. 1999. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease.* Baltimore, MD: Williams and Wilkins. P. 181.

## CAROTENOIDS

*Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids* (ISBN 0-309-06949-1), Chapter 8, pp. 372–382.

- Albanes D, Heinonen OP, Taylor PR, Virtamo J, Edwards BK, Rautalahti M, Hartman AM, Palmgren J, Freedman LS, Haapakoski J, Barrett MJ, Pietinen P, Malila N, Tala E, Liippo K, Salomaa ER, Tangrea JA, Teppo L, Askin FB, Taskinen E, Erozan Y, Greenwald P, Huttunen JK. 1996.  $\alpha$ -Tocopherol and  $\beta$ -carotene supplements and lung cancer incidence in the Alpha-Tocopherol Beta-Carotene Prevention Study: Effects of base-line characteristics and study compliance. *J Natl Cancer Inst* 88:1560–1570.
- Albanes D, Virtamo J, Taylor PR, Rautalahti M, Pietinen P, Heinonen OP. 1997. Effects of supplemental beta-carotene, cigarette smoking, and alcohol consumption on serum carotenoids in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. *Am J Clin Nutr* 66:366–372.
- Allard JP, Royall D, Kurian R, Muggli R, Jeejeebhoy KN. 1994. Effects of beta-carotene supplementation on lipid peroxidation in humans. *Am J Clin Nutr* 59:884–890.
- ATBC (Alpha-Tocopherol, Beta Carotene) Cancer Prevention Study Group. 1994. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. *N Engl J Med* 330:1029–1035.
- Baker DL, Krol ES, Jacobsen N, Liebler DC. 1999. Reactions of beta-carotene with cigarette smoke oxidants. Identification of carotenoid oxidation products and evaluation of the prooxidant/antioxidant effect. *Chem Res Toxicol* 12:535–543.
- Batieha AM, Armenian HK, Norkus EP, Morris JS, Spate VE, Comstock GW. 1993. Serum micronutrients and the subsequent risk of cervical cancer in a population-based nested case-control study. *Cancer Epidemiol Biomarkers Prev* 2:335–339.
- Bendich A. 1988. The safety of beta-carotene. *Nutr Cancer* 11:207–214.
- Block G, Patterson B, Subar A. 1992. Fruit, vegetables, and cancer prevention: A review of the epidemiological evidence. *Nutr Cancer* 18:1–29.
- Blot WJ, Li J-Y, Taylor PR, Guo W, Dawsey S, Wang G-Q, Yang CS, Zheng S-F, Gail M, Li G-Y, Yu Y, Liu B-Q, Tangrea J, Sun Y-H, Liu F, Fraumeni JF Jr, Zhang Y-H, Li B. 1993. Nutrition intervention trials in Linxian, China: Supplementation with specific vitamin/mineral combinations, cancer incidence, and disease-specific mortality in the general population. *J Natl Cancer Inst* 85: 1483–1492.
- Blot WJ, Li J-Y, Taylor PR, Li B. 1994. Lung cancer and vitamin supplementation. *N Engl J Med* 331:614.
- Boileau TW, Moore AC, Erdman JW Jr. 1999. Carotenoids and vitamin A. In: Papas AM, ed. *Antioxidant Status, Diet, Nutrition, and Health*. Boca Raton, FL: CRC Press. Pp. 133–158.
- Bone RA, Landrum JT, Tarsis SL. 1985. Preliminary identification of the human macular pigment. *Vision Res* 25:1531–1535.
- Bone RA, Landrum JT, Hime GW, Cains A, Zamor J. 1993. Stereochemistry of the human macular carotenoids. *Invest Ophthalmol Vis Sci* 34:2033–2040.
- Bonithon-Kopp C, Coudray C, Berr C, Touboul PJ, Feve JM, Favier A, Ducimetiere P. 1997. Combined effects of lipid peroxidation and antioxidant status on carotid atherosclerosis in a population aged 59–71 y: The EVA Study. *Am J Clin Nutr* 65:121–127.

- Brady WE, Mares-Perlman JA, Bowen P, Stacewicz-Sapuntzakis M. 1996. Human serum carotenoid concentrations are related to physiologic and lifestyle factors. *J Nutr* 126:129–137.
- Brown L, Rimm EB, Seddon JM, Giovannucci EL, Chasan-Taber L, Spiegelman D, Willett WC, Hankinson SE. 1999. A prospective study of carotenoid intake and risk of cataract extraction in US men. *Am J Clin Nutr* 70:517–524.
- Burri BJ, Dixon ZR, Fong AK, Kretsch MJ, Clifford AJ, Erdman JW Jr. 1993. Possible association of skin lesions with a low-carotene diet in premenopausal women. *Ann NY Acad Sci* 691:279–280.
- Butte NF, Calloway DH. 1981. Evaluation of lactational performance of Navajo women. *Am J Clin Nutr* 34:2210–2215.
- Calzada C, Bizzotto M, Paganga G, Miller NJ, Bruckdorfer KR, Diplock AT, Rice-Evans CA. 1995. Levels of antioxidant nutrients in plasma and low density lipoproteins: A human volunteer supplementation study. *Free Radic Res* 23:489–503.
- Canfield LM, Giuliano AR, Neilson EM, Yap HH, Graver EJ, Cui HA, Blashill BM. 1997. Beta-carotene in breast milk and serum is increased after a single beta-carotene dose. *Am J Clin Nutr* 66:52–61.
- Canfield LM, Giuliano AR, Neilson EM, Blashil BM, Graver EJ, Yap HH. 1998. Kinetics of the response of milk and serum beta-carotene to daily beta-carotene supplementation in healthy, lactating women. *Am J Clin Nutr* 67: 276–283.
- Castenmiller JJ, West CE. 1998. Bioavailability and bioconversion of carotenoids. *Annu Rev Nutr* 18:19–38.
- Chandler LA, Schwartz SJ. 1987. HPLC separation of *cis-trans* carotene isomers in fresh and processed fruits and vegetables. *J Food Sci* 52:669–672.
- Chappell JE, Francis T, Clandinin MT. 1985. Vitamin A and E content of human milk at early stages of lactation. *Early Hum Dev* 11:157–167.
- Chasan-Taber L, Willett WC, Seddon JM, Stampfer M, Rosner B, Colditz GA, Speizer FE, Hankinson SE. 1999. A prospective study of carotenoid and vitamin A intakes and risk of cataract extraction in US women. *Am J Clin Nutr* 70:509–516.
- Chow CK, Thacker RR, Changchit C, Bridges RB, Rehm SR, Humble J, Turbek J. 1986. Lower levels of vitamin C and carotenes in plasma of cigarette smokers. *J Am Coll Nutr* 5:305–312.
- Chug-Ahuja JK, Holden JM, Forman MR, Mangels AR, Beecher GR, Lanza E. 1993. The development and application of a carotenoid database for fruits, vegetables, and selected multicomponent foods. *J Am Diet Assoc* 93:318–323.
- Clevidence BA, Khachik F, Brown ED, Nair PP, Wiley ER, Prior RL, Cao G, Morel DW, Stone W, Gross M, Kramer TR. 1997. Human consumption of carotenoid-rich vegetables. In: Aruoma OI, Cuppett SL, eds. *Antioxidant Methodology: In Vivo and In Vitro Concepts*. Champaign, IL: AOCS Press. Pp 53–63.
- Clinton SK. 1998. Lycopene: Chemistry, biology, and implications for human health and disease. *Nutr Rev* 56:35–51.
- Clinton SK, Emenhiser C, Schwartz S, Bostwick DG, Williams AW, Moore BJ, Erdman JW Jr. 1996. *Cis-trans* lycopene isomers, carotenoids, and retinol in the human prostate. *Cancer Epidemiol Biomarkers Prev* 5:823–833.
- Comstock GW, Menkes MS, Schober SE, Vuilleumier J-P, Helsing KJ. 1988. Serum levels of retinol, beta-carotene, and alpha-tocopherol in older adults. *Am J Epidemiol* 127:114–123.

- Connell JE, Kuller LH, Kjelsberg MO, Polk BF, Collins G, Rider A, Hulley SB. 1989. Relationship between carotenoids and cancer. The Multiple Risk Factor Intervention Trial (MRFIT) Study. *Cancer* 64:126–134.
- Coodley GO, Nelson HD, Loveless MO, Folk C. 1993. Beta-carotene in HIV infection. *J Acquir Immune Defic Syndr* 6:272–276.
- de Pee S, West CE, Muhilal, Karyadi D, Hautvast J. 1995. Lack of improvement in vitamin A status with increased consumption of dark-green leafy vegetables. *Lancet* 346:75–81.
- de Pee S, West CE, Permaesih D, Martuti S, Muhilal, Hautvast J. 1998. Orange fruit is more effective than are dark-green, leafy vegetables in increasing serum concentrations of retinol and beta-carotene in schoolchildren in Indonesia. *Am J Clin Nutr* 68:1058–1067.
- Dietz JM, Kantha SS, Erdman JW Jr. 1988. Reversed phase HPLC analysis of alpha- and beta-carotene from selected raw and cooked vegetables. *Plant Food Hum Nutr* 38:333–341.
- Dixon ZR, Burri BJ, Clifford A, Frankel EN, Schneeman BO, Parks E, Keim NL, Barbieri T, Wu M-M, Fong AK, Kretsch MJ, Sowell AL, Erdman JW Jr. 1994. Effects of a carotene-deficient diet on measures of oxidative susceptibility and superoxide dismutase activity in adult women. *Free Radic Biol Med* 17:537–544.
- Dixon ZR, Shie F-S, Warden BA, Burri BJ, Neidlinger TR. 1998. The effect of a low carotenoid diet on malondialdehyde-thiobarbituric acid (MDA-TBA) concentrations in women: A placebo-controlled double-blind study. *J Am Coll Nutr* 17:54–58.
- EDCCSG (Eye Disease Case-Control Study Group). 1993. Antioxidant status and neovascular age-related macular degeneration. *Arch Ophthalmol* 111:104–109.
- Eichholzer M, Stahelin HB, Gey KF. 1992. Inverse correlation between essential antioxidants in plasma and subsequent risk to develop cancer, ischemic heart disease and stroke respectively: 12-year follow-up of the Prospective Basel Study. *Exp Suppl* 62:398–410.
- Elinder LS, Hadell K, Johansson J, Molgaard J, Holme I, Olsson AG, Walldius G. 1995. Probucol treatment decreases serum concentrations of diet-derived antioxidants. *Arterioscler Thromb Vasc Biol* 15:1057–1063.
- Erdman JW Jr, Bierer TL, Gugger ET. 1993. Absorption and transport of carotenoids. *Ann NY Acad Sci* 691:76–85.
- Fukao A, Tsubono Y, Kawamura M, Ido T, Akazawa N, Tsuji I, Komatsu S, Minami Y, Hisamichi S. 1996. The independent association of smoking and drinking with serum beta-carotene levels among males in Miyagi, Japan. *Int J Epidemiol* 25:300–306.
- Gartner C, Stahl W, Sies H. 1997. Lycopene is more bioavailable from tomato paste than from fresh tomatoes. *Am J Clin Nutr* 66:116–122.
- Gaziano JM, Hennekens CH. 1993. The role of beta-carotene in the prevention of cardiovascular disease. *Ann NY Acad Sci* 691:148–155.
- Gaziano JM, Hatta A, Flynn M, Johnson EJ, Krinsky NI, Ridker PM, Hennekens CH, Frei B. 1995. Supplementation with beta-carotene in vivo and in vitro does not inhibit low density lipoprotein oxidation. *Atherosclerosis* 112:187–195.
- Gebre-Medhin M, Vahlquist A, Hofvander Y, Uppsall L, Vahlquist B. 1976. Breast milk composition in Ethiopian and Swedish mothers. I. Vitamin A and beta-carotene. *Am J Clin Nutr* 29:441–451.

- Gey KF, Moser UK, Jordan P, Stahelin HB, Eichholzer M, Ludin E. 1993a. Increased risk of cardiovascular disease at suboptimal plasma concentrations of essential antioxidants: An epidemiological update with special attention to carotene and vitamin C. *Am J Clin Nutr* 57:787S–797S.
- Gey KF, Stähelin HB, Eichholzer M. 1993b. Poor plasma status of carotene and vitamin C is associated with higher morbidity from ischemic heart disease and stroke: Basel Prospective Study. *Clin Invest* 71:3–6.
- Giovannucci E. 1999. Tomatoes, tomato-based products, lycopene, and cancer: Review of the epidemiologic literature. *J Natl Cancer Inst* 91:317–331.
- Giovannucci E, Ascherio A, Rimm EB, Stampfer MJ, Colditz GA, Willett WC. 1995. Intake of carotenoids and retinol in relation to risk of prostate cancer. *J Natl Cancer Inst* 87:1767–1776.
- Giuliano AR, Neilson EM, Kelly BE, Canfield LM. 1992. Simultaneous quantitation and separation of carotenoids and retinol in human milk by high-performance liquid chromatography. *Methods Enzymol* 213:391–399.
- Giuliano AR, Neilson SM, Yap H-H, Baier M, Canfield LM. 1994. Quantitation of and inter/intra-individual variability in major carotenoids of mature human milk. *J Nutr Biochem* 5:551–556.
- Goodman DS, Blomstrand R, Werner B, Huang HS, Shiratori T. 1966. The intestinal absorption and metabolism of vitamin A and beta-carotene in man. *J Clin Invest* 45:1615–1623.
- Gottlieb K, Zarling EJ, Mobarhan S, Bowen P, Sugerman S. 1993. Beta-carotene decreases markers of lipid peroxidation in healthy volunteers. *Nutr Cancer* 19:207–212.
- Greenberg ER, Baron JA, Karagas MR, Stukel TA, Nierenberg DW, Stevens MM, Mandel JS, Haile RW. 1996. Mortality associated with low plasma concentration of beta carotene and the effect of oral supplementation. *J Am Med Assoc* 275:699–703.
- Hammond BR Jr, Fuld K. 1992. Interocular differences in macular pigment density. *Invest Ophthalmol Vis Sci* 33:350–355.
- Hammond BR Jr, Curran-Celentano J, Judd S, Fuld K, Krinsky NI, Wooten BR, Snodderly DM. 1996. Sex differences in macular pigment optical density: Relation to plasma carotenoid concentrations and dietary patterns. *Vision Res* 36:2001–2012.
- Hammond BR Jr, Johnson EJ, Russell RM, Krinsky NI, Yeum KJ, Edwards RB, Snodderly DM. 1997. Dietary modification of human macular pigment density. *Invest Ophthalmol Vis Sci* 38:1795–1801.
- Handelman GJ, Dratz EA, Reay CC, Van Kuijk JG. 1988. Carotenoids in the human macula and whole retina. *Invest Ophthalmol Vis Sci* 29:850–855.
- Handelman GJ, Packer L, Cross CE. 1996. Destruction of tocopherols, carotenoids, and retinol in human plasma by cigarette smoke. *Am J Clin Nutr* 63:559–565.
- Hanusch M, Stahl W, Schulz WA, Sies H. 1995. Induction of gap junctional communication by 4-oxoretnoic acid generated from its precursor canthaxanthin. *Arch Biochem Biophys* 317:423–428.
- Health Canada. 1997. *Canada's Food Guide to Healthy Eating*. Minister of Public Works and Government Services Canada.
- Hennekens CH, Buring JE, Manson JE, Stampfer M, Rosner B, Cook NR, Belanger C, LaMotte F, Gaziano JM, Ridker PM, Willett W, Peto R. 1996. Lack of effect of long-term supplementation with beta carotene on the incidence of malignant neoplasms and cardiovascular disease. *N Engl J Med* 334:1145–1149.

## ONLINE REFERENCES

## 855

- Herbeth B, Didelot-Barthelemy L, Lemoine A, Le Devehat C. 1988. Plasma fat-soluble vitamins and alcohol consumption. *Am J Clin Nutr* 47:343–344.
- Herbeth B, Chavance M, Musse N, Mejean L, Vernhes G. 1990. Determinants of plasma retinol, beta-carotene, and alpha-tocopherol. *Am J Epidemiol* 132:394–396.
- Heywood R, Palmer AK, Gregson RL, Hummeler H. 1985. The toxicity of beta-carotene. *Toxicology* 36:91–100.
- Hininger I, Chopra M, Thurnham DI, Laporte F, Richard M-J, Favier A, Roussel A-M. 1997. Effect of increased fruit and vegetable intake on the susceptibility of lipoprotein to oxidation in smokers. *Eur J Clin Nutr* 51:601–606.
- Holden JM, Eldridge AL, Beecher GR, Buzzard M, Bhagwat S, Davis CS, Douglass LW, Gebhardt S, Haytowitz D, Schakel S. 1999. Carotenoid content of U.S. foods: an update of the database. *Food Comp Anal* 12:169–196.
- Hollander D, Ruble RE. 1978. Beta-carotene intestinal absorption: bile, fatty acid, pH, and flow rate effects on transport. *Am J Physiology*. 235: e686–e691.
- Hughes DA, Wright AJ, Finglas PM, Peerless AC, Bailey AL, Astley SB, Pinder AC, Southon S. 1997. The effect of beta-carotene supplementation on the immune function of blood monocytes from healthy male nonsmokers. *J Lab Clin Med* 129:309–317.
- Jacques PF, Chylack LT Jr. 1991. Epidemiologic evidence of a role for the antioxidant vitamins and carotenoids in cataract prevention. *Am J Clin Nutr* 53:352S–355S.
- Jalal F, Nesheim MC, Agus Z, Sanjur D, Habicht JP. 1998. Serum retinol concentrations in children are affected by food sources of beta-carotene, fat intake, and anthelmintic drug treatment. *Am J Clin Nutr* 68:623–629.
- Johnson EJ, Russell RM. 1992. Distribution of orally administered beta-carotene among lipoproteins in healthy men. *Am J Clin Nutr* 56:128–135.
- Johnson EJ, Qin J, Krinsky NI, Russell RM. 1997. Beta-carotene isomers in human serum, breast milk and buccal mucosa cells after continuous oral doses of *all-trans* and *9-cis* beta-carotene. *J Nutr* 127:1993–1999.
- Kaplan LA, Lau JM, Stein EA. 1990. Carotenoid composition, concentrations, and relationships in various human organs. *Clin Physiol Biochem* 8:1–10.
- Khachik F, Bernstein PS, Garland DL. 1997a. Identification of lutein and zeaxanthin oxidation products in human and monkey retinas. *Invest Ophthalmol Vis Sci* 38:1802–1811.
- Khachik F, Spangler CJ, Smith JC, Canfield LM, Steck A, Pfander H. 1997b. Identification, quantification, and relative concentrations of carotenoids and their metabolites in human milk and serum. *Anal Chem* 69:1873–1881.
- Kobza A, Ramsay CA, Magnus IA. 1973. Oral carotene therapy in actinic reticuloid and solar urticaria. Failure to demonstrate a photoprotective effect against long wave ultraviolet and visible radiation. *Br J Dermatol* 88:157–166.
- Kohlmeier L, Hastings SB. 1995. Epidemiologic evidence of a role of carotenoids in cardiovascular disease prevention. *Am J Clin Nutr* 62:1370S–1376S.
- Kohlmeier L, Kark JD, Gomez-Gracia E, Martin BC, Steck SE, Kardinaal AF, Ringstad J, Thamm M, Masaev V, Riemersma R, Martin-Moreno JM, Huttunen JK, Kok FJ. 1997. Lycopene and myocardial infarction risk in the EURAMIC Study. *Am J Epidemiol* 146:618–626.
- Koontzovsky BP, Berry DA, Jones MB, Lin PY, Cooper DA, Jones DY, Jackson JE. 1997. Olestra affects serum concentrations of alpha-tocopherol and carotenoids but not vitamin D or vitamin K status in free-living subjects. *J Nutr* 127:1636S–1645S.

- Kostic D, White WS, Olson JA. 1995. Intestinal absorption, serum clearance, and interactions between lutein and beta-carotene when administered to human adults in separate or combined oral doses. *Am J Clin Nutr* 62:604–610.
- Kramer TR, Burri BJ. 1997. Modulated mitogenic proliferative responsiveness of lymphocytes in whole-blood cultures after a low-carotene diet and mixed-carotenoid supplementation in women. *Am J Clin Nutr* 65:871–875.
- Krinsky NI. 1993. Actions of carotenoids in biological systems. *Annu Rev Nutr* 13:561–587.
- Kuhnlein HV, Soueida R, Receveur O. 1996. Dietary nutrient profiles of Canadian Baffin Island Inuit differ by food source, season, and age. *J Am Diet Assoc* 96:155–162.
- Kushi LH, Folsom AR, Prineas RJ, Mink PJ, Wu Y, Bostick RM. 1996. Dietary antioxidant vitamins and death from coronary heart disease in postmenopausal women. *N Engl J Med* 334:1156–1162.
- Lachance PA. 1997. Nutrient addition to foods: The public health impact in countries with rapidly westernizing diets. In: Bendich A, Deckelbaum RJ, eds. *Preventive Nutrition: The Comprehensive Guide for Health Professionals*. Totowa, NJ: Humana Press. Pp. 441–454.
- Lascari AD. 1981. Carotenemia. A review. *Clin Pediatr* 20:25–29.
- Le Marchand L, Hankin JH, Kolonel LN, Beecher GR, Wilkens LR, Zhao LP. 1993. Intake of specific carotenoids and lung cancer risk. *Cancer Epidemiol Biomarkers Prev* 2:183–187.
- Lewis MB. 1972. The effect of beta-carotene on serum vitamin A levels in erythropoietic protoporphyrinia. *Australas J Dermatol* 13:75–78.
- Lin Y, Burri BJ, Neidlinger TR, Muller HG, Dueker SR, Cliffford A. 1998. Estimating the concentration of beta-carotene required for maximal protection of low-density lipoproteins in women. *Am J Clin Nutr* 67:837–845.
- LSRO/FASEB (Life Sciences Research Office/Federation of American Societies for Experimental Biology). 1995. *Third Report on Nutrition Monitoring in the United States*. Washington, DC: US Government Printing Office.
- Mahapatra S, Manorama R. 1997. The protective effect of red palm oil in comparison with massive vitamin A dose in combating vitamin A deficiency in Orissa, India. *Asia Pacific J Clin Nutr* 6:246–250.
- Mangels AR, Holden JM, Beecher GR, Forman MR, Lanza E. 1993. Carotenoid content of fruits and vegetables: An evaluation of analytic data. *J Am Diet Assoc* 93:284–296.
- Manson JE, Gaziano JM, Jonas MA, Hennekens CH. 1993. Antioxidants and cardiovascular disease: A review. *J Am Coll Nutr* 12:426–432.
- Mares-Perlman JA, Brady WE, Klein R, Klein BE, Palta M, Bowen P, Stacewicz-Sapuntzakis M. 1994. Serum levels of carotenoids and tocopherols in people with age-related maculopathy. *Invest Ophthalmol Vis Sci* 35:2004.
- Mares-Perlman JA, Brady WE, Klein BE, Klein R, Palta M, Bowen P, Stacewicz-Sapuntzakis M. 1995. Serum carotenoids and tocopherols and severity of nuclear and cortical opacities. *Invest Ophthalmol Vis Sci* 36:276–288.
- Margetts BM, Jackson AA. 1996. The determinants of plasma beta-carotene: Interaction between smoking and other lifestyle factors. *Eur J Clin Nutr* 50:236–238.
- Martini MC, Campbell DR, Gross MD, Grandits GA, Potter JD, Slavin JL. 1995. Plasma carotenoids as biomarkers of vegetable intake: The University of Minnesota Cancer Prevention Research Unit Feeding Studies. *Cancer Epidemiol Biomarkers Prev* 4:491–496.

- Mathews-Roth MM. 1986. Beta-carotene therapy for erythropoietic protoporphyrria and other photosensitivity diseases. *Biochimie* 68:875–884.
- Mathews-Roth MM, Pathak MA, Parrish J, Fitzpatrick TB, Kass EH, Toda K, Clemens W. 1972. A clinical trial of the effects of oral beta-carotene on the responses of human skin to solar radiation. *J Invest Dermatol* 59:349–353.
- Mathews-Roth MM, Pathak MA, Fitzpatrick TB, Harber LC, Kass EH. 1974. Beta-carotene as an oral photoprotective agent in erythropoietic protoporphyrria. *J Am Med Assoc* 228:1004–1008.
- Mayne ST. 1996. Beta-carotene, carotenoids, and disease prevention in humans. *FASEB J* 10:690–701.
- Mayne ST. 1998. Beta-carotene, Carotenoids and Cancer Prevention. In: DeVita VT Jr, Hellman S, Rosenberg SA, eds. *Principles and Practice of Oncology (PPO)*, 5th Edition Updates. Philadelphia, PA: Lippincott-Raven Publishers. Pp. 12:1–15.
- Mayne ST, Goodwin WJ Jr. 1993. Chemoprevention of head and neck cancer. *Current Opinion Otolaryn Head Neck Surg* 1:126–132.
- Mayne ST, Cartmel B, Silva F, Kim CS, Fallon BG, Briskin K, Zheng T, Baum M, Shor-Posner G, Goodwin WJ Jr. 1998. Effect of supplemental beta-carotene on plasma concentrations of carotenoids, retinol, and alpha-tocopherol in humans. *Am J Clin Nutr* 68:642–647.
- Menkes MS, Comstock GW, Vuilleumier JP, Helsing KJ, Rider AA, Brookmeyer R. 1986. Serum beta-carotene, vitamins A and E, selenium, and the risk of lung cancer. *N Engl J Med* 315:1250–1254.
- Micozzi MS, Brown ED, Edwards BK, Bieri JG, Taylor PR, Khachik F, Beecher GR, Smith JC. 1992. Plasma carotenoid response to chronic intake of selected foods and beta-carotene supplements in men. *Am J Clin Nutr* 55:1120–1125.
- Mobarhan S, Bowen P, Andersen B, Evans M, Stacewicz-Sapuntzakis M, Sugerman S, Simms P, Lucchesi D, Friedman H. 1990. Effects of beta-carotene repletion on beta-carotene absorption, lipid peroxidation, and neutrophil superoxide formation in young men. *Nutr Cancer* 14:195–206.
- Morris DL, Kritchevsky SB, Davis CE. 1994. Serum carotenoids and coronary heart disease: The Lipid Research Clinics Coronary Primary Prevention Trial and Follow-up Study. *J Am Med Assoc* 272:1439–1441.
- Mosca L, Rubenfire M, Mandel C, Rock C, Tarshis T, Tsai A, Pearson T. 1997. Antioxidant nutrient supplementation reduces the susceptibility of low density lipoprotein to oxidation in patients with coronary artery disease. *J Am Coll Cardiol* 30:392–399.
- Nebeling LC, Forman MR, Graubard BI, Snyder RA. 1997. Changes in carotenoid intake in the United States: The 1987 and 1992 National Health Interview Surveys. *J Am Diet Assoc* 97:991–996.
- Nierenberg DW, Dain BJ, Mott LA, Baron JA, Greenberg ER. 1997. Effects of 4 y of oral supplementation with beta-carotene on serum concentrations of retinol, tocopherol, and five carotenoids. *Am J Clin Nutr* 66:315–319.
- Nomura AM, Stemmermann GN, Heilbrun LK, Salkeld RM, Vuilleumier JP. 1985. Serum vitamin levels and the risk of cancer of specific sites in men of Japanese ancestry in Hawaii. *Cancer Res* 45:2369–2372.
- Nomura AM, Stemmermann GN, Lee J, Craft NE. 1997. Serum micronutrients and prostate cancer in Japanese Americans in Hawaii. *Cancer Epidemiol Biomarkers Prev* 6:487–491.
- Olson JA. 1989. Biological actions of carotenoids. *J Nutr* 119:94–95.

- Olson JA. 1994. Absorption, transport, and metabolism of carotenoids in humans. *Pure Appl Chem* 66:1011–1016.
- Olson JA. 1999. Carotenoids. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th edition. Baltimore, MD: Williams & Wilkins. Pp. 525–541.
- Omenn GS, Goodman GE, Thornquist MD, Balmes J, Cullen MR, Glass A, Keogh JP, Meyskens FL Jr, Valanis B, Williams JH Jr, Barnhart S, Cherniack MG, Brodkin CA, Hammar S. 1996a. Risk factors for lung cancer and for intervention effects in CARET, the Beta-Carotene and Retinol Efficacy Trial. *J Natl Cancer Inst* 88:1550–1559.
- Omenn GS, Goodman GE, Thornquist MD, Balmes J, Cullen MR, Glass A, Keogh JP, Meyskens FL Jr, Valanis B, Williams JH Jr, Barnhart S, Hammar S. 1996b. Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease. *N Engl J Med* 334:1150–1155.
- Ostrea EM Jr, Balun JE, Winkler R, Porter T. 1986. Influence of breast-feeding on the restoration of the low serum concentration of vitamin E and beta-carotene in the newborn infant. *Am J Obstet Gynecol* 154:1014–1017.
- Pamuk ER, Byers T, Coates RJ, Vann JW, Sowell AL, Gunter EW, Glass D. 1994. Effect of smoking on serum nutrient concentrations in African-American women. *Am J Clin Nutr* 59:891–895.
- Pandey DK, Shekelle R, Selwyn BJ, Tangney C, Stamler J. 1995. Dietary vitamin C and beta-carotene and risk of death in middle-aged men. The Western Electric Study. *Am J Epidemiol* 142:1269–1278.
- Parker RS. 1988. Carotenoid and tocopherol composition of human adipose tissue. *Am J Clin Nutr* 47:33–36.
- Parker RS. 1996. Absorption, metabolism, and transport of carotenoids. *FASEB J* 10:542–551.
- Patton S, Canfield LM, Huston GE, Ferris AM, Jensen RG. 1990. Carotenoids of human colostrum. *Lipids* 25:159–165.
- Pool-Zobel BL, Bub A, Muller H, Wollowski I, Rechkemmer G. 1997. Consumption of vegetables reduces genetic damage in humans: First results of a human intervention trial with carotenoid-rich foods. *Carcinogenesis* 18:1847–1850.
- Richards GA, Theron AJ, Van Rensburg CE, Van Rensburg AJ, Van der Merwe CA, Kuyl JM, Anderson R. 1990. Investigation of the effects of oral administration of vitamin E and beta-carotene on the chemiluminescence responses and the frequency of sister chromatid exchanges in circulating leukocytes from cigarette smokers. *Am Rev Respir Dis* 142:648–654.
- Riemersma RA, Wood DA, Macintyre CC, Elton RA, Gey KF, Oliver MF. 1991. Risk of angina pectoris and plasma concentrations of vitamins A, C, and E and carotene. *Lancet* 337:1–5.
- Rimm EB, Stampfer MJ, Ascherio A, Giovannucci E, Colditz GA, Willett WC. 1993. Vitamin E consumption and the risk of coronary heart disease in men. *N Engl J Med* 328:1450–1456.
- Rock CL, Swendseid ME. 1992. Plasma beta-carotene response in humans after meals supplemented with dietary pectin. *Am J Clin Nutr* 55:96–99.
- Rodriguez MS, Irwin MI. 1972. A conspectus of research on vitamin A requirements of man. *J Nutr* 102:909–968.
- Roels OA, Trout M, Dujacquier R. 1958. Carotene balances on boys in Ruanda where vitamin A deficiency is prevalent. *J Nutr* 65:115–127.

- Rust P, Eichler I, Renner S, Elmadfa I. 1998. Effects of long-term oral beta-carotene supplementation on lipid peroxidation in patients with cystic fibrosis. *Int J Vitam Nutr Res* 68:83–87.
- Sahyoun NR, Jacques PF, Russell RM. 1996. Carotenoids, vitamins C and E, and mortality in an elderly population. *Am J Epidemiol* 144:501–511.
- Salgo MG, Cueto R, Winston GW, Pryor WA. 1999. Beta carotene and its oxidation products have different effects on microsome mediated binding of benzo[a]pyrene to DNA. *Free Radic Biol Med* 26:162–173.
- Salonen JT, Nyssonnen K, Parviainen M, Kantola M, Korpela H, Salonen R. 1993. Low plasma beta-carotene, vitamin E and selenium levels associate with accelerated carotid atherogenesis in hypercholesterolemic eastern Finnish men. *Circulation* 87:678.
- Santos MS, Meydani SN, Leka L, Wu D, Fotouhi N, Meydani M, Hennekens CH, Gaziano JM. 1996. Natural killer cell activity in elderly men is enhanced by beta-carotene supplementation. *Am J Clin Nutr* 64:772–777.
- Santos MS, Gaziano JM, Leka LS, Beharka AA, Hennekens CH, Meydani SN. 1998. Beta-carotene-induced enhancement of natural killer cell activity in elderly men: An investigation of the role of cytokines. *Am J Clin Nutr* 68:164–170.
- Schmitz HH, Poor CL, Wellman RB, Erdman JW Jr. 1991. Concentrations of selected carotenoids and vitamin A in human liver, kidney and lung tissue. *J Nutr* 121:1613–1621.
- Seddon JM, Ajani UA, Sperduto RD, Hiller R, Blair N, Burton TC, Farber MD, Gragoudas ES, Haller J, Miller DT, Yannuzzi LA, Willett W. 1994. Dietary carotenoids, vitamins A, C, and E, and advanced age-related macular degeneration. *J Am Med Assoc* 272:1413–1420.
- Shoenfeld Y, Shaklai M, Ben-Baruch N, Hirschorn M, Pinkhaus J. 1982. Neutropenia induced by hypercarotenaemia. *Lancet* 1:1245.
- Sies H, Stahl W. 1997. Carotenoids and intercellular communication via gap junctions. *Int J Vitam Nutr Res* 67:364–367.
- Snodderly DM. 1995. Evidence for protection against age-related macular degeneration by carotenoids and antioxidant vitamins. *Am J Clin Nutr* 62:1448S–1461S.
- Stahelin HB, Gey KF, Eichholzer M, Ludin E, Bernasconi F, Thurneysen J, Brubacher G. 1991. Plasma antioxidant vitamins and subsequent cancer mortality in the 12-year follow-up of the Prospective Basel Study. *Am J Epidemiol* 133:766–775.
- Stahl W, Sies H. 1992. Uptake of lycopene and its geometrical isomers is greater from heat-processed than from unprocessed tomato juice in humans. *J Nutr* 122:2161–2166.
- Stahl W, Schwarz W, Sundquist AR, Sies H. 1992. *Cis-trans* isomers of lycopene and beta-carotene in human serum and tissues. *Arch Biochem Biophys* 294:173–177.
- Steinberg FM, Chait A. 1998. Antioxidant vitamin supplementation and lipid peroxidation in smokers. *Am J Clin Nutr* 68:319–327.
- Stryker WS, Kaplan LA, Stein EA, Stampfer MJ, Sober A, Willett WC. 1988. The relation of diet, cigarette smoking, and alcohol consumption to plasma beta-carotene and alpha-tocopherol levels. *Am J Epidemiol* 127:283–296.
- Taylor A. 1993. Cataract: Relationship between nutrition and oxidation. *J Am Coll Nutr* 12:138–146.
- Taylor A, Jacques PF, Epstein EM. 1995. Relations among aging, antioxidant status, and cataract. *Am J Clin Nutr* 62:1439S–1447S.

- Traber MG, Diamond SR, Lane JC, Brody RI, Kayden HJ. 1994. Beta-carotene transport in human lipoproteins. Comparisons with alpha-tocopherol. *Lipids* 29:665–669.
- VandenLangenberg GM, Brady WE, Nebeling LC, Block G, Forman M, Bowen PE, Stacewicz-Sapuntzakis M, Mares-Perlman JA. 1996. Influence of using different sources of carotenoid data in epidemiologic studies. *J Am Diet Assoc* 96:1271–1275.
- van het Hof KH, Brouwer IA, West CE, Haddeman E, Steegers-Theunissen RP, van Dusseldorf M, Weststrate JA, Eskes TK, Hautvast JG. 1999. Bioavailability of lutein from vegetables is 5 times higher than that of beta-carotene. *Am J Clin Nutr* 70:261–268.
- van Poppel G, Kok FJ, Duijzing P, de Vogel N. 1992a. No influence of beta-carotene on smoking-induced DNA damage as reflected by sister chromatid exchanges. *Int J Cancer* 51:355–358.
- van Poppel G, Kok FJ, Hermus RJ. 1992b. Beta-carotene supplementation in smokers reduces the frequency of micronuclei in sputum. *Br J Cancer* 66:1164–1168.
- van Poppel G, Poulsen H, Loft S, Verhagen H. 1995. No influence of beta carotene on oxidative DNA damage in male smokers. *J Natl Cancer Inst* 87:310–311.
- van Vliet T, Schreurs WH, van Den Berg H. 1995. Intestinal beta-carotene absorption and cleavage in men: Response of beta-carotene and retinyl esters in the triglyceride-rich lipoprotein fraction after a single oral dose of beta-carotene. *Am J Clin Nutr* 62:110–116.
- Wahlqvist ML, Wattanapenpaiboon N, Macrae FA, Lambert JR, MacLennan R, Hsu-Hage BH. 1994. Changes in serum carotenoids in subjects with colorectal adenomas after 24 mo of beta-carotene supplementation. Australian Polyp Prevention Project Investigators. *Am J Clin Nutr* 60:936–943.
- Wang X-D. 1994. Absorption and metabolism of beta-carotene. *J Am Coll Nutr* 13:314–325.
- Wang X-D, Liu C, Bronson RT, Smith DE, Krinsky NI, Russell RM. 1999. Retinoid signaling and activator protein-1 expression in ferrets given beta-carotene supplements and exposed to tobacco smoke. *J Natl Cancer Inst* 91:60–66.
- Wang Y, Ichiba M, Oishi H, Iyadomi M, Shono N, Tomokuni K. 1997. Relationship between plasma concentrations of beta-carotene and alpha-tocopherol and life-style factors and levels of DNA adducts in lymphocytes. *Nutr Cancer* 27:69–73.
- West S, Vitale S, Hallfrisch J, Munoz B, Muller D, Bressler S, Bressler NM. 1994. Are antioxidants or supplements protective for age-related macular degeneration? *Arch Ophthalmol* 112:222–227.
- Weststrate JA, Meijer GW. 1998. Plant sterol-enriched margarines and reduction of plasma total- and LDL-cholesterol concentrations in normocholesterolaemic and mildly hypercholesterolaemic subjects. *Eur J Clin Nutr* 52:334–343.
- Weststrate JA, van het Hof KH. 1995. Sucrose polyester and plasma carotenoid concentrations in healthy subjects. *Am J Clin Nutr* 62:591–597.
- White WS, Stacewicz-Sapuntzakis M, Erdman JW Jr, Bowen PE. 1994. Pharmacokinetics of beta-carotene and canthaxanthin after ingestion of individual and combined doses by human subjects. *J Am Coll Nutr* 13:665–671.
- Winklhofer-Roob BM, Puhl H, Khoschsorur G, van't Hof MA, Esterbauer H, Shmerling DH. 1995. Enhanced resistance to oxidation of low density lipoproteins and decreased lipid peroxide formation during beta-carotene supplementation in cystic fibrosis. *Free Radic Biol Med* 18:849–859.

- Witter FR, Blake DA, Baumgardner R, Mellits ED, Niebyl JR. 1982. Folate, carotene, and smoking. *Am J Obstet Gynecol* 144:857.
- WCRF/AICR (World Cancer Research Fund/American Institute for Cancer Research). 1997. *Food, Nutrition and the Prevention of Cancer: A Global Perspective*. Menasha, WI: BANTA Book Group.
- Yong LC, Forman MR, Beecher GR, Graubard BI, Campbell WS, Reichman ME, Taylor PR, Lanza E, Holden JM, Judd JT. 1994. Relationship between dietary intake and plasma concentrations of carotenoids in premenopausal women: Application of the USDA-NCI carotenoid food-composition database. *Am J Clin Nutr* 60:223–230.
- Zhang L-X, Cooney RV, Bertram JS. 1991. Carotenoids enhance gap junctional communication and inhibit lipid peroxidation in C3H/10T1/2 cells: Relationship to their cancer chemopreventive action. *Carcinogenesis* 12:2109–2114.
- Zheng W, Blot WJ, Diamond EL, Norkus EP, Spate V, Morris JS, Comstock GW. 1993. Serum micronutrients and the subsequent risk of oral and pharyngeal cancer. *Cancer Res* 53:795–798.
- Ziegler RG, Colavito EA, Hartge P, McAdams MJ, Schoenberg JB, Mason TJ, Fraumeni JF Jr. 1996a. Importance of alpha-carotene, beta-carotene, and other phytochemicals in the etiology of lung cancer. *J Natl Cancer Inst* 88:612–615.
- Ziegler RG, Mayne ST, Swanson CA. 1996b. Nutrition and lung cancer. *Cancer Causes Control* 7:157–177.
- Zino S, Skeaff M, Williams S, Mann J. 1997. Randomised controlled trial of effect of fruit and vegetable consumption on plasma concentrations of lipids and antioxidants. *Br Med J* 314:1787–1791.

Ibid., Chapter 9, 399–400.

- AIN (American Institute of Nutrition). 1990. Nomenclature policy: Generic descriptors and trivial names for vitamins and related compounds. *J Nutr* 120:12–19.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the third National Health and Nutrition Examination Survey: Underreporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- Horwitt MK. 1976. Vitamin E: A reexamination. *Am J Clin Nutr* 29:569–578.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances be Revised?* Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1997. *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1998. *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline*. Washington, DC: National Academy Press.
- IUPAC-IUB Commission on Biochemical Nomenclature. 1974. Nomenclature of tocopherols and related compounds. Recommendations 1973. *Eur J Biochem* 46:217–219.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.

- NRC (National Research Council). 1980. *Drinking Water and Health*, Volume 3. Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Swanson CA, Patterson BH, Levander OA, Veillon C, Taylor PR, Helzlsouer K, McAdam PA, Zech LA. 1991. Human [ $^{74}\text{Se}$ ]selenomethionine metabolism: A kinetic model. *Am J Clin Nutr* 54:917–926.
- Thomson CD, Robinson MF. 1986. Urinary and fecal excretions and absorption of a large supplement of selenium: Superiority of selenate over selenite. *Am J Clin Nutr* 44:659–663.
- USDA (U.S. Department of Agriculture). 1999. USDA Nutrient Database for Standard Reference, Release, [Online]. Available: <http://www.nal.usda.gov/fnic/foodcomp>.
- Weiser H, Vecchi M, Schlachter M. 1986. Stereoisomers of alpha-tocopherol acetate. IV. USP units and alpha-tocopherol equivalents of all-rac-, 2-ambo- and RRR-alpha-tocopherol evaluated by simultaneous determination of resorption-gestation, myopath and liver storage capacity in rats. *Int J Vitam Nutr Res* 56:45–56.
- Williams AW, Erdman JW Jr. 1999. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*. Baltimore, MD: Williams and Wilkins. P. 181.

## CHOLINE

*Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline* (ISBN 0-309-06411-2), Chapter 12, pp. 414–422.

- Acara M, Rennick B. 1973. Regulation of plasma choline by the renal tubule: Bidirectional transport of choline. *Am J Physiol* 225:1123–1128.
- Acara M, Rennick B, LaGraff S, Schroeder ET. 1983. Effect of renal transplantation on the levels of choline in the plasma of uremic humans. *Nephron* 35:241–243.
- Albright CD, Liu R, Bethea TC, da Costa KA, Salganik RI, Zeisel SH. 1996. Choline deficiency induces apoptosis in SV40-immortalized CWSV-1 rat hepatocytes in culture. *FASEB J* 10:510–516.
- Al-Waiz M, Ayesh R, Mitchell SC, Idle JR, Smith RL. 1988. Trimethylaminuria (“fish-odour syndrome”): A study of an affected family. *Clin Sci* 74:231–236.
- Al-Waiz M, Ayesh R, Mitchell SC, Idle JR, Smith RL. 1989. Trimethylaminuria: The detection of carriers using a trimethylamine load test. *J Inher Metab Dis* 12:80–85.
- Anonymous. 1997. Betaine for homocystinuria. *Med Lett Drugs Ther* 39:12.
- Aquilonius SM, Ceder G, Lying-Tunell U, Malmlund HO, Schuberth J. 1975. The arteriovenous difference of choline across the brain of man. *Brain Res* 99:430–433.
- Arvidson GA. 1968. Biosynthesis of phosphatidylcholines in rat liver. *Eur J Biochem* 5:415–421.
- Barak AJ, Kemmy RJ. 1982. Methotrexate effects on hepatic betaine levels in choline-supplemented and choline-deficient rats. *Drug Nutr Interact* 1:275–278.
- Barak AJ, Tuma DJ, Beckenhauer HC. 1984. Methotrexate hepatotoxicity. *J Am Coll Nutr* 3:93–96.
- Bartus RT, Dean RL, Goas JA, Lippa AS. 1980. Age-related changes in passive avoidance retention: Modulation with dietary choline. *Science* 209:301–303.
- Bauernschmitt HG, Kinne RK. 1993. Metabolism of the “organic osmolyte” glycerocephosphorylcholine in isolated rat inner medullary collecting duct cells. I. Pathways for synthesis and degradation. *Biochim Biophys Acta* 1148:331–341.
- Best CH, Huntsman ME. 1932. The effects of the components of lecithine upon deposition of fat in the liver. *J Physiol* 75:405–412.
- Bianchi G, Azzone GF. 1964. Oxidation of choline in rat liver mitochondria. *J Biol Chem* 239:3947–3955.
- Bjornstad P, Bremer J. 1966. In vivo studies on pathways for the biosynthesis of lecithin in the rat. *J Lipid Res* 7:38–45.
- Blair R, Newsome F. 1985. Involvement of water-soluble vitamins in diseases of swine. *J Anim Sci* 60:1508–1517.
- Blair R, Whitehead CC, Bannister DW, Evans AJ. 1973. Involvement of diet in fatty liver and kidney syndrome in broiler chickens. *Vet Rec* 92:118–119.
- Blusztajn JK, Zeisel SH, Wurtman RJ. 1979. Synthesis of lecithin (phosphatidylcholine) from phosphatidylethanolamine in bovine brain. *Brain Res* 179:319–327.
- Boyd WD, Graham-White J, Blackwood G, Glen I, McQueen J. 1977. Clinical effects of choline in Alzheimer senile dementia. *Lancet* 2:711.

- Bremer J, Greenberg D. 1961. Methyl transferring enzyme system of microsomes in the biosynthesis of lecithin (phosphatidylcholine). *Biochim Biophys Acta* 46:205–216.
- Buchman AL, Dubin M, Jenden D, Moukarzel A, Roch MH, Rice K, Gornbein J, Ament ME, Eckhert CD. 1992. Lecithin increases plasma free choline and decreases hepatic steatosis in long-term total parenteral nutrition patients. *Gastroenterology* 102:1363–1370.
- Buchman AL, Moukarzel A, Jenden DJ, Roch M, Rice K, Ament ME. 1993. Low plasma free choline is prevalent in patients receiving long term parenteral nutrition and is associated with hepatic aminotransferase abnormalities. *Clin Nutr* 12:33–37.
- Buchman AL, Dubin M, Moukarzel A, Jenden D, Roch M, Rice K, Gornbein J, Ament M. 1995. Choline deficiency: A cause of hepatic steatosis during parenteral nutrition that can be reversed with intravenous choline supplementation. *Hepatology* 22:1399–1403.
- Burg MB. 1995. Molecular basis of osmotic regulation. *Am J Physiol* 268:F983–F996.
- Burt ME, Hanin I, Brennan MF. 1980. Choline deficiency associated with total parenteral nutrition. *Lancet* 2:638–639.
- Cermak JM, Holler T, Jackson DA, Blusztajn JK. 1998. Prenatal availability of choline modifies development of the hippocampal cholinergic system. *FASEB J* 12:349–357.
- Cersosimo RJ, Matthews SJ. 1987. Hepatotoxicity associated with choline magnesium trisalicylate: Case report and review of salicylate-induced hepatotoxicity. *Drug Intell Clin Pharm* 21:621–625.
- Chawla RK, Wolf DC, Kutner MH, Bonkovsky HL. 1989. Choline may be an essential nutrient in malnourished patients with cirrhosis. *Gastroenterology* 97:1514–1520.
- Cheng W-L, Holmes-McNary MQ, Mar M-H, Lien EL, Zeisel SH. 1996. Bioavailability of choline and choline esters from milk in rat pups. *J Nutr Biochem* 7:457–464.
- Cohen BM, Renshaw PF, Stoll AL, Wurtman RJ, Yurgelun-Todd D, Babb SM. 1995. Decreased brain choline uptake in older adults. An in vivo proton magnetic resonance spectroscopy study. *J Am Med Assoc* 274:902–907.
- Cohen EL, Wurtman RJ. 1975. Brain acetylcholine: Increase after systemic choline administration. *Life Sci* 16:1095–1102.
- Conlay LA, Wurtman RJ, Blusztajn K, Coviella IL, Maher TJ, Evoniuk GE. 1986. Decreased plasma choline concentrations in marathon runners. *N Engl J Med* 315:892.
- Cornford EM, Cornford ME. 1986. Nutrient transport and the blood-brain barrier in developing animals. *Fed Proc* 45:2065–2072.
- Crews FT, Calderini G, Battistella A, Toffano G. 1981. Age-dependent changes in the methylation of rat brain phospholipids. *Brain Res* 229:256–259.
- Cui Z, Houweling M, Chen MH, Record M, Chap H, Vance DE, Tercé F. 1996. A genetic defect in phosphatidylcholine biosynthesis triggers apoptosis in Chinese hamster ovary cells. *J Biol Chem* 271:14668–14671.
- da Costa KA, Cochary EF, Blusztajn JK, Garner SC, Zeisel SH. 1993. Accumulation of 1,2-sn-diradylglycerol with increased membrane-associated protein kinase C may be the mechanism for spontaneous hepatocarcinogenesis in choline-deficient rats. *J Biol Chem* 268:2100–2105.

- da Costa KA, Garner SC, Chang J, Zeisel SH. 1995. Effects of prolonged (1 year) choline deficiency and subsequent re-feeding of choline on 1,2-sn-diradylglycerol, fatty acids and protein kinase C in rat liver. *Carcinogenesis* 16:327–334.
- Davis JE. 1944. Depression of normal erythrocyte number by soybean lecithin or choline. *Am J Physiol* 142:65–67.
- Davis KL, Berger PA, Hollister LE. 1975. Choline for tardive dyskinesia. *N Engl J Med* 293:152.
- Davis KL, Hollister LE, Berger PA. 1979. Choline chloride in schizophrenia. *Am J Psychiatry* 136:1581–1584.
- Drouva SV, LaPlante E, Leblanc P, Bechet JJ, Clauser H, Kordon C. 1986. Estradiol activates methylating enzyme(s) involved in the conversion of phosphatidyl-ethanolamine to phosphatidylcholine in rat pituitary membranes. *Endocrinology* 119:2611–2622.
- Dudman NP, Tyrrell PA, Wilcken DE. 1987. Homocysteinemia: Depressed plasma serine levels. *Metabolism* 36:198–201.
- Eagle H. 1955. The minimum vitamin requirements of the L and HeLa cells in tissue culture, the production of specific vitamin deficiencies, and their cure. *J Exp Med* 102:595–600.
- Engel RW. 1943. The choline content of animal and plant products. *J Nutr* 25:441–446.
- Exton JH. 1994. Phosphatidylcholine breakdown and signal transduction. *Biochim Biophys Acta* 1212:26–42.
- Fairbanks BW, Krider JL. 1945. Significance of the B vitamins in swine nutrition. *N Am Vet* 26:18–23.
- Finkelstein JD, Martin JJ, Harris BJ, Kyle WE. 1982. Regulation of the betaine content of rat liver. *Arch Biochem Biophys* 218:169–173.
- Finkelstein JD, Martin JJ, Harris BJ. 1988. Methionine metabolism in mammals. The methionine-sparing effect of cystine. *J Biol Chem* 263:11750–11754.
- Fischer T. 1984. Contact allergy to choline chloride. *Contact Dermatitis* 10:316–317.
- Freeman-Narrod M, Narrod SA, Custer RP. 1977. Chronic toxicity of methotrexate in rats: Partial to complete protection of the liver by choline. *J Natl Cancer Inst* 59:1013–1017.
- Frenkel R, Muguruma K, Johnston J. 1996. The biochemical role of platelet-activating factor in reproduction. *Prog Lipid Res* 35:155–168.
- Garcia-Perez A, Burg MB. 1991. Role of organic osmolytes in adaptation of renal cells to high osmolality. *J Membr Biol* 119:1–13.
- Garner SC, Mar MH, Zeisel SH. 1995. Choline distribution and metabolism in pregnant rats and fetuses are influenced by the choline content of the maternal diet. *J Nutr* 125:2851–2858.
- Gelenberg AJ, Doller-Wojcik J, Growdon JH. 1979. Choline and lecithin in the treatment of tardive dyskinesia: Preliminary results from a pilot study. *Am J Psychiatry* 136:772–776.
- Grossman EB, Hebert SC. 1989. Renal inner medullary choline dehydrogenase activity: Characterization and modulation. *Am J Physiol* 256:F107–F112.
- Growdon JH, Cohen EL, Wurtman RJ. 1977a. Huntington's disease: Clinical and chemical effects of choline administration. *Ann Neurol* 1:418–422.
- Growdon JH, Hirsch MJ, Wurtman RJ, Wiener W. 1977b. Oral choline administration to patients with tardive dyskinesia. *N Engl J Med* 297:524–527.
- Gwee MC, Sim MK. 1978. Free choline concentration and cephalin-N-methyltransferase activity in the maternal and foetal liver and placenta of pregnant rats. *Clin Exp Pharmacol Physiol* 5:649–653.

- Handler P. 1949. Response of guinea pigs to diets deficient in choline. *Proc Soc Exp Biol Med* 70:70–73.
- Hannun YA. 1994. The sphingomyelin cycle and the second messenger function of ceramide. *J Biol Chem* 269:3125–3128.
- Hartz SC, Russell RM, Rosenberg IH. 1992. *Nutrition in the Elderly. The Boston Nutritional Status Survey*. London: Smith-Gordon.
- Haubrich DR, Wedeking PW, Wang PF. 1974. Increase in tissue concentration of acetylcholine in guinea pigs in vivo induced by administration of choline. *Life Sci* 14:921–927.
- Hershey JM. 1931. Substitution of lecithin for raw pancreas in the diet of depancreatized dog. *Am J Physiol* 93:657–658.
- Herzberg GR, Lerner J. 1973. Intestinal absorption of choline in the chick. *Biochim Biophys Acta* 307:234–242.
- Herzberg GR, Sheerin H, Lerner J. 1971. Cationic amino acid transport in chicken small intestine. *Comp Biochem Physiol* 40A:229–247.
- Hirsch MJ, Growdon JH, Wurtman RJ. 1978. Relations between dietary choline or lecithin intake, serum choline levels, and various metabolic indices. *Metabolism* 27:953–960.
- Hodge HC. 1945. Chronic oral toxicology of choline chloride in rats. *Proc Exp Biol Med* 58:212–215.
- Hoffbauer FW, Zaki FG. 1965. Choline deficiency in baboon and rat compared. *Arch Pathol* 79:364–369.
- Holler T, Cermak JM, Blusztajn JK. 1996. Dietary choline supplementation in pregnant rats increases hippocampal phospholipase D activity of the offspring. *FASEB J* 10:1653–1659.
- Holmes-McNary MQ, Cheng WL, Mar MH, Fussell S, Zeisel SH. 1996. Choline and choline esters in human and rat milk and in infant formulas. *Am J Clin Nutr* 64:572–576.
- Holmes-McNary MQ, Loy R, Mar MH, Albright CD, Zeisel SH. 1997. Apoptosis is induced by choline deficiency in fetal brain and in PC12 cells. *Brain Res Dev Brain Res* 101:9–16.
- Horne DW, Cook RJ, Wagner C. 1989. Effect of dietary methyl group deficiency on folate metabolism in rats. *J Nutr* 119:618–621.
- Humbert JA, Hammond KB, Hathaway WE. 1970. Trimethylaminuria: The fish-odor syndrome. *Lancet* 2:770–771.
- Jacob RA, Pianalto FS, Henning SM, Zhang JZ, Swendseid ME. 1995. In vivo methylation capacity is not impaired in healthy men during short-term dietary folate and methyl group restriction. *J Nutr* 125:1495–1502.
- James ST, Miller BT, Basnakian AG, Pogribny IP, Pogribna M, Muskhelishvili L. 1997. Apoptosis and proliferation under conditions of deoxynucleotide pool imbalance in liver of folate/methyl deficient rats. *Carcinogenesis* 18:287–293.
- Jorswieck I. 1974. Proceedings: Penetration of choline through rat placenta in vivo. *Naunyn Schmiedebergs Arch Pharmakol* 282:R42.
- Kennedy EP, Weiss SB. 1956. The function of cytidine coenzymes in the biosynthesis of phospholipids. *J Biol Chem* 222:193–214.
- Ketola HG. 1976. Choline metabolism and nutritional requirement of lake trout (*Salvelinus namaycush*). *J Anim Sci* 43:474–477.
- Ketola HG, Nesheim MC. 1974. Influence of dietary protein and methionine levels on the requirement for choline by chickens. *J Nutr* 104:1484–1489.
- Ketola HG, Young RJ. 1973. The need for dietary choline by young Japanese quail. *Poult Sci* 52:2362–2363.

- Kim Y-I, Miller JW, da Costa K-A, Nadeau M, Smith D, Selhub J, Zeisel SH, Mason JB. 1994. Severe folate deficiency causes secondary depletion of choline and phosphocholine in rat liver. *J Nutr* 124:2197–2203.
- Kuczler FJ, Nahrwold DL, Rose RC. 1977. Choline influx across the brush border of guinea pig jejunum. *Biochim Biophys Acta* 465:131–137.
- Kuksis A, Mookerjea S. 1978. Choline. *Nutr Rev* 36:201–207.
- Lawrence CM, Millac P, Stout GS, Ward JW. 1980. The use of choline chloride in ataxic disorders. *J Neurol Neurosurg Psychiatry* 43:452–454.
- Le Kim D, Betzing H. 1976. Intestinal absorption of polyunsaturated phosphatidyl-choline in the rat. *Hoppe Seylers Z Physiol Chem* 357:1321–1331.
- Lindblad L, Schersten T. 1976. Incorporation rate in vitro of choline and methyl-methionine into human hepatic lecithins. *Scand J Gastroenterol* 11:587–591.
- Loffelholz K. 1981. Release of acetylcholine in the isolated heart. *Am J Physiol* 240:H431–H440.
- Loy R, Heyer D, Williams CL, Meck WH. 1991. Choline-induced spatial memory facilitation correlates with altered distribution and morphology of septal neurons. *Adv Exp Med Biol* 295:373–382.
- LSRO/FASEB (Life Sciences Research Office/Federation of American Societies for Experimental Biology). 1975. *Evaluation of the Health Aspects of Choline Chloride and Choline Bitartrate as Food Ingredients*. Report # PB-223 845/9. Washington, DC: Department of Health, Education and Welfare.
- LSRO/FASEB (Life Sciences Research Office/Federation of American Societies for Experimental Biology). 1981. *Effects of Consumption of Choline and Lecithin on Neurological and Cardiovascular Systems*. Report # PB-82-133257. Bethesda, MD: LSRO/FASEB.
- Lyman RL, Sheehan G, Tinoco J. 1971. Diet and <sup>14</sup>CH<sub>3</sub>-methionine incorporation into liver phosphatidylcholine fractions of male and female rats. *Can J Biochem* 49:71–79.
- McIntire JM, Schweigert BS, Elvehjem CA. 1944. The choline and pyridoxine content of meats. *J Nutr* 28:219–223.
- Meck WH, Williams CL. 1997a. Characterization of the facilitative effects of perinatal choline supplementation on timing and temporal memory. *Neuroreport* 8:2831–2835.
- Meck WH, Williams CL. 1997b. Perinatal choline supplementation increases the threshold for chunking in spatial memory. *Neuroreport* 8:3053–3059.
- Meck WH, Williams CL. 1997c. Simultaneous temporal processing is sensitive to prenatal choline availability in mature and aged rats. *Neuroreport* 8:3045–3051.
- Meck WH, Smith RA, Williams CL. 1988. Pre- and postnatal choline supplementation produces long-term facilitation of spatial memory. *Dev Psychobiol* 21:339–353.
- Meck WH, Smith RA, Williams CL. 1989. Organizational changes in cholinergic activity and enhanced visuospatial memory as a function of choline administered prenatally or postnatally or both. *Behav Neurosci* 103:1234–1241.
- Mody GM, Naidoo PD, Singh TG. 1983. Clinical evaluation of choline magnesium trisalicylate in rheumatoid arthritis. *S Afr Med J* 64:195–196.
- Mudd SH, Poole JR. 1975. Labile methyl balances for normal humans on various dietary regimens. *Metabolism* 24:721–735.
- Nadkarni MM, Peller CA, Retig J. 1992. Eosinophilic hepatitis after ingestion of choline magnesium trisalicylate. *Am J Gastroenterol* 87:151–153.
- Newberne PM, Rogers AE. 1986. Labile methyl groups and the promotion of cancer. *Annu Rev Nutr* 6:407–432.

- Perloff BP, Rizek RL, Haytowitz DB, Reid PR. 1990. Dietary intake methodology. II. USDA's Nutrient Data Base for Nationwide Dietary Intake Surveys. *J Nutr* 120:1530–1534.
- Poirier LA, Grantham PH, Rogers AE. 1977. The effects of a marginally lipotrope-deficient diet on the hepatic levels of S-adenosylmethionine and on the urinary metabolites of 2-acetylaminofluorene in rats. *Cancer Res* 37:744–748.
- Pomfret EA, da Costa K-A, Schurman LL, Zeisel SH. 1989. Measurement of choline and choline metabolite concentrations using high-pressure liquid chromatography and gas chromatography-mass spectrometry. *Analy Biochem* 180:85–90.
- Pomfret EA, da Costa K, Zeisel SH. 1990. Effects of choline deficiency and methotrexate treatment upon rat liver. *J Nutr Biochem* 1:533–541.
- Pyapali GK, Turner DA, Williams CL, Meck WH, Swartzwelder HS. 1998. Prenatal dietary choline supplementation decreases the threshold for induction of long-term potentiation in young adult rats. *J Neurophysiol* 79:1790–1796.
- Rennick B, Acara M, Hysert P, Mookerjee B. 1976. Choline loss during hemodialysis: Homeostatic control of plasma choline concentrations. *Kidney Int* 10:329–335.
- Rennick B, Acara M, Glor M. 1977. Relations of renal transport rate, transport maximum, and competitor potency for tetraethylammonium and choline. *Am J Physiol* 232:F443–F447.
- Ridgway ND, Vance DE. 1988. Kinetic mechanism of phosphatidylethanolamine N-methyltransferase. *J Biol Chem* 263:16864–16871.
- Rohlfis EM, Garner SC, Mar MH, Zeisel SH. 1993. Glycerophosphocholine and phosphocholine are the major choline metabolites in rat milk. *J Nutr* 123:1762–1768.
- Sahu AP. 1989. Effect of Choline and Mineral Fibres (Chrysotile Asbestos) on Guinea-pigs. Lyon, France: IARC Scientific Publications.
- Sahu AP, Saxena AK, Singh KP, Shanker R. 1986. Effect of chronic choline administration in rats. *Indian J Exp Biol* 24:91–96.
- Sandage BW, Sabounjian L, White R, Wurtman RJ. 1992. Choline citrate may enhance athletic performance. *Physiologist* 35:236.
- Savendahl L, Mar M-H, Underwood LE, Zeisel SH. 1997. Prolonged fasting in humans results in diminished plasma choline concentrations but does not cause liver dysfunction. *Am J Clin Nutr* 66:622–625.
- SCOGS/LSRO (Select Committee on GRAS Substances, Life Sciences Research Office). 1979. *Evaluation of the Health Aspects of Lecithin as a Food Ingredient*. Report # PB301405. Springfield, VA: National Technical Information Service.
- Selhub J, Seyoum E, Pomfret EA, Zeisel SH. 1991. Effects of choline deficiency and methotrexate treatment upon liver folate content and distribution. *Cancer Res* 51:16–21.
- Shapira G, Chawla RK, Berry CJ, Williams PJ, Roy RGB, Rudman D. 1986. Cysteine, tyrosine, choline and carnitine supplementation of patients on total parenteral nutrition. *Nutr Int* 2:334–339.
- Sheard NF, Zeisel SH. 1986. An in vitro study of choline uptake by intestine from neonatal and adult rats. *Pediatr Res* 20:768–772.
- Sheard NF, Tayek JA, Bistrian BR, Blackburn GL, Zeisel SH. 1986. Plasma choline concentration in humans fed parenterally. *Am J Clin Nutr* 43:219–224.
- Shelley ED, Shelley WB. 1984. The fish odor syndrome. Trimethylaminuria. *JAMA* 251:253–255.

- Shin OH, Mar MH, Albright CD, Citarella MT, daCosta KA, Zeisel SH. 1997. Methyl-group donors cannot prevent apoptotic death of rat hepatocytes induced by choline-deficiency. *J Cell Biochem* 64:196–208.
- Shivapurkar N, Poirier LA. 1983. Tissue levels of Sadenosylmethionine and S-adenosylhomocysteine in rats fed methyl-deficient, amino acid-defined diets for one to five weeks. *Carcinogenesis* 4:1051–1057.
- Sundler R, Akesson B. 1975. Regulation of phospholipid biosynthesis in isolated rat hepatocytes. Effect of different substrates. *J Biol Chem* 250:3359–3367.
- Svardal AM, Ueland PM, Berge RK, Aarsland A, Aarsaether N, Lonning PE, Refsum H. 1988. Effect of methotrexate on homocysteine and other sulfur compounds in tissues of rats fed a normal or a defined, choline-deficient diet. *Cancer Chemother Pharmacol* 21:313–318.
- Sweiry JH, Yudilevich DL. 1985. Characterization of choline transport at maternal and fetal interfaces of the perfused guinea-pig placenta. *J Physiol* 366:251–266.
- Sweiry JH, Page KR, Dacke CG, Abramovich DR, Yudilevich DL. 1986. Evidence of saturable uptake mechanisms at maternal and fetal sides of the perfused human placenta by rapid paired-tracer dilution: Studies with calcium and choline. *J Dev Physiol* 8:435–445.
- Tamminga CA, Smith RC, Chang S, Haraszti JS, Davis JM. 1976. Depression associated with oral choline. *Lancet* 2:905.
- Tani H, Suzuki S, Kobayashi M, Kotake Y. 1967. The physiological role of choline in guinea pigs. *J Nutr* 92:317–324.
- Tayek JA, Bistrian B, Sheard NF, Zeisel SH, Blackburn GL. 1990. Abnormal liver function in malnourished patients receiving total parenteral nutrition: A prospective randomized study. *J Am Coll Nutr* 9:76–83.
- Tessitore L, Sesca E, Greco M, Pani P, Dianzani M. 1995. Sexually differentiated response to choline in choline deficiency and ethionine intoxication. *Int J Exp Pathol* 76:125–129.
- Vance DE. 1990. Boehringer Mannheim Award lecture. Phosphatidylcholine metabolism: Masochistic enzymology, metabolic regulation, and lipoprotein assembly. *Biochem Cell Biol* 68:1151–1165.
- Vance DE, Ridgway ND. 1988. The methylation of phosphatidylethanolamine. *Prog Lipid Res* 27:61–79.
- Varela-Moreiras G, Ragel C, Perez de Miguel Sanz J. 1995. Choline deficiency and methotrexate treatment induces marked but reversible changes in hepatic folate concentrations, serum homocysteine and DNA methylation rates in rats. *J Am Coll Nutr* 14:480–485.
- Von Allworden HN, Horn S, Kahl J, Feldheim W. 1993. The influence of lecithin on plasma choline concentrations in triathletes and adolescent runners during exercise. *Eur J Appl Physiol* 67:87–91.
- Wecker L. 1986. Neurochemical effects of choline supplementation. *Can J Physiol Pharmacol* 64:329–333.
- Weihrauch JL, Son Y-S. 1983. The phospholipid content of foods. *J Am Oil Chem Soc* 60:1971–1978.
- Weinhold PA, Sanders R. 1973. The oxidation of choline by liver slices and mitochondria during liver development in the rat. *Life Sci* 13:621–629.
- Welsch F. 1976. Studies on accumulation and metabolic fate of (*N*-Me<sub>3</sub>H)choline in human term placenta fragments. *Biochem Pharmacol* 25:1021–1030.

- Welsch F. 1978. Choline metabolism in human term placenta—studies on de novo synthesis and the effects of some drugs on the metabolic fate of [*N*-methyl <sup>3</sup>H]choline. *Biochem Pharmacol* 27:1251–1257.
- Welsch F, Wenger WC, Stedman DB. 1981. Choline metabolism in placenta: Evidence for the biosynthesis of phosphatidylcholine in microsomes via the methylation pathway. *Placenta* 2:211–221.
- Wendel U, Bremer H. 1984. Betaine in the treatment of homocystinuria due to 5,10-methylenetetrahydrofolate reductase deficiency. *Eur J Pediatr* 142:147–150.
- Widdowson EM. 1963. Growth and composition of the fetus and newborn. In: Assali N, ed. *Biology of Gestation*, Vol. 2. New York: Academic Press. Pp. 1–51.
- Wilcken DE, Wilcken B, Dudman NP, Tyrrell PA. 1983. Homocystinuria—the effects of betaine in the treatment of patients not responsive to pyridoxine. *N Engl J Med* 309:448–453.
- Wilcken DE, Dudman NP, Tyrrell PA. 1985. Homocystinuria due to cystathione  $\beta$ -synthase deficiency—the effects of betaine treatment in pyridoxine-responsive patients. *Metabolism* 34:1115–1121.
- Williams CL, Meck WH, Heyer D, Loy R. 1998. Hypertrophy of basal forebrain neurons and enhanced visuospatial memory in perinatally choline-supplemented rats. *Brain Res* 794:225–238.
- Wong ER, Thompson W. 1972. Choline oxidation and labile methyl groups in normal and choline-deficient rat liver. *Biochim Biophys Acta* 260:259–271.
- Wood JL, Allison RG. 1982. Effects of consumption of choline and lecithin on neurological and cardiovascular systems. *Fed Proc* 41:3015–3021.
- Yang EK, Blusztajn JK, Pomfret EA, Zeisel SH. 1988. Rat and human mammary tissue can synthesize choline moiety via the methylation of phosphatidylethanolamine. *Biochem J* 256:821–828.
- Yao ZM, Vance DE. 1988. The active synthesis of phosphatidylcholine is required for very low density lipoprotein secretion from rat hepatocytes. *J Biol Chem* 263:2998–3004.
- Yao ZM, Vance DE. 1989. Head group specificity in the requirement of phosphatidylcholine biosynthesis for very low density lipoprotein secretion from cultured hepatocytes. *J Biol Chem* 264:11373–11380.
- Yao ZM, Vance DE. 1990. Reduction in VLDL, but not HDL, in plasma of rats deficient in choline. *Biochem Cell Biol* 68:552–558.
- Young DL. 1971. Estradiol- and testosterone-induced alterations in phosphatidylcholine and triglyceride synthesis in hepatic endoplasmic reticulum. *J Lipid Res* 12:590–595.
- Yudilevich DL, Sweiry JH. 1985. Membrane carriers and receptors at maternal and fetal sides of the placenta by single circulation paired-tracer dilution: Evidence for a choline transport system. *Contrib Gynecol Obstet* 13:158–161.
- Zeisel SH. 1981. Dietary choline: Biochemistry, physiology, and pharmacology. *Annu Rev Nutr* 1:95–121.
- Zeisel SH. 1987. Choline availability in the neonate. In: Dowdall MJ, Hawthorne JN, eds. *Cellular and Molecular Basis of Cholinergic Function*. Chichester, England: Horwood. Pp. 709–719.
- Zeisel SH. 1993. Choline phospholipids: Signal transduction and carcinogenesis. *FASEB J* 7:551–557.
- Zeisel SH, Blusztajn JK. 1994. Choline and human nutrition. *Annu Rev Nutr* 14:269–296.
- Zeisel SH, Wurtman RJ. 1981. Developmental changes in rat blood choline concentration. *Biochem J* 198:565–570.

- Zeisel SH, Epstein MF, Wurtman RJ. 1980a. Elevated choline concentration in neonatal plasma. *Life Sci* 26:1827–1831.
- Zeisel SH, Growdon JH, Wurtman RJ, Magil SG, Logue M. 1980b. Normal plasma choline responses to ingested lecithin. *Neurology* 30:1226–1229.
- Zeisel SH, Story DL, Wurtman RJ, Brunengraber H. 1980c. Uptake of free choline by isolated perfused rat liver. *Proc Natl Acad Sci USA* 77:4417–4419.
- Zeisel SH, Stanbury JB, Wurtman RJ, Brigida M, Fierro BR. 1982. Choline content of mothers' milk in Ecuador and Boston. *N Engl J Med* 306:175–176.
- Zeisel SH, Wishnok JS, Blusztajn JK. 1983. Formation of methylamines from ingested choline and lecithin. *J Pharmacol Exp Ther* 225:320–324.
- Zeisel SH, Char D, Sheard NF. 1986. Choline, phosphatidylcholine and sphingomyelin in human and bovine milk and infant formulas. *J Nutr* 116:50–58.
- Zeisel SH, Zola T, daCosta K, Pomfret EA. 1989. Effect of choline deficiency on S-adenosylmethionine and methionine concentrations in rat liver. *Biochem J* 259:725–729.
- Zeisel SH, daCosta K-A, Franklin PD, Alexander EA, Lamont JT, Sheard NF, Beiser A. 1991. Choline, an essential nutrient for humans. *FASEB J* 5:2093–2098.
- Zeisel SH, Mar M-H, Zhou Z-W, da Costa K-A. 1995. Pregnancy and lactation are associated with diminished concentrations of choline and its metabolites in rat liver. *J Nutr* 125:3049–3054.
- Zeisel SH, Albright CD, Shin O-H, Mar M-H, Salganik RI, da Costa K-A. 1997. Choline deficiency selects for resistance to p53-independent apoptosis and causes tumorigenic transformation of rat hepatocytes. *Carcinogenesis* 18:731–738.

Ibid., Chapter 13, p. 436.

- Beaton GH. 1994. Criteria of an adequate diet. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*, 8th ed. Philadelphia: Lea & Febiger. Pp. 1491–1505.
- Hegsted DM. 1972. Problems in the use and interpretation of the Recommended Dietary Allowances. *Ecol Food Nutr* 1:255–265.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- USDA (U.S. Department of Agriculture). 1992. *The Food Guide Pyramid*. Home and Garden Bulletin Number 252. Washington, DC: US Government Printing Office.
- WHO (World Health Organization). 1996. *Trace Elements in Human Nutrition and Health*. Prepared in collaboration with the Food and Agriculture Organization of the United Nations and the International Atomic Energy Agency. Geneva: WHO.

## VITAMIN D

*Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride* (ISBN 0-309-06350-7), pp. 325–374.

- Abbott L, Nadler J, Rude RK. 1994. Magnesium deficiency in alcoholism: Possible contribution to osteoporosis and cardiovascular disease in alcoholics. *Alcohol Clin Exp Res* 18:1976–1082.
- Abe E, Miyaura C, Sakagami H, Takeda M, Konno K, Yamazaki T, Yoshiki S, Suda T. 1981. Differentiation of mouse myeloid leukemia cells induced by 1 $\alpha$ 25-dihydroxyvitamin D<sub>3</sub>. *Proc Natl Acad Sci USA* 78:4990–4994.
- Abraham GE, Grewal H. 1990. A total dietary program emphasizing magnesium instead of calcium: Effect on the mineral density of calcaneous bone in post-menopausal women on hormonal therapy. *J Reprod Med* 35:503–507.
- Abrams SA, Stuff JE. 1994. Calcium metabolism in girls: Current dietary intakes lead to low rates of calcium absorption and retention during puberty. *Am J Clin Nutr* 60:739–743.
- Abrams SA, Sidbury JB, Muenzer J, Esteban NV, Vieira NE, Yerger AL. 1991. Stable isotopic measurement of endogenous fecal calcium excretion in children. *J Pediatr Gastroenterol Nutr* 12:469–473.
- Abrams SA, Esteban NV, Vieira NE, Sidbury JB, Specker BL, Yerger AL. 1992. Developmental changes in calcium kinetics in children assessed using stable isotopes. *J Bone Miner Res* 7:287–293.
- Abrams SA, Silber TJ, Esteban NV, Vieira NE, Stuff JE, Meyers R, Majd M, Yerger AL. 1993. Mineral balance and bone turnover in adolescents with anorexia nervosa. *J Pediatr* 123:326–331.
- Abrams SA, O'Brien KO, Stuff JE. 1996a. Changes in calcium kinetics associated with menarche. *J Clin Endocrinol Metab* 81:2017–2020.
- Abrams SA, O'Brien KO, Wen J, Liang LK, Stuff JE. 1996b. Absorption by 1-year-old children of an iron supplement given with cow's milk or juice. *Pediatr Res* 39:171–175.
- Abrams SA, Wen J, Stuff JE. 1997a. Absorption of calcium, zinc and iron from breast milk by 5- to 7-month-old infants. *Pediatr Res* 41:1–7.
- Abrams SA, Grusak MA, Stuff J, O'Brien KO. 1997b. Calcium and magnesium balance in 9- to 14-year-old children. *Am J Clin Nutr* 66:1172–1177.
- Abreo K, Adlakha A, Kilpatrick S, Flanagan R, Webb R, Shakamuri S. 1993. The Milk-Alkali Syndrome. A reversible form of acute renal failure. *Arch Intern Med* 153:1005–1010.
- Ackerman PG, Toro G. 1953. Calcium and phosphorus balance in elderly men. *J Gerontol* 8:298–300.
- ADA (American Dental Association Council on Dental Therapeutics). 1994. New fluoride guidelines proposed. *J Am Dent Assoc* 125:366.
- Adams JS. 1989. Vitamin D metabolite-mediated hypercalcemia. *Endocrinol Metab Clin North Am* 18:765–778.
- Adams JS, Beeker TG, Hongo T, Clemens TL. 1990. Constitutive expression of a vitamin D 1-hydroxylase in a myelomonocytic cell line: A model for studying 1,25-dihydroxyvitamin D production in vitro. *J Bone Miner Res* 5:1265–1269.
- Affinito P, Tommaselli GA, DiCarlo C, Guida F, Nappi C. 1996. Changes in bone mineral density and calcium metabolism in breast-feeding women: A one year follow-up study. *J Clin Endocrinol Metab* 81:2314–2318.

- Aksnes L, Aarskog D. 1982. Plasma concentrations of vitamin D metabolites in puberty: Effect of sexual maturation and implications for growth. *J Clin Endocrinol Metab* 55:94–101.
- Ala-Houhala M. 1985. 25-Hydroxyvitamin D levels during breast-feeding with or without maternal or infantile supplementation of vitamin D. *J Pediatr Gastroenterol Nutr* 4:220–226.
- Ala-Houhala M, Parvianinen MT, Pyyko K, Visakorpi JK. 1984. Serum 25-hydroxyvitamin D levels in Finnish children aged 2 to 17 years. *Acta Paediatr Scand* 73:232–236.
- Ala-Houhala M, Koskinen T, Terho A, Koivula T, Visakorpi J. 1986. Maternal compared with infant vitamin D supplementation. *Arch Dis Child* 61:1159–1163.
- Alaimo K, McDowell MA, Briefel RR, Bischof AM, Caughman CR, Loria CM, Johnson CL. 1994. *Dietary Intake of Vitamins, Minerals, and Fiber of Persons Ages 2 Months and Over in the United States: Third National Health and Nutrition Examination Survey, Phase I, 1988–91*. Advance data from vital and health statistics; no. 258. U.S. Department of Health and Human Services. Hyattsville, MD: National Center for Health Statistics.
- Albert DG, Morita Y, Iseri LT. 1958. Serum magnesium and plasma sodium levels in essential vascular hypertension. *Circulation* 17:761–764.
- Alderman BW, Weiss NS, Daling JR, Ure CL, Ballard JH. 1986. Reproductive history and postmenopausal risk of hip and forearm fracture. *Am J Epidemiol* 124:262–267.
- Alfrey AC, Miller NL, Butkus D. 1974. Evaluation of body magnesium stores. *J Lab Clin Med* 84:153–162.
- Allen JC, Keller RP, Archer P, Neville MC. 1991. Studies in human lactation: Milk composition and daily secretion rates of macronutrients in the first year of lactation. *Am J Clin Nutr* 54:69–80.
- Allen SH, Shah JH. 1992. Calcinosis and metastatic calcification due to vitamin D intoxication. A case report and review. *Horm Res* 37:68–77.
- Allender PS, Cutler JA, Follmann D, Cappuccio FP, Prysor J, Elliott P. 1996. Dietary calcium and blood pressure: A meta-analysis of randomized clinical trials. *Ann Intern Med* 124:825–831.
- Aloia JF, Vaswani AN, Yeh JK, Ross P, Ellis K, Cohn SH. 1983. Determinants of bone mass in postmenopausal women. *Arch Intern Med* 143:1700–1704.
- Aloia JF, Vaswani AN, Yeh JK, Ellis K, Cohn SH. 1984. Total body phosphorus in postmenopausal women. *Miner Electrolyte Metab* 10:73–76.
- Aloia JF, Vaswani A, Yeh JK, Ross PL, Flaster E, Dilmanian FA. 1994. Calcium supplementation with and without hormone replacement therapy to prevent postmenopausal bone loss. *Ann Intern Med* 120:97–103.
- Altura BT, Brust M, Bloom S, Barbour RL, Stempak JG, Altura BM. 1990. Magnesium dietary intake modulates blood lipid levels and atherogenesis. *Proc Natl Acad Sci USA* 87:1840–1844.
- Altura BT, Shirey TL, Hiti J, Dell'Orfano K, Handwerker SM, Altura BM. 1992. A new method for the rapid determination of ionized Mg<sup>2+</sup> in whole blood, serum and plasma. *Methods Find Exp Clin Pharmacol* 14:297–304.
- Altura BT, Wilimizig C, Trnovec T, Nyulassy S, Altura BM. 1994. Comparative effects of a Mg-enriched diet and different orally administered magnesium oxide preparations on ionized Mg, Mg metabolism and electrolytes in serum of human volunteers. *J Am Coll Nutr* 13:447–454.
- American Academy of Pediatrics. 1982. The promotion of breastfeeding: Policy statement based on task force report. *Pediatrics* 69:654–661.

- Anderson DM, Hollis BW, LeVine BR, Pittard WB III. 1988. Dietary assessment of maternal vitamin D intake and correlation with maternal and neonatal serum vitamin D concentrations at delivery. *J Perinatol* 8:46–48.
- Andon MB, Ilich JZ, Tzagournis MA, Matkovic V. 1996. Magnesium balance in adolescent females consuming a low- or high-calcium diet. *Am J Clin Nutr* 63:950–953.
- Angus RM, Sambrook PN, Pockock NA, Eisman JA. 1988. Dietary intake and bone mineral density. *Bone Miner* 4:265–277.
- Antman EM. 1996. Magnesium in acute myocardial infarction: Overview of available evidence. *Am Heart J* 132:487–495.
- Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin PH, Karanja N. 1997. A clinical trial of the effects of dietary patterns on blood pressure. *N Engl J Med* 336:1117–1124.
- Arnold FA Jr, Dean HT, Jay P, Knutson JW. 1956. Effect of fluoridated public water supplies on dental caries prevalence. Tenth year of the Grand Rapids-Muskegon Study. *Pub Hlth Rep* 71:652–658.
- Ascherio A, Rimm EB, Giovannucci EL, Colditz GA, Rosner B, Willett WC, Sacks F, Stampfer MJ. 1992. A prospective study of nutritional factors and hypertension among U.S. men. *Circulation* 86:1475–1484.
- Ashe JR, Schofield FA, Gram MR. 1979. The retention of calcium, iron, phosphorus, and magnesium during pregnancy: The adequacy of prenatal diets with and without supplementation. *Am J Clin Nutr* 32:286–291.
- Atkinson SA, Chappell JE, Clandinin MT. 1987. Calcium supplementation of mothers' milk for low birthweight infants: Problems related to absorption and excretion. *Nutr Res* 7:813–823.
- Atkinson SA, Alston-Mills BP, Lonnerdal B, Neville MC, Thompson MP. 1995. Major minerals and ionic constituents of human and bovine milk. In: Jensen RJ, ed. *Handbook of Milk Composition*. California: Academic Press. Pp. 593–619.
- Bainbridge RR, Mimouni FB, Landi T, Crossman M, Harris L, Tsang RC. 1996. Effect of rice cereal feedings on bone mineralization and calcium homeostasis in cow milk formula fed infants. *J Am Coll Nutr* 15:383–388.
- Baran D, Sorensen A, Grimes J, Lew R, Karella A, Johnson B, Roche J. 1990. Dietary modification with dairy products for preventing vertebral bone loss in premenopausal women: A three-year prospective study. *J Clin Endocrinol Metab* 70:264–270.
- Bardicef M, Bardicef O, Sorokin Y, Altura BM, Altura BT, Cotton DB, Resnick LM. 1995. Extracellular and intracellular magnesium depletion in pregnancy and gestational diabetes. *Am J Obstet Gynecol* 172:1009–1013.
- Barger-Lux MJ, Heaney RP. 1995. Caffeine and the calcium economy revisited. *Osteopor Int* 5:97–102.
- Barger-Lux MJ, Heaney RP, Stegman MR. 1990. Effects of moderate caffeine intake on the calcium economy of premenopausal women. *Am J Clin Nutr* 52:722–725.
- Barger-Lux MJ, Heaney RP, Lanspa SJ, Healy JC, DeLuca HF. 1995. An investigation of sources of variation in calcium absorption efficiency. *J Clin Endocrinol Metab* 80:406–411.
- Barger-Lux MJ, Heaney RP, Dowell S, Bierman J, Holick MF, Chen TC. 1996. Relative molar potency of 25-hydroxyvitamin D indicates a major role in calcium absorption. *J Bone Miner Res* 11:S423.

- Barnhart WE, Hiller LK, Leonard GJ, Michaels SE. 1974. Dentifrice usage and ingestion among four age groups. *J Dent Res* 53:1317–1322.
- Barragry JM, France MW, Corless D, Gupta SP, Switala S, Boucher BJ, Cohen RD. 1978. Intestinal cholecalciferol absorption in the elderly and in younger adults. *Clin Sci Molec Med* 55:213–220.
- Barrett-Connor E, Chang JC, Edelstein SL. 1994. Coffee-associated osteoporosis offset by daily milk consumption. The Rancho Bernardo Study. *J Am Med Assoc* 271:280–283.
- Bashir Y, Sneddon JF, Staunton HA, Haywood GA, Simpson IA, McKenna WJ, Camm AJ. 1993. Effects of long-term oral magnesium chloride replacement in congestive heart failure secondary to coronary artery disease. *Am J Cardiol* 72:1156–1162.
- Beall DP, Scofield RH. 1995. Milk-alkali syndrome associated with calcium carbonate consumption: Report of 7 patients with parathyroid hormone levels and an estimate of prevalence among patients hospitalized with hypercalcemia. *Medicine* 74:89–96.
- Beaton GH. 1994. Criteria of an adequate diet. In: Shils RE, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease, 8th edition*. Philadelphia: Lea & Febiger. Pp. 1491–1505.
- Beaton GH. 1996. Statistical approaches to establish mineral element recommendations. *J Nutr* 126:2302S–2328S.
- Begum A, Pereira SM. 1969. Calcium balance studies on children accustomed to low calcium intakes. *Br J Nutr* 23:905–911.
- Bell NH, Greene A, Epstein S, Oexmann MJ, Shaw S, Shary J. 1985. Evidence for alteration of the vitamin D-endocrine system in blacks. *J Clin Invest* 76:470–473.
- Bell NH, Shary J, Stevens J, Garza M, Gordon L, Edwards J. 1991. Demonstration that bone mass is greater in black than in white children. *J Bone Miner Res* 6:719–723.
- Bell NH, Yergey AL, Vieira NE, Oexmann MJ, Shary JR. 1993. Demonstration of a difference in urinary calcium, not calcium absorption, in black and white adolescents. *J Bone Miner Res* 8:1111–1115.
- Bell RA, Whitford GM, Barenie JT, Myers DR. 1985. Fluoride retention in children using self-applied topical fluoride products. *Clin Prev Dent* 7:22–27.
- Berkelhammer CH, Wood RJ, Sitrin MD. 1988. Acetate and hypercalciuria during total parenteral nutrition. *Am J Clin Nutr* 48:1482–1489.
- Bernstein DS, Sadowsky N, Hegsted DM, Guri CD, Stare FJ. 1966. Prevalence of osteoporosis in high- and low-fluoride areas in North Dakota. *J Am Med Assoc* 198:499–504.
- Bijvoet, OLM. 1969. Relation of plasma phosphate concentration to renal tubular reabsorption of phosphate. *Clin Sci* 37:23–26.
- Bikle DD, Gee E, Halloran B, Haddad JG. 1984. Free 1,25-dihydroxyvitamin D levels in serum from normal subjects, pregnant subjects, and subjects with liver disease. *J Clin Invest* 74:1966–1971.
- Birkeland JM, Charlton G. 1976. Effect of pH on the fluoride ion activity of plaque. *Caries Res* 10:72–80.
- Bishop NJ, Dahlenburg SL, Fewtrell MS, Morley R, Lucas A. 1996. Early diet of preterm infants and bone mineralization at age five years. *Acta Paediatr* 85:230–236.
- Bizik BK, Ding W, Cerklewski FL. 1996. Evidence that bone resorption of young men is not increased by high dietary phosphorus obtained from milk and cheese. *Nutr Res* 16:1143–1146.

- Black DM, Cummings SR, Genant HK, Nevitt MC, Palermo L, Browner W. 1992. Axial and appendicular bone density predict fractures in older women. *J Bone Miner Res* 7:633–638.
- Blank S, Scanlon KS, Sinks TH, Lett S, Falk H. 1995. An outbreak of hypervitaminosis D associated with the overfortification of milk from a home-delivery dairy. *Am J Publ Health* 85:656–659.
- Blayney JR, Hill IN. 1964. Evanston dental caries study XXIV. Prenatal fluorides—value of waterborne fluorides during pregnancy. *J Am Dent Assoc* 69:291–294.
- Bodanszky H, Leleiko N. 1985. Metabolic alkalosis with hypertonic dehydration in a patient with diarrhoea and magnesium oxide ingestion. *Acta Paediatr Hung* 26:241–246.
- Bogdonoff MD, Shock NW, Nichols MP. 1953. Calcium, phosphorus, nitrogen, and potassium balance studies in the aged male. *J Gerontol* 8:272–288.
- Bostick RM, Potter JD, Fosdick L, Grambsch P, Lampe JW, Wood JR, Louis TA, Ganz R, Grandits G. 1993. Calcium and colorectal epithelial cell proliferation: A preliminary randomized, double-blinded, placebo-controlled clinical trial. *J Natl Cancer Inst* 85:132–141.
- Boston JL, Beauchene RE, Cruikshank DP. 1989. Erythrocyte and plasma magnesium during teenage pregnancy: Relationship with blood pressure and pregnancy-induced hypertension. *Obstet Gynecol* 73:169–174.
- Bouillon R, Van Assche FA, Van Baelen H, Heyns W, De Moor P. 1981. Influence of the vitamin D-binding protein on the serum concentration of 1,25-dihydroxyvitamin D<sub>3</sub>. Significance of the free 1,25-dihydroxyvitamin D<sub>3</sub> concentration. *J Clin Invest* 67:589–596.
- Bour NJS, Soullier BA, Zemel MB. 1984. Effect of level and form of phosphorus and level of calcium intake on zinc, iron and copper bioavailability in man. *Nutr Res* 4:371–379.
- Bowden GH. 1990. Effects of fluoride on the microbial ecology of dental plaque. *J Dent Res* 69 (Spec Iss):653–659.
- Boyle DR, Chagnon M. 1995. An incidence of skeletal fluorosis associated with groundwaters of the maritime carboniferous basin, Gaspe Region, Quebec, Canada. *Environ Geochem Health* 17:5–12.
- BPA (British Paediatric Association). 1956. Hypercalcaemia in infants and Vitamin D. *Br Med J* 2:149.
- BPA (British Paediatric Association). 1964. Infantile hypercalcaemia, nutritional rickets, and infantile scurvy in Great Britain. *Br Med J* 1:1659–1661.
- Brambilla E, Belluomo G, Malerba A, Buscaglia M, Strohmenger L. 1994. Oral administration of fluoride in pregnant women, and the relation between concentration in maternal plasma and in amniotic fluid. *Arch Oral Biol* 39:991–994.
- Brandwein SL, Sigman, KM. 1994. Case report: Milk-alkali syndrome and pancreatitis. *Am J Med Sci* 308:173–176.
- Brannan PG, Vergne-Marini P, Pak CY, Hull AR, Fordtran JS. 1976. Magnesium absorption in the human small intestine. Results in normal subjects, patients with chronic renal disease, and patients with absorptive hypercalciuria. *J Clin Invest* 57:1412–1418.
- Bransby ER, Berry WTC, Taylor DM. 1964. Study of the vitamin-D intakes of infants in 1960. *Br Med J* 1:1661–1663.
- Brazier M, Kamel S, Maamer M, Agbomson F, Elesper I, Garabedian M, Desmet G, Sebert JL. 1995. Markers of bone remodeling in the elderly subject: Effects of vitamin D insufficiency and its correction. *J Bone Miner Res* 10:1753–1761.

- Brickman AS, Coburn JW, Massry SG. 1974. 1,25 dihydroxy-vitamin D<sub>3</sub> in normal man and patients with renal failure. *Ann Intern Med* 80:161–168.
- Brink EJ, Beynen AC. 1992. Nutrition and magnesium absorption: A review. *Prog Food Nutr Sci* 16:125–162.
- Brodehl J, Gellissen K, Weber H-P. 1982. Postnatal development of tubular phosphate reabsorption. *Clin Nephrol* 17:163–171.
- Brown WE, Gregory TM, Chow LC. 1977. Effects of fluoride on enamel solubility and cariostasis. *Caries Res* 11(Suppl 1):118–141.
- Brunelle JA, Carlos JP. 1990. Recent trends in dental caries in U.S. children and the effect of water fluoridation. *J Dent Res* 69(Spec Iss):723–727.
- Bruun C, Thylstrup A. 1988. Dentifrice usage among Danish children. *J Dent Res* 67:1114–1117.
- Bucher HC, Cook RJ, Guyatt GH, Lang JD, Cook DJ, Hatala R, Hunt DL. 1996. Effects of dietary calcium supplementation on blood pressure: A meta-analysis of randomized controlled trials. *J Am Med Assoc* 275:1016–1022.
- Bucuvalas JC, Heubi JE, Specker BL, Gregg DJ, Yerger AL, Vieira NE. 1990. Calcium absorption in bone disease associated with chronic cholestasis during childhood. *Hepatology* 12:1200–1205.
- Bullamore JR, Wilkinson R, Gallagher JC, Nordin BEC, Marshall DH. 1970. Effects of age on calcium absorption. *Lancet* 2:535–537.
- Bullimore DW, Miloszewski KJ. 1987. Raised parathyroid hormone levels in the milk-alkali syndrome: An appropriate response? *Postgrad Med J* 63:789–792.
- Burt BA. 1992. The changing patterns of systemic fluoride intake. *J Dent Res* 71:1228–1237.
- Burtis WJ, Gay L, Insogna KL, Ellison A, Broadus AE. 1994. Dietary hypercalciuria in patients with calcium oxalate kidney stones. *Am J Clin Nutr* 60:424–429.
- Bushe CJ. 1986. Profound hypophosphataemia in patients collapsing after a “fun run.” *Br Med J* 292:898–899.
- Butte NF, Garza C, Smith EO, Nichols BL. 1984. Human milk intake and growth in exclusively breast-fed infants. *J Pediatr* 104:187–195.
- Buzzard IM, Willett WC, eds. 1994. Dietary assessment methods. Proceedings of a conference held in St. Paul, MN. *Am J Clin Nutr* 59:143S–306S.
- Byrne J, Thomas MR, Chan GM. 1987. Calcium intake and bone density of lactating women in their late childbearing years. *J Am Diet Assoc* 87:883–887.
- Byrne PM, Freaney R, McKenna MJ. 1995. Vitamin D supplementation in the elderly: Review of safety and effectiveness of different regimens. *Calcif Tissue Int* 56:518–520.
- Caddell JL, Ratananon N, Trangratapit P. 1973. Parenteral magnesium load tests in postpartum Thai women. *Am J Clin Nutr* 26:612–615.
- Caddell JL, Saier FL, Thomason CA. 1975. Parenteral magnesium load tests in postpartum American women. *Am J Clin Nutr* 28:1099–1104.
- Calvo MS. 1993. Dietary phosphorus, calcium metabolism and bone. *J Nutr* 123:1627–1633.
- Calvo MS, Heath H III. 1988. Acute effects of oral phosphate-salt ingestion on serum phosphorus, serum ionized calcium, and parathyroid hormone in young adults. *Am J Clin Nutr* 47:1025–1029.
- Calvo MS, Park YK. 1996. Changing phosphorus content of the U.S. diet: Potential for adverse effects on bone. *J Nutr* 126:1168S–1180S.
- Calvo MS, Kumar R, Heath H III. 1988. Elevated secretion and action of serum parathyroid hormone in young adults consuming high phosphorus, low calcium diets assembled from common foods. *J Clin Endocrinol Metab* 66:823–829.

- Calvo MS, Kumar R, Heath H. 1990. Persistently elevated parathyroid hormone secretion and action in young women after four weeks of ingesting high phosphorus, low calcium diets. *J Clin Endocrinol Metab* 70:1334–1340.
- Campbell SB, MacFarlane DJ, Fleming SJ, Khafagi FA. 1994. Increased skeletal uptake of Tc-99m Methylene Disphosphonate in Milk-Alkali Syndrome. *Clin Nucl Med* 19:207–211.
- Canadian Paediatric Society (Nutrition Committee). 1991. Meeting the iron needs of infants and young children: An update. *Can Med Assoc J* 144:1451–1454.
- Canadian Paediatric Society. 1996. The use of fluoride in infants and children. *Paediatr Child Health* 1:131–134.
- Cappuccio FP, Markandu ND, Beynon GW, Shore AC, Sampson B, MacGregor GA. 1985. Lack of effect of oral magnesium on high blood pressure: A double blind study. *Br Med J Clin Res Ed* 291:235–238.
- Carlos JP, Gittelsohn AM, Haddon W Jr. 1962. Caries in deciduous teeth in relation to maternal ingestion of fluoride. *Pub Hlth Rep* 77:658–660.
- Carroll MD, Abraham S, Dresser CM. 1983. Dietary intake source data: United States, 1976–1980. Data from the National Health Survey. Vital and Health Statistics series 11, no. 231. DHHS Publ. No. (PHS) 83-1681. Hyattsville, MD: National Center for Health Statistics, Public Health Service, U.S. Department of Health and Human Services.
- Chan GM. 1991. Dietary calcium and bone mineral status of children and adolescents. *Am J Dis Child* 145:631–634.
- Chan GM, Roberts CC, Folland D, Jackson R. 1982a. Growth and bone mineralization of normal breast-fed infants and the effects of lactation on maternal bone mineral status. *Am J Clin Nutr* 36:438–443.
- Chan GM, Slater RN, Hollis J, Thomas MR. 1982b. Decreased bone mineral status in lactating adolescent mothers. *J Pediatr* 101:767–770.
- Chan GM, Leeper L, Book LS. 1987. Effects of soy formulas on mineral metabolism in term infants. *Am J Dis Child* 141:527–530.
- Chan GM, Hoffman K, McMurry M. 1995. Effects of dairy products on bone and body composition in pubertal girls. *J Pediatr* 126:551–556.
- Chan JT, Koh SH. 1996. Fluoride content in caffeinated, decaffeinated and herbal teas. *Caries Res* 30:88–92.
- Chan JT, Qui CC, Whitford GM, Weatherred JG. 1990. Influence of coffee on fluoride metabolism in rats. *Proc Soc Exp Biol Med* 194:43–47.
- Chandra RK. 1984. Physical growth of exclusively breast-fed infants. *Nutr Res* 2:275–276.
- Chapuy MC, Arlot ME, Duboeuf F, Brun J, Crouzet B, Arnaud S, Delmas PD, Meunier PJ. 1992. Vitamin D<sub>3</sub> and calcium to prevent hip fractures in elderly women. *N Engl J Med* 327:1637–1642.
- Charles P, Jensen FT, Mosekilde L, Hansen HH. 1983. Calcium metabolism evaluated by <sup>47</sup>Ca kinetics: Estimation of dermal calcium loss. *Clin Sci* 65:415–422.
- Chen TC, Castillo L, Korycka-Dahl M, DeLuca HF. 1974. Role of vitamin D metabolites in phosphate transport of rat intestine. *J Nutr* 104:1056–1060.
- Chen TC, Shao A, Heath H III, Holick MF. 1993. An update on the vitamin D content of fortified milk from the United States and Canada. *N Engl J Med* 329:1507.
- Chen X, Whitford GM. 1994. Lack of significant effect of coffee and caffeine on fluoride metabolism in rats. *J Dent Res* 73:1173–1179.
- Chesney RW. 1990. Requirements and upper limits of vitamin D intake in the term neonate, infant, and older child. *J Pediatr* 116:159–166.

- Chevalley T, Rizzoli R, Nydegger V, Slosman D, Rapin CH, Michel JP, Vasey H, Bonjour JP. 1994. Effects of calcium supplements on femoral bone mineral density and vertebral fracture rate in vitamin D-replete elderly patients. *Osteopor Int* 4:245–252.
- Chinn HI. 1981. Effects of dietary factors on skeletal integrity in adults: Calcium, phosphorus, vitamin D, and protein. Prepared for Bureau of Foods, Food and Drug Administration, U.S. Department of Health and Human Services, Washington, D.C.
- Cholak J. 1959. Fluorides: A critical review. I. The occurrence of fluoride in air, food and water. *J Occup Med* 1:501–511.
- Chow LC. 1990. Tooth-bound fluoride and dental caries. *J Dent Res* 69(Spec Iss):595–600.
- Clark DC, Hann HJ, Williamson MF, Berkowitz J. 1993. Aesthetic concerns of children and parents in relation to different classifications of the Tooth Surface Index of Fluorosis. *Community Dent Oral Epidemiol* 21:360–364.
- Clarkson EM, Warren RL, McDonald SJ, de Wardener HE. 1967. The effect of a high intake of calcium on magnesium metabolism in normal subjects and patients with chronic renal failure. *Clin Sci* 32:11–18.
- Clarkson PM, Haymes EM. 1995. Exercise and mineral status of athletes: Calcium, magnesium, phosphorus, and iron. *Med Sci Sports Exerc* 27:831–843.
- Clemens TL, Adams JS. 1996. Vitamin D metabolites. In: Favus MJ, Christakos S, eds. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 3rd edition*. Philadelphia, PA: Lippincott-Raven. Pp. 109–114.
- Clemens TL, Adams JS, Henderson SL, Holick MF. 1982. Increased skin pigment reduces the capacity of skin to synthesise vitamin D<sub>3</sub>. *Lancet* 1:74–76.
- Clemens TL, Zhou X, Myles M, Endres D, Lindsay R. 1986. Serum vitamin D<sub>2</sub> and vitamin D<sub>3</sub> metabolite concentrations and absorption of vitamin D<sub>2</sub> in elderly subjects. *J Clin Endocrinol Metab* 63:656–660.
- Cleveland LE, Goldman JD, Borrud LG. 1996. *Data Tables: Results from USDA's 1994 Continuing Survey of Food Intakes by Individuals and 1994 Diet and Health Knowledge Survey*. Beltsville, MD: Agricultural Research Service, U.S. Department of Agriculture.
- Clovis J, Hargreaves JA. 1988. Fluoride intake from beverage consumption. *Community Dent Oral Epidemiol* 16:11–15.
- CNPP, USDA (Center for Nutrition Policy and Promotion, U.S. Department of Agriculture). 1996. *Nutrient Content of the U.S. Food Supply, 1990–1994. Preliminary Data*. Washington, DC: U.S. Department of Agriculture.
- Cockburn F, Belton NR, Purvis RJ, Giles MM, Brown JK, Turner TL, Wilkinson EM, Forfar JO, Barrie WJM, McKay GS, Pocock SJ. 1980. Maternal vitamin D intake and mineral metabolism in mothers and their newborn infants. *Br Med J* 281:11–14.
- Coffin B, Azpiroz F, Guarner F, Malagelada JR. 1994. Selective gastric hypersensitivity and reflex hyporeactivity in functional dyspepsia. *Gastroenterology* 107:1345–1351.
- Cohen L. 1988. Recent data on magnesium and osteoporosis. *Magnes Res* 1:85–87.
- Cohen L, Laor A. 1990. Correlation between bone magnesium concentration and magnesium retention in the intravenous magnesium load test. *Magnes Res* 3:271–274.
- Cohn SH, Abesamis C, Yasumura S, Aloia JF, Zanzi I, Ellis KJ. 1977. Comparative skeletal mass and radial bone mineral content in black and white women. *Metabolism* 26:171–178.

- Colston K, Colston MJ, Feldman D. 1981. 1,25-dihydroxyvitamin D<sub>3</sub> and malignant melanoma: The presence of receptors and inhibition of cell growth in culture. *Endocrinol* 108:1083–1086.
- COMA (Committee on Medical Aspects of Food Policy). 1991. *Dietary Reference Values for Food Energy and Nutrients for the United Kingdom. Report on Health and Social Subjects, No. 41*. London: HMSO.
- Comstock GW. 1979. Water hardness and cardiovascular diseases. *Am J Epidemiol* 110:375–400.
- Conradt A, Weidinger H, Algayer H. 1984. On the role of magnesium in fetal hypotrophy, pregnancy induced hypertension and pre-eclampsia. *Magnes Bull* 2:68–76.
- Cooper C, Melton LJ III. 1992. Epidemiology of osteoporosis. *Trends Endocrinol Metab* 3:224–229.
- Cooper C, Campion G, Melton LJ III. 1992. Hip fractures in the elderly: A worldwide projection. *Osteopor Int* 2:285–289.
- Costello RB, Moser-Veillon PB, DiBianco R. 1997. Magnesium supplementation in patients with congestive heart failure. *J Am Coll Nutr* 16:22–31.
- Cowell DC, Taylor WH. 1981. Ionic fluoride: A study of its physiological variation in man. *Ann Clin Biochem* 18:76–83.
- Craig JM. 1959. Observations on the kidney after phosphate loading in the rat. *Arch Pathol* 68:306–315.
- Cramer CF. 1961. Progress and rate of absorption of radiophosphorus through the intestinal tract of rats. *Can J Biochem Physiol* 39:499–503.
- Cremer HD, Buttner W. 1970. *Absorption of Fluorides. Fluoride and Human Health*. Geneva, Switzerland: World Health Organization.
- Cross NA, Hillman LS, Allen SH, Krause GF, Vieira NE. 1995a. Calcium homeostasis and bone metabolism during pregnancy, lactation, and postweaning: A longitudinal study. *Am J Clin Nutr* 61:514–523.
- Cross NA, Hillman LS, Allen SH, Krasue GF. 1995b. Changes in bone mineral density and markers of bone remodeling during lactation and postweaning in women consuming high amounts of calcium. *J Bone Miner Res* 10:1312–1320.
- Cumming RG, Cummings SR, Nevitt MC, Scott J, Ensrud KE, Vogt TM, Fox K. 1997. Calcium intake and fracture risk: Results from the study of osteoporotic fractures. *Am J Epidemiol* 145:926–934.
- Cummings SR, Black DM, Nevitt MC, Browner W, Cauley J, Ensrud K, Genant HK, Palermo L, Scott J, Vogt TM. 1993. Bone density at various sites for prediction of hip fractures. The Study of Osteoporotic Fractures Research Group. *Lancet* 341:72–75.
- Cummings SR, Nevitt MC, Browner WS, Stone K, Fox KM, Ensrud KE, Cauley J, Black D, Vogt TM. 1995. Risk factors for hip fracture in white women: Study of Osteoporotic Fractures Research Group. *N Engl J Med* 332:767–773.
- Cunningham AS, Mazess RB. 1983. Bone mineral loss in lactating adolescents. *J Pediatr* 101:338–339.
- Curhan GC, Willett WC, Rimm EB, Stampfer MJ. 1993. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. *N Engl J Med* 328:833–838.
- Curhan GC, Willett WC, Speizer FE, Spiegelman D, Stampfer MJ. 1997. Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk for kidney stones in women. *Ann Intern Med* 126:497–504.

- Dabeka RW, McKenzie AD, Conacher HBS, Kirkpatrick DC. 1982. Determination of fluoride in Canadian infant foods and calculation of fluoride intakes by infants. *Can J Pub Hlth* 73:188–191.
- Dabeka RW, McKenzie AD, Lecroix GM. 1987. Dietary intakes of lead, cadmium, arsenic and fluoride by Canadian adults: A 24-hour duplicate diet study. *Food Addit Contam* 4:89–101.
- Dale G, Fleetwood JA, Inkster JS, Sainsbury JR. 1986. Profound hypophosphataemia in patients collapsing after a “fun run.” *Br Med J (Clin Res)* 292:447–448.
- Dalton MA, Sargent JD, O’Connor GT, Olmstead EM, Klein RZ. 1997. Calcium and phosphorus supplementation of iron-fortified infant formula: No effect on iron status of healthy full-term infants. *Am J Clin Nutr* 65:921–926.
- Davies M, Adams PH. 1978. The continuing risk of vitamin D intoxication. *Lancet* 2(8090):621–623.
- Davies M, Lawson DEM, Emberson C, Barnes JLC, Roberts GE, Barnes ND. 1982. Vitamin D from skin: Contribution to vitamin D status compared with oral vitamin D in normal and anti-convulsant-treated subjects. *Clin Sci* 63:461–472.
- Davies M, Hayes ME, Yin JA, Berry JL, Mawer EB. 1994. Abnormal synthesis of 1,25-dihydroxyvitamin D in patients with malignant lymphoma. *J Clin Endocrinol Metab* 78:1202–1207.
- Davis RH, Morgan DB, Rivlin RS. 1970. The excretion of calcium in the urine and its relation to calcium intake, sex and age. *Clin Sci* 39:1–12.
- Dawes C. 1989. Fluorides: Mechanisms of action and recommendations for use. *J Can Dent Assoc* 55:721–723.
- Dawson-Hughes B. 1996. Calcium. In: Marcus R, Feldman D, Kelsey J, eds. *Osteoporosis*. Orlando, FL: Academic Press, Inc. Pp. 1103, 1105.
- Dawson-Hughes B, Stern DT, Shipp CC, Rasmussen HM. 1988. Effect of lowering dietary calcium intake on fractional whole body calcium retention. *J Clin Endocrinol Metab* 67:62–68.
- Dawson-Hughes B, Dallal GE, Krall EA, Sadowski L, Sahyoun N, Tannenbaum S. 1990. A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women. *N Engl J Med* 323:878–883.
- Dawson-Hughes B, Dallal GE, Krall EA, Harris S, Sokoll LJ, Falconer G. 1991. Effect of vitamin D supplementation on wintertime and overall bone loss in healthy postmenopausal women. *Ann Intern Med* 115:505–512.
- Dawson-Hughes B, Harris S, Kramich C, Dallal G, Rasmussen HM. 1993. Calcium retention and hormone levels in black and white women on high- and low-calcium diets. *J Bone Miner Res* 8:779–787.
- Dawson-Hughes B, Harris SS, Krall EA, Dallal GE, Falconer G, Green CL. 1995. Rates of bone loss in postmenopausal women randomly assigned to one of two dosages of vitamin D. *Am J Clin Nutr* 61:1140–1145.
- Dawson-Hughes B, Fowler SE, Dalsky G, Gallagher C. 1996. Sodium excretion influences calcium homeostasis in elderly men and women. *J Nutr* 126:2107–2112.
- Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. 1997. Calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. *N Engl J Med* 337:670–676.
- Dean HT. 1942. The investigation of physiological effects by the epidemiological method. In: Moulton FR, ed. *Fluorine and Dental Health*. Washington, DC: American Association for the Advancement of Science. Pp. 23–31.
- Dean HT, Elvove E. 1937. Further studies on the minimal threshold of chronic endemic dental fluorosis. *Pub Hlth Rep* 52:1249–1264.

- Delmas PD. 1992. Clinical use of biochemical markers of bone remodeling in osteoporosis. *Bone* 13:S17–S21.
- Delmi M, Rapin CH, Bengoa JM, Delmas PD, Vasey H, Bonjour JP. 1990. Dietary supplementation in elderly patients with fractured neck of the femur. *Lancet* 335:1013–1016.
- DeLuca HF. 1984. The metabolism, physiology, and function of vitamin D. In: Kumar R, ed. *Vitamin D: Basic and Clinical Aspects*. Boston: M. Nijhoff Publishers.
- DeLuca HF. 1988. The vitamin D story: A collaborative effort of basic science and clinical medicine. *FASEB J* 2:224–236.
- Delvin EE, Salle BL, Glorieux FH, Adeleine P, David LS. 1986. Vitamin D supplementation during pregnancy: Effect on neonatal calcium homeostasis. *J Pediatr* 109:328–334.
- Demay MB. 1995. Hereditary defects in vitamin D metabolism and vitamin D receptor defects. In: DeGroot LJ, Besser M, Burger HG, Jameson JL, Loriaux DL, Marshall JC, O'Dell WD, Potts JT, Rubenstein AH, eds. *Endocrinology, Vol 2, Third edition*. Philadelphia, PA: WB Saunders. Pp. 1173–1178.
- Demirjian A. 1980. *Anthropometry Report. Height, Weight, and Body Dimensions: A Report from Nutrition Canada*. Ottawa: Minister of National Health and Welfare, Health and Promotion Directorate, Health Services and Promotion Branch.
- Dengel JL, Mangels AR, Moser-Veillon PB. 1994. Magnesium homeostasis: Conservation mechanism in lactating women consuming a controlled-magnesium diet. *Am J Clin Nutr* 59:990–994.
- Deurenberg P, Pieters JJ, Hautvast JG. 1990. The assessment of the body fat percentage by skinfold thickness measurements in childhood and young adolescence. *Br J Nutr* 63:293–303.
- Deuster PA, Singh A. 1993. Responses of plasma magnesium and other cations to fluid replacement during exercise. *J Am Coll Nutr* 12:286–293.
- Devine A, Criddle RA, Dick IM, Kerr DA, Prince RL. 1995. A longitudinal study of the effect of sodium and calcium intakes on regional bone density in postmenopausal women. *Am J Clin Nutr* 62:740–745.
- DeVizia B, Mansi A. 1992. Calcium and phosphorus metabolism in full-term infants. *Monatsschr Kinderheilkd* 140:S8–S12.
- DeVizia B, Fomon SJ, Nelson SE, Edwards BE, Zeigler EE. 1985. Effect of dietary calcium on metabolic balance of normal infants. *Pediatr Res* 19:800–806.
- Dewey KG, Finley DA, Lonnerdal B. 1984. Breast milk volume and composition during late lactation (7–20 months). *J Pediatr Gastroenterol Nutr* 3:713–720.
- DHHS (Department of Health and Human Services). 1988. *The Surgeon General's Report on Nutrition and Health*. Washington, DC: US Department of Health and Human Services, Public Health Service.
- DHHS (Department of Health and Human Services). 1990. *Healthy People 2000: National Health Promotion and Disease Prevention Objectives*. DHHS Publ. No. (PHS) 91-50212. Washington, DC: US Government Printing Office. Pp. 466–467.
- Diem K. 1970. *Documenta Geigy*. Ardsley, NY: Geigy Pharmaceuticals.
- Dobnig H, Kainer F, Stepan V, Winter R, Lipp R, Schaffer M, Kahr A, Nocnik S, Patterer G, Leb G. 1995. Elevated parathyroid hormone-related peptide levels after human gestation: Relationship to changes in bone and mineral metabolism. *J Clin Endocrinol Metab* 80:3699–3707.
- Dorsch TR. 1986. The milk-alkali syndrome, vitamin D, and parathyroid hormone. *Ann Intern Med* 105:800–801.

- Dorup I, Clausen T. 1993. Correlation between magnesium and potassium contents in muscle: Role of Na(+)-K<sup>+</sup> pump. *Am J Physiol* 264:C457–C463.
- Dourson ML, Stara JF. 1983. Regulatory history and experimental support of uncertainty (safety) factors. *Regul Toxicol Pharmacol* 3:224–238.
- Dowell TB. 1981. The use of toothpaste in infancy. *Br Dent J* 150:247–249.
- Drinkwater BL, Chesnut CH III. 1991. Bone density changes during pregnancy and lactation in active women: A longitudinal study. *Bone Miner* 14:153–160.
- Drinkwater B, Bruemner B, Chesnut C. 1990. Menstrual history as a determinant of current bone density in young athletes. *J Am Med Assoc* 263:545–548.
- Dwyer JT, Dietz WH, Hass G, Suskind R. 1979. Risk of nutritional rickets among vegetarian children. *Am J Dis Child* 133:134–140.
- Dyckner T, Wester PO. 1983. Effect of magnesium on blood pressure. *Br Med J (Clin Res)* 286:1847–1849.
- Dyckner T, Wester PO. 1985. Skeletal muscle magnesium and potassium determinations: Correlation with lymphocyte contents of magnesium and potassium. *J Am Coll Nutr* 4:619–625.
- Ebeling PR, Yergey AL, Vieira NE, Burritt MF, O'Fallon WM, Kumar R, Riggs BL. 1994. Influence of age on effects on endogenous 1,25-dihydroxy-vitamin D on calcium absorption in normal women. *Calcif Tissue Int* 55:330–334.
- Eble DM, Deaton TG, Wilson FC, Bawden JW. 1992. Fluoride concentrations in human and rat bone. *J Pub Hlth Dent* 52:288–291.
- Egsmose C, Lund B, McNair P, Lund B, Storm T, Sorensen OH. 1987. Low serum levels of 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D in institutionalized old people: Influence of solar exposure and vitamin D supplementation. *Age Ageing* 16:35–40.
- Eisman JA, Suva LJ, Sher E, Pearce PJ, Funder JW, Martin TJ. 1981. Frequency of 1,25-dihydroxyvitamin D<sub>3</sub> receptor in human breast cancer. *Cancer Res* 41:5121–5124.
- Ekstrand J, Ehrnebo M. 1979. Influence of milk products on fluoride bioavailability in man. *Eur J Clin Pharmacol* 16:211–215.
- Ekstrand J, Ehrnebo M. 1980. Absorption of fluoride from fluoride dentifrices. *Caries Res* 14:96–102.
- Ekstrand J, Boreus LO, de Chateau P. 1981. No evidence of transfer of fluoride from plasma to breast milk. *Br Med J* 283:761–762.
- Ekstrand J, Spak CJ, Falch J, Afseth J, Ulvestad H. 1984. Distribution of fluoride to human breast milk following intake of high doses of fluoride. *Caries Res* 18:93–95.
- Ekstrand J, Fomon SJ, Ziegler EE, Nelson SE. 1994a. Fluoride pharmacokinetics in infancy. *Pediatr Res* 35:157–163.
- Ekstrand J, Ziegler EE, Nelson SE, Fomon SJ. 1994b. Absorption and retention of dietary and supplemental fluoride by infants. *Adv Dent Res* 8:175–180.
- Elders PJ, Netelenbos JC, Lips P, van Ginkel FC, Khoe E, Leeuwenkamp OR, Hackeng WH, van der Stelt PF. 1991. Calcium supplementation reduces vertebral bone loss in perimenopausal women: A controlled trial in 248 women between 46 and 55 years of age. *J Clin Endocrinol Metab* 73:533–540.
- Elders PJ, Lips P, Netelenbos JC, van Ginkel FC, Khoe E, van der Vijgh WJ, van der Stelt PF. 1994. Long-term effect of calcium supplementation on bone loss in perimenopausal women. *J Bone Miner Res* 9:963–970.
- Elia M. 1992. Energy expenditure and the whole body. In: Kinney JM, Tucker HN, eds. *Energy Metabolism: Tissue Determinants and Cellular Corollaries*. New York: Raven Press Ltd. Pp. 19–59.

- Elin RJ. 1987. Assessment of magnesium status. *Clin Chem* 33:1965–1970.
- Elin RJ, Hosseini JM. 1985. Magnesium content of mononuclear blood cells. *Clin Chem* 31:377–380.
- Ellis KJ, Shypailo RJ, Hergenroeder A, Perez M, Abrams S. 1996. Total body calcium and bone mineral content: Comparison of dual-energy X-ray absorptiometry (DXA) with neutron activation analysis (NAA). *J Bone Miner Res* 11:843–848.
- Ellis KJ, Abrams SA, Wong WW. 1997. Body composition of a young, multiethnic female population. *Am J Clin Nutr* 65:724–731.
- EPA (U. S. Environmental Protection Agency). 1986. Guidelines for Carcinogen Risk Assessment. *Federal Register* 51(185):33992–34003.
- EPA (U. S. Environmental Protection Agency). 1996. Proposed Guidelines for Carcinogen Risk Assessment; Notice. *Federal Register* 61(79):17960–18011.
- Esala S, Vuori E, Helle A. 1982. Effect of maternal fluorine intake on breast milk fluorine content. *Br J Nutr* 48:201–204.
- Esveld RP, DeLuca HF. 1981. Calcitroic acid: Biological activity and tissue distribution studies. *Arch Biochem Biophys* 206:403–413.
- European Community. 1993. *Nutrient and Energy Intakes for the European Community*. Reports of the Scientific Committee for Food, Thirty-first Series.
- Evans RW. 1989. Changes in dental fluorosis following an adjustment to the fluoride concentration of Hong Kong's water supplies. *Adv Dent Res* 3:154–160.
- Evans RW, Darvell BW. 1995. Refining the estimate of the critical period for susceptibility to enamel fluorosis in human maxillary central incisors. *J Pub Hlth Dent* 55:238–249.
- Fairweather-Tait S, Prentice A, Heumann KG, Landing MAJ, Stirling DM, Wharf SG, Turnlund JR. 1995. Effect of calcium supplements and stage of lactation on the calcium absorption efficiency of lactating women accustomed to low calcium intakes. *Am J Clin Nutr* 62:1188–1192.
- FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization). 1982. *Evaluation of Certain Food Additives and Contaminants*. Twenty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives (WHO Technical Report Series No. 683).
- FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization, Expert Consultation). 1995. *The Application of Risk Analysis to Food Standard Issues*. Recommendations to the Codex Alimentarius Commission (ALINORM 95/9, Appendix 5).
- FAO/WHO/UNA (Food and Agriculture Organization of the United Nations/World Health Organization/United Nations). 1985. *Energy and Protein Requirements*. Report of a joint FAO/WHO/UNA Consultation Technical Report Series. No. 724. Geneva, Switzerland: World Health Organization.
- Fardellone P, Sebert JL, Garabedian M, Bellony R, Maamer M, Agbomson F, Brazier M. 1995. Prevalence and biological consequences of vitamin D deficiency in elderly institutionalized subjects. *Rev Rhum* 62:576–581.
- Farmer ME, White LR, Brody JA, Bailey KR. 1984. Race and sex differences in hip fracture incidence. *Am J Publ Health* 74:1374–1380.
- Fatemi S, Ryzen E, Flores J, Endres DB, Rude RK. 1991. Effect of experimental human magnesium depletion on parathyroid hormone secretion and 1,25-dihydroxyvitamin D metabolism. *J Clin Endocrinol Metab* 73:1067–1072.
- Faulkner KG, Cummings SR, Black D, Palermo L, Gluer CC, Genant HK. 1993. Simple measurement of femoral geometry predicts hip fracture: The study of osteoporotic fractures. *J Bone Miner Res* 8:1211–1217.

- Favus MJ, Christakos S. 1996. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 3rd Edition*. Philadelphia, PA: Lippincott-Raven.
- Featherstone JDB, Shields CP. 1988. *A Study of Fluoride in New York State Residents*. Final report to New York State Department of Health.
- Fehily AM, Coles RJ, Evans WD, Elwood PC. 1992. Factors affecting bone density in young adults. *Am J Clin Nutr* 56:579–586.
- Fejerskov O, Thylstrup A, Larsen MJ. 1977. Clinical and structural features and possible pathogenic mechanisms of dental fluorosis. *Scand J Dent Res* 85:510–534.
- Feldblum PJ, Zhang J, Rich LE, Fortney JA, Talmage RV. 1992. Lactation history and bone mineral density among perimenopausal women. *Epidemiology* 3:527–531.
- Feliciano ES, Ho ML, Specker BL, Falciglia G, Shui QM, Yin TA, Chen XC. 1994. Seasonal and geographical variations in the growth rate of infants in China receiving increasing dosages of vitamin D supplements. *J Trop Pediatr* 40:162–165.
- Feltman R, Kosel G. 1961. Prenatal and postnatal ingestion of fluorides—fourteen years of investigation. Final report. *J Dent Med* 16:190–198.
- Fieser LF, Fieser M. 1959. Vitamin D. In: *Steroids*. New York: Reinhold. Pp. 90–168.
- Filippo FA, Battistone GC. 1971. The fluoride content of a representative diet of the young adult male. *Clin Chim Acta* 31:453–457.
- Fine KD, Santa Ana CA, Porter JL, Fordtran JS. 1991a. Intestinal absorption of magnesium from food and supplements. *J Clin Invest* 88:396–402.
- Fine KD, Santa Ana CA, Fordtran JS. 1991b. Diagnosis of magnesium-induced diarrhea. *N Engl J Med* 324:1012–1017.
- Fink RI, Kolterman OG, Griffin J, Olefsky JM. 1983. Mechanisms of insulin resistance in aging. *J Clin Invest* 71:1523–1535.
- Fitzgerald MG, Fourman P. 1956. An experimental study of magnesium deficiency in man. *Clin Sci* 15:635.
- Fomon SJ, Nelson SE. 1993. Calcium, phosphorus, magnesium, and sulfur. In: Fomon SJ, ed. *Nutrition of Normal Infants*. St. Louis: Mosby-Year Book, Inc. Pp. 192–216.
- Fomon SJ, Younoszai MK, Thomas LN. 1966. Influence of vitamin D on linear growth of normal full-term infants. *J Nutr* 88:345–50.
- Fomon SJ, Haschke F, Ziegler EE, Nelson SE. 1982. Body composition of reference children from birth to age 10 years. *Am J Clin Nutr* 35:1169–1175.
- Franz KB. 1987. Magnesium intake during pregnancy. *Magnesium* 6:18–27.
- Franz KB. 1989. Influence of phosphorus on intestinal absorption of calcium and magnesium. In: Itokawa Y, Durlach J, eds. *Magnesium in Health and Disease*. London: John Libbey & Co. Pp. 71–78.
- Fraser DR. 1980. Regulation of the metabolism of vitamin D. *Physiol Rev* 60:551–613.
- Fraser DR. 1983. The physiological economy of vitamin D. *Lancet* 1:969–972.
- Freiman I, Pettifor JM, Moodley GM. 1982. Serum phosphorus in protein energy malnutrition. *J Pediatr Gastroenterol Nutr* 1:547–550.
- French JK, Koldaway IM, Williams LC. 1986. Milk-alkali syndrome following over-the-counter antacid self-medication. *N Zeal Med J* 99:322–323.
- Freudenheim JL, Johnson NE, Smith EL. 1986. Relationships between usual nutrient intake and bone-mineral content of women 35–65 years of age: Longitudinal and cross-sectional analysis. *Am J Clin Nutr* 44:863–876.

- Freyberg RH. 1942. Treatment of arthritis with vitamin and endocrine preparations. *J Am Med Assoc* 119:1165–1171.
- Frithz G, Wictorin B, Ronquist G. 1991. Calcium-induced constipation in a prepubescent boy. *Acta Paediatr Scand* 80:964–965.
- Frost HM. 1973. The origin and nature of transients in human bone remodeling dynamics. In: Frame B, Parfitt AM, Duncan H, eds. *Clinical Aspects of Metabolic Bone Disease*. Amsterdam: Excerpta Medica Series. Pp. 124–137.
- Frost HM. 1987. The mechanostat: A proposed pathogenic mechanism of osteoporosis and the bone mass effects of mechanical and nonmechanical agents. *Bone Miner* 2:73–85.
- Frost HM. 1997. Why do marathon runners have less bone than weight lifters? A vital-biomechanical view and explanation. *Bone* 20:183–189.
- Gadallah M, Massry SG, Bigazzi R, Horst RL, Eggema P, Campese VM. 1991. Intestinal absorption of calcium and calcium metabolism in patients with essential hypertension and normal renal function. *Am J Hypertens* 4:404–409.
- Galla JH, Booker BB, Luke RG. 1986. Role of the loop segment in the urinary concentrating defect of hypercalcemia. *Kidney Int* 29:977–982.
- Gallagher JC, Riggs BL, DeLuca HF. 1980. Effect of estrogen on calcium absorption and serum vitamin D metabolites in postmenopausal osteoporosis. *J Clin Endocrinol Metab* 51:1359–1364.
- Gallagher JC, Goldgar D, Moy A. 1987. Total bone calcium in women: Effect of age and menopause status. *J Bone Miner Res* 2:491–496.
- Garby L, Lammert O. 1984. Within-subjects between-days-and-weeks variation in energy expenditure at rest. *Human Nutr Clin Nutr* 38:395–397.
- Garfinkel L, Garfinkel D. 1985. Magnesium regulation of the glycolytic pathway and the enzymes involved. *Magnesium* 4:60–72.
- Garland C, Shekelle RB, Barrett-Connor E, Criqui MH, Rossof AH, Paul O. 1985. Dietary vitamin D and calcium and risk of colorectal cancer: A 19-year prospective study in men. *Lancet* 1:307–309.
- Garland FC, Garland CF, Gorham ED, Young JF. 1990. Geographic variation in breast cancer mortality in the United States: A hypothesis involving exposure to solar radiation. *Prev Med* 19:614–622.
- Garn SM. 1972. The course of bone gain and the phases of bone loss. *Orthop Clin North Am* 3:503–520.
- Gartside PS, Glueck CJ. 1995. The important role of modifiable dietary and behavioral characteristics in the causation and prevention of coronary heart disease hospitalization and mortality: The prospective NHANES I follow-up study. *J Am Coll Nutr* 14:71–79.
- Gedalia I, Brzezinski A, Portuguese N, Bercovici B. 1964. The fluoride content of teeth and bones of human foetuses. *Arch Oral Biol* 9:331–340.
- Geleijnse JM, Witteman JC, Bak AA, den Breeijen JH, Grobbee DE. 1994. Reduction in blood pressure with a low sodium, high potassium, high magnesium salt in older subjects with mild to moderate hypertension. *Br Med J* 309:436–440.
- German Society of Nutrition. 1991. *Recommendations on Nutrient Intake*. Abstract and Tables of the 157 Pages Booklet, 5th revised edition. Frankfurt: Druckerei Henrich.
- Gershoff SN, Legg MA, Hegsted DM. 1958. Adaptation to different calcium intakes in dogs. *J Nutr* 64:303–312.
- Gertner JM, Coustan DR, Kligler AS, Mallette LE, Ravin N, Broadus AE. 1986. Pregnancy as state of physiologic absorptive hypercalciuria. *Am J Med* 81:451–456.

- Gillman MW, Hood MY, Moore LL, Nguyen US, Singer MR, Andon MB. 1995. Effect of calcium supplementation on blood pressure in children. *J Pediatr* 127:186–192.
- Gilsanz V, Roe TF, Mora S, Costin G, Goodman WG. 1991. Changes in vertebral bone density in black girls and white girls during childhood and puberty. *N Engl J Med* 325:1597–1600.
- Glaser K, Parmelee AH, Hoffman WS. 1949. Comparative efficacy of vitamin D preparations in prophylactic treatment of premature infants. *Am J Dis Child* 77:1–14.
- Glass RL, Peterson JK, Zuckerberg DA, Naylor MN. 1975. Fluoride ingestion resulting from the use of a monofluorophosphate dentifrice by children. *Br Dent J* 138:423–426.
- Glenn FB. 1981. The rationale for the administration of a NaF tablet supplement during pregnancy and postnatally in a private practice setting. *J Dent Child* 48:118–122.
- Glenn FB, Glenn WD III, Duncan RC. 1984. Prenatal fluoride tablet supplementation and the fluoride content of teeth: Part VII. *J Dent Child* 51:344–351.
- Gloth FM III, Gundberg CM, Hollis BW, Haddad JG Jr, Tobin JD. 1995. Vitamin D deficiency in homebound elderly persons. *J Am Med Assoc* 274:1683–1686.
- Goeree R, O'Brien B, Pettitt D, Cuddy L, Ferraz M, Adachi J. 1996. An assessment of the burden of illness due to osteoporosis in Canada. *J SOGC*:15S–24S.
- Golden BE, Golden MH. 1981. Plasma zinc, rate of weight gain, and the energy cost of tissue deposition in children recovering from severe malnutrition on a cow's milk or soya protein-based diet. *Am J Clin Nutr* 34:892–899.
- Goldfarb S. 1994. Diet and nephrolithiasis. *Ann Rev Med* 45:235–243.
- Goldring SR, Krane SM, Avioli LV. 1995. Disorders of calcification: Osteomalacia and rickets. In: DeGroot LJ, ed. *Endocrinology*, Vol 2, *Third Edition*. Philadelphia: WB Saunders. Pp. 1204–1227.
- Golzarian J, Scott HW Jr, Richards WO. 1994. Hypermagnesemia-induced paralytic ileus. *Dig Dis Sci* 39:1138–1142.
- Gora ML, Seth SK, Bay WH, Visconti JA. 1989. Milk-alkali syndrome associated with use of chlorothiazide and calcium carbonate. *Clin Pharm* 8:227–229.
- Goren S, Silverstein LJ, Gonzales N. 1993. A survey of food service managers of Washington State boarding homes for the elderly. *J Nutr Elderly* 12:27–42.
- Graham S. 1959. Idiopathic hypercalcemia. *Postgraduate Med* 25:67–72.
- Gray TK, Lester GE, Lorenc RS. 1979. Evidence for extra-renal 1-hydroxylation of 25-hydroxyvitamin D<sub>3</sub> in pregnancy. *Science* 204:1311–1313.
- Greer FR. 1989. Calcium, phosphorus, and magnesium: How much is too much for infant formulas? *J Nutr* 119:1846–1851.
- Greer FR, Garn SM. 1982. Loss of bone mineral content in lactating adolescents. *J Pediatr* 101:718–719.
- Greer FR, Searcy JE, Levin RS, Steichen JJ, Steichen-Asche PS, Tsang RC. 1982a. Bone mineral content and serum 25-hydroxyvitamin D concentrations in breast-fed infants with and without supplemental vitamin D: One-year follow-up. *J Pediatr* 100:919–922.
- Greer FR, Tsang RC, Levin RS, Searcy JE, Wu R, Steichen JJ. 1982b. Increasing serum calcium and magnesium concentrations in breast-fed infants: Longitudinal studies of minerals in human milk and in sera of nursing mothers and their infants. *J Pediatr* 100:59–64.

- Greer FR, Steichen JJ, Tsang RC. 1982c. Effects of increased calcium, phosphorus, and vitamin D intake on bone mineralization in very low-birth-weight infants fed formulas with polycose and medium-chain triglycerides. *J Pediatr* 100:951–955.
- Greer FR, Lane J, Ho M. 1984. Elevated serum parathyroid hormone, calcitonin, and 1,25-dihydroxyvitamin D in lactating women nursing twins. *Am J Clin Nutr* 40:562–568.
- Greger JL, Baier MJ. 1983. Effect of dietary aluminum on mineral metabolism of adult males. *Am J Clin Nutr* 38:411–419.
- Greger JL, Baligar P, Abernathy RP, Bennett OA, Peterson T. 1978. Calcium, magnesium, phosphorus, copper, and manganese balance in adolescent females. *Am J Clin Nutr* 31:117–121.
- Greger JL, Huffman J, Abernathy RP, Bennett OA, Resnick SE. 1979. Phosphorus and magnesium balance of adolescent females fed two levels of zinc. *J Food Sci* 44:1765–1767.
- Greger JL, Smith SA, Snedeker SM. 1981. Effect of dietary calcium and phosphorus levels on the utilization of calcium, phosphorus, magnesium, manganese, and selenium by adult males. *Nutr Res* 1:315–325.
- Grill V, Martin TJ. 1993. Non-parathyroid hypercalcemias. In: Nordin BEC, Need AG, Morris HA, eds. *Metabolic Bone and Stone Disease*. Edinburgh: Churchill Livingstone. Pp. 133–145.
- Grimston SK, Morrison K, Harder JA, Hanley DA. 1992. Bone mineral density during puberty in Western Canadian children. *Bone Miner* 19:85–96.
- Groeneveld A, Van Eck AA, Backer-Dirks O. 1990. Fluoride in caries prevention: Is the effect pre- or post-eruptive? *J Dent Res* 69(Spec Iss):751–755.
- Gullestad L, Dolva LO, Waage A, Falch D, Fagerthun H, Kjekshus J. 1992. Magnesium deficiency diagnosed by an intravenous loading test. *Scan J Clin Lab Invest* 52:245–253.
- Gullestad L, Nes M, Ronneberg R, Midtveldt K, Falch D, Kjekshus J. 1994. Magnesium status in healthy free-living elderly Norwegians. *J Am Coll Nutr* 13:45–50.
- Gultekin A, Ozalp I, Hasanoglu A, Unal A. 1987. Serum-25-hydroxycholecalciferol levels in children and adolescents. *Turk J Pediatr* 29:155–162.
- Gunther T. 1993. Mechanisms and regulation of Mg<sup>2+</sup> efflux and Mg<sup>2+</sup> influx. *Miner Electrolyte Metab* 19:259–265.
- Guy WS. 1979. Inorganic and organic fluorine in human blood. In: Johansen E, Taves DR, Olsen TO, eds. *Continuing Evaluation of the Use of Fluorides*. AAAS Selected Symposium. Boulder, CO: Westview Press.
- Haddad JG, Jr. 1980. Competitive protein-binding radioassays for 25-OH-D; clinical applications. In: Norman, ed. *Vitamin D*, vol. 2. New York: Marcel Dekker, Inc., P. 587.
- Haddad JG, Hahn TJ. 1973. Natural and synthetic sources of circulating 25-hydroxyvitamin D in man. *Nature* 244:515–517.
- Hakim R, Tolis G, Goltzman D, Meltzer S, Friedman R. 1979. Severe hypercalcemia associated with hydrochlorothiazide and calcium carbonate therapy. *Can Med Assoc J* 21:591–594.
- Halioua L, Anderson JJ. 1989. Lifetime calcium intake and physical activity habits: Independent and combined effects on the radial bone of healthy premenopausal Caucasian women. *Am J Clin Nutr* 49:534–541.
- Hallberg L, Rossander-Hulten L, Brune M, Gleerup A. 1992. Calcium and iron absorption: Mechanism of action and nutritional importance. *Eur J Clin Nutr* 46:317–327.

- Hallfrisch J, Muller DC. 1993. Does diet provide adequate amounts of calcium, iron, magnesium, and zinc in a well-educated adult population? *Exper Gerontol* 28:473–483.
- Hamilton IR. 1990. Biochemical effects of fluoride on oral bacteria. *J Dent Res* 69(Spec Iss):660–667.
- Hammer DI, Heyden S. 1980. Water hardness and cardiovascular mortality. *J Am Med Assoc* 243:2399–2400.
- Hamuro Y, Shino A, Suzuki Z. 1970. Acute induction of soft tissue calcification with transient hyperphosphatemia in the KK mouse by modification in dietary contents of calcium, phosphorus, and magnesium. *J Nutr* 100:404–412.
- Handwerker SM, Altura BT, Altura BM. 1996. Serum ionized magnesium and other electrolytes in the antenatal period of human pregnancy. *J Am Coll Nutr* 15:36–43.
- Hardwick LL, Jones MR, Brautbar N, Lee DB. 1991. Magnesium absorption: Mechanisms and the influence of vitamin D, calcium and phosphate. *J Nutr* 121:13–23.
- Hargreaves JA. 1972. Fluoride content of deciduous tooth enamel from three different regions (Abstract). *J Dent Res* 51:274.
- Hargreaves JA. 1992. The level and timing of systemic exposure to fluoride with respect to caries resistance. *J Dent Res* 71:1244–1248.
- Hargreaves JA, Ingram GS, Wagg BJ. 1970. An extended excretion study on the ingestion of a monofluorophosphate toothpaste by children. *Acta Med Sci Hung* 27:413–419.
- Hargreaves JA, Ingram FF, Wagg BJ. 1972. A gravimetric based study of the ingestion of toothpaste by children. *Caries Res* 6:237–243.
- Hargreaves JA, Thompson GW, Pimlott JFL, Norbert LD. 1988. Commencement date of fluoride supplementation related to dental caries. *J Dent Res* 67:230.
- Harris SS, Dawson-Hughes B. 1994. Caffeine and bone loss in healthy postmenopausal women. *Am J Clin Nutr* 60:573–578.
- Hart M, Windle J, McHale M, Grissom R. 1982. Milk-alkali syndrome and hypercalcemia: A case report. *Nebr Med J* 67:128–130.
- Hasling C, Charles P, Jensen FT, Mosekilde L. 1990. Calcium metabolism in postmenopausal osteoporosis: The influence of dietary calcium and net absorbed calcium. *J Bone Miner Res* 5:939–946.
- Hayslip CC, Klein TA, Wray HL, Duncan WE. 1989. The effects of lactation on bone mineral content in healthy postpartum women. *Obstet Gynecol* 73:588–592.
- Health Canada. 1990. *Nutrition Recommendations. The Report of the Scientific Review Committee 1990*. Ottawa: Canadian Government Publishing Centre.
- Health Canada. 1993. *Health Risk Determination—The Challenge of Health Protection*. Health Canada, Health Protection Branch. Ottawa: Health Canada.
- Heaney RP. 1993. Protein intake and the calcium economy. *J Am Diet Assoc* 93:1259–1260.
- Heaney RP. 1997. Vitamin D: Role in the calcium economy. In: Feldman D, Glorieux FH, Pike JW, eds. *Vitamin D*. San Diego, CA: Academic Press. Pp. 485–497.
- Heaney RP, Recker RR. 1982. Effects of nitrogen, phosphorus, and caffeine on calcium balance in women. *J Lab Clin Med* 99:46–55.
- Heaney RP, Recker RR. 1987. Calcium supplements: Anion effects. *Bone Miner* 2:433–439.

- Heaney RP, Recker RR. 1994. Determinants of endogenous fecal calcium in healthy women. *J Bone Miner Res* 9:1621–1627.
- Heaney RP, Skillman TG. 1964. Secretion and excretion of calcium by the human gastrointestinal tract. *J Lab Clin Med* 64:29–41.
- Heaney RP, Skillman TG. 1971. Calcium metabolism in normal human pregnancy. *J Clin Endocrinol* 33:661–670.
- Heaney RP, Saville PD, Recker RR. 1975. Calcium absorption as a function of calcium intake. *J Lab Clin Med* 85:881–890.
- Heaney RP, Recker RR, Saville PD. 1977. Calcium balance and calcium requirements in middle-aged women. *Am J Clin Nutr* 30:1603–1611.
- Heaney RP, Recker RR, Saville PD. 1978. Menopausal changes in calcium balance performance. *J Lab Clin Med* 92:953–963.
- Heaney RP, Recker RR, Hinders SM. 1988. Variability of calcium absorption. *Am J Clin Nutr* 47:262–264.
- Heaney RP, Recker RR, Stegman MR, Moy AJ. 1989. Calcium absorption in women: Relationships to calcium intake, estrogen status, and age. *J Bone Miner Res* 4:469–475.
- Heaney RP, Recker RR, Weaver CM. 1990a. Absorbability of calcium sources: The limited role of solubility. *Calcif Tissue Int* 46:300–304.
- Heaney RP, Weaver CM, Fitzsimmons ML. 1990b. Influence of calcium load on absorption fraction. *J Bone Miner Res* 5:1135–1138.
- Heaney RP, Weaver CM, Fitzsimmons ML. 1991. Soybean phytate content: Effect on calcium absorption. *Am J Clin Nutr* 53:745–747.
- Heaton FW. 1969. The kidney and magnesium homeostasis. *Ann NY Acad Sci* 162:775–785.
- Hegsted DM. 1972. Problems in the use and interpretation of the Recommended Dietary Allowances. *Ecol Food Nutr* 1:255–265.
- Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. 1993. Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: The DARLING study. *Am J Clin Nutr* 58:152–161.
- Hemmingsen C, Staun M, Olgaard K. 1994. Effects of magnesium on renal and intestinal calbindin-D. *Miner Electrolyte Metab* 20:265–273.
- Herman-Giddens ME, Slora EJ, Wasserman RC, Bourdon CJ, Bhapkar MV, Koch GG, Hasemeier CM. 1997. Secondary sexual characteristics and menses in young girls seen in office practice: A study from the Pediatric Research in Office Settings Network. *Pediatrics* 99:505–512.
- Hill AB. 1971. *Principles of Medical Statistics, 9th Ed.* New York: Oxford University Press.
- Hillman LS. 1990. Mineral and vitamin D adequacy in infants fed human milk or formula between 6 and 12 months of age. *J Pediatr* 117:S134–S142.
- Hillman L, Sateesha S, Haussler M, Wiest W, Slatopolsky E, Haddad J. 1981. Control of mineral homeostasis during lactation: Interrelationships of 25-hydroxyvitamin D, 24,25-dihydroxyvitamin D, 1,25-dihydroxyvitamin D, parathyroid hormone, calcitonin, prolactin, and estradiol. *Am J Obstet Gynecol* 139:471–476.
- Hillman LS, Chow W, Salmons SJ, Weaver E, Erickson M, Hansen J. 1988. Vitamin D metabolism, mineral homeostasis and bone mineralization in term infants fed human milk, cow milk-based formula or soy-based formula. *J Pediatr* 112:864–874.
- Hodge HC, Smith FA. 1977. Occupational fluoride exposure. *J Occup Med* 19:12–39.

- Hodge HC. 1979. The safety of fluoride tablets or drops. In: Johansen E, Taves DR, Olson, TO, eds. *Continuing Evaluation of the Use of Fluorides, AAAS Selected Symposium 1*. Boulder, CO: Westview Press. Pp. 253–274.
- Hodgson E, Mailman RB, Chamber JE. 1988. *Dictionary of Toxicology*. New York: Van Nostrand Reinhold, Inc.
- Hoffman S, Grisso JA, Kelsey JL, Gammon MD, O'Brien LA. 1993. Parity, lactation and hip fracture. *Osteopor Int* 3:171–176.
- Hofvander Y, Hagman U, Hillervik C, Sjolin S. 1982. The amount of milk consumed by 1–3 months old breast- or bottle-fed infants. *Acta Pediatr Scand* 71:953–958.
- Holbrook TL, Barrett-Connor E, Wingard DL. 1988. Dietary calcium and risk of hip fracture: 14-year prospective population study. *Lancet* 2:1046–1049.
- Holick MF. 1986. Vitamin D requirements for the elderly. *Clin Nutr* 5:121–129.
- Holick MF. 1994. McCollum Award Lecture, 1994: Vitamin D: New horizons for the 21st century. *Am J Clin Nutr* 60:619–630.
- Holick MF. 1995. Vitamin D: Photobiology, metabolism, and clinical applications. In: DeGroot LJ, Besser M, Burger HG, Jameson JL, Loriaux DL, Marshall JC, O'Dell WD, Potts JL, Rubenstein AH, eds. *Endocrinology, 3rd Edition*. Philadelphia, PA: WB Saunders.
- Holick MF. 1996. Vitamin D: Photobiology, metabolism, mechanism of action, and clinical application. In: Favus MJ, ed. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 3rd Edition*. Philadelphia, PA: Lippincott-Raven. Pp. 74–81.
- Holick MF, Clark MB. 1978. The photobiogenesis and metabolism of vitamin D. *Fed Proc* 37:2567–2574.
- Holick MF, Schnoes HK, DeLuca HF. 1971. Identification of 1,25-dihydroxycholecalciferol, a form of vitamin D<sub>3</sub> metabolically active in the intestine. *Proc Natl Acad Sci USA* 68:803–804.
- Holick MF, Uskokovic M, Henley JW, MacLaughlin J, Holick SA, Potts JT Jr. 1980. The photoproduction of 1 $\alpha$ , 25-dihydroxyvitamin D<sub>3</sub> in skin: An approach to the therapy of vitamin-D-resistant syndromes. *N Engl J Med* 303:349–354.
- Holick MF, MacLaughlin JA, Doppelt SH. 1981. Regulation of cutaneous previtamin D<sub>3</sub> photosynthesis in man: Skin pigment is not an essential regulator. *Science* 211:590–593.
- Holick MF, Matsuoka LY, Wortsman J. 1989. Age, vitamin D, and solar ultraviolet. *Lancet* 2:1104–1105.
- Holick MF, Shao Q, Liu WW, Chen TC. 1992. The vitamin D content of fortified milk and infant formula. *N Engl J Med* 326:1178–1181.
- Hollifield JW. 1987. Magnesium depletion, diuretics, and arrhythmias. *Am J Med* 82(Suppl 3A):30–37.
- Hollis BW. 1996. Assessment of vitamin D nutritional and hormonal status: What to measure and how to do it. *Calcif Tissue Int* 58:4–5.
- Holmes RP, Kummerow FA. 1983. The relationship of adequate and excessive intake of vitamin D to health and disease. *J Am Coll Nutr* 2:173–199.
- Honkanen R, Alhava E, Parviainen M, Talasniemi S, Monkkonen R. 1990. The necessity and safety of calcium and vitamin D in the elderly. *J Am Geriatr Soc* 38:862–866.
- Hordon LD, Peacock M. 1987. Vitamin D metabolism in women with femoral neck fracture. *Bone Miner* 2:413–426.
- Horowitz HS. 1990. The future of water fluoridation and other systemic fluorides. *J Dent Res* 69(Spec Iss):760–764.

- Horowitz HS. 1996. The effectiveness of community water fluoridation in the United States. *J Pub Hlth Dent* 56:253–258.
- Horowitz HS, Heifetz SB. 1967. Effects of prenatal exposure to fluoridation on dental caries. *Pub Hlth Rep* 82:297–304.
- Horowitz M, Wishart J, Mundy L, Nordin BEC. 1987. Lactose and calcium absorption in postmenopausal osteoporosis. *Arch Intern Med* 147:534–536.
- Hoskova M. 1968. Fluoride tablets in the prevention of tooth decay. *Cesk Pediatr* 23:438–441.
- Howard JE, Hopkins TR, Connor TB. 1953. On certain physiologic responses to intravenous injection of calcium salts into normal, hyperparathyroid and hypoparathyroid persons. *J Clin Endocrinol Metab* 13:1–19.
- Hreshchyshyn MM, Hopkins A, Zylstra S, Anbar M. 1988. Associations of parity, breast-feeding, and birth control pills with lumbar spine and femoral neck bone densities. *Am J Obstet Gynecol* 159:318–322.
- Hua H, Gonzales J, Rude RK. 1995. Magnesium transport induced ex vivo by a pharmacological dose of insulin is impaired in non-insulin-dependent diabetes mellitus. *Magnes Res* 8:359–366.
- Huang Z, Himes JH, McGovern PG. 1996. Nutrition and subsequent hip fracture risk among a national cohort of white women. *Am J Epidemiol* 144:124–134.
- Hunt CD, Nielsen FH. 1981. Interaction between boron and cholecalciferol in the chick. In: McC Howell J, Gathorne JM, White CL, eds. *Trace Element Metabolism in Man and Animals, TEMA-4*. Canberra: Australian Academy of Science. Pp. 597–600.
- Hunt MS, Schofield FA. 1969. Magnesium balance and protein intake level in adult human female. *Am J Clin Nutr* 22:367–373.
- Hwang DL, Yen CF, Nadler JL. 1993. Insulin increases intracellular magnesium transport in human platelets. *J Clin Endocrinol Metab* 76:549–553.
- IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Report of the Subcommittee on Nutritional Status and Weight Gain During Pregnancy, Subcommittee on Dietary Intake and Nutrient Supplements During Pregnancy, Committee on Nutritional Status During Pregnancy and Lactation, Food and Nutrition Board. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1991. *Nutrition During Lactation*. Report of the Subcommittee on Nutrition During Lactation, Committee on Nutritional Status During Pregnancy and Lactation, Food and Nutrition Board. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Food and Nutrition Board. Washington, DC: National Academy Press.
- Ireland P, Fordtran JS. 1973. Effect of dietary calcium and age on jejunal calcium absorption in humans studied by intestinal perfusion. *J Clin Invest* 52:2672–2681.
- Irnell L. 1969. Metastatic calcification of soft tissue on overdose of vitamin D. *Acta Med Scand* 185:147–152.
- Iseri LT, French JH. 1984. Magnesium: Nature's physiologic calcium blocker. *Am Heart J* 108:188–193.
- ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. 1995. ISIS-4: A randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. *Lancet* 345:669–685.

- Ismail AI, Brodeur JM, Kavanagh M, Boisclair G, Tessier C, Picotte L. 1990. Prevalence of dental caries and dental fluorosis in students, 11–17 years of age, in fluoridated and non-fluoridated cities in Quebec. *Caries Res* 24:290–297.
- Jackman LA, Millane SS, Martin BR, Wood OB, McCabe GP, Peacock M, Weaver CM. 1997. Calcium retention in relation to calcium intake and postmenarcheal age in adolescent females. *Am J Clin Nutr* 66:327–333.
- Jackson D, Murray JJ, Fairpo CG. 1973. Life-long benefits of fluoride in drinking water. *Br Dent J* 134:419–422.
- Jacobus CH, Holick MF, Shao Q, Chen TC, Holm IA, Kolodny JM, Fuleihan GE, Seely EW. 1992. Hypervitaminosis D associated with drinking milk. *N Engl J Med* 326:1173–1177.
- Janas LM, Picone TA, Benson JD, MacLean WC. 1988. Influence of dietary calcium to phosphorus and parathormone during the first two weeks of life. *Pediatr Res* 23:485A.
- Janelle KC, Barr SI. 1995. Nutrient intakes and eating behavior scores of vegetarian and nonvegetarian women. *J Am Diet Assoc* 95:180–186.
- Jeans PC. 1950. Vitamin D. *J Am Med Assoc* 143:177–181.
- Jeans PC, Stearns G. 1938. The effect of vitamin D on linear growth in infancy. II. The effect of intakes above 1,800 USP units daily. *J Pediatr* 13:730–740.
- Joffres MR, Reed DM, Yano K. 1987. Relationship of magnesium intake and other dietary factors to blood pressure: The Honolulu heart study. *Am J Clin Nutr* 45:469–475.
- Johansson C, Mellström D, Milsom I. 1993. Reproductive factors as predictors of bone density and fractures in women at the age of 70. *Maturitas* 17:39–50.
- Johnson AO, Semenza JG, Buchowski MS, Enwonwu CO, Scrimshaw NS. 1993a. Correlation of lactose maldigestion, lactose intolerance, and milk intolerance. *Am J Clin Nutr* 57:399–401.
- Johnson AO, Semenza JG, Buchowski MS, Enwonwu CO, Scrimshaw NS. 1993b. Adaptation of lactose maldigesters to continued milk intakes. *Am J Clin Nutr* 58:879–881.
- Johnson CM, Wilson DM, O'Fallon WM, Malek RS, Kurland LT. 1979. Renal stone epidemiology: A 25-year study in Rochester, Minn. *Kidney Int* 16:624–631.
- Johnson J Jr, Bawden JW. 1987. The fluoride content of infant formulas available in 1985. *Pediatr Dent* 9:33–37.
- Johnson KR, Jobber J, Stonawski BJ. 1980. Prophylactic vitamin D in the elderly. *Age Ageing* 9:121–127.
- Johnston CC, Miller JZ, Slemenda CW, Reister TK, Hui S, Christian JC, Peacock M. 1992. Calcium supplementation and increases in bone mineral density in children. *N Engl J Med* 327:82–87.
- Jones JE, Manalo R, Flink EB. 1967. Magnesium requirements in adults. *Am J Clin Nutr* 20:632–635.
- Jowsey J, Balasubramaniam P. 1972. Effect of phosphate supplements on soft tissue calcification and bone turnover. *Clin Sci* 42:289–299.
- Junor JR, Catto GRD. 1976. Renal biopsy in the milk-alkali syndrome. *J Clin Path* 29:1074–1076.
- Kailis DG, Taylor SR, Davis GB, Bartlett LG, Fitzgerald DJ, Grose IJ, Newton PD. 1968. Fluoride and caries: Observations of the effects of prenatal and postnatal fluoride on some Perth pre-school children. *Med J Austral* 2:1037–1040.
- Kalkwarf HJ, Specker BL. 1995. Bone mineral loss during lactation and recovery after weaning. *Obstet Gynecol* 86:26–32.
- Kalkwarf HJ, Specker BL, Heubi JE, Vieira NE, Yerger AL. 1996. Intestinal calcium absorption of women during lactation and after weaning. *Am J Clin Nutr* 63:526–531.

- Kalkwarf HJ, Specker BL, Bianchi DC, Ranz J, Ho M. 1997. The effect of calcium supplementation on bone density during lactation and after weaning. *N Engl J Med* 337:523–528.
- Kallmeyer JC, Funston MR. 1983. The milk-alkali syndrome: A case report. *S Afr Med J* 64:287–288.
- Kamel S, Brazier M, Picard C, Boitte F, Samson L, Desmet G, Sebert JL. 1994. Urinary excretion of pyridinolines crosslinks measured by immunoassay and HPLC techniques in normal subjects and in elderly patients with vitamin D deficiency. *Bone Miner* 26:197–208.
- Kamel S, Brazier M, Rogez JC, Vincent O, Maamer M, Desmet G, Sebert JL. 1996. Different responses of free and peptide-bound cross-links to vitamin D and calcium supplementation in elderly women with vitamin D insufficiency. *J Clin Endocrinol Metab* 81:3717–3721.
- Kaminsky LS, Mahoney MC, Leach J, Melius J, Miller MJ. 1990. Fluoride: Benefits and risks of exposure. *Crit Rev Oral Biol Med* 1:261–281.
- Kanapka JA, Hamilton IR. 1971. Fluoride inhibition of enolase activity in vivo and its relationship to the inhibition of glucose-6-P formation in *Streptococcus salivarius*. *Arch Biochem Biophys* 146:167–174.
- Kanemitsu T, Koike A, Yamamoto S. 1985. Study of the cell proliferation kinetics in ulcerative colitis, adenomatous polyps, and cancer. *Cancer* 56:1094–1098.
- Kanis JA, Melton LJ III, Christiansen C, Johnston CC, Khaltaev N. 1994. The diagnosis of osteoporosis. *J Bone Miner Res* 9:1137–1141.
- Kapsner P, Langsdorf L, Marcus R, Kraemer FB, Hoffman AR. 1986. Milk-alkali syndrome in patients treated with calcium carbonate after cardiac transplantation. *Arch Intern Med* 146:1965–1968.
- Katzman DK, Bachrach LK, Carter DR, Marcus R. 1991. Clinical and anthropometric correlates of bone mineral acquisition in healthy adolescent girls. *J Clin Endocrinol Metab* 73:1332–1339.
- Kayne LH, Lee DB. 1993. Intestinal magnesium absorption. *Miner Electrolyte Metab* 19:210–217.
- Keddie KMG. 1987. Case report: Severe depressive illness in the context of hypervitaminosis D. *Br J Psych* 150:394–396.
- Kellie SE, Brody JA. 1990. Sex-specific and race-specific hip fracture rates. *Am J Pub Hlth* 80:326–328.
- Kelsay JL, Prather ES. 1983. Mineral balances of human subjects consuming spinach in a low-fiber diet and in a diet containing fruits and vegetables. *Am J Clin Nutr* 38:12–19.
- Kelsay JL, Behall KM, Prather ES. 1979. Effect of fiber from fruits and vegetables on metabolic responses of human subjects. II. Calcium, magnesium, iron, and silicon balances. *Am J Clin Nutr* 32:1876–1880.
- Kent GN, Price RI, Gutteridge DH, Smith M, Allen JR, Bhagat CI, Barnes MP, Hickling CJ, Retallack RW, Wilson SG, Devlin RD, Davies C, St. John A. 1990. Human lactation: Forearm trabecular bone loss, increased bone turnover, and renal conservation of calcium and inorganic phosphate with recovery of bone mass following weaning. *J Bone Miner Res* 5:361–369.
- Kent GN, Price RI, Gutteridge DH, Rosman KJ, Smith M, Allen JR, Hickling CJ, Blakeman SL. 1991. The efficiency of intestinal calcium absorption is increased in late pregnancy but not in established lactation. *Calcif Tissue Int* 48:293–295.
- Kesteloot H, Joossens JV. 1990. The relationship between dietary intake and urinary excretion of sodium, potassium, calcium and magnesium: Belgian Inter-university Research on Nutrition and Health. *J Hum Hypertension* 4:527–533.

- Kiel DP, Felson DT, Hannan MT, Anderson JJ, Wilson PW. 1990. Caffeine and the risk of hip fracture: The Framingham Study. *Am J Epidemiol* 132:675–684.
- Kinyamu HK, Gallagher JC, Balhorn KE, Petranick KM, Rafferty KA. 1997. Serum vitamin D metabolites and calcium absorption in normal young and elderly free-living women and in women living in nursing homes. *Am J Clin Nutr* 65:790–797.
- Klaassen CD, Amdur MO, Doull J. 1986. *Casarett and Doull's Toxicology: The Basic Science of Poisons, Third Edition*. New York: Macmillan Publishing Company.
- Kleerekoper M, Mendlovic DB. 1993. Sodium fluoride therapy of postmenopausal osteoporosis. *Endocrinol Rev* 14:312–323.
- Kleibeuker JH, Welberg JW, Mulder NH, van der Meer R, Cats A, Limburg AJ, Kreumer WM, Hardonk MJ, de Vries EG. 1993. Epithelial cell proliferation in the sigmoid colon of patients with adenomatous polyps increases during oral calcium supplementation. *Br J Cancer* 67:500–503.
- Klein CJ, Moser-Veillon PB, Douglass LW, Ruben KA, Trocki O. 1995. A longitudinal study of urinary calcium, magnesium, and zinc excretion in lactating and nonlactating postpartum women. *Am J Clin Nutr* 61:779–786.
- Kleiner SM, Bazzarre TL, Ainsworth BE. 1994. Nutritional status of nationally ranked elite bodybuilders. *Int J Sport Nutr* 4:54–69.
- Kleinman GE, Rodriguez H, Good MC, Caudle MR. 1991. Hypercalcemic crisis in pregnancy associated with excessive ingestion of calcium carbonate antacid (milk-alkali syndrome): Successful treatment with hemodialysis. *Obstet Gynecol* 73:496–499.
- Knochel JP. 1977. The pathophysiology and clinical characteristics of severe hypophosphatemia. *Arch Intern Med* 137:203–220.
- Knochel JP. 1985. The clinical status of hypophosphatemia: An update. *N Engl J Med* 313:447–449.
- Kobayashi A, Kawai S, Ohbe Y, Nagashima Y. 1975. Effects of dietary lactose and a lactase preparation on the intestinal absorption of calcium and magnesium in normal infants. *Am J Clin Nutr* 28:681–683.
- Kochersberger G, Westlund R, Lyles KW. 1991. The metabolic effects of calcium supplementation in the elderly. *J Am Geriatr Soc* 39:192–196.
- Koetting CA, Wardlaw GM. 1988. Wrist, spine, and hip bone density in women with variable histories of lactation. *Am J Clin Nutr* 48:1479–1481.
- Kohlmeier L, Mendez M, McDuffie J, Miller M. 1997. Computer-assisted self-interviewing: A multimedia approach to dietary assessment. *Am J Clin Nutr* 65:1275S–1281S.
- Koo W, Tsang R. 1997. Calcium, magnesium, phosphorus and vitamin D. In: *Nutrition During Infancy, 2nd Edition*. Cincinnati: Digital Education. Pp. 175–189.
- Koo W, Krug-Wispe S, Neylen M, Succop P, Oestreich AE, Tsang RC. 1995. Effect of three levels of vitamin D intake in preterm infants receiving high mineral-containing milk. *J Pediatr Gastroenterol Nutr* 21:182–189.
- Krall EA, Sahyoun N, Tannenbaum S, Dallal GE, Dawson-Hughes B. 1989. Effect of vitamin D intake on seasonal variations in parathyroid hormone secretion in postmenopausal women. *N Engl J Med* 321:1777–1783.
- Kramer L, Osis D, Wiatrowski E, Spenser H. 1974. Dietary fluoride in different areas of the United States. *Am J Clin Nutr* 27:590–594.
- Kreiger N, Kelsey JL, Holford TR, O'Connor T. 1982. An epidemiologic study of hip fracture in postmenopausal women. *Am J Epidemiol* 116:141–148.

- Krejs GJ, Nicar MJ, Zerwekh HE, Normal DA, Kane MG, Pak CY. 1983. Effect of 1,25-dihydroxyvitamin D<sub>3</sub> on calcium and magnesium absorption in the healthy human jejunum and ileum. *Am J Med* 75:973–976.
- Krishnamachari KA. 1986. Skeletal fluorosis in humans: A review of recent progress in the understanding of the disease. *Prog Food Nutr Sci* 10:279–314.
- Krook L, Whalen JP, Lesser GV, Berens DL. 1975. Experimental studies on osteoporosis. *Methods Achiev Exp Pathol* 7:72–108.
- Kröger H, Kotaniemi A, Vainio P, Alhava E. 1992. Bone densitometry of the spine and femur in children by dual-energy x-ray absorptiometry. *Bone Miner* 17:75–85.
- Kröger H, Kotaniemi A, Kröger L, Alhava E. 1993. Development of bone mass and bone density of the spine and femoral neck—a prospective study of 65 children and adolescents. *Bone Miner* 23:171–182.
- Kröger H, Alhava E, Honkanen R, Tuppurainen M, Saarikoski S. 1994. The effect of fluoridated drinking water on axial bone mineral density: A population-based study. *Bone Miner* 27:33–41.
- Kruse K, Bartels H, Kracht U. 1984. Parathyroid function in different stages of vitamin D deficiency rickets. *Eur J Pediatr* 141:158–162.
- Kumar JV, Green EL, Wallace W, Carnahan T. 1989. Trends in dental fluorosis and dental caries prevalences in Newburgh and Kingston, NY. *Am J Pub Hlth* 79:565–569.
- Kumar R. 1986. The metabolism and mechanism of action of 1,25-dihydroxyvitamin D<sub>3</sub>. *Kidney Int* 30:793–803.
- Kumar R, Cohen WR, Silva P, Epstein FH. 1979. Elevated 1,25-dihydroxyvitamin D plasma levels in normal human pregnancy and lactation. *J Clin Invest* 63:342–344.
- Kummerow FA, Simon Cho BH, Huang YT, Imai H, Kamio A, Deutsch MJ, Hooper WM. 1976. Additive risk factors in atherosclerosis. *Am J Clin Nutr* 29:579–584.
- Kurtz TW, Al-Bander HA, Morris RC. 1987. “Salt sensitive” essential hypertension in men. *N Engl J Med* 317:1043–1048.
- Kurzel RB. 1991. Serum magnesium levels in pregnancy and preterm labor. *Am J Perinatol* 8:119–127.
- Kuti V, Balazs M, Morvay F, Varenka Z, Szekely A, Szucs M. 1981. Effect of maternal magnesium supply on spontaneous abortion and premature birth and on intrauterine fetal development: Experimental epidemiological study. *Magnes Bull* 3:73–79.
- Ladizesky M, Lu Z, Oliveri B, San Roman N, Diaz S, Holick MF, Mautalen C. 1995. Solar ultraviolet B radiation and photoproduction of vitamin D<sub>3</sub> in central and southern areas of Argentina. *J Bone Miner Res* 10:545–549.
- Lafferty FW. 1991. Differential diagnosis of hypercalcemia. *J Bone Miner Res* 6:S51–S59.
- Lakshmanan LF, Rao RB, Kim WW, Kelsay JL. 1984. Magnesium intakes, balances, and blood levels of adults consuming self-selected diets. *Am J Clin Nutr* 40:1380–1389.
- Lamberg-Allardt C, von Knorring J, Slatis P, Holmstrom T. 1989. Vitamin D status and concentrations of serum vitamin D metabolites and osteocalcin in elderly patients with femoral neck fracture: A follow-up study. *Eur J Clin Nutr* 43:355–361.
- Lamberg-Allardt C, Karkkainen M, Seppanen R, Bistrom H. 1993. Low serum 25-hydroxyvitamin D concentrations and secondary hyperparathyroidism in middle-aged white strict vegetarians. *Am J Clin Nutr* 58:684–689.
- Largent EJ. 1952. Rates of elimination of fluoride stored in the tissues of man. *Arch Ind Hyg* 6:37–42.

- Larsen MJ, Senderovitz F, Kirkegaard E, Poulsen S, Fejerskov O. 1988. Dental fluorosis in the primary and permanent dentition in fluoridated areas with consumption of either powdered milk or natural cow's milk. *J Dent Res* 67:822–825.
- Lawson DE, Fraser DR, Kodicek E, Morris HR, Williams DH. 1971. Identification of 1,25-dihydroxycholecalciferol, a new kidney hormone controlling calcium metabolism. *Nature* 230:228–230.
- Lealman GT, Logan RW, Hutchison JH, Kerr MM, Fulton AM, Brown CA. 1976. Calcium, phosphorus, and magnesium concentrations in plasma during first week of life and their relation to type of milk feed. *Arch Dis Child* 51:377–384.
- LeBlanc A, Schneider V, Spector E, Evans H, Rowe R, Lane H, Demers L, Lipton A. 1995. Calcium absorption, endogenous excretion, and endocrine changes during and after long-term bed rest. *Bone* 16:301S–304S.
- Lebrun JB, Moffatt ME, Mundy RJ, Sangster RK, Postl BD, Dooley JP, Dilling LA, Godel JC, Haworth JC. 1993. Vitamin D deficiency in a Manitoba community. *Can J Pub Hlth* 84:394–396.
- Lee WT, Leung SS, Wang SH, Xu YC, Zeng WP, Lau J, Oppenheimer SJ, Cheng JC. 1994. Double-blind, controlled calcium supplementation and bone mineral accretion in children accustomed to a low-calcium diet. *Am J Clin Nutr* 60:744–750.
- Lee WT, Leung SS, Leung DM, Tsang HS, Lau J, Cheng JC. 1995. A randomized double-blind controlled calcium supplementation trial, and bone and height acquisition in children. *Br J Nutr* 74:125–139.
- Lee WT, Leung SS, Leung DM, Cheng JC. 1996. A follow-up study on the effects of calcium-supplement withdrawal and puberty on bone acquisition of children. *Am J Clin Nutr* 64:71–77.
- LeGeros RZ, Glenn FB, Lee DD, Glenn WD. 1985. Some physico-chemical properties of deciduous enamel with and without pre-natal fluoride supplementation (PNF). *J Dent Res* 64:465–469.
- Lehner NDM, Bullock BC, Clarkson TB, Lofland HB. 1967. Biologic activities of vitamin D<sub>2</sub> and D<sub>3</sub> for growing squirrel monkeys. *Lab Anim Care* 17:483.
- Leitch I, Aitken FC. 1959. The estimation of calcium requirement: A re-examination. *Nutr Abs Rev* 29:393–409.
- Lemann J Jr. 1996. Calcium and phosphate metabolism: An overview in health and in calcium stone formers. In: Coe FL, Favus MJ, Pak CY, Parks JH, Preminger GM, eds. *Kidney Stones: Medical and Surgical Management*. Philadelphia, PA: Lippincott-Raven. Pp. 259–288.
- Lemann J Jr, Worcester EM, Gray RW. 1991. Hypercalciuria and stones. *Am J Kidney Dis* 17:386–391.
- Lemke CW, Doherty JM, Arra MC. 1970. Controlled fluoridation: The dental effects of discontinuation in Antigo, Wisconsin. *J Am Dent Assoc* 80:782–786.
- Leone NC, Shimkin MB, Arnold FA, Stevenson CA, Zimmerman ER, Geiser PB, Lieberman JE. 1954. Medical aspects of excessive fluoride in a water supply. *Pub Hlth Rep* 69:925–936.
- Leone NC, Stevenson CA, Hilbush TF, Sosman MC. 1955. A roentgenologic study of a human population exposed to high-fluoride domestic water: A ten-year study. *Am J Roentg* 74:874–885.
- Leone NC, Stevenson CA, Besse B, Hawes, LE, Dawber TA. 1960. The effects of the absorption of fluoride. II. A radiological investigation of 546 human residents of an area in which the drinking water contained only a minute trace of fluoride. *Archs Ind Hlth* 21:326–327.

- Leoni V, Fabiani L, Ticchiarelli L. 1985. Water hardness and cardiovascular mortality rate in Abruzzo, Italy. *Arch Environ Health* 40:274–278.
- Leung SSF, Lui S, Swaminathan R. 1989. Vitamin D status of Hong Kong Chinese infants. *Acta Paediatr Scand* 78:303–306.
- Leverett DH. 1986. Prevalence of dental fluorosis in fluoridated and nonfluoridated communities—a preliminary investigation. *J Pub Hlth Dent* 46:184–187.
- Leverett DH, Adair SM, Vaughan BW, Proskin HM, Moss ME. 1997. Randomized clinical trial of the effect of prenatal fluoride supplements in preventing dental caries. *Caries Res* 31:174–179.
- Levine RJ, Hauth JC, Curet LB, Sibai BM, Catalano PM, Morris CD, DerSimonian R, Esterlitz JR, Raymond EG, Bild DE, Clemens JD, Cutler JA. 1997. Trial of calcium to prevent preeclampsia. *N Engl J Med* 337:69–76.
- Levy SM, Muchow G. 1992. Provider compliance with recommended dietary fluoride supplement protocol. *Am J Pub Hlth* 82:281–283.
- Levy SM, Kohout FJ, Kiritsy MC, Heilman JR, Wefel JS. 1995. Infants' fluoride ingestion from water, supplements and dentifrice. *J Am Dent Assoc* 126:1625–1632.
- Lewis DW. 1976. *An Evaluation of the Effects of Water Fluoridation, City of Toronto, 1963–1975*. Toronto, Canada: The Corporation of the City of Toronto.
- Lewis NM, Marcus MSK, Behling AR, Greger JL. 1989. Calcium supplements and milk: Effects on acid-base balance and on retention of calcium, magnesium, and phosphorus. *Am J Clin Nutr* 49:527–533.
- Liel Y, Edwards J, Shary J, Spicer KM, Gordon L, Bell NH. 1988. The effects of race and body habitus on bone mineral density of the radius, hip, and spine in premenopausal women. *J Clin Endocrinol Metab* 66:1247–1250.
- Lin S-H, Lin Y-F, Shieh S-D. 1996. Milk-alkali syndrome in an aged patient with osteoporosis and fractures. *Nephron* 73:496–497.
- Linden V. 1974. Vitamin D and myocardial infarction. *Br Med J* 3:647–650.
- Linkswiler HM, Zemel MB, Hegsted M, Schuette S. 1981. Protein-induced hypercalciuria. *Fed Proc* 40:2429–2433.
- Lips P, Wiersinga A, vanGinkel FC, Jongen MJ, Netelenbos JC, Hackeng WH, Delmas PD, vanderVijgh WJ. 1988. The effect of vitamin D supplementation on vitamin D status and parathyroid function in elderly subjects. *J Clin Endocrinol Metab* 67:644–650.
- Lips P, Graafmans WC, Ooms ME, Bezemer D, Bouter LM. 1996. Vitamin D supplementation and fracture incidence in elderly persons: A randomized, placebo-controlled clinical trial. *Ann Intern Med* 124:400–406.
- Lipski PS, Torrance A, Kelly PJ, James OF. 1993. A study of nutritional deficits of long-stay geriatric patients. *Age Aging* 22:244–255.
- Lissner L, Bengtsson C, Hansson T. 1991. Bone mineral content in relation to lactation history in pre- and postmenopausal women. *Calcif Tissue Int* 48:319–325.
- Livingstone MB, Prentice AM, Coward WA, Strain JJ, Black AE, Davies PS, Stewart CM, McKenna PG, Whitehead RG. 1992. Validation estimates of energy intake by weighted dietary record and diet history in children and adolescents. *Am J Clin Nutr* 56:29–35.
- Lloyd T, Schaeffer JM, Walker MA, Demers LM. 1991. Urinary hormonal concentrations and spinal bone densities of premenopausal vegetarian and nonvegetarian women. *Am J Clin Nutr* 54:1005–1010.

- Lloyd T, Andon MB, Rollings N, Martel JK, Landis R, Demers LM, Eggli DF, Kieselhorst K, Kulin HE. 1993. Calcium supplementation and bone mineral density in adolescent girls. *J Am Med Assoc* 270:841–844.
- Lo CW, Paris PW, Clemens TL, Nolan J, Holick MF. 1985. Vitamin D absorption in healthy subjects and in patients with intestinal malabsorption syndromes. *Am J Clin Nutr* 42:644–649.
- Lonnerdal B. 1997. Effects of milk and milk components on calcium, magnesium, and trace element absorption during infancy. *Physiol Rev* 77:643–669.
- Looker AC, Harris TB, Madans JH, Sempers CT. 1993. Dietary calcium and hip fracture risk: The NHANES I Epidemiology Follow-Up Study. *Osteopor Int* 3:177–184.
- Looker AC, Johnston CC Jr, Wahner HW, Dunn WL, Calvo MS, Harris TB, Heyse SP, Lindsay RL. 1995. Prevalence of low femoral bone density in older US women from NHANES III. *J Bone Miner Res* 10:796–802.
- Lopez JM, Gonzalez G, Reyes V, Campino C, Diaz S. 1996. Bone turnover and density in healthy women during breastfeeding and after weaning. *Osteopor Int* 6:153–159.
- Lotz M, Zisman E, Bartter FC. 1968. Evidence for a phosphorus-depletion syndrome in man. *N Engl J Med* 278:409–415.
- Lowenstein FW, Stanton MF. 1986. Serum magnesium levels in the United States, 1971–1974. *J Am Coll Nutr* 5:399–414.
- Lowik MR, van Dokkum W, Kistemaker C, Schaafsma G, Ockhuizen T. 1993. Body composition, health status and urinary magnesium excretion among elderly people (Dutch Nutrition Surveillance System). *Magnes Res* 6:223–232.
- LSRO/FASEB (Life Sciences Research Office/Federation of American Societies for Experimental Biology). 1986. *Guidelines for Use of Dietary Intake Data*. Anderson SA, ed. Bethesda, MD: LSRO/FASEB.
- Lu PW, Briody JN, Ogle GD, Morley K, Humphries IR, Allen J, Howman-Giles R, Sillence D, Cowell CT. 1994. Bone mineral density of total body, spine, and femoral neck in children and young adults: A cross-sectional and longitudinal study. *J Bone Miner Res* 9:1451–1458.
- Luckey MM, Meier DE, Mandeli JP, DaCosta MC, Hubbard ML, Goldsmith SJ. 1989. Radial and vertebral bone density in white and black women: Evidence for racial differences in premenopausal bone homeostasis. *J Clin Endocrinol Metab* 69:762–770.
- Lukert BP, Raisz LG. 1990. Glucocorticoid-induced osteoporosis: Pathogenesis and management. *Ann Intern Med* 112:352–364.
- Lund B, Sorensen OH. 1979. Measurement of 25-hydroxyvitamin D in serum and its relation to sunshine, age and vitamin D intake in the Danish population. *Scand J Clin Lab Invest* 39:23–30.
- Luoma H, Aromaa A, Helminen S, Murtomaa H, Kiviluoto L, Punstar S, Knekt P. 1983. Risk of myocardial infarction in Finnish men in relation to fluoride, magnesium and calcium concentration in drinking water. *Acta Med Scand* 213:171–176.
- Lutwak L, Lester L, Gitelman HJ, Fox M, Whedon GD. 1964. Effects of high dietary calcium and phosphorus on calcium, phosphorus, nitrogen and fat metabolism in children. *Am J Clin Nutr* 14:76–82.

- Ma J, Folsom AR, Melnick SL, Eckfeldt JH, Sharrett AR, Nabulsi AA, Hutchinson RG, Metcalf PA. 1995. Associations of serum and dietary magnesium with cardiovascular disease, hypertension, diabetes, insulin, and carotid arterial wall thickness: The ARIC study. *Atherosclerosis Risk in Community Study. J Clin Epidemiol* 48:927–940.
- MacLaughlin J, Holick MF. 1985. Aging decreases the capacity of human skin to produce vitamin D<sub>3</sub>. *J Clin Invest* 76:1536–1538.
- MacLaughlin JA, Anderson RR, Holick MF. 1982. Spectral character of sunlight modulates photosynthesis of previtamin D<sub>3</sub> and its photoisomers in human skin. *Science* 216:1001–1003.
- Maguire ME. 1984. Hormone-sensitive magnesium transport and magnesium regulation of adenylate cyclase. *Trends Pharmacol Sci* 5:73–77.
- Mahalko JR, Sandstead HH, Johnson LK, Milne DB. 1983. Effect of a moderate increase in dietary protein on the retention and excretion of Ca, Cu, Fe, Mg, P, and Zn by adult males. *Am J Clin Nutr* 37:8–14.
- Maheshwari UR, McDonald JT, Schneider VS, Brunetti AJ, Leybin L, Newbrun E, Hodge HC. 1981. Fluoride balance studies in ambulatory healthy men with and without fluoride supplements. *Am J Clin Nutr* 34:2679–2684.
- Maheshwari UR, King JC, Leybin L, Newbrun E, Hodge HC. 1983. Fluoride balances during early and late pregnancy. *J Occup Med* 25:587–590.
- Mallet E, Gugi B, Brunelle P, Henocq A, Basuyau JP, Lemeur H. 1986. Vitamin D supplementation in pregnancy: A controlled trial of two methods. *Obstet Gynecol* 68:300–304.
- Malm OJ. 1958. Calcium requirement and adaptation in adult men. *Scand J Clin Lab Invest* 10(Suppl 36):1–280.
- Malone DNS, Horn DB. 1971. Acute hypercalcemia and renal failure after antacid therapy. *Br Med J* 1:709–710.
- Manz F. 1992. Why is the phosphorus content of human milk exceptionally low? *Monatsschr Kinderheilkd* 140:S35–S39.
- Marcus R, Cann C, Madvig P, Minkoff J, Goddard M, Bayer M, Martin M, Gaudiani L, Haskell W, Genant H. 1985. Menstrual function and bone mass in elite women distance runners. Endocrine and metabolic features. *Ann Intern Med* 102:158–163.
- Margen S, Chu JY, Kaufmann NA, Calloway DH. 1974. Studies in calcium metabolism I. The calciuretic effect of dietary protein. *Am J Clin Nutr* 27:584–589.
- Margolis HC, Moreno EC. 1990. Physicochemical perspectives on the cariostatic mechanisms of systemic and topical fluorides. *J Dent Res* 69(Spec Iss):606–613.
- Marier JR. 1986. Magnesium content of the food supply in the modern-day world. *Magnesium* 5:1–8.
- Marken PA, Weart CW, Carson DS, Gums JG, Lopes-Virella MF. 1989. Effects of magnesium oxide on the lipid profile of healthy volunteers. *Atherosclerosis* 77:37–42.
- Markestad T, Elzouki AY. 1991. Vitamin-D deficiency rickets in northern Europe and Libya. In: Glorieux FH, ed. *Rickets: Nestle Nutrition Workshop Series, Vol 21*. New York, NY: Raven Press.
- Markestad T, Ulstein M, Bassoe HH, Aksnes L, Aarskog D. 1983. Vitamin D metabolism in normal and hypoparathyroid pregnancy and lactation. Case report. *Br J Obstet Gynaecol* 90:971–976.
- Markestad T, Ulstein M, Aksnes L, Aarskog D. 1986. Serum concentrations of vitamin D metabolites in vitamin D supplemented pregnant women. A longitudinal study. *Acta Obstet Gynecol Scand* 65:63–67.

- Marquis RE. 1995. Antimicrobial actions of fluoride for oral bacteria. *Can J Microbiol* 41:955–964.
- Marsh AG, Sanchez TV, Midkelsen O, Keiser J, Mayor G. 1980. Cortical bone density of adult lacto-ovo-vegetarian and omnivorous women. *J Am Diet Assoc* 76:148–151.
- Marshall DH, Nordin BEC, Speed R. 1976. Calcium, phosphorus and magnesium requirement. *Proc Nutr Soc* 35:163–173.
- Martin AD, Bailey DA, McKay HA. 1997. Bone mineral and calcium accretion during puberty. *Am J Clin Nutr* 66:611–615.
- Martin BJ. 1990. The magnesium load test: Experience in elderly subjects. *Aging (Milano)* 2:291–296.
- Martin TJ, Grill V. 1995. Hypercalcemia. *Clin Endocrinol* 42:535–538.
- Martinez ME, Salinas M, Miguel JL, Herrero E, Gomez P, Garcia J, Sanchez-Sicilia L, Montero A. 1985. Magnesium excretion in idiopathic hypercalciuria. *Nephron* 40: 446–450.
- Massey LK, Wise KJ. 1984. The effect of dietary caffeine on urinary excretion of calcium, magnesium, sodium and potassium in healthy young females. *Nutr Res* 4:43–50.
- Massey LK, Roman-Smith H, Sutton RA. 1993. Effect of dietary oxalate and calcium on urinary oxalate and risk of formation of calcium oxalate kidney stones. *J Am Diet Assoc* 93:901–906.
- Matkovic V. 1991. Calcium metabolism and calcium requirements during skeletal modeling and consolidation of bone mass. *Am J Clin Nutr* 54:245S–260S.
- Matkovic V, Heaney RP. 1992. Calcium balance during human growth: Evidence for threshold behavior. *Am J Clin Nutr* 55:992–996.
- Matkovic V, Fontana D, Tominac C, Goel P, Chesnut CH III. 1990. Factors that influence peak bone mass formation: A study of calcium balance and the inheritance of bone mass in adolescent females. *Am J Clin Nutr* 52:878–888.
- Matkovic V, Jelic T, Wardlaw GM, Illich JZ, Goel PK, Wright JK, Andon MB, Smith KT, Heaney RP. 1994. Timing of peak bone mass in Caucasian females and its implication for the prevention of osteoporosis. *J Clin Invest* 93:799–808.
- Matkovic V, Illich JZ, Andon MB, Hsieh LC, Tzagournis MA, Lagger BJ, Goel PK. 1995. Urinary calcium, sodium, and bone mass of young females. *Am J Clin Nutr* 62:417–425.
- Matsuda H. 1991. Magnesium gating of the inwardly rectifying K<sup>+</sup> channel. *Ann Rev Physiol* 53:289–298.
- Matsuoka LY, Ide L, Wortsman J, MacLaughlin JA, Holick MF. 1987. Sunscreens suppress cutaneous vitamin D<sub>3</sub> synthesis. *J Clin Endocrinol Metab* 64:1165–1168.
- Matsuoka LY, Wortsman J, Dannenberg MJ, Hollis BW, Lu Z, Holick MF. 1992. Clothing prevents ultraviolet-B radiation-dependent photosynthesis of vitamin D<sub>3</sub>. *J Clin Endocrinol Metab* 75:1099–1103.
- Mawer EB, Schaefer K, Lumb GA, Stanbury SW. 1971. The metabolism of isotopically labelled vitamin D<sub>3</sub> in man: The influence of the state of vitamin D nutrition. *Clin Sci* 40:39–53.
- Mawer EB, Backhouse J, Holman CA, Lumb GA, Stanbury DW. 1972. The distribution and storage of vitamin D and its metabolites in human tissues. *Clin Sci* 43:413–431.
- Mazariegos-Ramos E, Guerrero-Romero F, Rodriguez-Moran M, Lazcano-Burciaga G, Paniagua R, Amato D. 1995. Consumption of soft drinks with phosphoric acid as a risk factor for the development of hypocalcemia in children: A case-control study. *J Pediatr* 126:940–942.

- McCarron DA. 1983. Calcium and magnesium nutrition in human hypertension. *Ann Int Med* 98:800–805.
- McCarron DA, Morris CD. 1985. Blood pressure response to oral calcium in persons with mild to moderate hypertension: A randomized, double-blind, placebo-controlled, crossover trial. *Ann Intern Med* 103:825–831.
- McCarron DA, Morris CD, Young E, Roullet C, Drüeke T. 1991. Dietary calcium and blood pressure: Modifying factors in specific populations. *Am J Clin Nutr* 54:215S–219S.
- McCauley HB, McClure FJ. 1954. Effect of fluoride in drinking water on the osseous development of the hand and wrist in children. *Pub Hlth Rep* 69:671–683.
- McClure FJ. 1943. Ingestion of fluoride and dental caries. Quantitative relations based on food and water requirements of children one to twelve years old. *Am J Dis Child* 66:362–369.
- McClure FJ, Zipkin I. 1958. Physiologic effects of fluoride as related to water fluoridation. *Dent Clin North Am* 2:441–458.
- McCrory WW, Forman CW, McNamara H, Barnett HL. 1950. Renal excretion of phosphate in newborn infants: Observations in normal infants and in infants with hypocalcemic tetany. *Am J Dis Child* 80:512–513.
- McFarlane D. 1941. Experimental phosphate nephritis in the rat. *J Pathol* 52:17–24.
- McGrath N, Singh V, Cundy T. 1993. Severe vitamin D deficiency in Auckland. *N Zel Med J* 106:524–526.
- McKenna MJ. 1992. Differences in vitamin D status between countries in young adults and the elderly. *Am J Med* 93:69–77.
- McKnight-Hanes MC, Leverett DH, Adair SM, Shields CP. 1988. Fluoride content of infant formulas: Soy-based formulas as a potential factor in dental fluorosis. *Pediatr Dent* 10:189–194.
- Meier DE, Luckey MM, Wallenstein S, Clemens TL, Orwoll ES, Waslien CI. 1991. Calcium, vitamin D, and parathyroid hormone status in young white and black women: Association with racial differences in bone mass. *J Clin Endocrinol Metab* 72:703–710.
- Melton LJ III, Chrischilles EA, Cooper C, Lane AW, Riggs, BL. 1992. Perspective. How many women have osteoporosis? *J Bone Miner Res* 7:1005–1010.
- Melton LJ III, Atkinson EJ, O'Fallon WM, Wahner HW, Riggs BL. 1993a. Long-term fracture prediction by bone mineral assessed at different skeletal sites. *J Bone Miner Res* 8:1227–1233.
- Melton LJ III, Bryant SC, Wahner HW, O'Fallon WM, Malkasian GD, Judd HL, Riggs BL. 1993b. Influence of breastfeeding and other reproductive factors on bone mass later in life. *Osteopor Int* 3:76–83.
- Merke J, Klaus G, Hugel U, Waldherr R, Ritz E. 1986. No 1,25-dihydroxyvitamin D<sub>3</sub> receptors on osteoclasts of calcium-deficient chicken despite demonstrable receptors on circulating monocytes. *J Clin Invest* 77:312–314.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- Mertz W, Abernathy CO, Olin SS. 1994. *Risk Assessment of Essential Elements*. Washington, DC: ILSI Press.
- Meulmeester JF, vandenBerg H, Wedel M, Boshuis PG, Hulshof KF, Luyken R. 1990. Vitamin D status, parathyroid hormone and sunlight in Turkish, Moroccan and Caucasian children in The Netherlands. *Eur J Clin Nutr* 44:461–470.

- Meyer F, White E. 1993. Alcohol and nutrients in relation to colon cancer in middle-aged adults. *Am J Epidemiol* 138:225–236.
- Miller JZ, Smith DL, Flora L, Slemenda C, Jiang X, Johnston CC Jr. 1988. Calcium absorption from calcium carbonate and a new form of calcium (CCM) in healthy male and female adolescents. *Am J Clin Nutr* 48:1291–1294.
- Mimouni FB. 1996. The ion-selective magnesium electrode: A new tool for clinicians and investigators. *J Am Coll Nutr* 15:4–5.
- Mimouni F, Tsang RC, Hertzberg VS, Miodovnik M. 1986. Polycythemia hypomagnesemia and hypocalcemia infants of diabetic mothers. *Am J Dis Child* 140:798–800.
- Mimouni F, Campaigne B, Neylan M, Tsang RC. 1993. Bone mineralization in the first year of life in infants fed human milk, cow-milk formula, or soy-based formula. *J Pediatr* 122:348–354.
- Moncrief MW, Chance GW. 1969. Nephrotoxic effect of vitamin D therapy in vitamin D refractory rickets. *Arch Dis Child* 44:571–579.
- Montaldo MB, Benson JD. 1986. Nutrient intakes of older infants: Effect of different milk feedings. *J Am Coll Nutr* 5:331–341.
- Mordes JP, Wacker WEC. 1978. Excessive magnesium. *Pharmacol Rev* 29:273–300.
- Moser PB, Issa CF, Reynolds RD. 1983. Dietary magnesium intake and the concentration of magnesium in plasma and erythrocytes of postpartum women. *J Am Coll Nutr* 2:387–396.
- Moser PB, Reynolds RD, Acharya S, Howard MP, Andon MB. 1988. Calcium and magnesium dietary intakes and plasma and milk concentrations of Nepalese lactating women. *Am J Clin Nutr* 47:735–739.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance data from vital and health statistics, No. 174. Hyattsville, MD: National Center for Health Statistics.
- Motoyama T, Sano H, Fukuzaki H. 1989. Oral magnesium supplementation in patients with essential hypertension. *Hypertension* 13:227–232.
- Mountokalakis TD. 1987. Effects of aging, chronic disease, and multiple supplements on magnesium requirements. *Magnesium* 6:5–11.
- Moya M, Cortes E, Ballester MI, Vento M, Juste M. 1992. Short-term polycose substitution for lactose reduces calcium absorption in healthy term babies. *J Pediatr Gastroenterol Nutr* 14:57–61.
- Muhler JC. 1970. Ingestion from foods. In: Adler P, ed. *Fluorides and Human Health*. Monograph series no. 59. Geneva: World Health Organization. Pp. 32–40.
- Muldowney WP, Mazbar SA. 1996. Rolaids-yogurt syndrome: A 1990s version of milk-alkali syndrome. *Am J Kidney Dis* 27:270–272.
- Murphy SP, Calloway DH. 1986. Nutrient intakes of women in NHANES II, emphasizing trace minerals, fiber, and phytate. *J Am Diet Assoc* 86:1366–1372.
- Naccache H, Simard PL, Trahan L, Demers M, Lapointe C, Brodeur JM. 1990. Variability in the ingestion of toothpaste by preschool children. *Caries Res* 24:359–363.
- Naccache H, Simard PL, Trahan L, Brodeur JM, Demers M, Lachapelle D, Bernard PM. 1992. Factors affecting the ingestion of fluoride dentifrice by children. *J Pub Hlth Dent* 52:222–226.
- Nadler JL, Malayan S, Luong H, Shaw S, Natarajan RD, Rude RK. 1992. Intracellular free magnesium deficiency plays a key role in increased platelet reactivity in type II diabetes mellitus. *Diabetes Care* 15:835–841.

- Nadler JL, Buchanan T, Natarajan R, Antonipillai I, Bergman R, Rude RK. 1993. Magnesium deficiency produces insulin resistance and increased thromboxane synthesis. *Hypertension* 21:1024–1029.
- Nagubandi S, Kumar R, Londowski JM, Corradino RA, Tietz PS. 1980. Role of vitamin D glucosiduronate in calcium homeostasis. *J Clin Invest* 66:1274–1280.
- Nagy L, Tarnok F, Past T, Mozsik GY, Deak G, Tapsonyi Z, Fendler K, Javor T. 1988. Human tolerability and pharmacodynamic study of TISACID tablet in duodenal ulcer patients. A prospective, randomized, self-controlled clinico-pharmacological study. *Acta Medica Hung* 45:231–246.
- Nakamura T, Turner CH, Yoshikawa T, Slemenda CW, Peacock M, Burr DB, Mizuno Y, Orimo H, Ouchi Y, Johnston CC Jr. 1994. Do variations in hip geometry explain differences in hip fracture risk between Japanese and white Americans? *J Bone Miner Res* 9:1071–1076.
- Nakao H. 1988. Nutritional significance of human milk vitamin D in neonatal period. *Kobe J Med Sci* 34:121–128.
- Narang NK, Gupta RC, Jain MK. 1984. Role of vitamin D in pulmonary tuberculosis. *J Assoc Physicians India* 32:185–188.
- National Council for Nutrition (Conseil National de la Nutrition). 1994. *Recommendations nutritionnelles pour la Belgique*. Bruxelles, Belgium: Ministère des Affaires Sociales de la Santé Publique et de l’Environnement.
- National Food Administration. 1989. *Swedish Nutrition Recommendations, 2nd edition*. Uppsala, Sweden: National Food Administration.
- Need AG, Morris HA, Horowitz M, Nordin C. 1993. Effects of skin thickness, age, body fat, and sunlight on serum 25-hydroxyvitamin D. *Am J Clin Nutr* 58:882–885.
- Neri LC, Johansen HL. 1978. Water hardness and cardiovascular mortality. *Ann NY Acad Sci* 304:203–219.
- Neri LC, Johansen HL, Hewitt D, Marier J, Langner N. 1985. Magnesium and certain other elements and cardiovascular disease. *Sci Total Environ* 42:49–75.
- Netherlands Food and Nutrition Council. 1992. *Report on the Age Limit to be Adopted in Connection with “Guidelines for a Healthy Diet.”* The Hague: Netherlands Food and Nutrition Council.
- Neville MC, Keller R, Seacat J, Lutes V, Neifert M, Casey C, Allen J, Archer P. 1988. Studies in human lactation: Milk volumes in lactating women during the onset of lactation and full lactation. *Am J Clin Nutr* 48:1375–1386.
- Newmark K, Nugent P. 1993. Milk-alkali syndrome: A consequence of chronic antacid abuse. *Postgrad Med* 93:149–156.
- Ng K, St John A, Bruce DG. 1994. Secondary hyperparathyroidism, vitamin D deficiency and hip fracture: Importance of sampling times after fracture. *Bone Miner* 25:103–109.
- Niekamp RA, Baer JT. 1995. In-season dietary adequacy of trained male cross-country runners. *Int J Sport Nutr* 5:45–55.
- Nielsen FH. 1990. Studies on the relationship between boron and magnesium which possibly affects the formation and maintenance of bones. *Magnes Trace Elem* 9:61–69.
- Nielsen FH, Hunt CD, Mullen LM, Hunt JR. 1987. Effect of dietary boron on mineral, estrogen, and testosterone metabolism in postmenopausal women. *FASEB J* 1:394–397.
- Nieves JW, Golden AL, Siris E, Kelsey JL, Lindsay R. 1995. Teenage and current calcium intake are related to bone mineral density of the hip and forearm in women aged 30–39 years. *Am J Epidemiol* 141:342–351.

- NIH (National Institutes of Health). 1994. *Optimal Calcium Intake*. NIH Consensus Statement 12:4. Bethesda, MD: NIH.
- NIN (National Institute of Nutrition). 1995. Dairy products in the Canadian diet. NIN Review No. 24. Ontario, Canada: NIN.
- Nordin BEC. 1976. *Calcium, Phosphate and Magnesium Metabolism*. Edinburgh: Churchill Livingstone.
- Nordin BEC. 1989. Phosphorus. *J Food Nutr* 45:62–75.
- Nordin BEC, Polley KJ. 1987. Metabolic consequences of the menopause. A cross-sectional, longitudinal, and intervention study on 557 normal postmenopausal women. *Calcif Tissue Int* 41:S1–S59.
- Nose O, Iida Y, Kai H, Harada T, Ogawa M, Yabuuchi H. 1979. Breath hydrogen test for detecting lactose malabsorption in infants and children: Prevalence of lactose malabsorption in Japanese children and adults. *Arch Dis Child* 54:436–440.
- NRC (National Research Council). 1980. *Recommended Dietary Allowances, 9th Edition*. Committee on Dietary Allowances, Food and Nutrition Board. Washington, DC: National Academy Press.
- NRC (National Research Council). 1982. *Diet, Nutrition, and Cancer*. Report of the Committee on Diet, Nutrition, and Cancer, Assembly of Life Sciences. Washington, DC: National Academy Press.
- NRC (National Research Council). 1983. *Risk Assessment in the Federal Government: Managing the Process*. Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC (National Research Council). 1989a. *Recommended Dietary Allowances: 10th Edition*. Report of the Subcommittee on the Tenth Edition of the RDAs, Food and Nutrition Board, and the Commission on Life Sciences. Washington, DC: National Academy Press.
- NRC (National Research Council). 1989b. *Diet and Health: Implications for Reducing Chronic Disease Risk*. Report of the Committee on Diet and Health, Food and Nutrition Board, Commission on Life Sciences. Washington, DC: National Academy Press.
- NRC (National Research Council). 1993. *Health Effects of Ingested Fluoride*. Subcommittee on Health Effects of Ingested Fluoride. Washington, DC: National Academy Press.
- NRC (National Research Council). 1994. *Science and Judgment in Risk Assessment. Committee on Risk Assessment of Hazardous Air Pollutants*. Board on Environmental Studies and Toxicology. Washington, DC: National Academy Press.
- NRC (National Research Council). 1995. *Nutrient Requirements of Laboratory Animals*. Committee on Animal Nutrition, Board on Agriculture. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- O'Brien KO, Abrams SA, Stuff JE, Liang LK, Welch TR. 1996. Variables related to urinary calcium excretion in young girls. *J Pediatr Gastroenterol Nutr* 23:8–12.
- O'Dowd KJ, Clemens TL, Kelsey JL, Lindsay R. 1993. Exogenous calciferol (vitamin D) and vitamin D endocrine status among elderly nursing home residents in the New York City area. *J Am Geriatr Soc* 41:414–421.

- Ohlson MA, Brewer WD, Jackson L, Swanson PP, Roberts PH, Mangel M, Leverton RM, Chaloupka M, Gram MR, Reynolds MS, Lutz R. 1952. Intakes and retentions of nitrogen, calcium and phosphorus by 136 women between 30 and 85 years of age. *Fed Proc* 11:775–783.
- Oliveri MB, Ladizesky M, Mautalen CA, Alonso A, Martinez L. 1993. Seasonal variations of 25 hydroxyvitamin D and parathyroid hormone in Ushuaia (Argentina), the southernmost city in the world. *Bone Miner* 20:99–108.
- Ooms ME, Roos JC, Bezemer PD, VanDerVijgh WJ, Bouter LM, Lips P. 1995. Prevention of bone loss by vitamin D supplementation in elderly women: A randomized double-blind trial. *J Clin Endocrinol Metab* 80:1052–1058.
- Ophaug RH, Singer L, Harland BF. 1980a. Estimated fluoride intake of 6-month-old infants in four dietary regions of the United States. *Am J Clin Nutr* 33:324–327.
- Ophaug RH, Singer L, Harland BF. 1980b. Estimated fluoride intake of average two-year-old children in four dietary regions of the United States. *J Dent Res* 59:777–781.
- Ophaug RH, Singer L, Harland BF. 1985. Dietary fluoride intake of 6-month and 2-year-old children in four dietary regions of the United States. *Am J Clin Nutr* 42:701–707.
- Orimo H, Ouchi Y. 1990. The role of calcium and magnesium in the development of atherosclerosis. Experimental and clinical evidence. *Ann NY Acad Sci* 598:444–457.
- Orwoll ES. 1982. The milk-alkali syndrome: Current concepts. *Ann Intern Med* 97:242–248.
- Orwoll ES, Oviatt SK, McClung MR, Deftos LJ, Sexton G. 1990. The rate of bone mineral loss in normal men and the effects of calcium and cholecalciferol supplementation. *Ann Intern Med* 112:29–34.
- Osis D, Kramer L, Wiatrowski E, Spencer H. 1974. Dietary fluoride intake in man. *J Nutr* 104:1313–1318.
- Osteoporosis Society of Canada. 1993. Consensus on calcium nutrition. Official position of the Osteoporosis Society of Canada. *Nutr Quart* 18:62–69.
- Osuji OO, Leake JL, Chipman ML, Nikiforuk G, Locker D, Levine N. 1988. Risk factors for dental fluorosis in a fluoridated community. *J Dent Res* 67:1488–1492.
- OTA (Office of Technology Assessment). 1993. *Researching Health Risks*. Washington, DC: Office of Technology Assessment.
- Outhouse J, Kinsman G, Sheldon D, Tworney I, Smith J. 1939. The calcium requirements of five pre-school girls. *J Nutr* 17:199–211.
- Outhouse J, Breiter H, Rutherford E, Dwight J, Mills R, Armstrong W. 1941. The calcium requirement of man: Balance studies on seven adults. *J Nutr* 21:565–575.
- Paganini-Hill A, Chao A, Ross RK, Henderson BE. 1991. Exercise and other factors in the prevention of hip fracture: The Leisure World Study. *Epidemiology* 2:16–25.
- Pak CY. 1988. Medical management of nephrolithiasis in Dallas: Update 1987. *J Urol* 140:461–467.
- Pak CY, Sakhaei K, Rubin CD, Zerwekh JE. 1997. Sustained-release sodium fluoride in the management of established menopausal osteoporosis. *Am J Med Sci* 313:23–32.
- Pang DT, Phillips CL, Bawden JW. 1992. Fluoride intake from beverage consumption in a sample of North Carolina children. *J Dent Res* 71:1382–1388.

- Paolisso G, Passariello N, Pizza G, Marrazzo G, Giunta R, Sgambato S, Varricchio M, D'Onofrio F. 1989. Dietary magnesium supplements improve B-cell response to glucose and arginine in elderly non-insulin-dependent diabetic subjects. *Acta Endocrinol Copenh* 121:16–20.
- Paolisso G, Scheen A, D'Onofrio FD, Lefebvre P. 1990. Magnesium and glucose homeostasis. *Diabetologia* 33:511–514.
- Paolisso G, Sgambato S, Gambardella A, Pizza G, Tesauro P, Varricchio M, D'Onofrio F. 1992. Daily magnesium supplements improve glucose handling in elderly subjects. *Am J Clin Nutr* 55:1161–1167.
- Parfitt AM. 1977. Metacarpal cortical dimensions in hypoparathyroidism, primary hyperparathyroidism and chronic renal failure. *Calcif Tiss Res Suppl* 22:329–331.
- Parfitt AM. 1988. Bone remodeling: Relationship to the amount and structure of bone, and the pathogenesis and prevention of fractures. In: Riggs BL, Melton LJ III eds. *Osteoporosis: Etiology, Diagnosis, and Management*. New York, NY: Raven Press.
- Parfitt AM, Higgins BA, Nassim JR, Collins JA, Hilb A. 1964. Metabolic studies in patients with hypercalciuria. *Clin Sci* 27:463–482.
- Parfitt AM, Chir B, Gallagher JC, Heaney RP, Johnston CC, Neer R, Whedon GD. 1982. Vitamin D and bone health in the elderly. *Am J Clin Nutr* 36:1014–1031.
- Paunier L, Lacourt G, Pilloud P, Schlaepi P, Sizomenko PC. 1978. 25-hydroxyvitamin D and calcium levels in maternal, cord and infant serum in relation to maternal vitamin D intake. *Helv Paediatr Acta* 33:95–103.
- Peace H, Beattie JH. 1991. No effect of boron on bone mineral excretion and plasma sex steroid levels in healthy postmenopausal women. Monography, proceedings, roundtables, and discussions of the Seventh International Symposium on Trace Elements in Man and Animals, held May 20–25, 1990, in Dubrovnik, Croatia, Yugoslavia.
- Peacock M. 1991. Calcium absorption efficiency and calcium requirements in children and adolescents. *Am J Clin Nutr* 54:261S–265S.
- Pedersen AB, Bartholomew MJ, Dolence LA, Aljadir LP, Netteburg KL, Lloyd T. 1991. Menstrual differences due to vegetarian and nonvegetarian diets. *Am J Clin Nutr* 53:879–885.
- Pendrys DG, Katz RV. 1989. Risk of enamel fluorosis associated with fluoride supplementation, infant formula, and fluoride dentifrice use. *Am J Epidemiol* 130:1199–1208.
- Pendrys DG, Morse DE. 1990. Use of fluoride supplementation by children living in fluoridated communities. *J Dent Child* 57:343–347.
- Pendrys DG, Stamm JW. 1990. Relationship of total fluoride intake to beneficial effects and enamel fluorosis. *J Dent Res* 69(Spec Iss):529–538.
- Peng SK, Taylor CB. 1980. Editorial: Probable role of excesses of vitamin D in genesis of arteriosclerosis. *Arterial Wall* 6:63–68.
- Peng SK, Taylor CB, Tham P, Mikkelsen B. 1978. Role of mild excesses of vitamin D in arteriosclerosis. A study in squirrel monkeys. *Arterial Wall* 4:229.
- Pennington JA. 1994. *Bowes and Church's Food Values of Portions Commonly Used*. Philadelphia, PA: JB Lippincott.
- Pennington JA, Wilson DB. 1990. Daily intakes of nine nutritional elements: Analyzed vs. calculated values. *J Am Diet Assoc* 90:375–381.
- Pennington JA, Young BE. 1991. Total diet study nutritional elements, 1982–1989. *J Am Diet Assoc* 91:179–183.

- Perloff BP, Rizek RL, Haytowitz DB, Reid PR. 1990. Dietary intake methodology. II. USDA's Nutrient Data Base for Nationwide Dietary Intake Surveys. *J Nutr* 120:1530–1534.
- Petley A, Macklin B, Renwick AG, Wilkin TJ. 1995. The pharmacokinetics of niacinamide in humans and rodents. *Diabetes* 44:152–155.
- Pett LB, Ogilvie GH. 1956. The Canadian Weight-Height Survey. *Hum Biol* 28:177–188.
- Pettifor JM, Ross FP, Moodley G, Wang J, Marco G, Skjolde C. 1978a. Serum calcium, magnesium, phosphorus, alkaline phosphatase and 25-hydroxyvitamin D concentrations in children. *S Afr Med J* 53:751–754.
- Pettifor JM, Ross P, Wang J, Moodley G, Couper-Smith J. 1978b. Rickets in children of rural origin in South Africa: Is low dietary calcium a factor? *J Pediatr* 92:320–324.
- Pettifor JM, Bikle DD, Cavaleros M, Zachen D, Kamdar MC, Ross FP. 1995. Serum levels of free 1,25-dihydroxyvitamin D in vitamin D toxicity. *Ann Intern Med* 122:511–513.
- Pietschmann P, Woloszczuk W, Pietschmann H. 1990. Increased serum osteocalcin levels in elderly females with vitamin D deficiency. *Exp Clin Endocrinol* 95:275–278.
- Pillai S, Bikle DD, Elias PM. 1987. 1,25-Dihydroxyvitamin D production and receptor binding in human keratinocytes varies with differentiation. *J Biol Chem* 263:5390–5395.
- Pitkin RM, Reynolds WA, Williams GA, Hargis GK. 1979. Calcium metabolism in normal pregnancy: A longitudinal study. *Am J Obstet Gynecol* 133:781–787.
- Pittard WB III, Geddes KM, Sutherland SE, Miller MC, Hollis BW. 1990. Longitudinal changes in the bone mineral content of term and premature infants. *Am J Dis Child* 144:36–40.
- Pluckebaum JM, Chavez N. 1994. Nutritional status of Northwest Indiana Hispanics in a congregate meal program. *J Nutr Elderly* 13:1–22.
- PNUN (Standing Nordic Committee on Food). 1989. *Nordic Nutrition Recommendations*, 2nd Edition. Oslo: Nordic Council of Ministers.
- Ponder SW, McCormick DP, Fawcett HD, Palmer JL, McKernan MG, Brouhard BH. 1990. Spinal bone mineral density in children aged 5.00 through 11.99 years. *Am J Dis Child* 144:1346–1348.
- Ponz de Leon M, Roncucci L, Di Donato P, Tassi L, Smerieri O, Amorico MG, Malagoli G, De Maria D, Antonioli A, Chahin NJ. 1988. Pattern of epithelial cell proliferation in colorectal mucosa of normal subjects and of patients with adenomatous polyps or cancer of the large bowel. *Cancer Res* 48:4121–4126.
- Portale AA, Booth BE, Halloran BP, Morris RC Jr. 1984. Effect of dietary phosphorus on circulating concentrations of 1,25-dihydroxyvitamin D and immunoreactive parathyroid hormone in children with moderate renal insufficiency. *J Clin Invest* 73:1580–1589.
- Portale AA, Halloran BP, Murphy MM, Morris RC. 1986. Oral intake of phosphorus can determine the serum concentration of 1,25-dihydroxyvitamin D by determining its production rate in humans. *J Clin Invest* 77:7–12.
- Portale AA, Halloran BP, Morris RC Jr. 1987. Dietary intake of phosphorus modulates the circadian rhythm in serum concentration of phosphorus. Implications for the renal production of 1,25-dihydroxyvitamin D. *J Clin Invest* 80:1147–1154.

- Portale AA, Halloran BP, Morris RC Jr. 1989. Physiologic regulation of the serum concentration of 1,25-dihydroxyvitamin D by phosphorus in normal men. *J Clin Invest* 83:1494–1499.
- Prentice A, Laskey MA, Shaw J, Cole TJ, Fraser DR. 1990. Bone mineral content of Gambian and British children aged 0–36 months. *Bone Miner* 10:211–214.
- Prentice A, Jarjou LM, Cole TJ, Stirling DM, Dibba B, Fairweather-Tait S. 1995. Calcium requirements of lactating Gambian mothers: Effects of a calcium supplement on breast-milk calcium concentration, maternal bone mineral content, and urinary calcium excretion. *Am J Clin Nutr* 62:58–67.
- Prichard JL. 1969. The prenatal and postnatal effects of fluoride supplements on West Australian school children, aged 6, 7 and 8, Perth, 1967. *Austral Dent J* 14:335–338.
- Prince RL, Smith M, Dick IM, Price RI, Webb PG, Henderson NK, Harris MM. 1991. Prevention of postmenopausal osteoporosis. A comparative study of exercise, calcium supplementation, and hormone-replacement therapy. *N Engl J Med* 325:1189–1195.
- Prince R, Devine A, Dick I, Criddle A, Kerr D, Kent N, Price R, Randell A. 1995. The effects of calcium supplementation (milk powder or tablets) and exercise on bone density in postmenopausal women. *J Bone Miner Res* 10:1068–1075.
- Purdie DW, Aaron JE, Selby PL. 1988. Bone histology and mineral homeostasis in human pregnancy. *Br J Obstet Gynecol* 95:849–854.
- Quamme GA. 1989. Control of magnesium transport in the thick ascending limb. *Am J Physiol* 256:F197–F210.
- Quamme GA. 1993. Laboratory evaluation of magnesium status. Renal function and free intracellular magnesium concentration. *Clin Lab Med* 13:209–223.
- Quamme GA, Dirks JH. 1986. The physiology of renal magnesium handling. *Renal Physiol* 9:257–269.
- Raisz LG, Niemann I. 1969. Effect of phosphate, calcium and magnesium on bone resorption and hormonal responses in tissue culture. *Endocrinology* 85:446–452.
- Rajalakshmi K, Srikantia SG. 1980. Copper, zinc, and magnesium content of breast milk of Indian women. *Am J Clin Nutr* 33:664–669.
- Raman L, Rajalakshmi K, Krishnamachari KA, Sastry JG. 1978. Effect of calcium supplementation to undernourished mothers during pregnancy on the bone density of the neonates. *Am J Clin Nutr* 31:466–469.
- Randall RE, Cohen D, Spray CC, Rossmeisl EC. 1964. Hypermagnesemia in renal failure. *Ann Intern Med* 61:73–88.
- Rao DR, Bello H, Warren AP, Brown GE. 1994. Prevalence of lactose maldigestion. Influence and interaction of age, race, and sex. *Dig Dis Sci* 39:1519–1524.
- Rasmussen HS, McNair P, Goransson L, Balslev S, Larsen OG, Aurup P. 1988. Magnesium deficiency in patients with ischemic heart disease with and without acute myocardial infarction uncovered by an intravenous loading test. *Arch Intern Med* 148:329–332.
- Ray NF, Chan JK, Thamer M, Melton LJ III. 1997. Medical expenditures for the treatment of osteoporotic fractures in the United States in 1995: Report from the National Osteoporosis Foundation. *J Bone Miner Res* 12:24–35.
- Reasner CA II, Dunn JF, Fetchick DA, Liel Y, Hollis BW, Epstein S, Shary J, Mundy GR, Bell NH. 1990. Alteration of vitamin D metabolism in Mexican-Americans. *J Bone Miner Res* 5:13–17.
- Recker RR. 1985. Calcium absorption and achlorhydria. *N Engl J Med* 313:70–73.

- Recker RR, Hassing GS, Lau JR, Saville PD. 1973. The hyperphosphatemic effect of disodium ethane-1-hydroxy-1, 1-diphosphonate (EHDP): Renal handling of phosphorus and the renal response to parathyroid hormone. *J Lab Clin Med* 81:258–266.
- Recker RR, Davies KM, Hinders SM, Heaney RP, Stegman MR, Kimmel DB. 1992. Bone gain in young adult women. *J Am Med Assoc* 268:2403–2408.
- Recker RR, Hinders S, Davies KM, Heaney RP, Stegman MR, Lappe JM, Kimmel DB. 1996. Correcting calcium nutritional deficiency prevents spine fractures in elderly women. *J Bone Miner Res* 11:1961–1966.
- Reddy GS, Norman AW, Willis DM, Goltzman D, Guyda H, Solomon S, Philips DR, Bishop JE, Mayer E. 1983. Regulation of vitamin D metabolism in normal human pregnancy. *J Clin Endocrinol Metab* 56:363–370.
- Reed A, Haugen M, Pachman LM, Langman CB. 1990. Abnormalities in serum osteocalcin values in children with chronic rheumatic diseases. *J Pediatr* 116:574–580.
- Reed JA, Anderson JJ, Tylavsky FA, Gallagher PN Jr. 1994. Comparative changes in radial-bone density of elderly female lacto-ovovegetarians and omnivores. *Am J Clin Nutr* 59:1197S–1202S.
- Reginster JY, Strause L, Deroisy R, Lecart MP, Saltman P, Franchimont P. 1989. Preliminary report of decreased serum magnesium in postmenopausal osteoporosis. *Magnesium* 8:106–109.
- Reichel H, Koeffler HP, Norman AW. 1989. The role of vitamin D endocrine system in health and disease. *N Engl J Med* 320:980–991.
- Reid IR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. 1995. Long-term effects of calcium supplementation on bone loss and fractures in postmenopausal women: A randomized controlled trial. *Am J Med* 98:331–335.
- Reinhart RA. 1988. Magnesium metabolism. A review with special reference to the relationship between intracellular content and serum levels. *Arch Intern Med* 148:2415–2420.
- Reinhold JG, Fardadji B, Abadi P, Ismail-Beigi F. 1991. Decreased absorption of calcium, magnesium, zinc and phosphorus by humans due to increased fiber and phosphorus consumption as wheat bread. *Am J Clin Nutr* 49:204–206.
- Resnick LM, Gupta RK, Laragh JH. 1984. Intracellular free magnesium in erythrocytes of essential hypertension: Relation to blood pressure and serum divalent cations. *Proc Natl Acad Sci USA* 81:6511–6515.
- Resnick L, Gupta R, and Bhargava KK, Gruenspan H, Alderman MH, Laragh JH. 1991. Cellular ions in hypertension, diabetes and obesity: A nuclear magnetic resonance spectroscopic study. *Hypertension* 17:951–957.
- Riancho JA, delArco C, Arteaga R, Herranz JL, Albajar M, Macias JG. 1989. Influence of solar irradiation on vitamin D levels in children on anticonvulsant drugs. *Acta Neurol Scand* 79:296–299.
- Ricci JM, Hariharan S, Helfott A, Reed K, O'Sullivan MJ. 1991. Oral tocolysis with magnesium chloride: A randomized controlled prospective clinical trial. *Am J Obstet Gynecol* 165:603–610.
- Richards A, Mosekilde L, Søgaard CH. 1994. Normal age-related changes in fluoride content of vertebral trabecular bone—relation to bone quality. *Bone* 15:21–26.
- Riggs BL, Melton LJ III. 1995. The worldwide problem of osteoporosis: Insights afforded by epidemiology. *Bone* 17:505S–511S.

- Riggs BL, O'Fallon WM, Muse J, O'Conner MK, Melton LJ III. 1996. Long-term effects of calcium supplementation on serum PTH, bone turnover, and bone loss in elderly women. *J Bone Miner Res* 11:S118.
- Rigo J, Salle BL, Picaud JC, Putet G, Senterre J. 1995. Nutritional evaluation of protein hydrolysate formulas. *Eur J Clin Nutr* 49:S26–S38.
- Riis B, Thomsen K, Christiansen C. 1987. Does calcium supplementation prevent postmenopausal bone loss? *N Engl J Med* 316:173–177.
- Ritz E. 1982. Acute hypophosphatemia. *Kidney Int* 22:84–94.
- Rizzoli R, Stoermann C, Ammann P, Bonjour J-P. 1994. Hypercalcemia and hyperosteolysis in vitamin D intoxication: Effects of clodronate therapy. *Bone* 15:193–198.
- Robertson, WG. 1985. Dietary factors important in calcium stone formation. In: Schwillie PO, Smith LH, Robertson WG, Vahlensieck W, eds. *Urolithiasis and Related Clinical Research*. New York: Plenum Press. Pp. 61–68.
- Romani A, Marfella C, Scarpa A. 1993. Cell magnesium transport and homeostasis: Role of intracellular compartments. *Miner Electrolyte Metab* 19:282–289.
- Roncucci L, Scalmati A, Ponz de Leon M. 1991. Pattern of cell kinetics in colorectal mucosa of patients with different types of adenomatous polyps of the large bowel. *Cancer* 68:873–878.
- Ronis DL, Lang WP, Farghaly MM, Passow E. 1993. Tooth brushing, flossing, and preventive dental visits by Detroit-area residents in relation to demographic and socioeconomic factors. *J Pub Hlth Dent* 53:138–145.
- Rosado JL, Lopez P, Morales M, Munoz E, Allen LH. 1992. Bioavailability of energy, nitrogen, fat, zinc, iron and calcium from rural and urban Mexican diets. *Br J Nutr* 68:45–58.
- Rowe JW, Minaker KL, Pallotta JA, Flier JS. 1983. Characterization of the insulin resistance of aging. *J Clin Invest* 71:1581–1587.
- Rubenowitz E, Axelsson G, Rylander R. 1996. Magnesium in drinking water and death from acute myocardial infarction. *Am J Epidemiol* 143:456–462.
- Rubin H. 1975. Central role for magnesium in coordinate control of metabolism and growth in animal cells. *Proc Natl Acad Sci USA* 72:3551–3555.
- Rude RK. 1993. Magnesium metabolism and deficiency. *Endocrinol Metab Clin North Am* 22:377–395.
- Rude RK, Olerich M. 1996. Magnesium deficiency: Possible role in osteoporosis associated with gluten-sensitive enteropathy. *Osteopor Int* 6:453–461.
- Rude RK, Singer FR. 1980. Magnesium deficiency and excess. *Ann Rev Med* 32:245–259.
- Rude RK, Oldham SB, Singer FR. 1976. Functional hypoparathyroidism and parathyroid hormone end-organ resistance in human magnesium deficiency. *Clin Endocrinol* 5:209–224.
- Rude RK, Bethune JE, Singer FR. 1980. Renal tubular maximum for magnesium in normal, hyperparathyroid and hypoparathyroid man. *J Clin Endocrinol Metab* 51:1425–1431.
- Rude RK, Manoogian C, Ehrlich L, DeRusso P, Ryzen E, Nadler J. 1989. Mechanisms of blood pressure regulation by magnesium in man. *Magnesium* 8:266–278.
- Rude RK, Stephen A, Nadler J. 1991. Determination of red blood cell intracellular free magnesium by nuclear magnetic resonance as an assessment of magnesium depletion. *Magnes Trace Elem* 10:117–121.

- Rudloff S, Lonnerdal B. 1990. Calcium retention from milk-based infant formulas, whey-hydrolysate formula, and human milk in weanling rhesus monkeys. *Am J Dis Child* 144:360–363.
- Rudnicki M, Frolich A, Rasmussen WF, McNair P. 1991. The effect of magnesium on maternal blood pressure in pregnancy-induced hypertension. A randomized double-blind placebo-controlled trial. *Acta Obstet Gynecol Scand* 70:445–450.
- Ruiz JC, Mandel C, Garabedian M. 1995. Influence of spontaneous calcium intake and physical exercise on the vertebral and femoral bone mineral density of children and adolescents. *J Bone Miner Res* 10:675–682.
- Russell AL. 1949. Dental effects of exposure to fluoride-bearing Dakota sandstone waters at various ages and for various lengths of time. II. Patterns of dental caries inhibition as related to exposure span, to elapsed time since exposure, and to periods of calcification and eruption. *J Dent Res* 28:600–612.
- Russell AL, Elvove E. 1951. Domestic water and dental caries. VII. A study of the fluoride-dental caries relationship in an adult population. *Pub Hlth Rep* 66:1389–1401.
- Ryan MP. 1987. Diuretics and potassium/magnesium depletion. Directions for treatment. *Am J Med* 82:38–47.
- Ryzen E, Elbaum N, Singer FR, Rude RK. 1985. Parenteral magnesium tolerance testing in the evaluation of magnesium deficiency. *Magnesium* 4:137–147.
- Ryzen E, Elkayam U, Rude RK. 1986. Low blood mononuclear cell magnesium in intensive cardiac care unit patients. *Am Heart J* 111:475–480.
- Sacks FM, Brown LE, Appel L, Borhani NO, Evans D, Whelton P. 1995. Combinations of potassium, calcium, and magnesium supplements in hypertension. *Hypertension* 26:950–956.
- Sakhaee K, Baker S, Zerwekh J, Poindexter J, Garcia-Hernandez PA, Pak CY. 1994. Limited risk of kidney stone formation during long-term calcium citrate supplementation in nonstone forming subjects. *J Urol* 152:324–327.
- Salama F, Whitford GM, Barenie JT. 1989. Fluoride retention by children from toothbrushing. *J Dent Res* 68(Spec Issue):335.
- Salle BL, Delvin E, Glorieux F, David L. 1990. Human neonatal hypocalcemia. *Biol Neonate* 58:S22–S31.
- Sandberg AS, Larsen T, Sandstrom B. 1993. High dietary calcium level decreases colonic phytate degradation in pigs fed a rapeseed diet. *J Nutr* 123:559–566.
- Sanders TA, Purves R. 1981. An anthropometric and dietary assessment of the nutritional status of vegan preschool children. *J Human Nutr* 35:349–357.
- Sandler RB, Slemenda CW, LaPorte RE, Cauley JA, Schramm MM, Barresi ML, Kriska AM. 1985. Postmenopausal bone density and milk consumption in childhood and adolescence. *Am J Clin Nutr* 42:270–274.
- Saunders D, Sillery J, Chapman R. 1988. Effect of calcium carbonate and aluminum hydroxide on human intestinal function. *Dig Dis Sci* 33:409–412.
- Schanler RJ, Garza C, Smith EO. 1985. Fortified mothers' milk for very low birth weight infants: Results of macromineral balance studies. *J Pediatr* 107:767–774.
- Schendel DE, Berg CJ, Yeargin-Allsopp M, Boyle CA, Decoufle P. 1996. Prenatal magnesium sulfate exposure and the risk for cerebral palsy or mental retardation among very low-birth-weight children aged 3 to 5 years. *J Am Med Assoc* 276:1805–1810.
- Schiffl H, Binswanger U. 1982. Renal handling of fluoride in healthy man. *Renal Physiol* 5:192–196.

- Schiller L, Santa Ana C, Sheikh M, Emmett M, Fordtran J. 1989. Effect of the time of administration of calcium acetate on phosphorus binding. *N Engl J Med* 320:1110–1113.
- Schlesinger ES, Overton DE, Riverhead LI, Chase HC, Cantwell KT. 1956. Newburgh-Kingston caries-fluorine study XIII. Pediatric findings after ten years. *J Am Dent Assoc* 52:296–306.
- Schlesinger L, Arevalo M, Arredondo S, Diaz M, Lonnerdal B, Stekel A. 1992. Effect of a zinc-fortified formula on immunocompetence and growth of malnourished infants. *Am J Clin Nutr* 56:491–498.
- Schmidt LE, Arfken CL, Heins JM. 1994. Evaluation of nutrient intake in subjects with non-insulin-dependent diabetes mellitus. *J Am Diet Assoc* 94:773–774.
- Schmidt-Gayk H, Goossen J, Lendle F, Seidel D. 1977. Serum 25-hydroxycholecalciferol in myocardial infarction. *Atherosclerosis* 26:55–58.
- Schneider EL, Guralnik JM. 1990. The aging of America. Impact on health care costs. *J Am Med Assoc* 263:2335–2340.
- Schofield FA, and Morrell E. 1960. Calcium, phosphorus and magnesium. *Fed Proc* 19:1014–1016.
- Schuman CA, Jones HW III. 1985. The “milk-alkali” syndrome: Two case reports with discussion of pathogenesis. *Quart J Med (New Series)* 55:119–126.
- Schutzmansky G. 1971. Fluoride tablet application in pregnant females. *Dtsch Stomatol* 21:122–129.
- Schwartz E, Chokas WV, Panariello VA. 1964. Metabolic balance studies of high calcium intake in osteoporosis. *Am J Med* 36:233–249.
- Schwartz GG, Hulka BS. 1990. Is vitamin D deficiency a risk factor for prostate cancer? *Anticancer Res* 10:1307–1312.
- Schwartz R, Walker G, Linz MD, MacKellar I. 1973. Metabolic responses of adolescent boys to two levels of dietary magnesium and protein. I. Magnesium and nitrogen retention. *Am J Clin Nutr* 26:510–518.
- Schwartz R, Spencer H, Welsh JJ. 1984. Magnesium absorption in human subjects from leafy vegetables, intrinsically labeled with stable  $^{26}\text{Mg}$ . *Am J Clin Nutr* 39:571–576.
- Schwartz R, Apgar BJ, Wien EM. 1986. Apparent absorption and retention of Ca, Cu, Mg, Mn, and Zn from a diet containing bran. *Am J Clin Nutr* 43:444–455.
- Schwartzman MS, Franck WA. 1987. Vitamin D toxicity complicating the treatment of senile, postmenopausal, and glucocorticoid-induced osteoporosis: Four case reports and a critical commentary on the use of vitamin D in these disorders. *Am J Med* 82:224–229.
- Sebastian A, Harris ST, Ottaway JH, Todd KM, Morris RC Jr. 1994. Improved mineral balance and skeletal metabolism in postmenopausal women treated with potassium bicarbonate. *N Engl J Med* 330:1776–1781.
- Sebert JL, Garabedian M, Chauvenet M, Maamer M, Agbomson F, Brazier M. 1995. Evaluation of a new solid formulation of calcium and vitamin D in institutionalized elderly subjects: A randomized comparative trial versus separate administration of both constituents. *Rev Rhum* 62:288–294.
- Seelig MS. 1981. Magnesium requirements in human nutrition. *Magnes Bull* 3(suppl):26–47.
- Seelig MS. 1993. Interrelationship of magnesium and estrogen in cardiovascular and bone disorders, eclampsia, migraine and premenstrual syndrome. *J Am Coll Nutr* 12:442–458.
- Seelig MS, Elin RJ. 1996. Is there a place for magnesium in the treatment of acute myocardial infarction? *Am Heart J* 132:471–477.

- Seki K, Makimura N, Mitsui C, Hirata J, Nagata I. 1991. Calcium-regulating hormones and osteocalcin levels during pregnancy: A longitudinal study. *Am J Obstet Gynecol* 164:1248–1252.
- Selby PL. 1994. Calcium requirement—A reappraisal of the methods used in its determination and their application to patients with osteoporosis. *Am J Clin Nutr* 60:944–948.
- Selby PL, Davies M, Marks JS, Mawer EB. 1995. Vitamin D intoxication causes hypercalcemia by increased bone resorption which responds to pamidronate. *Clin Endocrinol* 43:531–536.
- Sentipal JM, Wardlaw GM, Mahan J, Matkovic V. 1991. Influence of calcium intake and growth indexes on vertebral bone mineral density in young females. *Am J Clin Nutr* 54:425–428.
- Seydoux J, Girardin E, Paunier L, Beguin F. 1992. Serum and intracellular magnesium during normal pregnancy and in patients with pre-eclampsia. *Br J Obstet Gynecol* 99:207–211.
- Shapses SA, Robins SP, Schwartz EI, Chowdhury H. 1995. Short-term changes in calcium but not protein intake alter the rate of bone resorption in healthy subjects as assessed by urinary pyridinium cross-link excretion. *J Nutr* 125:2814–2821.
- Sharma OP. 1996. Vitamin D, calcium, and sarcoidosis. *Chest* 109:535–539.
- Shen YW, Taves DR. 1974. Fluoride concentrations in the human placenta and maternal and cord blood. *Am J Obstet Gynecol* 119:205–207.
- Sherman HC, Hawley E. 1922. Calcium and phosphorus metabolism in childhood. *J Biol Chem* 52:375–399.
- Shils ME. 1969. Experimental human magnesium depletion. *Medicine* 46:61–85.
- Shils ME. 1994. Magnesium. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*. Philadelphia, PA: Lea & Febiger. Pp. 164–184.
- Shils ME, Rude RK. 1996. Deliberations and evaluations of the approaches, endpoints and paradigms for magnesium dietary recommendations. *J Nutr* 126:2398S–2403S.
- Sibai BM, Villar MA, Bray E. 1989. Magnesium supplementation during pregnancy: A double-blind randomized controlled clinical trial. *Am J Obstet Gynecol* 161:115–119.
- Siener R, Hesse A. 1995. Influence of a mixed and a vegetarian diet on urinary magnesium excretion and concentration. *Br J Nutr* 73:783–790.
- Silverberg SJ, Shane E, Clemens TL, Dempster DW, Segre GV, Lindsay R, Bilezikian JP. 1986. The effect of oral phosphate administration on major indices of skeletal metabolism in normal subjects. *J Bone Miner Res* 1:383–388.
- Silvis SE, Paragas PD Jr. 1972. Paresthesias, weakness, seizures, and hypophosphatemia in patients receiving hyperalimentation. *Gastroenterology* 62:513–520.
- Simard PL, Lachapelle C, Trahan L, Naccache H, Demers M, Broduer JM. 1989. The ingestion of fluoride dentifrice by young children. *J Dent Child* 56:177–181.
- Simard PL, Naccache H, Lachapelle D, Brodeur JM. 1991. Ingestion of fluoride from dentifrices by children aged 12 to 24 months. *Clin Pediatr Phila* 30:614–617.
- Simmer K, Khanum S, Carlsson L, Thompson RP. 1988. Nutritional rehabilitation in Bangladesh—the importance of zinc. *Am J Clin Nutr* 47:1036–1040.
- Singer L, Ophaug R. 1979. Total fluoride intake of infants. *Pediatrics* 63:460–466.
- Singer L, Ophaug RH, Harland BF. 1980. Fluoride intakes of young male adults in the United States. *Am J Clin Nutr* 33:328–332.
- Singer L, Ophaug RH, Harland BF. 1985. Dietary fluoride intake of 15–19-year-old male adults residing in the United States. *J Dent Res* 64:1302–1305.

- Singh A, Jolly SS. 1970. Chronic toxic effects on the skeletal system. In: *Fluorides and Human Health*. Geneva: World Health Organization. Pp 238–249.
- Skajaa K, Dorup I, Sandstrom BM. 1991. Magnesium intake and status and pregnancy outcome in a Danish population. *Br J Obstet Gynecol* 98:919–928.
- Slattery ML, Sorenson AW, Ford MH. 1988. Dietary calcium intake as a mitigating factor in colon cancer. *Am J Epidemiol* 128:504–514.
- Slemenda CW, Reister TK, Hui SL, Miller JZ, Christian JC, Johnston CC Jr. 1994. Influences on skeletal mineralization in children and adolescents: Evidence for varying effects of sexual maturation and physical activity. *J Pediatr* 125:201–207.
- Slemenda CW, Peacock M, Hui S, Zhou L, Johnston CC Jr. 1997. Reduced rates of skeletal remodeling are associated with increased bone mineral density during the development of peak skeletal mass. *J Bone Miner Res* 12:676–682.
- Slesinski MJ, Subar AF, Kahle LL. 1996. Dietary intake of fat, fiber, and other nutrients is related to the use of vitamin and mineral supplements in the United States: The 1992 National Health Interview Survey. *J Nutr* 126:3001–3008.
- Smilkstein MJ, Smolinske SC, Kulig KW, Rumack, BH. 1988. Severe hypermagnesemia due to multiple-dose cathartic therapy. *West J Med* 148:208–211.
- Smith EL, Gilligan C, Smith PE, Sempos CT. 1989. Calcium supplementation and bone loss in middle-aged women. *Am J Clin Nutr* 50:833–842.
- Smith KT, Heaney RP, Flora L, Hinders SM. 1987. Calcium absorption from a new calcium delivery system (CCM). *Calcif Tissue Int* 41:351–352.
- Smith R, Dent CE. 1969. Vitamin D requirements in adults. Clinical and metabolic studies on seven patients with nutritional osteomalacia. *Bibl Nutr Dieta* 13:44–45.
- Snedeker SM, Smith SA, Greger JL. 1982. Effect of dietary calcium and phosphorus levels on the utilization of iron, copper, and zinc by adult males. *J Nutr* 112:136–143.
- Sojka JE, Wastney ME, Abrams S, Froese S, Martin BR, Weaver CM. 1997. Magnesium kinetics in adolescent girls determined using stable isotopes: Effects of high and low calcium intakes. *Am J Physiol* 273:R170–R175.
- Sojka JE, Weaver CM. 1995. Magnesium supplementation and osteoporosis. *Nutr Rev* 53:71–74.
- Sokoll LJ, Dawson-Hughes B. 1992. Calcium supplementation and plasma ferritin concentrations in premenopausal women. *Am J Clin Nutr* 56:1045–1048.
- Sorva A, Risteli J, Risteli L, Valimaki M, Tilvis R. 1991. Effects of vitamin D and calcium on markers of bone metabolism in geriatric patients with low serum 25-hydroxyvitamin D levels. *Calcif Tissue Int* 49:S88–S89.
- Southgate DAT, Widdowson EM, Smits BJ, Cooke WT, Walker CHM, Mathers NP. 1969. Absorption and excretion of calcium and fat by young infants. *Lancet* 1:487–489.
- Sowers M, Wallace RB, Lemke JH. 1985. Correlates of forearm bone mass among women during maximal bone mineralization. *Prev Med* 14:585–596.
- Sowers M, Wallace RB, Lemke JH. 1986. The relationship of bone mass and fracture history to fluoride and calcium intake: A study of three communities. *Am J Clin Nutr* 44:889–898.
- Sowers M, Clark MK, Jannausch ML, Wallace RB. 1991. A prospective study of bone mineral content and fracture in communities with differential fluoride exposure. *Am J Epidemiol* 133:649–660.
- Sowers M, Corton G, Shapiro B, Jannausch ML, Crutchfield M, Smith ML, Randolph JF, Hollis B. 1993. Changes in bone density with lactation. *J Am Med Assoc* 269:3130–3135.

- Sowers M, Randolph J, Shapiro B, Jannaush M. 1995a. A prospective study of bone density and pregnancy after an extended period of lactation with bone loss. *Obstet Gynecol* 85:285–289.
- Sowers M, Eyre D, Hollis BW, Randolph JF, Shapiro B, Jannausch ML, Crutchfield M. 1995b. Biochemical markers of bone turnover in lactating and nonlactating postpartum women. *J Clin Endocrinol Metab*. 80:2210–2216.
- Spak CJ, Ekstrand J, Zylberstein D. 1982. Bioavailability of fluoride added by baby formula and milk. *Caries Res* 16:249–256.
- Spak CJ, Hardell LI, De Chateau P. 1983. Fluoride in human milk. *Acta Paediatr Scand* 72:699–701.
- Spatling L, Spatling G. 1988. Magnesium supplementation in pregnancy. A double blind study. *Br J Obstet Gynecol* 95:120–125.
- Specker BL. 1996. Evidence for an interaction between calcium intake and physical activity on changes in bone mineral density. *J Bone Miner Res* 11:1539–1544.
- Specker BL, Tsang RC. 1987. Cyclical serum 25-hydroxyvitamin D concentrations paralleling sunshine exposure in exclusively breast-fed infants. *J Pediatr* 110:744–747.
- Specker BL, Tsang RC, Hollis BW. 1985a. Effect of race and diet on human-milk vitamin D and 25-hydroxyvitamin D. *Am J Dis Child* 139:1134–1137.
- Specker BL, Valanis B, Hertzberg V, Edwards N, Tsang RC. 1985b. Sunshine exposure and serum 25-hydroxyvitamin D concentrations in exclusively breast-fed infants. *J Pediatr* 107:372–376.
- Specker BL, Lichtenstein P, Mimouni F, Gormley C, Tsang RC. 1986. Calcium-regulating hormones and minerals from birth to 18 months of age: A cross-sectional study. II. Effects of sex, race, age, season, and diet on serum minerals, parathyroid hormone, and calcitonin. *Pediatrics* 77:891–896.
- Specker BL, Tsang RC, Ho ML, Miller D. 1987. Effect of vegetarian diet on serum 1,25-dihydroxyvitamin D concentrations during lactation. *Obstet Gynecol* 70:870–874.
- Specker BL, Tsang RC, Ho ML. 1991a. Changes in calcium homeostasis over the first year postpartum: Effect of lactation and weaning. *Obstet Gynecol* 78:56–62.
- Specker BL, Tsang RC, Ho ML, Landi TM, Gratton TL. 1991b. Low serum calcium and high parathyroid hormone levels in neonates fed “humanized” cow’s milk-based formula. *Am J Dis Child* 145:941–945.
- Specker BL, Ho ML, Oestreich A, Yin TA, Shui QM, Chen XC, Tsang RC. 1992. Prospective study of vitamin D supplementation and rickets in China. *J Pediatr* 120:733–739.
- Specker BL, Vieira NE, O’Brien KO, Ho ML, Heubi JE, Abrams SA, Yerger AL. 1994. Calcium kinetics in lactating women with low and high calcium intakes. *Am J Clin Nutr* 59:593–599.
- Specker BL, Beck A, Kalkwarf H, Ho M. 1997. Randomized trial of varying mineral intake on total body bone mineral accretion during the first year of life. *Pediatrics* 99:e12.
- Spencer H, Menczel J, Lewin I, Samachson J. 1965. Effect of high phosphorus intake on calcium and phosphorus metabolism in man. *J Nutr* 86:125–132.
- Spencer H, Lewin I, Fowler J, Samachson J. 1969. Influence of dietary calcium intake on  $\text{Ca}^{47}$  absorption in man. *Am J Med* 46:197–205.
- Spencer H, Kramer L, Osis D, Norris C. 1978a. Effect of phosphorus on the absorption of calcium and on the calcium balance in man. *J Nutr* 108:447–457.
- Spencer H, Lesniak M, Gatzka CA, Kramer L, Norris C, Coffey J. 1978b. Magnesium-calcium interrelationships in man. *Trace Substances Environ Hlth* 12:241–247.

- Spencer H, Kramer L, Lesniak M, DeBartolo M, Norris C, Osis D. 1984. Calcium requirements in humans. Report of original data and a review. *Clin Orthop Relat Res* 184:270–280.
- Spencer H, Fuller H, Norris C, Williams D. 1994. Effect of magnesium on the intestinal absorption of calcium in man. *J Am Coll Nutr* 13:485–492.
- Spencer H, Osis D, Lender M. 1981. Studies of fluoride metabolism in man. A review and report of original data. *Sci Total Environ* 17:1–12.
- Stamp TCB, Haddad JG, Twigg CA. 1977. Comparison of oral 25-hydroxycholecalciferol, vitamin D, and ultraviolet light as determinants of circulating 25-hydroxyvitamin D. *Lancet* 1:1341–1343.
- Stanbury SW. 1971. The phosphate ion in chronic renal failure. In: Hioco DJ, ed. *Phosphate et Metabolisme Phosphocalcique*. Paris: Sandoz Laboratories.
- Stapleton FB. 1994. Hematuria associated with hypercalciuria and hyperuricosuria: A practical approach. *Pediatr Nephrol* 8:756–761.
- Stearns G. 1968. Early studies of vitamin D requirement during growth. *Am J Pub Hlth* 58:2027–2035.
- Steenbock H, Black A. 1924. The reduction of growth-promoting and calcifying properties in a ration by exposure to ultraviolet light. *J Biol Chem* 61:408–422.
- Steichen JJ, Tsang RC. 1987. Bone mineralization and growth in term infants fed soy-based or cow milk-based formula. *J Pediatr* 110:687–692.
- Stein JH, Smith WO, Ginn HE. 1966. Hypophosphatemia in acute alcoholism. *Am J Med Sci* 252:78–83.
- Stendig-Lindberg G, Tepper R, Leichter I. 1993. Trabecular bone density in a two year controlled trial of peroral magnesium in osteoporosis. *Magnes Res* 6:155–163.
- Stephen KW, McCall DR, Tullis JI. 1987. Caries prevalence in northern Scotland before, and 5 years after, water defluoridation. *Br Dent J* 163:324–326.
- Stevenson CA, Watson AR. 1957. Fluoride osteosclerosis. *Am J Roentg Rad Ther Nucl Med* 78:13–18.
- Stumpf WE, Sar M, Reid FA, Tanakay Y, DeLuca HF. 1979. Target cells for 1,25-dihydroxyvitamin D<sub>3</sub> in intestinal tract, stomach, kidney, skin, pituitary, and parathyroid. *Science* 206:1188–1190.
- Suarez FL, Savaiano DA, Levitt MD. 1995. A comparison of symptoms after the consumption of milk or lactose-hydrolyzed milk by people with self-reported severe lactose intolerance. *N Engl J Med* 333:1–4.
- Svenningsen NW, Lindquist B. 1974. Postnatal development of renal hydrogen ion excretion capacity in relation to age and protein intake. *Acta Paediatr Scand* 63:721–731.
- Switzer RL. 1971. Regulation and mechanism of phosphoribosylpyrophosphate synthetase. III. Kinetic studies of the reaction mechanism. *J Biol Chem* 246:2447–2458.
- Tanner JT, Smith J, Defibaugh P, Angyal G, Villalobos M, Bueno MP, McGarrahan ET, Wehr HM, Muniz JF, Hollis BW. 1988. Survey of vitamin content of fortified milk. *J Assoc Off Anal Chem* 71: 607–610.
- Tanner JM. 1990. *Growth at Adolescence*. Oxford: Oxford University Press.
- Tatevossian A. 1990. Fluoride in dental plaque and its effects. *J Dent Res* 69(Spec Iss): 645–652.
- Taves DR. 1978. Fluoridation and mortality due to heart disease. *Nature* 272:361–362.
- Taves DR. 1983. Dietary intake of fluoride ashed (total fluoride) v. unashed (inorganic fluoride) analysis of individual foods. *Br J Nutr* 49:295–301.

- Taves DR, Neuman WF. 1964. Factors controlling calcification in vitro: Fluoride and magnesium. *Arch Biochem Biophys* 108:390–397.
- Taylor AF, Norman ME. 1984. Vitamin D metabolite levels in normal children. *Pediatr Res* 18: 886–890.
- Taylor CB, Hass GM, Ho KJ, Liu LB. 1972. Risk factors in the pathogenesis of arteriosclerotic heart disease and generalized atherosclerosis. *Ann Clin Lab Sci* 2:239.
- Teegarden D, Proulx WR, Martin BR, Zhao J, McCabe GP, Lyle RM, Peacock M, Slemenda C, Johnston CC, Weaver CM. 1995. Peak bone mass in young women. *J Bone Miner Res* 10:711–715.
- Ten Cate JM. 1990. In vitro studies on the effects of fluoride on de- and remineralization. *J Dent Res* 69(Spec Iss):614–619.
- Terblanche S, Noakes TD, Dennis SC, Marais D, Eckert M. 1992. Failure of magnesium supplementation to influence marathon running performance or recovery in magnesium-replete subjects. *Int J Sport Nutr* 2:154–164.
- Tesar R, Notelovitz M, Shim E, Kauwell G, Brown J. 1992. Axial and peripheral bone density and nutrient intakes of postmenopausal vegetarian and omnivorous women. *Am J Clin Nutr* 56:699–704.
- Thatcher HS, Rock L. 1928. Clinical notes, suggestions and new instruments. *J Am Med Assoc* 91:1185–1186.
- Theintz G, Buchs B, Rizzoli R, Slosman D, Clavien H, Sizonenko PC, Bonjour JP. 1992. Longitudinal monitoring of bone mass accumulation in healthy adolescents: Evidence for a marked reduction after 16 years of age at the levels of lumbar spine and femoral neck in female subjects. *J Clin Endocrinol Metab* 75:1060–1065.
- Thompson FE, Byers T. 1994. Dietary assessment resource manual. *J Nutr* 124:224S–231S.
- Thys-Jacobs S, Ceccarelli S, Bierman A, Weisman H, Cohen M-A, Alvir J. 1989. Calcium supplementation in premenstrual syndrome: A randomized cross-over trial. *J Gen Intern Med* 4:183–189.
- Tillman DM, Semple PF. 1988. Calcium and magnesium in essential hypertension. *Clin Sci* 75:395–402.
- Touitou Y, Godard JP, Ferment O, Chastang C, Proust J, Bogdan A, Auzeby A, Touitou C. 1987. Prevalence of magnesium and potassium deficiencies in the elderly. *Clin Chem* 33:518–523.
- Travis SF, Sugerman HJ, Ruberg RL, Dudrick SJ, Delivoria-Papadopoulos M, Miller L, Osaki FA. 1971. Alterations of red cell glycolytic intermediates and oxygen transport as a consequence of hypophosphatemia in patients receiving intravenous hyperalimentation. *N Engl J Med* 285:763–768.
- Tremaine WJ, Newcomer AD, Riggs BL, McGill DB. 1986. Calcium absorption from milk in lactase-deficient and lactase-sufficient adults. *Dig Dis Sci* 31:376–378.
- Tsang RC, Strub R, Brown DR, Steichen J, Hartman C, Chen IW. 1976. Hypomagnesemia in infants of diabetic mothers: Perinatal studies. *J Pediatr* 89:115–119.
- Tucker K. 1996. The use of epidemiological approaches and meta-analysis to determine mineral element requirements. *J Nutr* 126:2365S–2372S.
- Tucker K, Kiel DP, Hannan MT, Felson DT. 1995. Magnesium intake is associated with bone-mineral density (BMD) in elderly women. *J Bone Miner Res* 10:S466.
- Tylavsky FA, Anderson JJ. 1988. Dietary factors in bone health of elderly lacto-ovo vegetarian and omnivorous women. *Am J Clin Nutr* 48:842–849.

- Urakabe S, Nakata K, Ando A, Orita Y, Abe Y. 1975. Hypokalemia and metabolic acidosis from overuse of magnesium oxide. *Jpn Circ J* 39:1135–1137.
- USDA (US Department of Agriculture). 1985. *Nationwide Food Consumption Survey. Continuing Survey of Food Intakes of Individuals*. Women 19–50 years and their children 1–5 years, 1 day, 1985. Report No. 85-1. Hyattsville, MD: Nutrition Monitoring Division, Human Nutrition Information Service, USDA.
- USDA (US Department of Agriculture). 1991. *Provisional Table on the Vitamin D Content of Foods*. Hyattsville, MD: Nutrient Data Research Branch, USDA.
- USDA (US Department of Agriculture), Center for Nutrition Policy and Promotion. 1997. *Nutrient Content of the U.S. Food Supply, 1909–1994*. Washington DC: Center for Nutrition Policy and Promotion, USDA.
- USPHS (US Public Health Service). 1991. *Ad Hoc Subcommittee on Fluoride: Review of Fluoride Benefits and Risks*. Bethesda, MD: Department of Health and Human Services.
- Venkataraman PS, Tsang RC, Greer FR, Noguchi A, Laskarzewski P, Steichen JJ. 1985. Late infantile tetany and secondary hyperparathyroidism in infants fed humanized cow milk formula. Longitudinal follow-up. *Am J Dis Child* 139:664–668.
- Vicchio D, Yergey A, O'Brien K, Allen L, Ray R, Holick MF. 1993. Quantification and kinetics of 25-hydroxyvitamin D<sub>3</sub> by isotope dilution liquid chromatography/thermospray mass spectrometry. *Biol Mass Spectrom* 22:53–58.
- Vik T, Try K, Thelle DS, Forde OH. 1979. Tromso heart study: Vitamin D metabolism and myocardial infarction. *Br Med J* 2:176.
- Villar J, Repke JT. 1990. Calcium supplementation during pregnancy may reduce preterm delivery in high-risk populations. *Am J Obstet Gynecol* 163:1124–1131.
- Villareal DT, Civitelli R, Chines A, Avioli LV. 1991. Subclinical vitamin D deficiency in postmenopausal women with low vertebral bone mass. *J Clin Endocrinol Metab* 72: 628–634.
- Wacker WE, Parisi AF. 1968. Magnesium metabolism. *N Engl J Med* 45:658–663, 712–717, 772–776.
- Wagener DK, Novrjah P, Horowitz AM. 1995. *Trends in Childhood Use of Dental Care Products Containing Fluoride: United States, 1983–1989*. Advance data from Vital Health Statistics of the Center for Disease Control. National Center for Health Statistics #219; Nov. 20, 1992. Hyattsville, MD: National Center for Health Statistics.
- Walker AR, Richardson B, Walker F. 1972. The influence of numerous pregnancies and lactations on bone dimensions in South African Bantu and Caucasian mothers. *Clin Sci* 42:189–196.
- Walker RM, Linkswiler HM. 1972. Calcium retention in the adult human male as affected by protein intake. *J Nutr* 102:1297–1302.
- Wallach S, Verch RL. 1986. Tissue magnesium in spontaneously hypertensive rats. *Magnesium* 5:33–38.
- Wang CC, Kern R, Kaucher M. 1930. Minimum requirement of calcium and phosphorus in children. *Am J Dis Child* 39:768–773.
- Wardlaw GM, Pike AM. 1986. The effect of lactation on peak adult shaft and ultra-distal forearm bone mass in women. *Am J Clin Nutr* 44:283–286.
- Wasnich R, Yano K, Vogel J. 1983. Postmenopausal bone loss at multiple skeletal sites: Relationship to estrogen use. *J Chron Dis* 36:781–790.
- Wastney ME, Ng J, Smith D, Martin BR, Peacock M, Weaver CM. 1996. Differences in calcium kinetics between adolescent girls and young women. *Am J Physiol* 271:R208–R216.

- Waterhouse C, Taves D, Munzer A. 1980. Serum inorganic fluoride: Changes related to previous fluoride intake, renal function and bone resorption. *Clin Sci* 58:145–152.
- Weaver CM. 1994. Age-related calcium requirements due to changes in absorption and utilization. *J Nutr* 124:1418S–1425S.
- Weaver CM, Martin BR, Plawecki KL, Peacock M, Wood OB, Smith DL, Wastney ME. 1995. Differences in calcium metabolism between adolescent and adult females. *Am J Clin Nutr* 61:577–581.
- Webb AR, Kline L, Holick MF. 1988. Influence of season and latitude on the cutaneous synthesis of vitamin D<sub>3</sub>: Exposure to winter sunlight in Boston and Edmonton will not promote vitamin D<sub>3</sub> synthesis in human skin. *J Clin Endocrinol Metab* 67:373–378.
- Webb AR, De Costa BR, Holick MF. 1989. Sunlight regulates the cutaneous production of vitamin D<sub>3</sub> by causing its photodegradation. *J Clin Endocrinol Metab* 68:882–887.
- Webb AR, Pilbeam C, Hanafin N, Holick MF. 1990. An evaluation of the relative contributions of exposure to sunlight and of diet to the circulating concentrations of 25-hydroxyvitamin D in an elderly nursing home population in Boston. *Am J Clin Nutr* 51:1075–1081.
- Wei SH, Hattab FN, Mellberg JR. 1989. Concentration of fluoride and selected other elements in teas. *Nutrition* 5:237–240.
- Weinsier RL, Krumdieck CL. 1981. Death resulting from overzealous total parenteral nutrition: The refeeding syndrome revisited. *Am J Clin Nutr* 34:393–399.
- Weisman Y, Harell A, Edelstein S, Spirer Z, Golander A. 1979. 1,25-dihydroxyvitamin D<sub>3</sub> and 24,25-dihydroxyvitamin D<sub>3</sub> in vitro synthesis by human decidua and placenta. *Nature* 281:317–319.
- Weissberg N, Schwartz G, Shemesh O, Brooks BA, Algur N, Eylath U, Abraham AS. 1992. Serum and mononuclear cell potassium, magnesium, sodium and calcium in pregnancy and labour and their relation to uterine muscle contraction. *Magnes Res* 5:173–177.
- Wester PO, Dyckner T. 1980. Diuretic treatment and magnesium losses. *Acta Med Scand* 647:145–152.
- Whitford GM. 1994. Effects of plasma fluoride and dietary calcium concentrations on GI absorption and secretion of fluoride in the rat. *Calcif Tissue Int* 54:421–425.
- Whitford GM. 1996. The metabolism and toxicity of fluoride. In Myers HM, ed. *Monographs in Oral Science*, 2nd Revised Edition. Basel, Switzerland: Karger.
- Whitford GM, Allmann DW, Shahed AR. 1987. Topical fluorides: Effects on physiologic and biochemical processes. *J Dent Res* 66:1072–1078.
- Whiting SJ, Pluhator MM. 1992. Comparison of in vitro and in vivo tests for determination of availability of calcium from calcium carbonate tablets. *J Am Coll Nutr* 11:553–560.
- Whiting SJ, Wood RJ. 1997. Adverse effects of high-calcium diets in humans. *Nutr Rev* 55:1–9.
- WHO (World Health Organization). 1984. *Fluorine and Fluorides*. Environmental Health Criteria 36. Geneva: World Health Organization. Pp. 77–79.
- WHO (World Health Organization). 1987. *Principles for the Safety Assessment of Food Additives and Contaminants in Food*. Environmental Health Criteria 70. Geneva: World Health Organization.

- WHO (World Health Organization). 1994. *Assessment of Fracture Risk and its Application to Screening for Postmenopausal Osteoporosis*. Technical Report Series 843. Geneva: World Health Organization.
- WHO (World Health Organization). 1996. *Trace Elements in Human Nutrition and Health*. Prepared in collaboration with the Food and Agriculture Organization of the United Nations and the International Atomic Energy Agency. Geneva: World Health Organization.
- Wickham CA, Walsh K, Cooper C, Barker DJ, Margetts BM, Morris J, Bruce SA. 1989. Dietary calcium, physical activity, and risk of hip fracture: A prospective study. *Br Med J* 299:889–892.
- Widdowson EM. 1965. Absorption and excretion of fat, nitrogen, and minerals from “filled” milks by babies one week old. *Lancet* 2:1099–1105.
- Widdowson EM, Dickerson JWT. 1964. The chemical composition of the body. In: Comar CL, Bronner F, eds. *Mineral Metabolism: An Advanced Treatise, Vol. II. The Elements, Part A*. New York: Academic Press.
- Widdowson EM, McCance RA, Spray CM. 1951. The chemical composition of the human body. *Clin Sci* 10:113–125.
- Widman L, Wester PO, Stegmayr BK, Wirell M. 1993. The dose-dependent reduction in blood pressure through administration of magnesium. A double blind placebo controlled cross-over study. *Am J Hypertens* 6:41–45.
- Wiktorsson AM, Martinsson T, Zimmerman M. 1992. Caries prevalence among adults in communities with optimal and low water fluoride concentrations. *Community Dent Oral Epidemiol* 20:359–363.
- Wilkinson R. 1976. Absorption of calcium, phosphorus, and magnesium. In: Nor din BEC, ed. *Calcium, Phosphate and Magnesium Metabolism*. Edinburgh: Churchill Livingstone. Pp. 36–112.
- Willett W. 1990. *Nutritional Epidemiology*. New York, NY: Oxford University Press.
- Willett WC, Sampson L, eds. 1997. Dietary assessment methods. *Am J Clin Nutr* 65:1097S–1368S.
- Williams JE, Zwemer JD. 1990. Community water fluoride levels, preschool dietary patterns, and the occurrence of fluoride dental opacities. *J Pub Hlth Dent* 50:276–281.
- Williams ML, Rose CS, Morrow G, Sloan SE, Barness LA. 1970. Calcium and fat absorption in neonatal period. *Am J Clin Nutr* 23:1322–1330.
- Wilson SG, Retallack RW, Kent JC, Worth GK, Gutteridge DH. 1990. Serum free 1,25-dihydroxyvitamin D and the free 1,25-dihydroxyvitamin D index during a longitudinal study of human pregnancy and lactation. *Clin Endocrinol* 32:613–622.
- Wise A, Gilbert DJ. 1982. Phytate hydrolysis by germfree and conventional rats. *Appl Environ Microbiol* 43:753–756.
- Wisker E, Nagel R, Tanudjaja TK, Feldheim W. 1991. Calcium, magnesium, zinc, and iron balances in young women: Effects of a low-phytate barley-fiber concentrate. *Am J Clin Nutr* 54:553–559.
- Witterman JC, Willett WC, Stampfer MJ, Colditz GA, Sacks FM, Speizer FE, Rosner B, Hennekens CH. 1989. A prospective study of nutritional factors and hypertension among U.S. women. *Circulation* 80:1320–1327.

- Witteman JC, Grobbee DE, Derkx FH, Bouillon R, de Brujin AM, Hofman A. 1994. Reduction of blood pressure with oral magnesium supplementation in women with mild to moderate hypertension. *Am J Clin Nutr* 60:129–135.
- Wong NL, Quamme GA, Dirks JH. 1986. Effects of acid-base disturbances on renal handling of magnesium in the dog. *Clin Sci* 70:277–284.
- Wood RJ, Zheng JJ. 1990. Milk consumption and zinc retention in postmenopausal women. *J Nutr* 120:398–403.
- Wood RJ, Sitrin MD, Rosenberg IH. 1988. Effect of phosphorus on endogenous calcium losses during total parenteral nutrition. *Am J Clin Nutr* 48:632–636.
- Woods KL, Fletcher S. 1994. Long-term outcome after intravenous magnesium sulphate in suspected acute myocardial infarction: The second Leicester Intravenous Magnesium Intervention Trial (LIMIT-2). *Lancet* 343:816–819.
- Workshop Reports. 1992. *J Dent Res* 71:1218–1227.
- Yamagata Z, Miyamura T, Iijima S, Asaka A, Sasaki M, Kato J, Koizumi K. 1994. Vitamin D receptor gene polymorphism and bone mineral density in healthy Japanese women. *Lancet* 344:1027.
- Yamamoto ME, Applegate WB, Klag MJ, Borhani NO, Cohen JD, Kirchner KA, Lakatos E, Sacks FM, Taylor JO, Hennekens CH. 1995. Lack of blood pressure effect with calcium and magnesium supplementation in adults with high-normal blood pressure. Results from Phase I of the Trials of Hypertension Prevention (TOHP). Trials of Hypertension Prevention (TOHP) Collaborative Research Group. *Ann Epidemiol* 5:96–107.
- Yano K, Heilbrun LK, Wasnich RD, Hankin JH, Vogel JM. 1985. The relationship between diet and bone mineral content of multiple skeletal sites in elderly Japanese men and women living in Hawaii. *Am J Clin Nutr* 42:877–888.
- Young GP, Thomas RJ, Bourne DW, Russell DM. 1985. Parenteral nutrition. *Med J Aust* 143:597–601.
- Zeghoud F, Vervel C, Guillozo H, Walrant-Debray O, Boutignon H, Garabedian M. 1997. Subclinical vitamin D deficiency in neonates: Definition and response to vitamin D supplements. *Am J Clin Nutr* 65:771–778.
- Zemel PC, Zemel MB, Urberg M, Douglas FL, Geiser R, Sower JR. 1990. Metabolic and hemodynamic effects of magnesium supplementation in patients with essential hypertension. *Am J Clin Nutr* 51:665–669.
- Ziegler EE, Fomon SJ. 1983. Lactose enhances mineral absorption in infancy. *J Pediatr Gastroenterol Nutr* 2:228–294.
- Zielhuis RL, van der Kreek FW. 1979. The use of a safety factor in setting health-based permissible levels for occupational exposure. *Int Arch Occup Environ Health* 42:191–201.
- Zipkin I, Zucas SM, Lavender DR, Fullmer HM, Schiffmann E, Corcoran BA. 1970. Fluoride and calcification of rat aorta. *Calcif Tissue Res* 6:173–182.

## VITAMIN E

*Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids* (ISBN 0-309-06949-1), Chapter 6, pp. 262–283.

- AAP (American Academy of Pediatrics). 1998. *Pediatric Nutrition Handbook*, 4th edition. Elk Grove Village, IL: AAP. P. 67.
- Abbasi S, Ludomirski A, Bhutani VK, Weiner S, Johnson L. 1990. Maternal and fetal plasma vitamin E to total lipid ratio and fetal RBC antioxidant function during gestational development. *J Am Coll Nutr* 9:314–319.
- Abdo KM, Rao G, Montgomery CA, Dinowitz M, Kanagalingam K. 1986. Thirteen-week toxicity study of *d*-alpha-tocopheryl acetate (vitamin E) in Fischer 344 rats. *Food Chem Toxicol* 24:1043–1050.
- Acuff RV, Thedford SS, Hidirogloiu NN, Papas AM, Odom TA. 1994. Relative bioavailability of *RRR*- and *all-rac*-alpha-tocopheryl acetate in humans: Studies using deuterated compounds. *Am J Clin Nutr* 60:397–402.
- Acuff RV, Webb LW, Brooks IJ, Papas AM, Lane JR. 1997. Pharmacokinetics of *RRR*-gamma-tocopherol in humans after a single dose administration of deuterium-labeled gamma-tocopherol in humans. *FASEB J* 11:A449.
- Adam O, Lemmen C, Kless T, Adam P, Denzlinger C, Hailer S. 1995. Low fat diet decreases alpha-tocopherol levels, and stimulates LDL oxidation and eicosanoid biosynthesis in man. *Eur J Med Res* 1:65–71.
- Adler LA, Edson R, Lavori P, Peselow E, Duncan E, Rosenthal M, Rotrosen J. 1998. Long-term treatment effects of vitamin E for tardive dyskinesia. *Biol Psychiatry* 43:868–872.
- AIN (American Institute of Nutrition). 1990. Nomenclature policy: Generic descriptors and trivial names for vitamins and related compounds. *J Nutr* 120:12–19.
- Ali J, Kader HA, Hassan K, Arshat H. 1986. Changes in human milk vitamin E and total lipids during the first twelve days of lactation. *Am J Clin Nutr* 43:925–930.
- Alexy U, Kersting M, Sichert-Hellert W, Manz F, Schöch G. 1999. Vitamin intake of 3- to 36-month-old German infants and children—Results of the DONALD-study. *Int J Vitam Nutr Res* 69:285–291.
- Allen JC, Keller RP, Archer P, Neville MC. 1991. Studies in human lactation: Milk composition and daily secretion rates of macronutrients in the first year of lactation. *Am J Clin Nutr* 54:69–80.
- Ames BN, Gold LS, Willett WC. 1995. The causes and prevention of cancer. *Proc Natl Acad Sci USA* 92:5258–5265.
- Amiel J, Maziere J, Beucler I, Koenig M, Reutenuer L, Loux N, Bonnefont D, Feo C, Landrieu P. 1995. Familial isolated vitamin E deficiency. Extensive study of a large family with a 5-year therapeutic follow-up. *J Inherit Metab Dis* 18:333–340.
- Anderson DM, Pittard WB. 1985. Vitamin E and C concentrations in human milk with maternal megadosing. A case report. *J Am Diet Assoc* 85:715–717.
- Anderson TW, Reid DB. 1974. A double-blind trial of vitamin E in angina pectoris. *Am J Clin Nutr* 27:1174–1178.
- Andersson SO, Wolk A, Bergstrom R, Giovannucci E, Lindgren C, Baron J, Adami HO. 1996. Energy, nutrient intake and prostate cancer risk: A population-based case-control study in Sweden. *Int J Cancer* 68:716–722.

- Arita M, Sato Y, Miyata A, Tanabe T, Takahashi E, Kayden H, Arai H, Inoue K. 1995. Human alpha-tocopherol transfer protein: cDNA cloning, expression and chromosomal localization. *Biochem J* 306:437–443.
- Ascherio A, Stampfer MJ, Colditz GA, Rimm EB, Litin L, Willett WC. 1992. Correlations of vitamin A and E intakes with the plasma concentrations of carotenoids and tocopherols among American men and women. *J Nutr* 122:1792–1801.
- ATBC (Alpha-Tocopherol, Beta Carotene) Cancer Prevention Study Group. 1994. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. *N Engl J Med* 330:1029–1035.
- Awad JA, Morrow JD, Hill KE, Roberts LJ II, Burk RF. 1994. Detection and localization of lipid peroxidation in selenium- and vitamin E-deficient rats using F<sub>2</sub>-isoprostanes. *J Nutr* 124:810–816.
- Azen SP, Mack WJ, Cashin-Hemphill L, LaBree L, Shircore AM, Selzer RH, Blanckenhorn DH, Hodis HN. 1996a. Progression of coronary artery disease predicts clinical coronary events. Long-term follow-up from the Cholesterol Lowering Atherosclerosis Study. *Circulation* 93:34–41.
- Azen SP, Qian D, Mack WJ, Sevanian A, Selzer RH, Liu CR, Liu CH, Hodis HN. 1996b. Effect of supplementary antioxidant vitamin intake on carotid arterial wall intima-media thickness in a controlled clinical trial of cholesterol lowering. *Circulation* 94:2369–2372.
- Azzi A, Boscoboinik D, Marilley D, Ozer NK, Stauble B, Tasinato A. 1995. Vitamin E: A sensor and an information transducer of the cell oxidation state. *Am J Clin Nutr* 62:1337S–1346S.
- Bae CY, Keenan JM, Fontaine P, Wenz J, Ripsin CM, McCaffrey DJ. 1993. Plasma lipid response and nutritional adequacy in hypercholesterolemic subjects on the American Heart Association Step-One Diet. *Arch Fam Med* 2:765–772.
- Bayliss EA, Hambidge KM, Sokol RJ, Stewart B, Lilly JR. 1995. Hepatic concentrations of zinc, copper and manganese in infants with extrahepatic biliary atresia. *J Trace Elem Med Biol* 9:40–43.
- Baynes JW. 1991. Role of oxidative stress in development of complications in diabetes. *Diabetes* 40:405–412.
- Bendich A. 1994. Role of antioxidants in the maintenance of immune functions. In: Frei B, ed. *Natural Antioxidants in Human Health and Disease*. San Diego: Academic Press. Pp. 447–467.
- Bendich A, Machlin LJ. 1988. Safety of oral intake of vitamin E. *Am J Clin Nutr* 48:612–619.
- Ben Hamida M, Belal S, Sirugo G, Ben Hamida C, Panayides K, Ionannou P, Beckmann J, Mandel JL, Hentati F, Koenig M, Middleton L. 1993. Friedreich's ataxia phenotype not linked to chromosome 9 and associated with selective autosomal recessive vitamin E deficiency in two inbred Tunisian families. *Neurology* 43:2179–2183.
- Bieri JG, Evarts RP. 1973. Tocopherols and fatty acids in American diets. The recommended allowance for vitamin E. *J Am Diet Assoc* 62:147–151.
- Bieri JG, Evarts RP. 1974. Gamma-tocopherol: Metabolism, biological activity and significance in human vitamin E nutrition. *Am J Clin Nutr* 27:980–986.
- Bieri JG, McKenna MC. 1981. Expressing dietary values for fat-soluble vitamins: Changes in concepts and terminology. *Am J Clin Nutr* 34:289–295.
- Bjørneboe A, Bjørneboe GE, Hagen BF, Nossen JO, Drevon CA. 1987. Secretion of alpha-tocopherol from cultured rat hepatocytes. *Biochim Biophys Acta* 922:199–205.

- Blomstrand R, Forsgren L. 1968. Labelled tocopherols in man. Intestinal absorption and thoracic-duct lymph transport of *dl*-alpha-tocopheryl-3,4-14C2 acetate *dl*-alpha-tocopheramine-3,4-14C2 *dl*-alpha-tocopherol-(5-methyl-3H) and *N*-(methyl-3H)-*dl*-gamma-tocopheramine. *Z Vitaminforsch* 38:328–344.
- Boda V, Finckh B, Durken M, Commentz J, Hellwege HH, Kohlschutter A. 1998. Monitoring erythrocyte free radical resistance in neonatal blood microsamples using a peroxy radical-mediated haemolysis test. *Scand J Clin Lab Invest* 58:317–322.
- Boersma ER, Offringa PJ, Muskiet FA, Chase WM, Simmons IJ. 1991. Vitamin E, lipid fractions, and fatty acid composition of colostrum, transitional milk, and mature milk: An international comparative study. *Am J Clin Nutr* 53:1197–1204.
- Boscoboinik D, Szewczyk A, Hensey C, Azzi A. 1991. Inhibition of cell proliferation by alpha-tocopherol. Role of protein kinase C. *J Biol Chem* 266:6188–6194.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Nutrition Examination Survey: Underreporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Brown K, Reid A, White T, Henderson T, Hukin S, Johnstone C, Glen A. 1998. Vitamin E, lipids, and lipid peroxidation products in tardive dyskinesia. *Biol Psychiatry* 43:863–867.
- Buettner GR. 1993. The pecking order of free radicals and antioxidants: Lipid peroxidation, alpha-tocopherol, and ascorbate. *Arch Biochem Biophys* 300:535–543.
- Burck U, Goebel HH, Kuhlendahl HD, Meier C, Goebel KM. 1981. Neuromyopathy and vitamin E deficiency in man. *Neuropediatrics* 12:267–278.
- Burton GW, Ingold KU. 1981. Autoxidation of biological molecules. I. The antioxidant activity of vitamin E and related chain-breaking phenolic antioxidants in vitro. *J Am Chem Soc* 103:6472–6477.
- Burton GW, Ingold KU. 1986. Vitamin E: Application of the principles of physical organic chemistry to the exploration of its structure and function. *Acc Chem Res* 19:194–201.
- Burton GW, Joyce A, Ingold KU. 1983. Is vitamin E the only lipid-soluble, chain-breaking antioxidant in human blood plasma and erythrocyte membranes? *Arch Biochem Biophys* 221:281–290.
- Burton GW, Doba T, Gabe EJ, Hughes L, Lee FL, Prasad L, Ingold KU. 1985. Autoxidation of biological molecules. 4. Maximizing the antioxidant activity of phenols. *J Am Chem Soc* 107:7053–7065.
- Burton GW, Traber MG, Acuff RV, Walters DN, Kayden H, Hughes L, Ingold KU. 1998. Human plasma and tissue alpha-tocopherol concentrations in response to supplementation with deuterated natural and synthetic vitamin E. *Am J Clin Nutr* 67:669–684.
- Butte NF, Garza C, Smith EO, Nichols BL. 1984. Human milk intake and growth in exclusively breast-fed infants. *J Pediatr* 104:187–195.
- Cachia O, Benna JE, Pedruzzoli E, Descomps B, Gougerot-Pocidalo MA, Leger CL. 1998. Alpha-tocopherol inhibits the respiratory burst in human monocytes. Attenuation of p47(phox) membrane translocation and phosphorylation. *J Biol Chem* 273:32801–32805.
- Calzada C, Bruckdorfer R, Rice-Evans CA. 1997. The influence of antioxidant nutrients on platelet function in healthy volunteers. *Atherosclerosis* 128:97–105.
- Catignani GL, Bieri JG. 1977. Rat liver alpha-tocopherol binding protein. *Biochim Biophys Acta* 497:349–357.

- Cavalier L, Ouahchi K, Kayden HJ, DiDonato S, Reutener L, Mandel J-L, Koenig M. 1998. Ataxia with isolated vitamin E deficiency: Heterogeneity of mutations and phenotypic variability in a large number of families. *Am J Hum Genet* 62:301–310.
- Ceballos-Picot I, Nicole A, Briand P, Grimer G, Delacourte A, Defossez A, Javoy-Agid F, Lafon M, Blouin JL, Sinet PM. 1991. Neuronal-specific expression of human copper-zinc superoxide dismutase gene in transgenic mice: Animal model of gene dosage effects in Down's syndrome. *Brain Res* 552:198–214.
- Ceriello A, Giugliano D, Quatraro A, Donzella C, Dipalo G, Lefebvre PJ. 1991. Vitamin E reduction of protein glycosylation in diabetes. New prospect for prevention of diabetic complications? *Diabetes Care* 14:68–72.
- Chan AC, Leith MK. 1981. Decreased prostacyclin synthesis in vitamin E-deficient rabbit aorta. *Am J Clin Nutr* 34:2341–2347.
- Chan AC, Tran K, Raynor T, Ganz PR, Chow CK. 1991. Regeneration of vitamin E in human platelets. *J Biol Chem* 266:17290–17295.
- Chan AC, Wagner M, Kennedy C, Chen E, Lanuville O, Mezl VA, Tran K, Choy PC. 1998a. Vitamin E up-regulates arachidonic acid release and phospholipase A<sup>2</sup> in megakaryocytes. *Mol Cell Biochem* 189:153–159.
- Chan AC, Wagner M, Kennedy C, Mroske C, Proulx P, Laneuville O, Tran K, Choy PC. 1998b. Vitamin E up-regulates phospholipase A<sup>2</sup>, arachidonic acid release and cyclooxygenase in endothelial cells. *Akt Ernahr-Med* 23:1–8.
- Chappell JE, Francis T, Clandinin MT. 1985. Vitamin A and E content of human milk at early stages of lactation. *Early Hum Devel* 11:157–167.
- Chatelain E, Boscoboinik DO, Bartoli GM, Kagan VE, Gey F, Packer L, Azzi A. 1993. Inhibition of smooth muscle cell proliferation and protein kinase C activity by tocopherols and tocotrienols. *Biochim Biophys Acta* 1176:83–89.
- Cheeseman KH, Holley AE, Kelly FJ, Wasil M, Hughes L, Burton G. 1995. Biokinetics in humans of RRR-alpha-tocopherol: The free phenol, acetate ester, and succinate ester forms of vitamin E. *Free Radic Biol Med* 19:591–598.
- Chen LH, Boissonneault GA, Glauert HP. 1988. Vitamin C, vitamin E and cancer. *Anticancer Res* 8:739–748.
- Chopra RK, Bhagavan HN. 1999. Relative bioavailabilities of natural and synthetic vitamin E formulations containing mixed tocopherols in human subjects. *Int J Vitam Nutr Res* 69:92–95.
- Church DF, Pryor WA. 1985. Free-radical chemistry of cigarette smoke and its toxicological implications. *Environ Hlth Perspect* 64:111–126.
- Clement M, Bourre JM. 1997. Graded dietary levels of RRR-gamma-tocopherol induce a marked increase in the concentrations of alpha- and gamma-tocopherol in nervous tissues, heart, liver and muscle of vitamin-E-deficient rats. *Biochim Biophys Acta* 1334:173–1781.
- Clement S, Tasinato A, Boscoboinik D, Azzi A. 1997. The effect of alpha-tocopherol on the synthesis, phosphorylation and activity of protein kinase C in smooth muscle cells after phorbol 12-myristate 13-acetate down-regulation. *Eur J Biochem* 246:745–749.
- Cohn W, Loechleiter F, Weber F. 1988. Alpha-tocopherol is secreted from rat liver in very low density lipoproteins. *J Lipid Res* 29:1359–1366.
- Colette C, Pares-Herbute N, Monnier LH, Cartry E. 1988. Platelet function in type I diabetes: Effects of supplementation with large doses of vitamin E. *Am J Clin Nutr* 47:256–261.

- Cominacini L, Garbin U, Pasini AF, Davoli A, Campagnola M, Contessi GB, Pastorino AM, Lo Cascio V. 1997. Antioxidants inhibit the expression of intercellular cell adhesion molecule-1 and vascular cell adhesion molecule-1 induced by oxidized LDL on human umbilical vein endothelial cells. *Free Radic Biol Med* 22:117–127.
- Comstock GW, Bush TL, Helzlsouer K. 1992. Serum retinol, beta-carotene, vitamin E, and selenium as related to subsequent cancer of specific sites. *Am J Epidemiol* 135:115–121.
- Comstock GW, Alberg AJ, Huang HY, Wu K, Burke AE, Hoffman SC, Norkus EP, Gross M, Cutler RG, Morris JS, Spate VL, Helzlsouer KJ. 1997. The risk of developing lung cancer associated with antioxidants in the blood: Ascorbic acid, carotenoids, alpha-tocopherol, selenium, and total peroxy radical absorbing capacity. *Cancer Epidemiol Biomarkers Prev* 6:907–916.
- Cornett CR, Markesberry WR, Ehmann WD. 1998. Imbalances of trace elements related to oxidative damage in Alzheimer's disease brain. *Neurotoxicology* 19: 339–345.
- Corrigan JJ Jr, Marcus FI. 1974. Coagulopathy associated with vitamin E ingestion. *J Am Med Assoc* 230:1300–1301.
- Cross CE, Eiserich JP, Halliwell B. 1997. General biological consequences of inhaled environmental toxicants. In: Crystal RG, West JB, Barnes PJ, Weibel ER, eds. *The Lung: Scientific Foundations*, 2nd edition. Philadelphia: Lippincott-Raven. Pp. 2421–2437.
- Cynamon HA, Milov DE, Valenstein E, Wagner M. 1988. Effect of vitamin E deficiency on neurologic function in patients with cystic fibrosis. *J Pediatr* 113:637–640.
- Dam H. 1962. Interrelations between vitamin E and polyunsaturated fatty acids in animals. *Vitam Horm* 20:527–540.
- Davi G, Ciabattoni G, Consoli A, Mezzetti A, Falco A, Santarone S, Pennese E, Vitacolonna E, Bucciarelli T, Costantini F, Capani F, Patrono C. 1999. In vivo formation of 8-iso-prostaglandin F2a and platelet activation in diabetes mellitus. Effects of improved metabolic control and vitamin E supplementation. *Circulation* 99:224–229.
- DeCosse JJ, Miller HH, Lesser ML. 1989. Effect of wheat fiber and vitamins C and E on rectal polyps in patients with familial adenomatous polyposis. *J Natl Cancer Inst* 81:1290–1297.
- Delanty N, Reilly M, Pratico D, FitzGerald DJ, Lawson JA, FitzGerald GA. 1996. 8-Epi PGF2 alpha: Specific analysis of an isoeicosanoid as an index of oxidant stress in vivo. *Br J Clin Pharmacol* 42:15–19.
- DeMaio SJ, King SB 3rd, Lembo NJ, Roubin GS, Hearn JA, Bhagavan HN, Sgoutas DS. 1992. Vitamin E supplementation, plasma lipids and incidence of restenosis after percutaneous transluminal coronary angioplasty (PTCA). *J Am Coll Nutr* 11:68–73.
- Devaraj S, Li D, Jialal I. 1996. The effects of alpha tocopherol supplementation on monocyte function. Decreased lipid oxidation, interleukin 1 $\beta$  secretion, and monocyte adhesion to endothelium. *J Clin Invest* 98:756–763.
- Devaraj S, Adams-Huet B, Fuller CJ, Jialal I. 1997. Dose-response comparison of *RRR*-alpha-tocopherol and all-racemic alpha-tocopherol on LDL oxidation. *Arterioscler Thromb Vasc Biol* 17:2273–2279.

- de Vries JH, Hollman PC, Meyboom S, Buysman MN, Zock PL, van Staveren WA, Katan MB. 1998. Plasma concentrations and urinary excretion of the antioxidant flavonols quercetin and kaempferol as biomarkers for dietary intake. *Am J Clin Nutr* 68:60–65.
- Dial S, Eitenmiller RR. 1995. Tocopherols and tocotrienols in key foods in the U.S. diet. In: Ong ASH, Niki E, Packer L, eds. *Nutrition, Lipids, Health, and Disease*. Champaign, IL: AOCS Press. Pp. 327–342.
- Dieber-Rotheneder M, Puhl H, Waeg G, Striegl G, Esterbauer H. 1991. Effect of oral supplementation with *d*-alpha-tocopherol on the vitamin E content of human low density lipoproteins and resistance to oxidation. *J Lipid Res* 32: 1325–1332.
- Dimitrov NV, Meyer C, Gilliland D, Ruppenthal M, Chenoweth W, Malone W. 1991. Plasma tocopherol concentrations in response to supplemental vitamin E. *Am J Clin Nutr* 53:723–729.
- Dimitrov NV, Meyer-Leece C, McMillan J, Gilliland D, Perloff M, Malone W. 1996. Plasma alpha-tocopherol concentrations after supplementation with water- and fat-soluble vitamin E. *Am J Clin Nutr* 64:329–335.
- Doba T, Burton GW, Ingold KU. 1985. Antioxidant and co-antioxidant activity of vitamin C. The effect of vitamin C, either alone or in the presence of vitamin E or a water-soluble vitamin E analogue, upon the peroxidation of aqueous multilamellar phospholipid liposomes. *Biochim Biophys Acta* 835:298–303.
- Dorgan JF, Sowell A, Swanson CA, Potischman N, Miller R, Schussler N, Stephenson HE. 1998. Relationships of serum carotenoids, retinol, alpha-tocopherol, and selenium with breast cancer risk: Results from a prospective study in Columbia, Missouri (United States). *Cancer Causes Control* 9:89–97.
- Draper HH. 1993. Interrelationships of vitamin E with other nutrients. In: Packer L, Fuchs J, eds. *Vitamin E in Health and Disease*. New York: Marcel Dekker. Pp. 53–61.
- Duthie GG, Arthur JR, James WP. 1991. Effects of smoking and vitamin E on blood antioxidant status. *Am J Clin Nutr* 53:1061S–1063S.
- Duthie SJ, Ross M, Collins AR. 1995. The influence of smoking and diet on the hypoxanthine phosphoribosyltransferase (hprt) mutant frequency in circulating T lymphocytes from a normal human population. *Mutat Res* 331:55–64.
- Duthie SJ, Ma A, Ross MA, Collins AR. 1996. Antioxidant supplementation decreases oxidative DNA damage in human lymphocytes. *Cancer Res* 56:1291–1295.
- Dysmsza HA, Park J. 1975. Excess dietary vitamin E in rats. *Fed Am Soc Exp Biol* 34:912.
- Egan MF, Hyde TM, Albers GW, Elkashef A, Alexander RC, Reeve A, Blum A, Saenz RE, Wyatt RJ. 1992. Treatment of tardive dyskinesia with vitamin E. *Am J Psychiatry* 149:773–777.
- Eichholzer M, Stahelin HB, Gey KF, Ludin E, Bernasconi F. 1996. Prediction of male cancer mortality by plasma levels of interacting vitamins: 17-year follow-up of the prospective Basel study. *Int J Cancer* 66:145–150.
- Eiserich JP, van der Vliet A, Handelman GJ, Halliwell B, Cross CE. 1995. Dietary antioxidants and cigarette smoke-induced biomolecular damage: A complex interaction. *Am J Clin Nutr* 62:1490S–1500S.
- Eiserich JP, Cross CE, Van der Vliet A. 1997. Nitrogen oxides are important contributors to cigarette smoke-induced ascorbate oxidation. In: Packer L, Fuchs J, eds. *Vitamin C in Health and Disease*. New York: Marcel Dekker. Pp. 399–412.

- Eitenmiller RR, Landen WO Jr. 1995. Vitamins. In: Jeon IJ, Ikins WG, eds. *Analyzing Food for Nutrition Labeling and Hazardous Contaminants*. New York: Marcel Dekker. Pp. 195–281.
- Elias E, Muller DP, Scott J. 1981. Association of spinocerebellar disorders with cystic fibrosis or chronic childhood cholestasis and very low serum vitamin E. *Lancet* 2:1319–1321.
- Elkashef AM, Ruskin PE, Bacher N, Barrett D. 1990. Vitamin E in the treatment of tardive dyskinesia. *Am J Psychiatry* 147:505–506.
- Ernster VL, Goodson WH, Hunt TK, Petrakis NL, Sickles EA, Miike R. 1985. Vitamin E and benign breast “disease”: A double-blind, randomized clinical trial. *Surgery* 97:490–494.
- Farrell PM, Bieri JG. 1975. Megavitamin E supplementation in man. *Am J Clin Nutr* 28:1381–1386.
- Farrell PM, Bieri JG, Fratantoni JF, Wood RE, Di Sant’Agnese PA. 1977. The occurrence and effects of human vitamin E deficiency. A study in patients with cystic fibrosis. *J Clin Invest* 60:233–241.
- Farrell PM, Mischler EH, Gutcher GR. 1982. Evaluation of vitamin E deficiency in children with lung disease. *Ann NY Acad Sci* 393:96–108.
- Faruqi R, de la Motte C, DiCorleto PE. 1994. Alpha-tocopherol inhibits agonist-induced monocytic cell adhesion to cultured human endothelial cells. *J Clin Invest* 94:592–600.
- Finer, NN, Peters, KL, Hayek, Z, Merkel, CL. 1984. Vitamin E and necrotizing enterocolitis. *Pediatrics* 73:387-93.
- Ford ES, Sowell A. 1999. Serum alpha-tocopherol status in the United States population: Findings from the Third National Health and Nutrition Examination Survey. *Am J Epidemiol* 150:290–300.
- Freedman JE, Farhat JH, Loscalzo J, Keaney JF Jr. 1996. Alpha-tocopherol inhibits aggregation of human platelets by a protein kinase C-dependent mechanism. *Circulation* 94:2434–2440.
- Fuller CJ, Chandalia M, Garg A, Grundy SM, Jialal I. 1996. *RRR*-alpha-Tocopheryl acetate supplementation at pharmacologic doses decreases low-density-lipoprotein oxidative susceptibility but not protein glycation in patients with diabetes mellitus. *Am J Clin Nutr* 63:753–759.
- Gallo-Torres HE. 1970. Obligatory role of bile for the intestinal absorption of vitamin E. *Lipids* 5:379–384.
- Gascón-Vila P, García-Closas R, Serra-Majem L, Pastor MC, Ribas L, Ramon JM, Marine-Font A, Salleras L. 1997. Determinants of the nutritional status of vitamin E in a non-smoking Mediterranean population. Analysis of the effect of vitamin E intake, alcohol consumption and body mass index on the serum alpha-tocopherol concentration. *Eur J Clin Nutr* 51:723–728.
- Ghalaut VS, Ghalaut PS, Kharb S, Singh GP. 1995. Vitamin E in intestinal fat malabsorption. *Ann Nutr Metab* 39:296–301.
- Gisinger C, Jeremy J, Speiser P, Mikhailidis D, Dandona P, Schernthaner G. 1988. Effect of vitamin E supplementation on platelet thromboxane A2 production in type I diabetic patients. Double-blind crossover trial. *Diabetes* 37:1260–1264.
- GISSI-Prevenzione Investigators. 1999. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: Results of the GISSI-Prevenzione Trial. *Lancet* 354:447–455.
- Gotoda T, Arita M, Arai H, Inoue K, Yokota T, Fukuo Y, Yazaki Y, Yamada N. 1995. Adult-onset spinocerebellar dysfunction caused by a mutation in the gene for the alpha-tocopherol-transfer protein. *N Engl J Med* 333:1313–1318.

- Greenberg ER, Baron JA, Tosteson TD, Freeman DH, Beck GJ, Bond JH, Colacicchio TA, Coller JA, Frankl HD, Haile RW, Mandel JS, Nierenberg DW, Rothstein R, Snover DC, Stevens MM, Summers RW, van Stolk RU. 1994. A clinical trial of antioxidant vitamins to prevent colorectal adenoma. *N Engl J Med* 331:141–147.
- Haddad EH, Berk LS, Kettering JD, Hubbard RW, Peters WR. 1999. Dietary intake and biochemical, hematologic, and immune status of vegans compared with nonvegetarians. *Am J Clin Nutr* 70:586S–593S.
- Halliwell B. 1999. Establishing the significance and optimal intake of dietary antioxidants: The biomarker concept. *Nutr Rev* 57:104–113.
- Hammans SR, Kennedy CR. 1998. Ataxia with isolated vitamin E deficiency presenting as mutation negative Friedreich's ataxia. *J Neurol Neurosurg Psychiatry* 64:368–370.
- Handelman GJ, Epstein WL, Peerson J, Spiegelman D, Machlin LJ, Dratz EA. 1994. Human adipose alpha-tocopherol and gamma-tocopherol kinetics during and after 1 y of alpha-tocopherol supplementation. *Am J Clin Nutr* 59:1025–1032.
- Hankinson SE, Stampfer MJ, Seddon JM, Colditz GA, Rosner B, Speizer FE, Willett WC. 1992. Nutrient intake and cataract extraction in women: A prospective study. *Br Med J* 305:335–339.
- Harding AE, Matthews S, Jones S, Ellis CJ, Booth IW, Muller DP. 1985. Spinocerebellar degeneration associated with a selective defect of vitamin E absorption. *N Engl J Med* 313:32–35.
- Harries JT, Muller DP. 1971. Absorption of different doses of fat soluble and water miscible preparations of vitamin E in children with cystic fibrosis. *Arch Dis Child* 46:341–344.
- Hartz SC, Otradovec CL, McGandy RB, Russell RM, Jacob RA, Sahyoun N, Peters H, Abrams D, Scura LA, Whinston-Perry RA. 1988. Nutrient supplement use by healthy elderly. *J Am Coll Nutr* 7:119–128.
- Hartz SC, Russell RM, Rosenberg IH. 1992. *Nutrition in the Elderly. The Boston Nutritional Status Survey*. London: Smith-Gordon. P. 106–108.
- Hassan H, Hashim SA, Van Itallie TB, Sebrell WH. 1966. Syndrome in premature infants associated with low plasma vitamin E levels and high polyunsaturated fatty acid diet. *Am J Clin Nutr* 19:147–157.
- Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. 1993. Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: The DARLING Study. *Am J Clin Nutr* 58:152–161.
- Heinonen OP, Albane D, Virtamo J, Taylor PR, Huttunen JK, Hartman AM, Haa-pakoski J, Malila N, Rautalahti M, Ripatti S, Mäenpää H, Teerenhovi L, Koss L, Virolainen M, Edwards BK. 1998. Prostate cancer and supplementation with alpha-tocopherol and beta-carotene: Incidence and mortality in a controlled trial. *J Natl Cancer Inst* 90:440–446.
- Higashi O, Kikuchi Y. 1974. Effects of vitamin E on the aggregation and the lipid peroxidation of platelets exposed to hydrogen peroxide. *Tohoku J Exp Med* 112:271–278.
- Hodis HN, Mack WJ, LaBree L, Cashin-Hemphill L, Sevanian A, Johnson R, Azen SP. 1995. Serial coronary angiographic evidence that antioxidant vitamin intake reduces progression of coronary artery atherosclerosis. *J Am Med Assoc* 273:1849–1854.

- Hofstad B, Almendingen K, Vatn M, Andersen S, Owen R, Larsen S, Osnes M. 1998. Growth and recurrence of colorectal polyps: A double-blind 3-year intervention with calcium and antioxidants. *Digestion* 59:148–156.
- HOPE Study Investigators. 2000. Vitamin E supplementation and cardiovascular events in high-risk patients. *N Engl J Med* 342:154–160.
- Horwitt MK. 1960. Vitamin E and lipid metabolism in man. *Am J Clin Nutr* 8:451–461.
- Horwitt MK. 1962. Interrelations between vitamin E and polyunsaturated fatty acids in adult men. *Vitam Horm* 20:541–558.
- Horwitt MK. 1974. Status of human requirements for vitamin E. *Am J Clin Nutr* 27:1182–1193.
- Horwitt MK. 1976. Vitamin E: A reexamination. *Am J Clin Nutr* 29:569–578.
- Horwitt MK, Harvey CC, Duncan GD, Wilson WC. 1956. Effects of limited tocopherol intake in man with relationships to erythrocyte hemolysis and lipid oxidations. *Am J Clin Nutr* 4:408–419.
- Horwitt MK, Century B, Zeman AA. 1963. Erythrocyte survival time and reticulocyte levels after tocopherol depletion in man. *Am J Clin Nutr* 12:99–106.
- Horwitt MK, Harvey CC, Dahm CH, Searcy MT. 1972. Relationship between tocopherol and serum lipid levels for determination of nutritional adequacy. *Ann NY Acad Sci* 203:223–236.
- Hosomi A, Arita M, Sato Y, Kiyose C, Ueda T, Igarashi O, Arai H, Inoue K. 1997. Affinity for alpha-tocopherol transfer protein as a determinant of the biological activities of vitamin E analogs. *FEBS Lett* 409:105–108.
- Ingold KU, Webb AC, Witter D, Burton GW, Metcalfe TA, Muller DPR. 1987. Vitamin E remains the major lipid-soluble, chain-breaking antioxidant in human plasma even in individuals suffering severe vitamin E deficiency. *Arch Biochem Biophys* 259:224–225.
- IOM (Institute of Medicine). 1991. *Nutrition During Lactation*. Washington, DC: National Academy Press. P. 179.
- Ishizuka T, Itaya S, Wada H, Ishizawa M, Kimura M, Kajita K, Kanoh Y, Miura A, Muto N, Yasuda K. 1998. Differential effect of the antidiabetic thiazolidinediones troglitazone and pioglitazone on human platelet aggregation mechanism. *Diabetes* 47:1494–1500.
- Islam KN, Devaraj S, Jialal I. 1998. Alpha-tocopherol enrichment of monocytes decreases agonist-induced adhesion to human endothelial cells. *Circulation* 98:2255–2261.
- IUPAC-IUB Commission on Biochemical Nomenclature. 1974. Nomenclature of tocopherols and related compounds. Recommendations 1973. *Eur J Biochem* 46:217–219.
- Jacob RA, Kutnink MA, Csallany AS, Daroszewska M, Burton GW. 1996. Vitamin C nutriture has little short-term effect on vitamin E concentrations in healthy women. *J Nutr* 126:2268–2277.
- Jacques PF, Chylack LT Jr. 1991. Epidemiologic evidence of a role for the antioxidant vitamins and carotenoids in cataract prevention. *Am J Clin Nutr* 53:352S–355S.
- Jacques PF, Chylack LT Jr, Taylor A. 1994. Relationships between natural antioxidants and cataract formation. In: Frei B, ed. *Natural Antioxidants in Human Health and Disease*. San Diego: Academic Press. Pp. 515–529.
- Jain SK, McVie R, Jaramillo JJ, Palmer M, Smith T. 1996a. Effect of modest vitamin E supplementation on blood glycated hemoglobin and triglyceride levels and red cell indices in type I diabetic patients. *J Am Coll Nutr* 15:458–461.

- Jain SK, McVie R, Jaramillo JJ, Palmer M, Smith T, Meachum ZD, Little RL. 1996b. The effect of modest vitamin E supplementation on lipid peroxidation products and other cardiovascular risk factors in diabetic patients. *Lipids* 31:S87–S90.
- Jain SK, Krueger KS, McVie R, Jaramillo JJ, Palmer M, Smith T. 1998. Relationship of blood thromboxane-B2 (TxB2) with lipid peroxides and effect of vitamin E and placebo supplementation on TxB2 and lipid peroxide levels in type 1 diabetic patients. *Diabetes Care* 21:1511–1516.
- Jansson L, Akesson B, Holmberg L. 1981. Vitamin E and fatty acid composition of human milk. *Am J Clin Nutr* 34:8–13.
- Jialal I, Fuller CJ, Huet BA. 1995. The effect of alpha-tocopherol supplementation on LDL oxidation. A dose-response study. *Arterioscler Thromb Vasc Biol* 15:190–198.
- Johnson L, Bowen FW, Abbasi S, Herrmann N, Weston M, Sacks L, Porat R, Stahl G, Peckham G, Delivoria-Papadopoulos M, Quinn G, Schaffer D. 1985. Relationship of prolonged pharmacologic serum levels of vitamin E to incidence of sepsis and necrotizing enterocolitis in infants with birth weight 1,500 grams or less. *Pediatrics* 75:619–638.
- Jones PJH, Kubow S. 1999. Lipids, sterols and their metabolism. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease, 9th edition*. Baltimore, MD: Williams & Wilkins. Pp. 347–362.
- Kalra V, Grover J, Ahuja GK, Rathi S, Khurana DS. 1998. Vitamin E deficiency and associated neurological deficits in children with protein-energy malnutrition. *J Trop Pediatr* 44:291–295.
- Kamal-Eldin A, Appelqvist LA. 1996. The chemistry and antioxidant properties of tocopherols and tocotrienols. *Lipids* 31:671–701.
- Kantoci D, Wechter WJ, Murray ED Jr, Dewind SA, Borchardt D, Khan SI. 1997. Endogenous natriuretic factors 6: The stereochemistry of a natriuretic gamma-tocopherol metabolite LLU-alpha. *J Pharmacol Exp Ther* 282:648–656.
- Kappus H, Diplock AT. 1992. Tolerance and safety of vitamin E: A toxicological position report. *Free Radic Biol Med* 13:55–74.
- Kardinaal AF, van 't Veer P, Brants HA, van den Berg H, van Schoonhoven J, Hermus RJ. 1995. Relations between antioxidant vitamins in adipose tissue, plasma, and diet. *Am J Epidemiol* 141:440–450.
- Kayden HJ, Hatam LJ, Traber MG. 1983. The measurement of nanograms of tocopherol from needle aspiration biopsies of adipose tissue: Normal and abetalipoproteinemic subjects. *J Lipid Res* 24:652–656.
- Kelleher J, Losowsky MS. 1970. The absorption of alpha-tocopherol in man. *Br J Nutr* 24:1033–1047.
- Keller JN, Pang Z, Geddes JW, Begley JG, Germeyer A, Waeg G, Mattson MP. 1997. Impairment of glucose and glutamate transport and induction of mitochondrial oxidative stress and dysfunction in synaptosomes by amyloid beta-peptide: Role of the lipid peroxidation product 4-hydroxynonenal. *J Neurochem* 69:273–284.
- Kim JM, White RH. 1996. Effect of vitamin E on the anticoagulant response to warfarin. *Am J Cardiol* 77:545–546.
- Kitagawa M, Mino M. 1989. Effects of elevated alpha (RRR)-tocopherol dosage in man. *J Nutr Sci Vitaminol* 35:133–142.
- Kiyose C, Muramatsu R, Fujiyama-Fujiwara Y, Ueda T, Igarashi O. 1995. Biodiscrimination of alpha-tocopherol stereoisomers during intestinal absorption. *Lipids* 30:1015–1018.

- Kiyose C, Muramatsu R, Kameyama Y, Ueda T, Igarashi O. 1997. Biodiscrimination of alpha-tocopherol stereoisomers in humans after oral administration. *Am J Clin Nutr* 65:785–789.
- Klein T, Reutter F, Schweer H, Seyberth HW, Nusing RM. 1997. Generation of the isoprostane 8-epi-prostaglandin F<sub>2alpha</sub> in vitro and in vivo via the cyclooxygenases. *J Pharmacol Exp Ther* 282:1658–1665.
- Knek P, Aromaa A, Maatela J, Aaran RK, Nikkari T, Hakama M, Hakulinen T, Peto R, Saxen E, Teppo L. 1988. Serum vitamin E and risk of cancer among Finnish men during a 10-year follow-up. *Am J Epidemiol* 127:28–41.
- Knek P, Heliovaara M, Rissanen A, Aromaa A, Aaran RK. 1992. Serum antioxidant vitamins and risk of cataract. *Br Med J* 305:1392–1394.
- Knek P, Reunanen A, Jarvinen R, Seppanen R, Heliovaara M, Aromaa A. 1994. Antioxidant vitamin intake and coronary mortality in a longitudinal population study. *Am J Epidemiol* 139:1180–1189.
- Kobayashi H, Kanno C, Yamauchi K, Tsugo T. 1975. Identification of alpha-, beta-, gamma-, and delta-tocopherols and their contents in human milk. *Biochim Biophys Acta* 380:282–290.
- Kohlschütter A, Hubner C, Jansen W, Lindner SG. 1988. A treatable familial neuromyopathy with vitamin E deficiency, normal absorption, and evidence of increased consumption of vitamin E. *J Inher Metab Dis* 11:149–152.
- Kostner GM, Oettl K, Jauhiainen M, Ehnholm C, Esterbauer H, Dieplinger H. 1995. Human plasma phospholipid transfer protein accelerates exchange/transfer of alpha-tocopherol between lipoproteins and cells. *Biochem J* 305:659–667.
- Krasavage WJ, Terhaar CJ. 1977. *d*-alpha-Tocopheryl poly(ethylene glycol) 1000 succinate. Acute toxicity, subchronic feeding, reproduction, and teratologic studies in the rat. *J Agric Food Chem* 25:273–278.
- Krendel DA, Gilchrist JM, Johnson AO, Bossen EH. 1987. Isolated deficiency of vitamin E with progressive neurologic deterioration. *Neurology* 37:538–540.
- Kuhlenkamp J, Ronk M, Yusin M, Stolz A, Kaplowitz N. 1993. Identification and purification of a human liver cytosolic tocopherol binding protein. *Protein Expr Purif* 4:382–389.
- Kunisaki M, Umeda F, Inoguchi T, Watanabe J, Nawata H. 1990. Effects of vitamin E administration on platelet function in diabetes mellitus. *Diabetes Res* 14:37–42.
- Kunisaki M, Bursell SE, Umeda F, Nawata H, King GL. 1994. Normalization of diacylglycerol-protein kinase C activation by vitamin E in aorta of diabetic rats and cultured rat smooth muscle cells exposed to elevated glucose levels. *Diabetes* 43:1372–1377.
- Kushi LH, Folsom AR, Prineas RJ, Mink PJ, Wu Y, Bostick RM. 1996. Dietary antioxidant vitamins and death from coronary heart disease in postmenopausal women. *N Engl J Med* 334:1156–1162.
- Laditan AA, Ette SI. 1982. Plasma alpha-tocopherol (vitamin E) levels and tocopherol-lipid ratio among children with protein-energy malnutrition (PEM). *Ann Trop Paediatr* 2:85–88.
- Lammi-Keefe CJ, Jensen RG, Clark RM, Ferris AM. 1985. Alpha tocopherol, total lipid and linoleic acid contents of human milk at 2, 6, 12, and 16 weeks. In: Schaub J, ed. *Composition and Physiological Properties of Human Milk*. New York: Elsevier Science. Pp. 241–245.
- Lammi-Keefe CJ, Ferris AM, Jensen RG. 1990. Changes in human milk at 0600, 1000, 1400, 1800, and 2200 h. *J Pediatr Gastroenterol Nutr* 11:83–88.

- Laplante P, Vanasse M, Michaud J, Geoffroy G, Brochu P. 1984. A progressive neurological syndrome associated with an isolated vitamin E deficiency. *Can J Neurol Sci* 11:561–564.
- Lehmann J, Martin HL, Lashley EL, Marshall MW, Judd JT. 1986. Vitamin E in foods from high and low linoleic acid diets. *J Am Diet Assoc* 86:1208–1216.
- Leo MA, Ahmed S, Aleynik SI, Siegel JH, Kasmin F, Lieber CS. 1995. Carotenoids and tocopherols in various hepatobiliary conditions. *J Hepatol* 23:550–556.
- Leske MC, Chylack LT Jr, Wu SY. 1991. The Lens Opacities Case-Control Study. Risk factors for cataract. *Arch Ophthalmol* 109:244–251.
- Lohr JB, Cadet JL, Lohr MA, Jeste DV, Wyatt RJ. 1987. Alpha-tocopherol in tardive dyskinesia. *Lancet* 1:913–914.
- Lohr JB, Kuczenski R, Bracha HS, Moir M, Jeste DV. 1990. Increased indices of free radical activity in the cerebrospinal fluid of patients with tardive dyskinesia. *Biol Psychiatry* 28:535–539.
- London RS, Sundaram GS, Murphy L, Manimekalai S, Reynolds M, Goldstein PJ. 1985. The effect of vitamin E on mammary dysplasia: A double-blind study. *Obstet Gynecol* 65:104–106.
- Losonczy KG, Harris TB, Havlik RJ. 1996. Vitamin E and vitamin C supplement use and risk of all-cause and coronary heart disease mortality in older persons: The Established Populations for Epidemiologic Studies of the Elderly. *Am J Clin Nutr* 64:190–196.
- Losowsky MS, Kelleher J, Walker BE, Davies T, Smith CL. 1972. Intake and absorption of tocopherol. *Ann NY Acad Sci* 203:212–222.
- Machlin LJ. 1989. Use and safety of elevated dosages of vitamin E in adults. *Int J Vitam Nutr Res* 30:56–68.
- MacMahon MT, Neale G. 1970. The absorption of alpha-tocopherol in control subjects and in patients with intestinal malabsorption. *Clin Sci* 38:197–210.
- Manach C, Morand C, Crespy V, Demigne C, Texier O, Regerat F, Remesy C. 1998. Quercetin is recovered in human plasma as conjugated derivatives which retain antioxidant properties. *FEBS Lett* 426:331–336.
- Mandel CH, Mosca L, Maimon E, Sievers J, Tsai A, Rock CL. 1997. Dietary intake and plasma concentrations of vitamin E, vitamin C, and beta carotene in patients with coronary artery disease. *J Am Diet Assoc* 97:655–657.
- March BE, Wong E, Seier L, Sim J, Biely J. 1973. Hypervitaminosis E in the chick. *J Nutr* 103:371–377.
- Mares-Perlman JA, Brady WE, Klein R, Klein BE, Palta M, Bowen P, Stacewicz-Sapuntzakis M. 1994a. Serum levels of carotenoids and tocopherols in people with age-related maculopathy. *Invest Ophthalmol Vis Sci* 35:2004.
- Mares-Perlman JA, Klein BE, Klein R, Ritter LL. 1994b. Relation between lens opacities and vitamin and mineral supplement use. *Ophthalmology* 101:315–325.
- Martin A, Foxall T, Blumberg JB, Meydani M. 1997. Vitamin E inhibits low-density lipoprotein-induced adhesion of monocytes to human aortic endothelial cells in vitro. *Arterioscler Thromb Vasc Biol* 17:429–436.
- Martinello F, Fardin P, Ottina M, Ricchieri GL, Koenig M, Cavalier L, Trevisan CP. 1998. Supplemental therapy in isolated vitamin E deficiency improves the peripheral neuropathy and prevents the progression of ataxia. *J Neurol Sci* 156:177–179.
- McCay PB. 1985. Vitamin E: Interactions with free radicals and ascorbate. *Annu Rev Nutr* 5:323–340.

- McKeown-Eyssen G, Holloway C, Jazmaji V, Bright-See E, Dion P, Bruce WR. 1988. A randomized trial of vitamins C and E in the prevention of recurrence of colorectal polyps. *Cancer Res* 48:4701–4705.
- McLaughlin PJ, Weihrauch JL. 1979. Vitamin E content of foods. *J Am Diet Assoc* 75:647–665.
- Mellette SJ, Leone LA. 1960. Influence of age, sex, strain of rat and fat soluble vitamins on hemorrhagic syndromes in rats fed irradiated beef. *New Aspects Nutr* 19:1045–1049.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- Meydani M, Cohn JS, Macauley JB, McNamara JR, Blumberg JB, Schaefer EJ. 1989. Postprandial changes in the plasma concentration of alpha- and gamma-tocopherol in human subjects fed a fat-rich meal supplemented with fat-soluble vitamins. *J Nutr* 119:1252–1258.
- Meydani SN, Meydani M, Blumberg JB, Leka LS, Siber G, Loszewski R, Thompson C, Pedrosa MC, Diamond RD, Stollar BD. 1997. Vitamin E supplementation and in vivo immune response in healthy elderly subjects. A randomized controlled trial. *J Am Med Assoc* 277:1380–1386.
- Meydani SN, Meydani M, Blumberg JB, Leka LS, Pedrosa M, Diamond R, Schaefer EJ. 1998. Assessment of the safety of supplementation with different amounts of vitamin E in healthy older adults. *Am J Clin Nutr* 68:311–318.
- Mezzetti A, Lapenna D, Pierdomenico SD, Calafiore AM, Costantini F, Riario-Sforza G, Imbastaro T, Neri M, Cuccurullo F. 1995. Vitamins E, C and lipid peroxidation in plasma and arterial tissue of smokers and non-smokers. *Atherosclerosis* 112:91–99.
- Mohan M, Sperduto R, Angra S, Milton R, Mathur R, Underwood B, Jaffery N, Pandya C, Chhabra V, Vajpayee RB. 1989. India-US case-control study of age-related cataracts. India-US Case-Control Study Group. *Arch Ophthalmol* 107: 670–676.
- Molenaar R, Visser WJ, Verkerk A, Koster JF, Jongkind JF. 1989. Peroxidative stress and in vitro ageing of endothelial cells increases the monocyte-endothelial cell adherence in a human in vitro system. *Atherosclerosis* 76:193–202.
- Moore AN, Ingold KU. 1997. Alpha-tocopheryl quinone is converted into vitamin E in man. *Free Radic Biol Med* 22:931–934.
- Moore K, Roberts LJ II. 1998. Measurement of lipid peroxidation. *Free Radic Res* 28:659–671.
- Morrow JD, Frei B, Longmire AW, Gaziano JM, Lynch SM, Shyr Y, Strauss WE, Oates JA, Roberts LJ II. 1995. Increase in circulating products of lipid peroxidation ( $F^2$ -isoprostanes) in smokers. *N Engl J Med* 332:1198–1203.
- Morrow JD, Zackert WE, Yang JP, Kurhts EH, Callewaert D, Dworski R, Kanai K, Taber D, Moore K, Oates JA, Roberts LJ. 1999. Quantification of the major urinary metabolite of 15-F $2$ t-isoprostane (8-iso-PGF $2\alpha$ ) by a stable isotope dilution mass spectrometric assay. *Anal Biochem* 269:326–331.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance Data, Vital and Health Statistics of the National Center for Health Statistics. Number 174. Hyattsville, MD: National Center for Health Statistics.

- Mullarkey CJ, Edelstein D, Brownlee M. 1990. Free radical generation by early glycation products: A mechanism for accelerated atherogenesis in diabetes. *Biochem Biophys Res Commun* 173:932–939.
- Muller DP. 1994. Vitamin E and other antioxidants in neurological function and disease. In: Frei B, ed. *Natural Antioxidants in Human Health and Disease*. San Diego: Academic Press. Pp. 535–565.
- Muller DP, Harries JT, Lloyd JK. 1974. The relative importance of the factors involved in the absorption of vitamin E in children. *Gut* 15:966–971.
- Muller DP, Lloyd JK, Wolff OH. 1985. The role of vitamin E in the treatment of the neurological features of abetalipoproteinaemia and other disorders of fat absorption. *J Inher Metab Dis* 8:88–92.
- Murphy SP, Subar AF, Block G. 1990. Vitamin E intakes and sources in the United States. *Am J Clin Nutr* 52:361–367.
- Murray ED Jr, Wechter WJ, Kantoci D, Wang WH, Pham T, Quiggle DD, Gibson KM, Leipold D, Anner B. 1997. Endogenous natriuretic factors 7: Biospecificity of a natriuretic gamma-tocopherol metabolite LLU-alpha. *J Pharmacol Exp Ther* 282:657–662.
- Niki E. 1987. Antioxidants in relation to lipid peroxidation. *Chem Phys Lipids* 44: 227–253.
- Niki E, Tsuchiya J, Tanimura R, Kamiya Y. 1982. Regeneration of vitamin E from alpha-chromanoxyl radical by glutathione and vitamin C. *Chem Lett* 6:789–792.
- NRC (National Research Council). 1989. *Recommended Dietary Allowances*, 10th edition. Washington, DC: National Academy Press.
- O'Neill CA, Halliwell B, van der Vliet A, Davis PA, Packer L, Tritschler H, Strohman WJ, Rieland T, Cross CE, Reznick AZ. 1994. Aldehyde-induced protein modifications in human plasma: Protection by glutathione and dihydrolipoic acid. *J Lab Clin Med* 124:359–370.
- Osaki FA, Barness LA. 1967. Vitamin E deficiency: A previously unrecognized cause of hemolytic anemia in the premature infant. *J Pediatr* 70:211–220.
- Packer L. 1994. Vitamin E is nature's master antioxidant. *Sci Am Sci Med* 1:54–63.
- Pallast EG, Schouten EG, de Waart FG, Fonk HC, Doeke G, von Blomberg BM, Kok FJ. 1999. Effect of 50- and 100-mg vitamin E supplements on cellular immune function in noninstitutionalized elderly persons. *Am J Clin Nutr* 69: 1273–1281.
- Paolisso G, D'Amore A, Galzerano D, Balbi V, Giugliano D, Varricchio M, D'Onofrio F. 1993. Daily vitamin E supplements improve metabolic control but not insulin secretion in elderly type II diabetic patients. *Diabetes Care* 16:1433–1437.
- Parker RA, Sabrah T, Cap M, Gill BT. 1995. Relation of vascular oxidative stress, alpha-tocopherol, and hypercholesterolemia to early atherosclerosis in hamsters. *Arterioscler Thromb Vasc Biol* 15:349–358.
- Parker RS. 1988. Carotenoid and tocopherol composition of human adipose tissue. *Am J Clin Nutr* 47:33–36.
- Parkinson Study Group. 1993. Effects of tocopherol and deprenyl on the progression of disability in early Parkinson's disease. *N Engl J Med* 328:176–183.
- Parkinson Study Group. 1998. Mortality in DATATOP: A multicenter trial in early Parkinson's disease. *Ann Neurol* 43:318–325.
- Peng Y-S, Peng Y-M, McGee D, Alberts D. 1994. Carotenoids, tocopherols, and retinoids in human buccal mucosal cells: Intra- and interindividual variability and storage stability. *Am J Clin Nutr* 59:636–643.

## ONLINE REFERENCES

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- Phelps DL, Rosenbaum AL, Isenberg SJ, Leake RD, Dorey FJ. 1987. Tocopherol efficacy and safety for preventing retinopathy of prematurity: A randomized, controlled, double-masked trial. *Pediatrics* 79:489–500.
- Pratico D, Tangirala RK, Rader DJ, Rokach J, FitzGerald GA. 1998. Vitamin E suppresses isoprostane generation in vivo and reduces atherosclerosis in ApoE-deficient mice. *Nat Med* 4:1189–1192.
- Pratico D, Rokach J, Tangirala RK. 1999. Brains of aged apolipoprotein E-deficient mice have increased levels of F<sup>2</sup>-isoprostanes, in vivo markers of lipid peroxidation. *J Neurochem* 73:736–741.
- Princen HMG, van Duyvenvoorde W, Buytenhek R, van der Laarse A, van Poppel G, Gevers Leuven JA, van Hinsbergh VWM. 1995. Supplementation with low doses of vitamin E protects LDL from lipid peroxidation in men and women. *Arterioscler Thromb Vasc Biol* 15:325–333.
- Pryor WA, Stone K. 1993. Oxidants in cigarette smoke. Radicals, hydrogen peroxide, peroxynitrate, and peroxynitrite. *Ann NY Acad Sci* 686:12–27.
- Rader DJ, Brewer HB. 1993. Abetalipoproteinemia. New insights into lipoprotein assembly and vitamin E metabolism from a rare genetic disease. *J Am Med Assoc* 270:865–869.
- Rapola JM, Virtamo J, Ripatti S, Huttunen JK, Albanes D, Taylor PR, Heinonen OP. 1997. Randomised trial of alpha-tocopherol and beta-carotene supplements on incidence of major coronary events in men with previous myocardial infarction. *Lancet* 349:1715–1720.
- Reaven P. 1995. Dietary and pharmacologic regimens to reduce lipid peroxidation in non-insulin-dependent diabetes mellitus. *Am J Clin Nutr* 62:1483S–1489S.
- Reaven PD, Khouw A, Beltz WF, Parthasarathy S, Witztum JL. 1993. Effect of dietary antioxidant combinations in humans. Protection of LDL by vitamin E but not by beta-carotene. *Arterioscler Thromb* 13:590–600.
- Reaven PD, Herold DA, Barnett J, Edelman S. 1995. Effects of vitamin E on susceptibility of low-density lipoprotein and low-density lipoprotein subfractions to oxidation and on protein glycation in NIDDM. *Diabetes Care* 18:807–816.
- Refat M, Moore TJ, Kazui M, Risby TH, Perman JA, Schwarz KB. 1991. Utility of breath ethane as a noninvasive biomarker of vitamin E status in children. *Pediatr Res* 30:396–403.
- Reilly M, Delanty N, Lawson JA, Fitzgerald GA. 1996. Modulation of oxidant stress in vivo in chronic cigarette smokers. *Circulation* 94:19–25.
- Retzlaff BM, Dowdy AA, Walden CE, McCann BS, Gey G, Cooper M, Knopp RH. 1991. Changes in vitamin and mineral intakes and serum concentrations among free-living men on cholesterol-lowering diets: The Dietary Alternatives Study. *Am J Clin Nutr* 53:890–898.
- Rimm EB, Stampfer MJ, Ascherio A, Giovannucci E, Colditz GA, Willett WC. 1993. Vitamin E consumption and the risk of coronary heart disease in men. *N Engl J Med* 328:1450–1456.
- Ritchie JH, Fish MB, McMasters V, Grossman M. 1968. Edema and hemolytic anemia in premature infants. A vitamin E deficiency syndrome. *N Engl J Med* 279:1185–1190.
- Robertson JM, Donner AP, Trevithick JR. 1989. Vitamin E intake and risk of cataracts in humans. *Ann NY Acad Sci* 570:372–382.
- Ross MA, Crosley LK, Brown KM, Duthie SJ, Collins AC, Arthur JR, Duthie GG. 1995. Plasma concentrations of carotenoids and antioxidant vitamins in Scottish males: Influences of smoking. *Eur J Clin Nutr* 49:861–865.

- Rota S, McWilliam NA, Baglin TP, Byrne CD. 1998. Atherogenic lipoproteins support assembly of the prothrombinase complex and thrombin generation: Modulation by oxidation and vitamin E. *Blood* 91:508–515.
- Sano M, Ernesto C, Thomas RG, Klauber MR, Schafer K, Grundman M, Woodbury P, Growdon J, Cotman CW, Pfeiffer E, Schneider LS, Thal LJ. 1997. A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzheimer's disease. The Alzheimer's Disease Cooperative Study. *N Engl J Med* 336:1216–1222.
- Sarkkinen ES, Uusitupa MI, Nyysönen K, Parviainen M, Penttilä I, Salonen JT. 1993. Effects of two low-fat diets, high and low in polyunsaturated fatty acids, on plasma lipid peroxides and serum vitamin E levels in free-living hypercholesterolaemic men. *Eur J Clin Nutr* 47:623–630.
- Sato Y, Hagiwara K, Arai H, Inoue K. 1991. Purification and characterization of the alpha-tocopherol transfer protein from rat liver. *FEBS Lett* 288:41–45.
- Schuelke M, Mayatepek E, Inter M, Becker M, Pfeiffer E, Speer A, Hubner C, Finckh B. 1999. Treatment of ataxia in isolated vitamin E deficiency caused by alpha-tocopherol transfer protein deficiency. *J Pediatr* 134:240–244.
- Schultz M, Leist M, Petrzika M, Gassmann B, Brigelius-Flohé R. 1995. Novel urinary metabolite of alpha-tocopherol, 2,5,7,8-tetramethyl-2(2'-carboxyethyl)-6-hydroxychroman, as an indicator of an adequate vitamin E supply? *Am J Clin Nutr* 62:1527S–1534S.
- Schultz M, Leist M, Elsner A, Brigelius-Flohé R. 1997. Alpha-carboxyethyl-6-hydroxychroman as urinary metabolite of vitamin E. *Methods Enzymol* 282:297–310.
- Schwab US, Sarkkinen ES, Lichtenstein AH, Li Z, Ordovas JM, Schaefer EJ, Uusitupa MI. 1998a. The effect of quality and amount of dietary fat on the susceptibility of low density lipoprotein to oxidation in subjects with impaired glucose tolerance. *Eur J Clin Nutr* 52:452–458.
- Schwab US, Vogel S, Lammi-Keeffe CJ, Ordovas JM, Schaefer EJ, Li Z, Ausman LM, Gaultier L, Goldin BR, Furr HC, Lichtenstein AH. 1998b. Varying dietary fat type of reduced-fat diets has little effect on the susceptibility of LDL to oxidative modification in moderately hypercholesterolemic subjects. *J Nutr* 128: 1703–1709.
- Semenkovich CF, Heinecke JW. 1997. The mystery of diabetes and atherosclerosis: Time for a new plot. *Diabetes* 46:327–334.
- Sheppard AJ, Pennington JAT, Weihrauch JL. 1993. Analysis and distribution of vitamin E in vegetable oils and foods. In: Packer L, Fuchs J, eds. *Vitamin E in Health and Disease*. New York: Marcel Dekker. Pp. 9–31.
- Shorer Z, Parvari R, Bril G, Sela BA, Moses S. 1996. Ataxia with isolated vitamin E deficiency in four siblings. *Pediatr Neurol* 15:340–343.
- Shoulson I. 1998. DATATOP: A decade of neuroprotective inquiry. Parkinson Study Group. Deprenyl and Tocopherol Antioxidative Therapy of Parkinsonism. *Ann Neurol* 44:S160–S166.
- Slesinski MJ, Subar AF, Kahle LL. 1996. Dietary intake of fat, fiber and other nutrients is related to the use of vitamin and mineral supplements in the United States: The 1992 National Health Interview Survey. *J Nutr* 126:3001–3008.
- Smith MA, Harris PL, Sayre LM, Perry G. 1997. Iron accumulation in Alzheimer disease is a source of redox-generated free radicals. *Proc Natl Acad Sci USA* 94:9866–9868.
- Sokol RJ. 1988. Vitamin E deficiency and neurologic disease. *Annu Rev Nutr* 8:351–373.

- Sokol RJ. 1993. Vitamin E deficiency and neurological disorders. In: Packer L, Fuchs J, eds. *Vitamin E in Health and Disease*. New York: Marcel Dekker. Pp. 815–849.
- Sokol RJ, Heubi JE, Iannaccone S, Bove KE, Balistreri WF. 1983. Mechanism causing vitamin E deficiency during chronic childhood cholestasis. *Gastroenterology* 85:1172–1182.
- Sokol RJ, Heubi JE, Iannaccone ST, Bove KE, Balistreri WF. 1984. Vitamin E deficiency with normal serum vitamin E concentrations in children with chronic cholestasis. *N Engl J Med* 310:1209–1212.
- Sokol RJ, Guggenheim M, Iannaccone ST, Barkhaus PE, Miller C, Silverman A, Balistreri WF, Heubi JE. 1985. Improved neurologic function after long-term correction of vitamin E deficiency in children with chronic cholestasis. *N Engl J Med* 313:1580–1586.
- Sokol RJ, Kayden HJ, Bettis DB, Traber MG, Neville H, Ringel S, Wilson WB, Stumpf DA. 1988. Isolated vitamin E deficiency in the absence of fat malabsorption—Familial and sporadic cases: Characterization and investigation of causes. *J Lab Clin Med* 111:548–559.
- Sokol RJ, Reardon MC, Accurso FJ, Stall C, Narkewicz M, Abman SH, Hammond KB. 1989. Fat-soluble-vitamin status during the first year of life in infants with cystic fibrosis identified by screening of newborns. *Am J Clin Nutr* 50:1064–1071.
- Sokol RJ, Butler-Simon N, Conner C, Heubi JE, Sinatra FR, Suchy FJ, Heyman MB, Perrault J, Rothbaum RJ, Levy J, Iannaccone ST, Shneider BL, Koch TK, Narkewicz MR. 1993. Multicenter trial of *d*-alpha-tocopheryl polyethylene glycol 1000 succinate for treatment of vitamin E deficiency in children with chronic cholestasis. *Gastroenterology* 104:1727–1735.
- Sparrow CP, Doepper TW, Olszewski J, Wu MS, Ventre J, Stevens KA, Chao YS. 1992. Low density lipoprotein is protected from oxidation and the progression of atherosclerosis is slowed in cholesterol-fed rabbits by the antioxidant *N,N'*-diphenyl-phenylenediamine. *J Clin Invest* 89:1885–1891.
- Speer ME, Blifeld C, Rudolph AJ, Chadda P, Holbein ME, Hittner HM. 1984. Intraventricular hemorrhage and vitamin E in the very low-birth-weight infant: Evidence for efficacy of early intramuscular vitamin E administration. *Pediatrics* 74:1107–1112.
- Stampfer MJ, Hennekens CH, Manson JE, Colditz GA, Rosner B, Willett WC. 1993. Vitamin E consumption and the risk of coronary disease in women. *N Engl J Med* 328:1444–1449.
- Stauble B, Boscoboinik D, Tasinato A, Azzi A. 1994. Modulation of activator protein-1 (AP-1) transcription factor and protein kinase C by hydrogen peroxide and *d*-alpha-tocopherol in vascular smooth muscle cells. *Eur J Biochem* 226:393–402.
- Stead RJ, Muller DP, Matthews S, Hodson ME, Batten JC. 1986. Effect of abnormal liver function on vitamin E status and supplementation in adults with cystic fibrosis. *Gut* 27:714–718.
- Steinberg D. 1997. Oxidative modification of LDL and atherogenesis. *Circulation* 95:1062–1071.
- Steinberg D, Parthasarathy S, Carew TE, Khoo JC, Witztum JL. 1989. Beyond cholesterol. Modifications of low-density lipoprotein that increase its atherogenicity. *N Engl J Med* 320:915–924.

- Steinbrecher UP, Parthasarathy S, Leake DS, Witztum JL, Steinberg D. 1984. Modification of low density lipoprotein by endothelial cells involves lipid peroxidation and degradation of low density lipoprotein phospholipids. *Proc Natl Acad Sci USA* 81:3883–3887.
- Steiner M, Anastasi J. 1976. Vitamin E. An inhibitor of the platelet release reaction. *J Clin Invest* 57:732–737.
- Stephens NG, Parsons A, Schofield PM, Kelly F, Cheeseman K, Mitchinson MJ. 1996. Randomised controlled trial of vitamin E in patients with coronary disease: Cambridge Heart Antioxidant Study (CHAOS). *Lancet* 347:781–786.
- Stocker R. 1999. The ambivalence of vitamin E in atherogenesis. *Trends Biochem Sci* 24:219–223.
- Stoyanovsky DA, Osipov AN, Quinn PJ, Kagan VE. 1995. Ubiquinone-dependent recycling of vitamin E radicals by superoxide. *Arch Biochem Biophys* 323:343–351.
- Stryker WS, Kaplan LA, Stein EA, Stampfer MJ, Sober A, Willett WC. 1988. The relation of diet, cigarette smoking, and alcohol consumption to plasma beta-carotene and alpha-tocopherol levels. *Am J Epidemiol* 127:283–296.
- Stumpf DA, Sokol R, Bettis D, Neville H, Ringel S, Angelini C, Bell R. 1987. Friedreich's disease: V. Variant form with vitamin E deficiency and normal fat absorption. *Neurology* 37:68–74.
- Subramaniam R, Koppal T, Green M, Yatin S, Jordan B, Drake J, Butterfield DA. 1998. The free radical antioxidant vitamin E protects cortical synaptosomal membranes from amyloid beta-peptide(25–35) toxicity but not from hydroxynonenal toxicity: Relevance to the free radical hypothesis of Alzheimer's disease. *Neurochem Res* 23:1403–1410.
- Swanson JE, Ben R, Burton GW, Parker RS. 1998. Urinary excretion of 2,7,8-trimethyl-2-(beta-carboxyethyl)-6-hydroxychroman (gamma-CEHC) represents a major pathway of elimination of gamma-tocopherol in humans. *FASEB J* 12:A658.
- Swanson JE, Ben RN, Burton GW, Parker RS. 1999. Urinary excretion of 2,7,8-trimethyl-2-(beta-carboxyethyl)-6-hydroxychroman is a major route of elimination of gamma-tocopherol in humans. *J Lipid Res* 40:665–671.
- Szczeklik A, Gryglewski RJ, Domagala B, Dworski R, Basista M. 1985. Dietary supplementation with vitamin E in hyperlipoproteinemias: Effects on plasma lipid peroxides, antioxidant activity, prostacyclin generation and platelet aggregability. *Thromb Haemostasis* 54:425–430.
- Takahashi O, Ichikawa H, Sasaki M. 1990. Hemorrhagic toxicity of d-alpha-tocopherol in the rat. *Toxicology* 63:157–165.
- Tappel AL. 1962. Vitamin E as the biological lipid antioxidant. *Vitam Horm* 20:493–510.
- Tasinato A, Boscoboinik D, Bartoli G, Maroni P, Azzi A. 1995. d-Alpha-tocopherol inhibition of vascular smooth muscle cell proliferation occurs at physiological concentrations, correlates with protein kinase C inhibition, and is independent of its antioxidant properties. *Proc Natl Acad Sci USA* 92:12190–12194.
- Taylor A. 1993. Cataract: Relationship between nutrition and oxidation. *J Am Coll Nutr* 12:138–146.
- Teikari JM, Rautalahti M, Haukka J, Jarvinen P, Hartman AM, Virtamo J, Albanes D, Heinonen O. 1998. Incidence of cataract operations in Finnish male smokers unaffected by alpha tocopherol or beta carotene supplements. *J Epidemiol Community Health* 52:468–472.

- Thomas MR, Pearsons MH, Demkowicz M, Chan IM, Lewis CG. 1981. Vitamin A and vitamin E concentration of the milk from mothers of pre-term infants and milk of mothers of full term infants. *Acta Vitaminol Enzymol* 3:135–144.
- Thorin E, Hamilton CA, Dominiczak MH, Reid JL. 1994. Chronic exposure of cultured bovine endothelial cells to oxidized LDL abolishes prostacyclin release. *Arterioscler Thromb* 14:453–459.
- Traber MG. 1999. Vitamin E. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th edition. Baltimore, MD: Williams & Wilkins. P. 347–362.
- Traber MG, Kayden HJ. 1987. Tocopherol distribution and intracellular localization in human adipose tissue. *Am J Clin Nutr* 46:488–495.
- Traber MG, Kayden HJ. 1989. Preferential incorporation of alpha-tocopherol vs gamma-tocopherol in human lipoproteins. *Am J Clin Nutr* 49:517–526.
- Traber MG, Kayden HJ, Green JB, Green MH. 1986. Absorption of water-miscible forms of vitamin E in a patient with cholestasis and in thoracic duct-cannulated rats. *Am J Clin Nutr* 44:914–923.
- Traber MG, Sokol RJ, Ringel SP, Neville HE, Thellman CA, Kayden HJ. 1987. Lack of tocopherol in peripheral nerves of vitamin E-deficient patients with peripheral neuropathy. *N Engl J Med* 317:262–265.
- Traber MG, Burton GW, Ingold KU, Kayden HJ. 1990a. *RRR*- and *SRR*-alpha-tocopherols are secreted without discrimination in human chylomicrons, but *RRR*-alpha-tocopherol is preferentially secreted in very low density lipoproteins. *J Lipid Res* 31:675–685.
- Traber MG, Rudel LL, Burton GW, Hughes L, Ingold KU, Kayden HJ. 1990b. Nascent VLDL from liver perfusions of cynomolgus monkeys are preferentially enriched in *RRR*- compared with *SRR*-alpha tocopherol: Studies using deuterated tocopherols. *J Lipid Res* 31:687–694.
- Traber MG, Burton GW, Hughes L, Ingold KU, Hidaka H, Malloy M, Kane J, Hyams J, Kayden HJ. 1992. Discrimination between forms of vitamin E by humans with and without genetic abnormalities of lipoprotein metabolism. *J Lipid Res* 33:1171–1182.
- Traber MG, Cohn W, Muller DP. 1993. Absorption, transport and delivery to tissues. In: Packer L, Fuchs J, eds. *Vitamin E in Health and Disease*. New York: Marcel Dekker. Pp. 35–51.
- Traber MG, Rader D, Acuff R, Brewer HB, Kayden HJ. 1994a. Discrimination between *RRR*- and all racemic-alpha-tocopherols labeled with deuterium by patients with abetalipoproteinemia. *Atherosclerosis* 108:27–37.
- Traber MG, Ramakrishnan R, Kayden HJ. 1994b. Human plasma vitamin E kinetics demonstrate rapid recycling of plasma *RRR*-alpha-tocopherol. *Proc Natl Acad Sci USA* 91:10005–10008.
- Traber MG, Elsner A, Brigelius-Flohé R. 1998. Synthetic as compared with natural vitamin E is preferentially excreted as alpha-CEHC in human urine: Studies using deuterated alpha-tocopheryl acetates. *FEBS Lett* 437:145–148.
- Trabert W, Stober T, Mielke U, Heck FS, Schimrigk K. 1989. Isolated vitamin E deficiency. *Fortschr Neurol Psychiatr* 57:495–501.
- Tran K, Chan AC. 1990. *R,R,R*-alpha-tocopherol potentiates prostacyclin release in human endothelial cells. Evidence for structural specificity of the tocopherol molecule. *Biochim Biophys Acta* 1043:189–197.
- Tran K, Proulx P, Chan AC. 1994. Vitamin E suppresses diacylglycerol (DAG) level in thrombin-stimulated endothelial cells through an increase of DAG kinase activity. *Biochim Biophys Acta* 1212:193–202.

- Tran K, Wong JT, Lee E, Chan AC, Choy PC. 1996. Vitamin E potentiates arachidonate release and phospholipase A<sup>2</sup> activity in rat heart myoblastic cells. *Biochem J* 319:385–391.
- Tsai AC, Kelley JJ, Peng B, Cook N. 1978. Study on the effect of megavitamin E supplementation in man. *Am J Clin Nutr* 31:831–837.
- Tsuchiya M, Thompson DF, Suzuki YJ, Cross CE, Packer L. 1992. Superoxide formed from cigarette smoke impairs polymorphonuclear leukocyte active oxygen generation activity. *Arch Biochem Biophys* 299:30–37.
- Tutuncu NB, Bayraktar M, Varli K. 1998. Reversal of defective nerve conduction with vitamin E supplementation in type 2 diabetes: A preliminary study. *Diabetes Care* 21:1915–1918.
- USP (The United States Pharmacopeia). 1979. *The United States Pharmacopeia. National Formulary*. Rockville, MD: United States Pharmacopeial Convention.
- USP (The United States Pharmacopeia). 1980. *The United States Pharmacopeia. National Formulary*. Rockville, MD: United States Pharmacopeial Convention.
- USP (The United States Pharmacopeia). 1999. *The United States Pharmacopeia 24. National Formulary 19*. Rockville, MD: United States Pharmacopeial Convention.
- Upston JM, Terentis AC, Stocker R. 1999. Tocopherol-mediated peroxidation of lipoproteins: Implications for vitamin E as a potential antiatherogenic supplement. *FASEB J* 13:977–994.
- van het Hof KH, Brouwer IA, West CE, Haddeman E, Steegers-Theunissen RPM, van Dusseldorp M, Weststrate JA, Eskes TKAB, Hautvast JGAJ. 1999. Bioavailability of lutein from vegetables is 5 times higher than that of β-carotene. *Am J Clin Nutr* 70:261–268.
- van 't Veer P, Strain JJ, Fernandez-Crehuet J, Martin BC, Thamm M, Kardinaal AF, Kohlmeier L, Huttunen JK, Martin-Moreno JM, Kok FJ. 1996. Tissue antioxidants and postmenopausal breast cancer: The European Community Multi-centre Study on Antioxidants, Myocardial Infarction, and Cancer of the Breast (EURAMIC). *Cancer Epidemiol Biomarkers Prev* 5:441–447.
- Vatassery GT, Fahn S, Kuskowski MA. 1998. Alpha tocopherol in CSF of subjects taking high-dose vitamin E in the DATATOP study. Parkinson Study Group. *Neurology* 50:1900–1902.
- Velthuis-te Wierik EJ, van den Berg H, Weststrate JA, van het Hof KH, de Graaf C. 1996. Consumption of reduced-fat products: Effects on parameters of anti-oxidative capacity. *Eur J Clin Nutr* 50:214–219.
- Verhoeven DT, Assen N, Goldbohm RA, Dorant E, van 't Veer P, Sturmans F, Hermus RJ, van den Brandt PA. 1997. Vitamins C and E, retinol, beta-carotene and dietary fibre in relation to breast cancer risk: A prospective cohort study. *Br J Cancer* 75:149–155.
- Vitale S, West S, Hallfrisch J, Alston C, Wang F, Moorman C, Muller D, Singh V, Taylor HR. 1993. Plasma antioxidants and risk of cortical and nuclear cataract. *Epidemiology* 4:195–203.
- Wander RC, Du SH, Ketchum SO, Rowe KE. 1996. Effects of interaction of RRR-alpha-tocopheryl acetate and fish oil on low-density-lipoprotein oxidation in postmenopausal women with and without hormone-replacement therapy. *Am J Clin Nutr* 63:184–193.
- Wechter WJ, Kantoci D, Murray ED, D'Amico DC, Jung ME, Wang W-H. 1996. A new endogenous natriuretic factor: LLU-alpha. *Proc Natl Acad Sci USA* 93:6002–6007.

- Weiser H, Vecchi M. 1981. Stereoisomers of alpha-tocopheryl acetate. Characterization of the samples by physico-chemical methods and determination of biological activities in the rat resorption-gestation test. *Int J Vitam Nutr Res* 51:100–113.
- Weiser H, Vecchi M. 1982. Stereoisomers of alpha-tocopheryl acetate. II. Biopotencies of all eight stereoisomers, individually or in mixtures, as determined by rat resorption-gestation tests. *Int J Vitam Nutr Res* 52:351–370.
- Weiser H, Vecchi M, Schlachter M. 1986. Stereoisomers of alpha-tocopheryl acetate. IV. USP units and alpha-tocopherol equivalents of all-rac-, 2-ambo- and RRR-alpha-tocopherol evaluated by simultaneous determination of resorption-gestation, myopathy and liver storage capacity in rats. *Int J Vitam Nutr Res* 56:45–56.
- Wheldon GH, Bhatt A, Keller P, Hummeler H. 1983. D,L-alpha-tocopheryl acetate (vitamin E): A long term toxicity and carcinogenicity study in rats. *Int J Vitam Nutr Res* 53:287–296.
- Winklhofer-Roob BM, Tuchschmid PE, Molinari L, Shmerling DH. 1996a. Response to a single oral dose of *all-rac*-alpha-tocopheryl acetate in patients with cystic fibrosis and in healthy individuals. *Am J Clin Nutr* 63:717–721.
- Winklhofer-Roob BM, van't Hof MA, Shmerling DH. 1996b. Long-term oral vitamin E supplementation in cystic fibrosis patients: *RRR*-alpha-tocopherol compared with *all-rac*-alpha-tocopheryl acetate preparations. *Am J Clin Nutr* 63:722–728.
- Winklhofer-Roob BM, van't Hof MA, Shmerling DH. 1997. Reference values for plasma concentrations of vitamin E and A and carotenoids in a Swiss population from infancy to adulthood, adjusted for seasonal influences. *Clin Chem* 43:146–153.
- Witting LA, Lee L. 1975. Dietary levels of vitamin E and polyunsaturated fatty acids and plasma vitamin E. *Am J Clin Nutr* 28:571–576.
- Yang NY, Desai ID. 1977. Effect of high levels of dietary vitamin E on hematological indices and biochemical parameters in rats. *J Nutr* 107:1410–1417.
- Yong LC, Brown CC, Schatzkin A, Dresser CM, Slesinski MJ, Cox CS, Taylor PR. 1997. Intake of vitamins E, C, and A and risk of lung cancer. The NHANES I Epidemiologic Followup Study. *Am J Epidemiol* 146:231–243.
- Yoshida H, Yusin M, Ren I, Kuhlenkamp J, Hirano T, Stolz A, Kaplowitz N. 1992. Identification, purification and immunochemical characterization of a tocopherol-binding protein in rat liver cytosol. *J Lipid Res* 33:343–350.
- Yoshida H, Ishikawa T, Nakamura H. 1997. Vitamin E/lipid peroxide ratio and susceptibility of LDL to oxidative modification in non-insulin-dependent diabetes mellitus. *Arterioscler Thromb Vasc Biol* 17:1438–1446.

Ibid., Chapter 9, 399–400.

- AIN (American Institute of Nutrition). 1990. Nomenclature policy: Generic descriptors and trivial names for vitamins and related compounds. *J Nutr* 120:12–19.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the third National Health and Nutrition Examination Survey: Underreporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- Horwitt MK. 1976. Vitamin E: A reexamination. *Am J Clin Nutr* 29:569–578.

- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances be Revised?* Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1997. *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride.* Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1998. *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline.* Washington, DC: National Academy Press.
- IUPAC-IUB Commission on Biochemical Nomenclature. 1974. Nomenclature of tocopherols and related compounds. Recommendations 1973. *Eur J Biochem* 46:217–219.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1980. *Drinking Water and Health*, Volume 3. Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys.* Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Swanson CA, Patterson BH, Levander OA, Veillon C, Taylor PR, Helzlsouer K, McAdam PA, Zech LA. 1991. Human [<sup>74</sup>Se]selenomethionine metabolism: A kinetic model. *Am J Clin Nutr* 54:917–926.
- Thomson CD, Robinson MF. 1986. Urinary and fecal excretions and absorption of a large supplement of selenium: Superiority of selenate over selenite. *Am J Clin Nutr* 44:659–663.
- USDA (U.S. Department of Agriculture). 1999. USDA Nutrient Database for Standard Reference, Release, [Online]. Available: <http://www.nal.usda.gov/fnic/foodcomp>.
- Weiser H, Vecchi M, Schlachter M. 1986. Stereoisomers of alpha-tocopherol acetate. IV. USP units and alpha-tocopherol equivalents of all-rac-, 2-ambo- and RRR-alpha-tocopherol evaluated by simultaneous determination of resorption-gestation, myopath and liver storage capacity in rats. *Int J Vitam Nutr Res* 56:45–56.
- Williams AW, Erdman JW Jr. 1999. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease.* Baltimore, MD: Williams and Wilkins. P. 181.

## FOLATE

*Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline* (ISBN 0-309-06411-2), Chapter 8, pp. 284–305.

- Abma J, Chandra A, Mosher W, Peterson L, Piccinino L. 1997. Fertility, Family Planning, and Women's Health: New Data from the 1995 National Survey of Family Growth. National Center for Health Statistics. *Vital Health Stat Series* 23, Number 19.
- Abou-Saleh MT, Coppen A. 1989. Serum and red blood cell folate in depression. *Acta Psychiatr Scand* 80:78–82.
- Adams MJ Jr, Khoury MJ, Scanlon KS, Stevenson RE, Knight GJ, Haddow JE, Sylvester GC, Cheek JE, Henry JP, Stabler SP. 1995. Elevated midtrimester serum methylmalonic acid levels as a risk factor for neural tube defects. *Teratology* 51:311–317.
- Agamanolis DP, Chester EM, Victor M, Kark JA, Hines JD, Harris JW. 1976. Neuropathology of experimental vitamin B<sub>12</sub> deficiency. *Neurology* 26:905–914.
- Allen RH, Stabler SP, Savage DG, Lindenbaum J. 1990. Diagnosis of cobalamin deficiency. I. Usefulness of serum methylmalonic acid and total homocysteine concentrations. *Am J Hematol* 34:90–98.
- Allen RH, Stabler SP, Lindenbaum J. 1993. Serum betaine, N,N-dimethylglycine and N-methylglycine levels in patients with cobalamin and folate deficiency and related inborn errors of metabolism. *Metabolism* 42:1448–1460.
- Alperin JB. 1966. Response to varied doses of folic acid and vitamin B<sub>12</sub> in megaloblastic anemia. *Clin Res* 14:52.
- Alpert JE, Fava M. 1997. Nutrition and depression: The role of folate. *Nutr Rev* 55:145–149.
- Andersson A, Hultberg B, Brattstrom L, Isaksson A. 1992. Decreased serum homocysteine in pregnancy. *Eur J Clin Chem Clin Biochem* 30:377–379.
- Arnaud J, Favier A, Herrmann MA, Pilorget JJ. 1992. Effect of folic acid and folinic acid on zinc absorption. *Ann Nutr Metab* 36:157–161.
- Asfour R, Wahbeh N, Waslien CI, Guindi S, Darby WJ. 1977. Folacin requirement of children. 3. Normal infants. *Am J Clin Nutr* 30:1098–1105.
- Baggott JE, Morgan SL, Ha TS, Vaughn WH, Hine RJ. 1992. Inhibition of folate-dependent enzymes by non-steroidal anti-inflammatory drugs. *Biochem J* 282:197–202.
- Bailey LB. 1988. Factors that affect folate bioavailability. *Food Technol* 42:206–212, 238.
- Bailey LB, Cerdá JJ, Bloch BS, Busby MJ, Vargas L, Chandler CJ, Halsted CH. 1984. Effect of age on poly- and monoglutamyl folacin absorption in human subjects. *J Nutr* 114:1770–1776.
- Bailey LB, Barton LE, Hillier SE, Cerdá JJ. 1988. Bioavailability of mono and polyglutamyl folate in human subjects. *Nutr Rep Int* 38:509–518.
- Baird PA. 1983. Neural tube defects in the Sikhs. *Am J Med Genet* 16:49–56.
- Baldwin CT, Hoth CF, Amos JA, da Silva EO, Milunsky A. 1992. An exonic mutation in the HuP2 paired domain gene causes Waardenburg's syndrome. *Nature* 355:637–638.
- Baldwin JN, Dalessio DJ. 1961. Folic acid therapy and spinal-cord degeneration in pernicious anemia. *N Engl J Med* 264:1339–1342.

- Bates CJ, Fleming M, Paul AA, Black AE, Mandal AR. 1980. Folate status and its relation to vitamin C in healthy elderly men and women. *Age Ageing* 9:241–248.
- Bates CJ, Mansoor MA, van der Pols J, Prentice A, Cole TJ, Finch S. 1997. Plasma total homocysteine in a representative sample of 972 British men and women aged 65 and over. *Eur J Clin Nutr* 51:691–697.
- Baxter MG, Millar AA, Webster RA. 1973. Some studies on the convulsant action of folic acid. *Br J Pharmacol* 48:350–351.
- Bell KM, Plon L, Bunney WE, Potkin SG. 1988. *S*-Adenosylmethionine treatment of depression: A controlled clinical trial. *Am J Psychiatry* 145:1110–1114.
- Beresford SA, Boushey CJ. 1997. Homocysteine, folic acid, and cardiovascular disease risk. In: Bendich A, Deckelbaum RJ, eds. *Preventive Nutrition: The Comprehensive Guide for Health Professionals*. Totowa, NJ: Humana Press.
- Bergmark C, Mansoor MA, Swedenborg J, de Faire U, Svardal AM, Ueland PM. 1993. Hyperhomocysteinemia in patients operated for lower extremity ischeamia below the age of 50—effect of smoking and extent of disease. *Eur J Vasc Surg* 7:391–396.
- Berk L, Bauer JL, Castle WB. 1948. A report of 12 patients treated with synthetic pteroylglutamic acid with comments on the pertinent literature. *S Afr Med J* 22:604–611.
- Best CN. 1959. Subacute combined degeneration of spinal cord after extensive resection of ileum in Crohn's disease: Report of a case. *Br Med J* 2:862–864.
- Bethell FH, Sturgis CC. 1948. The relations of therapy in pernicious anemia to changes in the nervous system. Early and late results in a series of cases observed for periods of not less than ten years, and early results of treatment with folic acid. *Blood* 3:57–67.
- Blaw ME, Woody RC. 1983. Valproic acid embryopathy? *Neurology* 33:255.
- Blount BC, Mack MM, Wehr CM, MacGregor JT, Hiatt RA, Wang G, Wickramasinghe SN, Everson RB, Ames BN. 1997. Folate deficiency causes uracil misincorporation into human DNA and chromosome breakage: Implications for cancer and neuronal damage. *Proc Natl Acad Sci USA* 94:3290–3295.
- Bonnette RE, Caudill MA, Bailey LB. 1998. Plasma homocysteine response to controlled folate intake in pregnant women. *Obstet Gynecol* 92:167–170.
- Borman GB, Smith AH, Howard JK. 1986. Risk factors in the prevalence of anencephalus and spina bifida in New Zealand. *Teratology* 33:221–230.
- Bottiglieri T, Hyland K, Reynolds EH. 1994. The clinical potential of ademetionine (*S*-adenosylmethionine) in neurological disorders. *Drugs* 48:137–152.
- Botto LD, Khoury MJ, Mulinare J, Erickson JD. 1996. Periconceptional multivitamin use and the occurrence of conotruncal heart defects: Results from a population-based, case-control study. *Pediatrics* 98:911–917.
- Boushey CJ, Beresford SA, Omenn GS, Motulsky AG. 1995. A quantitative assessment of plasma homocysteine as a risk factor for vascular disease. Probable benefits of increasing folic acid intakes. *J Am Med Assoc* 274:1049–1057.
- Bower C, Stanley FJ. 1989. Dietary folate as a risk factor for neural-tube defects: Evidence from a case-control study in Western Australia. *Med J Aust* 150:613–619.
- Bower C, Stanley FJ. 1992a. Dietary folate and nonneural midline birth defects: No evidence of an association from a case-control study in Western Australia. *Am J Med Genet* 44:647–650.

- Bower C, Stanley FJ. 1992b. Periconceptional vitamin supplementation and neural tube defects; evidence from a case-control study in Western Australia and a review of recent publications. *J Epidemiol Community Health* 46:157–161.
- Bower C, Hobbs M, Carney A, Simpson D. 1984. Neural tube defects in Western Australia 1966–81 and a review of Australian data 1942–81. *J Epidemiol Community Health* 38:208–213.
- Brattstrom LE, Herbebo JE, Hultberg BL. 1984. Moderate homocysteinemia—a possible risk factor for arteriosclerotic cerebrovascular disease. *Stroke* 15:1012–1016.
- Brattstrom LE, Israelsson B, Jeppsson JO, Hultberg BL. 1988. Folic acid—an innocuous means to reduce plasma homocysteine. *Scand J Clin Lab Invest* 48:215–221.
- Brattstrom LE, Israelsson B, Norrving B, Bergkvist D, Thorne J, Hultberg B, Hamfelt A. 1990. Impaired homocysteine metabolism in early-onset cerebral and peripheral occlusive arterial disease. Effects of pyridoxine and folic acid treatment. *Atherosclerosis* 81:51–60.
- Brock KE, Berry G, Mock PA, MacLennan R, Truswell AS, Brinton LA. 1988. Nutrients in diet and plasma and risk of in situ cervical cancer. *J Natl Cancer Inst* 80:580–585.
- Brown CM, Smith AM, Picciano MF. 1986. Forms of human milk folacin and variation patterns. *J Pediatr Gastroenterol Nutr* 5:278–282.
- Brown JE, Jacobs DR, Hartman TJ, Barosso GM, Stang JS, Gross MD, Zeuske MA. 1997. Predictors of red cell folate level in women attempting pregnancy. *J Am Med Assoc* 277:548–552.
- Bunduki V, Dommergues M, Zittoun J, Marquet J, Muller F, Dumez Y. 1995. Maternal-fetal folate status and neural tube defects: A case control study. *Biol Neonate* 67:154–159.
- Burke G, Robinson K, Refsum H, Stuart B, Drumm J, Graham I. 1992. Intrauterine growth retardation, perinatal death, and maternal homocysteine levels. *N Engl J Med* 326:69–70.
- Butterworth CE, Tamura T. 1989. Folic acid safety and toxicity: A brief review. *Am J Clin Nutr* 50:353–358.
- Butterworth CE Jr, Hatch K, Gore H, Meuller H, Krumdieck C. 1982. Improvement in cervical dysplasia associated with folic acid therapy in users of oral contraceptives. *Am J Clin Nutr* 35:73–82.
- Butterworth CE Jr, Hatch K, Cole P, Sauberlich HE, Tamura T, Cornwell PE, Soong S-J. 1988. Zinc concentration in plasma and erythrocytes of subjects receiving folic acid supplementation. *Am J Clin Nutr* 47:484–486.
- Butterworth CE Jr, Hatch K, Macaluso M, Cole P, Sauberlich HE, Soong S-J, Borst M, Baker V. 1992a. Folate deficiency and cervical dysplasia. *J Am Med Assoc* 267:528–533.
- Butterworth CE Jr, Hatch K, Soong S-J, Cole P, Tamura T, Sauberlich HE, Borst M, Macaluso M, Baker V. 1992b. Oral folic acid supplementation for cervical dysplasia: A clinical intervention trial. *Am J Obstet Gynecol* 166:803–809.
- Campbell NR. 1996. How safe are folic acid supplements? *Arch Intern Med* 156:1638–1644.
- Carmel R, Johnson CS. 1978. Racial patterns in pernicious anemia: Early age at onset and increased frequency of intrinsic-factor antibody in black women. *N Engl J Med* 298:647–650.

- Carney MW, Chary TK, Laundry M, Bottiglieri T, Chanarin I, Reynolds EH, Toone B. 1990. Red cell folate concentrations in psychiatric patients. *J Affect Disord* 19:207–213.
- Carter CO. 1974. Clues to the aetiology of neural tube malformations. *Dev Med Child Neurol* 16:3–15.
- Caudill MA, Cruz AC, Gregory JF 3rd, Hutson AD, Bailey LB. 1997. Folate status response to controlled folate intake in pregnant human subjects. *J Nutr* 127:2363–2370.
- Caudill MA, Gregory JF, Hutson AD, Bailey LB. 1998. Folate catabolism in pregnant and nonpregnant women with controlled folate intakes. *J Nutr* 128:204–208.
- CDC (Centers for Disease Control and Prevention). 1991. Use of folic acid for prevention of spina bifida and other neural tube defects—1983–1991. *Morb Mortal Wkly Rep* 40:513–516.
- CDC (Centers for Disease Control and Prevention). 1992. Recommendations for the use of folic acid to reduce the number of cases of spina bifida and other neural tube defects. *Morb Mortal Wkly Rep* 41:1–7.
- CDC (Centers for Disease Control and Prevention). 1998. Use of folic acid-containing supplements among women of childbearing age—United States, 1997. *Morb Mortal Wkly Rep* 47:131–134.
- Chadefaux B, Cooper BA, Gilfix BM, Lue-Shing H, Carson W, Gavsie A, Rosenblatt DS. 1994. Homocysteine: Relationship to serum cobalamin, serum folate, erythrocyte folate, and lobation of neutrophils. *Clin Invest Med* 17:540–550.
- Chanarin I, Rothman D, Ward A, Perry J. 1968. Folate status and requirement in pregnancy. *Br Med J* 2:390–394.
- Chanarin I, Deacon R, Lumb M, Perry J. 1989. Cobalamin-folate interrelations. *Blood Rev* 3:211–215.
- Chasan-Taber L, Selhub J, Rosenberg IH, Malinow MR, Terry M, Tishler PV, Willett W, Hennekens CH, Stampfer MJ. 1996. A prospective study of folate and vitamin B<sub>6</sub> and risk of myocardial infarction in U.S. physicians. *J Am Coll Nutr* 15:136–143.
- Chen LH, Liu ML, Hwang HY, Chen LS, Korenberg J, Shane B. 1997. Human methionine synthase, cDNA cloning, gene localization, and expression. *J Biol Chem* 272:3628–3634.
- Chodos RB, Ross JF. 1951. The effects of combined folic acid and liver extract therapy. *Blood* 6:1213–1233.
- Collins CS, Bailey LB, Hillier S, Cerdá JJ, Wilder BJ. 1988. Red blood cell uptake of supplemental folate in patients on anticonvulsant drug therapy. *Am J Clin Nutr* 48:1445–1450.
- Colman N. 1982. Addition of folic acid to staple foods as a selective nutrition intervention strategy. *Nutr Rev* 40:225–233.
- Colman N, Larsen JV, Barker M, Barker EA, Green R, Metz J. 1975. Prevention of folate deficiency by food fortification. 3. Effect in pregnant subjects of varying amounts of added folic acid. *Am J Clin Nutr* 28:465–470.
- Conley CL, Krevans JR. 1951. Development of neurologic manifestations of pernicious anemia during multivitamin therapy. *N Engl J Med* 245:529–531.
- Cooperman JM, Pesci-Bourel A, Luhby AL. 1970. Urinary excretion of folic acid activity in man. *Clin Chem* 16:375–381.
- Copp AJ, Bernfield M. 1994. Etiology and pathogenesis of human neural tube defects: Insights from mouse models. *Curr Opin Pediatr* 6:624–631.

- Coppen A, Abou-Saleh MT. 1982. Plasma folate and affective morbidity during long-term lithium therapy. *Br J Psychiatr* 141:87–89.
- Coppen A, Chaudhry S, Swade C. 1986. Folic acid enhances lithium prophylaxis. *J Affect Disord* 10:9–13.
- Cragan JD, Roberts HE, Edmonds LD, Khoury MJ, Kirby RS, Shaw GM, Velie EM, Merz RD, Forrester MB, Williamson RA. 1995. Surveillance for anencephaly and spina bifida and the impact of prenatal diagnosis—United States, 1985–1994. *CDC Surveill Summ* 44:1–13.
- Crosby WH. 1960. The danger of folic acid in multivitamin preparations. *Mil Med* 125:233–235.
- Cunningham FG, MacDonald PC, Grant NF. 1989. *Williams Obstetrics*. Norwalk, Conn.: Appleton & Lange.
- Curtis D, Sparrow R, Brennan L, Van der Weyden MB. 1994. Elevated serum homocysteine as a predictor for vitamin B<sub>12</sub> or folate deficiency. *Eur J Haematol* 52:227–232.
- Cuskelly GJ, McNulty H, Scott JM. 1996. Effect of increasing dietary folate on red-cell folate: Implications for prevention of neural tube defects. *Lancet* 347:657–659.
- Czeizel A. 1993. Prevention of congenital abnormalities by periconceptional multivitamin supplementation. *Br Med J* 306:1645–1648.
- Czeizel AE, Dudas I. 1992. Prevention of the first occurrence of neural-tube defects by periconceptional vitamin supplementation. *N Engl J Med* 327:1832–1835.
- Czeizel AE, Dudas I, Metneki J. 1994. Pregnancy outcomes in a randomized controlled trial of periconceptional multivitamin supplementation. Final report. *Arch Gynecol Obstet* 255:131–139.
- Czeizel AE, Toth M, Rockenbauer M. 1996. Population-based case control study of folic acid supplementation during pregnancy. *Teratology* 53:345–351.
- Dai WS, Hsu M-A, Itri LM. 1989. Safety of pregnancy after discontinuation of isotretinoin. *Arch Dermatol* 125:362–365.
- Dalery K, Lussier-Cacan S, Selhub J, Davignon J, Latour Y, Genest J. 1995. Homocysteine and coronary artery disease in French Canadian subjects: Relation with vitamins B<sub>12</sub>, B<sub>6</sub>, pyridoxal phosphate, and folate. *Am J Cardiol* 75:1107–1111.
- Daly LE, Kirke PN, Molloy A, Weir DG, Scott JM. 1995. Folate levels and neural tube defects. Implications for prevention. *J Am Med Assoc* 274:1698–1702.
- Daly S, Mills JL, Molloy AM, Conley M, Lee YJ, Kirke PN, Weir DG, Scott JM. 1997. Minimum effective dose of folic acid for food fortification to prevent neural tube defects. *Lancet* 350:1666–1669.
- Dawson DW. 1966. Microdoses of folic acid in pregnancy. *J Obstet Gynaecol Br Commonw* 73:44–48.
- DeSouza S, Eitenmiller R. 1990. Effects of different enzyme treatments on extraction of total folate from various foods prior to microbiological assay and radioassay. *J Micronutr Anal* 7:37–57.
- deFranchis R, Mancini FP, D'Angelo A, Sebastio G, Fermo I, DeStefano V, Margaglione M, Mazzola G, DiMinno G, Andria G. 1996. Elevated total plasma homocysteine and 677C→T mutation of the 5,10-methylenetetrahydrofolate reductase gene in thrombotic vascular disease. *Am J Hum Genet* 59:262–264.
- De Wals P, Trochet C, Pinsonneault L. 1999. Prevalence of neural tube defects in the province of Quebec, 1992. *Can J Public Health* 90:237–239.
- DHHS (U.S. Department of Health and Human Services). 1993a. Food and Drug Administration. Folic acid; proposed rules. *Fed Regist* 21:53293–53294.

- DHHS (U.S. Department of Health and Human Services). 1993b. Food and Drug Administration. Food standards: Amendment of the standards of identity for enriched grain products to require the addition of folic acid. *Fed Regist* 58:53305.
- DHHS (U.S. Department of Health and Human Services). 1996. Food and Drug Administration. Food standards: Amendment of the standards of identity for enriched grain products to require addition of folic acid. *Fed Regist* 61:8781–8807.
- Dolk H, De Wals P, Gillerot Y, Lechat MF, Ayme S, Cornel M, Cuschieri A, Garne E, Goujard J, Laurence KM. 1991. Heterogeneity of neural tube defects in Europe: The significance of site of defect and presence of other major anomalies in relation to geographic differences in prevalence. *Teratology* 44:547–559.
- Economides DL, Ferguson J, Mackenzie IZ, Darley J, Ware II, Holmes-Siedle M. 1992. Folate and vitamin B<sub>12</sub> concentrations in maternal and fetal blood, and amniotic fluid in second trimester pregnancies complicated by neural tube defects. *Br J Obstet Gynaecol* 99:23–25.
- Eichner ER, Hillman RS. 1971. The evolution of anemia in alcoholic patients. *Am J Med* 50:218–232.
- Eichner ER, Hillman RS. 1973. Effect of alcohol on serum folate level. *J Clin Invest* 52:584–591.
- Eichner ER, Pierce HI, Hillman RS. 1971. Folate balance in dietary-induced megaloblastic anemia. *N Engl J Med* 284:933–938.
- Eichner ER, Loewenstein JE, McDonald CR, Dickson VL. 1979. Effect of common drugs on serum level and binding of folate in man. In: Kisliuk RL, Brown GM, eds. *Chemistry and Biology of Pteridines*. New York: Elsevier North Holland. Pp. 537–542.
- Ek J. 1980. Plasma and red cell folate values in newborn infants and their mothers in relation to gestational age. *J Pediatr* 97:288–292.
- Ek J, Magnus EM. 1979. Plasma and red blood cell folate in breastfed infants. *Acta Paediatr Scand* 68:239–243.
- Ek J, Magnus E. 1982. Plasma and red cell folate values and folate requirements in formula-fed term infants. *J Pediatr* 100:738–744.
- Ellison ABC. 1960. Pernicious anemia masked by multivitamins containing folic acid. *J Am Med Assoc* 173:240–243.
- Elsborg L. 1974. Inhibition of intestinal absorption of folate by phenytoin. *Acta Haematol* 52:24–28.
- Elwood JM, Elwood JH. 1980. *Epidemiology of Anencephalus and Spina Bifida*. Oxford: Oxford University Press.
- Emery AE. 1986. *Methodology in Medical Genetics: An Introduction to Statistical Methods*. 2nd ed. Edinburgh: Churchill Livingstone.
- Essien FB. 1992. Maternal methionine supplementation promotes the remediation of axial defects in *Axd* mouse neural tube mutants. *Teratology* 45:205–212.
- Evans RW, Shaten BJ, Hempel JD, Cutler JA, Kuller LH. 1997. Homocyst(e)ine and risk of cardiovascular disease in the Multiple Risk Factor Intervention Trial. *Arterioscler Thromb Vasc Biol* 17:1947–1953.
- Fava M, Borus JS, Alpert JE, Nierenberg AA, Rosenbaum JF, Bottiglieri T. 1997. Folate, vitamin B<sub>12</sub>, and homocysteine in major depressive disorder. *Am J Psychiatry* 154:426–428.
- Felson DT, Anderson JJ, Meenan RF. 1990. The comparative efficacy and toxicity of second-line drugs in rheumatoid arthritis. Results of two metaanalyses. *Arthritis Rheum* 33:1449–1461.

- Fowler WM, Hendricks AB. 1949. Folic acid and the neurologic manifestations of pernicious anemia. *Am Pract* 3:609–613.
- Frosst P, Blom HJ, Milos R, Goyette P, Sheppard CA, Matthews RG, Boers GJ, den Heijer M, Kluijtmans LA, van den Heuvel LP, Rozen R. 1995. A candidate genetic risk factor for vascular disease: A common mutation in methylenetetrahydrofolate reductase. *Nat Genet* 10:111–113.
- Gailani SD, Carey RW, Holland JF, O’Malley JA. 1970. Studies of folate deficiency in patients with neoplastic diseases. *Cancer Res* 30:327–333.
- Gallagher PM, Meleady R, Shields DC, Tan KS, McMaster D, Rozen R, Evans A, Graham IM, Whitehead AS. 1996. Homocysteine and risk of premature coronary heart disease. Evidence for a common gene mutation. *Circulation* 94:2154–2158.
- Garry PJ, Goodwin JS, Hunt WC, Hooper EM, Leonard AG. 1982. Nutritional status in a healthy elderly population: Dietary and supplemental intakes. *Am J Clin Nutr* 36:319–331.
- Garry PJ, Goodwin JS, Hunt WC. 1984. Folate and vitamin B<sub>12</sub> status in a healthy elderly population. *J Am Geriatr Soc* 32:719–726.
- Gartler SM, Hornug SK, Motulsky AG. 1981. Effect of chronologic age on induction of cystathione synthase, uroporphyrinogen I synthase, and glucose 6-phosphate dehydrogenase activities in lymphocytes. *Proc Natl Acad Sci USA* 78:1916–1919.
- Gibberd FB, Nicholls A, Dunne JF, Chaput de Saintonge DM. 1970. Toxicity of folic acid. *Lancet* 1:360–361.
- Giles WH, Kittner SJ, Anda RF, Croft JB, Casper ML. 1995. Serum folate and risk for ischemic stroke. First National Health and Nutrition Examination Survey epidemiology follow-up study. *Stroke* 26:1166–1170.
- Giovannucci E, Stampfer MJ, Colditz GA, Rimm EB, Trichopolous D, Rosner BA, Speizer FE, Willett WC. 1993. Folate, methionine, and alcohol intake and risk of colorectal adenoma. *J Natl Cancer Inst* 85:875–884.
- Giovannucci E, Rimm EB, Ascherio A, Stampfer MJ, Colditz GA, Willett WC. 1995. Alcohol, low-methionine-low folate diets and risk of colon cancer in men. *J Natl Cancer Inst* 87:265–273.
- Glynn SA, Albanes D, Pietinen P, Brown CC, Rautalahti M, Tangrea JA, Gunter EW. 1996. Colorectal cancer and folate status: A nested case control study among male smokers. *Cancer Epidemiol Biomarkers Prev* 5:487–494.
- Goddijn-Wessel TA, Wouters MG, van de Molen EF, Spuijbroek MD, Steegers-Theunissen RP, Blom HJ, Boers GH, Eskes TK. 1996. Hyperhomocysteinemia: A risk factor for placental abruption or infarction. *Eur J Obstet Gynecol Reprod Biol* 66:23–29.
- Godfrey PS, Toone BK, Carney MW, Flynn TG, Bottiglieri T, Laundy M, Chanarin I, Reynolds EH. 1990. Enhancement of recovery from psychiatric illness by methylfolate. *Lancet* 336:392–395.
- Gomez MR. 1981. Possible teratogenicity of valproic acid. *J Pediatr* 98:508–509.
- Goodwin JS, Goodwin JM, Garry PJ. 1983. Association between nutritional status and cognitive functioning in a healthy elderly population. *J Am Med Assoc* 249:2917–2921.
- Gotz VP, Laufer RD. 1980. Folic acid hypersensitivity or tartrazine allergy? *Am J Hosp Pharm* 37:1470–1474.
- Grace E, Emans SJ, Drum DE. 1982. Hematologic abnormalities in adolescents who take oral contraceptive pills. *J Pediatr* 101:771–774.

- Graham IM, Daly LE, Refsum HM, Robinson K, Brattstrom LE, Ueland PM, Palma-Reis RJ, Boers GH, Sheahan RG, Israelsson B, Uiterwaal CS, Meleady R, McMaster D, Verhoef P, Witteman J, Rubba P, Bellet H, Wautrecht JC, de Valk HW, Sales Luis AC, Parrot-Rouland FM, Tan KS, Higgins I, Garcon D, Andria G. 1997. Plasma homocysteine as a risk factor for vascular disease. The European Concerted Action Project. *J Am Med Assoc* 277:1775–1781.
- Gregory JF 3rd. 1989. Chemical and nutritional aspects of folate research: Analytical procedures, methods of folate synthesis, stability and bioavailability of dietary folates. *Adv Food Nutr Res* 33:1–101.
- Gregory JF 3rd. 1995. The bioavailability of folate. In: Bailey LB, ed. *Folate in Health and Disease*. New York: Marcel Dekker. Pp. 195–235.
- Gregory JF 3rd. 1997. Bioavailability of folate. *Eur J Clin Nutr* 51: S54–S59.
- Gregory JF 3rd, Engelhardt R, Bhandari SD, Sartain DB, Gustafson SK. 1990. Adequacy of extraction techniques for determination of folate in foods and other biological materials. *J Food Comp Anal* 3:134–144.
- Gunter EW, Bowman BA, Caudill SP, Twite DB, Adams MJ, Sampson EJ. 1996. Results of an international round robin for serum and whole-blood folate. *Clin Chem* 42:1689–1694.
- Hall BE, Watkins CH. 1947. Experience with pteroylglutamic (synthetic folic acid) in the treatment of pernicious anemia. *J Lab Clin Med* 32:622–634.
- Halsted CH, Griggs RC, Harris JW. 1967. The effect of alcoholism on the absorption of folic acid ( $H^3$ -PGA) evaluated by plasma levels and urine excretion. *J Lab Clin Med* 69:116–131.
- Halsted CH, Robles EA, Mezey E. 1971. Decreased jejunal uptake of labeled folic acid ( $H^3$ -PGA) in alcoholic patients: Roles of alcohol and malnutrition. *N Engl J Med* 285:701–706.
- Halsted CH, Robles EA, Mezey E. 1973. Intestinal malabsorption in folate-deficient alcoholics. *Gastroenterology* 64:526–532.
- Halsted CH, Gandhi G, Tamura T. 1981. Sulfasalazine inhibits the absorption of folates in ulcerative colitis. *N Engl J Med* 305:1513–1517.
- Hambidge M, Hackshaw A, Wald N. 1993. Neural tube defects and serum zinc. *Br J Obstet Gynecol* 100:746–749.
- Hamon CG, Blair JA, Barford PA. 1986. The effect of tetrahydrofolate on tetrahydrobiopterin metabolism. *J Ment Defic Res* 30:179–183.
- Hansen H, Rybo G. 1967. Folic acid dosage in prophylactic treatment during pregnancy. *Acta Obstet Gynecol Scand* 46:107–112.
- Hansen HA, Weinfeld A. 1962. Metabolic effects and diagnostic value of small doses of folic acid and  $B_{12}$  in megaloblastic anemias. *Acta Med Scand* 172:427–443.
- Happle R, Traupe H, Bounameaux Y, Fisch T. 1984. Teratogenic effects of etretinate in humans. *Dtsch Med Wochenschr* 109:1476–1480.
- Harpel PC, Zhang X, Borth W. 1996. Homocysteine and hemostasis: Pathogenic mechanisms predisposing to thrombosis. *J Nutr* 126:12855–12895.
- Haworth JC, Dilling LA, Surtees RA, Seargent LE, Lue-Shing H, Cooper BA, Rosenblatt DS. 1993. Symptomatic and asymptomatic methylenetetrahydrofolate reductase deficiency in two adult brothers. *Am J Med Genet* 45:572–576.
- Hayes C, Werler MM, Willett WC, Mitchell AA. 1996. Case-control study of periconceptional folic acid supplementation and oral clefts. *Am J Epidemiol* 143:1229–1234.

- Health Canada. 1996. *Departmental Consolidation of the Food and Drugs Act and the Food and Drug Regulations with Amendments to December 19, 1996*. Ottawa: Canada Communications Group.
- Health Canada. 1997. Regulations amending the Food and Drug Regulations (1066). *Canada Gazette, Part I*, November 29. Pp. 3702-3705.
- Heimburger DC, Krumdieck CL, Alexander CB, Birch R, Dill SR, Bailey WC. 1987. Localized folic acid deficiency and bronchial metaplasia in smokers: Hypothesis and preliminary report. *Nutr Int* 3:54-60.
- Heimburger DC, Alexander CB, Birch R, Butterworth CE, Bailey WC, Krumdieck CL. 1988. Improvement in bronchial squamous metaplasia in smokers treated with folate and vitamin B<sub>12</sub>. Report of a preliminary randomized, double-blind intervention trial. *J Am Med Assoc* 259:1525-1530.
- Heinle RW, Welch AD. 1947. Folic acid in pernicious anemia: Failure to prevent neurologic relapse. *J Am Med Assoc* 133:739-741.
- Heinle RW, Dingle JT, Weisberger AS. 1947. Folic acid in the maintenance of pernicious anemia. *J Lab Clin Med* 32:970-981.
- Hellstrom L. 1971. Lack of toxicity of folic acid given in pharmacological doses to healthy volunteers. *Lancet* 1:59-61.
- Herbert V. 1962a. Experimental nutritional folate deficiency in man. *Trans Assoc Am Physicians* 75:307-320.
- Herbert V. 1962b. Minimal daily adult folate requirement. *Arch Intern Med* 110:649-652.
- Herbert V. 1963. Current concepts in therapy: Megaloblastic anemia. *N Engl J Med* 268:201-203, 368-371.
- Herbert V. 1968. Nutritional requirements for vitamin B<sub>12</sub> and folic acid. *Am J Clin Nutr* 21:743-752.
- Herbert V. 1987. Making sense of laboratory tests of folate status: Folate requirements to sustain normality. *Am J Hem* 26:199-207.
- Herbert V, Das KC. 1993. Folic acid and vitamin B<sub>12</sub>. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*, 8th ed. Philadelphia: Lea & Febiger. Pp. 402-425.
- Herbert V, Zalusky R, Davidson CS. 1963. Correlates of folate deficiency with alcoholism and associated macrocytosis, anemia, and liver disease. *Ann Intern Med* 58:977-988.
- Hibbard BM. 1964. The role of folic acid in pregnancy. *J Obstet Gynaecol Br Commonw* 71:529-542.
- Hill RM. 1984. Isotretinoin teratogenicity. *Lancet* 1:1465.
- Hirata F, Axelrod J. 1980. Phospholipid methylation and biological signal transmission. *Science* 209:1082-1090.
- Hobbins JC. 1991. Diagnosis and management of neural tube defects today. *N Engl J Med* 324:690-691.
- Hoffbrand AV, Newcombe BF, Mollin DL. 1966. Method of assay of red cell folate activity and the value of the assay as a test for folate deficiency. *J Clin Pathol* 19:17-28.
- Holmes-Siedle M, Lindenbaum RH, Galliard A. 1992. Recurrence of neural tube defect in a group of at risk women: A 10 year study of Pregnavite Forte F. *J Med Genet* 29:134-135.
- Hommes OR, Obbens EA. 1972. The epileptogenic action of Na-folate in the rat. *J Neurol Sci* 16:271-281.
- Hook EB, Czeizel AE. 1997. Can terathanasia explain the protective effect of folic-acid supplementation on birth defects? *Lancet* 350:513-515.

- Hoppner K, Lampi B. 1980. Folate levels in human liver from autopsies in Canada. *Am J Clin Nutr* 33:862–864.
- Houghton LA, Green TJ, Donovan UM, Gibson RS, Stephen AM, O'Connor DL. 1997. Association between dietary fiber intake and the folate status of a group of female adolescents. *Am J Clin Nutr* 66:1414–1421.
- Hultberg B, Andersson A, Sterner G. 1993. Plasma homocysteine in renal failure. *Clin Nephrol* 40:230–235.
- Hunter R, Barnes J, Oakeley HF, Matthews DM. 1970. Toxicity of folic acid given in pharmacological doses to healthy volunteers. *Lancet* 1:61–3.
- Israels MC, Wilkinson JF. 1949. Risk of neurological complications in pernicious anemia treated with folic acid. *Br Med J* 2:1072–1075.
- Jackson RC. 1984. Biological effects of folic acid antagonists with antineoplastic activity. *Pharmacol Ther* 25:61–82.
- Jacob RA, Wu M-M, Henning SM, Swendseid ME. 1994. Homocysteine increases as folate decreases in plasma of healthy men during short-term dietary folate and methyl group restriction. *J Nutr* 124:1072–1080.
- Jacob RA, Gretz DM, Taylor PC, James SJ, Pogribny IP, Miller BJ, Henning SM, Swendseid ME. 1998. Moderate folate depletion increases plasma homocysteine and decreases lymphocyte DNA methylation in postmenopausal women. *J Nutr* 128:1204–1212.
- Jacobsen DW, Gatautis VJ, Green R, Robinson K, Savon SR, Secic M, Ji J, Otto JM, Taylor LM. 1994. Rapid HPLC determination of total homocysteine and other thiols in serum and plasma: Sex differences and correlation with cobalamin and folate concentrations in healthy subjects. *Clin Chem* 40:873–881.
- Jacobson SD, Berman L, Axelrod AR, Vonder Heide EC. 1948. Folic acid therapy: Its effect as observed in two patients with pernicious anemia and neurologic symptoms. *J Am Med Assoc* 137:825–827.
- Jacques PF, Sulsky SI, Sadowski JA, Phillips JC, Rush D, Willett WC. 1993. Comparison of micronutrient intake measured by a dietary questionnaire and biochemical indicators of micronutrient status. *Am J Clin Nutr* 57:182–189.
- Jacques PF, Bostom AG, Williams RR, Ellison RC, Eckfeldt JH, Rosenberg IH, Selhub J, Rozen R. 1996. Relation between folate status, a common mutation in methylenetetrahydrofolate reductase, and plasma homocysteine concentrations. *Circulation* 93:7–9.
- Jägerstad M. 1977. Folate intake and blood folate in elderly subjects, a study using the double sampling portion technique. *Nutr Metab* 21:29–31.
- Jägerstad M, Westesson A-K. 1979. Folate. *Scand J Gastroenterol* 14:196–202.
- Joyal CC, Lalonde R, Vikis-Freibergs V, Botez MI. 1993. Are age-related behavioral disorders improved by folate administration? *Exp Aging Res* 19:367–376.
- Kang SS, Wong PW, Norusis M. 1987. Homocystinemia due to folate deficiency. *Metabolism* 36:458–462.
- Kang SS, Wong PW, Bock HG, Horwitz A, Grix A. 1991a. Intermediate hyperhomocystinemia resulting from compound heterozygosity of methylenetetrahydrofolate reductase mutations. *Am J Hum Genet* 48:546–551.
- Kang SS, Wong PW, Susmano A, Sora J, Norusis M, Ruggie N. 1991b. Thermolabile methylenetetrahydrofolate reductase: An inherited risk factor for coronary artery disease. *Am J Hum Genet* 48:536–545.
- Keagy PM, Oace SM. 1989. Rat bioassay of wheat bran folate and effects of intestinal bacteria. *J Nutr* 119:1932–1939.
- Keagy PM, Shane B, Oace SM. 1988. Folate bioavailability in humans: Effects of wheat bran and beans. *Am J Clin Nutr* 47:80–88.

- Keating JN, Wada L, Stokstad EL, King JC. 1987. Folic acid: Effect of zinc absorption in humans and in the rat. *Am J Clin Nutr* 46:835–839.
- Kehl SJ, McLennan H, Collingridge GL. 1984. Effects of folic and kainic acids on synaptic responses of hippocampal neurones. *Neuroscience* 11:111–124.
- Keizer SE, Gibson RS, O'Connor DL. 1995. Postpartum folic acid supplementation of adolescents: Impact on maternal folate and zinc status and milk composition. *Am J Clin Nutr* 62:377–384.
- Khoury MJ, Erickson JD, James LM. 1982. Etiologic heterogeneity of neural tube defects: Clues from epidemiology. *Am J Epidemiol* 115:538–548.
- Kim Y-I, Pogribny IP, Basnakian AG, Miller JW, Selhub J, James SJ, Mason JB. 1997. Folate deficiency in rats induces DNA strand breaks and hypomethylation with the p53 tumor suppressor gene. *Am J Clin Nutr* 65:46–52.
- Kirke PN, Daly LE, Elwood JH. 1992. A randomized trial of low-dose folic acid to prevent neural tube defects. *Arch Dis Child* 67:1442–1446.
- Kirke PN, Molloy AM, Daly LE, Burke H, Weir DG, Scott JM. 1993. Maternal plasma folate and vitamin B<sub>12</sub> are independent risk factors for neural tube defects. *Q J Med* 86:703–708.
- Klipstein FA. 1964. Subnormal serum folate and macrocytosis associated with anticonvulsant drug therapy. *Blood* 23:68–86.
- Kluijtmans LA, van den Heuvel LP, Boers GH, Frosst P, Stevens EM, van Oost BA, den Heijer M, Trijbels FJ, Rozen R, Blom HJ. 1996. Molecular genetic analysis in mild hyperhomocysteinemia: A common mutation in the methylenetetrahydrofolate reductase gene is a genetic risk factor for cardiovascular disease. *Am J Hum Genet* 58:35–41.
- Koehler KM, Romero LJ, Stauber PM, Pareo-Tubbeh SL, Liang HC, Baumgartner RN, Garry PJ, Allen RH, Stabler SP. 1996. Vitamin supplementation and other variables affecting serum homocysteine and methylmalonic acid concentrations in elderly men and women. *J Am Coll Nutr* 15:364–376.
- Krause LJ, Forsberg CW, O'Connor DL. 1996. Feeding human milk to rats increases bifidobacterium in the cecum and colon which correlates with enhanced folate status. *J Nutr* 126:1505–1511.
- Krumdieck CL, Fukushima K, Fukushima T, Shiota T, Butterworth CE Jr. 1978. A long-term study of the excretion of folate and pterins in a human subject after ingestion of <sup>14</sup>C folic acid, with observations on the effect of diphenylhydantoin administration. *Am J Clin Nutr* 31:88–93.
- Landgren F, Israelsson B, Lindgren A, Hultberg B, Andersson A, Brattstrom L. 1995. Plasma homocysteine in acute myocardial infarction: Homocysteine-lowering effect of folic acid. *J Intern Med* 237:381–388.
- Landon MJ, Oxley A. 1971. Relation between maternal and infant blood folate activities. *Arch Dis Child* 46:810–814.
- Lashner BA. 1993. Red blood cell folate is associated with the development of dysplasia and cancer in ulcerative colitis. *J Cancer Res Clin Oncol* 119:549–554.
- Lashner BA, Heidenreich PA, Su GL, Kane SV, Hanauer SB. 1989. The effect of folate supplementation on the incidence of dysplasia and cancer in chronic ulcerative colitis. A case-control study. *Gastroenterology* 97:255–259.
- Laurence KM. 1990. The genetics and prevention of neural tube defects and “uncomplicated” hydrocephalus. In: Emery AE, Rimoin DL, eds. *Principles and Practice of Medical Genetics*, 2nd ed., Vol. 1. Edinburgh: Churchill Livingstone. Pp. 323–346.

- Laurence KM, James N, Miller MH, Tennant GB, Campbell H. 1981. Double-blind randomized controlled trial of folate treatment before conception to prevent recurrence of neural tube defects. *Br Med J* 282:1509–1511.
- Lawrence VA, Loewenstein JE, Eichner ER. 1984. Aspirin and folate binding: In vivo and in vitro studies of serum binding and urinary excretion of endogenous folate. *J Lab Clin Med* 103:944–948.
- Lewis CA, Pancharuniti N, Sauberlich HE. 1992. Plasma folate adequacy as determined by homocysteine level. *Ann NY Acad Sci* 669:360–362.
- Li YN, Gulati S, Baker PJ, Brody LC, Banerjee R, Kruger WD. 1996. Cloning, mapping and RNA analysis of the human methionine synthase gene. *Hum Mol Genet* 5:1851–1858.
- Lim HS, Mackey AD, Tamura T, Picciano MF. 1997. Measurable folates in human milk are increased by treatment with  $\alpha$ -amylase and protease. *FASEB J* 11:A395.
- Lindenbaum J, Heaton EB, Savage DG, Brust JC, Garrett TJ, Podell ER, Marcell PD, Stabler SP, Allen RH. 1988. Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis. *N Engl J Med* 318:1720–1728.
- Lindseth RE. 1996. Myelomeningocele. In: Morrissey RT, Weinstein SL, eds. *Lovell and Winter's Pediatric Orthopaedics*, 4th ed., Vol. 1. Philadelphia: Lippincott-Raven. Pp. 503–505.
- Loots JM, Kramer S, Brennan MJW. 1982. The effect of folates on the reflex activity in the isolated hemisected frog spinal cord. *J Neural Transm* 54:239–249.
- Lowenstein L, Cantlie G, Ramos O, Brunton L. 1966. The incidence and prevention of folate deficiency in a pregnant clinic population. *Can Med Assoc J* 95:797–806.
- LSRO/FASEB (Life Sciences Research Office/Federation of American Societies for Experimental Biology). 1984. *Assessment of the Folate Nutritional Status of the U.S. Population Based on Data Collected in the Second National Health and Nutrition Examination Survey, 1976–1980*. Senti FR, Pilch SM, eds. Bethesda, MD: LSRO/FASEB.
- LSRO/FASEB (Life Sciences Research Office/Federation of American Societies for Experimental Biology). 1994. *Assessment of the Folate Methodology Used in the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994)*. Raiten DJ, Fisher KD, eds. Bethesda, MD: LSRO/FASEB.
- LSRO/FASEB (Life Sciences Research Office/Federation of American Societies for Experimental Biology). 1995. *Third Report on Nutrition Monitoring in the United States*. Washington DC: U.S. Government Printing Office.
- Ma J, Stampfer MJ, Hennekens CH, Frosst P, Selhub J, Horsford J, Malinow MR, Willett WC, Rozen R. 1996. Methylenetetrahydrofolate reductase polymorphism, plasma folate, homocysteine, and risk of myocardial infarction in U.S. physicians. *Circulation* 94:2410–2416.
- Ma J, Stampfer MJ, Giovannucci E, Artigas C, Hunter DJ, Fuchs C, Willett WC, Selhub J, Hennekens CH, Rozen R. 1997. Methylenetetrahydrofolate reductase polymorphism, dietary interactions, and risk of colorectal cancer. *Cancer Res* 57:1098–1102.
- Mackey AD, Lim HS, Picciano MF, Smiciklas-Wright H. 1997. Biochemical indices of folate adequacy diminish in women during lactation. *FASEB J* 11:A179.

- Malinow MR, Nieto FJ, Kruger WD, Duell PB, Hess DL, Gluckmann RA, Block PC, Holzgang CR, Anderson PH, Seltzer D, Upson B, Lin QR. 1997. The effects of folic acid supplementation on plasma total homocysteine are modulated by multivitamin use and methylenetetrahydrofolate reductase genotypes. *Arterioscler Thromb Vasc Biol* 17:1157–1162.
- Malpas JS, Spray GH, Witts LJ. 1966. Serum folic acid and vitamin B<sub>12</sub> levels in anticonvulsant therapy. *Br Med J* 1:955–957.
- Marshall RA, Jandl JH. 1960. Response to “physiologic” doses of folic acid on megaloblastic anemia. *AMA Arch Intern Med* 105:352–360.
- Martin JI, Landen WO, Soliman A-G, Eitenmiller RR. 1990. Application of a tri-enzyme extraction for total folate determination in foods. *J Assoc Offic Anal Chem* 73:805–808.
- Mason JB. 1995. Folate status: Effects on carcinogenesis. In: Bailey LB, ed. *Folate in Health and Disease*. New York: Marcel Dekker. Pp. 361–378.
- Mason JB, Levesque T. 1996. Folate: Effects on carcinogenesis and the potential for cancer chemoprevention. *Oncology* 10:1727–1736.
- Mathur BP. 1966. Sensitivity of folic acid: A case report. *Indian J Med Sci* 20:133–134.
- Mayer EL, Jacobsen DW, Robinson K. 1996. Homocysteine and coronary atherosclerosis. *J Am Coll Cardiol* 27:517–527.
- McMartin KE, Collins TD, Shiao CQ, Vidrine L, Redetzki HM. 1986. Study of dose-dependence and urinary folate excretion produced by ethanol in humans and rats. *Alcohol Clin Exp Res* 10:419–424.
- McPartlin J, Halligan A, Scott JM, Darling M, Weir DG. 1993. Accelerated folate breakdown in pregnancy. *Lancet* 341:148–149.
- Meenan J, O'Hallinan E, Lynch S, Molloy A, McPartlan J, Scott J, Weir DG. 1996. Folate status of gastrointestinal epithelial cells is not predicted by serum and red cell folate values in replete subjects. *Gut* 38:410–413.
- Meenan J, O'Hallinan E, Scott J, Weir DG. 1997. Epithelial cell folate depletion occurs in neoplastic but not adjacent normal colon mucosa. *Gastroenterology* 112:1163–1168.
- Metz J. 1970. Folate deficiency conditioned by lactation. *Am J Clin Nutr* 23:843–847.
- Metz J, van der Westhuyzen J. 1987. The fruit bat as an experimental model of the neuropathy of cobalamin deficiency. *Comp Biochem Physiol* 88A:171–177.
- Mills JL, Conley MR. 1996. Folic acid to prevent neural tube defects: Scientific advances and public health issues. *Curr Opin Obstet Gynecol* 8:394–397.
- Mills JL, Rhoads GG, Simpson JL, Cunningham GC, Conley MR, Lassman MR, Walden ME, Depp DR, Hoffman HJ. 1989. The absence of a relation between the periconceptional use of vitamins and neural tube defects. National Institute of Child Health and Human Development Neural Tube Defects Study Group. *N Engl J Med* 321:430–435.
- Mills JL, McPartlin JM, Kirke PN, Lee YJ, Conley MR, Weir DG, Scott JM. 1995. Homocysteine metabolism in pregnancies complicated by neural-tube defects. *Lancet* 345:149–151.
- Milne DB, Johnson LK, Mahalko JR, Sandstead HH. 1983. Folate status of adult males living in a metabolic unit: Possible relationships with iron nutriture. *Am J Clin Nutr* 37:768–773.
- Milne DB, Canfield WK, Mahalko JR, Sandstead HH. 1984. Effect of oral folic acid supplements on zinc, copper, and iron absorption and excretion. *Am J Clin Nutr* 39:535–539.

- Milunsky A, Jick H, Jick SS, Bruell CL, MacLaughlin DS, Rothman KJ, Willett W. 1989. Multivitamin/folic acid supplementation in early pregnancy reduces the prevalence of neural tube defects. *J Am Med Assoc* 262:2847–2852.
- Mitchell DC, Vilter RW, Vilter CF. 1949. Hypersensitivity to folic acid. *Ann Intern Med* 31:1102–1105.
- Mitchell LE, Duffy DL, Duffy P, Bellingham G, Martin NG. 1997. Genetic effects on variation in red-blood-cell folate in adults: Implications for the familial aggregation of neural tube defects. *Am J Hum Genet* 60:433–438.
- Molgaard J, Malinow MR, Lassvik C, Holm A-C, Upson B, Olsson AG. 1992. Hyperhomocyst(e)inaemia: An independent risk factor for intermittent claudication. *J Intern Med* 231:273–279.
- Molloy AM, Daly S, Mills JL, Kirke PN, Whitehead AS, Ramsbottom D, Conley MR, Weir DG, Scott JM. 1997. Thermolabile variant of 5,10-methylenetetrahydrofolate reductase associated with low red-cell folates: Implications for folate intake recommendations. *Lancet* 349:1591–1593.
- Moore CA, Li S, Li Z, Hong SX, Gu HQ, Berry RJ, Mulinare J, Erickson JD. 1997. Elevated rates of severe neural tube defects in a high-prevalence area in northern China. *Am J Med Genet* 73:113–118.
- Morgan SL, Baggott JE. 1995. Folate antagonists in nonneoplastic disease: Proposed mechanisms of efficacy and toxicity. In: Bailey LB, ed. *Folate in Health and Disease*. New York: Marcel Dekker. Pp. 405–433.
- Morgan SL, Baggott JE, Altz-Smith M. 1987. Folate status of rheumatoid arthritis patients receiving long term, low-dose methotrexate therapy. *Arthritis Rheum* 30:1348–1356.
- Morgan SL, Baggott JE, Vaughn WH, Austin JS, Veitch TA, Lee JY, Koopman WJ, Krumbiegel CL, Alarcon GS. 1994. Supplementation with folic acid during methotrexate therapy for rheumatoid arthritis. A double-blind, placebo-controlled trial. *Ann Intern Med* 121:833–841.
- Morgan SL, Baggott JE, Alarcon GS. 1997. Methotrexate in rheumatoid arthritis. Folate supplementation should always be given. *Bio Drugs* 8:164–175.
- Morrison HI, Schaubel D, Desmeules M, Wigle DT. 1996. Serum folate and risk of fatal coronary heart disease. *J Am Med Assoc* 275:1893–1896.
- Mudd SH, Skovby F, Levy HL, Pettigrew KD, Wilcken B, Pyeritz RE, Andria G, Boers GH, Bromberg IL, Cerone R, Fowler B, Gröbe H, Schmidt H, Schweitzer L. 1985. The natural history of homocystinuria due to cystathione  $\beta$ -synthase deficiency. *Am J Hum Genet* 37:1–31.
- Mukherjee MD, Sandstead HH, Ratnaparkhi MV, Johnson LK, Milne DB, Stelling HP. 1984. Maternal zinc, iron, folic acid and protein nutriture and outcome of human pregnancy. *Am J Clin Nutr* 40:496–507.
- Mulinare J, Cordero JF, Erickson JD, Berry RJ. 1988. Periconceptional use of multivitamins and the occurrence of neural tube defects. *J Am Med Assoc* 260:3141–3145.
- Munger R, Romitti P, West N, Murray J, Hanson J. 1997. Maternal intake of folate, vitamin B<sub>12</sub>, and zinc and risk of orofacial cleft birth defects. *Am J Epidemiol* 145:S30.
- Nakazawa Y, Chiba K, Imatoh N, Kotorii T, Sakamoto T, Ishizaki T. 1983. Serum folic acid levels and antipyrine clearance rates in smokers and nonsmokers. *Drug Alcohol Depend* 11:201–207.
- Nygård O, Nordrehaug JE, Fefsum H, Ueland PM, Farstad M, Vollset SE. 1997. Plasma homocysteine levels and mortality in patients with coronary artery disease. *N Engl J Med* 327:230–236.

- O'Connor DL, Tamura T, Picciano MF. 1991. Pteroylpolyglutamates in human milk. *Am J Clin Nutr* 53:930–934.
- O'Keefe CA, Bailey LB, Thomas EA, Hofler SA, Davis BA, Cerda JJ, Gregory JF 3rd. 1995. Controlled dietary folate affects folate status in nonpregnant women. *J Nutr* 125:2717–2725.
- Olney JW, Fuller TA, de Gubareff T, Labruyere J. 1981. Intrastriatal folic acid mimics the distant but not local brain damaging properties of kainic acid. *Neurosci Lett* 25:207–210.
- Omer A, Mowat AG. 1968. Nature of anaemia in rheumatoid arthritis. 9. Folate metabolism in patients with rheumatoid arthritis. *Ann Rheum Dis* 27:414–424.
- Ortega RM, Redondo R, Andres P, Eguileor I. 1993. Nutritional assessment of folate and cyanocobalamin status in a Spanish elderly group. *Int J Vitam Nutr Res* 63:17–21.
- Ortega RM, Lopez-Sobaler AM, Gonzalez-Gross MM, Redondo RM, Marzana I, Zamora MJ, Andres P. 1994. Influence of smoking on folate intake and blood folate concentrations in a group of elderly Spanish men. *J Am Coll Nutr* 13:68–72.
- Pancharuniti N, Lewis CA, Sauberlich HE, Perkins LL, Go RC, Alvarez JO, Macaluso M, Acton RT, Copeland RB, Cousins AL, Gore TB, Cornwell PE, Roseman JE. 1994. Plasma homocyst(e)ine, folate, and vitamin B<sub>12</sub> concentrations and risk for early-onset coronary artery disease. *Am J Clin Nutr* 59:940–948.
- Pfeiffer CM, Rogers LM, Bailey LB, Gregory JF 3rd. 1997a. Absorption of folate from fortified cereal-grain products and of supplemental folate consumed with or without food determined by using a dual-label stable-isotope protocol. *Am J Clin Nutr* 66:1388–1397.
- Pfeiffer CM, Rogers LM, Gregory JF 3rd. 1997b. Determination of folate in cereal-grain food products using trienzyme extraction and combined affinity and reversed-phase liquid chromatography. *J Agric Food Chem* 45:407–413.
- Picciano MF. 1996. Pregnancy and lactation. In: Ziegler EE, Filer LJ Jr., eds. *Present Knowledge in Nutrition*. Washington, DC: ILSI Press. Pp. 384–395.
- Piyathilake CJ, Macaluso M, Hine RJ, Richards EW, Krumdieck CL. 1994. Local and systemic effects of cigarette smoking on folate and vitamin B-12. *Am J Clin Nutr* 60:559–566.
- Potischman N, Brinton LA, Laiming VA, Reeves WC, Brenes MM, Herroro R, Tenorio F, de Britton RC, Gaitan E. 1991. A case-control study of serum folate levels and invasive cervical cancer. *Cancer Res* 51:4785–4789.
- Qvist I, Abdulla M, Jägerstad M, Svensson S. 1986. Iron, zinc and folate status during pregnancy and two months after delivery. *Acta Obstet Gynecol Scand* 65:15–22.
- Rajkovic A, Catalano PM, Malinow MR. 1997. Elevated homocyst(e)ine levels with preeclampsia. *Obstet Gynecol* 90:168–171.
- Ramsbottom D, Scott JM, Molloy A, Weir DG, Kirke PN, Mills JL, Gallagher PM, Whitehead AS. 1997. Are common mutations of cystathionine beta-synthase involved in the aetiology of neural tube defects? *Clin Genet* 51:39–42.
- Rasmussen K, Moller J, Lyngbak M, Pedersen A-M, Dybkjaer L. 1996. Age- and gender-specific reference intervals for total homocysteine and methylmalonic acid in plasma before and after vitamin supplementation. *Clin Chem* 42:630–636.
- Reed T, Malinow MR, Christian JC, Upson B. 1991. Estimates of heritability of plasma homocyst(e)ine levels in aging adult male twins. *Clin Genet* 39:425–428.

- Reisner EH Jr, Weiner L. 1952. Studies on mutual effect of suboptimal oral doses of vitamin B<sub>12</sub> and folic acid in pernicious anemia. *N Engl J Med* 247:15–17.
- Retief FP. 1969. Urinary folate excretion after ingestion of pteroylmonoglutamic acid and food folate. *Am J Clin Nutr* 22:352–355.
- Reynolds EH, Chanarin I, Milner G, Matthews DM. 1966. Anticonvulsant therapy, folic acid and vitamin B<sub>12</sub> metabolism and mental symptoms. *Epilepsia* 7:261–270.
- Reynolds EH, Rothfeld P, Pincus JH. 1973. Neurological disease associated with folate deficiency. *Br Med J* 2:398–400.
- Rhode BM, Cooper BA, Farmer FA. 1983. Effect of orange juice, folic acid, and oral contraceptives on serum folate in women taking a folate-restricted diet. *J Am Coll Nutr* 2:221–230.
- Richens A. 1971. Toxicity of folic acid. *Lancet* 1:912.
- Riggs KM, Spiro A, Tucker K, Rush D. 1996. Relations of vitamin B-12, vitamin B-6, folate, and homocysteine to cognitive performance in the Normative Aging Study. *Am J Clin Nutr* 63:306–314.
- Rimm EB, Willett WC, Hu FB, Sampson L, Colditz GA, Manson JE, Hennekens C, Stampfer MJ. 1998. Folate and vitamin B<sub>6</sub> from diet and supplements in relation to risk of coronary heart disease among women. *J Am Med Assoc* 279:359–364.
- Ritz ND, Meyer LM, Brahin C, Sawitsky A. 1951. Further observations on the oral treatment of pernicious anemia with subminimal doses of folic acid and vitamin B<sub>12</sub>. *Acta Hematol* 5:334–338.
- Rong N, Selhub J, Goldin BR, Rosenberg IH. 1991. Bacterially synthesized folate in rat large intestine is incorporated into host tissue folyl polyglutamates. *J Nutr* 121:1955–1959.
- Rosa FW. 1991. Spina bifida in infants of women treated with carbamazepine during pregnancy. *N Engl J Med* 324:674–677.
- Rosenberg IH. 1992. Folate. In: Hartz SC, Russell RM, Rosenberg IH, eds. *Nutrition in the Elderly*. The Boston Nutritional Status Survey. London: Smith-Gordon. Pp. 135–139.
- Ross JF, Belding H, Paegel BL. 1948. The development and progression of subacute combined degeneration of the spinal cord in patients with pernicious anemia treated with synthetic pteroylglutamic (folic) acid. *Blood* 3:68–90.
- Russell RM, Ismail-Beigi F, Reinhold JG. 1976. Folate content of Iranian breads and the effect of their fiber content on the intestinal absorption of folic acid. *Am J Clin Nutr* 29:799–802.
- Russell RM, Rosenberg IH, Wilson PD, Iber FL, Oaks EB, Giovetti AC, Otradovec CL, Karwoski PA, Press AW. 1983. Increased urinary excretion and prolonged turnover time of folic acid during ethanol ingestion. *Am J Clin Nutr* 38:64–70.
- Sahyoun N. 1992. Nutrient intake by the NSS elderly population. In: Hartz SC, Russell RM, Rosenberg IH, eds. *Nutrition in the Elderly*. The Boston Nutritional Status Survey. London: Smith-Gordon. Pp. 31–44.
- Sahyoun NR, Otradovec CL, Hartz SC, Jacob RA, Peters H, Russell RM, McGandy RB. 1988. Dietary intakes and biochemical indicators of nutritional status in an elderly, institutionalized population. *Am J Clin Nutr* 47:524–533.
- Saleh AM, Pheasant AE, Blair JA, Allan RN, Walters J. 1982. Folate metabolism in man: The effect of malignant disease. *Br J Cancer* 46:346–353.
- Salmenpera L, Perheentupa J, Siimes MA. 1986. Folate nutrition is optimal in exclusively breast-fed infants but inadequate in some of their mothers and in formula-fed infants. *J Pediatr Gastroenterol Nutr* 5:283–289.

- Sauberlich HE, Kretsch MJ, Skala JH, Johnson HL, Taylor PC. 1987. Folate requirement and metabolism in nonpregnant women. *Am J Clin Nutr* 46:1016–1028.
- Savage DG, Lindenbaum J, Stabler SP, Allen RH. 1994. Sensitivity of serum methylmalonic acid and total homocysteine determinations for diagnosing cobalamin and folate deficiencies. *Am J Med* 96:239–246.
- Scanlon KS, Ferencz C, Loffredo CA, Wilson PD, Correa-Villaseñor A, Khoury MJ, Willett WC. 1998. Preconceptional folate intake and malformations of the cardiac outflow tract. *Epidemiology* 9:95–98.
- Schmitz C, Lindpaintner K, Verhoef P, Gaziano JM, Buring J. 1996. Genetic polymorphism of methylenetetrahydrofolate reductase and myocardial infarction. A case-control study. *Circulation* 94:1812–1814.
- Scholl TO, Hediger ML, Bendich A, Schall JI, Smith WK, Krueger PM. 1997. Use of multivitamin/mineral prenatal supplements: Influence on the outcome of pregnancy. *Am J Epidemiol* 146:134–141.
- Schwartz SM, Siscovick DS, Malinow MR, Rosendaal FR, Beverly RK, Hess DL, Psaty BM, Longstreth WT, Koepsell TD, Raghunathan TE, Reitsma PH. 1997. Myocardial infarction in young women in relation to plasma total homocysteine, folate, and a common variant in the methylenetetrahydrofolate reductase gene. *Circulation* 96:412–417.
- Schwartz SO, Kaplan SR, Armstrong BE. 1950. The long-term evaluation of folic acid in the treatment of pernicious anemia. *J Lab Clin Med* 35:894–898.
- Selby JV, Friedman GD, Fireman BH. 1989. Screening prescription drugs for possible carcinogenecity: Eleven to fifteen years of follow-up. *Cancer Res* 49:5736–5747.
- Selhub J, Rosenberg IH. 1996. Folic acid. In: Ziegler EE, Filer LJ Jr., eds. *Present Knowledge in Nutrition*. Washington, DC: ILSI Press. Pp. 206–219.
- Selhub J, Dhar G, Rosenberg IH. 1978. Inhibition of folate enzymes by sulfasalazine. *J Clin Invest* 61:221–224.
- Selhub J, Jacques PF, Wilson PWF, Rush D, Rosenberg IH. 1993. Vitamin status and intake as primary determinants of homocysteinemia in an elderly population. *J Am Med Assoc* 270:2693–2698.
- Senti FR, Pilch SM. 1985. Analysis of folate data from the Second National Health and Nutrition Examination Survey (NHANES II). *J Nutr* 115:1398–1402.
- Sesin GP, Kirschenbaum H. 1979. Folic acid hypersensitivity and fever: A case report. *Am J Hosp Pharm* 36:1565–1567.
- Shaw GM, Lammer EJ, Wasserman CR, O'Malley CD, Tolarova MM. 1995a. Risks of orofacial clefts in children born to women using multivitamins containing folic acid periconceptionally. *Lancet* 346:393–396.
- Shaw GM, O'Malley CD, Wasserman CR, Tolarova MM, Lammer EJ. 1995b. Maternal periconceptional use of multivitamins and reduced risk for conotruncal heart defects and limb deficiencies among offspring. *Am J Med Genet* 59:536–545.
- Shaw GM, Schaffer D, Velie EM, Morland K, Harris JA. 1995c. Periconceptional vitamin use, dietary folate, and the occurrence of neural tube defects. *Epidemiology* 6:219–226.
- Sheehy TW. 1973. Folic acid: Lack of toxicity. *Lancet* 1:37.
- Sheehy TW, Rubini ME, Perez-Santiago E, Santini R Jr, Haddock J. 1961. The effect of “minute” and “titrated” amounts of folic acid on the megaloblastic anemia of tropical sprue. *Blood* 18:623–636.
- Shojaonia AM, Hornady G, Barnes PH. 1968. Oral contraceptives and serum-folate level. *Lancet* 1:1376–1377.

- Shojania AM, Hornady GJ, Barnes PH. 1971. The effect of oral contraceptives on folate metabolism. *Am J Obstet Gynecol* 111:782–791.
- Shorvon SD, Carney MW, Chanarin I, Reynolds EH. 1980. The neuropsychiatry of megaloblastic anaemia. *Br Med J* 281:1036–1038.
- Smith AM, Picciano MF, Deering RH. 1983. Folate supplementation during lactation: Maternal folate status, human milk folate content, and their relationship to infant folate status. *J Pediatr Gastroenterol Nutr* 2:622–628.
- Smith AM, Picciano MF, Deering RH. 1985. Folate intake and blood concentrations of term infants. *Am J Clin Nutr* 41:590–598.
- Smith JL, Goldsmith GA, Lawrence JD. 1975. Effect of oral contraceptive steroids on vitamin and lipid levels in serum. *Am J Clin Nutr* 28:371–376.
- Smithells RW, Sheppard S, Schorah CJ. 1976. Vitamin deficiencies and neural tube defects. *Arch Dis Child* 51:944–950.
- Smithells RW, Sheppard S, Schorah CJ, Seller MJ, Nevin NC, Harris R, Read AP, Fielding DW. 1981. Apparent prevention of neural tube defects by periconceptional vitamin supplementation. *Arch Dis Child* 56:911–918.
- Smithells RW, Nevin NC, Seller MJ, Sheppard S, Harris R, Read AP, Fielding DW, Walker S, Schorah CJ, Wild J. 1983. Further experience of vitamin supplementation for prevention of neural tube defect recurrences. *Lancet* 1:1027–1031.
- Sparling R, Abela M. 1985. Hypersensitivity to folic acid therapy. *Clin Lab Haematol* 7:184–185.
- Spector RG. 1972. Influence of folic acid on exitable tissues. *Nature* 240:247–249.
- Spies TD, Stone RE. 1947. Liver extract, folic acid, and thymine in pernicious anemia and subacute combined degeneration. *Lancet* 1:174–176.
- Spies TD, Stone RE, Lopez GG, Milanes F, Aramburu T, Toca RL. 1948. The association between gastric achlorhydria and subacute combined degeneration of the spinal cord. *Postgrad Med* 4:89–95.
- Stabler SP, Marcell PD, Podell ER, Allen RH, Savage DG, Lindenbaum J. 1988. Elevation of total homocysteine in the serum of patients with cobalamin or folate deficiency detected by capillary gas chromatography-mass spectrometry. *J Clin Invest* 81:466–474.
- Stabler SP, Lindenbaum J, Allen RH. 1996. The use of homocysteine and other metabolites in the specific diagnosis of vitamin B-12 deficiency. *J Nutr* 126:1266S–1272S.
- Stanley OH, Chambers TL. 1982. Sodium valproate and neural tube defects. *Lancet* 2:1282–1283.
- Steegers-Theunissen RP, Boers GH, Blom HJ, Trijbels FJ, Eskes TK. 1992. Hyperhomocysteinaemia and recurrent spontaneous abortion or abruptio placentae. *Lancet* 339:1122–1123.
- Steegers-Theunissen RP, Boers GH, Trijbels FJ, Finkelstein JD, Blom HJ, Thomas CM, Borm GF, Wouters MG, Eskes TK. 1994. Maternal hyperhomocysteinemia: A risk factor for neural tube defects? *Metabolism* 43:1475–1480.
- Stites TE, Bailey LB, Scott KC, Toth JP, Fisher WP, Gregory JF 3rd. 1997. Kinetic modeling of folate metabolism through use of chronic administration of deuterium-labeled folic acid in men. *Am J Clin Nutr* 65:53–60.
- Suarez RM, Spies TD, Suarez RM Jr. 1947. The use of folic acid in sprue. *Ann Intern Med* 26:643–677.
- Subar AF, Harlan LC, Mattson ME. 1990. Food and nutrient intake differences between smokers and non-smokers in the U.S. *Am J Public Health* 80:1323–1329.
- Tamura T. 1995. Nutrient interaction of folate and zinc. In: Bailey LB, ed. *Folate in Health and Disease*. New York: Marcel Dekker. Pp. 287–312.

- Tamura T, Stokstad EL. 1973. The availability of food folate in man. *Br J Haematol* 25:513–532.
- Tamura T, Yoshimura Y, Arakawa T. 1980. Human milk folate and folate status in lactating mothers and their infants. *Am J Clin Nutr* 33:193–197.
- Tamura T, Goldenberg RL, Freeberg LE, Cliver SP, Cutter GR, Hoffman HJ. 1992. Maternal serum folate and zinc concentrations and their relationships to pregnancy outcome. *Am J Clin Nutr* 56:365–370.
- Tamura T, Mizuno Y, Johnston KE, Jacob RA. 1997. Food folate assay with protease,  $\alpha$ -amylase, and folate conjugase treatments. *J Agric Food Chem* 45:135–139.
- Tassabehji M, Read AP, Newton VE, Patton M, Gross P, Harris R, Strachan T. 1993. Mutations in the *PAX3* gene causing Waardenburg syndrome type I and type 2. *Nat Genet* 3:26–30.
- Thiersch JB. 1952. Therapeutic abortions with folic acid antagonists, 4-amino pteroylglutamic acid administration by the oral route. *Am J Obstet Gynecol* 63:1298–1304.
- Thirkettle JL, Gough KR, Read AE. 1964. Diagnostic value of small oral doses of folic acid in megaloblastic anemia. *Br Med J* 1:1286–1289.
- Tolarova M, Harris J. 1995. Reduced recurrence of orofacial clefts after periconceptional supplementation with high-dose folic acid and multivitamins. *Teratology* 51:71–78.
- Tsai JC, Perrella MA, Yoshizumi M, Hsieh CM, Haber E, Schlegel R, Lee ME. 1994. Promotion of vascular smooth muscle cell growth by homocysteine: A link to atherosclerosis. *Proc Natl Acad Sci USA* 91:6369–6373.
- Tucker KL, Selhub J, Wilson PW, Rosenberg IH. 1996. Dietary intake pattern relates to plasma folate and homocysteine concentrations in the Framingham Heart Study. *J Nutr* 126:3025–3031.
- Turner AJ. 1977. Commentary: The roles of folate and pteridine derivatives in neurotransmitter metabolism. *Biochem Pharmacol* 26:1009–1014.
- Ubbink JB, Vermaak WJ, van der Merwe A, Becker PJ. 1993. Vitamin B-12, vitamin B-6, and folate nutritional status in men with hyperhomocysteinemia. *Am J Clin Nutr* 57:47–53.
- Ubbink JB, Becker PJ, Vermaak WJ, Delport R. 1995a. Results of B-vitamin supplementation study used in a prediction model to define a reference range for plasma homocysteine. *Clin Chem* 41:1033–1037.
- Ubbink JB, Vermaak WJ, Delport R, van der Merwe A, Becker PJ, Potgieter H. 1995b. Effective homocysteine metabolism may protect South African blacks against coronary heart disease. *Am J Clin Nutr* 62:802–808.
- Vanaerts LA, Blom HJ, Deabreu RA, Trijbels FJ, Eskes TK, Copius Peereboom-Stegeman JH, Noordhoek J. 1994. Prevention of neural tube defects by and toxicity of L-homocysteine in cultured postimplantation rat embryos. *Teratology* 50:348–360.
- van der Put NM, Steegers-Theunissen RP, Frosst P, Trijbels FJ, Eskes TK, van den Heuvel LP, Mariman EC, den Heyer M, Rozen R, Blom HJ. 1995. Mutated methylenetetrahydrofolate reductase as a risk factor for spina bifida. *Lancet* 346:1070–1071.
- van der Put NM, Thomas CM, Eskes TK, Trijbels FJ, Steegers-Theunissen RP, Mariman EC, De Graaf-Hess A, Smeitink JA, Blom HJ. 1997a. Altered folate and vitamin B<sub>12</sub> metabolism in families with spina bifida offspring. *Q J Med* 90:505–510.

- van der Put NM, van der Molen EF, Kluijtmans LA, Heil SG, Trijbels JM, Eskes TK, Van Oppenraaij-Emmerzaal D, Banerjee R, Blom HJ. 1997b. Sequence analysis of the coding region of human methionine synthase: Relevance to hyperhomocysteinaemia in neural-tube defects and vascular disease. *Q J Med* 90:511–517.
- van der Westhuyzen J, Metz J. 1983. Tissue Sadenosylmethionine levels in fruit bats with N<sub>2</sub>O-induced neuropathy. *Br J Nutr* 50:325–330.
- van der Westhuyzen J, Fernandes-Costa F, Metz J. 1982. Cobalamin inactivation by nitrous oxide produces severe neurological impairment in fruit bats: Protection by methionine and aggravation by folates. *Life Sci* 31:2001–2010.
- Varadi S, Abbott D, Elwis A. 1966. Correlation of peripheral white cell and bone marrow changes with folate levels in pregnancy and their clinical significance. *J Clin Pathol* 19:33–36.
- Velie EM, Shaw GM. 1996. Impact of prenatal diagnosis and elective termination on prevalence and risk estimates of neural tube defects in California, 1989–1991. *Am J Epidemiol* 144:473–479.
- Vergel RG, Sanchez LR, Heredero BL, Rodriguez PL, Martinez AJ. 1990. Primary prevention of neural tube defects with folic acid supplementation: Cuban experience. *Prenat Diagn* 10:149–152.
- Verhaar MC, Wever RM, Kastelein JJ, van Dam T, Koomans HA, Rabelink TJ. 1998. 5-Methyltetrahydrofolate, the active form of folic acid, restores endothelial function in familial hypercholesterolemia. *Circulation* 97:237–241.
- Verhoef P, Stampfer MJ, Buring JE, Gaziano JM, Allen RH, Stabler SP, Reynolds RD, Kok FJ, Hennekens CH, Willett WC. 1996. Homocysteine metabolism and risk of myocardial infarction: Relation with vitamins B<sub>6</sub>, B<sub>12</sub>, and folate. *Am J Epidemiol* 143:845–859.
- Verhoef P, Kok FJ, Kluijtmans LA, Blom HJ, Refsum H, Ueland PM, Kruyssen DA. 1997a. The 677C→T mutation in the methylenetetrahydrofolate reductase gene: Associations with plasma total homocysteine levels and risk of coronary atherosclerotic disease. *Atherosclerosis* 132:105–113.
- Verhoef P, Rimm EB, Hunter DJ, Chen J, Willett WC, Kelsey K, Stampfer MJ. 1997b. Methylenetetrahydrofolate reductase polymorphism and risk of coronary heart disease: Results from health professionals study and meta-analysis. *Am J Epidemiol* 145:307.
- Verreault R, Chu J, Mandelson M, Shy K. 1989. A case-control study of diet and invasive cervical cancer. *Int J Cancer* 43:1050–1054.
- Victor M, Lear AA. 1956. Subacute combined degeneration of the spinal cord. Current concepts of the disease process. Value of serum vitamin B<sub>12</sub> determinations in clarifying some of the common clinical problems. *Am J Med* 20:896–911.
- Vilter CF, Vilter RW, Spies TD. 1947. The treatment of pernicious and related anemias with synthetic folic acid. 1. Observations on the maintenance of a normal hematologic status and on the occurrence of combined system disease at the end of one year. *J Lab Clin Med* 32:262–273.
- Volpe JJ. 1995. *Neurology of the Newborn*, 3rd ed. Philadelphia: WB Saunders.
- Von der Porten AE, Gregory JF 3rd, Toth JP, Cerda JJ, Curry SH, Bailey LB. 1992. In vivo folate kinetics during chronic supplementation of human subjects with deuterium-labeled folic acid. *J Nutr* 122:1293–1299.
- Wagley PF. 1948. Neurologic disturbances with folic acid therapy. *N Engl J Med* 238:11–15.

- Wagner C. 1996. Symposium on the subcellular compartmentation of folate metabolism. *J Nutr* 126:1228S–1234S.
- Wahlin A, Hill RD, Winblad B, Backman L. 1996. Effects of serum vitamin B<sub>12</sub> and folate status on episodic memory performance in very old age: A population-based study. *Psychol Aging* 11:487–496.
- Wald NJ. 1994. Folic acid and neural tube defects: The current evidence and implications for prevention. *Ciba Found Symp* 181:192–208.
- Wald N, Sneddon J, Densem J, Frost C, Stone R. 1991. Prevention of neural tube defects: Results of the Medical Research Council vitamin study. *Lancet* 338:131–137.
- Watanabe M, Osada J, Aratani Y, Kluckman K, Reddick R, Malinow MR, Maeda N. 1995. Mice deficient in cystathione beta-synthase: Animal models for mild and severe homocyst(e)inemia. *Proc Natl Acad Sci USA* 92:1585–1589.
- Ward M, McNulty H, McPartlin J, Strain JJ, Weir DG, Scott JM. 1997. Plasma homocysteine, a risk factor for cardiovascular disease, is lowered by physiological doses of folic acid. *Q J Med* 90:519–524.
- Wei M-M, Bailey LB, Toth JP, Gregory JF 3rd. 1996. Bioavailability for humans of deuterium-labeled monoglutamyl and polyglutamyl folates is affected by selected foods. *J Nutr* 126:3100–3108.
- Weir DG, McGing PG, Scott JM. 1985. Commentary: Folate metabolism, the enterohepatic circulation and alcohol. *Biochem Pharmacol* 34:1–7.
- Weller M, Marini AM, Martin B, Paul SM. 1994. The reduced unsubstituted pteroate moiety is required for folate toxicity of cultured cerebellar granule neurons. *J Pharmacol Exp Ther* 269:393–401.
- Werler MM, Shapiro S, Mitchell AA. 1993. Periconceptional folic acid exposure and risk of occurrent neural tube defects. *J Am Med Assoc* 269:1257–1261.
- Whitehead AS, Gallagher P, Mills JL, Kirke PN, Burke H, Molloy AM, Weir DG, Shields DC, Scott JM. 1995. A genetic defect in 5, 10 methylenetetrahydrofolate reductase in neural tube defects. *Q J Med* 88:763–766.
- Whitehead VM. 1973. Polygammaglutamyl metabolites of folic acid in human liver. *Lancet* 1:743–745.
- Whitehead VM. 1986. Pharmacokinetics and physiological disposition of folate and its derivatives. In: Blakely RL, Whitehead VM, eds. *Folates and Pterins*, Vol. 3. New York: John Wiley & Sons. Pp. 177–205.
- Wilcken DE, Wilcken B. 1976. The pathogenesis of coronary artery disease. A possible role for methionine metabolism. *J Clin Invest* 57:1079–1082.
- Wilcken DE, Wang XL, Sim AS, McCredie RM. 1996. Distribution in healthy and coronary populations of the methylenetetrahydrofolate reductase (MTHFR) C677T mutation. *Arterioscler Thromb Vasc Biol* 16:878–882.
- Will JJ, Mueller JF, Brodine C, Kiely CE, Friedman B, Hawkins VR, Dutra J, Vilter RN. 1959. Folic acid and vitamin B<sub>12</sub> in pernicious anemia. Studies on patients treated with these substances over a ten-year period. *J Lab Clin Med* 53:22–38.
- Willard JE, Lange RA, Hillis LD. 1992. The use of aspirin in ischemic heart disease. *N Engl J Med* 327:175–181.
- Willoughby ML. 1967. An investigation of folic acid requirements in pregnancy. II. *Br J Haematol* 13:503–509.
- Willoughby ML, Jewell FJ. 1966. Investigation of folic acid requirements in pregnancy. *Br Med J* 2:1568–1571.
- Willoughby ML, Jewell FG. 1968. Folate status throughout pregnancy and in postpartum period. *Br Med J* 4:356–360.
- Wilson JG. 1973. *Environment and Birth Defects*. New York: Academic Press.
- Witter FR, Blake DA, Baumgardner R, Mellits ED, Niebyl JR. 1982. Folate, carotene, and smoking. *Am J Obstet Gynecol* 144:857.

- Wouters MG, Boers GH, Blom HJ, Trijbels FJ, Thomas CM, Borm GF, Steegers-Theunissen RP, Eskes TK. 1993. Hyperhomocysteinemia: A risk factor in women with unexplained recurrent early pregnancy loss. *Fertil Steril* 60:820–825.
- Wu A, Chanarin I, Slavin G, Levi AJ. 1975. Folate deficiency in the alcoholic—its relationship to clinical and haematological abnormalities, liver disease and folate stores. *Br J Haematol* 29:469–478.
- Yen IH, Khoury MJ, Erickson JD, James LM, Waters GD, Berry RJ. 1992. The changing epidemiology of neural tube defects: United States, 1968–1989. *Am J Dis Child* 146:857–861.
- Young SN, Ghadirian AM. 1989. Folic acid and psychopathology. *Prog Neuropsychopharmacol Biol Psychiatry* 13:841–863.
- Zalusky R, Herbert V. 1961. Megaloblastic anemia in scurvy with response to 50 micrograms of folic acid daily. *N Engl J Med* 265:1033–1038.
- Ziegler RG, Brinton LA, Hammon RF, Lehman HF, Levine RS, Mallin K, Norman SA, Rosenthal JF, Trumble AC, Hoover RN. 1990. Diet and risk of invasive cervical cancer among white women in the United States. *Am J Epidemiol* 132:432–445.
- Ziegler RG, Jones CJ, Brinton LA, Norman SA, Mallin K, Levine RS, Lehman HF, Hammon RF, Trumble AC, Rosenthal JF. 1991. Diet and risk of in situ cervical cancer among white women in the United States. *Cancer Causes Control* 2:17–29.
- Zimmerman J. 1990. Folic acid transport in organ-cultured mucosa of human intestine. Evidence for distinct carriers. *Gastroenterology* 99:964–972.

Ibid., Chapter 13, p. 436.

- Beaton GH. 1994. Criteria of an adequate diet. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*, 8th ed. Philadelphia: Lea & Febiger. Pp. 1491–1505.
- Hegsted DM. 1972. Problems in the use and interpretation of the Recommended Dietary Allowances. *Ecol Food Nutr* 1:255–265.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- USDA (U.S. Department of Agriculture). 1992. *The Food Guide Pyramid*. Home and Garden Bulletin Number 252. Washington, DC: US Government Printing Office.
- WHO (World Health Organization). 1996. *Trace Elements in Human Nutrition and Health*. Prepared in collaboration with the Food and Agriculture Organization of the United Nations and the International Atomic Energy Agency. Geneva: WHO.

## VITAMIN K

*Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*  
(ISBN 0-309-07290-5), Chapter 5, pp. 189–196.

- AAP (American Academy of Pediatrics). 1993. Controversies concerning vitamin K and the newborn. *Pediatrics* 91:1001–1003.
- Alexander GD, Suttie JW. 1999. The effects of vitamin E on vitamin K activity. *FASEB J* 13:A535.
- Allison PM, Mumma-Schendel LL, Kindberg CG, Harms CS, Bang NU, Suttie JW. 1987. Effects of a vitamin K-deficient diet and antibiotics in normal human volunteers. *J Lab Clin Med* 110:180–188.
- Anai T, Hirota Y, Yoshimatsu J, Oga M, Miyakawa I. 1993. Can prenatal vitamin K1 (phylloquinone) supplementation replace prophylaxis at birth? *Obstet Gynecol* 81:251–254.
- Ansell P, Bull D, Roman E. 1996. Childhood leukaemia and intramuscular vitamin K: Findings from a case-control study. *Br Med J* 313:204–205.
- Bach AU, Anderson SA, Foley AL, Williams EC, Suttie JW. 1996. Assessment of vitamin K status in human subjects administered “minidose” warfarin. *Am J Clin Nutr* 64:894–902.
- Badr M, Yoshihara H, Kauffman F, Thurman R. 1987. Menadione causes selective toxicity to periportal regions of the liver lobule. *Toxicol Lett* 35:241–246.
- Bettger WJ, Olson RE. 1982. Effect of alpha-tocopherol and alpha-tocopherolquinone on vitamin K-dependent carboxylation in the rat. *Fed Proc* 41:344.
- Binkley NC, Suttie JW. 1995. Vitamin K nutrition and osteoporosis. *J Nutr* 125:1812–1821.
- Binkley NC, Krueger D, Todd H, Foley A, Engelke J, Suttie J. 1999. Serum under-carboxylated osteocalcin concentration is reduced by vitamin K supplementation. *FASEB J* 13:A238.
- Blanchard RA, Furie BC, Jorgensen M, Kruger SF, Furie B. 1981. Acquired vitamin K-dependent carboxylation deficiency in liver disease. *N Engl J Med* 305:242–248.
- Booth SL, Suttie JW. 1998. Dietary intake and adequacy of vitamin K. *J Nutr* 128:785–788.
- Booth SL, Sadowski JA, Weihrauch JL, Ferland G. 1993. Vitamin K1 (phylloquinone) content of foods: A provisional table. *J Food Comp Anal* 6:109–120.
- Booth SL, Sokoll LJ, O'Brien ME, Tucker K, Dawson-Hughes B, Sadowski JA. 1995. Assessment of dietary phylloquinone intake and vitamin K status in post-menopausal women. *Eur J Clin Nutr* 49:832–841.
- Booth SL, Pennington JA, Sadowski JA. 1996a. Dihydro-vitamin K1: Primary food sources and estimated dietary intakes in the American diet. *Lipids* 31:715–720.
- Booth SL, Pennington JA, Sadowski JA. 1996b. Food sources and dietary intakes of vitamin K-1 (phylloquinone) in the American diet: Data from the FDA Total Diet Study. *J Am Diet Assoc* 96:149–154.
- Booth SL, Charnley JM, Sadowski JA, Saltzman E, Bovill EG, Cushman M. 1997a. Dietary vitamin K1 and stability of oral anticoagulation: Proposal of a diet with constant vitamin K1 content. *Thromb Haemost* 77:504–509.

- Booth SL, Tucker KL, McKeown NM, Davidson KW, Dallal GE, Sadowski JA. 1997b. Relationships between dietary intakes and fasting plasma concentrations of fat-soluble vitamins in humans. *J Nutr* 127:587–592.
- Booth SL, O'Brien-Morse ME, Dallal GE, Davidson KW, Gundberg CM. 1999a. Response of vitamin K status to different intakes and sources of phylloquinone-rich foods: Comparison of younger and older adults. *Am J Clin Nutr* 70:368–377.
- Booth SL, O'Brien-Morse ME, Saltzman E, Lichtenstein AH, McKeown NM, Wood RJ, Gundberg CM. 1999b. Influence of dietary vitamin K1 (phylloquinone) on bone resorption. *FASEB J* 13:A580.
- Booth SL, Webb DR, Peters JC. 1999c. Assessment of phylloquinone and dihydrophylloquinone dietary intakes among a nationally representative sample of US consumers using 14-day food diaries. *J Am Diet Assoc* 99:1072–1076.
- Canfield LM, Hopkinson JM, Lima AF, Martin GS, Sugimoto K, Burr J, Clark L, McGee DL. 1990. Quantitation of vitamin K in human milk. *Lipids* 25:406–411.
- Canfield LM, Hopkinson JM, Lima AF, Silva B, Garza C. 1991. Vitamin K in colostrum and mature human milk over the lactation period—A cross-sectional study. *Am J Clin Nutr* 53:730–735.
- Caraballo PJ, Gabriel SE, Castro MR, Atkinson EJ, Melton LJ III. 1999. Changes in bone density after exposure to oral anticoagulants: A meta-analysis. *Osteoporos Int* 9:441–448.
- Chiou TJ, Chou YT, Tzeng WF. 1998. Menadione-induced cell degeneration is related to lipid peroxidation in human cancer cells. *Proc Natl Sci Counc Repub China B* 22:13–21.
- Corrigan JJ Jr, Ulfers LL. 1981. Effect of vitamin E on prothrombin levels in warfarin-induced vitamin K deficiency. *Am J Clin Nutr* 34:1701–1705.
- CPS (Canadian Paediatric Society). 1998. Routine administration of vitamin K to newborns. Joint position paper of the Canadian Paediatric Society and the Committee on Child and Adolescent Health of the College of Family Physicians of Canada. *Can Fam Physician* 44:1083–1090.
- Davidson KW, Booth SL, Dolnikowski GG, Sadowski JA. 1996. The conversion of phylloquinone to 2',3'-dihydrophylloquinone during hydrogenation of vegetable oils. *J Agric Food Chem* 44:980–983.
- Davidson RT, Foley AL, Engelke JA, Suttie JW. 1998. Conversion of dietary phylloquinone to tissue menaquinone-4 in rats is not dependent on gut bacteria. *J Nutr* 128:220–223.
- Delmas PD, Christiansen C, Mann KG, Price PA. 1990a. Bone Gla protein (osteocalcin) assay standardization report. *J Bone Miner Res* 5:5–11.
- Delmas PD, Price PA, Mann KG. 1990b. Validation of the bone Gla protein (osteocalcin) assay. *J Bone Miner Res* 5:3–4.
- Dickson RC, Stubbs TM, Lazarchick J. 1994. Antenatal vitamin K therapy of the low-birth-weight infant. *Am J Obstet Gynecol* 170:85–89.
- Douglas AS, Robins SP, Hutchison JD, Porter RW, Stewart A, Reid DM. 1995. Carboxylation of osteocalcin in post-menopausal osteoporotic women following vitamin K and D supplementation. *Bone* 17:15–20.
- Dowd P, Zheng ZB. 1995. On the mechanism of the anticoagulant action of vitamin E quinone. *Proc Natl Acad Sci* 92:8171–8175.
- Ducy P, Desbois C, Boyce B, Pinero G, Story B, Dunstan C, Smith E, Bonadio J, Goldstein S, Gundberg C, Bradley A, Karsenty G. 1996. Increased bone formation in osteocalcin-deficient mice. *Nature* 382:448–452.

- Ekelund H, Finnstrom O, Gunnarskog J, Kallen B, Larsson Y. 1993. Administration of vitamin K to newborn infants and childhood cancer. *Br Med J* 307:89–91.
- Ferland G. 1998. The vitamin K-dependent proteins: An update. *Nutr Rev* 56:223–230.
- Ferland G, Sadowski JA, O'Brien ME. 1993. Dietary induced subclinical vitamin K deficiency in normal human subjects. *J Clin Invest* 91:1761–1768.
- Feskanich D, Weber P, Willett WC, Rockett H, Booth SL, Colditz GA. 1999. Vitamin K intake and hip fractures in women: A prospective study. *Am J Clin Nutr* 69:74–79.
- Fournier B, Leclercq M, Audigier-Petit C, Letoublon R, Got R, Frot-Coutaz J. 1987. Vitamin K<sub>1</sub> binding protein in milk. *Int J Vitamin Nutr Res* 57:145–150.
- Francis JL. 1988. A rapid and simple micromethod for the specific determination of descarboxylated prothrombin (PIVKA II). *Med Lab Sci* 45:69–73.
- Frick PG, Riedler G, Brogli H. 1967. Dose response and minimal daily requirement for vitamin K in man. *J Appl Physiol* 23:387–389.
- Garber AK, Binkley NC, Krueger DC, Suttie JW. 1999. Comparison of phylloquinone bioavailability from food sources or a supplement in human subjects. *J Nutr* 129:1201–1203.
- Gijsbers BL, van Haarlem LJ, Soute BA, Ebberink RH, Vermeer C. 1990. Characterization of a Gla-containing protein from calcified human atherosclerotic plaques. *Arteriosclerosis* 10:991–995.
- Gijsbers BL, Jie KS, Vermeer C. 1996. Effect of food composition on vitamin K absorption in human volunteers. *Br J Nutr* 76:223–229.
- Golding J, Paterson M, Kinlen LJ. 1990. Factors associated with childhood cancer in a national cohort study. *Br J Cancer* 62:304–308.
- Golding J, Greenwood R, Birmingham K, Mott M. 1992. Childhood cancer, intramuscular vitamin K, and pethidine given during labour. *Br Med J* 305:341–346.
- Greer FR. 1995. The importance of vitamin K as a nutrient during the first year of life. *Nutr Res* 15:289–310.
- Greer FR, Marshall S, Cherry J, Suttie JW. 1991. Vitamin K status of lactating mothers, human milk, and breast-feeding infants. *Pediatrics* 88:751–756.
- Greer FR, Marshall SP, Foley AL, Suttie JW. 1997. Improving the vitamin K status of breastfeeding infants with maternal vitamin K supplements. *Pediatrics* 99:88–92.
- Gundberg CM, Nieman SD, Abrams S, Rosen H. 1998. Vitamin K status and bone health: An analysis of methods for determination of undercarboxylated osteocalcin. *J Clin Endocrinol Metab* 83:3258–3266.
- Hara K, Akiyama Y, Nakamura T, Murota S, Morita I. 1995. The inhibitory effect of vitamin K<sub>2</sub> (menatetrenone) on bone resorption may be related to its side chain. *Bone* 16:179–184.
- Haroon Y, Shearer MJ, Rahim S, Gunn WG, McEnery G, Barkhan P. 1982. The content of phylloquinone (vitamin K<sub>1</sub>) in human milk, cows' milk and infant formula foods determined by high-performance liquid chromatography. *J Nutr* 112:1105–1117.
- Hart JP, Shearer MJ, Klenerman L, Catterall A, Reeve J, Sambrook PN, Dodds RA, Bitensky L, Chayen J. 1985. Electrochemical detection of depressed circulating levels of vitamin K<sub>1</sub> in osteoporosis. *J Clin Endocrinol Metab* 60:1268–1269.
- Hodges SJ, Pilkington MJ, Stamp TC, Catterall A, Shearer MJ, Bitensky L, Chayen J. 1991. Depressed levels of circulating menaquinones in patients with osteoporotic fractures of the spine and femoral neck. *Bone* 12:387–389.

- Hodges SJ, Akesson K, Vergnaud P, Obrant K, Delmas PD. 1993. Circulating levels of vitamins K1 and K2 decreased in elderly women with hip fracture. *J Bone Miner Res* 8:1241–1245.
- Hogenbirk K, Peters M, Bouman P, Sturk A, Buller HA. 1993. The effect of formula versus breast feeding and exogenous vitamin K1 supplementation on circulating levels of vitamin K1 and vitamin K-dependent clotting factors in newborns. *Eur J Pediatr* 152:72–74.
- Ichihashi T, Takagishi Y, Uchida K, Yamada H. 1992. Colonic absorption of menaquinone-4 and menaquinone-9 in rats. *J Nutr* 122:506–512.
- Indyk HE, Woollard DC. 1997. Vitamin K and infant formulas: Determination and distribution of phylloquinone and menaquinone-4. *Analyst* 122:465–469.
- Jie KS, Bots ML, Vermeer C, Witteman JC, Grobbee DE. 1995. Vitamin K intake and osteocalcin levels in women with and without aortic atherosclerosis: A population-based study. *Atherosclerosis* 116:117–123.
- Jones DY, Koonsvitsky BP, Ebert ML, Jones MB, Lin PY, Will BH, Suttie JW. 1991. Vitamin K status of free-living subjects consuming olestra. *Am J Clin Nutr* 53:943–946.
- Kanai T, Takagi T, Masuhiro K, Nakamura M, Iwata M, Saji F. 1997. Serum vitamin K level and bone mineral density in post-menopausal women. *Int J Gynaecol Obstet* 56:25–30.
- Kazzi NJ, Ilagan NB, Liang KC, Kazzi GM, Grietsell LA, Brans YW. 1990. Placental transfer of vitamin K1 in preterm pregnancy. *Obstet Gynecol* 75:334–337.
- Klebanoff MA, Read JS, Mills JL, Shiono PH. 1993. The risk of childhood cancer after neonatal exposure to vitamin K. *N Engl J Med* 329:905–908.
- Knapen MH, Hamulyak K, Vermeer C. 1989. The effect of vitamin K supplementation on circulating osteocalcin (bone Gla protein) and urinary calcium excretion. *Ann Intern Med* 111:1001–1005.
- Knapen MH, Jie KS, Hamulyak K, Vermeer C. 1993. Vitamin K-induced changes in markers for osteoblast activity and urinary calcium loss. *Calcif Tissue Int* 53:81–85.
- Knapen MH, Nieuwenhuijzen Kruseman AC, Wouters RS, Vermeer C. 1998. Correlation of serum osteocalcin fractions with bone mineral density in women during the first 10 years after menopause. *Calcif Tissue Int* 63:375–379.
- Kohlmeier M, Saupe J, Drossel HJ, Shearer MJ. 1995. Variation of phylloquinone (vitamin K1) concentrations in hemodialysis patients. *Thromb Haemost* 74:1252–1254.
- Kohlmeier M, Salomon A, Saupe J, Shearer MJ. 1996. Transport of vitamin K to bone in humans. *J Nutr* 126:1192S–1196S.
- Koivu TJ, Piironen VI, Henttonen SK, Mattila PH. 1997. Determination of phylloquinone in vegetables, fruits, and berries by high-performance liquid chromatography with electrochemical detection. *J Agric Food Chem* 45:4644–4649.
- Lamon-Fava S, Sadowski JA, Davidson KW, O'Brien ME, McNamara JR, Schaefer EJ. 1998. Plasma lipoproteins as carriers of phylloquinone (vitamin K1) in humans. *Am J Clin Nutr* 67:1226–1231.
- Lane PA, Hathaway WE. 1985. Vitamin K in infancy. *J Pediatr* 106:351–359.
- Levy RJ, Lian JB, Gallop P. 1979. Atherocalcin, a gamma-carboxyglutamic acid containing protein from atherosclerotic plaque. *Biochem Biophys Res Commun* 91:41–49.
- Liu G, Peacock M. 1998. Age-related changes in serum undercarboxylated osteocalcin and its relationships with bone density, bone quality, and hip fracture. *Calcif Tissue Int* 62:286–289.

- Lubetsky A, Dekel-Stern E, Chetrit A, Lubin F, Halkin H. 1999. Vitamin K intake and sensitivity to warfarin in patients consuming regular diets. *Thromb Haemost* 81:396–399.
- Luo G, Ducy P, McKee MD, Pinero GJ, Loyer E, Behringer RR, Karsenty G. 1997. Spontaneous calcification of arteries and cartilage in mice lacking matrix GLA protein. *Nature* 386:78–81.
- Mandelbrot L, Guillaumont M, Leclercq M, Lefrere JJ, Gozin D, Daffos F, Forestier F. 1988. Placental transfer of vitamin K1 and its implications in fetal hemostasis. *Thromb Haemost* 60:39–43.
- McCarthy DJ, Lindamood C 3d, Gundberg CM, Hill DL. 1989. Retinoid-induced hemorrhaging and bone toxicity in rats fed diets deficient in vitamin K. *Toxicol Appl Pharmacol* 97:300–310.
- McKinney PA, Juszczak E, Findlay E, Smith K. 1998. Case-control study of childhood leukaemia and cancer in Scotland: Findings for neonatal intramuscular vitamin K. *Br Med J* 316:173–177.
- Molitor H, Robinson J. 1940. Oral and parenteral toxicity of vitamin K1, phthiocol, and 2 methyl 1,4 naphthoquinone. *Proc Soc Exp Biol Med* 43:125–128.
- Morales WJ, Angel JL, O'Brien WF, Knuppel RA, Marsalisi F. 1988. The use of antenatal vitamin K in the prevention of early neonatal intraventricular hemorrhage. *Am J Obstet Gynecol* 159:774–779.
- Motohara K, Matsukane I, Endo F, Kiyota Y, Matsuda I. 1989. Relationship of milk intake and vitamin K supplementation to vitamin K status in newborns. *Pediatrics* 84:90–93.
- NRC (National Research Council). 1987. *Vitamin Tolerance of Animals*. Washington, DC: National Academy Press.
- Olsen JH, Hertz H, Blinkenberg K, Verder H. 1994. Vitamin K regimens and incidence of childhood cancer in Denmark. *Br Med J* 308:895–896.
- Orimo H, Shiraki M, Fujita T, Onomura T, Inoue T, Kushida K. 1992. Clinical evaluation of menatetrenone in the treatment of involutional osteoporosis—A double-blind multicenter comparative study with 1- $\alpha$ -hydroxyvitamin D<sub>3</sub>. *J Bone Miner Res* 7:S122.
- Parker L, Cole M, Craft AW, Hey EN. 1998. Neonatal vitamin K administration and childhood cancer in the north of England: Retrospective case-control study. *Br Med J* 316:189–193.
- Passmore SJ, Draper G, Brownbill P, Kroll M. 1998. Case-control studies of relation between childhood cancer and neonatal vitamin K administration. *Br Med J* 316:178–184.
- Pietschnig B, Haschke F, Vanura H, Shearer M, Veitl V, Kellner S, Schuster E. 1993. Vitamin K in breast milk: No influence of maternal dietary intake. *Eur J Clin Nutr* 47:209–215.
- Piironen V, Koivu T, Tammisalo O, Mattila P. 1997. Determination of phylloquinone in oils, margarines and butter by high-performance liquid chromatography with electrochemical detection. *Food Chem* 59:473–480.
- Plantalech L, Guillaumont M, Vergnaud P, Leclercq M, Delmas PD. 1991. Impairment of gamma carboxylation of circulating osteocalcin (bone gla protein) in elderly women. *J Bone Miner Res* 6:1211–1216.
- Price PA. 1988. Role of vitamin K-dependent proteins in bone metabolism. *Annu Rev Nutr* 8:565–583.
- Price R, Fenton S, Shearer MJ, Bolton-Smith C. 1996. Daily and seasonal variation in phylloquinone (vitamin K1) intake in Scotland. *Proc Nutr Soc* 55:244A.

- Rao GH, Mason KE. 1975. Antisterility and antivitamin K activity of d-alpha-tocopheryl hydroquinone in the vitamin E-deficient female rat. *J Nutr* 105:495–498.
- Ravn P, Fledelius C, Rosenquist C, Overgaard K, Christiansen C. 1996. High bone turnover is associated with low bone mass in both pre- and postmenopausal women. *Bone* 19:291–298.
- Rosen HN, Maitland LA, Suttie JW, Manning WJ, Glynn RJ, Greenspan SL. 1993. Vitamin K and maintenance of skeletal integrity in adults. *Am J Med* 94:62–68.
- Sadowski JA, Hood SJ, Dallal GE, Garry PJ. 1989. Phylloquinone in plasma from elderly and young adults: Factors influencing its concentration. *Am J Clin Nutr* 50:100–108.
- Saupe J, Shearer MJ, Kohlmeier M. 1993. Phylloquinone transport and its influence on gamma-carboxyglutamate residues of osteocalcin in patients on maintenance hemodialysis. *Am J Clin Nutr* 58:204–208.
- Savage D, Lindenbaum J. 1983. Clinical and experimental human vitamin K deficiency. In: Lindenbaum J, ed. *Nutrition in Hematology*. New York: Churchill Livingstone. Pp. 271–320.
- Schurgers LJ, Geleijnse JM, Grobbee DE, Pols HAP, Hofman A, Witteman JCM, Vermeer C. 1999. Nutritional intake of vitamins K1 (phylloquinone) and K2 (menaquinone) in The Netherlands. *J Nutr Environ Med* 9:115–122.
- Shah DV, Tews JK, Harper AE, Suttie JW. 1978. Metabolism and transport of gamma-carboxyglutamic acid. *Biochim Biophys Acta* 539:209–217.
- Shearer MJ. 1992. Vitamin K metabolism and nutriture. *Blood Rev* 6:92–104.
- Shearer MJ, Barkhan P, Webster GR. 1970. Absorption and excretion of an oral dose of tritiated vitamin K1 in man. *Br J Haematol* 18:297–308.
- Shearer MJ, McBurney A, Barkhan P. 1974. Studies on the absorption and metabolism of phylloquinone (vitamin K1) in man. *Vitam Horm* 32:513–542.
- Shearer MJ, Bach A, Kohlmeier M. 1996. Chemistry, nutritional sources, tissue distribution and metabolism of vitamin K with special reference to bone health. *J Nutr* 126:1181S–1186S.
- Sokoll LJ, Sadowski JA. 1996. Comparison of biochemical indexes for assessing vitamin K nutritional status in a healthy adult population. *Am J Clin Nutr* 63:566–573.
- Sokoll LJ, O'Brien ME, Camilo ME, Sadowski JA. 1995. Undercarboxylated osteocalcin and development of a method to determine vitamin K status. *Clin Chem* 41:1121–1128.
- Sokoll LJ, Booth SL, O'Brien ME, Davidson KW, Tsaioun KI, Sadowski JA. 1997. Changes in serum osteocalcin, plasma phylloquinone, and urinary gamma-carboxyglutamic acid in response to altered intakes of dietary phylloquinone in human subjects. *Am J Clin Nutr* 65:779–784.
- Suttie JW. 1992. Vitamin K and human nutrition. *J Am Diet Assoc* 92:585–590.
- Suttie JW. 1993. Synthesis of vitamin K-dependent proteins. *FASEB J* 7:445–452.
- Suttie JW. 1995. The importance of menaquinones in human nutrition. *Annu Rev Nutr* 15:399–417.
- Suttie JW, Mummah-Schendel LL, Shah DV, Lyle BJ, Greger JL. 1988. Vitamin K deficiency from dietary vitamin K restriction in humans. *Am J Clin Nutr* 47:475–480.
- Szulc P, Chapuy MC, Meunier PJ, Delmas PD. 1993. Serum undercarboxylated osteocalcin is a marker of the risk of hip fracture in elderly women. *J Clin Invest* 91:1769–1774.

- Szulc P, Chapuy MC, Meunier PJ, Delmas PD. 1996. Serum undercarboxylated osteocalcin is a marker of the risk of hip fracture: A three year follow-up study. *Bone* 18:487–488.
- Tamatani M, Morimoto S, Nakajima M, Fukuo K, Onishi T, Kitano S, Niinobu T, Ogihara T. 1998. Decreased circulating levels of vitamin K and 25-hydroxyvitamin D in osteopenic elderly men. *Metabolism* 47:195–199.
- Thijssen HH, Drittij-Reijnders MJ. 1994. Vitamin K distribution in rat tissues: Dietary phylloquinone is a source of tissue menaquinone-4. *Br J Nutr* 72:415–425.
- Thijssen HH, Drittij-Reijnders MJ. 1996. Vitamin K status in human tissues: Tissue-specific accumulation of phylloquinone and menaquinone-4. *Br J Nutr* 75:121–127.
- Udall JA. 1965. Human sources and absorption of vitamin K in relation to anti-coagulation stability. *J Am Med Assoc* 194:107–109.
- Usui Y, Tanimura H, Nishimura N, Kobayashi N, Okanoue T, Ozawa K. 1990. Vitamin K concentrations in the plasma and liver of surgical patients. *Am J Clin Nutr* 51:846–852.
- Vergnaud P, Garnero P, Meunier PJ, Breart G, Kamihagi K, Delmas PD. 1997. Undercarboxylated osteocalcin measured with a specific immunoassay predicts hip fracture in elderly women: The EPIDOS Study. *J Clin Endocrinol Metab* 82:719–724.
- Vermeer C, Jie KS, Knapen MH. 1995. Role of vitamin K in bone metabolism. *Annu Rev Nutr* 15:1–22.
- Vermeer C, Gijsbers BL, Craciun AM, Groenen-van Dooren MM, Knapen MH. 1996. Effects of vitamin K on bone mass and bone metabolism. *J Nutr* 126:1187S–1191S.
- von Kries R, Kreppel S, Becker A, Tangermann R, Gobel U. 1987a. Acarboxyprothrombin concentration after oral prophylactic vitamin K. *Arch Dis Child* 62:938–940.
- von Kries R, Shearer M, McCarthy PT, Haug M, Harzer G, Gobel U. 1987b. Vitamin K1 content of maternal milk: Influence of the stage of lactation, lipid composition, and vitamin K1 supplements given to the mother. *Pediatr Res* 22:513–517.
- von Kries R, Shearer MJ, Widdershoven J, Motohara K, Umbach G, Gobel U. 1992. Des-gamma-carboxyprothrombin (PIVKA II) and plasma vitamin K1 in newborns and their mothers. *Thromb Haemost* 68:383–387.
- von Kries R, Kordass U, Shearer M, Gobel U. 1993. Idiopathic late hemorrhagic disease of newborn and conjugated hyperbilirubinemia. *J Pediatr Gastroenterol Nutr* 16:328–330.
- von Kries R, Gobel U, Hachmeister A, Kaletsch U, Michaelis J. 1996. Vitamin K and childhood cancer: A population based case-control study in Lower Saxony, Germany. *Br Med J* 313:199–203.
- Weber P. 1997. Management of osteoporosis: Is there a role for vitamin K? *Int J Vitam Nutr Res* 67:350–356.
- Widdershoven J, Lambert W, Motohara K, Monnens L, de Leenheer A, Matsuda I, Endo F. 1988. Plasma concentrations of vitamin K1 and PIVKA-II in bottle-fed and breast-fed infants with and without vitamin K prophylaxis at birth. *Eur J Pediatr* 148:139–142.
- Woolley DW. 1945. Some biological effects produced by  $\alpha$ -tocopheral quinone. *J Biol Chem* 159:59–66.

## Ibid., Chapter 14, pp. 578–579.

- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Examination Survey: Under-reporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Gibson RS, Ferguson EL. 1998. Assessment of dietary zinc in a population. *Am J Clin Nutr* 68:430S–434S.
- Hallberg L, Hulthen L. 2000. Prediction of dietary iron absorption: An algorithm for calculating absorption and bioavailability of dietary iron. *Am J Clin Nutr* 71:1147–1160.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1980. *Recommended Dietary Allowances*, 9th ed. Washington, DC: National Academy Press.
- NRC. 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC. 1989. *Recommended Dietary Allowances*, 10th ed. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Schoeller DA. 1999. Recent advances from application of doubly labeled water to measurement of human energy expenditure. *J Nutr* 129:1765–1768.
- USDA (U.S. Department of Agriculture). 1999. *USDA Nutrient Database for Standard Reference*, Release 13. [Online.] Available: <http://www.nal.usda.gov/fnic/foodcomp> [accessed February 2000].
- WHO (World Health Organization). 1996. Zinc. In: *Trace Elements in Human Nutrition and Health*. Geneva: WHO. Pp. 72–104.

## NIACIN

*Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline* (ISBN 0-309-06411-2), Chapter 6, pp. 145–149.

- Bean WB, Spies TD. 1940. A study of the effects of nicotinic acid and related pyridine and pyrazine compounds on the temperature of the skin of human beings. *Am Heart J* 20:62–75.
- Bechgaard H, Jespersen S. 1977. GI absorption of niacin in humans. *J Pharm Sci* 66:871–872.
- Bernofsky C. 1980. Physiology aspects of pyridine nucleotide regulation in mammals. *Mol Cell Biochem* 33:135–143.
- Carpenter KJ, Lewin WJ. 1985. A reexamination of the composition of diets associated with pellagra. *J Nutr* 115:543–552.
- Carter EG, Carpenter KJ. 1982. The bioavailability for humans of bound niacin from wheat bran. *Am J Clin Nutr* 36:855–861.
- CDC (Centers for Disease Control and Prevention). 1983. Niacin intoxication from pumpernickel bagels—New York. *MMWR* 32:305.
- Clementz GL, Holmes AW. 1987. Nicotinic acid-induced fulminant hepatic failure. *J Clin Gastroenterol* 9:582–584.
- Committee on Nutrition. 1985. Composition of human milk: Normative data. In: *Pediatric Nutrition Handbook*, 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics. Pp. 363–368.
- Dalton TA, Berry RS. 1992. Hepatotoxicity associated with sustained-release niacin. *Am J Med* 93:102–104.
- Dillon JC, Malfait P, Demaux G, Foldihope C. 1992. Urinary metabolites of niacin during the course of pellagra. *Ann Nutr Metab* 36:181–185.
- Einstein N, Baker A, Galper J, Wolfe H. 1975. Jaundice due to nicotinic acid therapy. *Am J Dig Dis* 20:282–286.
- Estep DL, Gay GR, Rappolt RT Sr. 1977. Preliminary report of the effects of propranolol HCl on the discomfiture caused by niacin. *Clin Toxicol* 11:325–328.
- Etchason JA, Miller TD, Squires RW, Allison TG, Gau GT, Marttila JK, Kottke BA. 1991. Niacin-induced hepatitis: A potential side effect with low-dose time-release niacin. *Mayo Clin Proc* 66:23–28.
- Ferenchick G, Rovner D. 1989. Case report: Hepatitis and hematemesis complicating nicotinic acid use. *Am J Med Sci* 298:191–193.
- Ford JE, Zechaldo A, Murphy J, Brooke OG. 1983. Comparison of the B vitamin composition of milk from mothers of preterm and term babies. *Arch Dis Child* 58:367–372.
- Fraunfelder FW, Fraunfelder FT, Illingworth DR. 1995. Adverse ocular effects associated with niacin therapy. *Br J Ophthalmol* 79:54–56.
- Frost PH. 1991. All niacin is not the same. *Ann Intern Med* 114:1065.
- Fu CS, Swendseid ME, Jacob RA, McKee RW. 1989. Biochemical markers for assessment of niacin status in young men: Levels of erythrocyte niacin coenzymes and plasma tryptophan. *J Nutr* 119:1949–1955.
- Gass JD. 1973. Nicotinic acid maculopathy. *Am J Ophthalmol* 76:500–510.
- Gibbons LW, Gonzalez V, Gordon N, Grundy S. 1995. The prevalence of side effects with regular and sustained-release nicotinic acid. *Am J Med* 99:378–385.

- Goldsmith GA. 1958. Niacin-tryptophan relationships in man and niacin requirement. *Am J Clin Nutr* 6:479–486.
- Goldsmith GA, Sarett HP, Register UD, Gibbens J. 1952. Studies on niacin requirement in man. 1. Experimental pellagra in subjects on corn diets low in niacin and tryptophan. *J Clin Invest* 31:533–542.
- Goldsmith GA, Rosenthal HL, Gibbens J, Unglaub WG. 1955. Studies on niacin requirement in man. 2. Requirement on wheat and corn diets low in tryptophan. *J Nutr* 56:371–386.
- Goldsmith GA, Gibbens J, Unglaub WG, Miller ON. 1956. Studies on niacin requirement in man. 3. Comparative effects of diets containing lime-treated and untreated corn in the production of experimental pellagra. *Am J Clin Nutr* 4:151–160.
- Goldstein MR. 1988. Potential problems with the widespread use of niacin. *Am J Med* 85:881.
- Gray DR, Morgan T, Chretien SD, Kashyap ML. 1994. Efficacy and safety of controlled-release niacin in dyslipoproteinemic veterans. *Ann Intern Med* 121:252–258.
- Henderson LM, Gross CJ. 1979. Metabolism of niacin and niacinamide in perfused rat intestine. *J Nutr* 109:654–662.
- Henkin Y, Johnson KC, Segrest JP. 1990. Rechallenge with crystalline niacin after drug-induced hepatitis from sustained-release niacin. *J Am Med Assoc* 264:241–243.
- Hodis HN. 1990. Acute hepatic failure associated with the use of low-dose sustained-release niacin. *J Am Med Assoc* 264:181.
- Horwitt MK. 1958. Niacin-tryptophan requirements of man. *J Am Diet Assoc* 34:914–919.
- Horwitt MK, Harvey CC, Rothwell WS, Cutler JL, Haffron D. 1956. Tryptophan-niacin relationships in man: Studies with diets deficient in riboflavin and niacin, together with observations on the excretion of nitrogen and niacin metabolites. *J Nutr* 60:1–43.
- Horwitt MK, Harper AE, Henderson LM. 1981. Niacin-tryptophan relationships for evaluating niacin equivalents. *Am J Clin Nutr* 34:423–427.
- ICNND (Interdepartmental Committee on Nutrition for National Defense). 1963. *Manual for Nutrition Surveys*, 2nd ed. Bethesda, MD: National Institutes of Health. P. 244.
- Jacob RA, Swendseid ME, McKee RW, Fu CS, Clemens RA. 1989. Biochemical markers for assessment of niacin status in young men: Urinary and blood levels of niacin metabolites. *J Nutr* 119:591–598.
- Jacobson EL, Lange RA, Jacobson MK. 1979. Pyridine nucleotide synthesis in 3T3 cells. *J Cell Physiol* 99:417–425.
- Kim H, Jacobson EL, Jacobson MK. 1994. NAD glycohydrolases: A possible function in calcium homeostasis. *Mol Cell Biochem* 138:237–243.
- Knapp TR, Middleton RK. 1991. Adverse effects of sustained-release niacin. *Ann Pharmacother* 25:253–254.
- Knodel LC, Talbert RL. 1987. Adverse effects of hypolipidaemic drugs. *Med Toxicol* 2:10–32.
- Knopp RH. 1991. Niacin and hepatic failure. *Ann Intern Med* 111:769.
- Knox WE. 1951. Two mechanisms which increase in vivo the liver tryptophan peroxidase activity: Specific enzyme adaptation and stimulation of the pituitary-adrenal system. *Br J Exp Pathol* 32:462–469.

- Lan SJ, Henderson LM. 1968. Uptake of nicotinic acid and niacinamide by rat erythrocytes. *J Biol Chem* 243:3388–3394.
- Lautier D, Lagueux J, Thibodeau J, Menard L, Poirier GG. 1993. Molecular and biochemical features of poly (ADP-ribose) metabolism. *Mol Cell Biochem* 122:171–193.
- Lee HC, Walseth TF, Bratt GT, Hayes RN, Clapper DL. 1989. Structural determination of a cyclic metabolite of NAD<sup>+</sup> with intracellular CA2<sup>+</sup>-mobilizing activity. *J Biol Chem* 264:1608–1615.
- Leklem JE, Brown RR, Rose DP, Linkswiler H, Arend RA. 1975. Metabolism of tryptophan and niacin in oral contraceptive users receiving controlled intakes of vitamin B<sub>6</sub>. *Am J Clin Nutr* 28:146–156.
- Malfait P, Moren A, Dillon JC, Brodel A, Begkoyian G, Etchegorry MG, Malenga G, Hakewill P. 1993. An outbreak of pellagra related to changes in dietary niacin among Mozambican refugees in Malawi. *Int J Epidemiol* 22:504–511.
- McCormick DB. 1988. Niacin. In: Shils ME, Young VR, eds. *Modern Nutrition in Health and Disease*. Philadelphia: Lea & Febiger. Pp. 370–375.
- McCormick DB. 1989. Two interconnected B vitamins: Riboflavin and pyridoxine. *Physiol Rev* 69:1170–1198.
- McKenney JM, Proctor JD, Harris S, Chinchili VM. 1994. A comparison of the efficacy and toxic effects of sustained- vs immediate-release niacin in hypercholesterolemic patients. *J Am Med Assoc* 271:672–677.
- Miettinen TA, Taskinen M-R, Pelkonen R, Nikkila EA. 1969. Glucose tolerance and plasma insulin in man during acute and chronic administration of nicotinic acid. *Acta Med Scand* 186:247–253.
- Millay RH, Klein ML, Illingworth DR. 1988. Niacin maculopathy. *Ophthalmology* 95:930–936.
- Miller DR, Hayes KC. 1982. Vitamin excess and toxicity. In: Hathcock JN, ed. *Nutritional Toxicology*, Vol. 1. New York: Academic Press. Pp. 81–133.
- Montaldo MB, Benson JD, Martinez GA. 1985. Nutrient intake of formula-fed infants and infants fed cow's milk. *Pediatrics* 75:343–351.
- Morrow JD, Parsons WG 3rd, Roberts LJ 2nd. 1989. Release of markedly increased quantities of prostaglandin D2 in vivo in humans following the administration of nicotinic acid. *Prostaglandins* 38:263–274.
- Morrow JD, Awad JA, Oates JA, Roberts LJ. 1992. Identification of skin as a major site of prostaglandin D2 release following oral administration of niacin in humans. *J Invest Dermatol* 98:812–815.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance Data, Vital and Health Statistics of the National Center for Health Statistics, No. 174. Hyattsville, MD: National Center for Health Statistics.
- Mrochek JE, Jolley RL, Young DS, Turner WJ. 1976. Metabolic response of humans to ingestion of nicotinic acid and niacinamide. *Clin Chem* 22:1821–1827.
- Mullin GE, Greenson JK, Mitchel MC. 1989. Fulminant hepatic failure after ingestion of sustained-release nicotinic acid. *Ann Intern Med* 111:253–255.
- NRC (National Research Council). 1989. *Recommended Dietary Allowances*, 10th ed. Washington, DC: National Academy Press.
- Palumbo PJ. 1991. Rediscovery of crystalline niacin. *Mayo Clin Proc* 66:112–113.
- Pardue WO. 1961. Severe liver dysfunction during nicotinic acid therapy. *J Am Med Assoc* 175:137–138.

- Patterson JI, Brown RR, Linkswiler H, Harper AE. 1980. Excretion of tryptophan-niacin metabolites by young men: Effects of tryptophan, leucine, and vitamin B<sub>6</sub> intakes. *Am J Clin Nutr* 33:2157–2167.
- Patterson DJ, Dew EW, Gyorkey R, Graham GY. 1983. Niacin hepatitis. *South Med J* 76:239–241.
- Rader JI, Calvert RJ, Hathcock JN. 1992. Hepatic toxicity of unmodified and time-release preparations of niacin. *Am J Med* 92:77–81.
- Ribaya-Mercado JD, Russell RM, Rasmussen HM, Crim MC, Perrone-Petty G, Gershoff SN. 1997. Effect of niacin status on gastrointestinal function and serum lipids. *FASEB J* 11:A179.
- Rivin AU. 1959. Jaundice occurring during nicotinic acid therapy for hypercholesterolemia. *J Am Med Assoc* 170:2088–2089.
- Rose DP, Braidman IP. 1971. Excretion of tryptophan metabolites as affected by pregnancy, contraceptive steroids, and steroid hormones. *Am J Clin Nutr* 24:673–683.
- Sauberlich HE, Skala JH, Dowdy RP. 1974. *Laboratory Tests for the Assessment of Nutritional Status*. Boca Raton, FL: CRC Press.
- Schwartz ML. 1993. Severe reversible hyperglycemia as a consequence of niacin therapy. *Arch Intern Med* 153:2050–2052.
- Sebrell WH, Butler RE. 1938. A reaction to the oral administration of nicotinic acid. *J Am Med Assoc* 111:2286–2287.
- Shibata K, Matsuo H. 1989. Effect of supplementing low protein diets with the limiting amino acids on the excretion of N<sup>1</sup>-methylnicotinamide and its pyridones in rats. *J Nutr* 119:896–901.
- Spies TD, Bean WB, Stone RE. 1938. The treatment of subclinical and classic pellagra. *J Am Med Assoc* 111:584–592.
- Stern RH, Spence JD, Freeman DJ, Parbtani A. 1991. Tolerance to nicotinic acid flushing. *Clin Pharmacol Ther* 50:66–70.
- Stierum RH, Vanherwijnen MH, Hageman GJ, Kleinjans JC. 1994. Increased poly (ADP-ribose) polymerase activity during repair of (+/-)-anti-benzo[a]pyrene diolepoxyde-induced DNA damage in human peripheral blood lymphocytes in vitro. *Carcinogenesis* 15:745–751.
- Vivian VM, Chaloupka MM, Reynolds MS. 1958. Some aspects of tryptophan metabolism in human subjects. 1. Nitrogen balances, blood pyridine nucleotides, and urinary excretion of N-methylnicotinamide and N-methyl-2-pyridone-5-carboxamide on a low-niacin diet. *J Nutr* 66:587–598.
- Wertz AW, Lojkin ME, Bouchard BS, Derby MB. 1958. Tryptophan-niacin relationships in pregnancy. *J Nutr* 64:339–353.
- Winter SL, Boyer JL. 1973. Hepatic toxicity from large doses of vitamin B<sub>3</sub> (nicotinamide). *N Engl J Med* 289:1180–1182.

Ibid., Chapter 13, p. 436.

- Beaton GH. 1994. Criteria of an adequate diet. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*, 8th ed. Philadelphia: Lea & Febiger. Pp. 1491–1505.
- Hegsted DM. 1972. Problems in the use and interpretation of the Recommended Dietary Allowances. *Ecol Food Nutr* 1:255–265.

- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys.* Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- USDA (U.S. Department of Agriculture). 1992. *The Food Guide Pyramid.* Home and Garden Bulletin Number 252. Washington, DC: US Government Printing Office.
- WHO (World Health Organization). 1996. *Trace Elements in Human Nutrition and Health.* Prepared in collaboration with the Food and Agriculture Organization of the United Nations and the International Atomic Energy Agency. Geneva: WHO.

## PANTOTHENIC ACID

*Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline* (ISBN 0-309-06411-2), Chapter 10, pp. 371–373.

- Annous KF, Song WO. 1995. Pantothenic acid uptake and metabolism by red blood cells of rats. *J Nutr* 125:2586–2593.
- Baker H, Frank O, Thomson AD, Feingold S. 1969. Vitamin distribution in red blood cells, plasma, and other body fluids. *Am J Clin Nutr* 22:1469–1475.
- Bull NL, Buss DH. 1982. Biotin, pantothenic acid and vitamin E in the British household food supply. *Hum Nutr Appl Nutr* 36:190–196.
- Cohenour SH, Calloway DH. 1972. Blood, urine, and dietary pantothenic acid levels of pregnant teenagers. *Am J Clin Nutr* 25:512–517.
- Deodhar AD, Ramakrishnan CV. 1960. Studies on human lactation. Relation between the dietary intake of lactating women and the chemical composition of milk with regard to vitamin content. *J Trop Pediatr* 6:44–70.
- Eissenstat BR, Wyse BW, Hansen RG. 1986. Pantothenic acid status of adolescents. *Am J Clin Nutr* 44:931–937.
- Fenstermacher DK, Rose RC. 1986. Absorption of pantothenic acid in rat and chick intestine. *Am J Physiol* 250:G155–G160.
- Fox HM, Linkwiler H. 1961. Pantothenic acid excretion on three levels of intake. *J Nutr* 75:451–454.
- Fry PC, Fox HM, Tao HG. 1976. Metabolic response to a pantothenic acid deficient diet in humans. *J Nutr Sci Vitaminol (Tokyo)* 22:339–346.
- Glusman M. 1947. The syndrome of “burning feet” (nutritional melagia) as a manifestation of nutritional deficiency. *Am J Med* 3:211–223.
- Haslam RH, Dalby JT, Rademaker AW. 1984. Effects of megavitamin therapy on children with attention deficit disorders. *Pediatrics* 74:103–111.
- Hodges RE, Ohlson MA, Bean WB. 1958. Pantothenic acid deficiency in man. *J Clin Invest* 37:1642–1657.
- Hodges RE, Bean WB, Ohlson MA, Bleiler R. 1959. Human pantothenic acid deficiency produced by omega-methyl pantothenic acid. *J Clin Invest* 38:1421–1425.
- Kathman JV, Kies C. 1984. Pantothenic acid status of free living adolescent and young adults. *Nutr Res* 4:245–250.
- Kerrey E, Crispin S, Fox HM, Kies C. 1968. Nutritional status of preschool children. I. Dietary and biochemical findings. *Am J Clin Nutr* 21:1274–1279.
- Koyanagi T, Hareyama S, Kikuchi R, Takanohashi T, Oikawa K, Akazawa N. 1969. Effect of administration of thiamine, riboflavin, ascorbic acid and vitamin A to students on their pantothenic acid contents in serum and urine. *Tohoku J Exp Med* 98:357–362.
- Lewis CM, King JC. 1980. Effect of oral contraceptive agents on thiamin, riboflavin, and pantothenic acid status in young women. *Am J Clin Nutr* 33:832–838.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance Data, Vital and Health Statistics of the National Center for Health Statistics, No. 174. Hyattsville, MD: National Center for Health Statistics.
- Orr ML. 1969. *Pantothenic Acid, Vitamin B<sub>6</sub> and Vitamin B<sub>12</sub> in Foods*. Home Economics Research Report No. 36. Washington, DC: U.S. Department of Agriculture.

- Pace JK, Stier LB, Taylor DD, Goodman PS. 1961. Metabolic patterns in preadolescent children. 5. Intake and urinary excretion of pantothenic acid and of folic acid. *J Nutr* 74:345–351.
- Picciano MF. 1995. Vitamins in milk. Water-soluble vitamins in human milk. In: Jensen RG, ed. *Handbook of Milk Composition*. San Diego: Academic Press.
- Plesofsky-Vig N. 1996. Pantothenic acid. In: Ziegler EE, Filer LJ Jr, eds. *Present Knowledge in Nutrition*, 7th ed. Washington, DC: ILSI Press. Pp. 236–244.
- Robinson FA. 1966. *The Vitamin Co-Factors of Enzyme Systems*. Oxford: Pergamon Press.
- Romera JM, Ramirez M, Gil A. 1996. Determination of pantothenic acid in infant milk formulas by high performance liquid chromatography. *JDairy Sci* 79:523–526.
- Santé Québec. 1995. *Les Québécoises et les Québécois Mangent-Ils Mieux? Rapport de l'Enquête Québécoise sur la Nutrition, 1990*. Montréal: Ministère de la Santé et des Services Sociaux, Gouvernement du Québec.
- Sarrett HP, Bennett MJ, Riggs TR, Cheldelin VH. 1946. Thiamine, riboflavin, nicotinic acid, pantothenic acid and ascorbic acid content of restaurant foods. *J Nutr* 31:755.
- Schneider HA, Anderson CE, Coursin DB. 1983. *Nutritional Support of Medical Practice, 2nd Edition*. Philadelphia: Harper and Row.
- Schroeder HA. 1971. Losses of vitamins and trace minerals resulting from processing and preservation of foods. *Am J Clin Nutr* 24:562–573.
- Shibata K, Gross CJ, Henderson LM. 1983. Hydrolysis and absorption of pantothenate and its coenzymes in the rat small intestine. *J Nutr* 113:2107–2115.
- Song WO, Chan GM, Wyse BW, Hansen RG. 1984. Effect of pantothenic acid status on the content of the vitamin in human milk. *Am J Clin Nutr* 40:317–324.
- Song WO, Wyse BW, Hansen RG. 1985. Pantothenic acid status of pregnant and lactating women. *J Am Diet Assoc* 85:192–198.
- Srinivasan V, Christensen N, Wyse BW, Hansen RG. 1981. Pantothenic acid nutritional status in the elderly—institutionalized and noninstitutionalized. *Am J Clin Nutr* 34:1736–1742.
- Stein ED, Diamond JM. 1989. Do dietary levels of pantothenic acid regulate its intestinal uptake in mice? *J Nutr* 119:1973–1983.
- Tahiliani AG, Beinlich CJ. 1991. Pantothenic acid in health and disease. *Vitam Horm* 46:165–228.
- Tarr JB, Tamura T, Stokstad EL. 1981. Availability of vitamin B<sub>6</sub> and pantothenate in an average American diet in man. *Am J Clin Nutr* 34:1328–1337.
- Vaxman F, Olander S, Lambert A, Nisand G, Grenier JF. 1996. Can the wound healing process be improved by vitamin supplementation? Experimental study on humans. *Eur Surg Res* 28:306–314.
- Walsh JH, Wyse BW, Hansen RG. 1981. Pantothenic acid content of 75 processed and cooked foods. *J Am Diet Assoc* 78:140–144.
- Wittwer CT, Schweitzer C, Pearson J, Song WO, Windham CT, Wyse BW, Hansen RG. 1989. Enzymes for liberation of pantothenic acid in blood: Use of plasma pantetheinase. *Am J Clin Nutr* 50:1072–1078.
- Zook EG, MacArthur MJ, Toepfer EW. 1956. *Pantothenic Acid in Foods*. USDA Handbook. Washington, DC: U.S. Department of Agriculture. P. 97.

Ibid., Chapter 13, p. 436.

- Beaton GH. 1994. Criteria of an adequate diet. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*, 8th ed. Philadelphia: Lea & Febiger. Pp. 1491–1505.
- Hegsted DM. 1972. Problems in the use and interpretation of the Recommended Dietary Allowances. *Ecol Food Nutr* 1:255–265.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- USDA (U.S. Department of Agriculture). 1992. *The Food Guide Pyramid*. Home and Garden Bulletin Number 252. Washington, DC: US Government Printing Office.
- WHO (World Health Organization). 1996. *Trace Elements in Human Nutrition and Health*. Prepared in collaboration with the Food and Agriculture Organization of the United Nations and the International Atomic Energy Agency. Geneva: WHO.

## RIBOFLAVIN

*Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline* (ISBN 0-309-06411-2), Chapter 5, pp. 117–122.

- Alexander M, Emanuel G, Golin T, Pinto JT, Rivlin RS. 1984. Relation of riboflavin nutriture in healthy elderly to intake of calcium and vitamin supplements: Evidence against riboflavin supplementation. *Am J Clin Nutr* 39:540–546.
- Ali N, Uperti RK, Srivastava LP, Misra RB, Joshi PC, Kidwai AM. 1991. Membrane damaging potential of photosensitized riboflavin. *Indian J Exp Biol* 29:818–822.
- Aw TY, Jones DP, McCormick DB. 1983. Uptake of riboflavin by isolated rat liver cells. *J Nutr* 113:1249–1254.
- Badart-Smook A, van Houwelingen AC, Al MD, Kester AD, Hornstra G. 1997. Fetal growth is associated positively with maternal intake of riboflavin and negatively with maternal intake of linoleic acid. *J Am Diet Assoc* 97:867–870.
- Bamji MS. 1969. Glutathione reductase activity in red blood cells and riboflavin nutritional status in humans. *Clin Chim Acta* 26:263–269.
- Bamji MS. 1976. Enzymic evaluation of thiamin, riboflavin and pyridoxine status of parturient women and their newborn infants. *Br J Nutr* 35:259–265.
- Bamji MS, Chowdhury N, Ramalakshmi BA, Jacob CM. 1991. Enzymatic evaluation of riboflavin status of infants. *Eur J Clin Nutr* 45:309–313.
- Bates CJ. 1987. Human requirements for riboflavin. *Am J Clin Nutr* 47:122–123.
- Bates CJ, Prentice AM, Paul AA, Sutcliffe BA, Watkinson M, Whitehead RG. 1981. Riboflavin status in Gambian pregnant and lactating women and its implications for Recommended Dietary Allowances. *Am J Clin Nutr* 34:928–935.
- Bates CJ, Powers HJ, Downes R, Brubacher D, Sutcliffe V, Thurnhill A. 1989. Riboflavin status of adolescent vs elderly Gambian subjects before and during supplementation. *Am J Clin Nutr* 50:825–829.
- Belko AZ, Obarzanek E, Kalkwarf HJ, Rotter MA, Bogusz S, Miller D, Haas JD, Roe DA. 1983. Effects of exercise on riboflavin requirements of young women. *Am J Clin Nutr* 37:509–517.
- Belko AZ, Obarzanek E, Roach R, Rotter M, Urban G, Weinberg S, Roe DA. 1984. Effects of aerobic exercise and weight loss on riboflavin requirements of moderately obese, marginally deficient young women. *Am J Clin Nutr* 40:553–561.
- Belko AZ, Meredith MP, Kalkwarf HJ, Obarzanek E, Weinberg S, Roach R, McKeon G, Roe DA. 1985. Effects of exercise on riboflavin requirements: Biological validation in weight reducing women. *Am J Clin Nutr* 41:270–277.
- Bessey OA, Horwitt MK, Love RH. 1956. Dietary deprivation of riboflavin and blood riboflavin levels in man. *J Nutr* 58:367–383.
- Blot WJ, Li JY, Taylor PR, Guo W, Dawsey SM, Li B. 1995. The Linxian trials: Mortality rates by vitamin-mineral intervention group. *Am J Clin Nutr* 62:1424S–1426S.
- Boisvert WA, Mendoza I, Castañeda C, De Portocarrero L, Solomons NW, Gershoff SN, Russell RM. 1993. Riboflavin requirement of healthy elderly humans and its relationship to macronutrient composition of the diet. *J Nutr* 123:915–925.
- Bowman BB, McCormick DB, Rosenberg IH. 1989. Epithelial transport of water-soluble vitamins. *Ann Rev Nutr* 9:187–199.
- Brewer W, Porter T, Ingalls R, Ohlson MA. 1946. The urinary excretion of riboflavin by college women. *J Nutr* 32:583–596.

- Brown ML. 1990. *Present Knowledge in Nutrition*, 6th ed. Washington, DC: International Life Sciences Institute-Nutrition Foundation.
- Brzezinski A, Bromberg YM, Braun K. 1952. Riboflavin excretion during pregnancy and early lactation. *J Lab Clin Med* 39:84–90.
- Burch HB, Bessey OA, Lowry OH. 1948. Fluorometric measurements of riboflavin and its natural derivatives in small quantities of blood serum and cells. *J Biol Chem* 175:457–470.
- Chastain JL, McCormick DB. 1987. Flavin catabolites: Identification and quantitation in human urine. *Am J Clin Nutr* 46:830–834.
- Chia CP, Addison R, McCormick DB. 1978. Absorption, metabolism, and excretion of 8α-(amino acid) riboflavins in the rat. *J Nutr* 108:373–381.
- Cole HS, Lopez R, Cooperman JM. 1976. Riboflavin deficiency in children with diabetes mellitus. *Acta Diabetol Lat* 13:25–29.
- Committee on Nutrition. 1985. Composition of human milk: Normative data. In: *Pediatric Nutrition Handbook*, 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics. Pp. 363–368.
- Dancis J, Lehanka J, Levitz M. 1988. Placental transport of riboflavin: Differential rates of uptake at the maternal and fetal surfaces of the perfused human placenta. *Am J Obstet Gynecol* 158:204–210.
- Daniel H, Wille U, Rehner G. 1983. In vitro kinetics of the intestinal transport of riboflavin in rats. *J Nutr* 113:636–643.
- Darby WJ. 1981. *Annual Review of Nutrition*, Vol. 1. Palo Alto, CA: Annual Reviews.
- Davis MV, Oldham HG, Roberts LJ. 1946. Riboflavin excretions of young women on diets containing varying levels of the B vitamins. *J Nutr* 32:143–161.
- Floersheim GL. 1994. Allopurinol, indomethacin and riboflavin enhance radiation lethality in mice. *Radiat Res* 139:240–247.
- Frischer H, Bowman JE, Carson PE, Reickmann KH, Willerson D Jr, Colwell EJ. 1973. Erythrocyte glutathione reductase, glucose-6-phosphate dehydrogenase, and 6-phosphogluconic dehydrogenase deficiencies in populations of the United States, South Vietnam, Iran, and Ethiopia. *J Lab Clin Med* 81:603–612.
- Heller S, Salkeld RM, Korner WF. 1974. Riboflavin status in pregnancy. *Am J Clin Nutr* 27:1225–1230.
- Horwitt MK. 1972. Riboflavin. Requirements and factors influencing them. In: Sebrell WH Jr, Harris RS, eds. *The Vitamins*, 2nd ed., Vol. 5. New York: Academic Press.
- Horwitt MK, Hills OW, Harvey CC, Liebert E, Steinberg DL. 1949. Effects of dietary depletion of riboflavin. *J Nutr* 39:357–373.
- Horwitt MK, Harvey CC, Hills OW, Liebert E. 1950. Correlation of urinary excretion of riboflavin with dietary intake and symptoms of ariboflavinosis. *J Nutr* 41:247–264.
- Innis WS, McCormick DB, Merrill AH Jr. 1985. Variations in riboflavin binding by human plasma: Identification of immunoglobulins as the major proteins responsible. *Biochem Med* 34:151–165.
- Jansen AP, Jansen BC. 1954. Riboflavin-excretion with urine in pregnancy. *Int Z Vitaminforsch* 25:193–199.
- Jusko WJ, Levy G. 1967. Absorption, metabolism, and excretion of riboflavin 5'-phosphate in man. *J Pharmacol Sci* 156:58–62.
- Jusko WJ, Levy G. 1975. Absorption, protein binding and elimination of riboflavin. In: Rivlin RS, ed. *Riboflavin*. New York: Plenum Press. Pp. 99–152.
- Jusko WJ, Khanna N, Levy G, Stern L, Yaffe SJ. 1970. Riboflavin absorption and excretion in the neonate. *Pediatrics* 45:945–949.

- Keys A, Henschel AF, Mickelsen O, Brozek JM, Crawford JH. 1944. Physiological and biochemical functions in normal young men on a diet restricted in riboflavin. *J Nutr* 27:165–178.
- Komindr S, Nichoalds GE. 1980. Clinical significance of riboflavin deficiency. In: Brewster MA, Naito HK, eds. *Nutritional Elements in Clinical Biochemistry*. New York: Plenum Press. Pp. 15–68.
- Kuizon MD, Natera MG, Alberto SP, Perlas LA, Desnacido JA, Avena EM, Tajaon RT, Macapinlac MP. 1992. Riboflavin requirement of Filipino women. *Eur J Clin Nutr* 46:257–264.
- Lee SS, McCormick DB. 1983. Effect of riboflavin status on hepatic activities of flavin-metabolizing enzymes in rats. *J Nutr* 113:2274–2279.
- Leske MC, Wu SY, Hyman L, Sperduto R, Underwood B, Chylack LT, Milton RC, Srivastava S, Ansari N. 1995. Biochemical factors in the lens opacities. Case-control study. The Lens Opacities Case-Control Study Group. *Arch Ophthalmol* 113:1113–1119.
- Levy G, Jusko WJ. 1966. Factors affecting the absorption of riboflavin in man. *J Pharm Sci* 55:285–289.
- Lossy FT, Goldsmith GA, Sarett HP. 1951. A study of test dose excretion of five B complex vitamins in man. *J Nutr* 45:213.
- Mayersohn M, Feldman S, Gribaldi M. 1969. Bile salt enhancement of riboflavin and flavin mononucleotide absorption in man. *J Nutr* 98:288–296.
- McCormick DB. 1962. The intracellular localization, partial purification, and properties of flavokinase from rat liver. *J Biol Chem* 237:959–962.
- McCormick DB. 1977. Interactions of flavins with amino acid residues: Assessments from spectral and photochemical studies. *Photochem Photobiol* 26:169–182.
- McCormick DB. 1989. Two interconnected B vitamins: Riboflavin and pyridoxine. *Physiol Rev* 69:1170–1198.
- McCormick DB. 1994. Riboflavin. In: Shils ME, Olson JE, Shike M, eds. *Modern Nutrition in Health and Disease*. Philadelphia: Lea & Febiger. Pp. 366–375.
- McCormick DB, Greene HL. 1994. Vitamins. In: Burtis CA, Ashwood ER, eds. *Tietz Textbook of Clinical Chemistry*. Philadelphia: Saunders.
- Meinen M, Aepli R, Rehner G. 1977. Studies on the absorption of thiamine, riboflavin and pyridoxine in vitro. *Nutr Metab* 21:264–266.
- Merrill AH Jr, Lambeth JD, Edmondson DE, McCormick DB. 1981. Formation and mode of action of flavoproteins. *Annu Rev Nutr* 1:281–317.
- Merrill AH Jr, Foltz AT, McCormick DB. 1991. Vitamins and cancer. In: Alfin-Slater RB, Kritchevsky D, eds. *Cancer and Nutrition*. New York: Plenum. Pp. 261–320.
- Montaldo MB, Benson JD, Martinez GA. 1985. Nutrient intake of formula-fed infants and infants fed cow's milk. *Pediatrics* 75:343–351.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance Data, Vital and Health Statistics of the National Center for Health Statistics, No. 174. Hyattsville, MD: National Center for Health Statistics.
- Nail PA, Thomas MR, Eakin R. 1980. The effect of thiamin and riboflavin supplementation on the level of those vitamins in human breast milk and urine. *Am J Clin Nutr* 33:198–204.
- Natraj U, George S, Kadam P. 1988. Isolation and partial characterisation of human riboflavin carrier protein and the estimation of its levels during human pregnancy. *J Reprod Immunol* 13:1–16.

- Nichoalds GE. 1981. Riboflavin. Symposium in Laboratory Medicine. In: Labbae RF, ed. *Symposium on Laboratory Assessment of Nutritional Status*. Clinics in Laboratory Medicine Series, Vol. 1. Philadelphia: WB Saunders. Pp. 685–698.
- Oldham H, Johnston F, Kleiger S, Hedderich-Arismendi H. 1944. A study of the riboflavin and thiamine requirements of children of preschool age. *J Nutr* 27:435–446.
- Powers HJ, Bates CJ, Eccles M, Brown H, George E. 1987. Bicycling performance in Gambian children: Effects of supplements of riboflavin or ascorbic acid. *Hum Nutr Clin Nutr* 41:59–69.
- Prager MD, Hill JM, Speer RJ. 1958. Whole blood riboflavin levels in healthy individuals and in patients manifesting various blood dyscrasias. *J Lab Clin Med* 52:206.
- Prasad PA, Bamji MS, Lakshmi AV, Satyanarayana K. 1990. Functional impact of riboflavin supplementation in urban school children. *Nutr Res* 10:275–281.
- Ramsay VP, Neumann C, Clark V, Swendseid ME. 1983. Vitamin cofactor saturation indices for riboflavin, thiamine, and pyridoxine in placental tissue of Kenyan women. *Am J Clin Nutr* 37:969–973.
- Rivier DA. 1973. Kinetics and Na-dependence of riboflavin absorption by intestine in vivo. *Experientia* 29:1443–1446.
- Rivlin RS. 1975. Riboflavin and cancer. In: Rivlin RS, ed. *Riboflavin*. New York: Plenum Press. Pp. 369–391.
- Roe DA, Bogusz S, Sheu J, McCormick DB. 1982. Factors affecting riboflavin requirements of oral contraceptive users and nonusers. *Am J Clin Nutr* 35:495–501.
- Roughead ZK, McCormick DB. 1990a. Flavin composition of human milk. *Am J Clin Nutr* 52:854–857.
- Roughead ZK, McCormick DB. 1990b. Qualitative and quantitative assessment of flavins in cow's milk. *J Nutr* 120:382–388.
- Roughead ZK, McCormick DB. 1991. Urinary riboflavin and its metabolites: Effects of riboflavin supplementation in healthy residents of rural Georgia (USA). *Eur J Clin Nutr* 45:299–307.
- Sadowski JA. 1992. Riboflavin. In: Hartz SC, Russell RM, Rosenberg IH, eds. *Nutrition in the Elderly. The Boston Nutritional Status Survey*. London: Smith-Gordon. Pp. 119–125.
- Said HM, Ma TY. 1994. Mechanism of riboflavin uptake by Caco-2 human intestinal epithelial cells. *Am J Physiol* 266:G15–G21.
- Sauberlich HE, Judd JH Jr, Nichoalds GE, Broquist HP, Darby WJ. 1972. Application of the erythrocyte glutathione reductase assay in evaluating riboflavin nutritional status in a high school student population. *Am J Clin Nutr* 25:756–762.
- Sauberlich HE, Skala JH, Dowdy RP. 1974. *Laboratory Tests for the Assessment of Nutritional Status*. Boca Raton, FL: CRC Press.
- Schoenen J, Lenaerts M, Bastings E. 1994. Rapid communication: High-dose riboflavin as a prophylactic treatment of migraine: Results of an open pilot study. *Cephalalgia* 14:328–329.
- Sebrell WH Jr, Butler RE, Wooley JG, Isbell H. 1941. Human riboflavin requirement estimated by urinary excretion of subjects on controlled intake. *Public Health Rep* 56:510–519.
- Smith MD. 1980. Rapid method for determination of riboflavin in urine by high-performance liquid chromatography. *J Chromatogr* 182:285–291.

## ONLINE REFERENCES

987

- Soares MJ, Satyanarayana K, Bamji MS, Jacob CM, Ramana YV, Rao SS. 1993. The effect of exercise on the riboflavin status of adult men. *Br J Nutr* 69:541–551.
- Sorrell MF, Frank O, Thompson AD, Aquino H, Baker H. 1971. Absorption of vitamins from the large intestine in vivo. *Nutr Rep Int* 3:143–148.
- Spector A, Wang GM, Wang RR, Li WC, Kleiman NJ. 1995. A brief photochemically induced oxidative insult causes irreversible lens damage and cataracts. 2. Mechanism of action. *Exp Eye Res* 60:483–493.
- Steier M, Lopez R, Cooperman JM. 1976. Riboflavin deficiency in infants and children with heart disease. *Am Heart J* 92:139–143.
- Stripp B. 1965. Intestinal absorption of riboflavin by man. *Acta Pharmacol Toxicol* 22:353–362.
- Sugiyama M, Tsuzuki K, Lin X, Costa M. 1992. Potentiation of sodium chromate (VI)-induced chromosomal aberrations and mutation by vitamin B<sub>2</sub> in Chinese hamster V79 cells. *Mutat Res* 283:211–214.
- Thomas MR, Snead SM, Wei C, Nail PA, Wilson M, Sprinkle EE 3rd. 1980. The effects of vitamin C, vitamin B<sub>6</sub>, vitamin B<sub>12</sub>, folic acid, riboflavin, and thiamin on the breast milk and maternal status of well-nourished women at 6 months postpartum. *Am J Clin Nutr* 33:2151–2156.
- Tremblay A, Boilard M, Bratton MF, Bessette H, Roberge AB. 1984. The effects of a riboflavin supplementation on the nutritional status and performance of elite swimmers. *Nutr Res* 4:201–208.
- Tucker RG, Mickelsen O, Keys A. 1960. The influence of sleep, work, diuresis, heat, acute starvation, thiamine intake and bed rest on human riboflavin excretion. *J Nutr* 72:251–261.
- Vir SC, Love AH, Thompson W. 1981. Riboflavin status during pregnancy. *Am J Clin Nutr* 34:2699–2705.
- Weight LM, Noakes TD, Labadarios D, Graves J, Jacobs P, Berman PA. 1988. Vitamin and mineral status of trained athletes including the effects of supplementation. *Am J Clin Nutr* 47:186–191.
- WHO (World Health Organization). 1965. *Nutrition in Pregnancy and Lactation*. Report of a WHO Expert Committee. Technical Report Series No. 302. Geneva: World Health Organization.
- Williams RD, Mason HL, Cusick PL, Wilder RM. 1943. Observations on induced riboflavin deficiency and the riboflavin requirement of man. *J Nutr* 25:361–377.
- Wilson JA. 1983. Disorders of vitamins: Deficiency, excess and errors of metabolism. In: Petersdorf RG, Harrison TR, eds. *Harrison's Principles of Internal Medicine*, 10th ed. New York: McGraw-Hill. Pp. 461–470.
- Winters LR, Yoon JS, Kalkwarf HJ, Davies JC, Berkowitz MG, Haas J, Roe DA. 1992. Riboflavin requirements and exercise adaptation in older women. *Am J Clin Nutr* 56:526–532.
- Yamada Y, Merrill AH Jr, McCormick DB. 1990. Probable reaction mechanisms of flavokinase and FAD synthetase from rat liver. *Arch Biochem Biophys* 278:125–130.
- Zempleni J, Galloway JR, McCormick DB. 1996. Pharmacokinetics of orally and intravenously administered riboflavin in healthy humans. *Am J Clin Nutr* 63:54–66.

Ibid., Chapter 13, p. 436.

- Beaton GH. 1994. Criteria of an adequate diet. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*, 8th ed. Philadelphia: Lea & Febiger. Pp. 1491–1505.
- Hegsted DM. 1972. Problems in the use and interpretation of the Recommended Dietary Allowances. *Ecol Food Nutr* 1:255–265.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- USDA (U.S. Department of Agriculture). 1992. *The Food Guide Pyramid*. Home and Garden Bulletin Number 252. Washington, DC: US Government Printing Office.
- WHO (World Health Organization). 1996. *Trace Elements in Human Nutrition and Health*. Prepared in collaboration with the Food and Agriculture Organization of the United Nations and the International Atomic Energy Agency. Geneva: WHO.

## THIAMIN

*Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline* (ISBN 0-309-06411-2), Chapter 4, pp. 83–86.

- Anderson SH, Charles TJ, Nicol AD. 1985. Thiamine deficiency at a district general hospital: Report of five cases. *Q J Med* 55:15–32.
- Anderson SH, Vickery CA, Nicol AD. 1986. Adult thiamine requirements and the continuing need to fortify processed cereals. *Lancet* 2:85–89.
- Ariaey-Nejad MR, Balaghi M, Baker EM, Sauberlich HE. 1970. Thiamin metabolism in man. *Am J Clin Nutr* 23:764–778.
- Bailey AL, Finglas PM, Wright AJ, Southon S. 1994. Thiamin intake, erythrocyte transketolase (EC 2.2.1.1) activity and total erythrocyte thiamin in adolescents. *Br J Nutr* 72:111–125.
- Baines M, Davies G. 1988. The evaluation of erythrocyte thiamin diphosphate as an indicator of thiamin status in man, and its comparison with erythrocyte transketolase activity measurements. *Ann Clin Biochem* 25:698–705.
- Bamji MS. 1970. Transketolase activity and urinary excretion of thiamin in the assessment of thiamin-nutrition status of Indians. *Am J Clin Nutr* 23:52–58.
- Bayliss RM, Brookes R, McCulloch J, Kuyl JM, Metz J. 1984. Urinary thiamine excretion after oral physiological doses of the vitamin. *Int J Vitam Nutr Res* 54:161–164.
- Brin M. 1962. Erythrocyte transketolase in early thiamine deficiency. *Ann NY Acad Sci* 98:528–541.
- Brin M. 1964. Erythrocyte as a biopsy tissue for functional evaluation of thiamine adequacy. *J Am Med Assoc* 187:762–766.
- Brin M. 1970. Transketolase (sedoheptulose-7-phosphate: D-glyceraldehyde-3-phosphate dihydroxyacetone transferase, EC 2.2.1.1) and the TPP effect in assessing thiamine adequacy. In: McCormick DB, Wright LD, eds. *Methods in Enzymology*, Vol. 18, Part A. London: Academic Press. Pp. 125–133.
- Bueding E, Stein MH, Wortis H. 1941. Blood pyruvate curves following glucose ingestion in normal and thiamine-deficient subjects. *J Biol Chem* 140:697–703.
- Burgess RC. 1946. Deficiency diseases in prisoners-of-war at Changi, Singapore, February 1942 to August 1945. *Lancet* 2:411–418.
- Chong YH, Ho GS. 1970. Erythrocyte transketolase activity. *Am J Clin Nutr* 23:261–266.
- Committee on Nutrition. 1985. Composition of human milk: Normative data. In: *Pediatric Nutrition Handbook*, 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics. Pp. 363–368.
- Daum K, Tuttle WW, Wilson M, Rhoads H. 1948. Influence of various levels of thiamine intake on physiologic response. 2. Urinary excretion of thiamine. *J Am Diet Assoc* 24:1049.
- Davis RE, Icke GC, Thom J, Riley WJ. 1984. Intestinal absorption of thiamin in man compared with folate and pyridoxal and its subsequent urinary excretion. *J Nutr Sci Vitaminol (Tokyo)* 30:475–482.
- Dick EC, Chen SD, Bert M, Smith JM. 1958. Thiamine requirement of eight adolescent boys, as estimated from urinary thiamine excretion. *J Nutr* 66:173–188.
- Elsom KO, Reinhold JG, Nicholson JT, Chornock C. 1942. Studies of the B vitamins in the human subject. 5. The normal requirement for thiamine; some factors influencing its utilization and excretion. *Am J Med Sci* 203:569–577.

- Fogelholm M, Rehunen S, Gref CG, Laakso JT, Lehto J, Ruokonen I, Himberg JJ. 1992. Dietary intake and thiamin, iron, and zinc status in elite Nordic skiers during different training periods. *Int J Sport Nutr* 2:351–365.
- Fogelholm M, Ruokonen I, Laakso JT, Vuorimaa T, Himberg JJ. 1993. Lack of association between indices of vitamin B<sub>1</sub>, B<sub>2</sub>, and B<sub>6</sub> status and exercise-induced blood lactate in young adults. *Int J Sport Nutr* 3:165–176.
- Foltz EE, Barborka CJ, Ivy AC. 1944. The level of vitamin B-complex in the diet at which detectable symptoms of deficiency occur in man. *Gastroenterology* 2:323–344.
- Gans DA, Harper AE. 1991. Thiamin status of incarcerated and nonincarcerated adolescent males: Dietary intake and thiamin pyrophosphate response. *Am J Clin Nutr* 53:1471–1475.
- Hart M, Reynolds MS. 1957. Thiamine requirement of adolescent girls. *J Home Econ* 49:35–37.
- Hathaway ML, Strom JE. 1946. A comparison of thiamine synthesis and excretion in human subjects on synthetic and natural diets. *J Nutr* 32:1.
- Hayes KC, Hegsted DM. 1973. Toxicity of the vitamins. In: *Toxicants Occurring Naturally in Foods*. Washington, DC: National Academy Press. Pp. 235–253.
- Heller S, Salkeld RM, Korner WF. 1974. Vitamin B<sub>1</sub> status in pregnancy. *Am J Clin Nutr* 27:1221–1224.
- Henshaw JL, Noakes G, Morris SO, Bennion M, Gubler CJ. 1970. Method for evaluating thiamine adequacy in college women. *J Am Diet Assoc* 57:436–441.
- Hoorn RK, Flikweert JP, Westerink D. 1975. Vitamin B<sub>1</sub>, B<sub>2</sub> and B<sub>6</sub> deficiencies in geriatric patients, measured by coenzyme stimulation of enzyme activities. *Clin Chim Acta* 61:151–162.
- Horwitt MK, Liebert E, Kreisler O, Wittman P. 1948. *Investigations of Human Requirements for B-Complex Vitamins*. Bulletin of the National Research Council No. 116. Report of the Committee on Nutritional Aspects of Ageing, Food and Nutrition Board, Division of Biology and Agriculture. Washington, DC: National Academy of Sciences.
- Hyttén FE, Thomason AM. 1961. Nutrition of the lactating women. In: Kon SK, Cowie AT, eds. *Milk: The Mammary Gland and Its Secretion*. New York: Academic Press. Pp. 3–46.
- Inouye K, Katsura E. 1965. Etiology and pathology of beriberi. In: Shimazono N, Katsura E, eds. *Review of Japanese Literature on Beriberi and Thiamine*. Igaku Shoin, Tokyo: Vitamin B Research Committee of Japan. Pp. 1–28.
- Kraut H, Wildemann L, Böhm M. 1966. Human thiamine requirements. *Int Z Vitaminforsch* 36:157–193.
- Laws CL. 1941. Sensitization to thiamine hydrochloride. *J Am Med Assoc* 117:146.
- Leitner ZA. 1943. Untoward effects of vitamin B<sub>1</sub>. *Lancet* 2:474–475.
- Levy G, Hewitt RR. 1971. Evidence in man for different specialized intestinal transport mechanisms for riboflavin and thiamin. *Am J Clin Nutr* 24:401–404.
- Lockhart HS, Kirkwood S, Harris RS. 1943. The effect of pregnancy and puerperium on the thiamine status of women. *Am J Obstet Gynecol* 46:358–365.
- Lonsdale D, Shamberger RJ. 1980. Red cell transketolase as an indicator of nutritional deficiency. *Am J Clin Nutr* 33:205–211.
- McAlpine D, Hills GM. 1941. The clinical value of the thiochrome test for aneurin (vitamin B<sub>1</sub>) in urine. *Q J Med* 34:31–39.
- McCormick DB, Greene HL. 1994. Vitamins. In: Burtis CA, Ashwood ER, eds. *Tietz Textbook of Clinical Chemistry*. Philadelphia: Saunders. Pp. 1275–1316.

- Montaldo MB, Benson JD, Martinez GA. 1985. Nutrient intake of formula-fed infants and infants fed cow's milk. *Pediatrics* 75:343–351.
- Morrison AB, Campbell JA. 1960. Vitamin absorption studies. 1. Factors influencing the excretion of oral test doses of thiamine and riboflavin by human subjects. *J Nutr* 72:435–440.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance Data, Vital and Health Statistics of the National Center for Health Statistics, No. 174. Hyattsville, MD: National Center for Health Statistics.
- Nail PA, Thomas MR, Eakin R. 1980. The effect of thiamin and riboflavin supplementation on the level of those vitamins in human breast milk and urine. *Am J Clin Nutr* 33:198–204.
- Najjar VA, Holt LE Jr. 1940. Studies in thiamin excretion. *Bull Johns Hopkins Hosp* 67:107–124.
- Nichols HK, Basu TK. 1994. Thiamin status of the elderly: Dietary intake and thiamin pyrophosphate response. *J Am Coll Nutr* 13:57–61.
- O'Rourke NP, Bunker VW, Thomas AJ, Finglas PM, Bailey AL, Clayton BE. 1990. Thiamine status of healthy and institutionalized elderly subjects: Analysis of dietary intake and biochemical indices. *Age Ageing* 19:325–329.
- Oldham H. 1962. Thiamine requirements of women. *Ann NY Acad Sci* 98:542–549.
- Oldham HG, Davis MV, Roberts LJ. 1946. Thiamine excretions and blood levels of young women on diets containing varying levels of the B vitamins, with some observations on niacin and pantothenic acid. *J Nutr* 32:163–180.
- Oldham H, Sheft BB, Porter T. 1950. Thiamine and riboflavin intakes and excretions during pregnancy. *J Nutr* 41:231–245.
- Pekkarinen M, Koivula L, Rissanen A. 1974. Thiamine intake and evaluation of thiamine status among aged people in Finland. *Int J Vitam Nutr Res* 44:435–442.
- Platt BS. 1967. Thiamine deficiency in human beriberi and in Wernicke's encephalopathy. In: Wolstenholme GEW, O'Connor M, eds. *Thiamine Deficiency: Biochemical Lesions and their Clinical Significance*. Ciba Foundation Study Group No. 28. London: Churchill Livingstone. Pp. 135–143.
- Pratt JB, Hamil BM. 1951. Metabolism of women during the reproductive cycle. 18. The effect of multivitamin supplements on the secretion of B vitamins in human milk. *J Nutr* 44:141–157.
- Reingold IM, Webb FR. 1946. Sudden death following intravenous administration of thiamine hydrochloride. *J Am Med Assoc* 130:491–492.
- Reuter H, Gassmann B, Erhardt V. 1967. Contribution to the question of the human thiamine requirement. *Int Z Vitaminforsch* 37:315–328.
- Royer-Morrot MJ, Zhiri A, Paille F, Royer RJ. 1992. Plasma thiamine concentrations after intramuscular and oral multiple dosage regimens in healthy men. *Eur J Clin Pharmacol* 42:219–222.
- Sauberlich HE, Herman YF, Stevens CO, Herman RH. 1979. Thiamin requirement of the adult human. *Am J Clin Nutr* 32:2237–2248.
- Schiff L. 1941. Collapse following parenteral administration of solution of thiamine hydrochloride. *J Am Med Assoc* 117:609.
- Schrijver J. 1991. Biochemical markers for micronutrient status and their interpretation. In: Pietrzik K, ed. *Modern Lifestyles, Lower Energy Intake and Micronutrient Status*. London: Springer-Verlag. Pp. 55–85.

- SCOGS/LSRO (Select Committee on GRAS Substances, Life Sciences Research Office). 1978. *Evaluation of the Health Aspects of Thiamin Hydrochloride and Thiamin Mononitrate as Food Ingredients*. Bethesda, MD: LSRO/FASEB.
- Singleton CK, Pekovich SR, McCool BA, Martin, PR. 1995. The thiamine-dependent hysteretic behavior of human transketolase: Implications for thiamine deficiency. *J Nutr* 125:189–194.
- Slobody LB, Willner MM, Mestern J. 1949. Comparison of vitamin B<sub>1</sub> levels in mothers and their newborn infants. *Am J Dis Child* 77:736.
- Stein W, Morgenstern M. 1944. Sensitization to thiamine hydrochloride: Report of a case. *Ann Intern Med* 70:826–828.
- Stephen JM, Grant R, Yeh CS. 1992. Anaphylaxis from administration of intravenous thiamine. *Am J Emerg Med* 10:61–63.
- Stiles MH. 1941. Hypersensitivity to thiamine chloride, with a note on sensitivity to pyridoxine hydrochloride. *J Allergy* 12:507–509.
- Toverud KU. 1940. The excretion of aneurin in pregnant and lactating women and infants. *Z Vitaminforsch* 10:255–267.
- Tripathy K. 1968. Erythrocyte transketolase activity and thiamine transfer across human placenta. *Am J Clin Nutr* 21:739–742.
- van der Beek EJ, van Dokkum W, Wedel M, Schrijver J, van den Berg H. 1994. Thiamin, riboflavin and vitamin B<sub>6</sub>: Impact of restricted intake on physical performance in man. *J Am Coll Nutr* 13:629–640.
- Wilkinson TJ, Hanger HC, Elmslie J, George PM, Sainsbury R. 1997. The response to treatment of subclinical thiamine deficiency in the elderly. *Am J Clin Nutr* 66:925–928.
- Williams RD, Mason HL, Smith BF, Wilder RM. 1942. Induced thiamin (vitamin B<sub>1</sub>) deficiency and the thiamine requirement of man: Further observations. *Arch Intern Med* 69:721–738.
- Williams RD, Mason HL, Wilder RM. 1943. The minimum daily requirement of thiamine in man. *J Nutr* 25:71–97.
- Wilson JA. 1983. Disorders of vitamins: Deficiency, excess and errors of metabolism. In: Petersdorf RG, Harrison TR, eds. *Harrison's Principles of Internal Medicine*, 10th ed. New York: McGraw-Hill. Pp. 461–470.
- Wood B, Gijsbers A, Goode A, Davis S, Mulholland J, Breen K. 1980. A study of partial thiamin restriction in human volunteers. *Am J Clin Nutr* 33:848–861.
- Wrenn KD, Murphy F, Slovis CM. 1989. A toxicity study of parenteral thiamine hydrochloride. *Ann Emerg Med* 18:867–870.
- Wyatt DT, Nelson D, Hillman RE. 1991. Age-dependent changes in thiamin concentrations in whole blood and cerebrospinal fluid in infants and children. *Am J Clin Nutr* 53:530–536.
- Ziporin ZZ, Nunes WT, Powell RC, Waring PP, Sauberlich HE. 1965. Thiamine requirement in the adult human as measured by urinary excretion of thiamine metabolites. *J Nutr* 85:297–304.

Ibid., Chapter 13, p. 436.

- Beaton GH. 1994. Criteria of an adequate diet. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*, 8th ed. Philadelphia: Lea & Febiger. Pp. 1491–1505.
- Hegsted DM. 1972. Problems in the use and interpretation of the Recommended Dietary Allowances. *Ecol Food Nutr* 1:255–265.

- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys.* Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- USDA (U.S. Department of Agriculture). 1992. *The Food Guide Pyramid.* Home and Garden Bulletin Number 252. Washington, DC: US Government Printing Office.
- WHO (World Health Organization). 1996. *Trace Elements in Human Nutrition and Health.* Prepared in collaboration with the Food and Agriculture Organization of the United Nations and the International Atomic Energy Agency. Geneva: WHO.

## CALCIUM

*Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride (ISBN 0-309-06350-7)*, pp. 325–374.

- Abbott L, Nadler J, Rude RK. 1994. Magnesium deficiency in alcoholism: Possible contribution to osteoporosis and cardiovascular disease in alcoholics. *Alcohol Clin Exp Res* 18:1976–1082.
- Abe E, Miyaura C, Sakagami H, Takeda M, Konno K, Yamazaki T, Yoshiki S, Suda T. 1981. Differentiation of mouse myeloid leukemia cells induced by 1 $\alpha$ 25-dihydroxyvitamin D<sub>3</sub>. *Proc Natl Acad Sci USA* 78:4990–4994.
- Abraham GE, Grewal H. 1990. A total dietary program emphasizing magnesium instead of calcium: Effect on the mineral density of calcaneous bone in postmenopausal women on hormonal therapy. *J Reprod Med* 35:503–507.
- Abrams SA, Stuff JE. 1994. Calcium metabolism in girls: Current dietary intakes lead to low rates of calcium absorption and retention during puberty. *Am J Clin Nutr* 60:739–743.
- Abrams SA, Sidbury JB, Muenzer J, Esteban NV, Vieira NE, Yerger AL. 1991. Stable isotopic measurement of endogenous fecal calcium excretion in children. *J Pediatr Gastroenterol Nutr* 12:469–473.
- Abrams SA, Esteban NV, Vieira NE, Sidbury JB, Specker BL, Yerger AL. 1992. Developmental changes in calcium kinetics in children assessed using stable isotopes. *J Bone Miner Res* 7:287–293.
- Abrams SA, Silber TJ, Esteban NV, Vieira NE, Stuff JE, Meyers R, Majd M, Yerger AL. 1993. Mineral balance and bone turnover in adolescents with anorexia nervosa. *J Pediatr* 123:326–331.
- Abrams SA, O'Brien KO, Stuff JE. 1996a. Changes in calcium kinetics associated with menarche. *J Clin Endocrin Metab* 81:2017–2020.
- Abrams SA, O'Brien KO, Wen J, Liang LK, Stuff JE. 1996b. Absorption by 1-year-old children of an iron supplement given with cow's milk or juice. *Pediatr Res* 39:171–175.
- Abrams SA, Wen J, Stuff JE. 1997a. Absorption of calcium, zinc and iron from breast milk by 5- to 7-month-old infants. *Pediatr Res* 41:1–7.
- Abrams SA, Grusak MA, Stuff J, O'Brien KO. 1997b. Calcium and magnesium balance in 9- to 14-year-old children. *Am J Clin Nutr* 66:1172–1177.
- Abreo K, Adlakha A, Kilpatrick S, Flanagan R, Webb R, Shakamuri S. 1993. The Milk-Alkali Syndrome. A reversible form of acute renal failure. *Arch Intern Med* 153:1005–1010.
- Ackerman PG, Toro G. 1953. Calcium and phosphorus balance in elderly men. *J Gerontol* 8:298–300.
- ADA (American Dental Association Council on Dental Therapeutics). 1994. New fluoride guidelines proposed. *J Am Dent Assoc* 125:366.
- Adams JS. 1989. Vitamin D metabolite-mediated hypercalcemia. *Endocrinol Metab Clin North Am* 18:765–778.
- Adams JS, Beeker TG, Hongo T, Clemens TL. 1990. Constitutive expression of a vitamin D 1-hydroxylase in a myelomonocytic cell line: A model for studying 1,25-dihydroxyvitamin D production in vitro. *J Bone Miner Res* 5:1265–1269.
- Affinito P, Tommaselli GA, DiCarlo C, Guida F, Nappi C. 1996. Changes in bone mineral density and calcium metabolism in breast-feeding women: A one year follow-up study. *J Clin Endocrinol Metab* 81:2314–2318.

- Aksnes L, Aarskog D. 1982. Plasma concentrations of vitamin D metabolites in puberty: Effect of sexual maturation and implications for growth. *J Clin Endocrinol Metab* 55:94–101.
- Ala-Houhala M. 1985. 25-Hydroxyvitamin D levels during breast-feeding with or without maternal or infantile supplementation of vitamin D. *J Pediatr Gastroenterol Nutr* 4:220–226.
- Ala-Houhala M, Parvianinen MT, Pyyko K, Visakorpi JK. 1984. Serum 25-hydroxyvitamin D levels in Finnish children aged 2 to 17 years. *Acta Paediatr Scand* 73:232–236.
- Ala-Houhala M, Koskinen T, Terho A, Koivula T, Visakorpi J. 1986. Maternal compared with infant vitamin D supplementation. *Arch Dis Child* 61:1159–1163.
- Alaimo K, McDowell MA, Briefel RR, Bischof AM, Caughman CR, Loria CM, Johnson CL. 1994. *Dietary Intake of Vitamins, Minerals, and Fiber of Persons Ages 2 Months and Over in the United States: Third National Health and Nutrition Examination Survey, Phase I, 1988–91*. Advance data from vital and health statistics; no. 258. U.S. Department of Health and Human Services. Hyattsville, MD: National Center for Health Statistics.
- Albert DG, Morita Y, Iseri LT. 1958. Serum magnesium and plasma sodium levels in essential vascular hypertension. *Circulation* 17:761–764.
- Alderman BW, Weiss NS, Daling JR, Ure CL, Ballard JH. 1986. Reproductive history and postmenopausal risk of hip and forearm fracture. *Am J Epidemiol* 124:262–267.
- Alfrey AC, Miller NL, Butkus D. 1974. Evaluation of body magnesium stores. *J Lab Clin Med* 84:153–162.
- Allen JC, Keller RP, Archer P, Neville MC. 1991. Studies in human lactation: Milk composition and daily secretion rates of macronutrients in the first year of lactation. *Am J Clin Nutr* 54:69–80.
- Allen SH, Shah JH. 1992. Calcinosis and metastatic calcification due to vitamin D intoxication. A case report and review. *Horm Res* 37:68–77.
- Allender PS, Cutler JA, Follmann D, Cappuccio FP, Pryer J, Elliott P. 1996. Dietary calcium and blood pressure: A meta-analysis of randomized clinical trials. *Ann Intern Med* 124:825–831.
- Aloia JF, Vaswani AN, Yeh JK, Ross P, Ellis K, Cohn SH. 1983. Determinants of bone mass in postmenopausal women. *Arch Intern Med* 143:1700–1704.
- Aloia JF, Vaswani AN, Yeh JK, Ellis K, Cohn SH. 1984. Total body phosphorus in postmenopausal women. *Miner Electrolyte Metab* 10:73–76.
- Aloia JF, Vaswani A, Yeh JK, Ross PL, Flaster E, Dilmanian FA. 1994. Calcium supplementation with and without hormone replacement therapy to prevent postmenopausal bone loss. *Ann Intern Med* 120:97–103.
- Altura BT, Brust M, Bloom S, Barbour RL, Stempak JG, Altura BM. 1990. Magnesium dietary intake modulates blood lipid levels and atherogenesis. *Proc Natl Acad Sci USA* 87:1840–1844.
- Altura BT, Shirey TL, Hiti J, Dell'Orfano K, Handwerker SM, Altura BM. 1992. A new method for the rapid determination of ionized Mg<sup>2+</sup> in whole blood, serum and plasma. *Methods Find Exp Clin Pharmacol* 14:297–304.
- Altura BT, Wilimizig C, Trnovec T, Nyulassy S, Altura BM. 1994. Comparative effects of a Mg-enriched diet and different orally administered magnesium oxide preparations on ionized Mg, Mg metabolism and electrolytes in serum of human volunteers. *J Am Coll Nutr* 13:447–454.
- American Academy of Pediatrics. 1982. The promotion of breastfeeding: Policy statement based on task force report. *Pediatrics* 69:654–661.

- Anderson DM, Hollis BW, LeVine BR, Pittard WB III. 1988. Dietary assessment of maternal vitamin D intake and correlation with maternal and neonatal serum vitamin D concentrations at delivery. *J Perinatol* 8:46–48.
- Andon MB, Ilich JZ, Tzagournis MA, Matkovic V. 1996. Magnesium balance in adolescent females consuming a low- or high-calcium diet. *Am J Clin Nutr* 63:950–953.
- Angus RM, Sambrook PN, Pockock NA, Eisman JA. 1988. Dietary intake and bone mineral density. *Bone Miner* 4:265–277.
- Antman EM. 1996. Magnesium in acute myocardial infarction: Overview of available evidence. *Am Heart J* 132:487–495.
- Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin PH, Karanja N. 1997. A clinical trial of the effects of dietary patterns on blood pressure. *N Engl J Med* 336:1117–1124.
- Arnold FA Jr, Dean HT, Jay P, Knutson JW. 1956. Effect of fluoridated public water supplies on dental caries prevalence. Tenth year of the Grand Rapids-Muskegon Study. *Pub Hlth Rep* 71:652–658.
- Ascherio A, Rimm EB, Giovannucci EL, Colditz GA, Rosner B, Willett WC, Sacks F, Stampfer MJ. 1992. A prospective study of nutritional factors and hypertension among U.S. men. *Circulation* 86:1475–1484.
- Ashe JR, Schofield FA, Gram MR. 1979. The retention of calcium, iron, phosphorus, and magnesium during pregnancy: The adequacy of prenatal diets with and without supplementation. *Am J Clin Nutr* 32:286–291.
- Atkinson SA, Chappell JE, Clandinin MT. 1987. Calcium supplementation of mothers' milk for low birthweight infants: Problems related to absorption and excretion. *Nutr Res* 7:813–823.
- Atkinson SA, Alston-Mills BP, Lonnerdal B, Neville MC, Thompson MP. 1995. Major minerals and ionic constituents of human and bovine milk. In: Jensen RJ, ed. *Handbook of Milk Composition*. California: Academic Press. Pp. 593–619.
- Bainbridge RR, Mimouni FB, Landi T, Crossman M, Harris L, Tsang RC. 1996. Effect of rice cereal feedings on bone mineralization and calcium homeostasis in cow milk formula fed infants. *J Am Coll Nutr* 15:383–388.
- Baran D, Sorensen A, Grimes J, Lew R, Karella A, Johnson B, Roche J. 1990. Dietary modification with dairy products for preventing vertebral bone loss in premenopausal women: A three-year prospective study. *J Clin Endocrinol Metab* 70:264–270.
- Bardicef M, Bardicef O, Sorokin Y, Altura BM, Altura BT, Cotton DB, Resnick LM. 1995. Extracellular and intracellular magnesium depletion in pregnancy and gestational diabetes. *Am J Obstet Gynecol* 172:1009–1013.
- Barger-Lux MJ, Heaney RP. 1995. Caffeine and the calcium economy revisited. *Osteopor Int* 5:97–102.
- Barger-Lux MJ, Heaney RP, Stegman MR. 1990. Effects of moderate caffeine intake on the calcium economy of premenopausal women. *Am J Clin Nutr* 52:722–725.
- Barger-Lux MJ, Heaney RP, Lanspa SJ, Healy JC, DeLuca HF. 1995. An investigation of sources of variation in calcium absorption efficiency. *J Clin Endocrinol Metab* 80:406–411.
- Barger-Lux MJ, Heaney RP, Dowell S, Bierman J, Holick MF, Chen TC. 1996. Relative molar potency of 25-hydroxyvitamin D indicates a major role in calcium absorption. *J Bone Miner Res* 11:S423.

- Barnhart WE, Hiller LK, Leonard GJ, Michaels SE. 1974. Dentifrice usage and ingestion among four age groups. *J Dent Res* 53:1317–1322.
- Barragry JM, France MW, Corless D, Gupta SP, Switala S, Boucher BJ, Cohen RD. 1978. Intestinal cholecalciferol absorption in the elderly and in younger adults. *Clin Sci Molec Med* 55:213–220.
- Barrett-Connor E, Chang JC, Edelstein SL. 1994. Coffee-associated osteoporosis offset by daily milk consumption. The Rancho Bernardo Study. *J Am Med Assoc* 271:280–283.
- Bashir Y, Sneddon JF, Staunton HA, Haywood GA, Simpson IA, McKenna WJ, Camm AJ. 1993. Effects of long-term oral magnesium chloride replacement in congestive heart failure secondary to coronary artery disease. *Am J Cardiol* 72:1156–1162.
- Beall DP, Scofield RH. 1995. Milk-alkali syndrome associated with calcium carbonate consumption: Report of 7 patients with parathyroid hormone levels and an estimate of prevalence among patients hospitalized with hypercalcemia. *Medicine* 74:89–96.
- Beaton GH. 1994. Criteria of an adequate diet. In: Shils RE, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease, 8th edition*. Philadelphia: Lea & Febiger. Pp. 1491–1505.
- Beaton GH. 1996. Statistical approaches to establish mineral element recommendations. *J Nutr* 126:2302S–2328S.
- Begum A, Pereira SM. 1969. Calcium balance studies on children accustomed to low calcium intakes. *Br J Nutr* 23:905–911.
- Bell NH, Greene A, Epstein S, Oexmann MJ, Shaw S, Shary J. 1985. Evidence for alteration of the vitamin D-endocrine system in blacks. *J Clin Invest* 76:470–473.
- Bell NH, Shary J, Stevens J, Garza M, Gordon L, Edwards J. 1991. Demonstration that bone mass is greater in black than in white children. *J Bone Miner Res* 6:719–723.
- Bell NH, Yergey AL, Vieira NE, Oexmann MJ, Shary JR. 1993. Demonstration of a difference in urinary calcium, not calcium absorption, in black and white adolescents. *J Bone Miner Res* 8:1111–1115.
- Bell RA, Whitford GM, Barenie JT, Myers DR. 1985. Fluoride retention in children using self-applied topical fluoride products. *Clin Prev Dent* 7:22–27.
- Berkelhammer CH, Wood RJ, Sitrin MD. 1988. Acetate and hypercalciuria during total parenteral nutrition. *Am J Clin Nutr* 48:1482–1489.
- Bernstein DS, Sadowsky N, Hegsted DM, Guri CD, Stare FJ. 1966. Prevalence of osteoporosis in high- and low-fluoride areas in North Dakota. *J Am Med Assoc* 198:499–504.
- Bijvoet, OLM. 1969. Relation of plasma phosphate concentration to renal tubular reabsorption of phosphate. *Clin Sci* 37:23–26.
- Bikle DD, Gee E, Halloran B, Haddad JG. 1984. Free 1,25-dihydroxyvitamin D levels in serum from normal subjects, pregnant subjects, and subjects with liver disease. *J Clin Invest* 74:1966–1971.
- Birkeland JM, Charlton G. 1976. Effect of pH on the fluoride ion activity of plaque. *Caries Res* 10:72–80.
- Bishop NJ, Dahlenburg SL, Fewtrell MS, Morley R, Lucas A. 1996. Early diet of preterm infants and bone mineralization at age five years. *Acta Paediatr* 85:230–236.
- Bizik BK, Ding W, Cerklewski FL. 1996. Evidence that bone resorption of young men is not increased by high dietary phosphorus obtained from milk and cheese. *Nutr Res* 16:1143–1146.

- Black DM, Cummings SR, Genant HK, Nevitt MC, Palermo L, Browner W. 1992. Axial and appendicular bone density predict fractures in older women. *J Bone Miner Res* 7:633–638.
- Blank S, Scanlon KS, Sinks TH, Lett S, Falk H. 1995. An outbreak of hypervitaminosis D associated with the overfortification of milk from a home-delivery dairy. *Am J Publ Health* 85:656–659.
- Blayney JR, Hill IN. 1964. Evanston dental caries study XXIV. Prenatal fluorides—value of waterborne fluorides during pregnancy. *J Am Dent Assoc* 69:291–294.
- Bodanszky H, Leleiko N. 1985. Metabolic alkalosis with hypertonic dehydration in a patient with diarrhoea and magnesium oxide ingestion. *Acta Paediatr Hung* 26:241–246.
- Bogdonoff MD, Shock NW, Nichols MP. 1953. Calcium, phosphorus, nitrogen, and potassium balance studies in the aged male. *J Gerontol* 8:272–288.
- Bostick RM, Potter JD, Fosdick L, Grambsch P, Lampe JW, Wood JR, Louis TA, Ganz R, Grandits G. 1993. Calcium and colorectal epithelial cell proliferation: A preliminary randomized, double-blinded, placebo-controlled clinical trial. *J Natl Cancer Inst* 85:132–141.
- Boston JL, Beauchene RE, Cruikshank DP. 1989. Erythrocyte and plasma magnesium during teenage pregnancy: Relationship with blood pressure and pregnancy-induced hypertension. *Obstet Gynecol* 73:169–174.
- Bouillon R, Van Assche FA, Van Baelen H, Heyns W, De Moor P. 1981. Influence of the vitamin D-binding protein on the serum concentration of 1,25-dihydroxyvitamin D<sub>3</sub>. Significance of the free 1,25-dihydroxyvitamin D<sub>3</sub> concentration. *J Clin Invest* 67:589–596.
- Bour NJS, Soullier BA, Zemel MB. 1984. Effect of level and form of phosphorus and level of calcium intake on zinc, iron and copper bioavailability in man. *Nutr Res* 4:371–379.
- Bowden GH. 1990. Effects of fluoride on the microbial ecology of dental plaque. *J Dent Res* 69 (Spec Iss):653–659.
- Boyle DR, Chagnon M. 1995. An incidence of skeletal fluorosis associated with groundwaters of the maritime carboniferous basin, Gaspe Region, Quebec, Canada. *Environ Geochem Health* 17:5–12.
- BPA (British Paediatric Association). 1956. Hypercalcaemia in infants and Vitamin D. *Br Med J* 2:149.
- BPA (British Paediatric Association). 1964. Infantile hypercalcaemia, nutritional rickets, and infantile scurvy in Great Britain. *Br Med J* 1:1659–1661.
- Brambilla E, Belluomo G, Malerba A, Buscaglia M, Strohmenger L. 1994. Oral administration of fluoride in pregnant women, and the relation between concentration in maternal plasma and in amniotic fluid. *Arch Oral Biol* 39:991–994.
- Brandwein SL, Sigman, KM. 1994. Case report: Milk-alkali syndrome and pancreatitis. *Am J Med Sci* 308:173–176.
- Brannan PG, Vergne-Marini P, Pak CY, Hull AR, Fordtran JS. 1976. Magnesium absorption in the human small intestine. Results in normal subjects, patients with chronic renal disease, and patients with absorptive hypercalciuria. *J Clin Invest* 57:1412–1418.
- Bransby ER, Berry WTC, Taylor DM. 1964. Study of the vitamin-D intakes of infants in 1960. *Br Med J* 1:1661–1663.
- Brazier M, Kamel S, Maamer M, Agbomson F, Elesper I, Garabedian M, Desmet G, Sebert JL. 1995. Markers of bone remodeling in the elderly subject: Effects of vitamin D insufficiency and its correction. *J Bone Miner Res* 10:1753–1761.

- Brickman AS, Coburn JW, Massry SG. 1974. 1,25 dihydroxy-vitamin D<sub>3</sub> in normal man and patients with renal failure. *Ann Intern Med* 80:161–168.
- Brink EJ, Beynen AC. 1992. Nutrition and magnesium absorption: A review. *Prog Food Nutr Sci* 16:125–162.
- Brodehl J, Gellissen K, Weber H-P. 1982. Postnatal development of tubular phosphate reabsorption. *Clin Nephrol* 17:163–171.
- Brown WE, Gregory TM, Chow LC. 1977. Effects of fluoride on enamel solubility and cariostasis. *Caries Res* 11(Suppl 1):118–141.
- Brunelle JA, Carlos JP. 1990. Recent trends in dental caries in U.S. children and the effect of water fluoridation. *J Dent Res* 69(Spec Iss):723–727.
- Bruun C, Thylstrup A. 1988. Dentifrice usage among Danish children. *J Dent Res* 67:1114–1117.
- Bucher HC, Cook RJ, Guyatt GH, Lang JD, Cook DJ, Hatala R, Hunt DL. 1996. Effects of dietary calcium supplementation on blood pressure: A meta-analysis of randomized controlled trials. *J Am Med Assoc* 275:1016–1022.
- Bucuvalas JC, Heubi JE, Specker BL, Gregg DJ, Yerger AL, Vieira NE. 1990. Calcium absorption in bone disease associated with chronic cholestasis during childhood. *Hepatology* 12:1200–1205.
- Bullamore JR, Wilkinson R, Gallagher JC, Nordin BEC, Marshall DH. 1970. Effects of age on calcium absorption. *Lancet* 2:535–537.
- Bullimore DW, Miloszewski KJ. 1987. Raised parathyroid hormone levels in the milk-alkali syndrome: An appropriate response? *Postgrad Med J* 63:789–792.
- Burt BA. 1992. The changing patterns of systemic fluoride intake. *J Dent Res* 71:1228–1237.
- Burtis WJ, Gay L, Insogna KL, Ellison A, Broadus AE. 1994. Dietary hypercalciuria in patients with calcium oxalate kidney stones. *Am J Clin Nutr* 60:424–429.
- Bushe CJ. 1986. Profound hypophosphataemia in patients collapsing after a “fun run.” *Br Med J* 292:898–899.
- Butte NF, Garza C, Smith EO, Nichols BL. 1984. Human milk intake and growth in exclusively breast-fed infants. *J Pediatr* 104:187–195.
- Buzzard IM, Willett WC, eds. 1994. Dietary assessment methods. Proceedings of a conference held in St. Paul, MN. *Am J Clin Nutr* 59:143S–306S.
- Byrne J, Thomas MR, Chan GM. 1987. Calcium intake and bone density of lactating women in their late childbearing years. *J Am Diet Assoc* 87:883–887.
- Byrne PM, Freaney R, McKenna MJ. 1995. Vitamin D supplementation in the elderly: Review of safety and effectiveness of different regimens. *Calcif Tissue Int* 56:518–520.
- Caddell JL, Ratananon N, Trangratapit P. 1973. Parenteral magnesium load tests in postpartum Thai women. *Am J Clin Nutr* 26:612–615.
- Caddell JL, Saier FL, Thomason CA. 1975. Parenteral magnesium load tests in postpartum American women. *Am J Clin Nutr* 28:1099–1104.
- Calvo MS. 1993. Dietary phosphorus, calcium metabolism and bone. *J Nutr* 123:1627–1633.
- Calvo MS, Heath H III. 1988. Acute effects of oral phosphate-salt ingestion on serum phosphorus, serum ionized calcium, and parathyroid hormone in young adults. *Am J Clin Nutr* 47:1025–1029.
- Calvo MS, Park YK. 1996. Changing phosphorus content of the U.S. diet: Potential for adverse effects on bone. *J Nutr* 126:1168S–1180S.
- Calvo MS, Kumar R, Heath H III. 1988. Elevated secretion and action of serum parathyroid hormone in young adults consuming high phosphorus, low calcium diets assembled from common foods. *J Clin Endocrinol Metab* 66:823–829.

- Calvo MS, Kumar R, Heath H. 1990. Persistently elevated parathyroid hormone secretion and action in young women after four weeks of ingesting high phosphorus, low calcium diets. *J Clin Endocrinol Metab* 70:1334–1340.
- Campbell SB, MacFarlane DJ, Fleming SJ, Khafagi FA. 1994. Increased skeletal uptake of Tc-99m Methylene Disphosphonate in Milk-Alkali Syndrome. *Clin Nucl Med* 19:207–211.
- Canadian Paediatric Society (Nutrition Committee). 1991. Meeting the iron needs of infants and young children: An update. *Can Med Assoc J* 144:1451–1454.
- Canadian Paediatric Society. 1996. The use of fluoride in infants and children. *Paediatr Child Health* 1:131–134.
- Cappuccio FP, Markandu ND, Beynon GW, Shore AC, Sampson B, MacGregor GA. 1985. Lack of effect of oral magnesium on high blood pressure: A double blind study. *Br Med J Clin Res Ed* 291:235–238.
- Carlos JP, Gittelsohn AM, Haddon W Jr. 1962. Caries in deciduous teeth in relation to maternal ingestion of fluoride. *Pub Hlth Rep* 77:658–660.
- Carroll MD, Abraham S, Dresser CM. 1983. Dietary intake source data: United States, 1976–1980. Data from the National Health Survey. Vital and Health Statistics series 11, no. 231. DHHS Publ. No. (PHS) 83-1681. Hyattsville, MD: National Center for Health Statistics, Public Health Service, U.S. Department of Health and Human Services.
- Chan GM. 1991. Dietary calcium and bone mineral status of children and adolescents. *Am J Dis Child* 145:631–634.
- Chan GM, Roberts CC, Folland D, Jackson R. 1982a. Growth and bone mineralization of normal breast-fed infants and the effects of lactation on maternal bone mineral status. *Am J Clin Nutr* 36:438–443.
- Chan GM, Slater RN, Hollis J, Thomas MR. 1982b. Decreased bone mineral status in lactating adolescent mothers. *J Pediatr* 101:767–770.
- Chan GM, Leeper L, Book LS. 1987. Effects of soy formulas on mineral metabolism in term infants. *Am J Dis Child* 141:527–530.
- Chan GM, Hoffman K, McMurry M. 1995. Effects of dairy products on bone and body composition in pubertal girls. *J Pediatr* 126:551–556.
- Chan JT, Koh SH. 1996. Fluoride content in caffeinated, decaffeinated and herbal teas. *Caries Res* 30:88–92.
- Chan JT, Qui CC, Whitford GM, Weatherred JG. 1990. Influence of coffee on fluoride metabolism in rats. *Proc Soc Exp Biol Med* 194:43–47.
- Chandra RK. 1984. Physical growth of exclusively breast-fed infants. *Nutr Res* 2:275–276.
- Chapuy MC, Arlot ME, Duboeuf F, Brun J, Crouzet B, Arnaud S, Delmas PD, Meunier PJ. 1992. Vitamin D<sub>3</sub> and calcium to prevent hip fractures in elderly women. *N Engl J Med* 327:1637–1642.
- Charles P, Jensen FT, Mosekilde L, Hansen HH. 1983. Calcium metabolism evaluated by <sup>47</sup>Ca kinetics: Estimation of dermal calcium loss. *Clin Sci* 65:415–422.
- Chen TC, Castillo L, Korycka-Dahl M, DeLuca HF. 1974. Role of vitamin D metabolites in phosphate transport of rat intestine. *J Nutr* 104:1056–1060.
- Chen TC, Shao A, Heath H III, Holick MF. 1993. An update on the vitamin D content of fortified milk from the United States and Canada. *N Engl J Med* 329:1507.
- Chen X, Whitford GM. 1994. Lack of significant effect of coffee and caffeine on fluoride metabolism in rats. *J Dent Res* 73:1173–1179.
- Chesney RW. 1990. Requirements and upper limits of vitamin D intake in the term neonate, infant, and older child. *J Pediatr* 116:159–166.

- Chevalley T, Rizzoli R, Nydegger V, Slosman D, Rapin CH, Michel JP, Vasey H, Bonjour JP. 1994. Effects of calcium supplements on femoral bone mineral density and vertebral fracture rate in vitamin D-replete elderly patients. *Osteopor Int* 4:245–252.
- Chinn HI. 1981. Effects of dietary factors on skeletal integrity in adults: Calcium, phosphorus, vitamin D, and protein. Prepared for Bureau of Foods, Food and Drug Administration, U.S. Department of Health and Human Services, Washington, D.C.
- Cholak J. 1959. Fluorides: A critical review. I. The occurrence of fluoride in air, food and water. *J Occup Med* 1:501–511.
- Chow LC. 1990. Tooth-bound fluoride and dental caries. *J Dent Res* 69(Spec Iss):595–600.
- Clark DC, Hann HJ, Williamson MF, Berkowitz J. 1993. Aesthetic concerns of children and parents in relation to different classifications of the Tooth Surface Index of Fluorosis. *Community Dent Oral Epidemiol* 21:360–364.
- Clarkson EM, Warren RL, McDonald SJ, de Wardener HE. 1967. The effect of a high intake of calcium on magnesium metabolism in normal subjects and patients with chronic renal failure. *Clin Sci* 32:11–18.
- Clarkson PM, Haymes EM. 1995. Exercise and mineral status of athletes: Calcium, magnesium, phosphorus, and iron. *Med Sci Sports Exerc* 27:831–843.
- Clemens TL, Adams JS. 1996. Vitamin D metabolites. In: Favus MJ, Christakos S, eds. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 3rd edition*. Philadelphia, PA: Lippincott-Raven. Pp. 109–114.
- Clemens TL, Adams JS, Henderson SL, Holick MF. 1982. Increased skin pigment reduces the capacity of skin to synthesise vitamin D<sub>3</sub>. *Lancet* 1:74–76.
- Clemens TL, Zhou X, Myles M, Endres D, Lindsay R. 1986. Serum vitamin D<sub>2</sub> and vitamin D<sub>3</sub> metabolite concentrations and absorption of vitamin D<sub>2</sub> in elderly subjects. *J Clin Endocrinol Metab* 63:656–660.
- Cleveland LE, Goldman JD, Borrud LG. 1996. *Data Tables: Results from USDA's 1994 Continuing Survey of Food Intakes by Individuals and 1994 Diet and Health Knowledge Survey*. Beltsville, MD: Agricultural Research Service, U.S. Department of Agriculture.
- Clovis J, Hargreaves JA. 1988. Fluoride intake from beverage consumption. *Community Dent Oral Epidemiol* 16:11–15.
- CNPP, USDA (Center for Nutrition Policy and Promotion, U.S. Department of Agriculture). 1996. *Nutrient Content of the U.S. Food Supply, 1990–1994. Preliminary Data*. Washington, DC: U.S. Department of Agriculture.
- Cockburn F, Belton NR, Purvis RJ, Giles MM, Brown JK, Turner TL, Wilkinson EM, Forfar JO, Barrie WJM, McKay GS, Pocock SJ. 1980. Maternal vitamin D intake and mineral metabolism in mothers and their newborn infants. *Br Med J* 281:11–14.
- Coffin B, Azpiroz F, Guarner F, Malagelada JR. 1994. Selective gastric hypersensitivity and reflex hyporeactivity in functional dyspepsia. *Gastroenterology* 107:1345–1351.
- Cohen L. 1988. Recent data on magnesium and osteoporosis. *Magnes Res* 1:85–87.
- Cohen L, Laor A. 1990. Correlation between bone magnesium concentration and magnesium retention in the intravenous magnesium load test. *Magnes Res* 3:271–274.
- Cohn SH, Abesamis C, Yasumura S, Aloia JF, Zanzi I, Ellis KJ. 1977. Comparative skeletal mass and radial bone mineral content in black and white women. *Metabolism* 26:171–178.

- Colston K, Colston MJ, Feldman D. 1981. 1,25-dihydroxyvitamin D<sub>3</sub> and malignant melanoma: The presence of receptors and inhibition of cell growth in culture. *Endocrinol* 108:1083–1086.
- COMA (Committee on Medical Aspects of Food Policy). 1991. *Dietary Reference Values for Food Energy and Nutrients for the United Kingdom. Report on Health and Social Subjects, No. 41*. London: HMSO.
- Comstock GW. 1979. Water hardness and cardiovascular diseases. *Am J Epidemiol* 110:375–400.
- Conradt A, Weidinger H, Algayer H. 1984. On the role of magnesium in fetal hypotrophy, pregnancy induced hypertension and pre-eclampsia. *Magnes Bull* 2:68–76.
- Cooper C, Melton LJ III. 1992. Epidemiology of osteoporosis. *Trends Endocrinol Metab* 3:224–229.
- Cooper C, Campion G, Melton LJ III. 1992. Hip fractures in the elderly: A worldwide projection. *Osteopor Int* 2:285–289.
- Costello RB, Moser-Veillon PB, DiBianco R. 1997. Magnesium supplementation in patients with congestive heart failure. *J Am Coll Nutr* 16:22–31.
- Cowell DC, Taylor WH. 1981. Ionic fluoride: A study of its physiological variation in man. *Ann Clin Biochem* 18:76–83.
- Craig JM. 1959. Observations on the kidney after phosphate loading in the rat. *Arch Pathol* 68:306–315.
- Cramer CF. 1961. Progress and rate of absorption of radiophosphorus through the intestinal tract of rats. *Can J Biochem Physiol* 39:499–503.
- Cremer HD, Buttner W. 1970. *Absorption of Fluorides. Fluoride and Human Health*. Geneva, Switzerland: World Health Organization.
- Cross NA, Hillman LS, Allen SH, Krause GF, Vieira NE. 1995a. Calcium homeostasis and bone metabolism during pregnancy, lactation, and postweaning: A longitudinal study. *Am J Clin Nutr* 61:514–523.
- Cross NA, Hillman LS, Allen SH, Krasue GF. 1995b. Changes in bone mineral density and markers of bone remodeling during lactation and postweaning in women consuming high amounts of calcium. *J Bone Miner Res* 10:1312–1320.
- Cumming RG, Cummings SR, Nevitt MC, Scott J, Ensrud KE, Vogt TM, Fox K. 1997. Calcium intake and fracture risk: Results from the study of osteoporotic fractures. *Am J Epidemiol* 145:926–934.
- Cummings SR, Black DM, Nevitt MC, Browner W, Cauley J, Ensrud K, Genant HK, Palermo L, Scott J, Vogt TM. 1993. Bone density at various sites for prediction of hip fractures. The Study of Osteoporotic Fractures Research Group. *Lancet* 341:72–75.
- Cummings SR, Nevitt MC, Browner WS, Stone K, Fox KM, Ensrud KE, Cauley J, Black D, Vogt TM. 1995. Risk factors for hip fracture in white women: Study of Osteoporotic Fractures Research Group. *N Engl J Med* 332:767–773.
- Cunningham AS, Mazess RB. 1983. Bone mineral loss in lactating adolescents. *J Pediatr* 101:338–339.
- Curhan GC, Willett WC, Rimm EB, Stampfer MJ. 1993. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. *N Engl J Med* 328:833–838.
- Curhan GC, Willett WC, Speizer FE, Spiegelman D, Stampfer MJ. 1997. Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk for kidney stones in women. *Ann Intern Med* 126:497–504.

- Dabeka RW, McKenzie AD, Conacher HBS, Kirkpatrick DC. 1982. Determination of fluoride in Canadian infant foods and calculation of fluoride intakes by infants. *Can J Pub Hlth* 73:188–191.
- Dabeka RW, McKenzie AD, Lecroix GM. 1987. Dietary intakes of lead, cadmium, arsenic and fluoride by Canadian adults: A 24-hour duplicate diet study. *Food Addit Contam* 4:89–101.
- Dale G, Fleetwood JA, Inkster JS, Sainsbury JR. 1986. Profound hypophosphataemia in patients collapsing after a “fun run.” *Br Med J (Clin Res)* 292:447–448.
- Dalton MA, Sargent JD, O’Connor GT, Olmstead EM, Klein RZ. 1997. Calcium and phosphorus supplementation of iron-fortified infant formula: No effect on iron status of healthy full-term infants. *Am J Clin Nutr* 65:921–926.
- Davies M, Adams PH. 1978. The continuing risk of vitamin D intoxication. *Lancet* 2(8090):621–623.
- Davies M, Lawson DEM, Emberson C, Barnes JLC, Roberts GE, Barnes ND. 1982. Vitamin D from skin: Contribution to vitamin D status compared with oral vitamin D in normal and anti-convulsant-treated subjects. *Clin Sci* 63:461–472.
- Davies M, Hayes ME, Yin JA, Berry JL, Mawer EB. 1994. Abnormal synthesis of 1,25-dihydroxyvitamin D in patients with malignant lymphoma. *J Clin Endocrinol Metab* 78:1202–1207.
- Davis RH, Morgan DB, Rivlin RS. 1970. The excretion of calcium in the urine and its relation to calcium intake, sex and age. *Clin Sci* 39:1–12.
- Dawes C. 1989. Fluorides: Mechanisms of action and recommendations for use. *J Can Dent Assoc* 55:721–723.
- Dawson-Hughes B. 1996. Calcium. In: Marcus R, Feldman D, Kelsey J, eds. *Osteoporosis*. Orlando, FL: Academic Press, Inc. Pp. 1103, 1105.
- Dawson-Hughes B, Stern DT, Shipp CC, Rasmussen HM. 1988. Effect of lowering dietary calcium intake on fractional whole body calcium retention. *J Clin Endocrinol Metab* 67:62–68.
- Dawson-Hughes B, Dallal GE, Krall EA, Sadowski L, Sahyoun N, Tannenbaum S. 1990. A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women. *N Engl J Med* 323:878–883.
- Dawson-Hughes B, Dallal GE, Krall EA, Harris S, Sokoll LJ, Falconer G. 1991. Effect of vitamin D supplementation on wintertime and overall bone loss in healthy postmenopausal women. *Ann Intern Med* 115:505–512.
- Dawson-Hughes B, Harris S, Kramich C, Dallal G, Rasmussen HM. 1993. Calcium retention and hormone levels in black and white women on high- and low-calcium diets. *J Bone Miner Res* 8:779–787.
- Dawson-Hughes B, Harris SS, Krall EA, Dallal GE, Falconer G, Green CL. 1995. Rates of bone loss in postmenopausal women randomly assigned to one of two dosages of vitamin D. *Am J Clin Nutr* 61:1140–1145.
- Dawson-Hughes B, Fowler SE, Dalsky G, Gallagher C. 1996. Sodium excretion influences calcium homeostasis in elderly men and women. *J Nutr* 126:2107–2112.
- Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. 1997. Calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. *N Engl J Med* 337:670–676.
- Dean HT. 1942. The investigation of physiological effects by the epidemiological method. In: Moulton FR, ed. *Fluorine and Dental Health*. Washington, DC: American Association for the Advancement of Science. Pp. 23–31.
- Dean HT, Elvove E. 1937. Further studies on the minimal threshold of chronic endemic dental fluorosis. *Pub Hlth Rep* 52:1249–1264.

- Delmas PD. 1992. Clinical use of biochemical markers of bone remodeling in osteoporosis. *Bone* 13:S17–S21.
- Delmi M, Rapin CH, Bengoa JM, Delmas PD, Vasey H, Bonjour JP. 1990. Dietary supplementation in elderly patients with fractured neck of the femur. *Lancet* 335:1013–1016.
- DeLuca HF. 1984. The metabolism, physiology, and function of vitamin D. In: Kumar R, ed. *Vitamin D: Basic and Clinical Aspects*. Boston: M. Nijhoff Publishers.
- DeLuca HF. 1988. The vitamin D story: A collaborative effort of basic science and clinical medicine. *FASEB J* 2:224–236.
- Delvin EE, Salle BL, Glorieux FH, Adeleine P, David LS. 1986. Vitamin D supplementation during pregnancy: Effect on neonatal calcium homeostasis. *J Pediatr* 109:328–334.
- Demay MB. 1995. Hereditary defects in vitamin D metabolism and vitamin D receptor defects. In: DeGroot LJ, Besser M, Burger HG, Jameson JL, Loriaux DL, Marshall JC, O'Dell WD, Potts JT, Rubenstein AH, eds. *Endocrinology, Vol 2, Third edition*. Philadelphia, PA: WB Saunders. Pp. 1173–1178.
- Demirjian A. 1980. *Anthropometry Report. Height, Weight, and Body Dimensions: A Report from Nutrition Canada*. Ottawa: Minister of National Health and Welfare, Health and Promotion Directorate, Health Services and Promotion Branch.
- Dengel JL, Mangels AR, Moser-Veillon PB. 1994. Magnesium homeostasis: Conservation mechanism in lactating women consuming a controlled-magnesium diet. *Am J Clin Nutr* 59:990–994.
- Deurenberg P, Pieters JJ, Hautvast JG. 1990. The assessment of the body fat percentage by skinfold thickness measurements in childhood and young adolescence. *Br J Nutr* 63:293–303.
- Deuster PA, Singh A. 1993. Responses of plasma magnesium and other cations to fluid replacement during exercise. *J Am Coll Nutr* 12:286–293.
- Devine A, Criddle RA, Dick IM, Kerr DA, Prince RL. 1995. A longitudinal study of the effect of sodium and calcium intakes on regional bone density in postmenopausal women. *Am J Clin Nutr* 62:740–745.
- DeVizia B, Mansi A. 1992. Calcium and phosphorus metabolism in full-term infants. *Monatsschr Kinderheilkd* 140:S8–S12.
- DeVizia B, Fomon SJ, Nelson SE, Edwards BE, Zeigler EE. 1985. Effect of dietary calcium on metabolic balance of normal infants. *Pediatr Res* 19:800–806.
- Dewey KG, Finley DA, Lonnerdal B. 1984. Breast milk volume and composition during late lactation (7–20 months). *J Pediatr Gastroenterol Nutr* 3:713–720.
- DHHS (Department of Health and Human Services). 1988. *The Surgeon General's Report on Nutrition and Health*. Washington, DC: US Department of Health and Human Services, Public Health Service.
- DHHS (Department of Health and Human Services). 1990. *Healthy People 2000: National Health Promotion and Disease Prevention Objectives*. DHHS Publ. No. (PHS) 91-50212. Washington, DC: US Government Printing Office. Pp. 466–467.
- Diem K. 1970. *Documenta Geigy*. Ardsley, NY: Geigy Pharmaceuticals.
- Dobnig H, Kainer F, Stepan V, Winter R, Lipp R, Schaffer M, Kahr A, Nocnik S, Patterer G, Leb G. 1995. Elevated parathyroid hormone-related peptide levels after human gestation: Relationship to changes in bone and mineral metabolism. *J Clin Endocrinol Metab* 80:3699–3707.
- Dorsch TR. 1986. The milk-alkali syndrome, vitamin D, and parathyroid hormone. *Ann Intern Med* 105:800–801.

- Dorup I, Clausen T. 1993. Correlation between magnesium and potassium contents in muscle: Role of Na(+)-K<sup>+</sup> pump. *Am J Physiol* 264:C457–C463.
- Dourson ML, Stara JF. 1983. Regulatory history and experimental support of uncertainty (safety) factors. *Regul Toxicol Pharmacol* 3:224–238.
- Dowell TB. 1981. The use of toothpaste in infancy. *Br Dent J* 150:247–249.
- Drinkwater BL, Chesnut CH III. 1991. Bone density changes during pregnancy and lactation in active women: A longitudinal study. *Bone Miner* 14:153–160.
- Drinkwater B, Bruemner B, Chesnut C. 1990. Menstrual history as a determinant of current bone density in young athletes. *J Am Med Assoc* 263:545–548.
- Dwyer JT, Dietz WH, Hass G, Suskind R. 1979. Risk of nutritional rickets among vegetarian children. *Am J Dis Child* 133:134–140.
- Dyckner T, Wester PO. 1983. Effect of magnesium on blood pressure. *Br Med J (Clin Res)* 286:1847–1849.
- Dyckner T, Wester PO. 1985. Skeletal muscle magnesium and potassium determinations: Correlation with lymphocyte contents of magnesium and potassium. *J Am Coll Nutr* 4:619–625.
- Ebeling PR, Yergey AL, Vieira NE, Burritt MF, O'Fallon WM, Kumar R, Riggs BL. 1994. Influence of age on effects on endogenous 1,25-dihydroxy-vitamin D on calcium absorption in normal women. *Calcif Tissue Int* 55:330–334.
- Eble DM, Deaton TG, Wilson FC, Bawden JW. 1992. Fluoride concentrations in human and rat bone. *J Pub Hlth Dent* 52:288–291.
- Egsmose C, Lund B, McNair P, Lund B, Storm T, Sorensen OH. 1987. Low serum levels of 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D in institutionalized old people: Influence of solar exposure and vitamin D supplementation. *Age Ageing* 16:35–40.
- Eisman JA, Suva LJ, Sher E, Pearce PJ, Funder JW, Martin TJ. 1981. Frequency of 1,25-dihydroxyvitamin D<sub>3</sub> receptor in human breast cancer. *Cancer Res* 41:5121–5124.
- Ekstrand J, Ehrnebo M. 1979. Influence of milk products on fluoride bioavailability in man. *Eur J Clin Pharmacol* 16:211–215.
- Ekstrand J, Ehrnebo M. 1980. Absorption of fluoride from fluoride dentifrices. *Caries Res* 14:96–102.
- Ekstrand J, Boreus LO, de Chateau P. 1981. No evidence of transfer of fluoride from plasma to breast milk. *Br Med J* 283:761–762.
- Ekstrand J, Spak CJ, Falch J, Afseth J, Ulvestad H. 1984. Distribution of fluoride to human breast milk following intake of high doses of fluoride. *Caries Res* 18:93–95.
- Ekstrand J, Fomon SJ, Ziegler EE, Nelson SE. 1994a. Fluoride pharmacokinetics in infancy. *Pediatr Res* 35:157–163.
- Ekstrand J, Ziegler EE, Nelson SE, Fomon SJ. 1994b. Absorption and retention of dietary and supplemental fluoride by infants. *Adv Dent Res* 8:175–180.
- Elders PJ, Netelenbos JC, Lips P, van Ginkel FC, Khoe E, Leeuwenkamp OR, Hackeng WH, van der Stelt PF. 1991. Calcium supplementation reduces vertebral bone loss in perimenopausal women: A controlled trial in 248 women between 46 and 55 years of age. *J Clin Endocrinol Metab* 73:533–540.
- Elders PJ, Lips P, Netelenbos JC, van Ginkel FC, Khoe E, van der Vijgh WJ, van der Stelt PF. 1994. Long-term effect of calcium supplementation on bone loss in perimenopausal women. *J Bone Miner Res* 9:963–970.
- Elia M. 1992. Energy expenditure and the whole body. In: Kinney JM, Tucker HN, eds. *Energy Metabolism: Tissue Determinants and Cellular Corollaries*. New York: Raven Press Ltd. Pp. 19–59.

- Elin RJ. 1987. Assessment of magnesium status. *Clin Chem* 33:1965–1970.
- Elin RJ, Hosseini JM. 1985. Magnesium content of mononuclear blood cells. *Clin Chem* 31:377–380.
- Ellis KJ, Shypailo RJ, Hergenroeder A, Perez M, Abrams S. 1996. Total body calcium and bone mineral content: Comparison of dual-energy X-ray absorptiometry (DXA) with neutron activation analysis (NAA). *J Bone Miner Res* 11:843–848.
- Ellis KJ, Abrams SA, Wong WW. 1997. Body composition of a young, multiethnic female population. *Am J Clin Nutr* 65:724–731.
- EPA (U. S. Environmental Protection Agency). 1986. Guidelines for Carcinogen Risk Assessment. *Federal Register* 51(185):33992–34003.
- EPA (U. S. Environmental Protection Agency). 1996. Proposed Guidelines for Carcinogen Risk Assessment; Notice. *Federal Register* 61(79):17960–18011.
- Esala S, Vuori E, Helle A. 1982. Effect of maternal fluorine intake on breast milk fluorine content. *Br J Nutr* 48:201–204.
- Esveld RP, DeLuca HF. 1981. Calcitroic acid: Biological activity and tissue distribution studies. *Arch Biochem Biophys* 206:403–413.
- European Community. 1993. *Nutrient and Energy Intakes for the European Community*. Reports of the Scientific Committee for Food, Thirty-first Series.
- Evans RW. 1989. Changes in dental fluorosis following an adjustment to the fluoride concentration of Hong Kong's water supplies. *Adv Dent Res* 3:154–160.
- Evans RW, Darvell BW. 1995. Refining the estimate of the critical period for susceptibility to enamel fluorosis in human maxillary central incisors. *J Pub Hlth Dent* 55:238–249.
- Fairweather-Tait S, Prentice A, Heumann KG, Landing MAJ, Stirling DM, Wharf SG, Turnlund JR. 1995. Effect of calcium supplements and stage of lactation on the calcium absorption efficiency of lactating women accustomed to low calcium intakes. *Am J Clin Nutr* 62:1188–1192.
- FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization). 1982. *Evaluation of Certain Food Additives and Contaminants*. Twenty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives (WHO Technical Report Series No. 683).
- FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization, Expert Consultation). 1995. *The Application of Risk Analysis to Food Standard Issues*. Recommendations to the Codex Alimentarius Commission (ALINORM 95/9, Appendix 5).
- FAO/WHO/UNA (Food and Agriculture Organization of the United Nations/World Health Organization/United Nations). 1985. *Energy and Protein Requirements*. Report of a joint FAO/WHO/UNA Consultation Technical Report Series. No. 724. Geneva, Switzerland: World Health Organization.
- Fardellone P, Sebert JL, Garabedian M, Bellony R, Maamer M, Agbomson F, Brazier M. 1995. Prevalence and biological consequences of vitamin D deficiency in elderly institutionalized subjects. *Rev Rhum* 62:576–581.
- Farmer ME, White LR, Brody JA, Bailey KR. 1984. Race and sex differences in hip fracture incidence. *Am J Publ Health* 74:1374–1380.
- Fatemi S, Ryzen E, Flores J, Endres DB, Rude RK. 1991. Effect of experimental human magnesium depletion on parathyroid hormone secretion and 1,25-dihydroxyvitamin D metabolism. *J Clin Endocrinol Metab* 73:1067–1072.
- Faulkner KG, Cummings SR, Black D, Palermo L, Gluer CC, Genant HK. 1993. Simple measurement of femoral geometry predicts hip fracture: The study of osteoporotic fractures. *J Bone Miner Res* 8:1211–1217.

- Favus MJ, Christakos S. 1996. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 3rd Edition*. Philadelphia, PA: Lippincott-Raven.
- Featherstone JDB, Shields CP. 1988. *A Study of Fluoride in New York State Residents*. Final report to New York State Department of Health.
- Fehily AM, Coles RJ, Evans WD, Elwood PC. 1992. Factors affecting bone density in young adults. *Am J Clin Nutr* 56:579–586.
- Fejerskov O, Thylstrup A, Larsen MJ. 1977. Clinical and structural features and possible pathogenic mechanisms of dental fluorosis. *Scand J Dent Res* 85:510–534.
- Feldblum PJ, Zhang J, Rich LE, Fortney JA, Talmage RV. 1992. Lactation history and bone mineral density among perimenopausal women. *Epidemiology* 3:527–531.
- Feliciano ES, Ho ML, Specker BL, Falciglia G, Shui QM, Yin TA, Chen XC. 1994. Seasonal and geographical variations in the growth rate of infants in China receiving increasing dosages of vitamin D supplements. *J Trop Pediatr* 40:162–165.
- Feltman R, Kosel G. 1961. Prenatal and postnatal ingestion of fluorides—fourteen years of investigation. Final report. *J Dent Med* 16:190–198.
- Fieser LF, Fieser M. 1959. Vitamin D. In: *Steroids*. New York: Reinhold. Pp. 90–168.
- Filippo FA, Battistone GC. 1971. The fluoride content of a representative diet of the young adult male. *Clin Chim Acta* 31:453–457.
- Fine KD, Santa Ana CA, Porter JL, Fordtran JS. 1991a. Intestinal absorption of magnesium from food and supplements. *J Clin Invest* 88:396–402.
- Fine KD, Santa Ana CA, Fordtran JS. 1991b. Diagnosis of magnesium-induced diarrhea. *N Engl J Med* 324:1012–1017.
- Fink RI, Kolterman OG, Griffin J, Olefsky JM. 1983. Mechanisms of insulin resistance in aging. *J Clin Invest* 71:1523–1535.
- Fitzgerald MG, Fourman P. 1956. An experimental study of magnesium deficiency in man. *Clin Sci* 15:635.
- Fomon SJ, Nelson SE. 1993. Calcium, phosphorus, magnesium, and sulfur. In: Fomon SJ, ed. *Nutrition of Normal Infants*. St. Louis: Mosby-Year Book, Inc. Pp. 192–216.
- Fomon SJ, Younoszai MK, Thomas LN. 1966. Influence of vitamin D on linear growth of normal full-term infants. *J Nutr* 88:345–50.
- Fomon SJ, Haschke F, Ziegler EE, Nelson SE. 1982. Body composition of reference children from birth to age 10 years. *Am J Clin Nutr* 35:1169–1175.
- Franz KB. 1987. Magnesium intake during pregnancy. *Magnesium* 6:18–27.
- Franz KB. 1989. Influence of phosphorus on intestinal absorption of calcium and magnesium. In: Itokawa Y, Durlach J, eds. *Magnesium in Health and Disease*. London: John Libbey & Co. Pp. 71–78.
- Fraser DR. 1980. Regulation of the metabolism of vitamin D. *Physiol Rev* 60:551–613.
- Fraser DR. 1983. The physiological economy of vitamin D. *Lancet* 1:969–972.
- Freiman I, Pettifor JM, Moodley GM. 1982. Serum phosphorus in protein energy malnutrition. *J Pediatr Gastroenterol Nutr* 1:547–550.
- French JK, Koldaway IM, Williams LC. 1986. Milk-alkali syndrome following over-the-counter antacid self-medication. *N Zeal Med J* 99:322–323.
- Freudenheim JL, Johnson NE, Smith EL. 1986. Relationships between usual nutrient intake and bone-mineral content of women 35–65 years of age: Longitudinal and cross-sectional analysis. *Am J Clin Nutr* 44:863–876.

- Freyberg RH. 1942. Treatment of arthritis with vitamin and endocrine preparations. *J Am Med Assoc* 119:1165–1171.
- Frithz G, Wictorin B, Ronquist G. 1991. Calcium-induced constipation in a prepubescent boy. *Acta Paediatr Scand* 80:964–965.
- Frost HM. 1973. The origin and nature of transients in human bone remodeling dynamics. In: Frame B, Parfitt AM, Duncan H, eds. *Clinical Aspects of Metabolic Bone Disease*. Amsterdam: Excerpta Medica Series. Pp. 124–137.
- Frost HM. 1987. The mechanostat: A proposed pathogenic mechanism of osteoporosis and the bone mass effects of mechanical and nonmechanical agents. *Bone Miner* 2:73–85.
- Frost HM. 1997. Why do marathon runners have less bone than weight lifters? A vital-biomechanical view and explanation. *Bone* 20:183–189.
- Gadallah M, Massry SG, Bigazzi R, Horst RL, Eggema P, Campese VM. 1991. Intestinal absorption of calcium and calcium metabolism in patients with essential hypertension and normal renal function. *Am J Hypertens* 4:404–409.
- Galla JH, Booker BB, Luke RG. 1986. Role of the loop segment in the urinary concentrating defect of hypercalcemia. *Kidney Int* 29:977–982.
- Gallagher JC, Riggs BL, DeLuca HF. 1980. Effect of estrogen on calcium absorption and serum vitamin D metabolites in postmenopausal osteoporosis. *J Clin Endocrinol Metab* 51:1359–1364.
- Gallagher JC, Goldgar D, Moy A. 1987. Total bone calcium in women: Effect of age and menopause status. *J Bone Miner Res* 2:491–496.
- Garby L, Lammert O. 1984. Within-subjects between-days-and-weeks variation in energy expenditure at rest. *Human Nutr Clin Nutr* 38:395–397.
- Garfinkel L, Garfinkel D. 1985. Magnesium regulation of the glycolytic pathway and the enzymes involved. *Magnesium* 4:60–72.
- Garland C, Shekelle RB, Barrett-Connor E, Criqui MH, Rossof AH, Paul O. 1985. Dietary vitamin D and calcium and risk of colorectal cancer: A 19-year prospective study in men. *Lancet* 1:307–309.
- Garland FC, Garland CF, Gorham ED, Young JF. 1990. Geographic variation in breast cancer mortality in the United States: A hypothesis involving exposure to solar radiation. *Prev Med* 19:614–622.
- Garn SM. 1972. The course of bone gain and the phases of bone loss. *Orthop Clin North Am* 3:503–520.
- Gartside PS, Glueck CJ. 1995. The important role of modifiable dietary and behavioral characteristics in the causation and prevention of coronary heart disease hospitalization and mortality: The prospective NHANES I follow-up study. *J Am Coll Nutr* 14:71–79.
- Gedalia I, Brzezinski A, Portuguese N, Bercovici B. 1964. The fluoride content of teeth and bones of human foetuses. *Arch Oral Biol* 9:331–340.
- Geleijnse JM, Witteman JC, Bak AA, den Breeijen JH, Grobbee DE. 1994. Reduction in blood pressure with a low sodium, high potassium, high magnesium salt in older subjects with mild to moderate hypertension. *Br Med J* 309:436–440.
- German Society of Nutrition. 1991. *Recommendations on Nutrient Intake*. Abstract and Tables of the 157 Pages Booklet, 5th revised edition. Frankfurt: Druckerei Henrich.
- Gershoff SN, Legg MA, Hegsted DM. 1958. Adaptation to different calcium intakes in dogs. *J Nutr* 64:303–312.
- Gertner JM, Coustan DR, Kliger AS, Mallette LE, Ravin N, Broadus AE. 1986. Pregnancy as state of physiologic absorptive hypercalciuria. *Am J Med* 81:451–456.

## ONLINE REFERENCES

1009

- Gillman MW, Hood MY, Moore LL, Nguyen US, Singer MR, Andon MB. 1995. Effect of calcium supplementation on blood pressure in children. *J Pediatr* 127:186–192.
- Gilsanz V, Roe TF, Mora S, Costin G, Goodman WG. 1991. Changes in vertebral bone density in black girls and white girls during childhood and puberty. *N Engl J Med* 325:1597–1600.
- Glaser K, Parmelee AH, Hoffman WS. 1949. Comparative efficacy of vitamin D preparations in prophylactic treatment of premature infants. *Am J Dis Child* 77:1–14.
- Glass RL, Peterson JK, Zuckerberg DA, Naylor MN. 1975. Fluoride ingestion resulting from the use of a monofluorophosphate dentifrice by children. *Br Dent J* 138:423–426.
- Glenn FB. 1981. The rationale for the administration of a NaF tablet supplement during pregnancy and postnatally in a private practice setting. *J Dent Child* 48:118–122.
- Glenn FB, Glenn WD III, Duncan RC. 1984. Prenatal fluoride tablet supplementation and the fluoride content of teeth: Part VII. *J Dent Child* 51:344–351.
- Gloth FM III, Gundberg CM, Hollis BW, Haddad JG Jr, Tobin JD. 1995. Vitamin D deficiency in homebound elderly persons. *J Am Med Assoc* 274:1683–1686.
- Goeree R, O'Brien B, Pettitt D, Cuddy L, Ferraz M, Adachi J. 1996. An assessment of the burden of illness due to osteoporosis in Canada. *J SOGC*:15S–24S.
- Golden BE, Golden MH. 1981. Plasma zinc, rate of weight gain, and the energy cost of tissue deposition in children recovering from severe malnutrition on a cow's milk or soya protein-based diet. *Am J Clin Nutr* 34:892–899.
- Goldfarb S. 1994. Diet and nephrolithiasis. *Ann Rev Med* 45:235–243.
- Goldring SR, Krane SM, Avioli LV. 1995. Disorders of calcification: Osteomalacia and rickets. In: DeGroot LJ, ed. *Endocrinology*, Vol 2, *Third Edition*. Philadelphia: WB Saunders. Pp. 1204–1227.
- Golzarian J, Scott HW Jr, Richards WO. 1994. Hypermagnesemia-induced paralytic ileus. *Dig Dis Sci* 39:1138–1142.
- Gora ML, Seth SK, Bay WH, Visconti JA. 1989. Milk-alkali syndrome associated with use of chlorothiazide and calcium carbonate. *Clin Pharm* 8:227–229.
- Goren S, Silverstein LJ, Gonzales N. 1993. A survey of food service managers of Washington State boarding homes for the elderly. *J Nutr Elderly* 12:27–42.
- Graham S. 1959. Idiopathic hypercalcemia. *Postgraduate Med* 25:67–72.
- Gray TK, Lester GE, Lorenc RS. 1979. Evidence for extra-renal 1-hydroxylation of 25-hydroxyvitamin D<sub>3</sub> in pregnancy. *Science* 204:1311–1313.
- Greer FR. 1989. Calcium, phosphorus, and magnesium: How much is too much for infant formulas? *J Nutr* 119:1846–1851.
- Greer FR, Garn SM. 1982. Loss of bone mineral content in lactating adolescents. *J Pediatr* 101:718–719.
- Greer FR, Searcy JE, Levin RS, Steichen JJ, Steichen-Asche PS, Tsang RC. 1982a. Bone mineral content and serum 25-hydroxyvitamin D concentrations in breast-fed infants with and without supplemental vitamin D: One-year follow-up. *J Pediatr* 100:919–922.
- Greer FR, Tsang RC, Levin RS, Searcy JE, Wu R, Steichen JJ. 1982b. Increasing serum calcium and magnesium concentrations in breast-fed infants: Longitudinal studies of minerals in human milk and in sera of nursing mothers and their infants. *J Pediatr* 100:59–64.

- Greer FR, Steichen JJ, Tsang RC. 1982c. Effects of increased calcium, phosphorus, and vitamin D intake on bone mineralization in very low-birth-weight infants fed formulas with polycose and medium-chain triglycerides. *J Pediatr* 100:951–955.
- Greer FR, Lane J, Ho M. 1984. Elevated serum parathyroid hormone, calcitonin, and 1,25-dihydroxyvitamin D in lactating women nursing twins. *Am J Clin Nutr* 40:562–568.
- Greger JL, Baier MJ. 1983. Effect of dietary aluminum on mineral metabolism of adult males. *Am J Clin Nutr* 38:411–419.
- Greger JL, Baligar P, Abernathy RP, Bennett OA, Peterson T. 1978. Calcium, magnesium, phosphorus, copper, and manganese balance in adolescent females. *Am J Clin Nutr* 31:117–121.
- Greger JL, Huffman J, Abernathy RP, Bennett OA, Resnick SE. 1979. Phosphorus and magnesium balance of adolescent females fed two levels of zinc. *J Food Sci* 44:1765–1767.
- Greger JL, Smith SA, Snedeker SM. 1981. Effect of dietary calcium and phosphorus levels on the utilization of calcium, phosphorus, magnesium, manganese, and selenium by adult males. *Nutr Res* 1:315–325.
- Grill V, Martin TJ. 1993. Non-parathyroid hypercalcemias. In: Nordin BEC, Need AG, Morris HA, eds. *Metabolic Bone and Stone Disease*. Edinburgh: Churchill Livingstone. Pp. 133–145.
- Grimston SK, Morrison K, Harder JA, Hanley DA. 1992. Bone mineral density during puberty in Western Canadian children. *Bone Miner* 19:85–96.
- Groeneveld A, Van Eck AA, Backer-Dirks O. 1990. Fluoride in caries prevention: Is the effect pre- or post-eruptive? *J Dent Res* 69(Spec Iss):751–755.
- Gullestad L, Dolva LO, Waage A, Falch D, Fagerthun H, Kjekshus J. 1992. Magnesium deficiency diagnosed by an intravenous loading test. *Scan J Clin Lab Invest* 52:245–253.
- Gullestad L, Nes M, Ronneberg R, Midtveldt K, Falch D, Kjekshus J. 1994. Magnesium status in healthy free-living elderly Norwegians. *J Am Coll Nutr* 13:45–50.
- Gultekin A, Ozalp I, Hasanoglu A, Unal A. 1987. Serum-25-hydroxycholecalciferol levels in children and adolescents. *Turk J Pediatr* 29:155–162.
- Gunther T. 1993. Mechanisms and regulation of Mg<sup>2+</sup> efflux and Mg<sup>2+</sup> influx. *Miner Electrolyte Metab* 19:259–265.
- Guy WS. 1979. Inorganic and organic fluorine in human blood. In: Johansen E, Taves DR, Olsen TO, eds. *Continuing Evaluation of the Use of Fluorides*. AAAS Selected Symposium. Boulder, CO: Westview Press.
- Haddad JG, Jr. 1980. Competitive protein-binding radioassays for 25-OH-D; clinical applications. In: Norman, ed. *Vitamin D*, vol. 2. New York: Marcel Dekker, Inc., P. 587.
- Haddad JG, Hahn TJ. 1973. Natural and synthetic sources of circulating 25-hydroxyvitamin D in man. *Nature* 244:515–517.
- Hakim R, Tolis G, Goltzman D, Meltzer S, Friedman R. 1979. Severe hypercalcemia associated with hydrochlorothiazide and calcium carbonate therapy. *Can Med Assoc J* 21:591–594.
- Halioua L, Anderson JJ. 1989. Lifetime calcium intake and physical activity habits: Independent and combined effects on the radial bone of healthy premenopausal Caucasian women. *Am J Clin Nutr* 49:534–541.
- Hallberg L, Rossander-Hulten L, Brune M, Gleerup A. 1992. Calcium and iron absorption: Mechanism of action and nutritional importance. *Eur J Clin Nutr* 46:317–327.

## ONLINE REFERENCES

## 1011

- Hallfrisch J, Muller DC. 1993. Does diet provide adequate amounts of calcium, iron, magnesium, and zinc in a well-educated adult population? *Exper Gerontol* 28:473–483.
- Hamilton IR. 1990. Biochemical effects of fluoride on oral bacteria. *J Dent Res* 69(Spec Iss):660–667.
- Hammer DI, Heyden S. 1980. Water hardness and cardiovascular mortality. *J Am Med Assoc* 243:2399–2400.
- Hamuro Y, Shino A, Suzuki Z. 1970. Acute induction of soft tissue calcification with transient hyperphosphatemia in the KK mouse by modification in dietary contents of calcium, phosphorus, and magnesium. *J Nutr* 100:404–412.
- Handwerker SM, Altura BT, Altura BM. 1996. Serum ionized magnesium and other electrolytes in the antenatal period of human pregnancy. *J Am Coll Nutr* 15:36–43.
- Hardwick LL, Jones MR, Brautbar N, Lee DB. 1991. Magnesium absorption: Mechanisms and the influence of vitamin D, calcium and phosphate. *J Nutr* 121:13–23.
- Hargreaves JA. 1972. Fluoride content of deciduous tooth enamel from three different regions (Abstract). *J Dent Res* 51:274.
- Hargreaves JA. 1992. The level and timing of systemic exposure to fluoride with respect to caries resistance. *J Dent Res* 71:1244–1248.
- Hargreaves JA, Ingram GS, Wagg BJ. 1970. An extended excretion study on the ingestion of a monofluorophosphate toothpaste by children. *Acta Med Sci Hung* 27:413–419.
- Hargreaves JA, Ingram FF, Wagg BJ. 1972. A gravimetric based study of the ingestion of toothpaste by children. *Caries Res* 6:237–243.
- Hargreaves JA, Thompson GW, Pimlott JFL, Norbert LD. 1988. Commencement date of fluoride supplementation related to dental caries. *J Dent Res* 67:230.
- Harris SS, Dawson-Hughes B. 1994. Caffeine and bone loss in healthy postmenopausal women. *Am J Clin Nutr* 60:573–578.
- Hart M, Windle J, McHale M, Grissom R. 1982. Milk-alkali syndrome and hypercalcemia: A case report. *Nebr Med J* 67:128–130.
- Hasling C, Charles P, Jensen FT, Mosekilde L. 1990. Calcium metabolism in postmenopausal osteoporosis: The influence of dietary calcium and net absorbed calcium. *J Bone Miner Res* 5:939–946.
- Hayslip CC, Klein TA, Wray HL, Duncan WE. 1989. The effects of lactation on bone mineral content in healthy postpartum women. *Obstet Gynecol* 73:588–592.
- Health Canada. 1990. *Nutrition Recommendations. The Report of the Scientific Review Committee 1990*. Ottawa: Canadian Government Publishing Centre.
- Health Canada. 1993. *Health Risk Determination—The Challenge of Health Protection*. Health Canada, Health Protection Branch. Ottawa: Health Canada.
- Heaney RP. 1993. Protein intake and the calcium economy. *J Am Diet Assoc* 93:1259–1260.
- Heaney RP. 1997. Vitamin D: Role in the calcium economy. In: Feldman D, Glorieux FH, Pike JW, eds. *Vitamin D*. San Diego, CA: Academic Press. Pp. 485–497.
- Heaney RP, Recker RR. 1982. Effects of nitrogen, phosphorus, and caffeine on calcium balance in women. *J Lab Clin Med* 99:46–55.
- Heaney RP, Recker RR. 1987. Calcium supplements: Anion effects. *Bone Miner* 2:433–439.

- Heaney RP, Recker RR. 1994. Determinants of endogenous fecal calcium in healthy women. *J Bone Miner Res* 9:1621–1627.
- Heaney RP, Skillman TG. 1964. Secretion and excretion of calcium by the human gastrointestinal tract. *J Lab Clin Med* 64:29–41.
- Heaney RP, Skillman TG. 1971. Calcium metabolism in normal human pregnancy. *J Clin Endocrinol* 33:661–670.
- Heaney RP, Saville PD, Recker RR. 1975. Calcium absorption as a function of calcium intake. *J Lab Clin Med* 85:881–890.
- Heaney RP, Recker RR, Saville PD. 1977. Calcium balance and calcium requirements in middle-aged women. *Am J Clin Nutr* 30:1603–1611.
- Heaney RP, Recker RR, Saville PD. 1978. Menopausal changes in calcium balance performance. *J Lab Clin Med* 92:953–963.
- Heaney RP, Recker RR, Hinders SM. 1988. Variability of calcium absorption. *Am J Clin Nutr* 47:262–264.
- Heaney RP, Recker RR, Stegman MR, Moy AJ. 1989. Calcium absorption in women: Relationships to calcium intake, estrogen status, and age. *J Bone Miner Res* 4:469–475.
- Heaney RP, Recker RR, Weaver CM. 1990a. Absorbability of calcium sources: The limited role of solubility. *Calcif Tissue Int* 46:300–304.
- Heaney RP, Weaver CM, Fitzsimmons ML. 1990b. Influence of calcium load on absorption fraction. *J Bone Miner Res* 5:1135–1138.
- Heaney RP, Weaver CM, Fitzsimmons ML. 1991. Soybean phytate content: Effect on calcium absorption. *Am J Clin Nutr* 53:745–747.
- Heaton FW. 1969. The kidney and magnesium homeostasis. *Ann NY Acad Sci* 162:775–785.
- Hegsted DM. 1972. Problems in the use and interpretation of the Recommended Dietary Allowances. *Ecol Food Nutr* 1:255–265.
- Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. 1993. Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: The DARLING study. *Am J Clin Nutr* 58:152–161.
- Hemmingsen C, Staun M, Olgaard K. 1994. Effects of magnesium on renal and intestinal calbindin-D. *Miner Electrolyte Metab* 20:265–273.
- Herman-Giddens ME, Slora EJ, Wasserman RC, Bourdon CJ, Bhapkar MV, Koch GG, Hasemeier CM. 1997. Secondary sexual characteristics and menses in young girls seen in office practice: A study from the Pediatric Research in Office Settings Network. *Pediatrics* 99:505–512.
- Hill AB. 1971. *Principles of Medical Statistics, 9th Ed.* New York: Oxford University Press.
- Hillman LS. 1990. Mineral and vitamin D adequacy in infants fed human milk or formula between 6 and 12 months of age. *J Pediatr* 117:S134–S142.
- Hillman L, Sateesha S, Haussler M, Wiest W, Slatopolsky E, Haddad J. 1981. Control of mineral homeostasis during lactation: Interrelationships of 25-hydroxyvitamin D, 24,25-dihydroxyvitamin D, 1,25-dihydroxyvitamin D, parathyroid hormone, calcitonin, prolactin, and estradiol. *Am J Obstet Gynecol* 139:471–476.
- Hillman LS, Chow W, Salmons SJ, Weaver E, Erickson M, Hansen J. 1988. Vitamin D metabolism, mineral homeostasis and bone mineralization in term infants fed human milk, cow milk-based formula or soy-based formula. *J Pediatr* 112:864–874.
- Hodge HC, Smith FA. 1977. Occupational fluoride exposure. *J Occup Med* 19:12–39.

- Hodge HC. 1979. The safety of fluoride tablets or drops. In: Johansen E, Taves DR, Olson, TO, eds. *Continuing Evaluation of the Use of Fluorides, AAAS Selected Symposium 1*. Boulder, CO: Westview Press. Pp. 253–274.
- Hodgson E, Mailman RB, Chamber JE. 1988. *Dictionary of Toxicology*. New York: Van Nostrand Reinhold, Inc.
- Hoffman S, Grisso JA, Kelsey JL, Gammon MD, O'Brien LA. 1993. Parity, lactation and hip fracture. *Osteopor Int* 3:171–176.
- Hofvander Y, Hagman U, Hillervik C, Sjolin S. 1982. The amount of milk consumed by 1–3 months old breast- or bottle-fed infants. *Acta Pediatr Scand* 71:953–958.
- Holbrook TL, Barrett-Connor E, Wingard DL. 1988. Dietary calcium and risk of hip fracture: 14-year prospective population study. *Lancet* 2:1046–1049.
- Holick MF. 1986. Vitamin D requirements for the elderly. *Clin Nutr* 5:121–129.
- Holick MF. 1994. McCollum Award Lecture, 1994: Vitamin D: New horizons for the 21st century. *Am J Clin Nutr* 60:619–630.
- Holick MF. 1995. Vitamin D: Photobiology, metabolism, and clinical applications. In: DeGroot LJ, Besser M, Burger HG, Jameson JL, Loriaux DL, Marshall JC, O'Dell WD, Potts JL, Rubenstein AH, eds. *Endocrinology, 3rd Edition*. Philadelphia, PA: WB Saunders.
- Holick MF. 1996. Vitamin D: Photobiology, metabolism, mechanism of action, and clinical application. In: Favus MJ, ed. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 3rd Edition*. Philadelphia, PA: Lippincott-Raven. Pp. 74–81.
- Holick MF, Clark MB. 1978. The photobiogenesis and metabolism of vitamin D. *Fed Proc* 37:2567–2574.
- Holick MF, Schnoes HK, DeLuca HF. 1971. Identification of 1,25-dihydroxycholecalciferol, a form of vitamin D<sub>3</sub> metabolically active in the intestine. *Proc Natl Acad Sci USA* 68:803–804.
- Holick MF, Uskokovic M, Henley JW, MacLaughlin J, Holick SA, Potts JT Jr. 1980. The photoproduction of 1 $\alpha$ , 25-dihydroxyvitamin D<sub>3</sub> in skin: An approach to the therapy of vitamin-D-resistant syndromes. *N Engl J Med* 303:349–354.
- Holick MF, MacLaughlin JA, Doppelt SH. 1981. Regulation of cutaneous previtamin D<sub>3</sub> photosynthesis in man: Skin pigment is not an essential regulator. *Science* 211:590–593.
- Holick MF, Matsuoka LY, Wortsman J. 1989. Age, vitamin D, and solar ultraviolet. *Lancet* 2:1104–1105.
- Holick MF, Shao Q, Liu WW, Chen TC. 1992. The vitamin D content of fortified milk and infant formula. *N Engl J Med* 326:1178–1181.
- Hollifield JW. 1987. Magnesium depletion, diuretics, and arrhythmias. *Am J Med* 82(Suppl 3A):30–37.
- Hollis BW. 1996. Assessment of vitamin D nutritional and hormonal status: What to measure and how to do it. *Calcif Tissue Int* 58:4–5.
- Holmes RP, Kummerow FA. 1983. The relationship of adequate and excessive intake of vitamin D to health and disease. *J Am Coll Nutr* 2:173–199.
- Honkanen R, Alhava E, Parviainen M, Talasniemi S, Monkkonen R. 1990. The necessity and safety of calcium and vitamin D in the elderly. *J Am Geriatr Soc* 38:862–866.
- Hordon LD, Peacock M. 1987. Vitamin D metabolism in women with femoral neck fracture. *Bone Miner* 2:413–426.
- Horowitz HS. 1990. The future of water fluoridation and other systemic fluorides. *J Dent Res* 69(Spec Iss):760–764.

- Horowitz HS. 1996. The effectiveness of community water fluoridation in the United States. *J Pub Hlth Dent* 56:253–258.
- Horowitz HS, Heifetz SB. 1967. Effects of prenatal exposure to fluoridation on dental caries. *Pub Hlth Rep* 82:297–304.
- Horowitz M, Wishart J, Mundy L, Nordin BEC. 1987. Lactose and calcium absorption in postmenopausal osteoporosis. *Arch Intern Med* 147:534–536.
- Hoskova M. 1968. Fluoride tablets in the prevention of tooth decay. *Cesk Pediatr* 23:438–441.
- Howard JE, Hopkins TR, Connor TB. 1953. On certain physiologic responses to intravenous injection of calcium salts into normal, hyperparathyroid and hypoparathyroid persons. *J Clin Endocrinol Metab* 13:1–19.
- Hreshchyshyn MM, Hopkins A, Zylstra S, Anbar M. 1988. Associations of parity, breast-feeding, and birth control pills with lumbar spine and femoral neck bone densities. *Am J Obstet Gynecol* 159:318–322.
- Hua H, Gonzales J, Rude RK. 1995. Magnesium transport induced ex vivo by a pharmacological dose of insulin is impaired in non-insulin-dependent diabetes mellitus. *Magnes Res* 8:359–366.
- Huang Z, Himes JH, McGovern PG. 1996. Nutrition and subsequent hip fracture risk among a national cohort of white women. *Am J Epidemiol* 144:124–134.
- Hunt CD, Nielsen FH. 1981. Interaction between boron and cholecalciferol in the chick. In: McC Howell J, Gathorne JM, White CL, eds. *Trace Element Metabolism in Man and Animals, TEMA-4*. Canberra: Australian Academy of Science. Pp. 597–600.
- Hunt MS, Schofield FA. 1969. Magnesium balance and protein intake level in adult human female. *Am J Clin Nutr* 22:367–373.
- Hwang DL, Yen CF, Nadler JL. 1993. Insulin increases intracellular magnesium transport in human platelets. *J Clin Endocrinol Metab* 76:549–553.
- IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Report of the Subcommittee on Nutritional Status and Weight Gain During Pregnancy, Subcommittee on Dietary Intake and Nutrient Supplements During Pregnancy, Committee on Nutritional Status During Pregnancy and Lactation, Food and Nutrition Board. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1991. *Nutrition During Lactation*. Report of the Subcommittee on Nutrition During Lactation, Committee on Nutritional Status During Pregnancy and Lactation, Food and Nutrition Board. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Food and Nutrition Board. Washington, DC: National Academy Press.
- Ireland P, Fordtran JS. 1973. Effect of dietary calcium and age on jejunal calcium absorption in humans studied by intestinal perfusion. *J Clin Invest* 52:2672–2681.
- Irnell L. 1969. Metastatic calcification of soft tissue on overdose of vitamin D. *Acta Med Scand* 185:147–152.
- Iseri LT, French JH. 1984. Magnesium: Nature's physiologic calcium blocker. *Am Heart J* 108:188–193.
- ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. 1995. ISIS-4: A randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. *Lancet* 345:669–685.

- Ismail AI, Brodeur JM, Kavanagh M, Boisclair G, Tessier C, Picotte L. 1990. Prevalence of dental caries and dental fluorosis in students, 11–17 years of age, in fluoridated and non-fluoridated cities in Quebec. *Caries Res* 24:290–297.
- Jackman LA, Millane SS, Martin BR, Wood OB, McCabe GP, Peacock M, Weaver CM. 1997. Calcium retention in relation to calcium intake and postmenarcheal age in adolescent females. *Am J Clin Nutr* 66:327–333.
- Jackson D, Murray JJ, Fairpo CG. 1973. Life-long benefits of fluoride in drinking water. *Br Dent J* 134:419–422.
- Jacobus CH, Holick MF, Shao Q, Chen TC, Holm IA, Kolodny JM, Fuleihan GE, Seely EW. 1992. Hypervitaminosis D associated with drinking milk. *N Engl J Med* 326:1173–1177.
- Janas LM, Picone TA, Benson JD, MacLean WC. 1988. Influence of dietary calcium to phosphorus and parathormone during the first two weeks of life. *Pediatr Res* 23:485A.
- Janelle KC, Barr SI. 1995. Nutrient intakes and eating behavior scores of vegetarian and nonvegetarian women. *J Am Diet Assoc* 95:180–186.
- Jeans PC. 1950. Vitamin D. *J Am Med Assoc* 143:177–181.
- Jeans PC, Stearns G. 1938. The effect of vitamin D on linear growth in infancy. II. The effect of intakes above 1,800 USP units daily. *J Pediatr* 13:730–740.
- Joffres MR, Reed DM, Yano K. 1987. Relationship of magnesium intake and other dietary factors to blood pressure: The Honolulu heart study. *Am J Clin Nutr* 45:469–475.
- Johansson C, Mellström D, Milsom I. 1993. Reproductive factors as predictors of bone density and fractures in women at the age of 70. *Maturitas* 17:39–50.
- Johnson AO, Semenza JG, Buchowski MS, Enwonwu CO, Scrimshaw NS. 1993a. Correlation of lactose maldigestion, lactose intolerance, and milk intolerance. *Am J Clin Nutr* 57:399–401.
- Johnson AO, Semenza JG, Buchowski MS, Enwonwu CO, Scrimshaw NS. 1993b. Adaptation of lactose maldigesters to continued milk intakes. *Am J Clin Nutr* 58:879–881.
- Johnson CM, Wilson DM, O'Fallon WM, Malek RS, Kurland LT. 1979. Renal stone epidemiology: A 25-year study in Rochester, Minn. *Kidney Int* 16:624–631.
- Johnson J Jr, Bawden JW. 1987. The fluoride content of infant formulas available in 1985. *Pediatr Dent* 9:33–37.
- Johnson KR, Jobber J, Stonawski BJ. 1980. Prophylactic vitamin D in the elderly. *Age Ageing* 9:121–127.
- Johnston CC, Miller JZ, Slemenda CW, Reister TK, Hui S, Christian JC, Peacock M. 1992. Calcium supplementation and increases in bone mineral density in children. *N Engl J Med* 327:82–87.
- Jones JE, Manalo R, Flink EB. 1967. Magnesium requirements in adults. *Am J Clin Nutr* 20:632–635.
- Jowsey J, Balasubramaniam P. 1972. Effect of phosphate supplements on soft tissue calcification and bone turnover. *Clin Sci* 42:289–299.
- Junor JR, Catto GRD. 1976. Renal biopsy in the milk-alkali syndrome. *J Clin Path* 29:1074–1076.
- Kailis DG, Taylor SR, Davis GB, Bartlett LG, Fitzgerald DJ, Grose IJ, Newton PD. 1968. Fluoride and caries: Observations of the effects of prenatal and postnatal fluoride on some Perth pre-school children. *Med J Austral* 2:1037–1040.
- Kalkwarf HJ, Specker BL. 1995. Bone mineral loss during lactation and recovery after weaning. *Obstet Gynecol* 86:26–32.
- Kalkwarf HJ, Specker BL, Heubi JE, Vieira NE, Yerger AL. 1996. Intestinal calcium absorption of women during lactation and after weaning. *Am J Clin Nutr* 63:526–531.

- Kalkwarf HJ, Specker BL, Bianchi DC, Ranz J, Ho M. 1997. The effect of calcium supplementation on bone density during lactation and after weaning. *N Engl J Med* 337:523–528.
- Kallmeyer JC, Funston MR. 1983. The milk-alkali syndrome: A case report. *S Afr Med J* 64:287–288.
- Kamel S, Brazier M, Picard C, Boitte F, Samson L, Desmet G, Sebert JL. 1994. Urinary excretion of pyridinolines crosslinks measured by immunoassay and HPLC techniques in normal subjects and in elderly patients with vitamin D deficiency. *Bone Miner* 26:197–208.
- Kamel S, Brazier M, Rogez JC, Vincent O, Maamer M, Desmet G, Sebert JL. 1996. Different responses of free and peptide-bound cross-links to vitamin D and calcium supplementation in elderly women with vitamin D insufficiency. *J Clin Endocrinol Metab* 81:3717–3721.
- Kaminsky LS, Mahoney MC, Leach J, Melius J, Miller MJ. 1990. Fluoride: Benefits and risks of exposure. *Crit Rev Oral Biol Med* 1:261–281.
- Kanapka JA, Hamilton IR. 1971. Fluoride inhibition of enolase activity in vivo and its relationship to the inhibition of glucose-6-P formation in *Streptococcus salivarius*. *Arch Biochem Biophys* 146:167–174.
- Kanemitsu T, Koike A, Yamamoto S. 1985. Study of the cell proliferation kinetics in ulcerative colitis, adenomatous polyps, and cancer. *Cancer* 56:1094–1098.
- Kanis JA, Melton LJ III, Christiansen C, Johnston CC, Khaltaev N. 1994. The diagnosis of osteoporosis. *J Bone Miner Res* 9:1137–1141.
- Kapsner P, Langsdorf L, Marcus R, Kraemer FB, Hoffman AR. 1986. Milk-alkali syndrome in patients treated with calcium carbonate after cardiac transplantation. *Arch Intern Med* 146:1965–1968.
- Katzman DK, Bachrach LK, Carter DR, Marcus R. 1991. Clinical and anthropometric correlates of bone mineral acquisition in healthy adolescent girls. *J Clin Endocrinol Metab* 73:1332–1339.
- Kayne LH, Lee DB. 1993. Intestinal magnesium absorption. *Miner Electrolyte Metab* 19:210–217.
- Keddie KMG. 1987. Case report: Severe depressive illness in the context of hypervitaminosis D. *Br J Psych* 150:394–396.
- Kellie SE, Brody JA. 1990. Sex-specific and race-specific hip fracture rates. *Am J Pub Hlth* 80:326–328.
- Kelsay JL, Prather ES. 1983. Mineral balances of human subjects consuming spinach in a low-fiber diet and in a diet containing fruits and vegetables. *Am J Clin Nutr* 38:12–19.
- Kelsay JL, Behall KM, Prather ES. 1979. Effect of fiber from fruits and vegetables on metabolic responses of human subjects. II. Calcium, magnesium, iron, and silicon balances. *Am J Clin Nutr* 32:1876–1880.
- Kent GN, Price RI, Gutteridge DH, Smith M, Allen JR, Bhagat CI, Barnes MP, Hickling CJ, Retallack RW, Wilson SG, Devlin RD, Davies C, St. John A. 1990. Human lactation: Forearm trabecular bone loss, increased bone turnover, and renal conservation of calcium and inorganic phosphate with recovery of bone mass following weaning. *J Bone Miner Res* 5:361–369.
- Kent GN, Price RI, Gutteridge DH, Rosman KJ, Smith M, Allen JR, Hickling CJ, Blakeman SL. 1991. The efficiency of intestinal calcium absorption is increased in late pregnancy but not in established lactation. *Calcif Tissue Int* 48:293–295.
- Kesteloot H, Joossens JV. 1990. The relationship between dietary intake and urinary excretion of sodium, potassium, calcium and magnesium: Belgian Inter-university Research on Nutrition and Health. *J Hum Hypertension* 4:527–533.

- Kiel DP, Felson DT, Hannan MT, Anderson JJ, Wilson PW. 1990. Caffeine and the risk of hip fracture: The Framingham Study. *Am J Epidemiol* 132:675–684.
- Kinyamu HK, Gallagher JC, Balhorn KE, Petranick KM, Rafferty KA. 1997. Serum vitamin D metabolites and calcium absorption in normal young and elderly free-living women and in women living in nursing homes. *Am J Clin Nutr* 65:790–797.
- Klaassen CD, Amdur MO, Doull J. 1986. *Casarett and Doull's Toxicology: The Basic Science of Poisons, Third Edition*. New York: Macmillan Publishing Company.
- Kleerekoper M, Mendlovic DB. 1993. Sodium fluoride therapy of postmenopausal osteoporosis. *Endocrinol Rev* 14:312–323.
- Kleibeuker JH, Welberg JW, Mulder NH, van der Meer R, Cats A, Limburg AJ, Kreumer WM, Hardonk MJ, de Vries EG. 1993. Epithelial cell proliferation in the sigmoid colon of patients with adenomatous polyps increases during oral calcium supplementation. *Br J Cancer* 67:500–503.
- Klein CJ, Moser-Veillon PB, Douglass LW, Ruben KA, Trocki O. 1995. A longitudinal study of urinary calcium, magnesium, and zinc excretion in lactating and nonlactating postpartum women. *Am J Clin Nutr* 61:779–786.
- Kleiner SM, Bazzarre TL, Ainsworth BE. 1994. Nutritional status of nationally ranked elite bodybuilders. *Int J Sport Nutr* 4:54–69.
- Kleinman GE, Rodriguez H, Good MC, Caudle MR. 1991. Hypercalcemic crisis in pregnancy associated with excessive ingestion of calcium carbonate antacid (milk-alkali syndrome): Successful treatment with hemodialysis. *Obstet Gynecol* 73:496–499.
- Knochel JP. 1977. The pathophysiology and clinical characteristics of severe hypophosphatemia. *Arch Intern Med* 137:203–220.
- Knochel JP. 1985. The clinical status of hypophosphatemia: An update. *N Engl J Med* 313:447–449.
- Kobayashi A, Kawai S, Ohbe Y, Nagashima Y. 1975. Effects of dietary lactose and a lactase preparation on the intestinal absorption of calcium and magnesium in normal infants. *Am J Clin Nutr* 28:681–683.
- Kochersberger G, Westlund R, Lyles KW. 1991. The metabolic effects of calcium supplementation in the elderly. *J Am Geriatr Soc* 39:192–196.
- Koetting CA, Wardlaw GM. 1988. Wrist, spine, and hip bone density in women with variable histories of lactation. *Am J Clin Nutr* 48:1479–1481.
- Kohlmeier L, Mendez M, McDuffie J, Miller M. 1997. Computer-assisted self-interviewing: A multimedia approach to dietary assessment. *Am J Clin Nutr* 65:1275S–1281S.
- Koo W, Tsang R. 1997. Calcium, magnesium, phosphorus and vitamin D. In: *Nutrition During Infancy, 2nd Edition*. Cincinnati: Digital Education. Pp. 175–189.
- Koo W, Krug-Wispe S, Neylen M, Succop P, Oestreich AE, Tsang RC. 1995. Effect of three levels of vitamin D intake in preterm infants receiving high mineral-containing milk. *J Pediatr Gastroenterol Nutr* 21:182–189.
- Krall EA, Sahyoun N, Tannenbaum S, Dallal GE, Dawson-Hughes B. 1989. Effect of vitamin D intake on seasonal variations in parathyroid hormone secretion in postmenopausal women. *N Engl J Med* 321:1777–1783.
- Kramer L, Osis D, Wiatrowski E, Spenser H. 1974. Dietary fluoride in different areas of the United States. *Am J Clin Nutr* 27:590–594.
- Kreiger N, Kelsey JL, Holford TR, O'Connor T. 1982. An epidemiologic study of hip fracture in postmenopausal women. *Am J Epidemiol* 116:141–148.

- Krejs GJ, Nicar MJ, Zerwekh HE, Normal DA, Kane MG, Pak CY. 1983. Effect of 1,25-dihydroxyvitamin D<sub>3</sub> on calcium and magnesium absorption in the healthy human jejunum and ileum. *Am J Med* 75:973–976.
- Krishnamachari KA. 1986. Skeletal fluorosis in humans: A review of recent progress in the understanding of the disease. *Prog Food Nutr Sci* 10:279–314.
- Krook L, Whalen JP, Lesser GV, Berens DL. 1975. Experimental studies on osteoporosis. *Methods Achiev Exp Pathol* 7:72–108.
- Kröger H, Kotaniemi A, Vainio P, Alhava E. 1992. Bone densitometry of the spine and femur in children by dual-energy x-ray absorptiometry. *Bone Miner* 17:75–85.
- Kröger H, Kotaniemi A, Kröger L, Alhava E. 1993. Development of bone mass and bone density of the spine and femoral neck—a prospective study of 65 children and adolescents. *Bone Miner* 23:171–182.
- Kröger H, Alhava E, Honkanen R, Tuppurainen M, Saarikoski S. 1994. The effect of fluoridated drinking water on axial bone mineral density: A population-based study. *Bone Miner* 27:33–41.
- Kruse K, Bartels H, Kracht U. 1984. Parathyroid function in different stages of vitamin D deficiency rickets. *Eur J Pediatr* 141:158–162.
- Kumar JV, Green EL, Wallace W, Carnahan T. 1989. Trends in dental fluorosis and dental caries prevalences in Newburgh and Kingston, NY. *Am J Pub Hlth* 79:565–569.
- Kumar R. 1986. The metabolism and mechanism of action of 1,25-dihydroxyvitamin D<sub>3</sub>. *Kidney Int* 30:793–803.
- Kumar R, Cohen WR, Silva P, Epstein FH. 1979. Elevated 1,25-dihydroxyvitamin D plasma levels in normal human pregnancy and lactation. *J Clin Invest* 63:342–344.
- Kummerow FA, Simon Cho BH, Huang YT, Imai H, Kamio A, Deutsch MJ, Hooper WM. 1976. Additive risk factors in atherosclerosis. *Am J Clin Nutr* 29:579–584.
- Kurtz TW, Al-Bander HA, Morris RC. 1987. “Salt sensitive” essential hypertension in men. *N Engl J Med* 317:1043–1048.
- Kurzel RB. 1991. Serum magnesium levels in pregnancy and preterm labor. *Am J Perinatol* 8:119–127.
- Kuti V, Balazs M, Morvay F, Varenka Z, Szekely A, Szucs M. 1981. Effect of maternal magnesium supply on spontaneous abortion and premature birth and on intrauterine fetal development: Experimental epidemiological study. *Magnes Bull* 3:73–79.
- Ladizesky M, Lu Z, Oliveri B, San Roman N, Diaz S, Holick MF, Mautalen C. 1995. Solar ultraviolet B radiation and photoproduction of vitamin D<sub>3</sub> in central and southern areas of Argentina. *J Bone Miner Res* 10:545–549.
- Lafferty FW. 1991. Differential diagnosis of hypercalcemia. *J Bone Miner Res* 6:S51–S59.
- Lakshmanan LF, Rao RB, Kim WW, Kelsay JL. 1984. Magnesium intakes, balances, and blood levels of adults consuming self-selected diets. *Am J Clin Nutr* 40:1380–1389.
- Lamberg-Allardt C, von Knorring J, Slatis P, Holmstrom T. 1989. Vitamin D status and concentrations of serum vitamin D metabolites and osteocalcin in elderly patients with femoral neck fracture: A follow-up study. *Eur J Clin Nutr* 43:355–361.
- Lamberg-Allardt C, Karkkainen M, Seppanen R, Bistrom H. 1993. Low serum 25-hydroxyvitamin D concentrations and secondary hyperparathyroidism in middle-aged white strict vegetarians. *Am J Clin Nutr* 58:684–689.
- Largent EJ. 1952. Rates of elimination of fluoride stored in the tissues of man. *Arch Ind Hyg* 6:37–42.

- Larsen MJ, Senderovitz F, Kirkegaard E, Poulsen S, Fejerskov O. 1988. Dental fluorosis in the primary and permanent dentition in fluoridated areas with consumption of either powdered milk or natural cow's milk. *J Dent Res* 67:822–825.
- Lawson DE, Fraser DR, Kodicek E, Morris HR, Williams DH. 1971. Identification of 1,25-dihydroxycholecalciferol, a new kidney hormone controlling calcium metabolism. *Nature* 230:228–230.
- Lealman GT, Logan RW, Hutchison JH, Kerr MM, Fulton AM, Brown CA. 1976. Calcium, phosphorus, and magnesium concentrations in plasma during first week of life and their relation to type of milk feed. *Arch Dis Child* 51:377–384.
- LeBlanc A, Schneider V, Spector E, Evans H, Rowe R, Lane H, Demers L, Lipton A. 1995. Calcium absorption, endogenous excretion, and endocrine changes during and after long-term bed rest. *Bone* 16:301S–304S.
- Lebrun JB, Moffatt ME, Mundy RJ, Sangster RK, Postl BD, Dooley JP, Dilling LA, Godel JC, Haworth JC. 1993. Vitamin D deficiency in a Manitoba community. *Can J Pub Hlth* 84:394–396.
- Lee WT, Leung SS, Wang SH, Xu YC, Zeng WP, Lau J, Oppenheimer SJ, Cheng JC. 1994. Double-blind, controlled calcium supplementation and bone mineral accretion in children accustomed to a low-calcium diet. *Am J Clin Nutr* 60:744–750.
- Lee WT, Leung SS, Leung DM, Tsang HS, Lau J, Cheng JC. 1995. A randomized double-blind controlled calcium supplementation trial, and bone and height acquisition in children. *Br J Nutr* 74:125–139.
- Lee WT, Leung SS, Leung DM, Cheng JC. 1996. A follow-up study on the effects of calcium-supplement withdrawal and puberty on bone acquisition of children. *Am J Clin Nutr* 64:71–77.
- LeGeros RZ, Glenn FB, Lee DD, Glenn WD. 1985. Some physico-chemical properties of deciduous enamel with and without pre-natal fluoride supplementation (PNF). *J Dent Res* 64:465–469.
- Lechner NDM, Bullock BC, Clarkson TB, Lofland HB. 1967. Biologic activities of vitamin D<sub>2</sub> and D<sub>3</sub> for growing squirrel monkeys. *Lab Anim Care* 17:483.
- Leitch I, Aitken FC. 1959. The estimation of calcium requirement: A re-examination. *Nutr Abs Rev* 29:393–409.
- Lemann J Jr. 1996. Calcium and phosphate metabolism: An overview in health and in calcium stone formers. In: Coe FL, Favus MJ, Pak CY, Parks JH, Preminger GM, eds. *Kidney Stones: Medical and Surgical Management*. Philadelphia, PA: Lippincott-Raven. Pp. 259–288.
- Lemann J Jr, Worcester EM, Gray RW. 1991. Hypercalciuria and stones. *Am J Kidney Dis* 17:386–391.
- Lemke CW, Doherty JM, Arra MC. 1970. Controlled fluoridation: The dental effects of discontinuation in Antigo, Wisconsin. *J Am Dent Assoc* 80:782–786.
- Leone NC, Shimkin MB, Arnold FA, Stevenson CA, Zimmerman ER, Geiser PB, Lieberman JE. 1954. Medical aspects of excessive fluoride in a water supply. *Pub Hlth Rep* 69:925–936.
- Leone NC, Stevenson CA, Hilbush TF, Sosman MC. 1955. A roentgenologic study of a human population exposed to high-fluoride domestic water: A ten-year study. *Am J Roentg* 74:874–885.
- Leone NC, Stevenson CA, Besse B, Hawes, LE, Dawber TA. 1960. The effects of the absorption of fluoride. II. A radiological investigation of 546 human residents of an area in which the drinking water contained only a minute trace of fluoride. *Archs Ind Hlth* 21:326–327.

- Leoni V, Fabiani L, Ticchiarelli L. 1985. Water hardness and cardiovascular mortality rate in Abruzzo, Italy. *Arch Environ Health* 40:274–278.
- Leung SSF, Lui S, Swaminathan R. 1989. Vitamin D status of Hong Kong Chinese infants. *Acta Paediatr Scand* 78:303–306.
- Leverett DH. 1986. Prevalence of dental fluorosis in fluoridated and nonfluoridated communities—a preliminary investigation. *J Pub Hlth Dent* 46:184–187.
- Leverett DH, Adair SM, Vaughan BW, Proskin HM, Moss ME. 1997. Randomized clinical trial of the effect of prenatal fluoride supplements in preventing dental caries. *Caries Res* 31:174–179.
- Levine RJ, Hauth JC, Curet LB, Sibai BM, Catalano PM, Morris CD, DerSimonian R, Esterlitz JR, Raymond EG, Bild DE, Clemens JD, Cutler JA. 1997. Trial of calcium to prevent preeclampsia. *N Engl J Med* 337:69–76.
- Levy SM, Muchow G. 1992. Provider compliance with recommended dietary fluoride supplement protocol. *Am J Pub Hlth* 82:281–283.
- Levy SM, Kohout FJ, Kiritsy MC, Heilman JR, Wefel JS. 1995. Infants' fluoride ingestion from water, supplements and dentifrice. *J Am Dent Assoc* 126:1625–1632.
- Lewis DW. 1976. *An Evaluation of the Effects of Water Fluoridation, City of Toronto, 1963–1975*. Toronto, Canada: The Corporation of the City of Toronto.
- Lewis NM, Marcus MSK, Behling AR, Greger JL. 1989. Calcium supplements and milk: Effects on acid-base balance and on retention of calcium, magnesium, and phosphorus. *Am J Clin Nutr* 49:527–533.
- Liel Y, Edwards J, Shary J, Spicer KM, Gordon L, Bell NH. 1988. The effects of race and body habitus on bone mineral density of the radius, hip, and spine in premenopausal women. *J Clin Endocrinol Metab* 66:1247–1250.
- Lin S-H, Lin Y-F, Shieh S-D. 1996. Milk-alkali syndrome in an aged patient with osteoporosis and fractures. *Nephron* 73:496–497.
- Linden V. 1974. Vitamin D and myocardial infarction. *Br Med J* 3:647–650.
- Linkswiler HM, Zemel MB, Hegsted M, Schuette S. 1981. Protein-induced hypercalciuria. *Fed Proc* 40:2429–2433.
- Lips P, Wiersinga A, vanGinkel FC, Jongen MJ, Netelenbos JC, Hackeng WH, Delmas PD, vanderVijgh WJ. 1988. The effect of vitamin D supplementation on vitamin D status and parathyroid function in elderly subjects. *J Clin Endocrinol Metab* 67:644–650.
- Lips P, Graafmans WC, Ooms ME, Bezemer D, Bouter LM. 1996. Vitamin D supplementation and fracture incidence in elderly persons: A randomized, placebo-controlled clinical trial. *Ann Intern Med* 124:400–406.
- Lipski PS, Torrance A, Kelly PJ, James OF. 1993. A study of nutritional deficits of long-stay geriatric patients. *Age Aging* 22:244–255.
- Lissner L, Bengtsson C, Hansson T. 1991. Bone mineral content in relation to lactation history in pre- and postmenopausal women. *Calcif Tissue Int* 48:319–325.
- Livingstone MB, Prentice AM, Coward WA, Strain JJ, Black AE, Davies PS, Stewart CM, McKenna PG, Whitehead RG. 1992. Validation estimates of energy intake by weighted dietary record and diet history in children and adolescents. *Am J Clin Nutr* 56:29–35.
- Lloyd T, Schaeffer JM, Walker MA, Demers LM. 1991. Urinary hormonal concentrations and spinal bone densities of premenopausal vegetarian and nonvegetarian women. *Am J Clin Nutr* 54:1005–1010.

- Lloyd T, Andon MB, Rollings N, Martel JK, Landis R, Demers LM, Eggli DF, Kieselhorst K, Kulin HE. 1993. Calcium supplementation and bone mineral density in adolescent girls. *J Am Med Assoc* 270:841–844.
- Lo CW, Paris PW, Clemens TL, Nolan J, Holick MF. 1985. Vitamin D absorption in healthy subjects and in patients with intestinal malabsorption syndromes. *Am J Clin Nutr* 42:644–649.
- Lonnerdal B. 1997. Effects of milk and milk components on calcium, magnesium, and trace element absorption during infancy. *Physiol Rev* 77:643–669.
- Looker AC, Harris TB, Madans JH, Sempers CT. 1993. Dietary calcium and hip fracture risk: The NHANES I Epidemiology Follow-Up Study. *Osteopor Int* 3:177–184.
- Looker AC, Johnston CC Jr, Wahner HW, Dunn WL, Calvo MS, Harris TB, Heyse SP, Lindsay RL. 1995. Prevalence of low femoral bone density in older US women from NHANES III. *J Bone Miner Res* 10:796–802.
- Lopez JM, Gonzalez G, Reyes V, Campino C, Diaz S. 1996. Bone turnover and density in healthy women during breastfeeding and after weaning. *Osteopor Int* 6:153–159.
- Lotz M, Zisman E, Bartter FC. 1968. Evidence for a phosphorus-depletion syndrome in man. *N Engl J Med* 278:409–415.
- Lowenstein FW, Stanton MF. 1986. Serum magnesium levels in the United States, 1971–1974. *J Am Coll Nutr* 5:399–414.
- Lowik MR, van Dokkum W, Kistemaker C, Schaafsma G, Ockhuizen T. 1993. Body composition, health status and urinary magnesium excretion among elderly people (Dutch Nutrition Surveillance System). *Magnes Res* 6:223–232.
- LSRO/FASEB (Life Sciences Research Office/Federation of American Societies for Experimental Biology). 1986. *Guidelines for Use of Dietary Intake Data*. Anderson SA, ed. Bethesda, MD: LSRO/FASEB.
- Lu PW, Briody JN, Ogle GD, Morley K, Humphries IR, Allen J, Howman-Giles R, Sillence D, Cowell CT. 1994. Bone mineral density of total body, spine, and femoral neck in children and young adults: A cross-sectional and longitudinal study. *J Bone Miner Res* 9:1451–1458.
- Luckey MM, Meier DE, Mandeli JP, DaCosta MC, Hubbard ML, Goldsmith SJ. 1989. Radial and vertebral bone density in white and black women: Evidence for racial differences in premenopausal bone homeostasis. *J Clin Endocrinol Metab* 69:762–770.
- Lukert BP, Raisz LG. 1990. Glucocorticoid-induced osteoporosis: Pathogenesis and management. *Ann Intern Med* 112:352–364.
- Lund B, Sorensen OH. 1979. Measurement of 25-hydroxyvitamin D in serum and its relation to sunshine, age and vitamin D intake in the Danish population. *Scand J Clin Lab Invest* 39:23–30.
- Luoma H, Aromaa A, Helminen S, Murtomaa H, Kiviluoto L, Punstar S, Knekt P. 1983. Risk of myocardial infarction in Finnish men in relation to fluoride, magnesium and calcium concentration in drinking water. *Acta Med Scand* 213:171–176.
- Lutwak L, Lester L, Gitelman HJ, Fox M, Whedon GD. 1964. Effects of high dietary calcium and phosphorus on calcium, phosphorus, nitrogen and fat metabolism in children. *Am J Clin Nutr* 14:76–82.

- Ma J, Folsom AR, Melnick SL, Eckfeldt JH, Sharrett AR, Nabulsi AA, Hutchinson RG, Metcalf PA. 1995. Associations of serum and dietary magnesium with cardiovascular disease, hypertension, diabetes, insulin, and carotid arterial wall thickness: The ARIC study. *Atherosclerosis Risk in Community Study. J Clin Epidemiol* 48:927–940.
- MacLaughlin J, Holick MF. 1985. Aging decreases the capacity of human skin to produce vitamin D<sub>3</sub>. *J Clin Invest* 76:1536–1538.
- MacLaughlin JA, Anderson RR, Holick MF. 1982. Spectral character of sunlight modulates photosynthesis of previtamin D<sub>3</sub> and its photoisomers in human skin. *Science* 216:1001–1003.
- Maguire ME. 1984. Hormone-sensitive magnesium transport and magnesium regulation of adenylate cyclase. *Trends Pharmacol Sci* 5:73–77.
- Mahalko JR, Sandstead HH, Johnson LK, Milne DB. 1983. Effect of a moderate increase in dietary protein on the retention and excretion of Ca, Cu, Fe, Mg, P, and Zn by adult males. *Am J Clin Nutr* 37:8–14.
- Maheshwari UR, McDonald JT, Schneider VS, Brunetti AJ, Leybin L, Newbrun E, Hodge HC. 1981. Fluoride balance studies in ambulatory healthy men with and without fluoride supplements. *Am J Clin Nutr* 34:2679–2684.
- Maheshwari UR, King JC, Leybin L, Newbrun E, Hodge HC. 1983. Fluoride balances during early and late pregnancy. *J Occup Med* 25:587–590.
- Mallet E, Gugi B, Brunelle P, Henocq A, Basuyau JP, Lemeur H. 1986. Vitamin D supplementation in pregnancy: A controlled trial of two methods. *Obstet Gynecol* 68:300–304.
- Malm OJ. 1958. Calcium requirement and adaptation in adult men. *Scand J Clin Lab Invest* 10(Suppl 36):1–280.
- Malone DNS, Horn DB. 1971. Acute hypercalcemia and renal failure after antacid therapy. *Br Med J* 1:709–710.
- Manz F. 1992. Why is the phosphorus content of human milk exceptionally low? *Monatsschr Kinderheilkd* 140:S35–S39.
- Marcus R, Cann C, Madvig P, Minkoff J, Goddard M, Bayer M, Martin M, Gaudiani L, Haskell W, Genant H. 1985. Menstrual function and bone mass in elite women distance runners. Endocrine and metabolic features. *Ann Intern Med* 102:158–163.
- Margen S, Chu JY, Kaufmann NA, Calloway DH. 1974. Studies in calcium metabolism I. The calciuretic effect of dietary protein. *Am J Clin Nutr* 27:584–589.
- Margolis HC, Moreno EC. 1990. Physicochemical perspectives on the cariostatic mechanisms of systemic and topical fluorides. *J Dent Res* 69(Spec Iss):606–613.
- Marier JR. 1986. Magnesium content of the food supply in the modern-day world. *Magnesium* 5:1–8.
- Marken PA, Weart CW, Carson DS, Gums JG, Lopes-Virella MF. 1989. Effects of magnesium oxide on the lipid profile of healthy volunteers. *Atherosclerosis* 77:37–42.
- Markestad T, Elzouki AY. 1991. Vitamin-D deficiency rickets in northern Europe and Libya. In: Glorieux FH, ed. *Rickets: Nestle Nutrition Workshop Series, Vol 21*. New York, NY: Raven Press.
- Markestad T, Ulstein M, Bassoe HH, Aksnes L, Aarskog D. 1983. Vitamin D metabolism in normal and hypoparathyroid pregnancy and lactation. Case report. *Br J Obstet Gynaecol* 90:971–976.
- Markestad T, Ulstein M, Aksnes L, Aarskog D. 1986. Serum concentrations of vitamin D metabolites in vitamin D supplemented pregnant women. A longitudinal study. *Acta Obstet Gynecol Scand* 65:63–67.

- Marquis RE. 1995. Antimicrobial actions of fluoride for oral bacteria. *Can J Microbiol* 41:955–964.
- Marsh AG, Sanchez TV, Midkelsen O, Keiser J, Mayor G. 1980. Cortical bone density of adult lacto-ovo-vegetarian and omnivorous women. *J Am Diet Assoc* 76:148–151.
- Marshall DH, Nordin BEC, Speed R. 1976. Calcium, phosphorus and magnesium requirement. *Proc Nutr Soc* 35:163–173.
- Martin AD, Bailey DA, McKay HA. 1997. Bone mineral and calcium accretion during puberty. *Am J Clin Nutr* 66:611–615.
- Martin BJ. 1990. The magnesium load test: Experience in elderly subjects. *Aging (Milano)* 2:291–296.
- Martin TJ, Grill V. 1995. Hypercalcemia. *Clin Endocrinol* 42:535–538.
- Martinez ME, Salinas M, Miguel JL, Herrero E, Gomez P, Garcia J, Sanchez-Sicilia L, Montero A. 1985. Magnesium excretion in idiopathic hypercalciuria. *Nephron* 40: 446–450.
- Massey LK, Wise KJ. 1984. The effect of dietary caffeine on urinary excretion of calcium, magnesium, sodium and potassium in healthy young females. *Nutr Res* 4:43–50.
- Massey LK, Roman-Smith H, Sutton RA. 1993. Effect of dietary oxalate and calcium on urinary oxalate and risk of formation of calcium oxalate kidney stones. *J Am Diet Assoc* 93:901–906.
- Matkovic V. 1991. Calcium metabolism and calcium requirements during skeletal modeling and consolidation of bone mass. *Am J Clin Nutr* 54:245S–260S.
- Matkovic V, Heaney RP. 1992. Calcium balance during human growth: Evidence for threshold behavior. *Am J Clin Nutr* 55:992–996.
- Matkovic V, Fontana D, Tominac C, Goel P, Chesnut CH III. 1990. Factors that influence peak bone mass formation: A study of calcium balance and the inheritance of bone mass in adolescent females. *Am J Clin Nutr* 52:878–888.
- Matkovic V, Jelic T, Wardlaw GM, Illich JZ, Goel PK, Wright JK, Andon MB, Smith KT, Heaney RP. 1994. Timing of peak bone mass in Caucasian females and its implication for the prevention of osteoporosis. *J Clin Invest* 93:799–808.
- Matkovic V, Illich JZ, Andon MB, Hsieh LC, Tzagournis MA, Lagger BJ, Goel PK. 1995. Urinary calcium, sodium, and bone mass of young females. *Am J Clin Nutr* 62:417–425.
- Matsuda H. 1991. Magnesium gating of the inwardly rectifying K<sup>+</sup> channel. *Ann Rev Physiol* 53:289–298.
- Matsuoka LY, Ide L, Wortsman J, MacLaughlin JA, Holick MF. 1987. Sunscreens suppress cutaneous vitamin D<sub>3</sub> synthesis. *J Clin Endocrinol Metab* 64:1165–1168.
- Matsuoka LY, Wortsman J, Dannenberg MJ, Hollis BW, Lu Z, Holick MF. 1992. Clothing prevents ultraviolet-B radiation-dependent photosynthesis of vitamin D<sub>3</sub>. *J Clin Endocrinol Metab* 75:1099–1103.
- Mawer EB, Schaefer K, Lumb GA, Stanbury SW. 1971. The metabolism of isotopically labelled vitamin D<sub>3</sub> in man: The influence of the state of vitamin D nutrition. *Clin Sci* 40:39–53.
- Mawer EB, Backhouse J, Holman CA, Lumb GA, Stanbury DW. 1972. The distribution and storage of vitamin D and its metabolites in human tissues. *Clin Sci* 43:413–431.
- Mazariegos-Ramos E, Guerrero-Romero F, Rodriguez-Moran M, Lazcano-Burciaga G, Paniagua R, Amato D. 1995. Consumption of soft drinks with phosphoric acid as a risk factor for the development of hypocalcemia in children: A case-control study. *J Pediatr* 126:940–942.

- McCarron DA. 1983. Calcium and magnesium nutrition in human hypertension. *Ann Int Med* 98:800–805.
- McCarron DA, Morris CD. 1985. Blood pressure response to oral calcium in persons with mild to moderate hypertension: A randomized, double-blind, placebo-controlled, crossover trial. *Ann Intern Med* 103:825–831.
- McCarron DA, Morris CD, Young E, Roullet C, Drüeke T. 1991. Dietary calcium and blood pressure: Modifying factors in specific populations. *Am J Clin Nutr* 54:215S–219S.
- McCauley HB, McClure FJ. 1954. Effect of fluoride in drinking water on the osseous development of the hand and wrist in children. *Pub Hlth Rep* 69:671–683.
- McClure FJ. 1943. Ingestion of fluoride and dental caries. Quantitative relations based on food and water requirements of children one to twelve years old. *Am J Dis Child* 66:362–369.
- McClure FJ, Zipkin I. 1958. Physiologic effects of fluoride as related to water fluoridation. *Dent Clin North Am* 2:441–458.
- McCrory WW, Forman CW, McNamara H, Barnett HL. 1950. Renal excretion of phosphate in newborn infants: Observations in normal infants and in infants with hypocalcemic tetany. *Am J Dis Child* 80:512–513.
- McFarlane D. 1941. Experimental phosphate nephritis in the rat. *J Pathol* 52:17–24.
- McGrath N, Singh V, Cundy T. 1993. Severe vitamin D deficiency in Auckland. *N Zel Med J* 106:524–526.
- McKenna MJ. 1992. Differences in vitamin D status between countries in young adults and the elderly. *Am J Med* 93:69–77.
- McKnight-Hanes MC, Leverett DH, Adair SM, Shields CP. 1988. Fluoride content of infant formulas: Soy-based formulas as a potential factor in dental fluorosis. *Pediatr Dent* 10:189–194.
- Meier DE, Luckey MM, Wallenstein S, Clemens TL, Orwoll ES, Waslien CI. 1991. Calcium, vitamin D, and parathyroid hormone status in young white and black women: Association with racial differences in bone mass. *J Clin Endocrinol Metab* 72:703–710.
- Melton LJ III, Chrischilles EA, Cooper C, Lane AW, Riggs, BL. 1992. Perspective. How many women have osteoporosis? *J Bone Miner Res* 7:1005–1010.
- Melton LJ III, Atkinson EJ, O'Fallon WM, Wahner HW, Riggs BL. 1993a. Long-term fracture prediction by bone mineral assessed at different skeletal sites. *J Bone Miner Res* 8:1227–1233.
- Melton LJ III, Bryant SC, Wahner HW, O'Fallon WM, Malkasian GD, Judd HL, Riggs BL. 1993b. Influence of breastfeeding and other reproductive factors on bone mass later in life. *Osteopor Int* 3:76–83.
- Merke J, Klaus G, Hugel U, Waldherr R, Ritz E. 1986. No 1,25-dihydroxyvitamin D<sub>3</sub> receptors on osteoclasts of calcium-deficient chicken despite demonstrable receptors on circulating monocytes. *J Clin Invest* 77:312–314.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- Mertz W, Abernathy CO, Olin SS. 1994. *Risk Assessment of Essential Elements*. Washington, DC: ILSI Press.
- Meulmeester JF, vandenBerg H, Wedel M, Boshuis PG, Hulshof KF, Luyken R. 1990. Vitamin D status, parathyroid hormone and sunlight in Turkish, Moroccan and Caucasian children in The Netherlands. *Eur J Clin Nutr* 44:461–470.

- Meyer F, White E. 1993. Alcohol and nutrients in relation to colon cancer in middle-aged adults. *Am J Epidemiol* 138:225–236.
- Miller JZ, Smith DL, Flora L, Slemenda C, Jiang X, Johnston CC Jr. 1988. Calcium absorption from calcium carbonate and a new form of calcium (CCM) in healthy male and female adolescents. *Am J Clin Nutr* 48:1291–1294.
- Mimouni FB. 1996. The ion-selective magnesium electrode: A new tool for clinicians and investigators. *J Am Coll Nutr* 15:4–5.
- Mimouni F, Tsang RC, Hertzberg VS, Miodovnik M. 1986. Polycythemia hypomagnesemia and hypocalcemia infants of diabetic mothers. *Am J Dis Child* 140:798–800.
- Mimouni F, Campaigne B, Neylan M, Tsang RC. 1993. Bone mineralization in the first year of life in infants fed human milk, cow-milk formula, or soy-based formula. *J Pediatr* 122:348–354.
- Moncrief MW, Chance GW. 1969. Nephrotoxic effect of vitamin D therapy in vitamin D refractory rickets. *Arch Dis Child* 44:571–579.
- Montaldo MB, Benson JD. 1986. Nutrient intakes of older infants: Effect of different milk feedings. *J Am Coll Nutr* 5:331–341.
- Mordes JP, Wacker WEC. 1978. Excessive magnesium. *Pharmacol Rev* 29:273–300.
- Moser PB, Issa CF, Reynolds RD. 1983. Dietary magnesium intake and the concentration of magnesium in plasma and erythrocytes of postpartum women. *J Am Coll Nutr* 2:387–396.
- Moser PB, Reynolds RD, Acharya S, Howard MP, Andon MB. 1988. Calcium and magnesium dietary intakes and plasma and milk concentrations of Nepalese lactating women. *Am J Clin Nutr* 47:735–739.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance data from vital and health statistics, No. 174. Hyattsville, MD: National Center for Health Statistics.
- Motoyama T, Sano H, Fukuzaki H. 1989. Oral magnesium supplementation in patients with essential hypertension. *Hypertension* 13:227–232.
- Mountokalakis TD. 1987. Effects of aging, chronic disease, and multiple supplements on magnesium requirements. *Magnesium* 6:5–11.
- Moya M, Cortes E, Ballester MI, Vento M, Juste M. 1992. Short-term polycose substitution for lactose reduces calcium absorption in healthy term babies. *J Pediatr Gastroenterol Nutr* 14:57–61.
- Muhler JC. 1970. Ingestion from foods. In: Adler P, ed. *Fluorides and Human Health*. Monograph series no. 59. Geneva: World Health Organization. Pp. 32–40.
- Muldowney WP, Mazbar SA. 1996. Rolaids-yogurt syndrome: A 1990s version of milk-alkali syndrome. *Am J Kidney Dis* 27:270–272.
- Murphy SP, Calloway DH. 1986. Nutrient intakes of women in NHANES II, emphasizing trace minerals, fiber, and phytate. *J Am Diet Assoc* 86:1366–1372.
- Naccache H, Simard PL, Trahan L, Demers M, Lapointe C, Brodeur JM. 1990. Variability in the ingestion of toothpaste by preschool children. *Caries Res* 24:359–363.
- Naccache H, Simard PL, Trahan L, Brodeur JM, Demers M, Lachapelle D, Bernard PM. 1992. Factors affecting the ingestion of fluoride dentifrice by children. *J Pub Hlth Dent* 52:222–226.
- Nadler JL, Malayan S, Luong H, Shaw S, Natarajan RD, Rude RK. 1992. Intracellular free magnesium deficiency plays a key role in increased platelet reactivity in type II diabetes mellitus. *Diabetes Care* 15:835–841.

- Nadler JL, Buchanan T, Natarajan R, Antonipillai I, Bergman R, Rude RK. 1993. Magnesium deficiency produces insulin resistance and increased thromboxane synthesis. *Hypertension* 21:1024–1029.
- Nagubandi S, Kumar R, Londowski JM, Corradino RA, Tietz PS. 1980. Role of vitamin D glucosiduronate in calcium homeostasis. *J Clin Invest* 66:1274–1280.
- Nagy L, Tarnok F, Past T, Mozsik GY, Deak G, Tapsonyi Z, Fendler K, Javor T. 1988. Human tolerability and pharmacodynamic study of TISACID tablet in duodenal ulcer patients. A prospective, randomized, self-controlled clinico-pharmacological study. *Acta Medica Hung* 45:231–246.
- Nakamura T, Turner CH, Yoshikawa T, Slemenda CW, Peacock M, Burr DB, Mizuno Y, Orimo H, Ouchi Y, Johnston CC Jr. 1994. Do variations in hip geometry explain differences in hip fracture risk between Japanese and white Americans? *J Bone Miner Res* 9:1071–1076.
- Nakao H. 1988. Nutritional significance of human milk vitamin D in neonatal period. *Kobe J Med Sci* 34:121–128.
- Narang NK, Gupta RC, Jain MK. 1984. Role of vitamin D in pulmonary tuberculosis. *J Assoc Physicians India* 32:185–188.
- National Council for Nutrition (Conseil National de la Nutrition). 1994. *Recommendations nutritionnelles pour la Belgique*. Bruxelles, Belgium: Ministère des Affaires Sociales de la Santé Publique et de l’Environnement.
- National Food Administration. 1989. *Swedish Nutrition Recommendations, 2nd edition*. Uppsala, Sweden: National Food Administration.
- Need AG, Morris HA, Horowitz M, Nordin C. 1993. Effects of skin thickness, age, body fat, and sunlight on serum 25-hydroxyvitamin D. *Am J Clin Nutr* 58:882–885.
- Neri LC, Johansen HL. 1978. Water hardness and cardiovascular mortality. *Ann NY Acad Sci* 304:203–219.
- Neri LC, Johansen HL, Hewitt D, Marier J, Langner N. 1985. Magnesium and certain other elements and cardiovascular disease. *Sci Total Environ* 42:49–75.
- Netherlands Food and Nutrition Council. 1992. *Report on the Age Limit to be Adopted in Connection with “Guidelines for a Healthy Diet.”* The Hague: Netherlands Food and Nutrition Council.
- Neville MC, Keller R, Seacat J, Lutes V, Neifert M, Casey C, Allen J, Archer P. 1988. Studies in human lactation: Milk volumes in lactating women during the onset of lactation and full lactation. *Am J Clin Nutr* 48:1375–1386.
- Newmark K, Nugent P. 1993. Milk-alkali syndrome: A consequence of chronic antacid abuse. *Postgrad Med* 93:149–156.
- Ng K, St John A, Bruce DG. 1994. Secondary hyperparathyroidism, vitamin D deficiency and hip fracture: Importance of sampling times after fracture. *Bone Miner* 25:103–109.
- Niekamp RA, Baer JT. 1995. In-season dietary adequacy of trained male cross-country runners. *Int J Sport Nutr* 5:45–55.
- Nielsen FH. 1990. Studies on the relationship between boron and magnesium which possibly affects the formation and maintenance of bones. *Magnes Trace Elem* 9:61–69.
- Nielsen FH, Hunt CD, Mullen LM, Hunt JR. 1987. Effect of dietary boron on mineral, estrogen, and testosterone metabolism in postmenopausal women. *FASEB J* 1:394–397.
- Nieves JW, Golden AL, Siris E, Kelsey JL, Lindsay R. 1995. Teenage and current calcium intake are related to bone mineral density of the hip and forearm in women aged 30–39 years. *Am J Epidemiol* 141:342–351.

- NIH (National Institutes of Health). 1994. *Optimal Calcium Intake*. NIH Consensus Statement 12:4. Bethesda, MD: NIH.
- NIN (National Institute of Nutrition). 1995. Dairy products in the Canadian diet. NIN Review No. 24. Ontario, Canada: NIN.
- Nordin BEC. 1976. *Calcium, Phosphate and Magnesium Metabolism*. Edinburgh: Churchill Livingstone.
- Nordin BEC. 1989. Phosphorus. *J Food Nutr* 45:62–75.
- Nordin BEC, Polley KJ. 1987. Metabolic consequences of the menopause. A cross-sectional, longitudinal, and intervention study on 557 normal postmenopausal women. *Calcif Tissue Int* 41:S1–S59.
- Nose O, Iida Y, Kai H, Harada T, Ogawa M, Yabuuchi H. 1979. Breath hydrogen test for detecting lactose malabsorption in infants and children: Prevalence of lactose malabsorption in Japanese children and adults. *Arch Dis Child* 54:436–440.
- NRC (National Research Council). 1980. *Recommended Dietary Allowances, 9th Edition*. Committee on Dietary Allowances, Food and Nutrition Board. Washington, DC: National Academy Press.
- NRC (National Research Council). 1982. *Diet, Nutrition, and Cancer*. Report of the Committee on Diet, Nutrition, and Cancer, Assembly of Life Sciences. Washington, DC: National Academy Press.
- NRC (National Research Council). 1983. *Risk Assessment in the Federal Government: Managing the Process*. Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC (National Research Council). 1989a. *Recommended Dietary Allowances: 10th Edition*. Report of the Subcommittee on the Tenth Edition of the RDAs, Food and Nutrition Board, and the Commission on Life Sciences. Washington, DC: National Academy Press.
- NRC (National Research Council). 1989b. *Diet and Health: Implications for Reducing Chronic Disease Risk*. Report of the Committee on Diet and Health, Food and Nutrition Board, Commission on Life Sciences. Washington, DC: National Academy Press.
- NRC (National Research Council). 1993. *Health Effects of Ingested Fluoride*. Subcommittee on Health Effects of Ingested Fluoride. Washington, DC: National Academy Press.
- NRC (National Research Council). 1994. *Science and Judgment in Risk Assessment. Committee on Risk Assessment of Hazardous Air Pollutants*. Board on Environmental Studies and Toxicology. Washington, DC: National Academy Press.
- NRC (National Research Council). 1995. *Nutrient Requirements of Laboratory Animals*. Committee on Animal Nutrition, Board on Agriculture. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- O'Brien KO, Abrams SA, Stuff JE, Liang LK, Welch TR. 1996. Variables related to urinary calcium excretion in young girls. *J Pediatr Gastroenterol Nutr* 23:8–12.
- O'Dowd KJ, Clemens TL, Kelsey JL, Lindsay R. 1993. Exogenous calciferol (vitamin D) and vitamin D endocrine status among elderly nursing home residents in the New York City area. *J Am Geriatr Soc* 41:414–421.

- Ohlson MA, Brewer WD, Jackson L, Swanson PP, Roberts PH, Mangel M, Leverton RM, Chaloupka M, Gram MR, Reynolds MS, Lutz R. 1952. Intakes and retentions of nitrogen, calcium and phosphorus by 136 women between 30 and 85 years of age. *Fed Proc* 11:775–783.
- Oliveri MB, Ladizesky M, Mautalen CA, Alonso A, Martinez L. 1993. Seasonal variations of 25 hydroxyvitamin D and parathyroid hormone in Ushuaia (Argentina), the southernmost city in the world. *Bone Miner* 20:99–108.
- Ooms ME, Roos JC, Bezemer PD, VanDerVijgh WJ, Bouter LM, Lips P. 1995. Prevention of bone loss by vitamin D supplementation in elderly women: A randomized double-blind trial. *J Clin Endocrinol Metab* 80:1052–1058.
- Ophaug RH, Singer L, Harland BF. 1980a. Estimated fluoride intake of 6-month-old infants in four dietary regions of the United States. *Am J Clin Nutr* 33:324–327.
- Ophaug RH, Singer L, Harland BF. 1980b. Estimated fluoride intake of average two-year-old children in four dietary regions of the United States. *J Dent Res* 59:777–781.
- Ophaug RH, Singer L, Harland BF. 1985. Dietary fluoride intake of 6-month and 2-year-old children in four dietary regions of the United States. *Am J Clin Nutr* 42:701–707.
- Orimo H, Ouchi Y. 1990. The role of calcium and magnesium in the development of atherosclerosis. Experimental and clinical evidence. *Ann NY Acad Sci* 598:444–457.
- Orwoll ES. 1982. The milk-alkali syndrome: Current concepts. *Ann Intern Med* 97:242–248.
- Orwoll ES, Oviatt SK, McClung MR, Deftos LJ, Sexton G. 1990. The rate of bone mineral loss in normal men and the effects of calcium and cholecalciferol supplementation. *Ann Intern Med* 112:29–34.
- Osis D, Kramer L, Wiatrowski E, Spencer H. 1974. Dietary fluoride intake in man. *J Nutr* 104:1313–1318.
- Osteoporosis Society of Canada. 1993. Consensus on calcium nutrition. Official position of the Osteoporosis Society of Canada. *Nutr Quart* 18:62–69.
- Osuji OO, Leake JL, Chipman ML, Nikiforuk G, Locker D, Levine N. 1988. Risk factors for dental fluorosis in a fluoridated community. *J Dent Res* 67:1488–1492.
- OTA (Office of Technology Assessment). 1993. *Researching Health Risks*. Washington, DC: Office of Technology Assessment.
- Outhouse J, Kinsman G, Sheldon D, Tworney I, Smith J. 1939. The calcium requirements of five pre-school girls. *J Nutr* 17:199–211.
- Outhouse J, Breiter H, Rutherford E, Dwight J, Mills R, Armstrong W. 1941. The calcium requirement of man: Balance studies on seven adults. *J Nutr* 21:565–575.
- Paganini-Hill A, Chao A, Ross RK, Henderson BE. 1991. Exercise and other factors in the prevention of hip fracture: The Leisure World Study. *Epidemiology* 2:16–25.
- Pak CY. 1988. Medical management of nephrolithiasis in Dallas: Update 1987. *J Urol* 140:461–467.
- Pak CY, Sakhaei K, Rubin CD, Zerwekh JE. 1997. Sustained-release sodium fluoride in the management of established menopausal osteoporosis. *Am J Med Sci* 313:23–32.
- Pang DT, Phillips CL, Bawden JW. 1992. Fluoride intake from beverage consumption in a sample of North Carolina children. *J Dent Res* 71:1382–1388.

- Paolisso G, Passariello N, Pizza G, Marrazzo G, Giunta R, Sgambato S, Varricchio M, D'Onofrio F. 1989. Dietary magnesium supplements improve B-cell response to glucose and arginine in elderly non-insulin-dependent diabetic subjects. *Acta Endocrinol Copenh* 121:16–20.
- Paolisso G, Scheen A, D'Onofrio FD, Lefebvre P. 1990. Magnesium and glucose homeostasis. *Diabetologia* 33:511–514.
- Paolisso G, Sgambato S, Gambardella A, Pizza G, Tesauro P, Varricchio M, D'Onofrio F. 1992. Daily magnesium supplements improve glucose handling in elderly subjects. *Am J Clin Nutr* 55:1161–1167.
- Parfitt AM. 1977. Metacarpal cortical dimensions in hypoparathyroidism, primary hyperparathyroidism and chronic renal failure. *Calcif Tiss Res Suppl* 22:329–331.
- Parfitt AM. 1988. Bone remodeling: Relationship to the amount and structure of bone, and the pathogenesis and prevention of fractures. In: Riggs BL, Melton LJ III eds. *Osteoporosis: Etiology, Diagnosis, and Management*. New York, NY: Raven Press.
- Parfitt AM, Higgins BA, Nassim JR, Collins JA, Hilb A. 1964. Metabolic studies in patients with hypercalciuria. *Clin Sci* 27:463–482.
- Parfitt AM, Chir B, Gallagher JC, Heaney RP, Johnston CC, Neer R, Whedon GD. 1982. Vitamin D and bone health in the elderly. *Am J Clin Nutr* 36:1014–1031.
- Paunier L, Lacourt G, Pilloud P, Schlaeppi P, Sizomenko PC. 1978. 25-hydroxyvitamin D and calcium levels in maternal, cord and infant serum in relation to maternal vitamin D intake. *Helv Paediatr Acta* 33:95–103.
- Peace H, Beattie JH. 1991. No effect of boron on bone mineral excretion and plasma sex steroid levels in healthy postmenopausal women. Monography, proceedings, roundtables, and discussions of the Seventh International Symposium on Trace Elements in Man and Animals, held May 20–25, 1990, in Dubrovnik, Croatia, Yugoslavia.
- Peacock M. 1991. Calcium absorption efficiency and calcium requirements in children and adolescents. *Am J Clin Nutr* 54:261S–265S.
- Pedersen AB, Bartholomew MJ, Dolence LA, Aljadir LP, Netteburg KL, Lloyd T. 1991. Menstrual differences due to vegetarian and nonvegetarian diets. *Am J Clin Nutr* 53:879–885.
- Pendrys DG, Katz RV. 1989. Risk of enamel fluorosis associated with fluoride supplementation, infant formula, and fluoride dentifrice use. *Am J Epidemiol* 130:1199–1208.
- Pendrys DG, Morse DE. 1990. Use of fluoride supplementation by children living in fluoridated communities. *J Dent Child* 57:343–347.
- Pendrys DG, Stamm JW. 1990. Relationship of total fluoride intake to beneficial effects and enamel fluorosis. *J Dent Res* 69(Spec Iss):529–538.
- Peng SK, Taylor CB. 1980. Editorial: Probable role of excesses of vitamin D in genesis of arteriosclerosis. *Arterial Wall* 6:63–68.
- Peng SK, Taylor CB, Tham P, Mikkelsen B. 1978. Role of mild excesses of vitamin D in arteriosclerosis. A study in squirrel monkeys. *Arterial Wall* 4:229.
- Pennington JA. 1994. *Bowes and Church's Food Values of Portions Commonly Used*. Philadelphia, PA: JB Lippincott.
- Pennington JA, Wilson DB. 1990. Daily intakes of nine nutritional elements: Analyzed vs. calculated values. *J Am Diet Assoc* 90:375–381.
- Pennington JA, Young BE. 1991. Total diet study nutritional elements, 1982–1989. *J Am Diet Assoc* 91:179–183.

- Perloff BP, Rizek RL, Haytowitz DB, Reid PR. 1990. Dietary intake methodology. II. USDA's Nutrient Data Base for Nationwide Dietary Intake Surveys. *J Nutr* 120:1530–1534.
- Petley A, Macklin B, Renwick AG, Wilkin TJ. 1995. The pharmacokinetics of niacinamide in humans and rodents. *Diabetes* 44:152–155.
- Pett LB, Ogilvie GH. 1956. The Canadian Weight-Height Survey. *Hum Biol* 28:177–188.
- Pettifor JM, Ross FP, Moodley G, Wang J, Marco G, Skjolde C. 1978a. Serum calcium, magnesium, phosphorus, alkaline phosphatase and 25-hydroxyvitamin D concentrations in children. *S Afr Med J* 53:751–754.
- Pettifor JM, Ross P, Wang J, Moodley G, Couper-Smith J. 1978b. Rickets in children of rural origin in South Africa: Is low dietary calcium a factor? *J Pediatr* 92:320–324.
- Pettifor JM, Bikle DD, Cavaleros M, Zachen D, Kamdar MC, Ross FP. 1995. Serum levels of free 1,25-dihydroxyvitamin D in vitamin D toxicity. *Ann Intern Med* 122:511–513.
- Pietschmann P, Woloszczuk W, Pietschmann H. 1990. Increased serum osteocalcin levels in elderly females with vitamin D deficiency. *Exp Clin Endocrinol* 95:275–278.
- Pillai S, Bikle DD, Elias PM. 1987. 1,25-Dihydroxyvitamin D production and receptor binding in human keratinocytes varies with differentiation. *J Biol Chem* 263:5390–5395.
- Pitkin RM, Reynolds WA, Williams GA, Hargis GK. 1979. Calcium metabolism in normal pregnancy: A longitudinal study. *Am J Obstet Gynecol* 133:781–787.
- Pittard WB III, Geddes KM, Sutherland SE, Miller MC, Hollis BW. 1990. Longitudinal changes in the bone mineral content of term and premature infants. *Am J Dis Child* 144:36–40.
- Pluckebaum JM, Chavez N. 1994. Nutritional status of Northwest Indiana Hispanics in a congregate meal program. *J Nutr Elderly* 13:1–22.
- PNUN (Standing Nordic Committee on Food). 1989. *Nordic Nutrition Recommendations*, 2nd Edition. Oslo: Nordic Council of Ministers.
- Ponder SW, McCormick DP, Fawcett HD, Palmer JL, McKernan MG, Brouhard BH. 1990. Spinal bone mineral density in children aged 5.00 through 11.99 years. *Am J Dis Child* 144:1346–1348.
- Ponz de Leon M, Roncucci L, Di Donato P, Tassi L, Smerieri O, Amorico MG, Malagoli G, De Maria D, Antonioli A, Chahin NJ. 1988. Pattern of epithelial cell proliferation in colorectal mucosa of normal subjects and of patients with adenomatous polyps or cancer of the large bowel. *Cancer Res* 48:4121–4126.
- Portale AA, Booth BE, Halloran BP, Morris RC Jr. 1984. Effect of dietary phosphorus on circulating concentrations of 1,25-dihydroxyvitamin D and immunoreactive parathyroid hormone in children with moderate renal insufficiency. *J Clin Invest* 73:1580–1589.
- Portale AA, Halloran BP, Murphy MM, Morris RC. 1986. Oral intake of phosphorus can determine the serum concentration of 1,25-dihydroxyvitamin D by determining its production rate in humans. *J Clin Invest* 77:7–12.
- Portale AA, Halloran BP, Morris RC Jr. 1987. Dietary intake of phosphorus modulates the circadian rhythm in serum concentration of phosphorus. Implications for the renal production of 1,25-dihydroxyvitamin D. *J Clin Invest* 80:1147–1154.

- Portale AA, Halloran BP, Morris RC Jr. 1989. Physiologic regulation of the serum concentration of 1,25-dihydroxyvitamin D by phosphorus in normal men. *J Clin Invest* 83:1494–1499.
- Prentice A, Laskey MA, Shaw J, Cole TJ, Fraser DR. 1990. Bone mineral content of Gambian and British children aged 0–36 months. *Bone Miner* 10:211–214.
- Prentice A, Jarjou LM, Cole TJ, Stirling DM, Dibba B, Fairweather-Tait S. 1995. Calcium requirements of lactating Gambian mothers: Effects of a calcium supplement on breast-milk calcium concentration, maternal bone mineral content, and urinary calcium excretion. *Am J Clin Nutr* 62:58–67.
- Prichard JL. 1969. The prenatal and postnatal effects of fluoride supplements on West Australian school children, aged 6, 7 and 8, Perth, 1967. *Austral Dent J* 14:335–338.
- Prince RL, Smith M, Dick IM, Price RI, Webb PG, Henderson NK, Harris MM. 1991. Prevention of postmenopausal osteoporosis. A comparative study of exercise, calcium supplementation, and hormone-replacement therapy. *N Engl J Med* 325:1189–1195.
- Prince R, Devine A, Dick I, Criddle A, Kerr D, Kent N, Price R, Randell A. 1995. The effects of calcium supplementation (milk powder or tablets) and exercise on bone density in postmenopausal women. *J Bone Miner Res* 10:1068–1075.
- Purdie DW, Aaron JE, Selby PL. 1988. Bone histology and mineral homeostasis in human pregnancy. *Br J Obstet Gynecol* 95:849–854.
- Quamme GA. 1989. Control of magnesium transport in the thick ascending limb. *Am J Physiol* 256:F197–F210.
- Quamme GA. 1993. Laboratory evaluation of magnesium status. Renal function and free intracellular magnesium concentration. *Clin Lab Med* 13:209–223.
- Quamme GA, Dirks JH. 1986. The physiology of renal magnesium handling. *Renal Physiol* 9:257–269.
- Raisz LG, Niemann I. 1969. Effect of phosphate, calcium and magnesium on bone resorption and hormonal responses in tissue culture. *Endocrinology* 85:446–452.
- Rajalakshmi K, Srikantia SG. 1980. Copper, zinc, and magnesium content of breast milk of Indian women. *Am J Clin Nutr* 33:664–669.
- Raman L, Rajalakshmi K, Krishnamachari KA, Sastry JG. 1978. Effect of calcium supplementation to undernourished mothers during pregnancy on the bone density of the neonates. *Am J Clin Nutr* 31:466–469.
- Randall RE, Cohen D, Spray CC, Rossmeisl EC. 1964. Hypermagnesemia in renal failure. *Ann Intern Med* 61:73–88.
- Rao DR, Bello H, Warren AP, Brown GE. 1994. Prevalence of lactose maldigestion. Influence and interaction of age, race, and sex. *Dig Dis Sci* 39:1519–1524.
- Rasmussen HS, McNair P, Goransson L, Balslev S, Larsen OG, Aurup P. 1988. Magnesium deficiency in patients with ischemic heart disease with and without acute myocardial infarction uncovered by an intravenous loading test. *Arch Intern Med* 148:329–332.
- Ray NF, Chan JK, Thamer M, Melton LJ III. 1997. Medical expenditures for the treatment of osteoporotic fractures in the United States in 1995: Report from the National Osteoporosis Foundation. *J Bone Miner Res* 12:24–35.
- Reasner CA II, Dunn JF, Fetchick DA, Liel Y, Hollis BW, Epstein S, Shary J, Mundy GR, Bell NH. 1990. Alteration of vitamin D metabolism in Mexican-Americans. *J Bone Miner Res* 5:13–17.
- Recker RR. 1985. Calcium absorption and achlorhydria. *N Engl J Med* 313:70–73.

- Recker RR, Hassing GS, Lau JR, Saville PD. 1973. The hyperphosphatemic effect of disodium ethane-1-hydroxy-1, 1-diphosphonate (EHDP): Renal handling of phosphorus and the renal response to parathyroid hormone. *J Lab Clin Med* 81:258–266.
- Recker RR, Davies KM, Hinders SM, Heaney RP, Stegman MR, Kimmel DB. 1992. Bone gain in young adult women. *J Am Med Assoc* 268:2403–2408.
- Recker RR, Hinders S, Davies KM, Heaney RP, Stegman MR, Lappe JM, Kimmel DB. 1996. Correcting calcium nutritional deficiency prevents spine fractures in elderly women. *J Bone Miner Res* 11:1961–1966.
- Reddy GS, Norman AW, Willis DM, Goltzman D, Guyda H, Solomon S, Philips DR, Bishop JE, Mayer E. 1983. Regulation of vitamin D metabolism in normal human pregnancy. *J Clin Endocrinol Metab* 56:363–370.
- Reed A, Haugen M, Pachman LM, Langman CB. 1990. Abnormalities in serum osteocalcin values in children with chronic rheumatic diseases. *J Pediatr* 116:574–580.
- Reed JA, Anderson JJ, Tylavsky FA, Gallagher PN Jr. 1994. Comparative changes in radial-bone density of elderly female lacto-ovovegetarians and omnivores. *Am J Clin Nutr* 59:1197S–1202S.
- Reginster JY, Strause L, Deroisy R, Lecart MP, Saltman P, Franchimont P. 1989. Preliminary report of decreased serum magnesium in postmenopausal osteoporosis. *Magnesium* 8:106–109.
- Reichel H, Koeffler HP, Norman AW. 1989. The role of vitamin D endocrine system in health and disease. *N Engl J Med* 320:980–991.
- Reid IR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. 1995. Long-term effects of calcium supplementation on bone loss and fractures in postmenopausal women: A randomized controlled trial. *Am J Med* 98:331–335.
- Reinhart RA. 1988. Magnesium metabolism. A review with special reference to the relationship between intracellular content and serum levels. *Arch Intern Med* 148:2415–2420.
- Reinhold JG, Fardadji B, Abadi P, Ismail-Beigi F. 1991. Decreased absorption of calcium, magnesium, zinc and phosphorus by humans due to increased fiber and phosphorus consumption as wheat bread. *Am J Clin Nutr* 49:204–206.
- Resnick LM, Gupta RK, Laragh JH. 1984. Intracellular free magnesium in erythrocytes of essential hypertension: Relation to blood pressure and serum divalent cations. *Proc Natl Acad Sci USA* 81:6511–6515.
- Resnick L, Gupta R, and Bhargava KK, Gruenspan H, Alderman MH, Laragh JH. 1991. Cellular ions in hypertension, diabetes and obesity: A nuclear magnetic resonance spectroscopic study. *Hypertension* 17:951–957.
- Riancho JA, delArco C, Arteaga R, Herranz JL, Albajar M, Macias JG. 1989. Influence of solar irradiation on vitamin D levels in children on anticonvulsant drugs. *Acta Neurol Scand* 79:296–299.
- Ricci JM, Hariharan S, Helfott A, Reed K, O'Sullivan MJ. 1991. Oral tocolysis with magnesium chloride: A randomized controlled prospective clinical trial. *Am J Obstet Gynecol* 165:603–610.
- Richards A, Mosekilde L, Søgaard CH. 1994. Normal age-related changes in fluoride content of vertebral trabecular bone—relation to bone quality. *Bone* 15:21–26.
- Riggs BL, Melton LJ III. 1995. The worldwide problem of osteoporosis: Insights afforded by epidemiology. *Bone* 17:505S–511S.

- Riggs BL, O'Fallon WM, Muse J, O'Conner MK, Melton LJ III. 1996. Long-term effects of calcium supplementation on serum PTH, bone turnover, and bone loss in elderly women. *J Bone Miner Res* 11:S118.
- Rigo J, Salle BL, Picaud JC, Putet G, Senterre J. 1995. Nutritional evaluation of protein hydrolysate formulas. *Eur J Clin Nutr* 49:S26–S38.
- Riis B, Thomsen K, Christiansen C. 1987. Does calcium supplementation prevent postmenopausal bone loss? *N Engl J Med* 316:173–177.
- Ritz E. 1982. Acute hypophosphatemia. *Kidney Int* 22:84–94.
- Rizzoli R, Stoermann C, Ammann P, Bonjour J-P. 1994. Hypercalcemia and hyperosteolysis in vitamin D intoxication: Effects of clodronate therapy. *Bone* 15:193–198.
- Robertson, WG. 1985. Dietary factors important in calcium stone formation. In: Schwillie PO, Smith LH, Robertson WG, Vahlensieck W, eds. *Urolithiasis and Related Clinical Research*. New York: Plenum Press. Pp. 61–68.
- Romani A, Marfella C, Scarpa A. 1993. Cell magnesium transport and homeostasis: Role of intracellular compartments. *Miner Electrolyte Metab* 19:282–289.
- Roncucci L, Scalmati A, Ponz de Leon M. 1991. Pattern of cell kinetics in colorectal mucosa of patients with different types of adenomatous polyps of the large bowel. *Cancer* 68:873–878.
- Ronis DL, Lang WP, Farghaly MM, Passow E. 1993. Tooth brushing, flossing, and preventive dental visits by Detroit-area residents in relation to demographic and socioeconomic factors. *J Pub Hlth Dent* 53:138–145.
- Rosado JL, Lopez P, Morales M, Munoz E, Allen LH. 1992. Bioavailability of energy, nitrogen, fat, zinc, iron and calcium from rural and urban Mexican diets. *Br J Nutr* 68:45–58.
- Rowe JW, Minaker KL, Pallotta JA, Flier JS. 1983. Characterization of the insulin resistance of aging. *J Clin Invest* 71:1581–1587.
- Rubenowitz E, Axelsson G, Rylander R. 1996. Magnesium in drinking water and death from acute myocardial infarction. *Am J Epidemiol* 143:456–462.
- Rubin H. 1975. Central role for magnesium in coordinate control of metabolism and growth in animal cells. *Proc Natl Acad Sci USA* 72:3551–3555.
- Rude RK. 1993. Magnesium metabolism and deficiency. *Endocrinol Metab Clin North Am* 22:377–395.
- Rude RK, Olerich M. 1996. Magnesium deficiency: Possible role in osteoporosis associated with gluten-sensitive enteropathy. *Osteopor Int* 6:453–461.
- Rude RK, Singer FR. 1980. Magnesium deficiency and excess. *Ann Rev Med* 32:245–259.
- Rude RK, Oldham SB, Singer FR. 1976. Functional hypoparathyroidism and parathyroid hormone end-organ resistance in human magnesium deficiency. *Clin Endocrinol* 5:209–224.
- Rude RK, Bethune JE, Singer FR. 1980. Renal tubular maximum for magnesium in normal, hyperparathyroid and hypoparathyroid man. *J Clin Endocrinol Metab* 51:1425–1431.
- Rude RK, Manoogian C, Ehrlich L, DeRusso P, Ryzen E, Nadler J. 1989. Mechanisms of blood pressure regulation by magnesium in man. *Magnesium* 8:266–278.
- Rude RK, Stephen A, Nadler J. 1991. Determination of red blood cell intracellular free magnesium by nuclear magnetic resonance as an assessment of magnesium depletion. *Magnes Trace Elem* 10:117–121.

- Rudloff S, Lonnerdal B. 1990. Calcium retention from milk-based infant formulas, whey-hydrolysate formula, and human milk in weanling rhesus monkeys. *Am J Dis Child* 144:360–363.
- Rudnicki M, Frolich A, Rasmussen WF, McNair P. 1991. The effect of magnesium on maternal blood pressure in pregnancy-induced hypertension. A randomized double-blind placebo-controlled trial. *Acta Obstet Gynecol Scand* 70:445–450.
- Ruiz JC, Mandel C, Garabedian M. 1995. Influence of spontaneous calcium intake and physical exercise on the vertebral and femoral bone mineral density of children and adolescents. *J Bone Miner Res* 10:675–682.
- Russell AL. 1949. Dental effects of exposure to fluoride-bearing Dakota sandstone waters at various ages and for various lengths of time. II. Patterns of dental caries inhibition as related to exposure span, to elapsed time since exposure, and to periods of calcification and eruption. *J Dent Res* 28:600–612.
- Russell AL, Elvove E. 1951. Domestic water and dental caries. VII. A study of the fluoride-dental caries relationship in an adult population. *Pub Hlth Rep* 66:1389–1401.
- Ryan MP. 1987. Diuretics and potassium/magnesium depletion. Directions for treatment. *Am J Med* 82:38–47.
- Ryzen E, Elbaum N, Singer FR, Rude RK. 1985. Parenteral magnesium tolerance testing in the evaluation of magnesium deficiency. *Magnesium* 4:137–147.
- Ryzen E, Elkayam U, Rude RK. 1986. Low blood mononuclear cell magnesium in intensive cardiac care unit patients. *Am Heart J* 111:475–480.
- Sacks FM, Brown LE, Appel L, Borhani NO, Evans D, Whelton P. 1995. Combinations of potassium, calcium, and magnesium supplements in hypertension. *Hypertension* 26:950–956.
- Sakhaee K, Baker S, Zerwekh J, Poindexter J, Garcia-Hernandez PA, Pak CY. 1994. Limited risk of kidney stone formation during long-term calcium citrate supplementation in nonstone forming subjects. *J Urol* 152:324–327.
- Salama F, Whitford GM, Barenie JT. 1989. Fluoride retention by children from toothbrushing. *J Dent Res* 68(Spec Issue):335.
- Salle BL, Delvin E, Glorieux F, David L. 1990. Human neonatal hypocalcemia. *Biol Neonate* 58:S22–S31.
- Sandberg AS, Larsen T, Sandstrom B. 1993. High dietary calcium level decreases colonic phytate degradation in pigs fed a rapeseed diet. *J Nutr* 123:559–566.
- Sanders TA, Purves R. 1981. An anthropometric and dietary assessment of the nutritional status of vegan preschool children. *J Human Nutr* 35:349–357.
- Sandler RB, Slemenda CW, LaPorte RE, Cauley JA, Schramm MM, Barresi ML, Kriska AM. 1985. Postmenopausal bone density and milk consumption in childhood and adolescence. *Am J Clin Nutr* 42:270–274.
- Saunders D, Sillery J, Chapman R. 1988. Effect of calcium carbonate and aluminum hydroxide on human intestinal function. *Dig Dis Sci* 33:409–412.
- Schanler RJ, Garza C, Smith EO. 1985. Fortified mothers' milk for very low birth weight infants: Results of macromineral balance studies. *J Pediatr* 107:767–774.
- Schendel DE, Berg CJ, Yeargin-Allsopp M, Boyle CA, Decoufle P. 1996. Prenatal magnesium sulfate exposure and the risk for cerebral palsy or mental retardation among very low-birth-weight children aged 3 to 5 years. *J Am Med Assoc* 276:1805–1810.
- Schiff H, Binswanger U. 1982. Renal handling of fluoride in healthy man. *Renal Physiol* 5:192–196.

- Schiller L, Santa Ana C, Sheikh M, Emmett M, Fordtran J. 1989. Effect of the time of administration of calcium acetate on phosphorus binding. *N Engl J Med* 320:1110–1113.
- Schlesinger ES, Overton DE, Riverhead LI, Chase HC, Cantwell KT. 1956. Newburgh-Kingston caries-fluorine study XIII. Pediatric findings after ten years. *J Am Dent Assoc* 52:296–306.
- Schlesinger L, Arevalo M, Arredondo S, Diaz M, Lonnerdal B, Stekel A. 1992. Effect of a zinc-fortified formula on immunocompetence and growth of malnourished infants. *Am J Clin Nutr* 56:491–498.
- Schmidt LE, Arfken CL, Heins JM. 1994. Evaluation of nutrient intake in subjects with non-insulin-dependent diabetes mellitus. *J Am Diet Assoc* 94:773–774.
- Schmidt-Gayk H, Goossen J, Lendle F, Seidel D. 1977. Serum 25-hydroxycholecalciferol in myocardial infarction. *Atherosclerosis* 26:55–58.
- Schneider EL, Guralnik JM. 1990. The aging of America. Impact on health care costs. *J Am Med Assoc* 263:2335–2340.
- Schofield FA, and Morrell E. 1960. Calcium, phosphorus and magnesium. *Fed Proc* 19:1014–1016.
- Schuman CA, Jones HW III. 1985. The “milk-alkali” syndrome: Two case reports with discussion of pathogenesis. *Quart J Med (New Series)* 55:119–126.
- Schutzmansky G. 1971. Fluoride tablet application in pregnant females. *Dtsch Stomatol* 21:122–129.
- Schwartz E, Chokas WV, Panariello VA. 1964. Metabolic balance studies of high calcium intake in osteoporosis. *Am J Med* 36:233–249.
- Schwartz GG, Hulka BS. 1990. Is vitamin D deficiency a risk factor for prostate cancer? *Anticancer Res* 10:1307–1312.
- Schwartz R, Walker G, Linz MD, MacKellar I. 1973. Metabolic responses of adolescent boys to two levels of dietary magnesium and protein. I. Magnesium and nitrogen retention. *Am J Clin Nutr* 26:510–518.
- Schwartz R, Spencer H, Welsh JJ. 1984. Magnesium absorption in human subjects from leafy vegetables, intrinsically labeled with stable  $^{26}\text{Mg}$ . *Am J Clin Nutr* 39:571–576.
- Schwartz R, Apgar BJ, Wien EM. 1986. Apparent absorption and retention of Ca, Cu, Mg, Mn, and Zn from a diet containing bran. *Am J Clin Nutr* 43:444–455.
- Schwartzman MS, Franck WA. 1987. Vitamin D toxicity complicating the treatment of senile, postmenopausal, and glucocorticoid-induced osteoporosis: Four case reports and a critical commentary on the use of vitamin D in these disorders. *Am J Med* 82:224–229.
- Sebastian A, Harris ST, Ottaway JH, Todd KM, Morris RC Jr. 1994. Improved mineral balance and skeletal metabolism in postmenopausal women treated with potassium bicarbonate. *N Engl J Med* 330:1776–1781.
- Sebert JL, Garabedian M, Chauvenet M, Maamer M, Agbomson F, Brazier M. 1995. Evaluation of a new solid formulation of calcium and vitamin D in institutionalized elderly subjects: A randomized comparative trial versus separate administration of both constituents. *Rev Rhum* 62:288–294.
- Seelig MS. 1981. Magnesium requirements in human nutrition. *Magnes Bull* 3(suppl):26–47.
- Seelig MS. 1993. Interrelationship of magnesium and estrogen in cardiovascular and bone disorders, eclampsia, migraine and premenstrual syndrome. *J Am Coll Nutr* 12:442–458.
- Seelig MS, Elin RJ. 1996. Is there a place for magnesium in the treatment of acute myocardial infarction? *Am Heart J* 132:471–477.

- Seki K, Makimura N, Mitsui C, Hirata J, Nagata I. 1991. Calcium-regulating hormones and osteocalcin levels during pregnancy: A longitudinal study. *Am J Obstet Gynecol* 164:1248–1252.
- Selby PL. 1994. Calcium requirement—A reappraisal of the methods used in its determination and their application to patients with osteoporosis. *Am J Clin Nutr* 60:944–948.
- Selby PL, Davies M, Marks JS, Mawer EB. 1995. Vitamin D intoxication causes hypercalcemia by increased bone resorption which responds to pamidronate. *Clin Endocrinol* 43:531–536.
- Sentipal JM, Wardlaw GM, Mahan J, Matkovic V. 1991. Influence of calcium intake and growth indexes on vertebral bone mineral density in young females. *Am J Clin Nutr* 54:425–428.
- Seydoux J, Girardin E, Paunier L, Beguin F. 1992. Serum and intracellular magnesium during normal pregnancy and in patients with pre-eclampsia. *Br J Obstet Gynecol* 99:207–211.
- Shapses SA, Robins SP, Schwartz EI, Chowdhury H. 1995. Short-term changes in calcium but not protein intake alter the rate of bone resorption in healthy subjects as assessed by urinary pyridinium cross-link excretion. *J Nutr* 125:2814–2821.
- Sharma OP. 1996. Vitamin D, calcium, and sarcoidosis. *Chest* 109:535–539.
- Shen YW, Taves DR. 1974. Fluoride concentrations in the human placenta and maternal and cord blood. *Am J Obstet Gynecol* 119:205–207.
- Sherman HC, Hawley E. 1922. Calcium and phosphorus metabolism in childhood. *J Biol Chem* 52:375–399.
- Shils ME. 1969. Experimental human magnesium depletion. *Medicine* 46:61–85.
- Shils ME. 1994. Magnesium. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*. Philadelphia, PA: Lea & Febiger. Pp. 164–184.
- Shils ME, Rude RK. 1996. Deliberations and evaluations of the approaches, endpoints and paradigms for magnesium dietary recommendations. *J Nutr* 126:2398S–2403S.
- Sibai BM, Villar MA, Bray E. 1989. Magnesium supplementation during pregnancy: A double-blind randomized controlled clinical trial. *Am J Obstet Gynecol* 161:115–119.
- Siener R, Hesse A. 1995. Influence of a mixed and a vegetarian diet on urinary magnesium excretion and concentration. *Br J Nutr* 73:783–790.
- Silverberg SJ, Shane E, Clemens TL, Dempster DW, Segre GV, Lindsay R, Bilezikian JP. 1986. The effect of oral phosphate administration on major indices of skeletal metabolism in normal subjects. *J Bone Miner Res* 1:383–388.
- Silvis SE, Paragas PD Jr. 1972. Paresthesias, weakness, seizures, and hypophosphatemia in patients receiving hyperalimentation. *Gastroenterology* 62:513–520.
- Simard PL, Lachapelle C, Trahan L, Naccache H, Demers M, Broduer JM. 1989. The ingestion of fluoride dentifrice by young children. *J Dent Child* 56:177–181.
- Simard PL, Naccache H, Lachapelle D, Brodeur JM. 1991. Ingestion of fluoride from dentifrices by children aged 12 to 24 months. *Clin Pediatr Phila* 30:614–617.
- Simmer K, Khanum S, Carlsson L, Thompson RP. 1988. Nutritional rehabilitation in Bangladesh—the importance of zinc. *Am J Clin Nutr* 47:1036–1040.
- Singer L, Ophaug R. 1979. Total fluoride intake of infants. *Pediatrics* 63:460–466.
- Singer L, Ophaug RH, Harland BF. 1980. Fluoride intakes of young male adults in the United States. *Am J Clin Nutr* 33:328–332.
- Singer L, Ophaug RH, Harland BF. 1985. Dietary fluoride intake of 15–19-year-old male adults residing in the United States. *J Dent Res* 64:1302–1305.

## ONLINE REFERENCES

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- Singh A, Jolly SS. 1970. Chronic toxic effects on the skeletal system. In: *Fluorides and Human Health*. Geneva: World Health Organization. Pp 238–249.
- Skajaa K, Dorup I, Sandstrom BM. 1991. Magnesium intake and status and pregnancy outcome in a Danish population. *Br J Obstet Gynecol* 98:919–928.
- Slattery ML, Sorenson AW, Ford MH. 1988. Dietary calcium intake as a mitigating factor in colon cancer. *Am J Epidemiol* 128:504–514.
- Slemenda CW, Reister TK, Hui SL, Miller JZ, Christian JC, Johnston CC Jr. 1994. Influences on skeletal mineralization in children and adolescents: Evidence for varying effects of sexual maturation and physical activity. *J Pediatr* 125:201–207.
- Slemenda CW, Peacock M, Hui S, Zhou L, Johnston CC Jr. 1997. Reduced rates of skeletal remodeling are associated with increased bone mineral density during the development of peak skeletal mass. *J Bone Miner Res* 12:676–682.
- Slesinski MJ, Subar AF, Kahle LL. 1996. Dietary intake of fat, fiber, and other nutrients is related to the use of vitamin and mineral supplements in the United States: The 1992 National Health Interview Survey. *J Nutr* 126:3001–3008.
- Smilkstein MJ, Smolinske SC, Kulig KW, Rumack, BH. 1988. Severe hypermagnesemia due to multiple-dose cathartic therapy. *West J Med* 148:208–211.
- Smith EL, Gilligan C, Smith PE, Sempos CT. 1989. Calcium supplementation and bone loss in middle-aged women. *Am J Clin Nutr* 50:833–842.
- Smith KT, Heaney RP, Flora L, Hinders SM. 1987. Calcium absorption from a new calcium delivery system (CCM). *Calcif Tissue Int* 41:351–352.
- Smith R, Dent CE. 1969. Vitamin D requirements in adults. Clinical and metabolic studies on seven patients with nutritional osteomalacia. *Bibl Nutr Dieta* 13:44–45.
- Snedeker SM, Smith SA, Greger JL. 1982. Effect of dietary calcium and phosphorus levels on the utilization of iron, copper, and zinc by adult males. *J Nutr* 112:136–143.
- Sojka JE, Wastney ME, Abrams S, Froese S, Martin BR, Weaver CM. 1997. Magnesium kinetics in adolescent girls determined using stable isotopes: Effects of high and low calcium intakes. *Am J Physiol* 273:R170–R175.
- Sojka JE, Weaver CM. 1995. Magnesium supplementation and osteoporosis. *Nutr Rev* 53:71–74.
- Sokoll LJ, Dawson-Hughes B. 1992. Calcium supplementation and plasma ferritin concentrations in premenopausal women. *Am J Clin Nutr* 56:1045–1048.
- Sorva A, Risteli J, Risteli L, Valimaki M, Tilvis R. 1991. Effects of vitamin D and calcium on markers of bone metabolism in geriatric patients with low serum 25-hydroxyvitamin D levels. *Calcif Tissue Int* 49:S88–S89.
- Southgate DAT, Widdowson EM, Smits BJ, Cooke WT, Walker CHM, Mathers NP. 1969. Absorption and excretion of calcium and fat by young infants. *Lancet* 1:487–489.
- Sowers M, Wallace RB, Lemke JH. 1985. Correlates of forearm bone mass among women during maximal bone mineralization. *Prev Med* 14:585–596.
- Sowers M, Wallace RB, Lemke JH. 1986. The relationship of bone mass and fracture history to fluoride and calcium intake: A study of three communities. *Am J Clin Nutr* 44:889–898.
- Sowers M, Clark MK, Jannausch ML, Wallace RB. 1991. A prospective study of bone mineral content and fracture in communities with differential fluoride exposure. *Am J Epidemiol* 133:649–660.
- Sowers M, Corton G, Shapiro B, Jannausch ML, Crutchfield M, Smith ML, Randolph JF, Hollis B. 1993. Changes in bone density with lactation. *J Am Med Assoc* 269:3130–3135.

- Sowers M, Randolph J, Shapiro B, Jannaush M. 1995a. A prospective study of bone density and pregnancy after an extended period of lactation with bone loss. *Obstet Gynecol* 85:285–289.
- Sowers M, Eyre D, Hollis BW, Randolph JF, Shapiro B, Jannausch ML, Crutchfield M. 1995b. Biochemical markers of bone turnover in lactating and nonlactating postpartum women. *J Clin Endocrinol Metab*. 80:2210–2216.
- Spak CJ, Ekstrand J, Zylberstein D. 1982. Bioavailability of fluoride added by baby formula and milk. *Caries Res* 16:249–256.
- Spak CJ, Hardell LI, De Chateau P. 1983. Fluoride in human milk. *Acta Paediatr Scand* 72:699–701.
- Spatling L, Spatling G. 1988. Magnesium supplementation in pregnancy. A double blind study. *Br J Obstet Gynecol* 95:120–125.
- Specker BL. 1996. Evidence for an interaction between calcium intake and physical activity on changes in bone mineral density. *J Bone Miner Res* 11:1539–1544.
- Specker BL, Tsang RC. 1987. Cyclical serum 25-hydroxyvitamin D concentrations paralleling sunshine exposure in exclusively breast-fed infants. *J Pediatr* 110:744–747.
- Specker BL, Tsang RC, Hollis BW. 1985a. Effect of race and diet on human-milk vitamin D and 25-hydroxyvitamin D. *Am J Dis Child* 139:1134–1137.
- Specker BL, Valanis B, Hertzberg V, Edwards N, Tsang RC. 1985b. Sunshine exposure and serum 25-hydroxyvitamin D concentrations in exclusively breast-fed infants. *J Pediatr* 107:372–376.
- Specker BL, Lichtenstein P, Mimouni F, Gormley C, Tsang RC. 1986. Calcium-regulating hormones and minerals from birth to 18 months of age: A cross-sectional study. II. Effects of sex, race, age, season, and diet on serum minerals, parathyroid hormone, and calcitonin. *Pediatrics* 77:891–896.
- Specker BL, Tsang RC, Ho ML, Miller D. 1987. Effect of vegetarian diet on serum 1,25-dihydroxyvitamin D concentrations during lactation. *Obstet Gynecol* 70:870–874.
- Specker BL, Tsang RC, Ho ML. 1991a. Changes in calcium homeostasis over the first year postpartum: Effect of lactation and weaning. *Obstet Gynecol* 78:56–62.
- Specker BL, Tsang RC, Ho ML, Landi TM, Gratton TL. 1991b. Low serum calcium and high parathyroid hormone levels in neonates fed “humanized” cow’s milk-based formula. *Am J Dis Child* 145:941–945.
- Specker BL, Ho ML, Oestreich A, Yin TA, Shui QM, Chen XC, Tsang RC. 1992. Prospective study of vitamin D supplementation and rickets in China. *J Pediatr* 120:733–739.
- Specker BL, Vieira NE, O’Brien KO, Ho ML, Heubi JE, Abrams SA, Yerger AL. 1994. Calcium kinetics in lactating women with low and high calcium intakes. *Am J Clin Nutr* 59:593–599.
- Specker BL, Beck A, Kalkwarf H, Ho M. 1997. Randomized trial of varying mineral intake on total body bone mineral accretion during the first year of life. *Pediatrics* 99:e12.
- Spencer H, Menczel J, Lewin I, Samachson J. 1965. Effect of high phosphorus intake on calcium and phosphorus metabolism in man. *J Nutr* 86:125–132.
- Spencer H, Lewin I, Fowler J, Samachson J. 1969. Influence of dietary calcium intake on  $\text{Ca}^{47}$  absorption in man. *Am J Med* 46:197–205.
- Spencer H, Kramer L, Osis D, Norris C. 1978a. Effect of phosphorus on the absorption of calcium and on the calcium balance in man. *J Nutr* 108:447–457.
- Spencer H, Lesniak M, Gatzka CA, Kramer L, Norris C, Coffey J. 1978b. Magnesium-calcium interrelationships in man. *Trace Substances Environ Hlth* 12:241–247.

- Spencer H, Kramer L, Lesniak M, DeBartolo M, Norris C, Osis D. 1984. Calcium requirements in humans. Report of original data and a review. *Clin Orthop Relat Res* 184:270–280.
- Spencer H, Fuller H, Norris C, Williams D. 1994. Effect of magnesium on the intestinal absorption of calcium in man. *J Am Coll Nutr* 13:485–492.
- Spencer H, Osis D, Lender M. 1981. Studies of fluoride metabolism in man. A review and report of original data. *Sci Total Environ* 17:1–12.
- Stamp TCB, Haddad JG, Twigg CA. 1977. Comparison of oral 25-hydroxycholecalciferol, vitamin D, and ultraviolet light as determinants of circulating 25-hydroxyvitamin D. *Lancet* 1:1341–1343.
- Stanbury SW. 1971. The phosphate ion in chronic renal failure. In: Hioco DJ, ed. *Phosphate et Metabolisme Phosphocalcique*. Paris: Sandoz Laboratories.
- Stapleton FB. 1994. Hematuria associated with hypercalciuria and hyperuricosuria: A practical approach. *Pediatr Nephrol* 8:756–761.
- Stearns G. 1968. Early studies of vitamin D requirement during growth. *Am J Pub Hlth* 58:2027–2035.
- Steenbock H, Black A. 1924. The reduction of growth-promoting and calcifying properties in a ration by exposure to ultraviolet light. *J Biol Chem* 61:408–422.
- Steichen JJ, Tsang RC. 1987. Bone mineralization and growth in term infants fed soy-based or cow milk-based formula. *J Pediatr* 110:687–692.
- Stein JH, Smith WO, Ginn HE. 1966. Hypophosphatemia in acute alcoholism. *Am J Med Sci* 252:78–83.
- Stendig-Lindberg G, Tepper R, Leichter I. 1993. Trabecular bone density in a two year controlled trial of peroral magnesium in osteoporosis. *Magnes Res* 6:155–163.
- Stephen KW, McCall DR, Tullis JI. 1987. Caries prevalence in northern Scotland before, and 5 years after, water defluoridation. *Br Dent J* 163:324–326.
- Stevenson CA, Watson AR. 1957. Fluoride osteosclerosis. *Am J Roentg Rad Ther Nucl Med* 78:13–18.
- Stumpf WE, Sar M, Reid FA, Tanakay Y, DeLuca HF. 1979. Target cells for 1,25-dihydroxyvitamin D<sub>3</sub> in intestinal tract, stomach, kidney, skin, pituitary, and parathyroid. *Science* 206:1188–1190.
- Suarez FL, Savaiano DA, Levitt MD. 1995. A comparison of symptoms after the consumption of milk or lactose-hydrolyzed milk by people with self-reported severe lactose intolerance. *N Engl J Med* 333:1–4.
- Svenningsen NW, Lindquist B. 1974. Postnatal development of renal hydrogen ion excretion capacity in relation to age and protein intake. *Acta Paediatr Scand* 63:721–731.
- Switzer RL. 1971. Regulation and mechanism of phosphoribosylpyrophosphate synthetase. III. Kinetic studies of the reaction mechanism. *J Biol Chem* 246:2447–2458.
- Tanner JT, Smith J, Defibaugh P, Angyal G, Villalobos M, Bueno MP, McGarrahan ET, Wehr HM, Muniz JF, Hollis BW. 1988. Survey of vitamin content of fortified milk. *J Assoc Off Anal Chem* 71: 607–610.
- Tanner JM. 1990. *Growth at Adolescence*. Oxford: Oxford University Press.
- Tatevossian A. 1990. Fluoride in dental plaque and its effects. *J Dent Res* 69(Spec Iss): 645–652.
- Taves DR. 1978. Fluoridation and mortality due to heart disease. *Nature* 272:361–362.
- Taves DR. 1983. Dietary intake of fluoride ashed (total fluoride) v. unashed (inorganic fluoride) analysis of individual foods. *Br J Nutr* 49:295–301.

- Taves DR, Neuman WF. 1964. Factors controlling calcification in vitro: Fluoride and magnesium. *Arch Biochem Biophys* 108:390–397.
- Taylor AF, Norman ME. 1984. Vitamin D metabolite levels in normal children. *Pediatr Res* 18: 886–890.
- Taylor CB, Hass GM, Ho KJ, Liu LB. 1972. Risk factors in the pathogenesis of arteriosclerotic heart disease and generalized atherosclerosis. *Ann Clin Lab Sci* 2:239.
- Teegarden D, Proulx WR, Martin BR, Zhao J, McCabe GP, Lyle RM, Peacock M, Slemenda C, Johnston CC, Weaver CM. 1995. Peak bone mass in young women. *J Bone Miner Res* 10:711–715.
- Ten Cate JM. 1990. In vitro studies on the effects of fluoride on de- and remineralization. *J Dent Res* 69(Spec Iss):614–619.
- Terblanche S, Noakes TD, Dennis SC, Marais D, Eckert M. 1992. Failure of magnesium supplementation to influence marathon running performance or recovery in magnesium-replete subjects. *Int J Sport Nutr* 2:154–164.
- Tesar R, Notelovitz M, Shim E, Kauwell G, Brown J. 1992. Axial and peripheral bone density and nutrient intakes of postmenopausal vegetarian and omnivorous women. *Am J Clin Nutr* 56:699–704.
- Thatcher HS, Rock L. 1928. Clinical notes, suggestions and new instruments. *J Am Med Assoc* 91:1185–1186.
- Theintz G, Buchs B, Rizzoli R, Slosman D, Clavien H, Sizonenko PC, Bonjour JP. 1992. Longitudinal monitoring of bone mass accumulation in healthy adolescents: Evidence for a marked reduction after 16 years of age at the levels of lumbar spine and femoral neck in female subjects. *J Clin Endocrinol Metab* 75:1060–1065.
- Thompson FE, Byers T. 1994. Dietary assessment resource manual. *J Nutr* 124:224S–231S.
- Thys-Jacobs S, Ceccarelli S, Bierman A, Weisman H, Cohen M-A, Alvir J. 1989. Calcium supplementation in premenstrual syndrome: A randomized cross-over trial. *J Gen Intern Med* 4:183–189.
- Tillman DM, Semple PF. 1988. Calcium and magnesium in essential hypertension. *Clin Sci* 75:395–402.
- Touitou Y, Godard JP, Ferment O, Chastang C, Proust J, Bogdan A, Auzeby A, Touitou C. 1987. Prevalence of magnesium and potassium deficiencies in the elderly. *Clin Chem* 33:518–523.
- Travis SF, Sugerman HJ, Ruberg RL, Dudrick SJ, Delivoria-Papadopoulos M, Miller L, Osaki FA. 1971. Alterations of red cell glycolytic intermediates and oxygen transport as a consequence of hypophosphatemia in patients receiving intravenous hyperalimentation. *N Engl J Med* 285:763–768.
- Tremaine WJ, Newcomer AD, Riggs BL, McGill DB. 1986. Calcium absorption from milk in lactase-deficient and lactase-sufficient adults. *Dig Dis Sci* 31:376–378.
- Tsang RC, Strub R, Brown DR, Steichen J, Hartman C, Chen IW. 1976. Hypomagnesemia in infants of diabetic mothers: Perinatal studies. *J Pediatr* 89:115–119.
- Tucker K. 1996. The use of epidemiological approaches and meta-analysis to determine mineral element requirements. *J Nutr* 126:2365S–2372S.
- Tucker K, Kiel DP, Hannan MT, Felson DT. 1995. Magnesium intake is associated with bone-mineral density (BMD) in elderly women. *J Bone Miner Res* 10:S466.
- Tylavsky FA, Anderson JJ. 1988. Dietary factors in bone health of elderly lacto-ovo vegetarian and omnivorous women. *Am J Clin Nutr* 48:842–849.

- Urakabe S, Nakata K, Ando A, Orita Y, Abe Y. 1975. Hypokalemia and metabolic acidosis from overuse of magnesium oxide. *Jpn Circ J* 39:1135–1137.
- USDA (US Department of Agriculture). 1985. *Nationwide Food Consumption Survey. Continuing Survey of Food Intakes of Individuals*. Women 19–50 years and their children 1–5 years, 1 day, 1985. Report No. 85-1. Hyattsville, MD: Nutrition Monitoring Division, Human Nutrition Information Service, USDA.
- USDA (US Department of Agriculture). 1991. *Provisional Table on the Vitamin D Content of Foods*. Hyattsville, MD: Nutrient Data Research Branch, USDA.
- USDA (US Department of Agriculture), Center for Nutrition Policy and Promotion. 1997. *Nutrient Content of the U.S. Food Supply, 1909–1994*. Washington DC: Center for Nutrition Policy and Promotion, USDA.
- USPHS (US Public Health Service). 1991. *Ad Hoc Subcommittee on Fluoride: Review of Fluoride Benefits and Risks*. Bethesda, MD: Department of Health and Human Services.
- Venkataraman PS, Tsang RC, Greer FR, Noguchi A, Laskarzewski P, Steichen JJ. 1985. Late infantile tetany and secondary hyperparathyroidism in infants fed humanized cow milk formula. Longitudinal follow-up. *Am J Dis Child* 139:664–668.
- Vicchio D, Yergey A, O'Brien K, Allen L, Ray R, Holick MF. 1993. Quantification and kinetics of 25-hydroxyvitamin D<sub>3</sub> by isotope dilution liquid chromatography/thermospray mass spectrometry. *Biol Mass Spectrom* 22:53–58.
- Vik T, Try K, Thelle DS, Forde OH. 1979. Tromso heart study: Vitamin D metabolism and myocardial infarction. *Br Med J* 2:176.
- Villar J, Repke JT. 1990. Calcium supplementation during pregnancy may reduce preterm delivery in high-risk populations. *Am J Obstet Gynecol* 163:1124–1131.
- Villareal DT, Civitelli R, Chines A, Avioli LV. 1991. Subclinical vitamin D deficiency in postmenopausal women with low vertebral bone mass. *J Clin Endocrinol Metab* 72: 628–634.
- Wacker WE, Parisi AF. 1968. Magnesium metabolism. *N Engl J Med* 45:658–663, 712–717, 772–776.
- Wagener DK, Novrjah P, Horowitz AM. 1995. *Trends in Childhood Use of Dental Care Products Containing Fluoride: United States, 1983–1989*. Advance data from Vital Health Statistics of the Center for Disease Control. National Center for Health Statistics #219; Nov. 20, 1992. Hyattsville, MD: National Center for Health Statistics.
- Walker AR, Richardson B, Walker F. 1972. The influence of numerous pregnancies and lactations on bone dimensions in South African Bantu and Caucasian mothers. *Clin Sci* 42:189–196.
- Walker RM, Linkswiler HM. 1972. Calcium retention in the adult human male as affected by protein intake. *J Nutr* 102:1297–1302.
- Wallach S, Verch RL. 1986. Tissue magnesium in spontaneously hypertensive rats. *Magnesium* 5:33–38.
- Wang CC, Kern R, Kaucher M. 1930. Minimum requirement of calcium and phosphorus in children. *Am J Dis Child* 39:768–773.
- Wardlaw GM, Pike AM. 1986. The effect of lactation on peak adult shaft and ultra-distal forearm bone mass in women. *Am J Clin Nutr* 44:283–286.
- Wasnich R, Yano K, Vogel J. 1983. Postmenopausal bone loss at multiple skeletal sites: Relationship to estrogen use. *J Chron Dis* 36:781–790.
- Wastney ME, Ng J, Smith D, Martin BR, Peacock M, Weaver CM. 1996. Differences in calcium kinetics between adolescent girls and young women. *Am J Physiol* 271:R208–R216.

- Waterhouse C, Taves D, Munzer A. 1980. Serum inorganic fluoride: Changes related to previous fluoride intake, renal function and bone resorption. *Clin Sci* 58:145–152.
- Weaver CM. 1994. Age-related calcium requirements due to changes in absorption and utilization. *J Nutr* 124:1418S–1425S.
- Weaver CM, Martin BR, Plawecki KL, Peacock M, Wood OB, Smith DL, Wastney ME. 1995. Differences in calcium metabolism between adolescent and adult females. *Am J Clin Nutr* 61:577–581.
- Webb AR, Kline L, Holick MF. 1988. Influence of season and latitude on the cutaneous synthesis of vitamin D<sub>3</sub>: Exposure to winter sunlight in Boston and Edmonton will not promote vitamin D<sub>3</sub> synthesis in human skin. *J Clin Endocrinol Metab* 67:373–378.
- Webb AR, De Costa BR, Holick MF. 1989. Sunlight regulates the cutaneous production of vitamin D<sub>3</sub> by causing its photodegradation. *J Clin Endocrinol Metab* 68:882–887.
- Webb AR, Pilbeam C, Hanafin N, Holick MF. 1990. An evaluation of the relative contributions of exposure to sunlight and of diet to the circulating concentrations of 25-hydroxyvitamin D in an elderly nursing home population in Boston. *Am J Clin Nutr* 51:1075–1081.
- Wei SH, Hattab FN, Mellberg JR. 1989. Concentration of fluoride and selected other elements in teas. *Nutrition* 5:237–240.
- Weinsier RL, Krumdieck CL. 1981. Death resulting from overzealous total parenteral nutrition: The refeeding syndrome revisited. *Am J Clin Nutr* 34:393–399.
- Weisman Y, Harell A, Edelstein S, Spirer Z, Golander A. 1979. 1,25-dihydroxyvitamin D<sub>3</sub> and 24,25-dihydroxyvitamin D<sub>3</sub> in vitro synthesis by human decidua and placenta. *Nature* 281:317–319.
- Weissberg N, Schwartz G, Shemesh O, Brooks BA, Algur N, Eylath U, Abraham AS. 1992. Serum and mononuclear cell potassium, magnesium, sodium and calcium in pregnancy and labour and their relation to uterine muscle contraction. *Magnes Res* 5:173–177.
- Wester PO, Dyckner T. 1980. Diuretic treatment and magnesium losses. *Acta Med Scand* 647:145–152.
- Whitford GM. 1994. Effects of plasma fluoride and dietary calcium concentrations on GI absorption and secretion of fluoride in the rat. *Calcif Tissue Int* 54:421–425.
- Whitford GM. 1996. The metabolism and toxicity of fluoride. In Myers HM, ed. *Monographs in Oral Science*, 2nd Revised Edition. Basel, Switzerland: Karger.
- Whitford GM, Allmann DW, Shahed AR. 1987. Topical fluorides: Effects on physiologic and biochemical processes. *J Dent Res* 66:1072–1078.
- Whiting SJ, Pluhator MM. 1992. Comparison of in vitro and in vivo tests for determination of availability of calcium from calcium carbonate tablets. *J Am Coll Nutr* 11:553–560.
- Whiting SJ, Wood RJ. 1997. Adverse effects of high-calcium diets in humans. *Nutr Rev* 55:1–9.
- WHO (World Health Organization). 1984. *Fluorine and Fluorides*. Environmental Health Criteria 36. Geneva: World Health Organization. Pp. 77–79.
- WHO (World Health Organization). 1987. *Principles for the Safety Assessment of Food Additives and Contaminants in Food*. Environmental Health Criteria 70. Geneva: World Health Organization.

- WHO (World Health Organization). 1994. *Assessment of Fracture Risk and its Application to Screening for Postmenopausal Osteoporosis*. Technical Report Series 843. Geneva: World Health Organization.
- WHO (World Health Organization). 1996. *Trace Elements in Human Nutrition and Health*. Prepared in collaboration with the Food and Agriculture Organization of the United Nations and the International Atomic Energy Agency. Geneva: World Health Organization.
- Wickham CA, Walsh K, Cooper C, Barker DJ, Margetts BM, Morris J, Bruce SA. 1989. Dietary calcium, physical activity, and risk of hip fracture: A prospective study. *Br Med J* 299:889–892.
- Widdowson EM. 1965. Absorption and excretion of fat, nitrogen, and minerals from “filled” milks by babies one week old. *Lancet* 2:1099–1105.
- Widdowson EM, Dickerson JWT. 1964. The chemical composition of the body. In: Comar CL, Bronner F, eds. *Mineral Metabolism: An Advanced Treatise, Vol. II. The Elements, Part A*. New York: Academic Press.
- Widdowson EM, McCance RA, Spray CM. 1951. The chemical composition of the human body. *Clin Sci* 10:113–125.
- Widman L, Wester PO, Stegmayr BK, Wirell M. 1993. The dose-dependent reduction in blood pressure through administration of magnesium. A double blind placebo controlled cross-over study. *Am J Hypertens* 6:41–45.
- Wiktorsson AM, Martinsson T, Zimmerman M. 1992. Caries prevalence among adults in communities with optimal and low water fluoride concentrations. *Community Dent Oral Epidemiol* 20:359–363.
- Wilkinson R. 1976. Absorption of calcium, phosphorus, and magnesium. In: Nor din BEC, ed. *Calcium, Phosphate and Magnesium Metabolism*. Edinburgh: Churchill Livingstone. Pp. 36–112.
- Willett W. 1990. *Nutritional Epidemiology*. New York, NY: Oxford University Press.
- Willett WC, Sampson L, eds. 1997. Dietary assessment methods. *Am J Clin Nutr* 65:1097S–1368S.
- Williams JE, Zwemer JD. 1990. Community water fluoride levels, preschool dietary patterns, and the occurrence of fluoride dental opacities. *J Pub Hlth Dent* 50:276–281.
- Williams ML, Rose CS, Morrow G, Sloan SE, Barness LA. 1970. Calcium and fat absorption in neonatal period. *Am J Clin Nutr* 23:1322–1330.
- Wilson SG, Retallack RW, Kent JC, Worth GK, Gutteridge DH. 1990. Serum free 1,25-dihydroxyvitamin D and the free 1,25-dihydroxyvitamin D index during a longitudinal study of human pregnancy and lactation. *Clin Endocrinol* 32:613–622.
- Wise A, Gilbert DJ. 1982. Phytate hydrolysis by germfree and conventional rats. *Appl Environ Microbiol* 43:753–756.
- Wisker E, Nagel R, Tanudjaja TK, Feldheim W. 1991. Calcium, magnesium, zinc, and iron balances in young women: Effects of a low-phytate barley-fiber concentrate. *Am J Clin Nutr* 54:553–559.
- Witteman JC, Willett WC, Stampfer MJ, Colditz GA, Sacks FM, Speizer FE, Rosner B, Hennekens CH. 1989. A prospective study of nutritional factors and hypertension among U.S. women. *Circulation* 80:1320–1327.
- Witteman JC, Grobbee DE, Derkx FH, Bouillon R, de Bruijn AM, Hofman A. 1994. Reduction of blood pressure with oral magnesium supplementation in women with mild to moderate hypertension. *Am J Clin Nutr* 60:129–135.
- Wong NL, Quamme GA, Dirks JH. 1986. Effects of acid-base disturbances on renal handling of magnesium in the dog. *Clin Sci* 70:277–284.

- Wood RJ, Zheng JJ. 1990. Milk consumption and zinc retention in postmenopausal women. *J Nutr* 120:398–403.
- Wood RJ, Sitrin MD, Rosenberg IH. 1988. Effect of phosphorus on endogenous calcium losses during total parenteral nutrition. *Am J Clin Nutr* 48:632–636.
- Woods KL, Fletcher S. 1994. Long-term outcome after intravenous magnesium sulphate in suspected acute myocardial infarction: The second Leicester Intravenous Magnesium Intervention Trial (LIMIT-2). *Lancet* 343:816–819.
- Workshop Reports. 1992. *J Dent Res* 71:1218–1227.
- Yamagata Z, Miyamura T, Iijima S, Asaka A, Sasaki M, Kato J, Koizumi K. 1994. Vitamin D receptor gene polymorphism and bone mineral density in healthy Japanese women. *Lancet* 344:1027.
- Yamamoto ME, Applegate WB, Klag MJ, Borhani NO, Cohen JD, Kirchner KA, Lakatos E, Sacks FM, Taylor JO, Hennekens CH. 1995. Lack of blood pressure effect with calcium and magnesium supplementation in adults with high-normal blood pressure. Results from Phase I of the Trials of Hypertension Prevention (TOHP). Trials of Hypertension Prevention (TOHP) Collaborative Research Group. *Ann Epidemiol* 5:96–107.
- Yano K, Heilbrun LK, Wasnich RD, Hankin JH, Vogel JM. 1985. The relationship between diet and bone mineral content of multiple skeletal sites in elderly Japanese men and women living in Hawaii. *Am J Clin Nutr* 42:877–888.
- Young GP, Thomas RJ, Bourne DW, Russell DM. 1985. Parenteral nutrition. *Med J Aust* 143:597–601.
- Zeghoud F, Vervel C, Guillozo H, Walrant-Debray O, Boutignon H, Garabedian M. 1997. Subclinical vitamin D deficiency in neonates: Definition and response to vitamin D supplements. *Am J Clin Nutr* 65:771–778.
- Zemel PC, Zemel MB, Urberg M, Douglas FL, Geiser R, Sower JR. 1990. Metabolic and hemodynamic effects of magnesium supplementation in patients with essential hypertension. *Am J Clin Nutr* 51:665–669.
- Ziegler EE, Fomon SJ. 1983. Lactose enhances mineral absorption in infancy. *J Pediatr Gastroenterol Nutr* 2:228–294.
- Zielhuis RL, van der Kreek FW. 1979. The use of a safety factor in setting health-based permissible levels for occupational exposure. *Int Arch Occup Environ Health* 42:191–201.
- Zipkin I, Zucas SM, Lavender DR, Fullmer HM, Schiffmann E, Corcoran BA. 1970. Fluoride and calcification of rat aorta. *Calcif Tissue Res* 6:173–182.

## CHROMIUM

*Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*  
(ISBN 0-309-07290-5), Chapter 6, pp. 217–223.

- Al-Hamood MH, Elbetieha A, Bataineh H. 1998. Sexual maturation and fertility of male and female mice exposed prenatally and postnatally to trivalent and hexavalent chromium compounds. *Reprod Fertil Dev* 10:179–183.
- Anderson RA. 1987. Chromium. In: Mertz W, ed. *Trace Elements in Human and Animal Nutrition*, Vol. I. San Diego: Academic Press. Pp. 225–244.
- Anderson RA. 1997. Chromium as an essential nutrient for humans. *Regul Toxicol Pharmacol* 26:S35–S41.
- Anderson R, Bryden NA. 1983. Concentration, insulin potentiation, and absorption of chromium in beer. *J Agric Food Chem* 31:308–311.
- Anderson RA, Kozlovsky AS. 1985. Chromium intake, absorption and excretion of subjects consuming self-selected diets. *Am J Clin Nutr* 41:1177–1183.
- Anderson RA, Polansky MM, Bryden NA, Roginski EE, Patterson KY, Reamer DC. 1982. Effect of exercise (running) on serum glucose, insulin, glucagon, and chromium excretion. *Diabetes* 31:212–216.
- Anderson RA, Polansky MM, Bryden NA, Patterson KY, Veillon C, Glinsmann WH. 1983. Effects of chromium supplementation on urinary Cr excretion of human subjects and correlation of Cr excretion with selected clinical parameters. *J Nutr* 113:276–281.
- Anderson RA, Polansky MM, Bryden NA. 1984. Strenuous running: Acute effects on chromium, copper, zinc, and selected clinical variables in urine and serum of male runners. *Biol Trace Elem Res* 6:327–336.
- Anderson RA, Bryden NA, Polansky MM. 1988a. Chromium content of selected breakfast cereals. *J Food Comp Anal* 1:303–308.
- Anderson RA, Bryden NA, Polansky MM, Deuster PA. 1988b. Exercise effects on chromium excretion of trained and untrained men consuming a constant diet. *J Appl Physiol* 64:249–252.
- Anderson RA, Bryden NA, Polansky MM, Reiser S. 1990. Urinary chromium excretion and insulinogenic properties of carbohydrates. *Am J Clin Nutr* 51:864–868.
- Anderson RA, Polansky MM, Bryden NA, Canary JJ. 1991. Supplemental-chromium effects on glucose, insulin, glucagon, and urinary chromium losses in subjects consuming controlled low-chromium diets. *Am J Clin Nutr* 54:909–916.
- Anderson RA, Bryden NA, Polansky MM. 1992. Dietary chromium intake. Freely chosen diets, institutional diets, and individual foods. *Biol Trace Elem Res* 32:117–121.
- Anderson RA, Bryden NA, Patterson KY, Veillon C, Andon MB, Moser-Veillon PB. 1993a. Breast milk chromium and its association with chromium intake, chromium excretion, and serum chromium. *Am J Clin Nutr* 57:519–523.
- Anderson RA, Bryden NA, Polansky MM. 1993b. Dietary intake of calcium, chromium, copper, iron, magnesium, manganese, and zinc: Duplicate plate values corrected using derived nutrient intake. *J Am Diet Assoc* 93:462–464.
- Anderson RA, Bryden NA, Polansky MM. 1997a. Lack of toxicity of chromium chloride and chromium picolinate in rats. *J Am Coll Nutr* 16:273–279.

- Anderson RA, Cheng N, Bryden NA, Polansky MM, Cheng N, Chi J, Feng J. 1997b. Elevated intakes of supplemental chromium improve glucose and insulin variables in individuals with type 2 diabetes. *Diabetes* 46:1786–1791.
- Aquilio E, Spagnoli R, Seri S, Bottone G, Spennati G. 1996. Trace element content in human milk during lactation of preterm newborns. *Biol Trace Elem Res* 51:63–70.
- ATSDR (Agency for Toxic Substances and Disease Registry). 1998. *Toxicological Profile for Chromium (Update)*. Atlanta: Centers for Disease Control and Prevention.
- Bagchi D, Bagchi M, Balmoori J, Ye X, Stohs SJ. 1997. Comparative induction of oxidative stress in cultured J774A.1 macrophage cells by chromium picolinate and chromium nicotinate. *Res Comm Mol Pathol Pharmacol* 97:335–346.
- Bataineh H, Al-Hamood MH, Elbetieha A, Bani Hani I. 1997. Effect of long-term ingestion of chromium compounds on aggression, sex behavior and fertility in adult male rat. *Drug Chem Toxicol* 20:133–149.
- Briefel RR, McDowell MA, Alaimo K, Caughman CR, Bischof AL, Carroll MD, Johnson CL. 1995. Total energy intake of the US population: The Third National Health and Nutrition Examination Survey, 1988–1991. *Am J Clin Nutr* 62:1072S–1080S.
- Brown RO, Forloines-Lynn S, Cross RE, Heizer WD. 1986. Chromium deficiency after long-term parenteral nutrition. *Dig Dis Sci* 31:661–664.
- Bunker VW, Lawson MS, Delves HT, Clayton BE. 1984. The uptake and excretion of chromium by the elderly. *Am J Clin Nutr* 39:797–802.
- Cabrera-Vique C, Teissedre PL, Cabanis MT, Cabanis JC. 1997. Determination and levels of chromium in French wine and grapes by graphite furnace atomic absorption spectrometry. *J Agric Food Chem* 45:1808–1811.
- Campbell WW, Beard JL, Joseph LJ, Davey SL, Evans WJ. 1997. Chromium picolinate supplementation and resistive training by older men: Effects on iron status and hematologic indexes. *Am J Clin Nutr* 66:944–949.
- Carmichael S, Abrams B, Selvin S. 1997. The pattern of maternal weight gain in women with good pregnancy outcomes. *Am J Pub Health* 87:1984–1988.
- Casey CE, Hambridge KM. 1984. Chromium in human milk from American mothers. *Br J Nutr* 52:73–77.
- Casey CE, Hambridge KM, Neville MC. 1985. Studies in human lactation: Zinc, copper, manganese and chromium in human milk in the first month of lactation. *Am J Clin Nutr* 41:1193–1200.
- Cerulli J, Grabe DW, Gauthier I, Malone M, McGoldrick MD. 1998. Chromium picolinate toxicity. *Ann Pharmacotherapy* 32:428–431.
- Chen NSC, Tsai A, Dyer IA. 1973. Effect of chelating agents on chromium absorption in rats. *J Nutr* 103:1182–1186.
- Clydesdale FM. 1988. Mineral interactions in foods. In: Bodwell CE, Erdman JW, eds. *Nutrient Interactions*. New York: Marcel Dekker. Pp. 73–113.
- Cocho JA, Cervilla JR, Rey-Goldar ML, Fdez-Lorenzo JR, Fraga JM. 1992. Chromium content in human milk, cow's milk, and infant formulas. *Biol Trace Elem Res* 32:105–107.
- Cupo DY, Wetterhahn KE. 1985. Binding of chromium to chromatin and DNA from liver and kidney of rats treated with sodium dichromate and chromium(III) chloride in vivo. *Cancer Res* 45:1146–1151.
- Davies S, McLaren Howard J, Hunnisett A, Howard M. 1997. Age-related decreases in chromium levels in 51,665 hair, sweat, and serum samples from 40,872 patients—Implications for the prevention of cardiovascular disease and type II diabetes mellitus. *Metabolism* 46:469–473.

- Davis CM, Vincent JB. 1997a. Chromium oligopeptide activates insulin receptor tyrosine kinase activity. *Biochemistry* 36:4382–4385.
- Davis CM, Vincent JB. 1997b. Isolation and characterization of a biologically active chromium oligopeptide from bovine liver. *Arch Biochem Biophys* 339:335–343.
- Davis ML, Seaborn CD, Stoecker BJ. 1995. Effects of over-the-counter drugs on <sup>51</sup>chromium retention and urinary excretion in rats. *Nutr Res* 15:201–210.
- Davis-Whitenack ML, Adeleye BO, Rolf LL, Stoecker BJ. 1996. Biliary excretion of <sup>51</sup>chromium in bile-duct cannulated rats. *Nutr Res* 16:1009–1015.
- Do Canto OM, Sargent T III, Liehn JC. 1995. Chromium (III) metabolism in diabetic patients. In: Sive Subramanian KN, Wastney ME, eds. *Kinetic Models of Trace Element and Mineral Metabolism during Development*. Boca Raton, FL: CRC Press. Pp. 205–219.
- Doisy RJ, Streeten DHP, Souma ML, Kalafer ME, Rekant SI, Dalakos TG. 1971. Metabolism of chromium-51 in human subjects—Normal, elderly, and diabetic subjects. In: Mertz W, Cornatzer WE, eds. *Newer Trace Elements in Nutrition*. New York: Marcel Dekker. Pp 155–168.
- Dowling HJ, Offenbacher EG, Pi-Sunyer FX. 1990. Effects of amino acids on the absorption of trivalent chromium and its retention by regions of the rat small intestine. *Nutr Res* 10:1261–1271.
- Elbetieha A, Al-Hamood MH. 1997. Long-term exposure of male and female mice to trivalent and hexavalent chromium compounds: Effect on fertility. *Toxicology* 116:39–47.
- Engelhardt S, Moser-Veillon PB, Mangels AR, Patterson KY, Veillon C. 1990. Appearance of an oral dose of chromium (<sup>53</sup>Cr) in breast milk? In: Atkinson SA, Hanson LA, Chandra RK, eds. *Human Lactation 4. Breastfeeding, Nutrition, Infection and Infant Growth in Developed and Emerging Countries*. St. Johns, Newfoundland: ARTS Biomedical. Pp. 485–487.
- Ernst E. 1990. Testicular toxicity following short-term exposure to tri- and hexavalent chromium: An experimental study in the rat. *Toxicol Lett* 51:269–275.
- Flodin NW. 1990. Micronutrient supplements: Toxicity and drug interactions. *Prog Food Nutr Sci* 14:277–331.
- Fomon SJ. 1974. *Infant Nutrition*, 2nd ed. Philadelphia: WB Saunders. Pp. 24–25.
- Fornace AJ Jr, Seres DS, Lechner JF, Harris CC. 1981. DNA-protein cross-linking by chromium salts. *Chem Biol Interact* 36:345–354.
- Freund H, Atamian S, Fischer JE. 1979. Chromium deficiency during total parenteral nutrition. *J Am Med Assoc* 241:496–498.
- Fristedt B, Lindqvist B, Schutz A, Ovrum P. 1965. Survival in a case of acute oral chromic acid poisoning with acute renal failure treated by haemodialysis. *Acta Med Scand* 177:153–159.
- Gibson RS, Scythes CA. 1984. Chromium, selenium, and other trace element intakes of a selected sample of Canadian premenopausal women. *Biol Trace Elem Res* 6:105–116.
- Gibson RS, MacDonald AC, Martinez OB. 1985. Dietary chromium and manganese intakes of a selected sample of Canadian elderly women. *Hum Nutr Appl Nutr* 39:43–52.
- Greenwood NN, Earnshaw A. 1997. *Chemistry of the Elements*, 2nd ed. Oxford: Butterworth-Heinemann. Pp. 1002–1039.
- Hamamy HA, Al-Hakkak ZS, Hussain AF. 1987. Chromosome aberrations in workers at a tannery in Iraq. *Mutat Res* 189:395–398.

- Hambidge KM. 1971. Chromium nutrition in the mother and the growing child. In: Mertz W, Cornatzer WE, eds. *Newer Trace Elements in Nutrition*. New York: Marcel Dekker. Pp. 169–194.
- Harris DC. 1977. Different metal-binding properties of the two sites of human transferrin. *Biochemistry* 16:560–564.
- Harris MI, Flegal KM, Cowie CC, Eberhardt MS, Goldstein DE, Little RR, Wiedmeyer HM, Byrd-Holt DD. 1998. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. *Diabetes Care* 21:518–524.
- Hathcock JN. 1997. Vitamins and minerals: Efficacy and safety. *Am J Clin Nutr* 66:427–437.
- Hopkins LL Jr. 1965. Distribution in the rat of physiological amounts of injected Cr<sup>51</sup>(III) with time. *Am J Physiol* 209:731–735.
- Hopkins LL Jr, Majaj AS. 1967. Improvements of impaired glucose tolerance by chromium(III) in malnourished infants. In: Kuhnau J, ed. *Proceedings of the Seventh International Congress of Nutrition. Vol. 5: Physiology and Biochemistry of Food Components*. London: Pergamon Press. Pp. 721–723.
- Hopkins LL Jr, Ransome-Kuti O, Majaj AS. 1968. Improvement of impaired carbohydrate metabolism by chromium (III) in malnourished infants. *Am J Clin Nutr* 21:203–211.
- IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Washington, DC: National Academy Press. Pp. 96–120.
- Itoh S, Shimada H. 1996. Micronucleus induction by chromium and selenium, and suppression by metallothionein inducer. *Mutat Res* 367:233–236.
- Ivankovic S, Preussmann R. 1975. Absence of toxic and carcinogenic effects after administration of high doses of chromic oxide pigment in subacute and long-term feeding experiments in rats. *Food Cosmet Toxicol* 13:347–351.
- Jeejeebhoy KN, Chu RC, Marliss EB, Greenberg GR, Bruce-Robertson A. 1977. Chromium deficiency, glucose intolerance, and neuropathy reversed by chromium supplementation, in a patient receiving long-term total parenteral nutrition. *Am J Clin Nutr* 30:531–538.
- Kamath SM, Stoecker BJ, Davis-Whitenack ML, Smith MM, Adeleye BO, Sangiah S. 1997. Absorption, retention and urinary excretion of chromium-51 in rats pretreated with indomethacin and dosed with dimethylprostaglandin E<sub>2</sub>, misoprostol or prostacyclin. *J Nutr* 127:478–482.
- Kaufman DB, DiNicola W, McIntosh R. 1970. Acute potassium dichromate poisoning. Treated by peritoneal dialysis. *Am J Dis Child* 119:374–376.
- Keim KS, Stoecker BJ, Henley S. 1987. Chromium status of the rat as affected by phytate. *Nutr Res* 7:253–263.
- Kerger BD, Finley BL, Corbett GE, Dodge DG, Paustenbach DJ. 1997. Ingestion of chromium(VI) in drinking water by human volunteers: Absorption, distribution, and excretion of single and repeated doses. *J Toxicol Environ Health* 50:67–95.
- Kim WW, Mertz W, Judd JT, Marshall MW, Kelsay JL, Prather ES. 1984. Effect of making duplicate food collections on nutrient intakes calculated from diet records. *Am J Clin Nutr* 40:1333–1337.
- Kozlovsky AS, Moser PB, Reiser S, Anderson RA. 1986. Effects of diets high in simple sugars on urinary chromium losses. *Metabolism* 35:515–518.
- Kusiak RA, Ritchie AC, Springer J, Muller J. 1993. Mortality from stomach cancer in Ontario miners. *Br J Ind Med* 50:117–126.

- Kuykendall JR, Kerger BD, Jarvi EJ, Corbett GE, Paustenbach DJ. 1996. Measurement of DNA-protein cross-links in human leukocytes following acute ingestion of chromium in drinking water. *Carcinogenesis* 17:1971–1977.
- Levis AG, Majone F. 1979. Cytotoxic and clastogenic effects of soluble chromium compounds on mammalian cell cultures. *Br J Cancer* 40:523–533.
- Lim TH, Sargent T III, Kusubov N. 1983. Kinetics of trace element chromium(III) in the human body. *Am J Physiol* 244:R445–R454.
- Loubieres Y, de Lassence A, Bernier M, Vieillard-Baron A, Schmitt JM, Page B, Jardin F. 1999. Acute, fatal, oral chromic acid poisoning. *J Toxicol Clin Toxicol* 37:333–336.
- Lukaski HC, Bolonchuk WW, Siders WA, Milne DB. 1996. Chromium supplementation and resistance training: Effects on body composition, strength, and trace element status of men. *Am J Clin Nutr* 63:954–965.
- Mackenzie RD, Byerrum RU, Decker CF, Hoppert CA, Langham RF. 1958. Chronic toxicity studies. II. Hexavalent and trivalent chromium administered in drinking water to rats. *AMA Arch Industr Health* 18:232–234.
- Mahalko JR, Bennion M. 1976. The effect of parity and time between pregnancies on maternal hair chromium concentration. *Am J Clin Nutr* 29:1069–1072.
- Martin WR, Fuller RE. 1998. Suspected chromium picolinate-induced rhabdomyolysis. *Pharmacotherapy* 18:860–862.
- Martinez OB, MacDonald AC, Gibson RS, Bourn D. 1985. Dietary chromium and effect of chromium supplementation on glucose tolerance of elderly Canadian women. *Nutr Res* 5:609–620.
- Mertz W. 1969. Chromium occurrence and function in biological systems. *Physiol Rev* 49:163–239.
- Mertz W. 1993. Chromium in human nutrition: A review. *J Nutr* 123:626–633.
- Mertz W, Roginski EE, Schwarz K. 1961. Effect of trivalent chromium complexes on glucose uptake by epididymal fat tissue of rats. *J Biol Chem* 236:318–322.
- Mertz W, Roginski EE, Reba RC. 1965. Biological activity and fate of trace quantities of intravenous chromium(III) in the rat. *Am J Physiol* 209:489–494.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- Mohamedshah FY, Moser-Veillon PB, Yamini S, Douglass LW, Anderson RA, Veillon C. 1998. Distribution of a stable isotope of chromium ( $^{53}\text{Cr}$ ) in serum, urine, and breast milk in lactating women. *Am J Clin Nutr* 67:1250–1255.
- Moshtagchie AA, Ani M, Bazrafshan MR. 1992. Comparative binding study of aluminum and chromium to human transferrin: Effect of iron. *Biol Trace Elem Res* 32:39–46.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance Data, Vital and Health Statistics of the National Center for Health Statistics, No. 174. Hyattsville, MD: National Center for Health Statistics.
- Nakamuro K, Yoshikawa K, Sayato Y, Kurata H. 1978. Comparative studies of chromosomal aberration and mutagenicity of the trivalent and hexavalent chromium. *Mutat Res* 58:175–181.
- Newbold RF, Amos J, Connell JR. 1979. The cytotoxic, mutagenic and clastogenic effects of chromium-containing compounds on mammalian cells in culture. *Mutat Res* 67:55–63.

- Offenbacher EG. 1994. Promotion of chromium absorption by ascorbic acid. *Trace Elem Elect* 11:178–181.
- Offenbacher EG, Pi-Sunyer FX. 1983. Temperature and pH effects on the release of chromium from stainless steel into water and fruit juices. *J Agric Food Chem* 31:89–92.
- Offenbacher EG, Spencer H, Dowling HJ, Pi-Sunyer FX. 1986. Metabolic chromium balances in men. *Am J Clin Nutr* 44:77–82.
- Offenbacher EG, Pi-Sunyer FX, Stoecker BJ. 1997. Chromium. In: O'Dell BL, Sunde RA, eds. *Handbook of Nutritionally Essential Mineral Elements*. New York: Marcel Dekker. Pp. 389–411.
- O'Flaherty EJ. 1994. Comparison of reference dose with estimated safe and adequate daily dietary intake for chromium. In: Mertz W, Abernathy CO, Olin SS, eds. *Risk Assessment of Essential Elements*. Washington, DC: ILSI Press. Pp. 213–218.
- Onkelinx C. 1977. Compartment analysis of metabolism of chromium(III) in rats of various ages. *Am J Physiol* 232:E478–E484.
- Paschal DC, Ting BG, Morrow JC, Pirkle JL, Jackson RJ, Sampson EJ, Miller DT, Caldwell KL. 1998. Trace metals in the urine of United States residents: reference range concentrations. *Environ Res* 76:53–59.
- Raffetto G, Parodi S, Parodi C, De Ferrari M, Troiano R, Brambilla G. 1977. Direct interaction with cellular targets as the mechanism for chromium carcinogenesis. *Tumori* 63:503–512.
- Rubin MA, Miller JP, Ryan AS, Treuth MS, Patterson KY, Pratley RE, Hurley BF, Veillon C, Moser-Veillon PB, Anderson RA. 1998. Acute and chronic resistive exercise increase urinary chromium excretion in men as measured with an enriched chromium stable isotope. *J Nutr* 128:73–78.
- Saner G. 1981. The effect of parity on maternal hair chromium concentration and the changes during pregnancy. *Am J Clin Nutr* 34:853–855.
- Sargent T III, Lim TH, Jenson RL. 1979. Reduced chromium retention in patients with hemochromatosis, a possible basis of hemochromatotic diabetes. *Metabolism* 28:70–79.
- Schroeder HA, Balassa JJ, Tipton IH. 1962. Abnormal trace metals in man—Chromium. *J Chron Dis* 15:941–964.
- Schroeder HA, Balassa JJ, Vinton WH Jr. 1965. Chromium, cadmium and lead in rats: Effects on life span, tumors and tissue levels. *J Nutr* 86:51–66.
- Schwarz K, Mertz W. 1959. Chromium(III) and the glucose tolerance factor. *Arch Biochem Biophys* 85:292–295.
- Seaborn CD, Stoecker BJ. 1989. Effects of starch, sucrose, fructose, and glucose on chromium absorption and tissue concentrations in obese and lean mice. *J Nutr* 119:1444–1451.
- Seaborn CD, Stoecker BJ. 1990. Effects of antacid or ascorbic acid on tissue accumulation and urinary excretion of  $^{51}\text{Cr}$ chromium. *Nutr Res* 10:1401–1407.
- Speetjens JK, Collins RA, Vincent JB, Woski SA. 1999. The nutritional supplement chromium (III) tris(picolinate) cleaves DNA. *Chem Res Toxicol* 12:483–487.
- Stearns DM, Wise JP, Patierno SR, Wetterhahn KE. 1995. Chromium(III) picolinate produces chromosome damage in Chinese hamster ovary cells. *FASEB J* 9:1643–1648.
- Stella M, Montaldi A, Rossi R, Rossi G, Levis AG. 1982. Clastogenic effects of chromium on human lymphocytes in vitro and in vivo. *Mutat Res* 101:151–164.
- Stoecker BJ. 1996. Chromium. In: Ziegler EE, Filer LJ Jr, eds. *Present Knowledge in Nutrition*, 7th ed. Washington, DC: ILSI Press. Pp. 344–352.

- Stoecker BJ. 1999. Chromium. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th ed. Baltimore, MD: Williams & Wilkins. Pp. 281.
- Tsuda H, Kato K. 1977. Chromosomal aberrations and morphological transformation in hamster embryonic cells treated with potassium dichromate in vitro. *Mutat Res* 46:87–94.
- Umeda M, Nishimura M. 1979. Inducibility of chromosomal aberrations by metal compounds in cultured mammalian cells. *Mutat Res* 67:221–229.
- Veillon C. 1989. Analytical chemistry of chromium. *Sci Total Environ* 86:65–68.
- Venier P, Montaldi A, Majone F, Bianchi V, Levis AG. 1982. Cytotoxic, mutagenic and clastogenic effects of industrial chromium compounds. *Carcinogenesis* 3:1331–1338.
- Vincent JB. 1999. Mechanisms of chromium action: Low-molecular-weight chromium-binding substance. *J Am Coll Nutr* 18:6–12.
- Wasser WG, Feldman NS, D'Agati VD. 1997. Chronic renal failure after ingestion of over-the-counter chromium picolinate. *Ann Intern Med* 126:410.
- Welch RM, Cary EE. 1975. Concentration of chromium, nickel, and vanadium in plant materials. *J Agric Food Chem* 23:479–482.
- Whiting RF, Stich HF, Koropatnick DJ. 1979. DNA damage and DNA repair in cultured human cells exposed to chromate. *Chem Biol Interact* 26:267–280.

Ibid., Chapter 14, pp. 578–579.

- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Examination Survey: Under-reporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Gibson RS, Ferguson EL. 1998. Assessment of dietary zinc in a population. *Am J Clin Nutr* 68:430S–434S.
- Hallberg L, Hulthen L. 2000. Prediction of dietary iron absorption: An algorithm for calculating absorption and bioavailability of dietary iron. *Am J Clin Nutr* 71:1147–1160.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1980. *Recommended Dietary Allowances*, 9th ed. Washington, DC: National Academy Press.
- NRC. 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC. 1989. *Recommended Dietary Allowances*, 10th ed. Washington, DC: National Academy Press.

- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Schoeller DA. 1999. Recent advances from application of doubly labeled water to measurement of human energy expenditure. *J Nutr* 129:1765–1768.
- USDA (U.S. Department of Agriculture). 1999. *USDA Nutrient Database for Standard Reference*, Release 13. [Online.] Available: <http://www.nal.usda.gov/fnic/foodcomp> [accessed February 2000].
- WHO (World Health Organization). 1996. Zinc. In: *Trace Elements in Human Nutrition and Health*. Geneva: WHO. Pp. 72–104.

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*Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*  
 (ISBN 0-309-07290-5), Chapter 7, pp. 252–257.

- Anderson RR. 1992. Comparison of trace elements in milk of four species. *J Dairy Sci* 75:3050–3055.
- Anderson RR. 1993. Longitudinal changes of trace elements in human milk during the first 5 months of lactation. *Nutr Res* 13:499–510.
- ATSDR (Agency for Toxic Substances and Disease Registry). 1990. *Toxicological Profile for Copper*. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.
- August D, Janghorbani M, Young VR. 1989. Determination of zinc and copper absorption at three dietary Zn-Cu ratios by using stable isotopic methods in young adult and elderly subjects. *Am J Clin Nutr* 50:1457–1463.
- Baker A, Harvey L, Majask-Newman G, Fairweather-Tait S, Flynn A, Cashman K. 1999. Effect of dietary copper intakes on biochemical markers of bone metabolism in healthy adults. *Eur J Clin Nutr* 53:408–412.
- Berg R, Lundh S. 1981. Copper contamination of drinking water as a cause of diarrhea in children. *Halsovardskontakt* 1:6–10.
- Bhathena SJ, Werman MJ, Turnlund JR. 1998. Opioid peptides, adrenocorticotrophic hormone and dietary copper intake in humans. *Nutr Neurosci* 1:59–67.
- Biego GH, Joyeux M, Hartemann P, Debry G. 1998. Determination of mineral contents in different kinds of milk and estimation of dietary intake in infants. *Food Addit Contam* 15:775–781.
- Botash AS, Nasca J, Dubowy R, Weinberger HL, Oliphant M. 1992. Zinc-induced copper deficiency in an infant. *Am J Dis Child* 146:709–711.
- Brewer GJ, Hill GM, Prasad AS, Cossack ZT, Rabbani P. 1983. Oral zinc therapy for Wilson's disease. *Ann Intern Med* 99:314–319.
- Butte NF, Garza C, Smith EO, Wills C, Nichols BL. 1987. Macro- and trace-mineral intakes of exclusively breast-fed infants. *Am J Clin Nutr* 45:42–48.
- Casey CE, Hambidge KM, Neville MC. 1985. Studies in human lactation: Zinc, copper, manganese and chromium in human milk in the first month of lactation. *Am J Clin Nutr* 41:1193–1200.
- Casey CE, Neville MC, Hambidge KM. 1989. Studies in human lactation: Secretion of zinc, copper, and manganese in human milk. *Am J Clin Nutr* 49:773–785.
- Cordano A, Baertl JM, Graham GG. 1964. Copper deficiency in infancy. *Pediatrics* 34:324–336.
- Danks DM. 1988. Copper deficiency in humans. *Ann Rev Nutr* 8:235–257.
- da Silva FJ, Williams RJ. 1991. Copper: Extracytoplasmic oxidases and matrix formation. In: da Silva FJ, Williams RJ, eds. *The Biological Chemistry of the Elements: The Inorganic Chemistry of Life*. Oxford: Clarendon Press. Pp. 388–399.
- Davis GK, Mertz W. 1987. Copper. In: Mertz W, ed. *Trace Elements in Human and Animal Nutrition*, 5th ed. New York: Academic Press. Pp. 301–364.
- Dewey KG, Lonnerdal B. 1983. Milk and nutrient intake of breast-fed infants from 1 to 6 months: Relation to growth and fatness. *J Pediatr Gastroenterol Nutr* 2:497–506.

- Donohue J. 1997. New ideas after five years of the lead and copper rule: A fresh look at the MCLG for copper. In: Lagos GE, Badilla-Ohlbaum R, eds. *Advances in Risk Assessment of Copper in the Environment*. Santiago, Chile: Catholic University of Chile. Pp. 265–272.
- Dorner K, Dziadzka S, Hohn A, Sievers E, Oldigs HD, Schulz-Lell G, Schaub J. 1989. Longitudinal manganese and copper balances in young infants and preterm infants fed on breast-milk and adapted cow's milk formulas. *Br J Nutr* 61:559–572.
- EPA (Environmental Protection Agency). 1987. *Summary Review of the Health Effects Associated with Copper. Health Issue Assessment*. EPA/600/8-87/001. Cincinnati, OH: Environmental Criteria and Assessment Office, EPA.
- Fields M, Ferretti RJ, Smith JC, Reiser S. 1984. The interaction of type of dietary carbohydrates with copper deficiency. *Am J Clin Nutr* 39:289–295.
- Fransson GB, Lonnerdal B. 1983. Distribution of trace elements and minerals in human and cow's milk. *Pediatr Res* 17:912–915.
- Fransson GB, Lonnerdal B. 1984. Iron, copper, zinc, calcium, and magnesium in human milk fat. *Am J Clin Nutr* 39:185–189.
- Fujita M, Itakura T, Takagi Y, Okada A. 1989. Copper deficiency during total parenteral nutrition: Clinical analysis of three cases. *J Parent Enter Nutr* 13:421–425.
- Graham GG, Cordano A. 1969. Copper depletion and deficiency in the malnourished infant. *Johns Hopkins Med J* 124:139–150.
- Harris ED. 1997. Copper. In: O'Dell BL, Sunde RA, eds. *Handbook of Nutritionally Essential Mineral Elements*. New York: Marcel Dekker. Pp. 231–273.
- Harris ZL, Gitlin JD. 1996. Genetic and molecular basis for copper toxicity. *Am J Clin Nutr* 63:836S–841S.
- Haschke F, Ziegler EE, Edwards BB, Foman SJ. 1986. Effect of iron fortification of infant formula on trace mineral absorption. *J Pediatr Gastroenterol Nutr* 5:768–773.
- Higashi A, Ikeda T, Uehara I, Matsuda I. 1982. Zinc and copper contents in breast milk of Japanese women. *Tohoku J Exp Med* 137:41–47.
- Higuchi S, Higashi A, Nakamura T, Matsuda I. 1988. Nutritional copper deficiency in severely handicapped patients on a low copper enteral diet for a prolonged period: Estimation of the required dose of dietary copper. *J Pediatr Gastroenterol Nutr* 7:583–587.
- IPCS (International Programme on Chemical Safety). 1998. *Environmental Health Criteria 200: Copper*. Geneva: World Health Organization.
- Johnson PE, Canfield WK. 1989. Stable zinc and copper absorption in free-living infants fed breast milk or formula. *J Trace Elem Exp Med* 2:285–295.
- Johnson MA, Fisher JG, Kays SE. 1992. Is copper an antioxidant nutrient? *Crit Rev Food Sci Nutr* 32:1–31.
- Jones AA, Di Silvestro RA, Coleman M, Wagner TL. 1997. Copper supplementation of adult men: Effects on blood copper enzyme activities and indicators of cardiovascular disease risk. *Metabolism* 46:1380–1383.
- Joshi RM, Kagawala TY, Bharucha BA, Vaidya VU, Pandya AL, Parikh AP, Kumta NB. 1987. Wilson's disease (a study of 12 cases). *Indian J Gastroenterol* 6:227–228.
- Kehoe CA, Turley E, Bonham MP, O'Conner JM, McKeown A, Faughnan MS, Coulter JS, Gilmore WS, Howard AN, Strain JJ. 2000. Response of putative indices of copper status to copper supplementation in human subjects. *Br J Nutr* 84:151–156.

- Kelley DS, Daudu PA, Taylor PC, Mackey BE, Turnlund JR. 1995. Effects of low-copper diets on human immune response. *Am J Clin Nutr* 62:412–416.
- King RL, Luick JR, Litman II, Jennings WG, Dunkley WL. 1959. Distribution of natural and added copper and iron in milk. *J Dairy Sci* 42:780–790.
- Kishore N, Prasad R. 1993. A new concept: Pathogenesis of Indian childhood cirrhosis (ICC)—Hereditary alpha-I-antitrypsin deficiency. *J Trop Pediatr* 39:191–192.
- Klevay LM. 1989. Ischemic heart disease as copper deficiency. *Adv Exp Med Biol* 258:197–208.
- Klevay LM, Inman L, Johnson LK, Lawler M, Mahalko JR, Milne DB, Lukaski HC, Bolonchuk W, Sandstead HH. 1984. Increased cholesterol in plasma in a young man during experimental copper depletion. *Metabolism* 33:1112–1118.
- Klevay LM, Canfield WK, Gallagher SK, Henriksen LK, Lukaski HC, Bolonchuk W, Johnson LK, Milne DB, Sandstead HH. 1986. Decreased glucose tolerance in two men during experimental copper depletion. *Nutr Rep Int* 33:371–382.
- Knobeloch L, Ziarnik M, Howard J, Theis B, Farmer D, Anderson H, Proctor M. 1994. Gastrointestinal upsets associated with ingestion of copper-contaminated water. *Environ Health Perspect* 102:958–961.
- Lentner C. 1984. *Geigy Scientific Tables. Volume 3: Physical Chemistry of Blood, Hematology, Somatometric Data*. West Caldwell, NJ: CIBA-Geigy.
- Levy Y, Zeharia A, Grunebaum M, Nitzan M, Steinherz R. 1985. Copper deficiency in infants fed cow milk. *J Pediatr* 106:786–788.
- Linder MC, Hazegh-Azam M. 1996. Copper biochemistry and molecular biology. *Am J Clin Nutr* 63:797S–811S.
- Lipsman S, Dewey KG, Lonnerdal B. 1985. Breast-feeding among teenage mothers: Milk composition, infant growth, and maternal dietary intake. *J Pediatr Gastroenterol Nutr* 4:426–434.
- Lonnerdal B, Hernell O. 1994. Iron, zinc, copper and selenium status of breast-fed infants and infants fed trace element fortified milk-based infant formula. *Acta Paediatr* 83:367–373.
- Lukaski HC, Klevay LM, Milne DB. 1988. Effects of dietary copper on human autonomic cardiovascular function. *Eur J Appl Physiol* 58:74–80.
- Mason KE. 1979. A conspectus of research on copper metabolism and requirements of man. *J Nutr* 109:1979–2066.
- Medeiros DM, Milton A, Brunett E, Stacy L. 1991. Copper supplementation effects on indicators of copper status and serum cholesterol in adult males. *Biol Trace Elem Res* 30:19–35.
- Mertz W. 1987. Use and misuse of balance studies. *J Nutr* 117:1811–1813.
- Milne DB. 1994. Assessment of copper nutritional status. *Clin Chem* 40:1479–1484.
- Milne DB. 1998. Copper intake and assessment of copper status. *Am J Clin Nutr* 67:1041S–1045S.
- Milne DB, Nielsen FH. 1996. Effects of a diet low in copper on copper-status indicators in postmenopausal women. *Am J Clin Nutr* 63:358–364.
- Milne DB, Klevay LM, Hunt JR. 1988. Effects of ascorbic acid supplements and a diet marginal in copper on indices of copper nutriture in women. *Nutr Res* 8: 865–873.
- Milne DB, Nielsen FH, Lykken GI. 1991. Effects of dietary copper and sulfur amino acids on copper homeostasis and selected indices of copper status in men. *Trace Elem Man Anim* 7:5-12–5-13.

- Morais MB, Fisberg M, Suzuki HU, Amancio OM, Machado NL. 1994. Effects of oral iron therapy on serum copper and serum ceruloplasmin in children. *J Trop Pediatr* 40:51–52.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance Data, Vital and Health Statistics of the National Center for Health Statistics, Number 174. Hyattsville, MD: National Center for Health Statistics.
- NRC (National Research Council). 1977. *Medical and Biological Effects of Environmental Pollutants: Copper*. Washington, DC: National Academy of Sciences.
- O'Donohue J, Reid MA, Varghese A, Portmann B, Williams R. 1993. Micronodular cirrhosis and acute liver failure due to chronic copper self-intoxication. *Eur J Gastroenterol Hepatol* 5:561–562.
- Olivares M, Uauy R. 1996. Limits of metabolic tolerance to copper and biological basis for present recommendations and regulations. *Am J Clin Nutr* 63:846S–852S.
- Olivares M, Pizarro F, Speisky H, Lonnerdal B, Uauy R. 1998. Copper in infant nutrition: Safety of World Health Organization provisional guideline value for copper content of drinking water. *J Pediatr Gastroenterol Nutr* 26:251–257.
- Pandit A, Bhave S. 1996. Present interpretation of the role of copper in Indian childhood cirrhosis. *Am J Clin Nutr* 63:830S–835S.
- Pena MM, Lee J, Thiele DJ. 1999. A delicate balance: Homeostatic control of copper uptake and distribution. *J Nutr* 129:1251–1260.
- Pennington JA, Schoen SA, Salmon GD, Young B, Johnson RD, Marts RW. 1995. Composition of core foods of the U.S. food supply, 1982–1991. III. Copper, manganese, selenium, and iodine. *J Food Comp Anal* 8:171–217.
- Picciano MF, Guthrie HA. 1976. Copper, iron, and zinc contents of mature human milk. *Am J Clin Nutr* 29:242–254.
- Pizarro F, Olivares M, Uauy R, Contreras P, Rebelo A, Gidi V. 1999. Acute gastrointestinal effects of graded levels of copper in drinking water. *Environ Health Perspect* 107:117–121.
- Pratt WB, Omdahl JL, Sorenson JR. 1985. Lack of effects of copper gluconate supplementation. *Am J Clin Nutr* 42:681–682.
- Prohaska JR, Tamura T, Percy AK, Turnlund JR. 1997. In vitro copper stimulation of plasma peptidylglycine  $\alpha$ -amidating monooxygenase in Menkes disease variant with occipital horns. *Pediatr Res* 42:862–865.
- Raiten DJ, Talbot JM, Walters JH. 1998. Assessment of nutrient requirements for infant formulas. *J Nutr* 128:2059S–2294S.
- Reiser S, Smith JC, Mertz W, Holbrook JT, Scholfield DJ, Powell AS, Canfield WK, Canary JJ. 1985. Indices of copper status in humans consuming a typical American diet containing either fructose or starch. *Am J Clin Nutr* 42:242–251.
- Rossipal E, Krachler M. 1998. Pattern of trace elements in human milk during the course of lactation. *Nutr Res* 18:11–24.
- Salmenpera L, Perheentupa J, Pakarinen P, Siimes MA. 1986. Cu nutrition in infants during prolonged exclusive breast-feeding: Low intake but rising serum concentrations of Cu and ceruloplasmin. *Am J Clin Nutr* 43:251–257.
- Scheinberg IH, Sternlieb I. 1994. Is non-Indian childhood cirrhosis caused by excess dietary copper? *Lancet* 344:1002–1004.
- Scheinberg IH, Sternlieb I. 1996. Wilson disease and idiopathic copper toxicosis. *Am J Clin Nutr* 63:842S–845S.

- Schoenemann HM, Failla ML, Steele NC. 1990. Consequences of severe copper deficiency are independent of dietary carbohydrate in young pigs. *Am J Clin Nutr* 52:147–154.
- Shaw JCL. 1992. Copper deficiency in term and preterm infants. In: Fomon SJ, Zlotkin S, eds. *Nutritional Anemias*. New York: Vevey/Raven Press. Pp. 105–117.
- Shike M, Roulet M, Kurian R, Whitwell J, Steward S, Jeejeebhoy KN. 1981. Copper metabolism and requirements in total parenteral nutrition. *Gastroenterology* 81:290–297.
- Spitalny KC, Brondum J, Vogt RL, Sargent HE, Kappel S. 1984. Drinking-water-induced copper intoxication in a Vermont family. *Pediatrics* 74:1103–1106.
- Tanner MS. 1998. Role of copper in Indian childhood cirrhosis. *Am J Clin Nutr* 67:1074S–1081S.
- Toyokuni S, Sagripanti JL. 1994. Increased 8-hydroxydeoxyguanosine in kidney and liver of rats continuously exposed to copper. *Toxicol Appl Pharmacol* 126:91–97.
- Turnlund JR. 1998. Human whole-body copper metabolism. *Am J Clin Nutr* 67:960S–964S.
- Turnlund JR. 1999. Copper. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th ed. Baltimore: Williams & Wilkins. Pp. 241–252.
- Turnlund JR, Swanson CA, King JC. 1983. Copper absorption and retention in pregnant women fed diets based on animal and plant proteins. *J Nutr* 113:2346–2352.
- Turnlund JR, Keyes WR, Anderson HL, Acord LL. 1989. Copper absorption and retention in young men at three levels of dietary copper by use of the stable isotope  $^{65}\text{Cu}$ . *Am J Clin Nutr* 49:870–878.
- Turnlund JR, Keen CL, Smith RG. 1990. Copper status and urinary and salivary copper in young men at three levels of dietary copper. *Am J Clin Nutr* 51:658–664.
- Turnlund JR, Scott KC, Peiffer GL, Jang AM, Keyes WR, Keen CL, Sakanashi TM. 1997. Copper status of young men consuming a low-copper diet. *Am J Clin Nutr* 65:72–78.
- Turnlund JR, Keyes WR, Peiffer GL, Scott KC. 1998. Copper absorption, excretion, and retention by young men consuming low dietary copper determined by using the stable isotope  $^{65}\text{Cu}$ . *Am J Clin Nutr* 67:1219–1225.
- Uauy R, Castillo-Duran C, Fisberg M, Fernandez N, Valenzuela A. 1985. Red cell superoxide dismutase activity as an index of human copper nutrition. *J Nutr* 115:1650–1655.
- Vaughan LA, Weber CW, Kemberling SR. 1979. Longitudinal changes in the mineral content of human milk. *Am J Clin Nutr* 32:2301–2306.
- Vulpe CD, Kuo YM, Murphy TL, Cowley L, Askwith C, Libina N, Gitschier J, Anderson GJ. 1999. Hephaestin, a ceruloplasmin homologue implicated in intestinal iron transport, is defective in the *sla* mouse. *Nat Genet* 21:195–199.
- Vuori E, Kuitunen P. 1979. The concentrations of copper and zinc in human milk. A longitudinal study. *Acta Paediatr Scand* 68:33–37.
- Vuori E, Makinen SM, Kara R, Kuitunen P. 1980. The effects of the dietary intakes of copper, iron, manganese, and zinc on the trace element content of human milk. *Am J Clin Nutr* 33:227–231.
- Werman MJ, Bhathena SJ, Turnlund JR. 1997. Dietary copper intake influences skin lysyl oxidase in young men. *J Nutr Biochem* 8:201–204.

- WHO (World Health Organization). 1996. Copper. In: *Trace Elements in Human Nutrition and Health*. Geneva: WHO. Pp. 123–143.
- Widdowson EM, Dickerson JWT. 1964. Chemical composition of the body. In: Comar CL, Bronner F, eds. *Mineral Metabolism: An Advanced Treatise*, Vol. II, Part A. New York: Academic Press. Pp. 1–248.
- Wylie J. 1957. Copper poisoning at a cocktail party. *Am J Public Health* 47:617.
- Yuzbasiyan-Gurkan V, Grider A, Nostrant T, Cousins RJ, Brewer GJ. 1992. Treatment of Wilson's disease with zinc: X. Intestinal metallothionein induction. *J Lab Clin Med* 120:380–386.

Ibid., Chapter 14, pp. 578–579.

- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Examination Survey: Under-reporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Gibson RS, Ferguson EL. 1998. Assessment of dietary zinc in a population. *Am J Clin Nutr* 68:430S–434S.
- Hallberg L, Hulthen L. 2000. Prediction of dietary iron absorption: An algorithm for calculating absorption and bioavailability of dietary iron. *Am J Clin Nutr* 71:1147–1160.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1980. *Recommended Dietary Allowances*, 9th ed. Washington, DC: National Academy Press.
- NRC. 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC. 1989. *Recommended Dietary Allowances*, 10th ed. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Schoeller DA. 1999. Recent advances from application of doubly labeled water to measurement of human energy expenditure. *J Nutr* 129:1765–1768.
- USDA (U.S. Department of Agriculture). 1999. *USDA Nutrient Database for Standard Reference*, Release 13. [Online.] Available: <http://www.nal.usda.gov/fnic/foodcomp> [accessed February 2000].
- WHO (World Health Organization). 1996. Zinc. In: *Trace Elements in Human Nutrition and Health*. Geneva: WHO. Pp. 72–104.

## FLUORIDE

*Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride (ISBN 0-309-06350-7)*, pp. 325–374.

- Abbott L, Nadler J, Rude RK. 1994. Magnesium deficiency in alcoholism: Possible contribution to osteoporosis and cardiovascular disease in alcoholics. *Alcohol Clin Exp Res* 18:1976–1082.
- Abe E, Miyaura C, Sakagami H, Takeda M, Konno K, Yamazaki T, Yoshiki S, Suda T. 1981. Differentiation of mouse myeloid leukemia cells induced by 1 $\alpha$ 25-dihydroxyvitamin D<sub>3</sub>. *Proc Natl Acad Sci USA* 78:4990–4994.
- Abraham GE, Grewal H. 1990. A total dietary program emphasizing magnesium instead of calcium: Effect on the mineral density of calcaneous bone in postmenopausal women on hormonal therapy. *J Reprod Med* 35:503–507.
- Abrams SA, Stuff JE. 1994. Calcium metabolism in girls: Current dietary intakes lead to low rates of calcium absorption and retention during puberty. *Am J Clin Nutr* 60:739–743.
- Abrams SA, Sidbury JB, Muenzer J, Esteban NV, Vieira NE, Yerger AL. 1991. Stable isotopic measurement of endogenous fecal calcium excretion in children. *J Pediatr Gastroenterol Nutr* 12:469–473.
- Abrams SA, Esteban NV, Vieira NE, Sidbury JB, Specker BL, Yerger AL. 1992. Developmental changes in calcium kinetics in children assessed using stable isotopes. *J Bone Miner Res* 7:287–293.
- Abrams SA, Silber TJ, Esteban NV, Vieira NE, Stuff JE, Meyers R, Majd M, Yerger AL. 1993. Mineral balance and bone turnover in adolescents with anorexia nervosa. *J Pediatr* 123:326–331.
- Abrams SA, O'Brien KO, Stuff JE. 1996a. Changes in calcium kinetics associated with menarche. *J Clin Endocrin Metab* 81:2017–2020.
- Abrams SA, O'Brien KO, Wen J, Liang LK, Stuff JE. 1996b. Absorption by 1-year-old children of an iron supplement given with cow's milk or juice. *Pediatr Res* 39:171–175.
- Abrams SA, Wen J, Stuff JE. 1997a. Absorption of calcium, zinc and iron from breast milk by 5- to 7-month-old infants. *Pediatr Res* 41:1–7.
- Abrams SA, Grusak MA, Stuff J, O'Brien KO. 1997b. Calcium and magnesium balance in 9- to 14-year-old children. *Am J Clin Nutr* 66:1172–1177.
- Abreo K, Adlakha A, Kilpatrick S, Flanagan R, Webb R, Shakamuri S. 1993. The Milk-Alkali Syndrome. A reversible form of acute renal failure. *Arch Intern Med* 153:1005–1010.
- Ackerman PG, Toro G. 1953. Calcium and phosphorus balance in elderly men. *J Gerontol* 8:298–300.
- ADA (American Dental Association Council on Dental Therapeutics). 1994. New fluoride guidelines proposed. *J Am Dent Assoc* 125:366.
- Adams JS. 1989. Vitamin D metabolite-mediated hypercalcemia. *Endocrinol Metab Clin North Am* 18:765–778.
- Adams JS, Beeker TG, Hongo T, Clemens TL. 1990. Constitutive expression of a vitamin D 1-hydroxylase in a myelomonocytic cell line: A model for studying 1,25-dihydroxyvitamin D production in vitro. *J Bone Miner Res* 5:1265–1269.
- Affinito P, Tommaselli GA, DiCarlo C, Guida F, Nappi C. 1996. Changes in bone mineral density and calcium metabolism in breast-feeding women: A one year follow-up study. *J Clin Endocrinol Metab* 81:2314–2318.

- Aksnes L, Aarskog D. 1982. Plasma concentrations of vitamin D metabolites in puberty: Effect of sexual maturation and implications for growth. *J Clin Endocrinol Metab* 55:94–101.
- Ala-Houhala M. 1985. 25-Hydroxyvitamin D levels during breast-feeding with or without maternal or infantile supplementation of vitamin D. *J Pediatr Gastroenterol Nutr* 4:220–226.
- Ala-Houhala M, Parvianinen MT, Pyyko K, Visakorpi JK. 1984. Serum 25-hydroxyvitamin D levels in Finnish children aged 2 to 17 years. *Acta Paediatr Scand* 73:232–236.
- Ala-Houhala M, Koskinen T, Terho A, Koivula T, Visakorpi J. 1986. Maternal compared with infant vitamin D supplementation. *Arch Dis Child* 61:1159–1163.
- Alaimo K, McDowell MA, Briefel RR, Bischof AM, Caughman CR, Loria CM, Johnson CL. 1994. *Dietary Intake of Vitamins, Minerals, and Fiber of Persons Ages 2 Months and Over in the United States: Third National Health and Nutrition Examination Survey, Phase I, 1988–91*. Advance data from vital and health statistics; no. 258. U.S. Department of Health and Human Services. Hyattsville, MD: National Center for Health Statistics.
- Albert DG, Morita Y, Iseri LT. 1958. Serum magnesium and plasma sodium levels in essential vascular hypertension. *Circulation* 17:761–764.
- Alderman BW, Weiss NS, Daling JR, Ure CL, Ballard JH. 1986. Reproductive history and postmenopausal risk of hip and forearm fracture. *Am J Epidemiol* 124:262–267.
- Alfrey AC, Miller NL, Butkus D. 1974. Evaluation of body magnesium stores. *J Lab Clin Med* 84:153–162.
- Allen JC, Keller RP, Archer P, Neville MC. 1991. Studies in human lactation: Milk composition and daily secretion rates of macronutrients in the first year of lactation. *Am J Clin Nutr* 54:69–80.
- Allen SH, Shah JH. 1992. Calcinosis and metastatic calcification due to vitamin D intoxication. A case report and review. *Horm Res* 37:68–77.
- Allender PS, Cutler JA, Follmann D, Cappuccio FP, Pryer J, Elliott P. 1996. Dietary calcium and blood pressure: A meta-analysis of randomized clinical trials. *Ann Intern Med* 124:825–831.
- Aloia JF, Vaswani AN, Yeh JK, Ross P, Ellis K, Cohn SH. 1983. Determinants of bone mass in postmenopausal women. *Arch Intern Med* 143:1700–1704.
- Aloia JF, Vaswani AN, Yeh JK, Ellis K, Cohn SH. 1984. Total body phosphorus in postmenopausal women. *Miner Electrolyte Metab* 10:73–76.
- Aloia JF, Vaswani A, Yeh JK, Ross PL, Flaster E, Dilmanian FA. 1994. Calcium supplementation with and without hormone replacement therapy to prevent postmenopausal bone loss. *Ann Intern Med* 120:97–103.
- Altura BT, Brust M, Bloom S, Barbour RL, Stempak JG, Altura BM. 1990. Magnesium dietary intake modulates blood lipid levels and atherogenesis. *Proc Natl Acad Sci USA* 87:1840–1844.
- Altura BT, Shirey TL, Hiti J, Dell'Orfano K, Handwerker SM, Altura BM. 1992. A new method for the rapid determination of ionized Mg<sup>2+</sup> in whole blood, serum and plasma. *Methods Find Exp Clin Pharmacol* 14:297–304.
- Altura BT, Wilimzig C, Trnovec T, Nyulassy S, Altura BM. 1994. Comparative effects of a Mg-enriched diet and different orally administered magnesium oxide preparations on ionized Mg, Mg metabolism and electrolytes in serum of human volunteers. *J Am Coll Nutr* 13:447–454.
- American Academy of Pediatrics. 1982. The promotion of breastfeeding: Policy statement based on task force report. *Pediatrics* 69:654–661.

- Anderson DM, Hollis BW, LeVine BR, Pittard WB III. 1988. Dietary assessment of maternal vitamin D intake and correlation with maternal and neonatal serum vitamin D concentrations at delivery. *J Perinatol* 8:46–48.
- Andon MB, Ilich JZ, Tzagournis MA, Matkovic V. 1996. Magnesium balance in adolescent females consuming a low- or high-calcium diet. *Am J Clin Nutr* 63:950–953.
- Angus RM, Sambrook PN, Pockock NA, Eisman JA. 1988. Dietary intake and bone mineral density. *Bone Miner* 4:265–277.
- Antman EM. 1996. Magnesium in acute myocardial infarction: Overview of available evidence. *Am Heart J* 132:487–495.
- Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin PH, Karanja N. 1997. A clinical trial of the effects of dietary patterns on blood pressure. *N Engl J Med* 336:1117–1124.
- Arnold FA Jr, Dean HT, Jay P, Knutson JW. 1956. Effect of fluoridated public water supplies on dental caries prevalence. Tenth year of the Grand Rapids-Muskegon Study. *Pub Hlth Rep* 71:652–658.
- Ascherio A, Rimm EB, Giovannucci EL, Colditz GA, Rosner B, Willett WC, Sacks F, Stampfer MJ. 1992. A prospective study of nutritional factors and hypertension among U.S. men. *Circulation* 86:1475–1484.
- Ashe JR, Schofield FA, Gram MR. 1979. The retention of calcium, iron, phosphorus, and magnesium during pregnancy: The adequacy of prenatal diets with and without supplementation. *Am J Clin Nutr* 32:286–291.
- Atkinson SA, Chappell JE, Clandinin MT. 1987. Calcium supplementation of mothers' milk for low birthweight infants: Problems related to absorption and excretion. *Nutr Res* 7:813–823.
- Atkinson SA, Alston-Mills BP, Lonnerdal B, Neville MC, Thompson MP. 1995. Major minerals and ionic constituents of human and bovine milk. In: Jensen RJ, ed. *Handbook of Milk Composition*. California: Academic Press. Pp. 593–619.
- Bainbridge RR, Mimouni FB, Landi T, Crossman M, Harris L, Tsang RC. 1996. Effect of rice cereal feedings on bone mineralization and calcium homeostasis in cow milk formula fed infants. *J Am Coll Nutr* 15:383–388.
- Baran D, Sorensen A, Grimes J, Lew R, Karella A, Johnson B, Roche J. 1990. Dietary modification with dairy products for preventing vertebral bone loss in premenopausal women: A three-year prospective study. *J Clin Endocrinol Metab* 70:264–270.
- Bardicef M, Bardicef O, Sorokin Y, Altura BM, Altura BT, Cotton DB, Resnick LM. 1995. Extracellular and intracellular magnesium depletion in pregnancy and gestational diabetes. *Am J Obstet Gynecol* 172:1009–1013.
- Barger-Lux MJ, Heaney RP. 1995. Caffeine and the calcium economy revisited. *Osteopor Int* 5:97–102.
- Barger-Lux MJ, Heaney RP, Stegman MR. 1990. Effects of moderate caffeine intake on the calcium economy of premenopausal women. *Am J Clin Nutr* 52:722–725.
- Barger-Lux MJ, Heaney RP, Lanspa SJ, Healy JC, DeLuca HF. 1995. An investigation of sources of variation in calcium absorption efficiency. *J Clin Endocrinol Metab* 80:406–411.
- Barger-Lux MJ, Heaney RP, Dowell S, Bierman J, Holick MF, Chen TC. 1996. Relative molar potency of 25-hydroxyvitamin D indicates a major role in calcium absorption. *J Bone Miner Res* 11:S423.

- Barnhart WE, Hiller LK, Leonard GJ, Michaels SE. 1974. Dentifrice usage and ingestion among four age groups. *J Dent Res* 53:1317–1322.
- Barragry JM, France MW, Corless D, Gupta SP, Switala S, Boucher BJ, Cohen RD. 1978. Intestinal cholecalciferol absorption in the elderly and in younger adults. *Clin Sci Molec Med* 55:213–220.
- Barrett-Connor E, Chang JC, Edelstein SL. 1994. Coffee-associated osteoporosis offset by daily milk consumption. The Rancho Bernardo Study. *J Am Med Assoc* 271:280–283.
- Bashir Y, Sneddon JF, Staunton HA, Haywood GA, Simpson IA, McKenna WJ, Camm AJ. 1993. Effects of long-term oral magnesium chloride replacement in congestive heart failure secondary to coronary artery disease. *Am J Cardiol* 72:1156–1162.
- Beall DP, Scofield RH. 1995. Milk-alkali syndrome associated with calcium carbonate consumption: Report of 7 patients with parathyroid hormone levels and an estimate of prevalence among patients hospitalized with hypercalcemia. *Medicine* 74:89–96.
- Beaton GH. 1994. Criteria of an adequate diet. In: Shils RE, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease, 8th edition*. Philadelphia: Lea & Febiger. Pp. 1491–1505.
- Beaton GH. 1996. Statistical approaches to establish mineral element recommendations. *J Nutr* 126:2302S–2328S.
- Begum A, Pereira SM. 1969. Calcium balance studies on children accustomed to low calcium intakes. *Br J Nutr* 23:905–911.
- Bell NH, Greene A, Epstein S, Oexmann MJ, Shaw S, Shary J. 1985. Evidence for alteration of the vitamin D-endocrine system in blacks. *J Clin Invest* 76:470–473.
- Bell NH, Shary J, Stevens J, Garza M, Gordon L, Edwards J. 1991. Demonstration that bone mass is greater in black than in white children. *J Bone Miner Res* 6:719–723.
- Bell NH, Yergey AL, Vieira NE, Oexmann MJ, Shary JR. 1993. Demonstration of a difference in urinary calcium, not calcium absorption, in black and white adolescents. *J Bone Miner Res* 8:1111–1115.
- Bell RA, Whitford GM, Barenie JT, Myers DR. 1985. Fluoride retention in children using self-applied topical fluoride products. *Clin Prev Dent* 7:22–27.
- Berkelhammer CH, Wood RJ, Sitrin MD. 1988. Acetate and hypercalciuria during total parenteral nutrition. *Am J Clin Nutr* 48:1482–1489.
- Bernstein DS, Sadowsky N, Hegsted DM, Guri CD, Stare FJ. 1966. Prevalence of osteoporosis in high- and low-fluoride areas in North Dakota. *J Am Med Assoc* 198:499–504.
- Bijvoet, OLM. 1969. Relation of plasma phosphate concentration to renal tubular reabsorption of phosphate. *Clin Sci* 37:23–26.
- Bikle DD, Gee E, Halloran B, Haddad JG. 1984. Free 1,25-dihydroxyvitamin D levels in serum from normal subjects, pregnant subjects, and subjects with liver disease. *J Clin Invest* 74:1966–1971.
- Birkeland JM, Charlton G. 1976. Effect of pH on the fluoride ion activity of plaque. *Caries Res* 10:72–80.
- Bishop NJ, Dahlenburg SL, Fewtrell MS, Morley R, Lucas A. 1996. Early diet of preterm infants and bone mineralization at age five years. *Acta Paediatr* 85:230–236.
- Bizik BK, Ding W, Cerklewski FL. 1996. Evidence that bone resorption of young men is not increased by high dietary phosphorus obtained from milk and cheese. *Nutr Res* 16:1143–1146.

- Black DM, Cummings SR, Genant HK, Nevitt MC, Palermo L, Browner W. 1992. Axial and appendicular bone density predict fractures in older women. *J Bone Miner Res* 7:633–638.
- Blank S, Scanlon KS, Sinks TH, Lett S, Falk H. 1995. An outbreak of hypervitaminosis D associated with the overfortification of milk from a home-delivery dairy. *Am J Publ Health* 85:656–659.
- Blayney JR, Hill IN. 1964. Evanston dental caries study XXIV. Prenatal fluorides—value of waterborne fluorides during pregnancy. *J Am Dent Assoc* 69:291–294.
- Bodanszky H, Leleiko N. 1985. Metabolic alkalosis with hypertonic dehydration in a patient with diarrhoea and magnesium oxide ingestion. *Acta Paediatr Hung* 26:241–246.
- Bogdonoff MD, Shock NW, Nichols MP. 1953. Calcium, phosphorus, nitrogen, and potassium balance studies in the aged male. *J Gerontol* 8:272–288.
- Bostick RM, Potter JD, Fosdick L, Grambsch P, Lampe JW, Wood JR, Louis TA, Ganz R, Grandits G. 1993. Calcium and colorectal epithelial cell proliferation: A preliminary randomized, double-blinded, placebo-controlled clinical trial. *J Natl Cancer Inst* 85:132–141.
- Boston JL, Beauchene RE, Cruikshank DP. 1989. Erythrocyte and plasma magnesium during teenage pregnancy: Relationship with blood pressure and pregnancy-induced hypertension. *Obstet Gynecol* 73:169–174.
- Bouillon R, Van Assche FA, Van Baelen H, Heuvel W, De Moor P. 1981. Influence of the vitamin D-binding protein on the serum concentration of 1,25-dihydroxyvitamin D<sub>3</sub>. Significance of the free 1,25-dihydroxyvitamin D<sub>3</sub> concentration. *J Clin Invest* 67:589–596.
- Bour NJS, Soullier BA, Zemel MB. 1984. Effect of level and form of phosphorus and level of calcium intake on zinc, iron and copper bioavailability in man. *Nutr Res* 4:371–379.
- Bowden GH. 1990. Effects of fluoride on the microbial ecology of dental plaque. *J Dent Res* 69 (Spec Iss):653–659.
- Boyle DR, Chagnon M. 1995. An incidence of skeletal fluorosis associated with groundwaters of the maritime carboniferous basin, Gaspe Region, Quebec, Canada. *Environ Geochem Health* 17:5–12.
- BPA (British Paediatric Association). 1956. Hypercalcaemia in infants and Vitamin D. *Br Med J* 2:149.
- BPA (British Paediatric Association). 1964. Infantile hypercalcaemia, nutritional rickets, and infantile scurvy in Great Britain. *Br Med J* 1:1659–1661.
- Brambilla E, Belluomo G, Malerba A, Buscaglia M, Strohmenger L. 1994. Oral administration of fluoride in pregnant women, and the relation between concentration in maternal plasma and in amniotic fluid. *Arch Oral Biol* 39:991–994.
- Brandwein SL, Sigman, KM. 1994. Case report: Milk-alkali syndrome and pancreatitis. *Am J Med Sci* 308:173–176.
- Brannan PG, Vergne-Marini P, Pak CY, Hull AR, Fordtran JS. 1976. Magnesium absorption in the human small intestine. Results in normal subjects, patients with chronic renal disease, and patients with absorptive hypercalciuria. *J Clin Invest* 57:1412–1418.
- Bransby ER, Berry WTC, Taylor DM. 1964. Study of the vitamin-D intakes of infants in 1960. *Br Med J* 1:1661–1663.
- Brazier M, Kamel S, Maamer M, Agbomson F, Elesper I, Garabedian M, Desmet G, Sebert JL. 1995. Markers of bone remodeling in the elderly subject: Effects of vitamin D insufficiency and its correction. *J Bone Miner Res* 10:1753–1761.

- Brickman AS, Coburn JW, Massry SG. 1974. 1,25 dihydroxy-vitamin D<sub>3</sub> in normal man and patients with renal failure. *Ann Intern Med* 80:161–168.
- Brink EJ, Beynen AC. 1992. Nutrition and magnesium absorption: A review. *Prog Food Nutr Sci* 16:125–162.
- Brodehl J, Gellissen K, Weber H-P. 1982. Postnatal development of tubular phosphate reabsorption. *Clin Nephrol* 17:163–171.
- Brown WE, Gregory TM, Chow LC. 1977. Effects of fluoride on enamel solubility and cariostasis. *Caries Res* 11(Suppl 1):118–141.
- Brunelle JA, Carlos JP. 1990. Recent trends in dental caries in U.S. children and the effect of water fluoridation. *J Dent Res* 69(Spec Iss):723–727.
- Bruun C, Thylstrup A. 1988. Dentifrice usage among Danish children. *J Dent Res* 67:1114–1117.
- Bucher HC, Cook RJ, Guyatt GH, Lang JD, Cook DJ, Hatala R, Hunt DL. 1996. Effects of dietary calcium supplementation on blood pressure: A meta-analysis of randomized controlled trials. *J Am Med Assoc* 275:1016–1022.
- Bucuvalas JC, Heubi JE, Specker BL, Gregg DJ, Yerger AL, Vieira NE. 1990. Calcium absorption in bone disease associated with chronic cholestasis during childhood. *Hepatology* 12:1200–1205.
- Bullamore JR, Wilkinson R, Gallagher JC, Nordin BEC, Marshall DH. 1970. Effects of age on calcium absorption. *Lancet* 2:535–537.
- Bullimore DW, Miloszewski KJ. 1987. Raised parathyroid hormone levels in the milk-alkali syndrome: An appropriate response? *Postgrad Med J* 63:789–792.
- Burt BA. 1992. The changing patterns of systemic fluoride intake. *J Dent Res* 71:1228–1237.
- Burtis WJ, Gay L, Insogna KL, Ellison A, Broadus AE. 1994. Dietary hypercalciuria in patients with calcium oxalate kidney stones. *Am J Clin Nutr* 60:424–429.
- Bushe CJ. 1986. Profound hypophosphataemia in patients collapsing after a “fun run.” *Br Med J* 292:898–899.
- Butte NF, Garza C, Smith EO, Nichols BL. 1984. Human milk intake and growth in exclusively breast-fed infants. *J Pediatr* 104:187–195.
- Buzzard IM, Willett WC, eds. 1994. Dietary assessment methods. Proceedings of a conference held in St. Paul, MN. *Am J Clin Nutr* 59:143S–306S.
- Byrne J, Thomas MR, Chan GM. 1987. Calcium intake and bone density of lactating women in their late childbearing years. *J Am Diet Assoc* 87:883–887.
- Byrne PM, Freaney R, McKenna MJ. 1995. Vitamin D supplementation in the elderly: Review of safety and effectiveness of different regimens. *Calcif Tissue Int* 56:518–520.
- Caddell JL, Ratananon N, Trangratapit P. 1973. Parenteral magnesium load tests in postpartum Thai women. *Am J Clin Nutr* 26:612–615.
- Caddell JL, Saier FL, Thomason CA. 1975. Parenteral magnesium load tests in postpartum American women. *Am J Clin Nutr* 28:1099–1104.
- Calvo MS. 1993. Dietary phosphorus, calcium metabolism and bone. *J Nutr* 123:1627–1633.
- Calvo MS, Heath H III. 1988. Acute effects of oral phosphate-salt ingestion on serum phosphorus, serum ionized calcium, and parathyroid hormone in young adults. *Am J Clin Nutr* 47:1025–1029.
- Calvo MS, Park YK. 1996. Changing phosphorus content of the U.S. diet: Potential for adverse effects on bone. *J Nutr* 126:1168S–1180S.
- Calvo MS, Kumar R, Heath H III. 1988. Elevated secretion and action of serum parathyroid hormone in young adults consuming high phosphorus, low calcium diets assembled from common foods. *J Clin Endocrinol Metab* 66:823–829.

- Calvo MS, Kumar R, Heath H. 1990. Persistently elevated parathyroid hormone secretion and action in young women after four weeks of ingesting high phosphorus, low calcium diets. *J Clin Endocrinol Metab* 70:1334–1340.
- Campbell SB, MacFarlane DJ, Fleming SJ, Khafagi FA. 1994. Increased skeletal uptake of Tc-99m Methylene Disphosphonate in Milk-Alkali Syndrome. *Clin Nucl Med* 19:207–211.
- Canadian Paediatric Society (Nutrition Committee). 1991. Meeting the iron needs of infants and young children: An update. *Can Med Assoc J* 144:1451–1454.
- Canadian Paediatric Society. 1996. The use of fluoride in infants and children. *Paediatr Child Health* 1:131–134.
- Cappuccio FP, Markandu ND, Beynon GW, Shore AC, Sampson B, MacGregor GA. 1985. Lack of effect of oral magnesium on high blood pressure: A double blind study. *Br Med J Clin Res Ed* 291:235–238.
- Carlos JP, Gittelsohn AM, Haddon W Jr. 1962. Caries in deciduous teeth in relation to maternal ingestion of fluoride. *Pub Hlth Rep* 77:658–660.
- Carroll MD, Abraham S, Dresser CM. 1983. Dietary intake source data: United States, 1976–1980. Data from the National Health Survey. Vital and Health Statistics series 11, no. 231. DHHS Publ. No. (PHS) 83-1681. Hyattsville, MD: National Center for Health Statistics, Public Health Service, U.S. Department of Health and Human Services.
- Chan GM. 1991. Dietary calcium and bone mineral status of children and adolescents. *Am J Dis Child* 145:631–634.
- Chan GM, Roberts CC, Folland D, Jackson R. 1982a. Growth and bone mineralization of normal breast-fed infants and the effects of lactation on maternal bone mineral status. *Am J Clin Nutr* 36:438–443.
- Chan GM, Slater RN, Hollis J, Thomas MR. 1982b. Decreased bone mineral status in lactating adolescent mothers. *J Pediatr* 101:767–770.
- Chan GM, Leeper L, Book LS. 1987. Effects of soy formulas on mineral metabolism in term infants. *Am J Dis Child* 141:527–530.
- Chan GM, Hoffman K, McMurry M. 1995. Effects of dairy products on bone and body composition in pubertal girls. *J Pediatr* 126:551–556.
- Chan JT, Koh SH. 1996. Fluoride content in caffeinated, decaffeinated and herbal teas. *Caries Res* 30:88–92.
- Chan JT, Qui CC, Whitford GM, Weatherred JG. 1990. Influence of coffee on fluoride metabolism in rats. *Proc Soc Exp Biol Med* 194:43–47.
- Chandra RK. 1984. Physical growth of exclusively breast-fed infants. *Nutr Res* 2:275–276.
- Chapuy MC, Arlot ME, Duboeuf F, Brun J, Crouzet B, Arnaud S, Delmas PD, Meunier PJ. 1992. Vitamin D<sub>3</sub> and calcium to prevent hip fractures in elderly women. *N Engl J Med* 327:1637–1642.
- Charles P, Jensen FT, Mosekilde L, Hansen HH. 1983. Calcium metabolism evaluated by <sup>47</sup>Ca kinetics: Estimation of dermal calcium loss. *Clin Sci* 65:415–422.
- Chen TC, Castillo L, Korycka-Dahl M, DeLuca HF. 1974. Role of vitamin D metabolites in phosphate transport of rat intestine. *J Nutr* 104:1056–1060.
- Chen TC, Shao A, Heath H III, Holick MF. 1993. An update on the vitamin D content of fortified milk from the United States and Canada. *N Engl J Med* 329:1507.
- Chen X, Whitford GM. 1994. Lack of significant effect of coffee and caffeine on fluoride metabolism in rats. *J Dent Res* 73:1173–1179.
- Chesney RW. 1990. Requirements and upper limits of vitamin D intake in the term neonate, infant, and older child. *J Pediatr* 116:159–166.

- Chevalley T, Rizzoli R, Nydegger V, Slosman D, Rapin CH, Michel JP, Vasey H, Bonjour JP. 1994. Effects of calcium supplements on femoral bone mineral density and vertebral fracture rate in vitamin D-replete elderly patients. *Osteopor Int* 4:245–252.
- Chinn HI. 1981. Effects of dietary factors on skeletal integrity in adults: Calcium, phosphorus, vitamin D, and protein. Prepared for Bureau of Foods, Food and Drug Administration, U.S. Department of Health and Human Services, Washington, D.C.
- Cholak J. 1959. Fluorides: A critical review. I. The occurrence of fluoride in air, food and water. *J Occup Med* 1:501–511.
- Chow LC. 1990. Tooth-bound fluoride and dental caries. *J Dent Res* 69(Spec Iss):595–600.
- Clark DC, Hann HJ, Williamson MF, Berkowitz J. 1993. Aesthetic concerns of children and parents in relation to different classifications of the Tooth Surface Index of Fluorosis. *Community Dent Oral Epidemiol* 21:360–364.
- Clarkson EM, Warren RL, McDonald SJ, de Wardener HE. 1967. The effect of a high intake of calcium on magnesium metabolism in normal subjects and patients with chronic renal failure. *Clin Sci* 32:11–18.
- Clarkson PM, Haymes EM. 1995. Exercise and mineral status of athletes: Calcium, magnesium, phosphorus, and iron. *Med Sci Sports Exerc* 27:831–843.
- Clemens TL, Adams JS. 1996. Vitamin D metabolites. In: Favus MJ, Christakos S, eds. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 3rd edition*. Philadelphia, PA: Lippincott-Raven. Pp. 109–114.
- Clemens TL, Adams JS, Henderson SL, Holick MF. 1982. Increased skin pigment reduces the capacity of skin to synthesise vitamin D<sub>3</sub>. *Lancet* 1:74–76.
- Clemens TL, Zhou X, Myles M, Endres D, Lindsay R. 1986. Serum vitamin D<sub>2</sub> and vitamin D<sub>3</sub> metabolite concentrations and absorption of vitamin D<sub>2</sub> in elderly subjects. *J Clin Endocrinol Metab* 63:656–660.
- Cleveland LE, Goldman JD, Borrud LG. 1996. *Data Tables: Results from USDA's 1994 Continuing Survey of Food Intakes by Individuals and 1994 Diet and Health Knowledge Survey*. Beltsville, MD: Agricultural Research Service, U.S. Department of Agriculture.
- Clovis J, Hargreaves JA. 1988. Fluoride intake from beverage consumption. *Community Dent Oral Epidemiol* 16:11–15.
- CNPP, USDA (Center for Nutrition Policy and Promotion, U.S. Department of Agriculture). 1996. *Nutrient Content of the U.S. Food Supply, 1990–1994. Preliminary Data*. Washington, DC: U.S. Department of Agriculture.
- Cockburn F, Belton NR, Purvis RJ, Giles MM, Brown JK, Turner TL, Wilkinson EM, Forfar JO, Barrie WJM, McKay GS, Pocock SJ. 1980. Maternal vitamin D intake and mineral metabolism in mothers and their newborn infants. *Br Med J* 281:11–14.
- Coffin B, Azpiroz F, Guarner F, Malagelada JR. 1994. Selective gastric hypersensitivity and reflex hyporeactivity in functional dyspepsia. *Gastroenterology* 107:1345–1351.
- Cohen L. 1988. Recent data on magnesium and osteoporosis. *Magnes Res* 1:85–87.
- Cohen L, Laor A. 1990. Correlation between bone magnesium concentration and magnesium retention in the intravenous magnesium load test. *Magnes Res* 3:271–274.
- Cohn SH, Abesamis C, Yasumura S, Aloia JF, Zanzi I, Ellis KJ. 1977. Comparative skeletal mass and radial bone mineral content in black and white women. *Metabolism* 26:171–178.

## ONLINE REFERENCES

## 1067

- Colston K, Colston MJ, Feldman D. 1981. 1,25-dihydroxyvitamin D<sub>3</sub> and malignant melanoma: The presence of receptors and inhibition of cell growth in culture. *Endocrinol* 108:1083–1086.
- COMA (Committee on Medical Aspects of Food Policy). 1991. *Dietary Reference Values for Food Energy and Nutrients for the United Kingdom. Report on Health and Social Subjects, No. 41*. London: HMSO.
- Comstock GW. 1979. Water hardness and cardiovascular diseases. *Am J Epidemiol* 110:375–400.
- Conradt A, Weidinger H, Algayer H. 1984. On the role of magnesium in fetal hypotrophy, pregnancy induced hypertension and pre-eclampsia. *Magnes Bull* 2:68–76.
- Cooper C, Melton LJ III. 1992. Epidemiology of osteoporosis. *Trends Endocrinol Metab* 3:224–229.
- Cooper C, Campion G, Melton LJ III. 1992. Hip fractures in the elderly: A worldwide projection. *Osteopor Int* 2:285–289.
- Costello RB, Moser-Veillon PB, DiBianco R. 1997. Magnesium supplementation in patients with congestive heart failure. *J Am Coll Nutr* 16:22–31.
- Cowell DC, Taylor WH. 1981. Ionic fluoride: A study of its physiological variation in man. *Ann Clin Biochem* 18:76–83.
- Craig JM. 1959. Observations on the kidney after phosphate loading in the rat. *Arch Pathol* 68:306–315.
- Cramer CF. 1961. Progress and rate of absorption of radiophosphorus through the intestinal tract of rats. *Can J Biochem Physiol* 39:499–503.
- Cremer HD, Buttner W. 1970. *Absorption of Fluorides. Fluoride and Human Health*. Geneva, Switzerland: World Health Organization.
- Cross NA, Hillman LS, Allen SH, Krause GF, Vieira NE. 1995a. Calcium homeostasis and bone metabolism during pregnancy, lactation, and postweaning: A longitudinal study. *Am J Clin Nutr* 61:514–523.
- Cross NA, Hillman LS, Allen SH, Krasue GF. 1995b. Changes in bone mineral density and markers of bone remodeling during lactation and postweaning in women consuming high amounts of calcium. *J Bone Miner Res* 10:1312–1320.
- Cumming RG, Cummings SR, Nevitt MC, Scott J, Ensrud KE, Vogt TM, Fox K. 1997. Calcium intake and fracture risk: Results from the study of osteoporotic fractures. *Am J Epidemiol* 145:926–934.
- Cummings SR, Black DM, Nevitt MC, Browner W, Cauley J, Ensrud K, Genant HK, Palermo L, Scott J, Vogt TM. 1993. Bone density at various sites for prediction of hip fractures. The Study of Osteoporotic Fractures Research Group. *Lancet* 341:72–75.
- Cummings SR, Nevitt MC, Browner WS, Stone K, Fox KM, Ensrud KE, Cauley J, Black D, Vogt TM. 1995. Risk factors for hip fracture in white women: Study of Osteoporotic Fractures Research Group. *N Engl J Med* 332:767–773.
- Cunningham AS, Mazess RB. 1983. Bone mineral loss in lactating adolescents. *J Pediatr* 101:338–339.
- Curhan GC, Willett WC, Rimm EB, Stampfer MJ. 1993. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. *N Engl J Med* 328:833–838.
- Curhan GC, Willett WC, Speizer FE, Spiegelman D, Stampfer MJ. 1997. Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk for kidney stones in women. *Ann Intern Med* 126:497–504.

- Dabeka RW, McKenzie AD, Conacher HBS, Kirkpatrick DC. 1982. Determination of fluoride in Canadian infant foods and calculation of fluoride intakes by infants. *Can J Pub Hlth* 73:188–191.
- Dabeka RW, McKenzie AD, Lecroix GM. 1987. Dietary intakes of lead, cadmium, arsenic and fluoride by Canadian adults: A 24-hour duplicate diet study. *Food Addit Contam* 4:89–101.
- Dale G, Fleetwood JA, Inkster JS, Sainsbury JR. 1986. Profound hypophosphataemia in patients collapsing after a “fun run.” *Br Med J (Clin Res)* 292:447–448.
- Dalton MA, Sargent JD, O’Connor GT, Olmstead EM, Klein RZ. 1997. Calcium and phosphorus supplementation of iron-fortified infant formula: No effect on iron status of healthy full-term infants. *Am J Clin Nutr* 65:921–926.
- Davies M, Adams PH. 1978. The continuing risk of vitamin D intoxication. *Lancet* 2(8090):621–623.
- Davies M, Lawson DEM, Emberson C, Barnes JLC, Roberts GE, Barnes ND. 1982. Vitamin D from skin: Contribution to vitamin D status compared with oral vitamin D in normal and anti-convulsant-treated subjects. *Clin Sci* 63:461–472.
- Davies M, Hayes ME, Yin JA, Berry JL, Mawer EB. 1994. Abnormal synthesis of 1,25-dihydroxyvitamin D in patients with malignant lymphoma. *J Clin Endocrinol Metab* 78:1202–1207.
- Davis RH, Morgan DB, Rivlin RS. 1970. The excretion of calcium in the urine and its relation to calcium intake, sex and age. *Clin Sci* 39:1–12.
- Dawes C. 1989. Fluorides: Mechanisms of action and recommendations for use. *J Can Dent Assoc* 55:721–723.
- Dawson-Hughes B. 1996. Calcium. In: Marcus R, Feldman D, Kelsey J, eds. *Osteoporosis*. Orlando, FL: Academic Press, Inc. Pp. 1103, 1105.
- Dawson-Hughes B, Stern DT, Shipp CC, Rasmussen HM. 1988. Effect of lowering dietary calcium intake on fractional whole body calcium retention. *J Clin Endocrinol Metab* 67:62–68.
- Dawson-Hughes B, Dallal GE, Krall EA, Sadowski L, Sahyoun N, Tannenbaum S. 1990. A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women. *N Engl J Med* 323:878–883.
- Dawson-Hughes B, Dallal GE, Krall EA, Harris S, Sokoll LJ, Falconer G. 1991. Effect of vitamin D supplementation on wintertime and overall bone loss in healthy postmenopausal women. *Ann Intern Med* 115:505–512.
- Dawson-Hughes B, Harris S, Kramich C, Dallal G, Rasmussen HM. 1993. Calcium retention and hormone levels in black and white women on high- and low-calcium diets. *J Bone Miner Res* 8:779–787.
- Dawson-Hughes B, Harris SS, Krall EA, Dallal GE, Falconer G, Green CL. 1995. Rates of bone loss in postmenopausal women randomly assigned to one of two dosages of vitamin D. *Am J Clin Nutr* 61:1140–1145.
- Dawson-Hughes B, Fowler SE, Dalsky G, Gallagher C. 1996. Sodium excretion influences calcium homeostasis in elderly men and women. *J Nutr* 126:2107–2112.
- Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. 1997. Calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. *N Engl J Med* 337:670–676.
- Dean HT. 1942. The investigation of physiological effects by the epidemiological method. In: Moulton FR, ed. *Fluorine and Dental Health*. Washington, DC: American Association for the Advancement of Science. Pp. 23–31.
- Dean HT, Elvove E. 1937. Further studies on the minimal threshold of chronic endemic dental fluorosis. *Pub Hlth Rep* 52:1249–1264.

- Delmas PD. 1992. Clinical use of biochemical markers of bone remodeling in osteoporosis. *Bone* 13:S17–S21.
- Delmi M, Rapin CH, Bengoa JM, Delmas PD, Vasey H, Bonjour JP. 1990. Dietary supplementation in elderly patients with fractured neck of the femur. *Lancet* 335:1013–1016.
- DeLuca HF. 1984. The metabolism, physiology, and function of vitamin D. In: Kumar R, ed. *Vitamin D: Basic and Clinical Aspects*. Boston: M. Nijhoff Publishers.
- DeLuca HF. 1988. The vitamin D story: A collaborative effort of basic science and clinical medicine. *FASEB J* 2:224–236.
- Delvin EE, Salle BL, Glorieux FH, Adeleine P, David LS. 1986. Vitamin D supplementation during pregnancy: Effect on neonatal calcium homeostasis. *J Pediatr* 109:328–334.
- Demay MB. 1995. Hereditary defects in vitamin D metabolism and vitamin D receptor defects. In: DeGroot LJ, Besser M, Burger HG, Jameson JL, Loriaux DL, Marshall JC, O'Dell WD, Potts JT, Rubenstein AH, eds. *Endocrinology, Vol 2, Third edition*. Philadelphia, PA: WB Saunders. Pp. 1173–1178.
- Demirjian A. 1980. *Anthropometry Report. Height, Weight, and Body Dimensions: A Report from Nutrition Canada*. Ottawa: Minister of National Health and Welfare, Health and Promotion Directorate, Health Services and Promotion Branch.
- Dengel JL, Mangels AR, Moser-Veillon PB. 1994. Magnesium homeostasis: Conservation mechanism in lactating women consuming a controlled-magnesium diet. *Am J Clin Nutr* 59:990–994.
- Deurenberg P, Pieters JJ, Hautvast JG. 1990. The assessment of the body fat percentage by skinfold thickness measurements in childhood and young adolescence. *Br J Nutr* 63:293–303.
- Deuster PA, Singh A. 1993. Responses of plasma magnesium and other cations to fluid replacement during exercise. *J Am Coll Nutr* 12:286–293.
- Devine A, Criddle RA, Dick IM, Kerr DA, Prince RL. 1995. A longitudinal study of the effect of sodium and calcium intakes on regional bone density in postmenopausal women. *Am J Clin Nutr* 62:740–745.
- DeVizia B, Mansi A. 1992. Calcium and phosphorus metabolism in full-term infants. *Monatsschr Kinderheilkd* 140:S8–S12.
- DeVizia B, Fomon SJ, Nelson SE, Edwards BE, Zeigler EE. 1985. Effect of dietary calcium on metabolic balance of normal infants. *Pediatr Res* 19:800–806.
- Dewey KG, Finley DA, Lonnerdal B. 1984. Breast milk volume and composition during late lactation (7–20 months). *J Pediatr Gastroenterol Nutr* 3:713–720.
- DHHS (Department of Health and Human Services). 1988. *The Surgeon General's Report on Nutrition and Health*. Washington, DC: US Department of Health and Human Services, Public Health Service.
- DHHS (Department of Health and Human Services). 1990. *Healthy People 2000: National Health Promotion and Disease Prevention Objectives*. DHHS Publ. No. (PHS) 91-50212. Washington, DC: US Government Printing Office. Pp. 466–467.
- Diem K. 1970. *Documenta Geigy*. Ardsley, NY: Geigy Pharmaceuticals.
- Dobnig H, Kainer F, Stepan V, Winter R, Lipp R, Schaffer M, Kahr A, Nocnik S, Patterer G, Leb G. 1995. Elevated parathyroid hormone-related peptide levels after human gestation: Relationship to changes in bone and mineral metabolism. *J Clin Endocrinol Metab* 80:3699–3707.
- Dorsch TR. 1986. The milk-alkali syndrome, vitamin D, and parathyroid hormone. *Ann Intern Med* 105:800–801.

- Dorup I, Clausen T. 1993. Correlation between magnesium and potassium contents in muscle: Role of Na(+)-K<sup>+</sup> pump. *Am J Physiol* 264:C457–C463.
- Dourson ML, Stara JF. 1983. Regulatory history and experimental support of uncertainty (safety) factors. *Regul Toxicol Pharmacol* 3:224–238.
- Dowell TB. 1981. The use of toothpaste in infancy. *Br Dent J* 150:247–249.
- Drinkwater BL, Chesnut CH III. 1991. Bone density changes during pregnancy and lactation in active women: A longitudinal study. *Bone Miner* 14:153–160.
- Drinkwater B, Bruemner B, Chesnut C. 1990. Menstrual history as a determinant of current bone density in young athletes. *J Am Med Assoc* 263:545–548.
- Dwyer JT, Dietz WH, Hass G, Suskind R. 1979. Risk of nutritional rickets among vegetarian children. *Am J Dis Child* 133:134–140.
- Dyckner T, Wester PO. 1983. Effect of magnesium on blood pressure. *Br Med J (Clin Res)* 286:1847–1849.
- Dyckner T, Wester PO. 1985. Skeletal muscle magnesium and potassium determinations: Correlation with lymphocyte contents of magnesium and potassium. *J Am Coll Nutr* 4:619–625.
- Ebeling PR, Yergey AL, Vieira NE, Burritt MF, O'Fallon WM, Kumar R, Riggs BL. 1994. Influence of age on effects on endogenous 1,25-dihydroxy-vitamin D on calcium absorption in normal women. *Calcif Tissue Int* 55:330–334.
- Eble DM, Deaton TG, Wilson FC, Bawden JW. 1992. Fluoride concentrations in human and rat bone. *J Pub Hlth Dent* 52:288–291.
- Egsmose C, Lund B, McNair P, Lund B, Storm T, Sorensen OH. 1987. Low serum levels of 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D in institutionalized old people: Influence of solar exposure and vitamin D supplementation. *Age Ageing* 16:35–40.
- Eisman JA, Suva LJ, Sher E, Pearce PJ, Funder JW, Martin TJ. 1981. Frequency of 1,25-dihydroxyvitamin D<sub>3</sub> receptor in human breast cancer. *Cancer Res* 41:5121–5124.
- Ekstrand J, Ehrnebo M. 1979. Influence of milk products on fluoride bioavailability in man. *Eur J Clin Pharmacol* 16:211–215.
- Ekstrand J, Ehrnebo M. 1980. Absorption of fluoride from fluoride dentifrices. *Caries Res* 14:96–102.
- Ekstrand J, Boreus LO, de Chateau P. 1981. No evidence of transfer of fluoride from plasma to breast milk. *Br Med J* 283:761–762.
- Ekstrand J, Spak CJ, Falch J, Afseth J, Ulvestad H. 1984. Distribution of fluoride to human breast milk following intake of high doses of fluoride. *Caries Res* 18:93–95.
- Ekstrand J, Fomon SJ, Ziegler EE, Nelson SE. 1994a. Fluoride pharmacokinetics in infancy. *Pediatr Res* 35:157–163.
- Ekstrand J, Ziegler EE, Nelson SE, Fomon SJ. 1994b. Absorption and retention of dietary and supplemental fluoride by infants. *Adv Dent Res* 8:175–180.
- Elders PJ, Netelenbos JC, Lips P, van Ginkel FC, Khoe E, Leeuwenkamp OR, Hackeng WH, van der Stelt PF. 1991. Calcium supplementation reduces vertebral bone loss in perimenopausal women: A controlled trial in 248 women between 46 and 55 years of age. *J Clin Endocrinol Metab* 73:533–540.
- Elders PJ, Lips P, Netelenbos JC, van Ginkel FC, Khoe E, van der Vijgh WJ, van der Stelt PF. 1994. Long-term effect of calcium supplementation on bone loss in perimenopausal women. *J Bone Miner Res* 9:963–970.
- Elia M. 1992. Energy expenditure and the whole body. In: Kinney JM, Tucker HN, eds. *Energy Metabolism: Tissue Determinants and Cellular Corollaries*. New York: Raven Press Ltd. Pp. 19–59.

- Elin RJ. 1987. Assessment of magnesium status. *Clin Chem* 33:1965–1970.
- Elin RJ, Hosseini JM. 1985. Magnesium content of mononuclear blood cells. *Clin Chem* 31:377–380.
- Ellis KJ, Shypailo RJ, Hergenroeder A, Perez M, Abrams S. 1996. Total body calcium and bone mineral content: Comparison of dual-energy X-ray absorptiometry (DXA) with neutron activation analysis (NAA). *J Bone Miner Res* 11:843–848.
- Ellis KJ, Abrams SA, Wong WW. 1997. Body composition of a young, multiethnic female population. *Am J Clin Nutr* 65:724–731.
- EPA (U. S. Environmental Protection Agency). 1986. Guidelines for Carcinogen Risk Assessment. *Federal Register* 51(185):33992–34003.
- EPA (U. S. Environmental Protection Agency). 1996. Proposed Guidelines for Carcinogen Risk Assessment; Notice. *Federal Register* 61(79):17960–18011.
- Esala S, Vuori E, Helle A. 1982. Effect of maternal fluorine intake on breast milk fluorine content. *Br J Nutr* 48:201–204.
- Esveld RP, DeLuca HF. 1981. Calcitroic acid: Biological activity and tissue distribution studies. *Arch Biochem Biophys* 206:403–413.
- European Community. 1993. *Nutrient and Energy Intakes for the European Community*. Reports of the Scientific Committee for Food, Thirty-first Series.
- Evans RW. 1989. Changes in dental fluorosis following an adjustment to the fluoride concentration of Hong Kong's water supplies. *Adv Dent Res* 3:154–160.
- Evans RW, Darvell BW. 1995. Refining the estimate of the critical period for susceptibility to enamel fluorosis in human maxillary central incisors. *J Pub Hlth Dent* 55:238–249.
- Fairweather-Tait S, Prentice A, Heumann KG, Landing MAJ, Stirling DM, Wharf SG, Turnlund JR. 1995. Effect of calcium supplements and stage of lactation on the calcium absorption efficiency of lactating women accustomed to low calcium intakes. *Am J Clin Nutr* 62:1188–1192.
- FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization). 1982. *Evaluation of Certain Food Additives and Contaminants*. Twenty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives (WHO Technical Report Series No. 683).
- FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization, Expert Consultation). 1995. *The Application of Risk Analysis to Food Standard Issues*. Recommendations to the Codex Alimentarius Commission (ALINORM 95/9, Appendix 5).
- FAO/WHO/UNA (Food and Agriculture Organization of the United Nations/World Health Organization/United Nations). 1985. *Energy and Protein Requirements*. Report of a joint FAO/WHO/UNA Consultation Technical Report Series. No. 724. Geneva, Switzerland: World Health Organization.
- Fardellone P, Sebert JL, Garabedian M, Bellony R, Maamer M, Agbomson F, Brazier M. 1995. Prevalence and biological consequences of vitamin D deficiency in elderly institutionalized subjects. *Rev Rhum* 62:576–581.
- Farmer ME, White LR, Brody JA, Bailey KR. 1984. Race and sex differences in hip fracture incidence. *Am J Publ Health* 74:1374–1380.
- Fatemi S, Ryzen E, Flores J, Endres DB, Rude RK. 1991. Effect of experimental human magnesium depletion on parathyroid hormone secretion and 1,25-dihydroxyvitamin D metabolism. *J Clin Endocrinol Metab* 73:1067–1072.
- Faulkner KG, Cummings SR, Black D, Palermo L, Gluer CC, Genant HK. 1993. Simple measurement of femoral geometry predicts hip fracture: The study of osteoporotic fractures. *J Bone Miner Res* 8:1211–1217.

- Favus MJ, Christakos S. 1996. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 3rd Edition*. Philadelphia, PA: Lippincott-Raven.
- Featherstone JDB, Shields CP. 1988. *A Study of Fluoride in New York State Residents*. Final report to New York State Department of Health.
- Fehily AM, Coles RJ, Evans WD, Elwood PC. 1992. Factors affecting bone density in young adults. *Am J Clin Nutr* 56:579–586.
- Fejerskov O, Thylstrup A, Larsen MJ. 1977. Clinical and structural features and possible pathogenic mechanisms of dental fluorosis. *Scand J Dent Res* 85:510–534.
- Feldblum PJ, Zhang J, Rich LE, Fortney JA, Talmage RV. 1992. Lactation history and bone mineral density among perimenopausal women. *Epidemiology* 3:527–531.
- Feliciano ES, Ho ML, Specker BL, Falciglia G, Shui QM, Yin TA, Chen XC. 1994. Seasonal and geographical variations in the growth rate of infants in China receiving increasing dosages of vitamin D supplements. *J Trop Pediatr* 40:162–165.
- Feltman R, Kosel G. 1961. Prenatal and postnatal ingestion of fluorides—fourteen years of investigation. Final report. *J Dent Med* 16:190–198.
- Fieser LF, Fieser M. 1959. Vitamin D. In: *Steroids*. New York: Reinhold. Pp. 90–168.
- Filippo FA, Battistone GC. 1971. The fluoride content of a representative diet of the young adult male. *Clin Chim Acta* 31:453–457.
- Fine KD, Santa Ana CA, Porter JL, Fordtran JS. 1991a. Intestinal absorption of magnesium from food and supplements. *J Clin Invest* 88:396–402.
- Fine KD, Santa Ana CA, Fordtran JS. 1991b. Diagnosis of magnesium-induced diarrhea. *N Engl J Med* 324:1012–1017.
- Fink RI, Kolterman OG, Griffin J, Olefsky JM. 1983. Mechanisms of insulin resistance in aging. *J Clin Invest* 71:1523–1535.
- Fitzgerald MG, Fourman P. 1956. An experimental study of magnesium deficiency in man. *Clin Sci* 15:635.
- Fomon SJ, Nelson SE. 1993. Calcium, phosphorus, magnesium, and sulfur. In: Fomon SJ, ed. *Nutrition of Normal Infants*. St. Louis: Mosby-Year Book, Inc. Pp. 192–216.
- Fomon SJ, Younoszai MK, Thomas LN. 1966. Influence of vitamin D on linear growth of normal full-term infants. *J Nutr* 88:345–50.
- Fomon SJ, Haschke F, Ziegler EE, Nelson SE. 1982. Body composition of reference children from birth to age 10 years. *Am J Clin Nutr* 35:1169–1175.
- Franz KB. 1987. Magnesium intake during pregnancy. *Magnesium* 6:18–27.
- Franz KB. 1989. Influence of phosphorus on intestinal absorption of calcium and magnesium. In: Itokawa Y, Durlach J, eds. *Magnesium in Health and Disease*. London: John Libbey & Co. Pp. 71–78.
- Fraser DR. 1980. Regulation of the metabolism of vitamin D. *Physiol Rev* 60:551–613.
- Fraser DR. 1983. The physiological economy of vitamin D. *Lancet* 1:969–972.
- Freiman I, Pettifor JM, Moodley GM. 1982. Serum phosphorus in protein energy malnutrition. *J Pediatr Gastroenterol Nutr* 1:547–550.
- French JK, Koldaway IM, Williams LC. 1986. Milk-alkali syndrome following over-the-counter antacid self-medication. *N Zeal Med J* 99:322–323.
- Freudenheim JL, Johnson NE, Smith EL. 1986. Relationships between usual nutrient intake and bone-mineral content of women 35–65 years of age: Longitudinal and cross-sectional analysis. *Am J Clin Nutr* 44:863–876.

- Freyberg RH. 1942. Treatment of arthritis with vitamin and endocrine preparations. *J Am Med Assoc* 119:1165–1171.
- Frithz G, Wictorin B, Ronquist G. 1991. Calcium-induced constipation in a prepubescent boy. *Acta Paediatr Scand* 80:964–965.
- Frost HM. 1973. The origin and nature of transients in human bone remodeling dynamics. In: Frame B, Parfitt AM, Duncan H, eds. *Clinical Aspects of Metabolic Bone Disease*. Amsterdam: Excerpta Medica Series. Pp. 124–137.
- Frost HM. 1987. The mechanostat: A proposed pathogenic mechanism of osteoporosis and the bone mass effects of mechanical and nonmechanical agents. *Bone Miner* 2:73–85.
- Frost HM. 1997. Why do marathon runners have less bone than weight lifters? A vital-biomechanical view and explanation. *Bone* 20:183–189.
- Gadallah M, Massry SG, Bigazzi R, Horst RL, Eggema P, Campese VM. 1991. Intestinal absorption of calcium and calcium metabolism in patients with essential hypertension and normal renal function. *Am J Hypertens* 4:404–409.
- Galla JH, Booker BB, Luke RG. 1986. Role of the loop segment in the urinary concentrating defect of hypercalcemia. *Kidney Int* 29:977–982.
- Gallagher JC, Riggs BL, DeLuca HF. 1980. Effect of estrogen on calcium absorption and serum vitamin D metabolites in postmenopausal osteoporosis. *J Clin Endocrinol Metab* 51:1359–1364.
- Gallagher JC, Goldgar D, Moy A. 1987. Total bone calcium in women: Effect of age and menopause status. *J Bone Miner Res* 2:491–496.
- Garby L, Lammert O. 1984. Within-subjects between-days-and-weeks variation in energy expenditure at rest. *Human Nutr Clin Nutr* 38:395–397.
- Garfinkel L, Garfinkel D. 1985. Magnesium regulation of the glycolytic pathway and the enzymes involved. *Magnesium* 4:60–72.
- Garland C, Shekelle RB, Barrett-Connor E, Criqui MH, Rossof AH, Paul O. 1985. Dietary vitamin D and calcium and risk of colorectal cancer: A 19-year prospective study in men. *Lancet* 1:307–309.
- Garland FC, Garland CF, Gorham ED, Young JF. 1990. Geographic variation in breast cancer mortality in the United States: A hypothesis involving exposure to solar radiation. *Prev Med* 19:614–622.
- Garn SM. 1972. The course of bone gain and the phases of bone loss. *Orthop Clin North Am* 3:503–520.
- Gartside PS, Glueck CJ. 1995. The important role of modifiable dietary and behavioral characteristics in the causation and prevention of coronary heart disease hospitalization and mortality: The prospective NHANES I follow-up study. *J Am Coll Nutr* 14:71–79.
- Gedalia I, Brzezinski A, Portuguese N, Bercovici B. 1964. The fluoride content of teeth and bones of human foetuses. *Arch Oral Biol* 9:331–340.
- Geleijnse JM, Witteman JC, Bak AA, den Breeijen JH, Grobbee DE. 1994. Reduction in blood pressure with a low sodium, high potassium, high magnesium salt in older subjects with mild to moderate hypertension. *Br Med J* 309:436–440.
- German Society of Nutrition. 1991. *Recommendations on Nutrient Intake*. Abstract and Tables of the 157 Pages Booklet, 5th revised edition. Frankfurt: Druckerei Henrich.
- Gershoff SN, Legg MA, Hegsted DM. 1958. Adaptation to different calcium intakes in dogs. *J Nutr* 64:303–312.
- Gertner JM, Coustan DR, Kliger AS, Mallette LE, Ravin N, Broadus AE. 1986. Pregnancy as state of physiologic absorptive hypercalciuria. *Am J Med* 81:451–456.

- Gillman MW, Hood MY, Moore LL, Nguyen US, Singer MR, Andon MB. 1995. Effect of calcium supplementation on blood pressure in children. *J Pediatr* 127:186–192.
- Gilsanz V, Roe TF, Mora S, Costin G, Goodman WG. 1991. Changes in vertebral bone density in black girls and white girls during childhood and puberty. *N Engl J Med* 325:1597–1600.
- Glaser K, Parmelee AH, Hoffman WS. 1949. Comparative efficacy of vitamin D preparations in prophylactic treatment of premature infants. *Am J Dis Child* 77:1–14.
- Glass RL, Peterson JK, Zuckerberg DA, Naylor MN. 1975. Fluoride ingestion resulting from the use of a monofluorophosphate dentifrice by children. *Br Dent J* 138:423–426.
- Glenn FB. 1981. The rationale for the administration of a NaF tablet supplement during pregnancy and postnatally in a private practice setting. *J Dent Child* 48:118–122.
- Glenn FB, Glenn WD III, Duncan RC. 1984. Prenatal fluoride tablet supplementation and the fluoride content of teeth: Part VII. *J Dent Child* 51:344–351.
- Gloth FM III, Gundberg CM, Hollis BW, Haddad JG Jr, Tobin JD. 1995. Vitamin D deficiency in homebound elderly persons. *J Am Med Assoc* 274:1683–1686.
- Goeree R, O'Brien B, Pettitt D, Cuddy L, Ferraz M, Adachi J. 1996. An assessment of the burden of illness due to osteoporosis in Canada. *J SOGC*:15S–24S.
- Golden BE, Golden MH. 1981. Plasma zinc, rate of weight gain, and the energy cost of tissue deposition in children recovering from severe malnutrition on a cow's milk or soya protein-based diet. *Am J Clin Nutr* 34:892–899.
- Goldfarb S. 1994. Diet and nephrolithiasis. *Ann Rev Med* 45:235–243.
- Goldring SR, Krane SM, Avioli LV. 1995. Disorders of calcification: Osteomalacia and rickets. In: DeGroot LJ, ed. *Endocrinology*, Vol 2, *Third Edition*. Philadelphia: WB Saunders. Pp. 1204–1227.
- Golzarian J, Scott HW Jr, Richards WO. 1994. Hypermagnesemia-induced paralytic ileus. *Dig Dis Sci* 39:1138–1142.
- Gora ML, Seth SK, Bay WH, Visconti JA. 1989. Milk-alkali syndrome associated with use of chlorothiazide and calcium carbonate. *Clin Pharm* 8:227–229.
- Goren S, Silverstein LJ, Gonzales N. 1993. A survey of food service managers of Washington State boarding homes for the elderly. *J Nutr Elderly* 12:27–42.
- Graham S. 1959. Idiopathic hypercalcemia. *Postgraduate Med* 25:67–72.
- Gray TK, Lester GE, Lorenc RS. 1979. Evidence for extra-renal 1-hydroxylation of 25-hydroxyvitamin D<sub>3</sub> in pregnancy. *Science* 204:1311–1313.
- Greer FR. 1989. Calcium, phosphorus, and magnesium: How much is too much for infant formulas? *J Nutr* 119:1846–1851.
- Greer FR, Garn SM. 1982. Loss of bone mineral content in lactating adolescents. *J Pediatr* 101:718–719.
- Greer FR, Searcy JE, Levin RS, Steichen JJ, Steichen-Asche PS, Tsang RC. 1982a. Bone mineral content and serum 25-hydroxyvitamin D concentrations in breast-fed infants with and without supplemental vitamin D: One-year follow-up. *J Pediatr* 100:919–922.
- Greer FR, Tsang RC, Levin RS, Searcy JE, Wu R, Steichen JJ. 1982b. Increasing serum calcium and magnesium concentrations in breast-fed infants: Longitudinal studies of minerals in human milk and in sera of nursing mothers and their infants. *J Pediatr* 100:59–64.

- Greer FR, Steichen JJ, Tsang RC. 1982c. Effects of increased calcium, phosphorus, and vitamin D intake on bone mineralization in very low-birth-weight infants fed formulas with polycose and medium-chain triglycerides. *J Pediatr* 100:951–955.
- Greer FR, Lane J, Ho M. 1984. Elevated serum parathyroid hormone, calcitonin, and 1,25-dihydroxyvitamin D in lactating women nursing twins. *Am J Clin Nutr* 40:562–568.
- Greger JL, Baier MJ. 1983. Effect of dietary aluminum on mineral metabolism of adult males. *Am J Clin Nutr* 38:411–419.
- Greger JL, Baligar P, Abernathy RP, Bennett OA, Peterson T. 1978. Calcium, magnesium, phosphorus, copper, and manganese balance in adolescent females. *Am J Clin Nutr* 31:117–121.
- Greger JL, Huffman J, Abernathy RP, Bennett OA, Resnick SE. 1979. Phosphorus and magnesium balance of adolescent females fed two levels of zinc. *J Food Sci* 44:1765–1767.
- Greger JL, Smith SA, Snedeker SM. 1981. Effect of dietary calcium and phosphorus levels on the utilization of calcium, phosphorus, magnesium, manganese, and selenium by adult males. *Nutr Res* 1:315–325.
- Grill V, Martin TJ. 1993. Non-parathyroid hypercalcemias. In: Nordin BEC, Need AG, Morris HA, eds. *Metabolic Bone and Stone Disease*. Edinburgh: Churchill Livingstone. Pp. 133–145.
- Grimston SK, Morrison K, Harder JA, Hanley DA. 1992. Bone mineral density during puberty in Western Canadian children. *Bone Miner* 19:85–96.
- Groeneveld A, Van Eck AA, Backer-Dirks O. 1990. Fluoride in caries prevention: Is the effect pre- or post-eruptive? *J Dent Res* 69(Spec Iss):751–755.
- Gullestad L, Dolva LO, Waage A, Falch D, Fagerthun H, Kjekshus J. 1992. Magnesium deficiency diagnosed by an intravenous loading test. *Scan J Clin Lab Invest* 52:245–253.
- Gullestad L, Nes M, Ronneberg R, Midtveldt K, Falch D, Kjekshus J. 1994. Magnesium status in healthy free-living elderly Norwegians. *J Am Coll Nutr* 13:45–50.
- Gultekin A, Ozalp I, Hasanoglu A, Unal A. 1987. Serum-25-hydroxycholecalciferol levels in children and adolescents. *Turk J Pediatr* 29:155–162.
- Gunther T. 1993. Mechanisms and regulation of Mg<sup>2+</sup> efflux and Mg<sup>2+</sup> influx. *Miner Electrolyte Metab* 19:259–265.
- Guy WS. 1979. Inorganic and organic fluorine in human blood. In: Johansen E, Taves DR, Olsen TO, eds. *Continuing Evaluation of the Use of Fluorides*. AAAS Selected Symposium. Boulder, CO: Westview Press.
- Haddad JG, Jr. 1980. Competitive protein-binding radioassays for 25-OH-D; clinical applications. In: Norman, ed. *Vitamin D*, vol. 2. New York: Marcel Dekker, Inc., P. 587.
- Haddad JG, Hahn TJ. 1973. Natural and synthetic sources of circulating 25-hydroxyvitamin D in man. *Nature* 244:515–517.
- Hakim R, Tolis G, Goltzman D, Meltzer S, Friedman R. 1979. Severe hypercalcemia associated with hydrochlorothiazide and calcium carbonate therapy. *Can Med Assoc J* 21:591–594.
- Halioua L, Anderson JJ. 1989. Lifetime calcium intake and physical activity habits: Independent and combined effects on the radial bone of healthy premenopausal Caucasian women. *Am J Clin Nutr* 49:534–541.
- Hallberg L, Rossander-Hulten L, Brune M, Gleerup A. 1992. Calcium and iron absorption: Mechanism of action and nutritional importance. *Eur J Clin Nutr* 46:317–327.

- Hallfrisch J, Muller DC. 1993. Does diet provide adequate amounts of calcium, iron, magnesium, and zinc in a well-educated adult population? *Exper Gerontol* 28:473–483.
- Hamilton IR. 1990. Biochemical effects of fluoride on oral bacteria. *J Dent Res* 69(Spec Iss):660–667.
- Hammer DI, Heyden S. 1980. Water hardness and cardiovascular mortality. *J Am Med Assoc* 243:2399–2400.
- Hamuro Y, Shino A, Suzuki Z. 1970. Acute induction of soft tissue calcification with transient hyperphosphatemia in the KK mouse by modification in dietary contents of calcium, phosphorus, and magnesium. *J Nutr* 100:404–412.
- Handwerker SM, Altura BT, Altura BM. 1996. Serum ionized magnesium and other electrolytes in the antenatal period of human pregnancy. *J Am Coll Nutr* 15:36–43.
- Hardwick LL, Jones MR, Brautbar N, Lee DB. 1991. Magnesium absorption: Mechanisms and the influence of vitamin D, calcium and phosphate. *J Nutr* 121:13–23.
- Hargreaves JA. 1972. Fluoride content of deciduous tooth enamel from three different regions (Abstract). *J Dent Res* 51:274.
- Hargreaves JA. 1992. The level and timing of systemic exposure to fluoride with respect to caries resistance. *J Dent Res* 71:1244–1248.
- Hargreaves JA, Ingram GS, Wagg BJ. 1970. An extended excretion study on the ingestion of a monofluorophosphate toothpaste by children. *Acta Med Sci Hung* 27:413–419.
- Hargreaves JA, Ingram FF, Wagg BJ. 1972. A gravimetric based study of the ingestion of toothpaste by children. *Caries Res* 6:237–243.
- Hargreaves JA, Thompson GW, Pimlott JFL, Norbert LD. 1988. Commencement date of fluoride supplementation related to dental caries. *J Dent Res* 67:230.
- Harris SS, Dawson-Hughes B. 1994. Caffeine and bone loss in healthy postmenopausal women. *Am J Clin Nutr* 60:573–578.
- Hart M, Windle J, McHale M, Grissom R. 1982. Milk-alkali syndrome and hypercalcemia: A case report. *Nebr Med J* 67:128–130.
- Hasling C, Charles P, Jensen FT, Mosekilde L. 1990. Calcium metabolism in postmenopausal osteoporosis: The influence of dietary calcium and net absorbed calcium. *J Bone Miner Res* 5:939–946.
- Hayslip CC, Klein TA, Wray HL, Duncan WE. 1989. The effects of lactation on bone mineral content in healthy postpartum women. *Obstet Gynecol* 73:588–592.
- Health Canada. 1990. *Nutrition Recommendations. The Report of the Scientific Review Committee 1990*. Ottawa: Canadian Government Publishing Centre.
- Health Canada. 1993. *Health Risk Determination—The Challenge of Health Protection*. Health Canada, Health Protection Branch. Ottawa: Health Canada.
- Heaney RP. 1993. Protein intake and the calcium economy. *J Am Diet Assoc* 93:1259–1260.
- Heaney RP. 1997. Vitamin D: Role in the calcium economy. In: Feldman D, Glorieux FH, Pike JW, eds. *Vitamin D*. San Diego, CA: Academic Press. Pp. 485–497.
- Heaney RP, Recker RR. 1982. Effects of nitrogen, phosphorus, and caffeine on calcium balance in women. *J Lab Clin Med* 99:46–55.
- Heaney RP, Recker RR. 1987. Calcium supplements: Anion effects. *Bone Miner* 2:433–439.

- Heaney RP, Recker RR. 1994. Determinants of endogenous fecal calcium in healthy women. *J Bone Miner Res* 9:1621–1627.
- Heaney RP, Skillman TG. 1964. Secretion and excretion of calcium by the human gastrointestinal tract. *J Lab Clin Med* 64:29–41.
- Heaney RP, Skillman TG. 1971. Calcium metabolism in normal human pregnancy. *J Clin Endocrinol* 33:661–670.
- Heaney RP, Saville PD, Recker RR. 1975. Calcium absorption as a function of calcium intake. *J Lab Clin Med* 85:881–890.
- Heaney RP, Recker RR, Saville PD. 1977. Calcium balance and calcium requirements in middle-aged women. *Am J Clin Nutr* 30:1603–1611.
- Heaney RP, Recker RR, Saville PD. 1978. Menopausal changes in calcium balance performance. *J Lab Clin Med* 92:953–963.
- Heaney RP, Recker RR, Hinders SM. 1988. Variability of calcium absorption. *Am J Clin Nutr* 47:262–264.
- Heaney RP, Recker RR, Stegman MR, Moy AJ. 1989. Calcium absorption in women: Relationships to calcium intake, estrogen status, and age. *J Bone Miner Res* 4:469–475.
- Heaney RP, Recker RR, Weaver CM. 1990a. Absorbability of calcium sources: The limited role of solubility. *Calcif Tissue Int* 46:300–304.
- Heaney RP, Weaver CM, Fitzsimmons ML. 1990b. Influence of calcium load on absorption fraction. *J Bone Miner Res* 5:1135–1138.
- Heaney RP, Weaver CM, Fitzsimmons ML. 1991. Soybean phytate content: Effect on calcium absorption. *Am J Clin Nutr* 53:745–747.
- Heaton FW. 1969. The kidney and magnesium homeostasis. *Ann NY Acad Sci* 162:775–785.
- Hegsted DM. 1972. Problems in the use and interpretation of the Recommended Dietary Allowances. *Ecol Food Nutr* 1:255–265.
- Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. 1993. Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: The DARLING study. *Am J Clin Nutr* 58:152–161.
- Hemmingsen C, Staun M, Olgaard K. 1994. Effects of magnesium on renal and intestinal calbindin-D. *Miner Electrolyte Metab* 20:265–273.
- Herman-Giddens ME, Slora EJ, Wasserman RC, Bourdon CJ, Bhapkar MV, Koch GG, Hasemeier CM. 1997. Secondary sexual characteristics and menses in young girls seen in office practice: A study from the Pediatric Research in Office Settings Network. *Pediatrics* 99:505–512.
- Hill AB. 1971. *Principles of Medical Statistics, 9th Ed.* New York: Oxford University Press.
- Hillman LS. 1990. Mineral and vitamin D adequacy in infants fed human milk or formula between 6 and 12 months of age. *J Pediatr* 117:S134–S142.
- Hillman L, Sateesha S, Haussler M, Wiest W, Slatopolsky E, Haddad J. 1981. Control of mineral homeostasis during lactation: Interrelationships of 25-hydroxyvitamin D, 24,25-dihydroxyvitamin D, 1,25-dihydroxyvitamin D, parathyroid hormone, calcitonin, prolactin, and estradiol. *Am J Obstet Gynecol* 139:471–476.
- Hillman LS, Chow W, Salmons SJ, Weaver E, Erickson M, Hansen J. 1988. Vitamin D metabolism, mineral homeostasis and bone mineralization in term infants fed human milk, cow milk-based formula or soy-based formula. *J Pediatr* 112:864–874.
- Hodge HC, Smith FA. 1977. Occupational fluoride exposure. *J Occup Med* 19:12–39.

- Hodge HC. 1979. The safety of fluoride tablets or drops. In: Johansen E, Taves DR, Olson, TO, eds. *Continuing Evaluation of the Use of Fluorides, AAAS Selected Symposium 1*. Boulder, CO: Westview Press. Pp. 253–274.
- Hodgson E, Mailman RB, Chamber JE. 1988. *Dictionary of Toxicology*. New York: Van Nostrand Reinhold, Inc.
- Hoffman S, Grisso JA, Kelsey JL, Gammon MD, O'Brien LA. 1993. Parity, lactation and hip fracture. *Osteopor Int* 3:171–176.
- Hofvander Y, Hagman U, Hillervik C, Sjolin S. 1982. The amount of milk consumed by 1–3 months old breast- or bottle-fed infants. *Acta Pediatr Scand* 71:953–958.
- Holbrook TL, Barrett-Connor E, Wingard DL. 1988. Dietary calcium and risk of hip fracture: 14-year prospective population study. *Lancet* 2:1046–1049.
- Holick MF. 1986. Vitamin D requirements for the elderly. *Clin Nutr* 5:121–129.
- Holick MF. 1994. McCollum Award Lecture, 1994: Vitamin D: New horizons for the 21st century. *Am J Clin Nutr* 60:619–630.
- Holick MF. 1995. Vitamin D: Photobiology, metabolism, and clinical applications. In: DeGroot LJ, Besser M, Burger HG, Jameson JL, Loriaux DL, Marshall JC, O'Dell WD, Potts JL, Rubenstein AH, eds. *Endocrinology, 3rd Edition*. Philadelphia, PA: WB Saunders.
- Holick MF. 1996. Vitamin D: Photobiology, metabolism, mechanism of action, and clinical application. In: Favus MJ, ed. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 3rd Edition*. Philadelphia, PA: Lippincott-Raven. Pp. 74–81.
- Holick MF, Clark MB. 1978. The photobiogenesis and metabolism of vitamin D. *Fed Proc* 37:2567–2574.
- Holick MF, Schnoes HK, DeLuca HF. 1971. Identification of 1,25-dihydroxycholecalciferol, a form of vitamin D<sub>3</sub> metabolically active in the intestine. *Proc Natl Acad Sci USA* 68:803–804.
- Holick MF, Uskokovic M, Henley JW, MacLaughlin J, Holick SA, Potts JT Jr. 1980. The photoproduction of 1 $\alpha$ , 25-dihydroxyvitamin D<sub>3</sub> in skin: An approach to the therapy of vitamin-D-resistant syndromes. *N Engl J Med* 303:349–354.
- Holick MF, MacLaughlin JA, Doppelt SH. 1981. Regulation of cutaneous previtamin D<sub>3</sub> photosynthesis in man: Skin pigment is not an essential regulator. *Science* 211:590–593.
- Holick MF, Matsuoka LY, Wortsman J. 1989. Age, vitamin D, and solar ultraviolet. *Lancet* 2:1104–1105.
- Holick MF, Shao Q, Liu WW, Chen TC. 1992. The vitamin D content of fortified milk and infant formula. *N Engl J Med* 326:1178–1181.
- Hollifield JW. 1987. Magnesium depletion, diuretics, and arrhythmias. *Am J Med* 82(Suppl 3A):30–37.
- Hollis BW. 1996. Assessment of vitamin D nutritional and hormonal status: What to measure and how to do it. *Calcif Tissue Int* 58:4–5.
- Holmes RP, Kummerow FA. 1983. The relationship of adequate and excessive intake of vitamin D to health and disease. *J Am Coll Nutr* 2:173–199.
- Honkanen R, Alhava E, Parviainen M, Talasniemi S, Monkkonen R. 1990. The necessity and safety of calcium and vitamin D in the elderly. *J Am Geriatr Soc* 38:862–866.
- Hordon LD, Peacock M. 1987. Vitamin D metabolism in women with femoral neck fracture. *Bone Miner* 2:413–426.
- Horowitz HS. 1990. The future of water fluoridation and other systemic fluorides. *J Dent Res* 69(Spec Iss):760–764.

- Horowitz HS. 1996. The effectiveness of community water fluoridation in the United States. *J Pub Hlth Dent* 56:253–258.
- Horowitz HS, Heifetz SB. 1967. Effects of prenatal exposure to fluoridation on dental caries. *Pub Hlth Rep* 82:297–304.
- Horowitz M, Wishart J, Mundy L, Nordin BEC. 1987. Lactose and calcium absorption in postmenopausal osteoporosis. *Arch Intern Med* 147:534–536.
- Hoskova M. 1968. Fluoride tablets in the prevention of tooth decay. *Cesk Pediatr* 23:438–441.
- Howard JE, Hopkins TR, Connor TB. 1953. On certain physiologic responses to intravenous injection of calcium salts into normal, hyperparathyroid and hypoparathyroid persons. *J Clin Endocrinol Metab* 13:1–19.
- Hreshchyshyn MM, Hopkins A, Zylstra S, Anbar M. 1988. Associations of parity, breast-feeding, and birth control pills with lumbar spine and femoral neck bone densities. *Am J Obstet Gynecol* 159:318–322.
- Hua H, Gonzales J, Rude RK. 1995. Magnesium transport induced ex vivo by a pharmacological dose of insulin is impaired in non-insulin-dependent diabetes mellitus. *Magnes Res* 8:359–366.
- Huang Z, Himes JH, McGovern PG. 1996. Nutrition and subsequent hip fracture risk among a national cohort of white women. *Am J Epidemiol* 144:124–134.
- Hunt CD, Nielsen FH. 1981. Interaction between boron and cholecalciferol in the chick. In: McC Howell J, Gathorne JM, White CL, eds. *Trace Element Metabolism in Man and Animals, TEMA-4*. Canberra: Australian Academy of Science. Pp. 597–600.
- Hunt MS, Schofield FA. 1969. Magnesium balance and protein intake level in adult human female. *Am J Clin Nutr* 22:367–373.
- Hwang DL, Yen CF, Nadler JL. 1993. Insulin increases intracellular magnesium transport in human platelets. *J Clin Endocrinol Metab* 76:549–553.
- IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Report of the Subcommittee on Nutritional Status and Weight Gain During Pregnancy, Subcommittee on Dietary Intake and Nutrient Supplements During Pregnancy, Committee on Nutritional Status During Pregnancy and Lactation, Food and Nutrition Board. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1991. *Nutrition During Lactation*. Report of the Subcommittee on Nutrition During Lactation, Committee on Nutritional Status During Pregnancy and Lactation, Food and Nutrition Board. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Food and Nutrition Board. Washington, DC: National Academy Press.
- Ireland P, Fordtran JS. 1973. Effect of dietary calcium and age on jejunal calcium absorption in humans studied by intestinal perfusion. *J Clin Invest* 52:2672–2681.
- Irnell L. 1969. Metastatic calcification of soft tissue on overdose of vitamin D. *Acta Med Scand* 185:147–152.
- Iseri LT, French JH. 1984. Magnesium: Nature's physiologic calcium blocker. *Am Heart J* 108:188–193.
- ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. 1995. ISIS-4: A randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. *Lancet* 345:669–685.

- Ismail AI, Brodeur JM, Kavanagh M, Boisclair G, Tessier C, Picotte L. 1990. Prevalence of dental caries and dental fluorosis in students, 11–17 years of age, in fluoridated and non-fluoridated cities in Quebec. *Caries Res* 24:290–297.
- Jackman LA, Millane SS, Martin BR, Wood OB, McCabe GP, Peacock M, Weaver CM. 1997. Calcium retention in relation to calcium intake and postmenarcheal age in adolescent females. *Am J Clin Nutr* 66:327–333.
- Jackson D, Murray JJ, Fairpo CG. 1973. Life-long benefits of fluoride in drinking water. *Br Dent J* 134:419–422.
- Jacobus CH, Holick MF, Shao Q, Chen TC, Holm IA, Kolodny JM, Fuleihan GE, Seely EW. 1992. Hypervitaminosis D associated with drinking milk. *N Engl J Med* 326:1173–1177.
- Janas LM, Picone TA, Benson JD, MacLean WC. 1988. Influence of dietary calcium to phosphorus and parathormone during the first two weeks of life. *Pediatr Res* 23:485A.
- Janelle KC, Barr SI. 1995. Nutrient intakes and eating behavior scores of vegetarian and nonvegetarian women. *J Am Diet Assoc* 95:180–186.
- Jeans PC. 1950. Vitamin D. *J Am Med Assoc* 143:177–181.
- Jeans PC, Stearns G. 1938. The effect of vitamin D on linear growth in infancy. II. The effect of intakes above 1,800 USP units daily. *J Pediatr* 13:730–740.
- Joffres MR, Reed DM, Yano K. 1987. Relationship of magnesium intake and other dietary factors to blood pressure: The Honolulu heart study. *Am J Clin Nutr* 45:469–475.
- Johansson C, Mellström D, Milsom I. 1993. Reproductive factors as predictors of bone density and fractures in women at the age of 70. *Maturitas* 17:39–50.
- Johnson AO, Semenza JG, Buchowski MS, Enwonwu CO, Scrimshaw NS. 1993a. Correlation of lactose maldigestion, lactose intolerance, and milk intolerance. *Am J Clin Nutr* 57:399–401.
- Johnson AO, Semenza JG, Buchowski MS, Enwonwu CO, Scrimshaw NS. 1993b. Adaptation of lactose maldigesters to continued milk intakes. *Am J Clin Nutr* 58:879–881.
- Johnson CM, Wilson DM, O'Fallon WM, Malek RS, Kurland LT. 1979. Renal stone epidemiology: A 25-year study in Rochester, Minn. *Kidney Int* 16:624–631.
- Johnson J Jr, Bawden JW. 1987. The fluoride content of infant formulas available in 1985. *Pediatr Dent* 9:33–37.
- Johnson KR, Jobber J, Stonawski BJ. 1980. Prophylactic vitamin D in the elderly. *Age Ageing* 9:121–127.
- Johnston CC, Miller JZ, Slemenda CW, Reister TK, Hui S, Christian JC, Peacock M. 1992. Calcium supplementation and increases in bone mineral density in children. *N Engl J Med* 327:82–87.
- Jones JE, Manalo R, Flink EB. 1967. Magnesium requirements in adults. *Am J Clin Nutr* 20:632–635.
- Jowsey J, Balasubramaniam P. 1972. Effect of phosphate supplements on soft tissue calcification and bone turnover. *Clin Sci* 42:289–299.
- Junor JR, Catto GRD. 1976. Renal biopsy in the milk-alkali syndrome. *J Clin Path* 29:1074–1076.
- Kailis DG, Taylor SR, Davis GB, Bartlett LG, Fitzgerald DJ, Grose IJ, Newton PD. 1968. Fluoride and caries: Observations of the effects of prenatal and postnatal fluoride on some Perth pre-school children. *Med J Austral* 2:1037–1040.
- Kalkwarf HJ, Specker BL. 1995. Bone mineral loss during lactation and recovery after weaning. *Obstet Gynecol* 86:26–32.
- Kalkwarf HJ, Specker BL, Heubi JE, Vieira NE, Yergey AL. 1996. Intestinal calcium absorption of women during lactation and after weaning. *Am J Clin Nutr* 63:526–531.

- Kalkwarf HJ, Specker BL, Bianchi DC, Ranz J, Ho M. 1997. The effect of calcium supplementation on bone density during lactation and after weaning. *N Engl J Med* 337:523–528.
- Kallmeyer JC, Funston MR. 1983. The milk-alkali syndrome: A case report. *S Afr Med J* 64:287–288.
- Kamel S, Brazier M, Picard C, Boitte F, Samson L, Desmet G, Sebert JL. 1994. Urinary excretion of pyridinolines crosslinks measured by immunoassay and HPLC techniques in normal subjects and in elderly patients with vitamin D deficiency. *Bone Miner* 26:197–208.
- Kamel S, Brazier M, Rogez JC, Vincent O, Maamer M, Desmet G, Sebert JL. 1996. Different responses of free and peptide-bound cross-links to vitamin D and calcium supplementation in elderly women with vitamin D insufficiency. *J Clin Endocrinol Metab* 81:3717–3721.
- Kaminsky LS, Mahoney MC, Leach J, Melius J, Miller MJ. 1990. Fluoride: Benefits and risks of exposure. *Crit Rev Oral Biol Med* 1:261–281.
- Kanapka JA, Hamilton IR. 1971. Fluoride inhibition of enolase activity in vivo and its relationship to the inhibition of glucose-6-P formation in *Streptococcus salivarius*. *Arch Biochem Biophys* 146:167–174.
- Kanemitsu T, Koike A, Yamamoto S. 1985. Study of the cell proliferation kinetics in ulcerative colitis, adenomatous polyps, and cancer. *Cancer* 56:1094–1098.
- Kanis JA, Melton LJ III, Christiansen C, Johnston CC, Khaltaev N. 1994. The diagnosis of osteoporosis. *J Bone Miner Res* 9:1137–1141.
- Kapsner P, Langsdorf L, Marcus R, Kraemer FB, Hoffman AR. 1986. Milk-alkali syndrome in patients treated with calcium carbonate after cardiac transplantation. *Arch Intern Med* 146:1965–1968.
- Katzman DK, Bachrach LK, Carter DR, Marcus R. 1991. Clinical and anthropometric correlates of bone mineral acquisition in healthy adolescent girls. *J Clin Endocrinol Metab* 73:1332–1339.
- Kayne LH, Lee DB. 1993. Intestinal magnesium absorption. *Miner Electrolyte Metab* 19:210–217.
- Keddie KMG. 1987. Case report: Severe depressive illness in the context of hypervitaminosis D. *Br J Psych* 150:394–396.
- Kellie SE, Brody JA. 1990. Sex-specific and race-specific hip fracture rates. *Am J Pub Hlth* 80:326–328.
- Kelsay JL, Prather ES. 1983. Mineral balances of human subjects consuming spinach in a low-fiber diet and in a diet containing fruits and vegetables. *Am J Clin Nutr* 38:12–19.
- Kelsay JL, Behall KM, Prather ES. 1979. Effect of fiber from fruits and vegetables on metabolic responses of human subjects. II. Calcium, magnesium, iron, and silicon balances. *Am J Clin Nutr* 32:1876–1880.
- Kent GN, Price RI, Gutteridge DH, Smith M, Allen JR, Bhagat CI, Barnes MP, Hickling CJ, Retallack RW, Wilson SG, Devlin RD, Davies C, St. John A. 1990. Human lactation: Forearm trabecular bone loss, increased bone turnover, and renal conservation of calcium and inorganic phosphate with recovery of bone mass following weaning. *J Bone Miner Res* 5:361–369.
- Kent GN, Price RI, Gutteridge DH, Rosman KJ, Smith M, Allen JR, Hickling CJ, Blakeman SL. 1991. The efficiency of intestinal calcium absorption is increased in late pregnancy but not in established lactation. *Calcif Tissue Int* 48:293–295.
- Kesteloot H, Joossens JV. 1990. The relationship between dietary intake and urinary excretion of sodium, potassium, calcium and magnesium: Belgian Inter-university Research on Nutrition and Health. *J Hum Hypertension* 4:527–533.

- Kiel DP, Felson DT, Hannan MT, Anderson JJ, Wilson PW. 1990. Caffeine and the risk of hip fracture: The Framingham Study. *Am J Epidemiol* 132:675–684.
- Kinyamu HK, Gallagher JC, Balhorn KE, Petranick KM, Rafferty KA. 1997. Serum vitamin D metabolites and calcium absorption in normal young and elderly free-living women and in women living in nursing homes. *Am J Clin Nutr* 65:790–797.
- Klaassen CD, Amdur MO, Doull J. 1986. *Casarett and Doull's Toxicology: The Basic Science of Poisons, Third Edition*. New York: Macmillan Publishing Company.
- Kleerekoper M, Mendlovic DB. 1993. Sodium fluoride therapy of postmenopausal osteoporosis. *Endocrinol Rev* 14:312–323.
- Kleibeuker JH, Welberg JW, Mulder NH, van der Meer R, Cats A, Limburg AJ, Kreumer WM, Hardonk MJ, de Vries EG. 1993. Epithelial cell proliferation in the sigmoid colon of patients with adenomatous polyps increases during oral calcium supplementation. *Br J Cancer* 67:500–503.
- Klein CJ, Moser-Veillon PB, Douglass LW, Ruben KA, Trocki O. 1995. A longitudinal study of urinary calcium, magnesium, and zinc excretion in lactating and nonlactating postpartum women. *Am J Clin Nutr* 61:779–786.
- Kleiner SM, Bazzarre TL, Ainsworth BE. 1994. Nutritional status of nationally ranked elite bodybuilders. *Int J Sport Nutr* 4:54–69.
- Kleinman GE, Rodriguez H, Good MC, Caudle MR. 1991. Hypercalcemic crisis in pregnancy associated with excessive ingestion of calcium carbonate antacid (milk-alkali syndrome): Successful treatment with hemodialysis. *Obstet Gynecol* 73:496–499.
- Knochel JP. 1977. The pathophysiology and clinical characteristics of severe hypophosphatemia. *Arch Intern Med* 137:203–220.
- Knochel JP. 1985. The clinical status of hypophosphatemia: An update. *N Engl J Med* 313:447–449.
- Kobayashi A, Kawai S, Ohbe Y, Nagashima Y. 1975. Effects of dietary lactose and a lactase preparation on the intestinal absorption of calcium and magnesium in normal infants. *Am J Clin Nutr* 28:681–683.
- Kochersberger G, Westlund R, Lyles KW. 1991. The metabolic effects of calcium supplementation in the elderly. *J Am Geriatr Soc* 39:192–196.
- Koetting CA, Wardlaw GM. 1988. Wrist, spine, and hip bone density in women with variable histories of lactation. *Am J Clin Nutr* 48:1479–1481.
- Kohlmeier L, Mendez M, McDuffie J, Miller M. 1997. Computer-assisted self-interviewing: A multimedia approach to dietary assessment. *Am J Clin Nutr* 65:1275S–1281S.
- Koo W, Tsang R. 1997. Calcium, magnesium, phosphorus and vitamin D. In: *Nutrition During Infancy, 2nd Edition*. Cincinnati: Digital Education. Pp. 175–189.
- Koo W, Krug-Wispe S, Neylen M, Succop P, Oestreich AE, Tsang RC. 1995. Effect of three levels of vitamin D intake in preterm infants receiving high mineral-containing milk. *J Pediatr Gastroenterol Nutr* 21:182–189.
- Krall EA, Sahyoun N, Tannenbaum S, Dallal GE, Dawson-Hughes B. 1989. Effect of vitamin D intake on seasonal variations in parathyroid hormone secretion in postmenopausal women. *N Engl J Med* 321:1777–1783.
- Kramer L, Osis D, Wiatrowski E, Spenser H. 1974. Dietary fluoride in different areas of the United States. *Am J Clin Nutr* 27:590–594.
- Kreiger N, Kelsey JL, Holford TR, O'Connor T. 1982. An epidemiologic study of hip fracture in postmenopausal women. *Am J Epidemiol* 116:141–148.

- Krejs GJ, Nicar MJ, Zerwekh HE, Normal DA, Kane MG, Pak CY. 1983. Effect of 1,25-dihydroxyvitamin D<sub>3</sub> on calcium and magnesium absorption in the healthy human jejunum and ileum. *Am J Med* 75:973–976.
- Krishnamachari KA. 1986. Skeletal fluorosis in humans: A review of recent progress in the understanding of the disease. *Prog Food Nutr Sci* 10:279–314.
- Krook L, Whalen JP, Lesser GV, Berens DL. 1975. Experimental studies on osteoporosis. *Methods Achiev Exp Pathol* 7:72–108.
- Kröger H, Kotaniemi A, Vainio P, Alhava E. 1992. Bone densitometry of the spine and femur in children by dual-energy x-ray absorptiometry. *Bone Miner* 17:75–85.
- Kröger H, Kotaniemi A, Kröger L, Alhava E. 1993. Development of bone mass and bone density of the spine and femoral neck—a prospective study of 65 children and adolescents. *Bone Miner* 23:171–182.
- Kröger H, Alhava E, Honkanen R, Tuppurainen M, Saarikoski S. 1994. The effect of fluoridated drinking water on axial bone mineral density: A population-based study. *Bone Miner* 27:33–41.
- Kruse K, Bartels H, Kracht U. 1984. Parathyroid function in different stages of vitamin D deficiency rickets. *Eur J Pediatr* 141:158–162.
- Kumar JV, Green EL, Wallace W, Carnahan T. 1989. Trends in dental fluorosis and dental caries prevalences in Newburgh and Kingston, NY. *Am J Pub Hlth* 79:565–569.
- Kumar R. 1986. The metabolism and mechanism of action of 1,25-dihydroxyvitamin D<sub>3</sub>. *Kidney Int* 30:793–803.
- Kumar R, Cohen WR, Silva P, Epstein FH. 1979. Elevated 1,25-dihydroxyvitamin D plasma levels in normal human pregnancy and lactation. *J Clin Invest* 63:342–344.
- Kummerow FA, Simon Cho BH, Huang YT, Imai H, Kamio A, Deutsch MJ, Hooper WM. 1976. Additive risk factors in atherosclerosis. *Am J Clin Nutr* 29:579–584.
- Kurtz TW, Al-Bander HA, Morris RC. 1987. “Salt sensitive” essential hypertension in men. *N Engl J Med* 317:1043–1048.
- Kurzel RB. 1991. Serum magnesium levels in pregnancy and preterm labor. *Am J Perinatol* 8:119–127.
- Kuti V, Balazs M, Morvay F, Varenka Z, Szekely A, Szucs M. 1981. Effect of maternal magnesium supply on spontaneous abortion and premature birth and on intrauterine fetal development: Experimental epidemiological study. *Magnes Bull* 3:73–79.
- Ladizesky M, Lu Z, Oliveri B, San Roman N, Diaz S, Holick MF, Mautalen C. 1995. Solar ultraviolet B radiation and photoproduction of vitamin D<sub>3</sub> in central and southern areas of Argentina. *J Bone Miner Res* 10:545–549.
- Lafferty FW. 1991. Differential diagnosis of hypercalcemia. *J Bone Miner Res* 6:S51–S59.
- Lakshmanan LF, Rao RB, Kim WW, Kelsay JL. 1984. Magnesium intakes, balances, and blood levels of adults consuming self-selected diets. *Am J Clin Nutr* 40:1380–1389.
- Lamberg-Allardt C, von Knorring J, Slatis P, Holmstrom T. 1989. Vitamin D status and concentrations of serum vitamin D metabolites and osteocalcin in elderly patients with femoral neck fracture: A follow-up study. *Eur J Clin Nutr* 43:355–361.
- Lamberg-Allardt C, Karkkainen M, Seppanen R, Bistrom H. 1993. Low serum 25-hydroxyvitamin D concentrations and secondary hyperparathyroidism in middle-aged white strict vegetarians. *Am J Clin Nutr* 58:684–689.
- Largent EJ. 1952. Rates of elimination of fluoride stored in the tissues of man. *Arch Ind Hyg* 6:37–42.

- Larsen MJ, Senderovitz F, Kirkegaard E, Poulsen S, Fejerskov O. 1988. Dental fluorosis in the primary and permanent dentition in fluoridated areas with consumption of either powdered milk or natural cow's milk. *J Dent Res* 67:822–825.
- Lawson DE, Fraser DR, Kodicek E, Morris HR, Williams DH. 1971. Identification of 1,25-dihydroxycholecalciferol, a new kidney hormone controlling calcium metabolism. *Nature* 230:228–230.
- Lealman GT, Logan RW, Hutchison JH, Kerr MM, Fulton AM, Brown CA. 1976. Calcium, phosphorus, and magnesium concentrations in plasma during first week of life and their relation to type of milk feed. *Arch Dis Child* 51:377–384.
- LeBlanc A, Schneider V, Spector E, Evans H, Rowe R, Lane H, Demers L, Lipton A. 1995. Calcium absorption, endogenous excretion, and endocrine changes during and after long-term bed rest. *Bone* 16:301S–304S.
- Lebrun JB, Moffatt ME, Mundy RJ, Sangster RK, Postl BD, Dooley JP, Dilling LA, Godel JC, Haworth JC. 1993. Vitamin D deficiency in a Manitoba community. *Can J Pub Hlth* 84:394–396.
- Lee WT, Leung SS, Wang SH, Xu YC, Zeng WP, Lau J, Oppenheimer SJ, Cheng JC. 1994. Double-blind, controlled calcium supplementation and bone mineral accretion in children accustomed to a low-calcium diet. *Am J Clin Nutr* 60:744–750.
- Lee WT, Leung SS, Leung DM, Tsang HS, Lau J, Cheng JC. 1995. A randomized double-blind controlled calcium supplementation trial, and bone and height acquisition in children. *Br J Nutr* 74:125–139.
- Lee WT, Leung SS, Leung DM, Cheng JC. 1996. A follow-up study on the effects of calcium-supplement withdrawal and puberty on bone acquisition of children. *Am J Clin Nutr* 64:71–77.
- LeGeros RZ, Glenn FB, Lee DD, Glenn WD. 1985. Some physico-chemical properties of deciduous enamel with and without pre-natal fluoride supplementation (PNF). *J Dent Res* 64:465–469.
- Lechner NDM, Bullock BC, Clarkson TB, Lofland HB. 1967. Biologic activities of vitamin D<sub>2</sub> and D<sub>3</sub> for growing squirrel monkeys. *Lab Anim Care* 17:483.
- Leitch I, Aitken FC. 1959. The estimation of calcium requirement: A re-examination. *Nutr Abs Rev* 29:393–409.
- Lemann J Jr. 1996. Calcium and phosphate metabolism: An overview in health and in calcium stone formers. In: Coe FL, Favus MJ, Pak CY, Parks JH, Preminger GM, eds. *Kidney Stones: Medical and Surgical Management*. Philadelphia, PA: Lippincott-Raven. Pp. 259–288.
- Lemann J Jr, Worcester EM, Gray RW. 1991. Hypercalciuria and stones. *Am J Kidney Dis* 17:386–391.
- Lemke CW, Doherty JM, Arra MC. 1970. Controlled fluoridation: The dental effects of discontinuation in Antigo, Wisconsin. *J Am Dent Assoc* 80:782–786.
- Leone NC, Shimkin MB, Arnold FA, Stevenson CA, Zimmerman ER, Geiser PB, Lieberman JE. 1954. Medical aspects of excessive fluoride in a water supply. *Pub Hlth Rep* 69:925–936.
- Leone NC, Stevenson CA, Hilbush TF, Sosman MC. 1955. A roentgenologic study of a human population exposed to high-fluoride domestic water: A ten-year study. *Am J Roentg* 74:874–885.
- Leone NC, Stevenson CA, Besse B, Hawes, LE, Dawber TA. 1960. The effects of the absorption of fluoride. II. A radiological investigation of 546 human residents of an area in which the drinking water contained only a minute trace of fluoride. *Archs Ind Hlth* 21:326–327.

- Leoni V, Fabiani L, Ticchiarelli L. 1985. Water hardness and cardiovascular mortality rate in Abruzzo, Italy. *Arch Environ Health* 40:274–278.
- Leung SSF, Lui S, Swaminathan R. 1989. Vitamin D status of Hong Kong Chinese infants. *Acta Paediatr Scand* 78:303–306.
- Leverett DH. 1986. Prevalence of dental fluorosis in fluoridated and nonfluoridated communities—a preliminary investigation. *J Pub Hlth Dent* 46:184–187.
- Leverett DH, Adair SM, Vaughan BW, Proskin HM, Moss ME. 1997. Randomized clinical trial of the effect of prenatal fluoride supplements in preventing dental caries. *Caries Res* 31:174–179.
- Levine RJ, Hauth JC, Curet LB, Sibai BM, Catalano PM, Morris CD, DerSimonian R, Esterlitz JR, Raymond EG, Bild DE, Clemens JD, Cutler JA. 1997. Trial of calcium to prevent preeclampsia. *N Engl J Med* 337:69–76.
- Levy SM, Muchow G. 1992. Provider compliance with recommended dietary fluoride supplement protocol. *Am J Pub Hlth* 82:281–283.
- Levy SM, Kohout FJ, Kiritsy MC, Heilman JR, Wefel JS. 1995. Infants' fluoride ingestion from water, supplements and dentifrice. *J Am Dent Assoc* 126:1625–1632.
- Lewis DW. 1976. *An Evaluation of the Effects of Water Fluoridation, City of Toronto, 1963–1975*. Toronto, Canada: The Corporation of the City of Toronto.
- Lewis NM, Marcus MSK, Behling AR, Greger JL. 1989. Calcium supplements and milk: Effects on acid-base balance and on retention of calcium, magnesium, and phosphorus. *Am J Clin Nutr* 49:527–533.
- Liel Y, Edwards J, Shary J, Spicer KM, Gordon L, Bell NH. 1988. The effects of race and body habitus on bone mineral density of the radius, hip, and spine in premenopausal women. *J Clin Endocrinol Metab* 66:1247–1250.
- Lin S-H, Lin Y-F, Shieh S-D. 1996. Milk-alkali syndrome in an aged patient with osteoporosis and fractures. *Nephron* 73:496–497.
- Linden V. 1974. Vitamin D and myocardial infarction. *Br Med J* 3:647–650.
- Linkswiler HM, Zemel MB, Hegsted M, Schuette S. 1981. Protein-induced hypercalciuria. *Fed Proc* 40:2429–2433.
- Lips P, Wiersinga A, vanGinkel FC, Jongen MJ, Netelenbos JC, Hackeng WH, Delmas PD, vanderVijgh WJ. 1988. The effect of vitamin D supplementation on vitamin D status and parathyroid function in elderly subjects. *J Clin Endocrinol Metab* 67:644–650.
- Lips P, Graafmans WC, Ooms ME, Bezemer D, Bouter LM. 1996. Vitamin D supplementation and fracture incidence in elderly persons: A randomized, placebo-controlled clinical trial. *Ann Intern Med* 124:400–406.
- Lipski PS, Torrance A, Kelly PJ, James OF. 1993. A study of nutritional deficits of long-stay geriatric patients. *Age Aging* 22:244–255.
- Lissner L, Bengtsson C, Hansson T. 1991. Bone mineral content in relation to lactation history in pre- and postmenopausal women. *Calcif Tissue Int* 48:319–325.
- Livingstone MB, Prentice AM, Coward WA, Strain JJ, Black AE, Davies PS, Stewart CM, McKenna PG, Whitehead RG. 1992. Validation estimates of energy intake by weighted dietary record and diet history in children and adolescents. *Am J Clin Nutr* 56:29–35.
- Lloyd T, Schaeffer JM, Walker MA, Demers LM. 1991. Urinary hormonal concentrations and spinal bone densities of premenopausal vegetarian and nonvegetarian women. *Am J Clin Nutr* 54:1005–1010.

- Lloyd T, Andon MB, Rollings N, Martel JK, Landis R, Demers LM, Eggli DF, Kieselhorst K, Kulin HE. 1993. Calcium supplementation and bone mineral density in adolescent girls. *J Am Med Assoc* 270:841–844.
- Lo CW, Paris PW, Clemens TL, Nolan J, Holick MF. 1985. Vitamin D absorption in healthy subjects and in patients with intestinal malabsorption syndromes. *Am J Clin Nutr* 42:644–649.
- Lonnerdal B. 1997. Effects of milk and milk components on calcium, magnesium, and trace element absorption during infancy. *Physiol Rev* 77:643–669.
- Looker AC, Harris TB, Madans JH, Sempers CT. 1993. Dietary calcium and hip fracture risk: The NHANES I Epidemiology Follow-Up Study. *Osteopor Int* 3:177–184.
- Looker AC, Johnston CC Jr, Wahner HW, Dunn WL, Calvo MS, Harris TB, Heyse SP, Lindsay RL. 1995. Prevalence of low femoral bone density in older US women from NHANES III. *J Bone Miner Res* 10:796–802.
- Lopez JM, Gonzalez G, Reyes V, Campino C, Diaz S. 1996. Bone turnover and density in healthy women during breastfeeding and after weaning. *Osteopor Int* 6:153–159.
- Lotz M, Zisman E, Bartter FC. 1968. Evidence for a phosphorus-depletion syndrome in man. *N Engl J Med* 278:409–415.
- Lowenstein FW, Stanton MF. 1986. Serum magnesium levels in the United States, 1971–1974. *J Am Coll Nutr* 5:399–414.
- Lowik MR, van Dokkum W, Kistemaker C, Schaafsma G, Ockhuizen T. 1993. Body composition, health status and urinary magnesium excretion among elderly people (Dutch Nutrition Surveillance System). *Magnes Res* 6:223–232.
- LSRO/FASEB (Life Sciences Research Office/Federation of American Societies for Experimental Biology). 1986. *Guidelines for Use of Dietary Intake Data*. Anderson SA, ed. Bethesda, MD: LSRO/FASEB.
- Lu PW, Briody JN, Ogle GD, Morley K, Humphries IR, Allen J, Howman-Giles R, Sillence D, Cowell CT. 1994. Bone mineral density of total body, spine, and femoral neck in children and young adults: A cross-sectional and longitudinal study. *J Bone Miner Res* 9:1451–1458.
- Luckey MM, Meier DE, Mandeli JP, DaCosta MC, Hubbard ML, Goldsmith SJ. 1989. Radial and vertebral bone density in white and black women: Evidence for racial differences in premenopausal bone homeostasis. *J Clin Endocrinol Metab* 69:762–770.
- Lukert BP, Raisz LG. 1990. Glucocorticoid-induced osteoporosis: Pathogenesis and management. *Ann Intern Med* 112:352–364.
- Lund B, Sorensen OH. 1979. Measurement of 25-hydroxyvitamin D in serum and its relation to sunshine, age and vitamin D intake in the Danish population. *Scand J Clin Lab Invest* 39:23–30.
- Luoma H, Aromaa A, Helminen S, Murtomaa H, Kiviluoto L, Punstar S, Knekt P. 1983. Risk of myocardial infarction in Finnish men in relation to fluoride, magnesium and calcium concentration in drinking water. *Acta Med Scand* 213:171–176.
- Lutwak L, Lester L, Gitelman HJ, Fox M, Whedon GD. 1964. Effects of high dietary calcium and phosphorus on calcium, phosphorus, nitrogen and fat metabolism in children. *Am J Clin Nutr* 14:76–82.

- Ma J, Folsom AR, Melnick SL, Eckfeldt JH, Sharrett AR, Nabulsi AA, Hutchinson RG, Metcalf PA. 1995. Associations of serum and dietary magnesium with cardiovascular disease, hypertension, diabetes, insulin, and carotid arterial wall thickness: The ARIC study. *Atherosclerosis Risk in Community Study. J Clin Epidemiol* 48:927–940.
- MacLaughlin J, Holick MF. 1985. Aging decreases the capacity of human skin to produce vitamin D<sub>3</sub>. *J Clin Invest* 76:1536–1538.
- MacLaughlin JA, Anderson RR, Holick MF. 1982. Spectral character of sunlight modulates photosynthesis of previtamin D<sub>3</sub> and its photoisomers in human skin. *Science* 216:1001–1003.
- Maguire ME. 1984. Hormone-sensitive magnesium transport and magnesium regulation of adenylate cyclase. *Trends Pharmacol Sci* 5:73–77.
- Mahalko JR, Sandstead HH, Johnson LK, Milne DB. 1983. Effect of a moderate increase in dietary protein on the retention and excretion of Ca, Cu, Fe, Mg, P, and Zn by adult males. *Am J Clin Nutr* 37:8–14.
- Maheshwari UR, McDonald JT, Schneider VS, Brunetti AJ, Leybin L, Newbrun E, Hodge HC. 1981. Fluoride balance studies in ambulatory healthy men with and without fluoride supplements. *Am J Clin Nutr* 34:2679–2684.
- Maheshwari UR, King JC, Leybin L, Newbrun E, Hodge HC. 1983. Fluoride balances during early and late pregnancy. *J Occup Med* 25:587–590.
- Mallet E, Gugi B, Brunelle P, Henocq A, Basuyau JP, Lemeur H. 1986. Vitamin D supplementation in pregnancy: A controlled trial of two methods. *Obstet Gynecol* 68:300–304.
- Malm OJ. 1958. Calcium requirement and adaptation in adult men. *Scand J Clin Lab Invest* 10(Suppl 36):1–280.
- Malone DNS, Horn DB. 1971. Acute hypercalcemia and renal failure after antacid therapy. *Br Med J* 1:709–710.
- Manz F. 1992. Why is the phosphorus content of human milk exceptionally low? *Monatsschr Kinderheilkd* 140:S35–S39.
- Marcus R, Cann C, Madvig P, Minkoff J, Goddard M, Bayer M, Martin M, Gaudiani L, Haskell W, Genant H. 1985. Menstrual function and bone mass in elite women distance runners. Endocrine and metabolic features. *Ann Intern Med* 102:158–163.
- Margen S, Chu JY, Kaufmann NA, Calloway DH. 1974. Studies in calcium metabolism I. The calciuretic effect of dietary protein. *Am J Clin Nutr* 27:584–589.
- Margolis HC, Moreno EC. 1990. Physicochemical perspectives on the cariostatic mechanisms of systemic and topical fluorides. *J Dent Res* 69(Spec Iss):606–613.
- Marier JR. 1986. Magnesium content of the food supply in the modern-day world. *Magnesium* 5:1–8.
- Marken PA, Weart CW, Carson DS, Gums JG, Lopes-Virella MF. 1989. Effects of magnesium oxide on the lipid profile of healthy volunteers. *Atherosclerosis* 77:37–42.
- Markestad T, Elzouki AY. 1991. Vitamin-D deficiency rickets in northern Europe and Libya. In: Glorieux FH, ed. *Rickets: Nestle Nutrition Workshop Series, Vol 21*. New York, NY: Raven Press.
- Markestad T, Ulstein M, Bassoe HH, Aksnes L, Aarskog D. 1983. Vitamin D metabolism in normal and hypoparathyroid pregnancy and lactation. Case report. *Br J Obstet Gynaecol* 90:971–976.
- Markestad T, Ulstein M, Aksnes L, Aarskog D. 1986. Serum concentrations of vitamin D metabolites in vitamin D supplemented pregnant women. A longitudinal study. *Acta Obstet Gynecol Scand* 65:63–67.

- Marquis RE. 1995. Antimicrobial actions of fluoride for oral bacteria. *Can J Microbiol* 41:955–964.
- Marsh AG, Sanchez TV, Midkelsen O, Keiser J, Mayor G. 1980. Cortical bone density of adult lacto-ovo-vegetarian and omnivorous women. *J Am Diet Assoc* 76:148–151.
- Marshall DH, Nordin BEC, Speed R. 1976. Calcium, phosphorus and magnesium requirement. *Proc Nutr Soc* 35:163–173.
- Martin AD, Bailey DA, McKay HA. 1997. Bone mineral and calcium accretion during puberty. *Am J Clin Nutr* 66:611–615.
- Martin BJ. 1990. The magnesium load test: Experience in elderly subjects. *Aging (Milano)* 2:291–296.
- Martin TJ, Grill V. 1995. Hypercalcemia. *Clin Endocrinol* 42:535–538.
- Martinez ME, Salinas M, Miguel JL, Herrero E, Gomez P, Garcia J, Sanchez-Sicilia L, Montero A. 1985. Magnesium excretion in idiopathic hypercalciuria. *Nephron* 40: 446–450.
- Massey LK, Wise KJ. 1984. The effect of dietary caffeine on urinary excretion of calcium, magnesium, sodium and potassium in healthy young females. *Nutr Res* 4:43–50.
- Massey LK, Roman-Smith H, Sutton RA. 1993. Effect of dietary oxalate and calcium on urinary oxalate and risk of formation of calcium oxalate kidney stones. *J Am Diet Assoc* 93:901–906.
- Matkovic V. 1991. Calcium metabolism and calcium requirements during skeletal modeling and consolidation of bone mass. *Am J Clin Nutr* 54:245S–260S.
- Matkovic V, Heaney RP. 1992. Calcium balance during human growth: Evidence for threshold behavior. *Am J Clin Nutr* 55:992–996.
- Matkovic V, Fontana D, Tominac C, Goel P, Chesnut CH III. 1990. Factors that influence peak bone mass formation: A study of calcium balance and the inheritance of bone mass in adolescent females. *Am J Clin Nutr* 52:878–888.
- Matkovic V, Jelic T, Wardlaw GM, Illich JZ, Goel PK, Wright JK, Andon MB, Smith KT, Heaney RP. 1994. Timing of peak bone mass in Caucasian females and its implication for the prevention of osteoporosis. *J Clin Invest* 93:799–808.
- Matkovic V, Illich JZ, Andon MB, Hsieh LC, Tzagournis MA, Lagger BJ, Goel PK. 1995. Urinary calcium, sodium, and bone mass of young females. *Am J Clin Nutr* 62:417–425.
- Matsuda H. 1991. Magnesium gating of the inwardly rectifying K<sup>+</sup> channel. *Ann Rev Physiol* 53:289–298.
- Matsuoka LY, Ide L, Wortsman J, MacLaughlin JA, Holick MF. 1987. Sunscreens suppress cutaneous vitamin D<sub>3</sub> synthesis. *J Clin Endocrinol Metab* 64:1165–1168.
- Matsuoka LY, Wortsman J, Dannenberg MJ, Hollis BW, Lu Z, Holick MF. 1992. Clothing prevents ultraviolet-B radiation-dependent photosynthesis of vitamin D<sub>3</sub>. *J Clin Endocrinol Metab* 75:1099–1103.
- Mawer EB, Schaefer K, Lumb GA, Stanbury SW. 1971. The metabolism of isotopically labelled vitamin D<sub>3</sub> in man: The influence of the state of vitamin D nutrition. *Clin Sci* 40:39–53.
- Mawer EB, Backhouse J, Holman CA, Lumb GA, Stanbury DW. 1972. The distribution and storage of vitamin D and its metabolites in human tissues. *Clin Sci* 43:413–431.
- Mazariegos-Ramos E, Guerrero-Romero F, Rodriguez-Moran M, Lazcano-Burciaga G, Paniagua R, Amato D. 1995. Consumption of soft drinks with phosphoric acid as a risk factor for the development of hypocalcemia in children: A case-control study. *J Pediatr* 126:940–942.

- McCarron DA. 1983. Calcium and magnesium nutrition in human hypertension. *Ann Int Med* 98:800–805.
- McCarron DA, Morris CD. 1985. Blood pressure response to oral calcium in persons with mild to moderate hypertension: A randomized, double-blind, placebo-controlled, crossover trial. *Ann Intern Med* 103:825–831.
- McCarron DA, Morris CD, Young E, Roullet C, Drüeke T. 1991. Dietary calcium and blood pressure: Modifying factors in specific populations. *Am J Clin Nutr* 54:215S–219S.
- McCauley HB, McClure FJ. 1954. Effect of fluoride in drinking water on the osseous development of the hand and wrist in children. *Pub Hlth Rep* 69:671–683.
- McClure FJ. 1943. Ingestion of fluoride and dental caries. Quantitative relations based on food and water requirements of children one to twelve years old. *Am J Dis Child* 66:362–369.
- McClure FJ, Zipkin I. 1958. Physiologic effects of fluoride as related to water fluoridation. *Dent Clin North Am* 2:441–458.
- McCrory WW, Forman CW, McNamara H, Barnett HL. 1950. Renal excretion of phosphate in newborn infants: Observations in normal infants and in infants with hypocalcemic tetany. *Am J Dis Child* 80:512–513.
- McFarlane D. 1941. Experimental phosphate nephritis in the rat. *J Pathol* 52:17–24.
- McGrath N, Singh V, Cundy T. 1993. Severe vitamin D deficiency in Auckland. *N Zel Med J* 106:524–526.
- McKenna MJ. 1992. Differences in vitamin D status between countries in young adults and the elderly. *Am J Med* 93:69–77.
- McKnight-Hanes MC, Leverett DH, Adair SM, Shields CP. 1988. Fluoride content of infant formulas: Soy-based formulas as a potential factor in dental fluorosis. *Pediatr Dent* 10:189–194.
- Meier DE, Luckey MM, Wallenstein S, Clemens TL, Orwoll ES, Waslien CI. 1991. Calcium, vitamin D, and parathyroid hormone status in young white and black women: Association with racial differences in bone mass. *J Clin Endocrinol Metab* 72:703–710.
- Melton LJ III, Chrischilles EA, Cooper C, Lane AW, Riggs, BL. 1992. Perspective. How many women have osteoporosis? *J Bone Miner Res* 7:1005–1010.
- Melton LJ III, Atkinson EJ, O'Fallon WM, Wahner HW, Riggs BL. 1993a. Long-term fracture prediction by bone mineral assessed at different skeletal sites. *J Bone Miner Res* 8:1227–1233.
- Melton LJ III, Bryant SC, Wahner HW, O'Fallon WM, Malkasian GD, Judd HL, Riggs BL. 1993b. Influence of breastfeeding and other reproductive factors on bone mass later in life. *Osteopor Int* 3:76–83.
- Merke J, Klaus G, Hugel U, Waldherr R, Ritz E. 1986. No 1,25-dihydroxyvitamin D<sub>3</sub> receptors on osteoclasts of calcium-deficient chicken despite demonstrable receptors on circulating monocytes. *J Clin Invest* 77:312–314.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- Mertz W, Abernathy CO, Olin SS. 1994. *Risk Assessment of Essential Elements*. Washington, DC: ILSI Press.
- Meulmeester JF, vandenBerg H, Wedel M, Boshuis PG, Hulshof KF, Luyken R. 1990. Vitamin D status, parathyroid hormone and sunlight in Turkish, Moroccan and Caucasian children in The Netherlands. *Eur J Clin Nutr* 44:461–470.

- Meyer F, White E. 1993. Alcohol and nutrients in relation to colon cancer in middle-aged adults. *Am J Epidemiol* 138:225–236.
- Miller JZ, Smith DL, Flora L, Slemenda C, Jiang X, Johnston CC Jr. 1988. Calcium absorption from calcium carbonate and a new form of calcium (CCM) in healthy male and female adolescents. *Am J Clin Nutr* 48:1291–1294.
- Mimouni FB. 1996. The ion-selective magnesium electrode: A new tool for clinicians and investigators. *J Am College Nutr* 15:4–5.
- Mimouni F, Tsang RC, Hertzberg VS, Miodovnik M. 1986. Polycythemia hypomagnesemia and hypocalcemia infants of diabetic mothers. *Am J Dis Child* 140:798–800.
- Mimouni F, Campaigne B, Neylan M, Tsang RC. 1993. Bone mineralization in the first year of life in infants fed human milk, cow-milk formula, or soy-based formula. *J Pediatr* 122:348–354.
- Moncrief MW, Chance GW. 1969. Nephrotoxic effect of vitamin D therapy in vitamin D refractory rickets. *Arch Dis Child* 44:571–579.
- Montaldo MB, Benson JD. 1986. Nutrient intakes of older infants: Effect of different milk feedings. *J Am Coll Nutr* 5:331–341.
- Mordes JP, Wacker WEC. 1978. Excessive magnesium. *Pharmacol Rev* 29:273–300.
- Moser PB, Issa CF, Reynolds RD. 1983. Dietary magnesium intake and the concentration of magnesium in plasma and erythrocytes of postpartum women. *J Am Coll Nutr* 2:387–396.
- Moser PB, Reynolds RD, Acharya S, Howard MP, Andon MB. 1988. Calcium and magnesium dietary intakes and plasma and milk concentrations of Nepalese lactating women. *Am J Clin Nutr* 47:735–739.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance data from vital and health statistics, No. 174. Hyattsville, MD: National Center for Health Statistics.
- Motoyama T, Sano H, Fukuzaki H. 1989. Oral magnesium supplementation in patients with essential hypertension. *Hypertension* 13:227–232.
- Mountokalakis TD. 1987. Effects of aging, chronic disease, and multiple supplements on magnesium requirements. *Magnesium* 6:5–11.
- Moya M, Cortes E, Ballester MI, Vento M, Juste M. 1992. Short-term polycose substitution for lactose reduces calcium absorption in healthy term babies. *J Pediatr Gastroenterol Nutr* 14:57–61.
- Muhler JC. 1970. Ingestion from foods. In: Adler P, ed. *Fluorides and Human Health*. Monograph series no. 59. Geneva: World Health Organization. Pp. 32–40.
- Muldowney WP, Mazbar SA. 1996. Rolaids-yogurt syndrome: A 1990s version of milk-alkali syndrome. *Am J Kidney Dis* 27:270–272.
- Murphy SP, Calloway DH. 1986. Nutrient intakes of women in NHANES II, emphasizing trace minerals, fiber, and phytate. *J Am Diet Assoc* 86:1366–1372.
- Naccache H, Simard PL, Trahan L, Demers M, Lapointe C, Brodeur JM. 1990. Variability in the ingestion of toothpaste by preschool children. *Caries Res* 24:359–363.
- Naccache H, Simard PL, Trahan L, Brodeur JM, Demers M, Lachapelle D, Bernard PM. 1992. Factors affecting the ingestion of fluoride dentifrice by children. *J Pub Hlth Dent* 52:222–226.
- Nadler JL, Malayan S, Luong H, Shaw S, Natarajan RD, Rude RK. 1992. Intracellular free magnesium deficiency plays a key role in increased platelet reactivity in type II diabetes mellitus. *Diabetes Care* 15:835–841.

- Nadler JL, Buchanan T, Natarajan R, Antonipillai I, Bergman R, Rude RK. 1993. Magnesium deficiency produces insulin resistance and increased thromboxane synthesis. *Hypertension* 21:1024–1029.
- Nagubandi S, Kumar R, Londowski JM, Corradino RA, Tietz PS. 1980. Role of vitamin D glucosiduronate in calcium homeostasis. *J Clin Invest* 66:1274–1280.
- Nagy L, Tarnok F, Past T, Mozsik GY, Deak G, Tapsonyi Z, Fendler K, Javor T. 1988. Human tolerability and pharmacodynamic study of TISACID tablet in duodenal ulcer patients. A prospective, randomized, self-controlled clinico-pharmacological study. *Acta Medica Hung* 45:231–246.
- Nakamura T, Turner CH, Yoshikawa T, Slemenda CW, Peacock M, Burr DB, Mizuno Y, Orimo H, Ouchi Y, Johnston CC Jr. 1994. Do variations in hip geometry explain differences in hip fracture risk between Japanese and white Americans? *J Bone Miner Res* 9:1071–1076.
- Nakao H. 1988. Nutritional significance of human milk vitamin D in neonatal period. *Kobe J Med Sci* 34:121–128.
- Narang NK, Gupta RC, Jain MK. 1984. Role of vitamin D in pulmonary tuberculosis. *J Assoc Physicians India* 32:185–188.
- National Council for Nutrition (Conseil National de la Nutrition). 1994. *Recommendations nutritionnelles pour la Belgique*. Bruxelles, Belgium: Ministère des Affaires Sociales de la Santé Publique et de l’Environnement.
- National Food Administration. 1989. *Swedish Nutrition Recommendations, 2nd edition*. Uppsala, Sweden: National Food Administration.
- Need AG, Morris HA, Horowitz M, Nordin C. 1993. Effects of skin thickness, age, body fat, and sunlight on serum 25-hydroxyvitamin D. *Am J Clin Nutr* 58:882–885.
- Neri LC, Johansen HL. 1978. Water hardness and cardiovascular mortality. *Ann NY Acad Sci* 304:203–219.
- Neri LC, Johansen HL, Hewitt D, Marier J, Langner N. 1985. Magnesium and certain other elements and cardiovascular disease. *Sci Total Environ* 42:49–75.
- Netherlands Food and Nutrition Council. 1992. *Report on the Age Limit to be Adopted in Connection with “Guidelines for a Healthy Diet.”* The Hague: Netherlands Food and Nutrition Council.
- Neville MC, Keller R, Seacat J, Lutes V, Neifert M, Casey C, Allen J, Archer P. 1988. Studies in human lactation: Milk volumes in lactating women during the onset of lactation and full lactation. *Am J Clin Nutr* 48:1375–1386.
- Newmark K, Nugent P. 1993. Milk-alkali syndrome: A consequence of chronic antacid abuse. *Postgrad Med* 93:149–156.
- Ng K, St John A, Bruce DG. 1994. Secondary hyperparathyroidism, vitamin D deficiency and hip fracture: Importance of sampling times after fracture. *Bone Miner* 25:103–109.
- Niekamp RA, Baer JT. 1995. In-season dietary adequacy of trained male cross-country runners. *Int J Sport Nutr* 5:45–55.
- Nielsen FH. 1990. Studies on the relationship between boron and magnesium which possibly affects the formation and maintenance of bones. *Magnes Trace Elem* 9:61–69.
- Nielsen FH, Hunt CD, Mullen LM, Hunt JR. 1987. Effect of dietary boron on mineral, estrogen, and testosterone metabolism in postmenopausal women. *FASEB J* 1:394–397.
- Nieves JW, Golden AL, Siris E, Kelsey JL, Lindsay R. 1995. Teenage and current calcium intake are related to bone mineral density of the hip and forearm in women aged 30–39 years. *Am J Epidemiol* 141:342–351.

- NIH (National Institutes of Health). 1994. *Optimal Calcium Intake*. NIH Consensus Statement 12:4. Bethesda, MD: NIH.
- NIN (National Institute of Nutrition). 1995. Dairy products in the Canadian diet. NIN Review No. 24. Ontario, Canada: NIN.
- Nordin BEC. 1976. *Calcium, Phosphate and Magnesium Metabolism*. Edinburgh: Churchill Livingstone.
- Nordin BEC. 1989. Phosphorus. *J Food Nutr* 45:62–75.
- Nordin BEC, Polley KJ. 1987. Metabolic consequences of the menopause. A cross-sectional, longitudinal, and intervention study on 557 normal postmenopausal women. *Calcif Tissue Int* 41:S1–S59.
- Nose O, Iida Y, Kai H, Harada T, Ogawa M, Yabuuchi H. 1979. Breath hydrogen test for detecting lactose malabsorption in infants and children: Prevalence of lactose malabsorption in Japanese children and adults. *Arch Dis Child* 54:436–440.
- NRC (National Research Council). 1980. *Recommended Dietary Allowances, 9th Edition*. Committee on Dietary Allowances, Food and Nutrition Board. Washington, DC: National Academy Press.
- NRC (National Research Council). 1982. *Diet, Nutrition, and Cancer*. Report of the Committee on Diet, Nutrition, and Cancer, Assembly of Life Sciences. Washington, DC: National Academy Press.
- NRC (National Research Council). 1983. *Risk Assessment in the Federal Government: Managing the Process*. Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC (National Research Council). 1989a. *Recommended Dietary Allowances: 10th Edition*. Report of the Subcommittee on the Tenth Edition of the RDAs, Food and Nutrition Board, and the Commission on Life Sciences. Washington, DC: National Academy Press.
- NRC (National Research Council). 1989b. *Diet and Health: Implications for Reducing Chronic Disease Risk*. Report of the Committee on Diet and Health, Food and Nutrition Board, Commission on Life Sciences. Washington, DC: National Academy Press.
- NRC (National Research Council). 1993. *Health Effects of Ingested Fluoride*. Subcommittee on Health Effects of Ingested Fluoride. Washington, DC: National Academy Press.
- NRC (National Research Council). 1994. *Science and Judgment in Risk Assessment. Committee on Risk Assessment of Hazardous Air Pollutants*. Board on Environmental Studies and Toxicology. Washington, DC: National Academy Press.
- NRC (National Research Council). 1995. *Nutrient Requirements of Laboratory Animals*. Committee on Animal Nutrition, Board on Agriculture. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- O'Brien KO, Abrams SA, Stuff JE, Liang LK, Welch TR. 1996. Variables related to urinary calcium excretion in young girls. *J Pediatr Gastroenterol Nutr* 23:8–12.
- O'Dowd KJ, Clemens TL, Kelsey JL, Lindsay R. 1993. Exogenous calciferol (vitamin D) and vitamin D endocrine status among elderly nursing home residents in the New York City area. *J Am Geriatr Soc* 41:414–421.

- Ohlson MA, Brewer WD, Jackson L, Swanson PP, Roberts PH, Mangel M, Leverton RM, Chaloupka M, Gram MR, Reynolds MS, Lutz R. 1952. Intakes and retentions of nitrogen, calcium and phosphorus by 136 women between 30 and 85 years of age. *Fed Proc* 11:775–783.
- Oliveri MB, Ladizesky M, Mautalen CA, Alonso A, Martinez L. 1993. Seasonal variations of 25 hydroxyvitamin D and parathyroid hormone in Ushuaia (Argentina), the southernmost city in the world. *Bone Miner* 20:99–108.
- Ooms ME, Roos JC, Bezemer PD, VanDerVijgh WJ, Bouter LM, Lips P. 1995. Prevention of bone loss by vitamin D supplementation in elderly women: A randomized double-blind trial. *J Clin Endocrinol Metab* 80:1052–1058.
- Ophaug RH, Singer L, Harland BF. 1980a. Estimated fluoride intake of 6-month-old infants in four dietary regions of the United States. *Am J Clin Nutr* 33:324–327.
- Ophaug RH, Singer L, Harland BF. 1980b. Estimated fluoride intake of average two-year-old children in four dietary regions of the United States. *J Dent Res* 59:777–781.
- Ophaug RH, Singer L, Harland BF. 1985. Dietary fluoride intake of 6-month and 2-year-old children in four dietary regions of the United States. *Am J Clin Nutr* 42:701–707.
- Orimo H, Ouchi Y. 1990. The role of calcium and magnesium in the development of atherosclerosis. Experimental and clinical evidence. *Ann NY Acad Sci* 598:444–457.
- Orwoll ES. 1982. The milk-alkali syndrome: Current concepts. *Ann Intern Med* 97:242–248.
- Orwoll ES, Oviatt SK, McClung MR, Deftos LJ, Sexton G. 1990. The rate of bone mineral loss in normal men and the effects of calcium and cholecalciferol supplementation. *Ann Intern Med* 112:29–34.
- Osis D, Kramer L, Wiatrowski E, Spencer H. 1974. Dietary fluoride intake in man. *J Nutr* 104:1313–1318.
- Osteoporosis Society of Canada. 1993. Consensus on calcium nutrition. Official position of the Osteoporosis Society of Canada. *Nutr Quart* 18:62–69.
- Osuji OO, Leake JL, Chipman ML, Nikiforuk G, Locker D, Levine N. 1988. Risk factors for dental fluorosis in a fluoridated community. *J Dent Res* 67:1488–1492.
- OTA (Office of Technology Assessment). 1993. *Researching Health Risks*. Washington, DC: Office of Technology Assessment.
- Outhouse J, Kinsman G, Sheldon D, Tworney I, Smith J. 1939. The calcium requirements of five pre-school girls. *J Nutr* 17:199–211.
- Outhouse J, Breiter H, Rutherford E, Dwight J, Mills R, Armstrong W. 1941. The calcium requirement of man: Balance studies on seven adults. *J Nutr* 21:565–575.
- Paganini-Hill A, Chao A, Ross RK, Henderson BE. 1991. Exercise and other factors in the prevention of hip fracture: The Leisure World Study. *Epidemiology* 2:16–25.
- Pak CY. 1988. Medical management of nephrolithiasis in Dallas: Update 1987. *J Urol* 140:461–467.
- Pak CY, Sakhaei K, Rubin CD, Zerwekh JE. 1997. Sustained-release sodium fluoride in the management of established menopausal osteoporosis. *Am J Med Sci* 313:23–32.
- Pang DT, Phillips CL, Bawden JW. 1992. Fluoride intake from beverage consumption in a sample of North Carolina children. *J Dent Res* 71:1382–1388.

- Paolisso G, Passariello N, Pizza G, Marrazzo G, Giunta R, Sgambato S, Varricchio M, D'Onofrio F. 1989. Dietary magnesium supplements improve B-cell response to glucose and arginine in elderly non-insulin-dependent diabetic subjects. *Acta Endocrinol Copenh* 121:16–20.
- Paolisso G, Scheen A, D'Onofrio FD, Lefebvre P. 1990. Magnesium and glucose homeostasis. *Diabetologia* 33:511–514.
- Paolisso G, Sgambato S, Gambardella A, Pizza G, Tesauro P, Varricchio M, D'Onofrio F. 1992. Daily magnesium supplements improve glucose handling in elderly subjects. *Am J Clin Nutr* 55:1161–1167.
- Parfitt AM. 1977. Metacarpal cortical dimensions in hypoparathyroidism, primary hyperparathyroidism and chronic renal failure. *Calcif Tiss Res Suppl* 22:329–331.
- Parfitt AM. 1988. Bone remodeling: Relationship to the amount and structure of bone, and the pathogenesis and prevention of fractures. In: Riggs BL, Melton LJ III eds. *Osteoporosis: Etiology, Diagnosis, and Management*. New York, NY: Raven Press.
- Parfitt AM, Higgins BA, Nassim JR, Collins JA, Hilb A. 1964. Metabolic studies in patients with hypercalciuria. *Clin Sci* 27:463–482.
- Parfitt AM, Chir B, Gallagher JC, Heaney RP, Johnston CC, Neer R, Whedon GD. 1982. Vitamin D and bone health in the elderly. *Am J Clin Nutr* 36:1014–1031.
- Paunier L, Lacourt G, Pilloud P, Schlaeppi P, Sizomenko PC. 1978. 25-hydroxyvitamin D and calcium levels in maternal, cord and infant serum in relation to maternal vitamin D intake. *Helv Paediatr Acta* 33:95–103.
- Peace H, Beattie JH. 1991. No effect of boron on bone mineral excretion and plasma sex steroid levels in healthy postmenopausal women. Monography, proceedings, roundtables, and discussions of the Seventh International Symposium on Trace Elements in Man and Animals, held May 20–25, 1990, in Dubrovnik, Croatia, Yugoslavia.
- Peacock M. 1991. Calcium absorption efficiency and calcium requirements in children and adolescents. *Am J Clin Nutr* 54:261S–265S.
- Pedersen AB, Bartholomew MJ, Dolence LA, Aljadir LP, Netteburg KL, Lloyd T. 1991. Menstrual differences due to vegetarian and nonvegetarian diets. *Am J Clin Nutr* 53:879–885.
- Pendrys DG, Katz RV. 1989. Risk of enamel fluorosis associated with fluoride supplementation, infant formula, and fluoride dentifrice use. *Am J Epidemiol* 130:1199–1208.
- Pendrys DG, Morse DE. 1990. Use of fluoride supplementation by children living in fluoridated communities. *J Dent Child* 57:343–347.
- Pendrys DG, Stamm JW. 1990. Relationship of total fluoride intake to beneficial effects and enamel fluorosis. *J Dent Res* 69(Spec Iss):529–538.
- Peng SK, Taylor CB. 1980. Editorial: Probable role of excesses of vitamin D in genesis of arteriosclerosis. *Arterial Wall* 6:63–68.
- Peng SK, Taylor CB, Tham P, Mikkelsen B. 1978. Role of mild excesses of vitamin D in arteriosclerosis. A study in squirrel monkeys. *Arterial Wall* 4:229.
- Pennington JA. 1994. *Bowes and Church's Food Values of Portions Commonly Used*. Philadelphia, PA: JB Lippincott.
- Pennington JA, Wilson DB. 1990. Daily intakes of nine nutritional elements: Analyzed vs. calculated values. *J Am Diet Assoc* 90:375–381.
- Pennington JA, Young BE. 1991. Total diet study nutritional elements, 1982–1989. *J Am Diet Assoc* 91:179–183.

- Perloff BP, Rizek RL, Haytowitz DB, Reid PR. 1990. Dietary intake methodology. II. USDA's Nutrient Data Base for Nationwide Dietary Intake Surveys. *J Nutr* 120:1530–1534.
- Petley A, Macklin B, Renwick AG, Wilkin TJ. 1995. The pharmacokinetics of niacinamide in humans and rodents. *Diabetes* 44:152–155.
- Pett LB, Ogilvie GH. 1956. The Canadian Weight-Height Survey. *Hum Biol* 28:177–188.
- Pettifor JM, Ross FP, Moodley G, Wang J, Marco G, Skjolde C. 1978a. Serum calcium, magnesium, phosphorus, alkaline phosphatase and 25-hydroxyvitamin D concentrations in children. *S Afr Med J* 53:751–754.
- Pettifor JM, Ross P, Wang J, Moodley G, Couper-Smith J. 1978b. Rickets in children of rural origin in South Africa: Is low dietary calcium a factor? *J Pediatr* 92:320–324.
- Pettifor JM, Bikle DD, Cavaleros M, Zachen D, Kamdar MC, Ross FP. 1995. Serum levels of free 1,25-dihydroxyvitamin D in vitamin D toxicity. *Ann Intern Med* 122:511–513.
- Pietschmann P, Woloszczuk W, Pietschmann H. 1990. Increased serum osteocalcin levels in elderly females with vitamin D deficiency. *Exp Clin Endocrinol* 95:275–278.
- Pillai S, Bikle DD, Elias PM. 1987. 1,25-Dihydroxyvitamin D production and receptor binding in human keratinocytes varies with differentiation. *J Biol Chem* 263:5390–5395.
- Pitkin RM, Reynolds WA, Williams GA, Hargis GK. 1979. Calcium metabolism in normal pregnancy: A longitudinal study. *Am J Obstet Gynecol* 133:781–787.
- Pittard WB III, Geddes KM, Sutherland SE, Miller MC, Hollis BW. 1990. Longitudinal changes in the bone mineral content of term and premature infants. *Am J Dis Child* 144:36–40.
- Pluckebaum JM, Chavez N. 1994. Nutritional status of Northwest Indiana Hispanics in a congregate meal program. *J Nutr Elderly* 13:1–22.
- PNUN (Standing Nordic Committee on Food). 1989. *Nordic Nutrition Recommendations*, 2nd Edition. Oslo: Nordic Council of Ministers.
- Ponder SW, McCormick DP, Fawcett HD, Palmer JL, McKernan MG, Brouhard BH. 1990. Spinal bone mineral density in children aged 5.00 through 11.99 years. *Am J Dis Child* 144:1346–1348.
- Ponz de Leon M, Roncucci L, Di Donato P, Tassi L, Smerieri O, Amorico MG, Malagoli G, De Maria D, Antonioli A, Chahin NJ. 1988. Pattern of epithelial cell proliferation in colorectal mucosa of normal subjects and of patients with adenomatous polyps or cancer of the large bowel. *Cancer Res* 48:4121–4126.
- Portale AA, Booth BE, Halloran BP, Morris RC Jr. 1984. Effect of dietary phosphorus on circulating concentrations of 1,25-dihydroxyvitamin D and immunoreactive parathyroid hormone in children with moderate renal insufficiency. *J Clin Invest* 73:1580–1589.
- Portale AA, Halloran BP, Murphy MM, Morris RC. 1986. Oral intake of phosphorus can determine the serum concentration of 1,25-dihydroxyvitamin D by determining its production rate in humans. *J Clin Invest* 77:7–12.
- Portale AA, Halloran BP, Morris RC Jr. 1987. Dietary intake of phosphorus modulates the circadian rhythm in serum concentration of phosphorus. Implications for the renal production of 1,25-dihydroxyvitamin D. *J Clin Invest* 80:1147–1154.

- Portale AA, Halloran BP, Morris RC Jr. 1989. Physiologic regulation of the serum concentration of 1,25-dihydroxyvitamin D by phosphorus in normal men. *J Clin Invest* 83:1494–1499.
- Prentice A, Laskey MA, Shaw J, Cole TJ, Fraser DR. 1990. Bone mineral content of Gambian and British children aged 0–36 months. *Bone Miner* 10:211–214.
- Prentice A, Jarjou LM, Cole TJ, Stirling DM, Dibba B, Fairweather-Tait S. 1995. Calcium requirements of lactating Gambian mothers: Effects of a calcium supplement on breast-milk calcium concentration, maternal bone mineral content, and urinary calcium excretion. *Am J Clin Nutr* 62:58–67.
- Prichard JL. 1969. The prenatal and postnatal effects of fluoride supplements on West Australian school children, aged 6, 7 and 8, Perth, 1967. *Austral Dent J* 14:335–338.
- Prince RL, Smith M, Dick IM, Price RI, Webb PG, Henderson NK, Harris MM. 1991. Prevention of postmenopausal osteoporosis. A comparative study of exercise, calcium supplementation, and hormone-replacement therapy. *N Engl J Med* 325:1189–1195.
- Prince R, Devine A, Dick I, Criddle A, Kerr D, Kent N, Price R, Randell A. 1995. The effects of calcium supplementation (milk powder or tablets) and exercise on bone density in postmenopausal women. *J Bone Miner Res* 10:1068–1075.
- Purdie DW, Aaron JE, Selby PL. 1988. Bone histology and mineral homeostasis in human pregnancy. *Br J Obstet Gynecol* 95:849–854.
- Quamme GA. 1989. Control of magnesium transport in the thick ascending limb. *Am J Physiol* 256:F197–F210.
- Quamme GA. 1993. Laboratory evaluation of magnesium status. Renal function and free intracellular magnesium concentration. *Clin Lab Med* 13:209–223.
- Quamme GA, Dirks JH. 1986. The physiology of renal magnesium handling. *Renal Physiol* 9:257–269.
- Raisz LG, Niemann I. 1969. Effect of phosphate, calcium and magnesium on bone resorption and hormonal responses in tissue culture. *Endocrinology* 85:446–452.
- Rajalakshmi K, Srikantia SG. 1980. Copper, zinc, and magnesium content of breast milk of Indian women. *Am J Clin Nutr* 33:664–669.
- Raman L, Rajalakshmi K, Krishnamachari KA, Sastry JG. 1978. Effect of calcium supplementation to undernourished mothers during pregnancy on the bone density of the neonates. *Am J Clin Nutr* 31:466–469.
- Randall RE, Cohen D, Spray CC, Rossmeisl EC. 1964. Hypermagnesemia in renal failure. *Ann Intern Med* 61:73–88.
- Rao DR, Bello H, Warren AP, Brown GE. 1994. Prevalence of lactose maldigestion. Influence and interaction of age, race, and sex. *Dig Dis Sci* 39:1519–1524.
- Rasmussen HS, McNair P, Goransson L, Balslev S, Larsen OG, Aurup P. 1988. Magnesium deficiency in patients with ischemic heart disease with and without acute myocardial infarction uncovered by an intravenous loading test. *Arch Intern Med* 148:329–332.
- Ray NF, Chan JK, Thamer M, Melton LJ III. 1997. Medical expenditures for the treatment of osteoporotic fractures in the United States in 1995: Report from the National Osteoporosis Foundation. *J Bone Miner Res* 12:24–35.
- Reasner CA II, Dunn JF, Fetchick DA, Liel Y, Hollis BW, Epstein S, Shary J, Mundy GR, Bell NH. 1990. Alteration of vitamin D metabolism in Mexican-Americans. *J Bone Miner Res* 5:13–17.
- Recker RR. 1985. Calcium absorption and achlorhydria. *N Engl J Med* 313:70–73.

## ONLINE REFERENCES

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- Recker RR, Hassing GS, Lau JR, Saville PD. 1973. The hyperphosphatemic effect of disodium ethane-1-hydroxy-1, 1-diphosphonate (EHDP): Renal handling of phosphorus and the renal response to parathyroid hormone. *J Lab Clin Med* 81:258–266.
- Recker RR, Davies KM, Hinders SM, Heaney RP, Stegman MR, Kimmel DB. 1992. Bone gain in young adult women. *J Am Med Assoc* 268:2403–2408.
- Recker RR, Hinders S, Davies KM, Heaney RP, Stegman MR, Lappe JM, Kimmel DB. 1996. Correcting calcium nutritional deficiency prevents spine fractures in elderly women. *J Bone Miner Res* 11:1961–1966.
- Reddy GS, Norman AW, Willis DM, Goltzman D, Guyda H, Solomon S, Philips DR, Bishop JE, Mayer E. 1983. Regulation of vitamin D metabolism in normal human pregnancy. *J Clin Endocrinol Metab* 56:363–370.
- Reed A, Haugen M, Pachman LM, Langman CB. 1990. Abnormalities in serum osteocalcin values in children with chronic rheumatic diseases. *J Pediatr* 116:574–580.
- Reed JA, Anderson JJ, Tylavsky FA, Gallagher PN Jr. 1994. Comparative changes in radial-bone density of elderly female lacto-ovovegetarians and omnivores. *Am J Clin Nutr* 59:1197S–1202S.
- Reginster JY, Strause L, Deroisy R, Lecart MP, Saltman P, Franchimont P. 1989. Preliminary report of decreased serum magnesium in postmenopausal osteoporosis. *Magnesium* 8:106–109.
- Reichel H, Koeffler HP, Norman AW. 1989. The role of vitamin D endocrine system in health and disease. *N Engl J Med* 320:980–991.
- Reid IR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. 1995. Long-term effects of calcium supplementation on bone loss and fractures in postmenopausal women: A randomized controlled trial. *Am J Med* 98:331–335.
- Reinhart RA. 1988. Magnesium metabolism. A review with special reference to the relationship between intracellular content and serum levels. *Arch Intern Med* 148:2415–2420.
- Reinhold JG, Fardadji B, Abadi P, Ismail-Beigi F. 1991. Decreased absorption of calcium, magnesium, zinc and phosphorus by humans due to increased fiber and phosphorus consumption as wheat bread. *Am J Clin Nutr* 49:204–206.
- Resnick LM, Gupta RK, Laragh JH. 1984. Intracellular free magnesium in erythrocytes of essential hypertension: Relation to blood pressure and serum divalent cations. *Proc Natl Acad Sci USA* 81:6511–6515.
- Resnick L, Gupta R, and Bhargava KK, Gruenspan H, Alderman MH, Laragh JH. 1991. Cellular ions in hypertension, diabetes and obesity: A nuclear magnetic resonance spectroscopic study. *Hypertension* 17:951–957.
- Riancho JA, delArco C, Arteaga R, Herranz JL, Albajar M, Macias JG. 1989. Influence of solar irradiation on vitamin D levels in children on anticonvulsant drugs. *Acta Neurol Scand* 79:296–299.
- Ricci JM, Hariharan S, Helfott A, Reed K, O'Sullivan MJ. 1991. Oral tocolysis with magnesium chloride: A randomized controlled prospective clinical trial. *Am J Obstet Gynecol* 165:603–610.
- Richards A, Mosekilde L, Søgaard CH. 1994. Normal age-related changes in fluoride content of vertebral trabecular bone—relation to bone quality. *Bone* 15:21–26.
- Riggs BL, Melton LJ III. 1995. The worldwide problem of osteoporosis: Insights afforded by epidemiology. *Bone* 17:505S–511S.

- Riggs BL, O'Fallon WM, Muse J, O'Conner MK, Melton LJ III. 1996. Long-term effects of calcium supplementation on serum PTH, bone turnover, and bone loss in elderly women. *J Bone Miner Res* 11:S118.
- Rigo J, Salle BL, Picaud JC, Putet G, Senterre J. 1995. Nutritional evaluation of protein hydrolysate formulas. *Eur J Clin Nutr* 49:S26–S38.
- Riis B, Thomsen K, Christiansen C. 1987. Does calcium supplementation prevent postmenopausal bone loss? *N Engl J Med* 316:173–177.
- Ritz E. 1982. Acute hypophosphatemia. *Kidney Int* 22:84–94.
- Rizzoli R, Stoermann C, Ammann P, Bonjour J-P. 1994. Hypercalcemia and hyperosteolysis in vitamin D intoxication: Effects of clodronate therapy. *Bone* 15:193–198.
- Robertson, WG. 1985. Dietary factors important in calcium stone formation. In: Schwillie PO, Smith LH, Robertson WG, Vahlensieck W, eds. *Urolithiasis and Related Clinical Research*. New York: Plenum Press. Pp. 61–68.
- Romani A, Marfella C, Scarpa A. 1993. Cell magnesium transport and homeostasis: Role of intracellular compartments. *Miner Electrolyte Metab* 19:282–289.
- Roncucci L, Scalmati A, Ponz de Leon M. 1991. Pattern of cell kinetics in colorectal mucosa of patients with different types of adenomatous polyps of the large bowel. *Cancer* 68:873–878.
- Ronis DL, Lang WP, Farghaly MM, Passow E. 1993. Tooth brushing, flossing, and preventive dental visits by Detroit-area residents in relation to demographic and socioeconomic factors. *J Pub Hlth Dent* 53:138–145.
- Rosado JL, Lopez P, Morales M, Munoz E, Allen LH. 1992. Bioavailability of energy, nitrogen, fat, zinc, iron and calcium from rural and urban Mexican diets. *Br J Nutr* 68:45–58.
- Rowe JW, Minaker KL, Pallotta JA, Flier JS. 1983. Characterization of the insulin resistance of aging. *J Clin Invest* 71:1581–1587.
- Rubenowitz E, Axelsson G, Rylander R. 1996. Magnesium in drinking water and death from acute myocardial infarction. *Am J Epidemiol* 143:456–462.
- Rubin H. 1975. Central role for magnesium in coordinate control of metabolism and growth in animal cells. *Proc Natl Acad Sci USA* 72:3551–3555.
- Rude RK. 1993. Magnesium metabolism and deficiency. *Endocrinol Metab Clin North Am* 22:377–395.
- Rude RK, Olerich M. 1996. Magnesium deficiency: Possible role in osteoporosis associated with gluten-sensitive enteropathy. *Osteopor Int* 6:453–461.
- Rude RK, Singer FR. 1980. Magnesium deficiency and excess. *Ann Rev Med* 32:245–259.
- Rude RK, Oldham SB, Singer FR. 1976. Functional hypoparathyroidism and parathyroid hormone end-organ resistance in human magnesium deficiency. *Clin Endocrinol* 5:209–224.
- Rude RK, Bethune JE, Singer FR. 1980. Renal tubular maximum for magnesium in normal, hyperparathyroid and hypoparathyroid man. *J Clin Endocrinol Metab* 51:1425–1431.
- Rude RK, Manoogian C, Ehrlich L, DeRusso P, Ryzen E, Nadler J. 1989. Mechanisms of blood pressure regulation by magnesium in man. *Magnesium* 8:266–278.
- Rude RK, Stephen A, Nadler J. 1991. Determination of red blood cell intracellular free magnesium by nuclear magnetic resonance as an assessment of magnesium depletion. *Magnes Trace Elem* 10:117–121.

- Rudloff S, Lonnerdal B. 1990. Calcium retention from milk-based infant formulas, whey-hydrolysate formula, and human milk in weanling rhesus monkeys. *Am J Dis Child* 144:360–363.
- Rudnicki M, Frolich A, Rasmussen WF, McNair P. 1991. The effect of magnesium on maternal blood pressure in pregnancy-induced hypertension. A randomized double-blind placebo-controlled trial. *Acta Obstet Gynecol Scand* 70:445–450.
- Ruiz JC, Mandel C, Garabedian M. 1995. Influence of spontaneous calcium intake and physical exercise on the vertebral and femoral bone mineral density of children and adolescents. *J Bone Miner Res* 10:675–682.
- Russell AL. 1949. Dental effects of exposure to fluoride-bearing Dakota sandstone waters at various ages and for various lengths of time. II. Patterns of dental caries inhibition as related to exposure span, to elapsed time since exposure, and to periods of calcification and eruption. *J Dent Res* 28:600–612.
- Russell AL, Elvove E. 1951. Domestic water and dental caries. VII. A study of the fluoride-dental caries relationship in an adult population. *Pub Hlth Rep* 66:1389–1401.
- Ryan MP. 1987. Diuretics and potassium/magnesium depletion. Directions for treatment. *Am J Med* 82:38–47.
- Ryzen E, Elbaum N, Singer FR, Rude RK. 1985. Parenteral magnesium tolerance testing in the evaluation of magnesium deficiency. *Magnesium* 4:137–147.
- Ryzen E, Elkayam U, Rude RK. 1986. Low blood mononuclear cell magnesium in intensive cardiac care unit patients. *Am Heart J* 111:475–480.
- Sacks FM, Brown LE, Appel L, Borhani NO, Evans D, Whelton P. 1995. Combinations of potassium, calcium, and magnesium supplements in hypertension. *Hypertension* 26:950–956.
- Sakhaee K, Baker S, Zerwekh J, Poindexter J, Garcia-Hernandez PA, Pak CY. 1994. Limited risk of kidney stone formation during long-term calcium citrate supplementation in nonstone forming subjects. *J Urol* 152:324–327.
- Salama F, Whitford GM, Barenie JT. 1989. Fluoride retention by children from toothbrushing. *J Dent Res* 68(Spec Issue):335.
- Salle BL, Delvin E, Glorieux F, David L. 1990. Human neonatal hypocalcemia. *Biol Neonate* 58:S22–S31.
- Sandberg AS, Larsen T, Sandstrom B. 1993. High dietary calcium level decreases colonic phytate degradation in pigs fed a rapeseed diet. *J Nutr* 123:559–566.
- Sanders TA, Purves R. 1981. An anthropometric and dietary assessment of the nutritional status of vegan preschool children. *J Human Nutr* 35:349–357.
- Sandler RB, Slemenda CW, LaPorte RE, Cauley JA, Schramm MM, Barresi ML, Kriska AM. 1985. Postmenopausal bone density and milk consumption in childhood and adolescence. *Am J Clin Nutr* 42:270–274.
- Saunders D, Sillery J, Chapman R. 1988. Effect of calcium carbonate and aluminum hydroxide on human intestinal function. *Dig Dis Sci* 33:409–412.
- Schanler RJ, Garza C, Smith EO. 1985. Fortified mothers' milk for very low birth weight infants: Results of macromineral balance studies. *J Pediatr* 107:767–774.
- Schendel DE, Berg CJ, Yeargin-Allsopp M, Boyle CA, Decoufle P. 1996. Prenatal magnesium sulfate exposure and the risk for cerebral palsy or mental retardation among very low-birth-weight children aged 3 to 5 years. *J Am Med Assoc* 276:1805–1810.
- Schiffl H, Binswanger U. 1982. Renal handling of fluoride in healthy man. *Renal Physiol* 5:192–196.

- Schiller L, Santa Ana C, Sheikh M, Emmett M, Fordtran J. 1989. Effect of the time of administration of calcium acetate on phosphorus binding. *N Engl J Med* 320:1110–1113.
- Schlesinger ES, Overton DE, Riverhead LI, Chase HC, Cantwell KT. 1956. Newburgh-Kingston caries-fluorine study XIII. Pediatric findings after ten years. *J Am Dent Assoc* 52:296–306.
- Schlesinger L, Arevalo M, Arredondo S, Diaz M, Lonnerdal B, Stekel A. 1992. Effect of a zinc-fortified formula on immunocompetence and growth of malnourished infants. *Am J Clin Nutr* 56:491–498.
- Schmidt LE, Arfken CL, Heins JM. 1994. Evaluation of nutrient intake in subjects with non-insulin-dependent diabetes mellitus. *J Am Diet Assoc* 94:773–774.
- Schmidt-Gayk H, Goossen J, Lendle F, Seidel D. 1977. Serum 25-hydroxycholecalciferol in myocardial infarction. *Atherosclerosis* 26:55–58.
- Schneider EL, Guralnik JM. 1990. The aging of America. Impact on health care costs. *J Am Med Assoc* 263:2335–2340.
- Schofield FA, and Morrell E. 1960. Calcium, phosphorus and magnesium. *Fed Proc* 19:1014–1016.
- Schuman CA, Jones HW III. 1985. The “milk-alkali” syndrome: Two case reports with discussion of pathogenesis. *Quart J Med (New Series)* 55:119–126.
- Schutzmansky G. 1971. Fluoride tablet application in pregnant females. *Dtsch Stomatol* 21:122–129.
- Schwartz E, Chokas WV, Panariello VA. 1964. Metabolic balance studies of high calcium intake in osteoporosis. *Am J Med* 36:233–249.
- Schwartz GG, Hulka BS. 1990. Is vitamin D deficiency a risk factor for prostate cancer? *Anticancer Res* 10:1307–1312.
- Schwartz R, Walker G, Linz MD, MacKellar I. 1973. Metabolic responses of adolescent boys to two levels of dietary magnesium and protein. I. Magnesium and nitrogen retention. *Am J Clin Nutr* 26:510–518.
- Schwartz R, Spencer H, Welsh JJ. 1984. Magnesium absorption in human subjects from leafy vegetables, intrinsically labeled with stable  $^{26}\text{Mg}$ . *Am J Clin Nutr* 39:571–576.
- Schwartz R, Apgar BJ, Wien EM. 1986. Apparent absorption and retention of Ca, Cu, Mg, Mn, and Zn from a diet containing bran. *Am J Clin Nutr* 43:444–455.
- Schwartzman MS, Franck WA. 1987. Vitamin D toxicity complicating the treatment of senile, postmenopausal, and glucocorticoid-induced osteoporosis: Four case reports and a critical commentary on the use of vitamin D in these disorders. *Am J Med* 82:224–229.
- Sebastian A, Harris ST, Ottaway JH, Todd KM, Morris RC Jr. 1994. Improved mineral balance and skeletal metabolism in postmenopausal women treated with potassium bicarbonate. *N Engl J Med* 330:1776–1781.
- Sebert JL, Garabedian M, Chauvenet M, Maamer M, Agbomson F, Brazier M. 1995. Evaluation of a new solid formulation of calcium and vitamin D in institutionalized elderly subjects: A randomized comparative trial versus separate administration of both constituents. *Rev Rhum* 62:288–294.
- Seelig MS. 1981. Magnesium requirements in human nutrition. *Magnes Bull* 3(suppl):26–47.
- Seelig MS. 1993. Interrelationship of magnesium and estrogen in cardiovascular and bone disorders, eclampsia, migraine and premenstrual syndrome. *J Am Coll Nutr* 12:442–458.
- Seelig MS, Elin RJ. 1996. Is there a place for magnesium in the treatment of acute myocardial infarction? *Am Heart J* 132:471–477.

- Seki K, Makimura N, Mitsui C, Hirata J, Nagata I. 1991. Calcium-regulating hormones and osteocalcin levels during pregnancy: A longitudinal study. *Am J Obstet Gynecol* 164:1248–1252.
- Selby PL. 1994. Calcium requirement—A reappraisal of the methods used in its determination and their application to patients with osteoporosis. *Am J Clin Nutr* 60:944–948.
- Selby PL, Davies M, Marks JS, Mawer EB. 1995. Vitamin D intoxication causes hypercalcemia by increased bone resorption which responds to pamidronate. *Clin Endocrinol* 43:531–536.
- Sentipal JM, Wardlaw GM, Mahan J, Matkovic V. 1991. Influence of calcium intake and growth indexes on vertebral bone mineral density in young females. *Am J Clin Nutr* 54:425–428.
- Seydoux J, Girardin E, Paunier L, Beguin F. 1992. Serum and intracellular magnesium during normal pregnancy and in patients with pre-eclampsia. *Br J Obstet Gynecol* 99:207–211.
- Shapses SA, Robins SP, Schwartz EI, Chowdhury H. 1995. Short-term changes in calcium but not protein intake alter the rate of bone resorption in healthy subjects as assessed by urinary pyridinium cross-link excretion. *J Nutr* 125:2814–2821.
- Sharma OP. 1996. Vitamin D, calcium, and sarcoidosis. *Chest* 109:535–539.
- Shen YW, Taves DR. 1974. Fluoride concentrations in the human placenta and maternal and cord blood. *Am J Obstet Gynecol* 119:205–207.
- Sherman HC, Hawley E. 1922. Calcium and phosphorus metabolism in childhood. *J Biol Chem* 52:375–399.
- Shils ME. 1969. Experimental human magnesium depletion. *Medicine* 46:61–85.
- Shils ME. 1994. Magnesium. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*. Philadelphia, PA: Lea & Febiger. Pp. 164–184.
- Shils ME, Rude RK. 1996. Deliberations and evaluations of the approaches, endpoints and paradigms for magnesium dietary recommendations. *J Nutr* 126:2398S–2403S.
- Sibai BM, Villar MA, Bray E. 1989. Magnesium supplementation during pregnancy: A double-blind randomized controlled clinical trial. *Am J Obstet Gynecol* 161:115–119.
- Siener R, Hesse A. 1995. Influence of a mixed and a vegetarian diet on urinary magnesium excretion and concentration. *Br J Nutr* 73:783–790.
- Silverberg SJ, Shane E, Clemens TL, Dempster DW, Segre GV, Lindsay R, Bilezikian JP. 1986. The effect of oral phosphate administration on major indices of skeletal metabolism in normal subjects. *J Bone Miner Res* 1:383–388.
- Silvis SE, Paragas PD Jr. 1972. Paresthesias, weakness, seizures, and hypophosphatemia in patients receiving hyperalimentation. *Gastroenterology* 62:513–520.
- Simard PL, Lachapelle C, Trahan L, Naccache H, Demers M, Broduer JM. 1989. The ingestion of fluoride dentifrice by young children. *J Dent Child* 56:177–181.
- Simard PL, Naccache H, Lachapelle D, Brodeur JM. 1991. Ingestion of fluoride from dentifrices by children aged 12 to 24 months. *Clin Pediatr Phila* 30:614–617.
- Simmer K, Khanum S, Carlsson L, Thompson RP. 1988. Nutritional rehabilitation in Bangladesh—the importance of zinc. *Am J Clin Nutr* 47:1036–1040.
- Singer L, Ophaug R. 1979. Total fluoride intake of infants. *Pediatrics* 63:460–466.
- Singer L, Ophaug RH, Harland BF. 1980. Fluoride intakes of young male adults in the United States. *Am J Clin Nutr* 33:328–332.
- Singer L, Ophaug RH, Harland BF. 1985. Dietary fluoride intake of 15–19-year-old male adults residing in the United States. *J Dent Res* 64:1302–1305.

- Singh A, Jolly SS. 1970. Chronic toxic effects on the skeletal system. In: *Fluorides and Human Health*. Geneva: World Health Organization. Pp 238–249.
- Skajaa K, Dorup I, Sandstrom BM. 1991. Magnesium intake and status and pregnancy outcome in a Danish population. *Br J Obstet Gynecol* 98:919–928.
- Slattery ML, Sorenson AW, Ford MH. 1988. Dietary calcium intake as a mitigating factor in colon cancer. *Am J Epidemiol* 128:504–514.
- Slemenda CW, Reister TK, Hui SL, Miller JZ, Christian JC, Johnston CC Jr. 1994. Influences on skeletal mineralization in children and adolescents: Evidence for varying effects of sexual maturation and physical activity. *J Pediatr* 125:201–207.
- Slemenda CW, Peacock M, Hui S, Zhou L, Johnston CC Jr. 1997. Reduced rates of skeletal remodeling are associated with increased bone mineral density during the development of peak skeletal mass. *J Bone Miner Res* 12:676–682.
- Slesinski MJ, Subar AF, Kahle LL. 1996. Dietary intake of fat, fiber, and other nutrients is related to the use of vitamin and mineral supplements in the United States: The 1992 National Health Interview Survey. *J Nutr* 126:3001–3008.
- Smilkstein MJ, Smolinske SC, Kulig KW, Rumack, BH. 1988. Severe hypermagnesemia due to multiple-dose cathartic therapy. *West J Med* 148:208–211.
- Smith EL, Gilligan C, Smith PE, Sempos CT. 1989. Calcium supplementation and bone loss in middle-aged women. *Am J Clin Nutr* 50:833–842.
- Smith KT, Heaney RP, Flora L, Hinders SM. 1987. Calcium absorption from a new calcium delivery system (CCM). *Calcif Tissue Int* 41:351–352.
- Smith R, Dent CE. 1969. Vitamin D requirements in adults. Clinical and metabolic studies on seven patients with nutritional osteomalacia. *Bibl Nutr Dieta* 13:44–45.
- Snedeker SM, Smith SA, Greger JL. 1982. Effect of dietary calcium and phosphorus levels on the utilization of iron, copper, and zinc by adult males. *J Nutr* 112:136–143.
- Sojka JE, Wastney ME, Abrams S, Froese S, Martin BR, Weaver CM. 1997. Magnesium kinetics in adolescent girls determined using stable isotopes: Effects of high and low calcium intakes. *Am J Physiol* 273:R170–R175.
- Sojka JE, Weaver CM. 1995. Magnesium supplementation and osteoporosis. *Nutr Rev* 53:71–74.
- Sokoll LJ, Dawson-Hughes B. 1992. Calcium supplementation and plasma ferritin concentrations in premenopausal women. *Am J Clin Nutr* 56:1045–1048.
- Sorva A, Risteli J, Risteli L, Valimaki M, Tilvis R. 1991. Effects of vitamin D and calcium on markers of bone metabolism in geriatric patients with low serum 25-hydroxyvitamin D levels. *Calcif Tissue Int* 49:S88–S89.
- Southgate DAT, Widdowson EM, Smits BJ, Cooke WT, Walker CHM, Mathers NP. 1969. Absorption and excretion of calcium and fat by young infants. *Lancet* 1:487–489.
- Sowers M, Wallace RB, Lemke JH. 1985. Correlates of forearm bone mass among women during maximal bone mineralization. *Prev Med* 14:585–596.
- Sowers M, Wallace RB, Lemke JH. 1986. The relationship of bone mass and fracture history to fluoride and calcium intake: A study of three communities. *Am J Clin Nutr* 44:889–898.
- Sowers M, Clark MK, Jannausch ML, Wallace RB. 1991. A prospective study of bone mineral content and fracture in communities with differential fluoride exposure. *Am J Epidemiol* 133:649–660.
- Sowers M, Corton G, Shapiro B, Jannausch ML, Crutchfield M, Smith ML, Randolph JF, Hollis B. 1993. Changes in bone density with lactation. *J Am Med Assoc* 269:3130–3135.

- Sowers M, Randolph J, Shapiro B, Jannaush M. 1995a. A prospective study of bone density and pregnancy after an extended period of lactation with bone loss. *Obstet Gynecol* 85:285–289.
- Sowers M, Eyre D, Hollis BW, Randolph JF, Shapiro B, Jannausch ML, Crutchfield M. 1995b. Biochemical markers of bone turnover in lactating and nonlactating postpartum women. *J Clin Endocrinol Metab*. 80:2210–2216.
- Spak CJ, Ekstrand J, Zylberstein D. 1982. Bioavailability of fluoride added by baby formula and milk. *Caries Res* 16:249–256.
- Spak CJ, Hardell LI, De Chateau P. 1983. Fluoride in human milk. *Acta Paediatr Scand* 72:699–701.
- Spatling L, Spatling G. 1988. Magnesium supplementation in pregnancy. A double blind study. *Br J Obstet Gynecol* 95:120–125.
- Specker BL. 1996. Evidence for an interaction between calcium intake and physical activity on changes in bone mineral density. *J Bone Miner Res* 11:1539–1544.
- Specker BL, Tsang RC. 1987. Cyclical serum 25-hydroxyvitamin D concentrations paralleling sunshine exposure in exclusively breast-fed infants. *J Pediatr* 110:744–747.
- Specker BL, Tsang RC, Hollis BW. 1985a. Effect of race and diet on human-milk vitamin D and 25-hydroxyvitamin D. *Am J Dis Child* 139:1134–1137.
- Specker BL, Valanis B, Hertzberg V, Edwards N, Tsang RC. 1985b. Sunshine exposure and serum 25-hydroxyvitamin D concentrations in exclusively breast-fed infants. *J Pediatr* 107:372–376.
- Specker BL, Lichtenstein P, Mimouni F, Gormley C, Tsang RC. 1986. Calcium-regulating hormones and minerals from birth to 18 months of age: A cross-sectional study. II. Effects of sex, race, age, season, and diet on serum minerals, parathyroid hormone, and calcitonin. *Pediatrics* 77:891–896.
- Specker BL, Tsang RC, Ho ML, Miller D. 1987. Effect of vegetarian diet on serum 1,25-dihydroxyvitamin D concentrations during lactation. *Obstet Gynecol* 70:870–874.
- Specker BL, Tsang RC, Ho ML. 1991a. Changes in calcium homeostasis over the first year postpartum: Effect of lactation and weaning. *Obstet Gynecol* 78:56–62.
- Specker BL, Tsang RC, Ho ML, Landi TM, Gratton TL. 1991b. Low serum calcium and high parathyroid hormone levels in neonates fed “humanized” cow’s milk-based formula. *Am J Dis Child* 145:941–945.
- Specker BL, Ho ML, Oestreich A, Yin TA, Shui QM, Chen XC, Tsang RC. 1992. Prospective study of vitamin D supplementation and rickets in China. *J Pediatr* 120:733–739.
- Specker BL, Vieira NE, O’Brien KO, Ho ML, Heubi JE, Abrams SA, Yerger AL. 1994. Calcium kinetics in lactating women with low and high calcium intakes. *Am J Clin Nutr* 59:593–599.
- Specker BL, Beck A, Kalkwarf H, Ho M. 1997. Randomized trial of varying mineral intake on total body bone mineral accretion during the first year of life. *Pediatrics* 99:e12.
- Spencer H, Menczel J, Lewin I, Samachson J. 1965. Effect of high phosphorus intake on calcium and phosphorus metabolism in man. *J Nutr* 86:125–132.
- Spencer H, Lewin I, Fowler J, Samachson J. 1969. Influence of dietary calcium intake on  $\text{Ca}^{47}$  absorption in man. *Am J Med* 46:197–205.
- Spencer H, Kramer L, Osis D, Norris C. 1978a. Effect of phosphorus on the absorption of calcium and on the calcium balance in man. *J Nutr* 108:447–457.
- Spencer H, Lesniak M, Gatzka CA, Kramer L, Norris C, Coffey J. 1978b. Magnesium–calcium interrelationships in man. *Trace Substances Environ Hlth* 12:241–247.

- Spencer H, Kramer L, Lesniak M, DeBartolo M, Norris C, Osis D. 1984. Calcium requirements in humans. Report of original data and a review. *Clin Orthop Relat Res* 184:270–280.
- Spencer H, Fuller H, Norris C, Williams D. 1994. Effect of magnesium on the intestinal absorption of calcium in man. *J Am Coll Nutr* 13:485–492.
- Spencer H, Osis D, Lender M. 1981. Studies of fluoride metabolism in man. A review and report of original data. *Sci Total Environ* 17:1–12.
- Stamp TCB, Haddad JG, Twigg CA. 1977. Comparison of oral 25-hydroxycholecalciferol, vitamin D, and ultraviolet light as determinants of circulating 25-hydroxyvitamin D. *Lancet* 1:1341–1343.
- Stanbury SW. 1971. The phosphate ion in chronic renal failure. In: Hioco DJ, ed. *Phosphate et Metabolisme Phosphocalcique*. Paris: Sandoz Laboratories.
- Stapleton FB. 1994. Hematuria associated with hypercalciuria and hyperuricosuria: A practical approach. *Pediatr Nephrol* 8:756–761.
- Stearns G. 1968. Early studies of vitamin D requirement during growth. *Am J Pub Hlth* 58:2027–2035.
- Steenbock H, Black A. 1924. The reduction of growth-promoting and calcifying properties in a ration by exposure to ultraviolet light. *J Biol Chem* 61:408–422.
- Steichen JJ, Tsang RC. 1987. Bone mineralization and growth in term infants fed soy-based or cow milk-based formula. *J Pediatr* 110:687–692.
- Stein JH, Smith WO, Ginn HE. 1966. Hypophosphatemia in acute alcoholism. *Am J Med Sci* 252:78–83.
- Stendig-Lindberg G, Tepper R, Leichter I. 1993. Trabecular bone density in a two year controlled trial of peroral magnesium in osteoporosis. *Magnes Res* 6:155–163.
- Stephen KW, McCall DR, Tullis JI. 1987. Caries prevalence in northern Scotland before, and 5 years after, water defluoridation. *Br Dent J* 163:324–326.
- Stevenson CA, Watson AR. 1957. Fluoride osteosclerosis. *Am J Roentg Rad Ther Nucl Med* 78:13–18.
- Stumpf WE, Sar M, Reid FA, Tanakay Y, DeLuca HF. 1979. Target cells for 1,25-dihydroxyvitamin D<sub>3</sub> in intestinal tract, stomach, kidney, skin, pituitary, and parathyroid. *Science* 206:1188–1190.
- Suarez FL, Savaiano DA, Levitt MD. 1995. A comparison of symptoms after the consumption of milk or lactose-hydrolyzed milk by people with self-reported severe lactose intolerance. *N Engl J Med* 333:1–4.
- Svenningsen NW, Lindquist B. 1974. Postnatal development of renal hydrogen ion excretion capacity in relation to age and protein intake. *Acta Paediatr Scand* 63:721–731.
- Switzer RL. 1971. Regulation and mechanism of phosphoribosylpyrophosphate synthetase. III. Kinetic studies of the reaction mechanism. *J Biol Chem* 246:2447–2458.
- Tanner JT, Smith J, Defibaugh P, Angyal G, Villalobos M, Bueno MP, McGarrahan ET, Wehr HM, Muniz JF, Hollis BW. 1988. Survey of vitamin content of fortified milk. *J Assoc Off Anal Chem* 71: 607–610.
- Tanner JM. 1990. *Growth at Adolescence*. Oxford: Oxford University Press.
- Tatevossian A. 1990. Fluoride in dental plaque and its effects. *J Dent Res* 69(Spec Iss): 645–652.
- Taves DR. 1978. Fluoridation and mortality due to heart disease. *Nature* 272:361–362.
- Taves DR. 1983. Dietary intake of fluoride ashed (total fluoride) v. unashed (inorganic fluoride) analysis of individual foods. *Br J Nutr* 49:295–301.

- Taves DR, Neuman WF. 1964. Factors controlling calcification in vitro: Fluoride and magnesium. *Arch Biochem Biophys* 108:390–397.
- Taylor AF, Norman ME. 1984. Vitamin D metabolite levels in normal children. *Pediatr Res* 18: 886–890.
- Taylor CB, Hass GM, Ho KJ, Liu LB. 1972. Risk factors in the pathogenesis of arteriosclerotic heart disease and generalized atherosclerosis. *Ann Clin Lab Sci* 2:239.
- Teegarden D, Proulx WR, Martin BR, Zhao J, McCabe GP, Lyle RM, Peacock M, Slemenda C, Johnston CC, Weaver CM. 1995. Peak bone mass in young women. *J Bone Miner Res* 10:711–715.
- Ten Cate JM. 1990. In vitro studies on the effects of fluoride on de- and remineralization. *J Dent Res* 69(Spec Iss):614–619.
- Terblanche S, Noakes TD, Dennis SC, Marais D, Eckert M. 1992. Failure of magnesium supplementation to influence marathon running performance or recovery in magnesium-replete subjects. *Int J Sport Nutr* 2:154–164.
- Tesar R, Notelovitz M, Shim E, Kauwell G, Brown J. 1992. Axial and peripheral bone density and nutrient intakes of postmenopausal vegetarian and omnivorous women. *Am J Clin Nutr* 56:699–704.
- Thatcher HS, Rock L. 1928. Clinical notes, suggestions and new instruments. *J Am Med Assoc* 91:1185–1186.
- Theintz G, Buchs B, Rizzoli R, Slosman D, Clavien H, Sizonenko PC, Bonjour JP. 1992. Longitudinal monitoring of bone mass accumulation in healthy adolescents: Evidence for a marked reduction after 16 years of age at the levels of lumbar spine and femoral neck in female subjects. *J Clin Endocrinol Metab* 75:1060–1065.
- Thompson FE, Byers T. 1994. Dietary assessment resource manual. *J Nutr* 124:224S–231S.
- Thys-Jacobs S, Ceccarelli S, Bierman A, Weisman H, Cohen M-A, Alvir J. 1989. Calcium supplementation in premenstrual syndrome: A randomized cross-over trial. *J Gen Intern Med* 4:183–189.
- Tillman DM, Semple PF. 1988. Calcium and magnesium in essential hypertension. *Clin Sci* 75:395–402.
- Touitou Y, Godard JP, Ferment O, Chastang C, Proust J, Bogdan A, Auzeby A, Touitou C. 1987. Prevalence of magnesium and potassium deficiencies in the elderly. *Clin Chem* 33:518–523.
- Travis SF, Sugerman HJ, Ruberg RL, Dudrick SJ, Delivoria-Papadopoulos M, Miller L, Osaki FA. 1971. Alterations of red cell glycolytic intermediates and oxygen transport as a consequence of hypophosphatemia in patients receiving intravenous hyperalimentation. *N Engl J Med* 285:763–768.
- Tremaine WJ, Newcomer AD, Riggs BL, McGill DB. 1986. Calcium absorption from milk in lactase-deficient and lactase-sufficient adults. *Dig Dis Sci* 31:376–378.
- Tsang RC, Strub R, Brown DR, Steichen J, Hartman C, Chen IW. 1976. Hypomagnesemia in infants of diabetic mothers: Perinatal studies. *J Pediatr* 89:115–119.
- Tucker K. 1996. The use of epidemiological approaches and meta-analysis to determine mineral element requirements. *J Nutr* 126:2365S–2372S.
- Tucker K, Kiel DP, Hannan MT, Felson DT. 1995. Magnesium intake is associated with bone-mineral density (BMD) in elderly women. *J Bone Miner Res* 10:S466.
- Tylavsky FA, Anderson JJ. 1988. Dietary factors in bone health of elderly lacto-ovo vegetarian and omnivorous women. *Am J Clin Nutr* 48:842–849.

- Urakabe S, Nakata K, Ando A, Orita Y, Abe Y. 1975. Hypokalemia and metabolic acidosis from overuse of magnesium oxide. *Jpn Circ J* 39:1135–1137.
- USDA (US Department of Agriculture). 1985. *Nationwide Food Consumption Survey. Continuing Survey of Food Intakes of Individuals*. Women 19–50 years and their children 1–5 years, 1 day, 1985. Report No. 85-1. Hyattsville, MD: Nutrition Monitoring Division, Human Nutrition Information Service, USDA.
- USDA (US Department of Agriculture). 1991. *Provisional Table on the Vitamin D Content of Foods*. Hyattsville, MD: Nutrient Data Research Branch, USDA.
- USDA (US Department of Agriculture), Center for Nutrition Policy and Promotion. 1997. *Nutrient Content of the U.S. Food Supply, 1909–1994*. Washington DC: Center for Nutrition Policy and Promotion, USDA.
- USPHS (US Public Health Service). 1991. *Ad Hoc Subcommittee on Fluoride: Review of Fluoride Benefits and Risks*. Bethesda, MD: Department of Health and Human Services.
- Venkataraman PS, Tsang RC, Greer FR, Noguchi A, Laskarzewski P, Steichen JJ. 1985. Late infantile tetany and secondary hyperparathyroidism in infants fed humanized cow milk formula. Longitudinal follow-up. *Am J Dis Child* 139:664–668.
- Vicchio D, Yergey A, O'Brien K, Allen L, Ray R, Holick MF. 1993. Quantification and kinetics of 25-hydroxyvitamin D<sub>3</sub> by isotope dilution liquid chromatography/thermospray mass spectrometry. *Biol Mass Spectrom* 22:53–58.
- Vik T, Try K, Thelle DS, Forde OH. 1979. Tromso heart study: Vitamin D metabolism and myocardial infarction. *Br Med J* 2:176.
- Villar J, Repke JT. 1990. Calcium supplementation during pregnancy may reduce preterm delivery in high-risk populations. *Am J Obstet Gynecol* 163:1124–1131.
- Villareal DT, Civitelli R, Chines A, Avioli LV. 1991. Subclinical vitamin D deficiency in postmenopausal women with low vertebral bone mass. *J Clin Endocrinol Metab* 72: 628–634.
- Wacker WE, Parisi AF. 1968. Magnesium metabolism. *N Engl J Med* 45:658–663, 712–717, 772–776.
- Wagener DK, Novrjah P, Horowitz AM. 1995. *Trends in Childhood Use of Dental Care Products Containing Fluoride: United States, 1983–1989*. Advance data from Vital Health Statistics of the Center for Disease Control. National Center for Health Statistics #219; Nov. 20, 1992. Hyattsville, MD: National Center for Health Statistics.
- Walker AR, Richardson B, Walker F. 1972. The influence of numerous pregnancies and lactations on bone dimensions in South African Bantu and Caucasian mothers. *Clin Sci* 42:189–196.
- Walker RM, Linkswiler HM. 1972. Calcium retention in the adult human male as affected by protein intake. *J Nutr* 102:1297–1302.
- Wallach S, Verch RL. 1986. Tissue magnesium in spontaneously hypertensive rats. *Magnesium* 5:33–38.
- Wang CC, Kern R, Kaucher M. 1930. Minimum requirement of calcium and phosphorus in children. *Am J Dis Child* 39:768–773.
- Wardlaw GM, Pike AM. 1986. The effect of lactation on peak adult shaft and ultra-distal forearm bone mass in women. *Am J Clin Nutr* 44:283–286.
- Wasnich R, Yano K, Vogel J. 1983. Postmenopausal bone loss at multiple skeletal sites: Relationship to estrogen use. *J Chron Dis* 36:781–790.
- Wastney ME, Ng J, Smith D, Martin BR, Peacock M, Weaver CM. 1996. Differences in calcium kinetics between adolescent girls and young women. *Am J Physiol* 271:R208–R216.

- Waterhouse C, Taves D, Munzer A. 1980. Serum inorganic fluoride: Changes related to previous fluoride intake, renal function and bone resorption. *Clin Sci* 58:145–152.
- Weaver CM. 1994. Age-related calcium requirements due to changes in absorption and utilization. *J Nutr* 124:1418S–1425S.
- Weaver CM, Martin BR, Plawecki KL, Peacock M, Wood OB, Smith DL, Wastney ME. 1995. Differences in calcium metabolism between adolescent and adult females. *Am J Clin Nutr* 61:577–581.
- Webb AR, Kline L, Holick MF. 1988. Influence of season and latitude on the cutaneous synthesis of vitamin D<sub>3</sub>: Exposure to winter sunlight in Boston and Edmonton will not promote vitamin D<sub>3</sub> synthesis in human skin. *J Clin Endocrinol Metab* 67:373–378.
- Webb AR, De Costa BR, Holick MF. 1989. Sunlight regulates the cutaneous production of vitamin D<sub>3</sub> by causing its photodegradation. *J Clin Endocrinol Metab* 68:882–887.
- Webb AR, Pilbeam C, Hanafin N, Holick MF. 1990. An evaluation of the relative contributions of exposure to sunlight and of diet to the circulating concentrations of 25-hydroxyvitamin D in an elderly nursing home population in Boston. *Am J Clin Nutr* 51:1075–1081.
- Wei SH, Hattab FN, Mellberg JR. 1989. Concentration of fluoride and selected other elements in teas. *Nutrition* 5:237–240.
- Weinsier RL, Krumdieck CL. 1981. Death resulting from overzealous total parenteral nutrition: The refeeding syndrome revisited. *Am J Clin Nutr* 34:393–399.
- Weisman Y, Harell A, Edelstein S, Spirer Z, Golander A. 1979. 1,25-dihydroxyvitamin D<sub>3</sub> and 24,25-dihydroxyvitamin D<sub>3</sub> in vitro synthesis by human decidua and placenta. *Nature* 281:317–319.
- Weissberg N, Schwartz G, Shemesh O, Brooks BA, Algur N, Eylath U, Abraham AS. 1992. Serum and mononuclear cell potassium, magnesium, sodium and calcium in pregnancy and labour and their relation to uterine muscle contraction. *Magnes Res* 5:173–177.
- Wester PO, Dyckner T. 1980. Diuretic treatment and magnesium losses. *Acta Med Scand* 647:145–152.
- Whitford GM. 1994. Effects of plasma fluoride and dietary calcium concentrations on GI absorption and secretion of fluoride in the rat. *Calcif Tissue Int* 54:421–425.
- Whitford GM. 1996. The metabolism and toxicity of fluoride. In Myers HM, ed. *Monographs in Oral Science*, 2nd Revised Edition. Basel, Switzerland: Karger.
- Whitford GM, Allmann DW, Shahed AR. 1987. Topical fluorides: Effects on physiologic and biochemical processes. *J Dent Res* 66:1072–1078.
- Whiting SJ, Pluhator MM. 1992. Comparison of in vitro and in vivo tests for determination of availability of calcium from calcium carbonate tablets. *J Am Coll Nutr* 11:553–560.
- Whiting SJ, Wood RJ. 1997. Adverse effects of high-calcium diets in humans. *Nutr Rev* 55:1–9.
- WHO (World Health Organization). 1984. *Fluorine and Fluorides*. Environmental Health Criteria 36. Geneva: World Health Organization. Pp. 77–79.
- WHO (World Health Organization). 1987. *Principles for the Safety Assessment of Food Additives and Contaminants in Food*. Environmental Health Criteria 70. Geneva: World Health Organization.

- WHO (World Health Organization). 1994. *Assessment of Fracture Risk and its Application to Screening for Postmenopausal Osteoporosis*. Technical Report Series 843. Geneva: World Health Organization.
- WHO (World Health Organization). 1996. *Trace Elements in Human Nutrition and Health*. Prepared in collaboration with the Food and Agriculture Organization of the United Nations and the International Atomic Energy Agency. Geneva: World Health Organization.
- Wickham CA, Walsh K, Cooper C, Barker DJ, Margetts BM, Morris J, Bruce SA. 1989. Dietary calcium, physical activity, and risk of hip fracture: A prospective study. *Br Med J* 299:889–892.
- Widdowson EM. 1965. Absorption and excretion of fat, nitrogen, and minerals from “filled” milks by babies one week old. *Lancet* 2:1099–1105.
- Widdowson EM, Dickerson JWT. 1964. The chemical composition of the body. In: Comar CL, Bronner F, eds. *Mineral Metabolism: An Advanced Treatise, Vol. II. The Elements, Part A*. New York: Academic Press.
- Widdowson EM, McCance RA, Spray CM. 1951. The chemical composition of the human body. *Clin Sci* 10:113–125.
- Widman L, Wester PO, Stegmayr BK, Wirell M. 1993. The dose-dependent reduction in blood pressure through administration of magnesium. A double blind placebo controlled cross-over study. *Am J Hypertens* 6:41–45.
- Wiktorsson AM, Martinsson T, Zimmerman M. 1992. Caries prevalence among adults in communities with optimal and low water fluoride concentrations. *Community Dent Oral Epidemiol* 20:359–363.
- Wilkinson R. 1976. Absorption of calcium, phosphorus, and magnesium. In: Nor din BEC, ed. *Calcium, Phosphate and Magnesium Metabolism*. Edinburgh: Churchill Livingstone. Pp. 36–112.
- Willett W. 1990. *Nutritional Epidemiology*. New York, NY: Oxford University Press.
- Willett WC, Sampson L, eds. 1997. Dietary assessment methods. *Am J Clin Nutr* 65:1097S–1368S.
- Williams JE, Zwemer JD. 1990. Community water fluoride levels, preschool dietary patterns, and the occurrence of fluoride dental opacities. *J Pub Hlth Dent* 50:276–281.
- Williams ML, Rose CS, Morrow G, Sloan SE, Barness LA. 1970. Calcium and fat absorption in neonatal period. *Am J Clin Nutr* 23:1322–1330.
- Wilson SG, Retallack RW, Kent JC, Worth GK, Gutteridge DH. 1990. Serum free 1,25-dihydroxyvitamin D and the free 1,25-dihydroxyvitamin D index during a longitudinal study of human pregnancy and lactation. *Clin Endocrinol* 32:613–622.
- Wise A, Gilbert DJ. 1982. Phytate hydrolysis by germfree and conventional rats. *Appl Environ Microbiol* 43:753–756.
- Wisker E, Nagel R, Tanudjaja TK, Feldheim W. 1991. Calcium, magnesium, zinc, and iron balances in young women: Effects of a low-phytate barley-fiber concentrate. *Am J Clin Nutr* 54:553–559.
- Witteman JC, Willett WC, Stampfer MJ, Colditz GA, Sacks FM, Speizer FE, Rosner B, Hennekens CH. 1989. A prospective study of nutritional factors and hypertension among U.S. women. *Circulation* 80:1320–1327.
- Witteman JC, Grobbee DE, Derkx FH, Bouillon R, de Bruijn AM, Hofman A. 1994. Reduction of blood pressure with oral magnesium supplementation in women with mild to moderate hypertension. *Am J Clin Nutr* 60:129–135.
- Wong NL, Quamme GA, Dirks JH. 1986. Effects of acid-base disturbances on renal handling of magnesium in the dog. *Clin Sci* 70:277–284.

- Wood RJ, Zheng JJ. 1990. Milk consumption and zinc retention in postmenopausal women. *J Nutr* 120:398–403.
- Wood RJ, Sitrin MD, Rosenberg IH. 1988. Effect of phosphorus on endogenous calcium losses during total parenteral nutrition. *Am J Clin Nutr* 48:632–636.
- Woods KL, Fletcher S. 1994. Long-term outcome after intravenous magnesium sulphate in suspected acute myocardial infarction: The second Leicester Intravenous Magnesium Intervention Trial (LIMIT-2). *Lancet* 343:816–819.
- Workshop Reports. 1992. *J Dent Res* 71:1218–1227.
- Yamagata Z, Miyamura T, Iijima S, Asaka A, Sasaki M, Kato J, Koizumi K. 1994. Vitamin D receptor gene polymorphism and bone mineral density in healthy Japanese women. *Lancet* 344:1027.
- Yamamoto ME, Applegate WB, Klag MJ, Borhani NO, Cohen JD, Kirchner KA, Lakatos E, Sacks FM, Taylor JO, Hennekens CH. 1995. Lack of blood pressure effect with calcium and magnesium supplementation in adults with high-normal blood pressure. Results from Phase I of the Trials of Hypertension Prevention (TOHP). Trials of Hypertension Prevention (TOHP) Collaborative Research Group. *Ann Epidemiol* 5:96–107.
- Yano K, Heilbrun LK, Wasnich RD, Hankin JH, Vogel JM. 1985. The relationship between diet and bone mineral content of multiple skeletal sites in elderly Japanese men and women living in Hawaii. *Am J Clin Nutr* 42:877–888.
- Young GP, Thomas RJ, Bourne DW, Russell DM. 1985. Parenteral nutrition. *Med J Aust* 143:597–601.
- Zeghoud F, Vervel C, Guillozo H, Walrant-Debray O, Boutignon H, Garabedian M. 1997. Subclinical vitamin D deficiency in neonates: Definition and response to vitamin D supplements. *Am J Clin Nutr* 65:771–778.
- Zemel PC, Zemel MB, Urberg M, Douglas FL, Geiser R, Sower JR. 1990. Metabolic and hemodynamic effects of magnesium supplementation in patients with essential hypertension. *Am J Clin Nutr* 51:665–669.
- Ziegler EE, Fomon SJ. 1983. Lactose enhances mineral absorption in infancy. *J Pediatr Gastroenterol Nutr* 2:228–294.
- Zielhuis RL, van der Kreek FW. 1979. The use of a safety factor in setting health-based permissible levels for occupational exposure. *Int Arch Occup Environ Health* 42:191–201.
- Zipkin I, Zucas SM, Lavender DR, Fullmer HM, Schiffmann E, Corcoran BA. 1970. Fluoride and calcification of rat aorta. *Calcif Tissue Res* 6:173–182.

## IODINE

*Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*  
 (ISBN 0-309-07290-5), Chapter 8, pp. 284–289.

- Albert A, Keating FR Jr. 1949. Metabolic studies with  $I^{131}$  labeled thyroid compounds. *J Clin Endocrinol* 9:1406–1421.
- Ayromloo J. 1972. Congenital goiter due to maternal ingestion of iodides. *Obstet Gynecol* 39:818–822.
- Benmiloud M, Chaouki ML, Gutekunst R, Teichert HM, Wood WG, Dunn JT. 1994. Oral iodized oil for correcting iodine deficiency: Optimal dosing and outcome indicator selection. *J Clin Endocrinol Metab* 79:20–24.
- Berghout A, Wiersinga W. 1998. Thyroid size and thyroid function during pregnancy: An analysis. *Eur J Endocrinol* 138:536–542.
- Berson SA, Yalow RS. 1954. Quantitative aspects of iodine metabolism. The exchangeable organic iodine pool, and the rates of thyroidal secretion, peripheral degradation and fecal excretion of endogenously synthesized organically bound iodine. *J Clin Invest* 15:33–1552.
- Bleichrodt N, Born MP. 1994. A meta-analysis of research on iodine and its relationship to cognitive development. In: Stanbury JB, ed. *The Damaged Brain of Iodine Deficiency: Cognitive, Behavioral, Neuromotor, Educative Aspects*. NY: Cognizant Communication. Pp. 195–200.
- Bourdoux P. 1998. Evaluation of the iodine intake: Problems of the iodine/creatinine ratio—Comparison with iodine excretion and daily fluctuations of iodine concentration. *Exp Clin Endocrinol Diabetes* 106:S17–S20.
- Buchinger W, Lorenz-Wawschinek O, Semlitsch G, Langsteiger W, Binter G, Bonelli RM, Eber O. 1997. Thyrotropin and thyroglobulin as an index of optimal iodine intake: Correlation with iodine excretion of 39,913 euthyroid patients. *Thyroid* 7:593–597.
- Carnell NE, Valente WA. 1998. Thyroid nodules in Graves' disease: Classification, characterization, and response to treatment. *Thyroid* 8:647–652.
- Carswell F, Kerr MM, Hutchison JH. 1970. Congenital goitre and hypothyroidism produced by maternal ingestion of iodides. *Lancet* 1:1241–1243.
- Chow CC, Phillips DI, Lazarus JH, Parkes AB. 1991. Effect of low dose iodide supplementation on thyroid function in potentially susceptible subjects: Are dietary iodide levels in Britain acceptable? *Clin Endocrinol* 34:413–416.
- Croxson MS, Hall TD, Kletzky OA, Jaramillo JE, Nicoloff JT. 1977. Decreased serum thyrotropin induced by fasting. *J Clin Endocrinol Metab* 45:560–568.
- DeGroot LJ. 1966. Kinetic analysis of iodine metabolism. *J Clin Endocrinol Metab* 26:149–173.
- Delange F. 1989. Iodine nutrition and congenital hypothyroidism. In: Delange F, Fisher DA, Glinoer D, eds. *Research in Congenital Hypothyroidism*. New York: Plenum Press.
- Delange F. 1993. Requirements of iodine in humans. In: Delange F, Dunn JT, Glinoer D, eds. *Iodine Deficiency in Europe: A Continuing Concern*. New York: Plenum Press. Pp. 5–13.
- Delange F, Burgi H. 1989. Iodine deficiency disorders in Europe. *Bull World Health Organ* 67:317–325.

- Delange F, Ermans AM. 1991. Iodine deficiency. In: Braverman LE, Utiger RD, eds. *Werner and Ingbar's the Thyroid: A Fundamental and Clinical Text*, 6th ed. Philadelphia: JD Lippincott.
- Delange F, Lecomte P. 2000. Iodine supplementation: Benefits outweigh risks. *Drug Safety* 22:89–95.
- Delange F, Bourdoux P, Vo Thi LD, Ermans AM, Senterre J. 1984. Negative iodine balance in preterm infants. *Ann Endocrinol* 45:77.
- Delange F, Dunn JT, Glinoer D. 1993. In: *Iodine Deficiency in Europe. A Continuing Concern*. New York: Plenum Press.
- Delange F, Benker G, Caron P, Eber O, Ott W, Peter F, Podoba J, Simescu M, Szybinsky Z, Vertongen F, Vitti P, Wiersinga W, Zamrazil V. 1997. Thyroid volume and urinary iodine in European schoolchildren: Standardization of values for assessment of iodine deficiency. *Eur J Endocrinol* 136:180–187.
- Delange F, de Benoist B, Alnwick D. 1999. Risks of iodine-induced hyperthyroidism after correction of iodine deficiency by iodized salt. *Thyroid* 9:545–556.
- Dunn JT, Crutchfield HE, Gutekunst R, Dunn AD. 1993. Two simple methods for measuring iodine in urine. *Thyroid* 3:119–123.
- Dunn JT, Semigran MJ, Delange F. 1998. The prevention and management of iodine-induced hyperthyroidism and its cardiac features. *Thyroid* 8:101–106.
- Dworkin HJ, Jacquez JA, Beierwaltes WH. 1966. Relationship of iodine ingestion to iodine excretion in pregnancy. *J Clin Endocrinol Metab* 26:1329–1342.
- Emrich D, Karkavitsas N, Facorro U, Schurnbrand P, Schreibvogel I, Schicha H, Dirks H. 1982. Influence of increasing iodine intake on thyroid function in euthyroid and hyperthyroid states. *J Clin Endocrinol Metab* 54:1236–1241.
- Ermans AM, Dumont JE, Bastenie PA. 1963. Thyroid function in a goiter endemic: I. Impairment of hormone synthesis and secretion in the goitrous gland. *J Clin Endocrinol* 23:539–549.
- Eskin BA. 1977. Iodine and mammary cancer. *Adv Exp Med Biol* 91:293–304.
- Etling N, Padovani E, Fouque F, Tato L. 1986. First-month variations in total iodine content of human breast milks. *Early Hum Dev* 13:81–85.
- Farwell AP, Braverman LE. 1996. Thyroid and Antithyroid Drugs. In: Hardman JG, Limbird LE, Molinoff PB, Ruddon RW, Gilman AG, eds. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*, 9th ed. New York: McGraw-Hill. Pp. 1383–1409.
- Finkelstein R, Jacobi M. 1937. Fatal iodine poisoning: A clinicopathologic and experimental study. *Ann Intern Med* 10:1283–1296.
- Fischer PW, Giroux A. 1987. Iodine content of a representative Canadian diet. *J Can Diet Assoc* 48:24–27.
- Fisher DA, Oddie TH. 1969a. Thyroidal radioiodine clearance and thyroid iodine accumulation: Contrast between random daily variation and population data. *J Clin Endocrinol Metab* 29:111–115.
- Fisher DA, Oddie TH. 1969b. Thyroid iodine content and turnover in euthyroid subjects: Validity of estimation of thyroid iodine accumulation from short-term clearance studies. *J Clin Endocrinol Metab* 29:721–727.
- Foley TP Jr. 1992. The relationship between autoimmune thyroid disease and iodine intake: A review. *Endokrynol Pol* 43:53–69.
- Franceschi S. 1998. Iodine intake and thyroid carcinoma—A potential risk factor. *Exp Clin Endocrinol Diabetes* 106:S38–S44.
- Gaitan E. 1989. *Environmental Goitrogenesis*. Boca Raton: CRC Press.

- Gardner DF, Kaplan MM, Stanley CA, Utiger RD. 1979. Effect of tri-iodothyronine replacement on the metabolic and pituitary responses to starvation. *N Engl J Med* 300:579–584.
- Gardner DF, Utiger RD, Schwartz SL, Witorsch P, Myers B, Braverman LA, Witorsch RJ. 1987. Effects of oral erythrosine (2',4',5',7-tetraiodofluorescein) on thyroid function in normal men. *Toxicol Appl Pharmacol* 91:299–304.
- Gardner DF, Centor RM, Utiger RD. 1988. Effects of low dose oral iodide supplementation on thyroid function in normal men. *Clin Endocrinol* 28:283–288.
- Ghent WR, Eskin BA, Low DA, Hill LP. 1993. Iodine replacement in fibrocystic disease of the breast. *Can J Surg* 36:453–460.
- Glinner D. 1998. Iodine supplementation during pregnancy: Importance and biochemical assessment. *Exp Clin Endocrinol Diabetes* 106:S21.
- Gushurst CA, Mueller JA, Green JA, Sedor F. 1984. Breast milk iodine: Reassessment in the 1980s. *Pediatrics* 73:354–357.
- Gutekunst R, Smolarek H, Hasenpusch U, Stubbe P, Friedrich HJ, Wood WG, Scriba PC. 1986. Goitre epidemiology: Thyroid volume, iodine excretion, thyroglobulin and thyrotropin in Germany and Sweden. *Acta Endocrinol* 112:494–501.
- Harrison MT. 1968. Iodine balance in man. *Postgrad Med J* 44:69–71.
- Harrison MT, Harden R, Alexander WD, Wayne E. 1965. Iodine balance studies in patients with normal and abnormal thyroid function. *J Clin Endocrinol* 25:1077–1084.
- Hays MT. 1991. Localization of human thyroxine absorption. *Thyroid* 1:241–248.
- Hemken RW. 1980. Milk and meat iodine content: Relation to human health. *J Am Vet Med Assoc* 176:1119–1121.
- Hetzell BS, Maberly GF. 1986. Iodine. In: Mertz W, ed. *Trace Elements in Human and Animal Nutrition*, Vol. 2. Orlando: Academic Press. Pp. 139–208.
- Hollowell JG, Staehling NW, Hannon WH, Flanders DW, Gunter EW, Maberly GF, Braverman LE, Pino S, Miller DT, Garbe PL, DeLozier DM, Jackson RJ. 1998. Iodine nutrition in the United States. Trends and public health implications: Iodine excretion data from National Health and Nutrition Examination Surveys I and III (1971–1974 and 1988–1994). *J Clin Endocrinol Metab* 83:3401–3408.
- Ingenbleek Y, Malvaux P. 1974. Iodine balance studies in protein-calorie malnutrition. *Arch Dis Child* 49:305–309.
- Jackson IM. 1982. Thyrotropin-releasing hormone. *New Engl J Med* 306:145–155.
- Johnson LA, Ford HC, Doran J, Richardson VF. 1990. A survey of the iodide concentration of human milk. *N Z Med J* 103:393–394.
- Jooste PL, Weight MJ, Lombard CJ. 2000. Short-term effectiveness of mandatory iodization of table salt, at an elevated iodine concentration, on the iodine and goiter status of school children with endemic goiter. *Am J Clin Nutr* 71:75–80.
- Kahaly G, Dienes HP, Beyer J, Hommel G. 1997. Randomized, double blind, placebo-controlled trial of low dose iodide in endemic goiter. *J Clin Endocrinol Metab* 82:4049–4053.
- Klebanoff SJ. 1967. Iodination of bacteria: A bacterial mechanism. *J Exp Med* 126:1063–1078.
- Klein AH, Meltzer S, Kenny FM. 1972. Improved prognosis in congenital hypothyroidism treated before age three months. *J Pediatr* 81:912–915.
- Kurt TL, Morgan ML, Hnilica V, Bost R, Petty CS. 1996. Fatal iatrogenic iodine toxicity in a nine-week old infant. *J Toxicol Clin Toxicol* 34:231–234.

## ONLINE REFERENCES

## 1113

- LaFranchi SH, Buist NR, Murphey WH, Larsen PR, Foley TP Jr. 1977. Transient neonatal hypothyroidism detected by newborn screening program. *Pediatrics* 60:539–541.
- Larsson G, Victor A. 1988. Micturition patterns in a healthy female population, studied with a frequency/volume chart. *Scand J Urol Nephrol* 114:53–57.
- Laurberg P, Pedersen KM, Hreidarsson A, Sigfusson N, Iversen E, Knudsen PR. 1998. Iodine intake and the pattern of thyroid disorders: A comparative epidemiological study of thyroid abnormalities in the elderly in Iceland and in Jutland, Denmark. *J Clin Endocrinol Metab* 83:765–769.
- Lind P, Langsteger W, Molnar M, Gallowitsch HJ, Mikosch P, Gomez I. 1998. Epidemiology of thyroid diseases in iodine sufficiency. *Thyroid* 8:1179–1183.
- Loh KC. 2000. Amiodarone-induced thyroid disorders: A clinical review. *Postgrad Med J* 76:133–140.
- Malamos B, Koutras DA, Marketos SG, Rigopoulos GA, Yataganas XA, Binopoulos D, Sfontouris J, Pharmakiotis AD, Vought RL, London WT. 1967. Endemic goiter in Greece: An iodine balance study in the field. *J Clin Endocrinol Metab* 27:1372–1380.
- Malvaux P, Beckers C, de Visscher M. 1969. Iodine balance studies in nongoitrous children and in adolescents on low iodine intake. *J Clin Endocrinol Metab* 29:79–84.
- Massoudi MS, Meilahn EN, Orchard TJ, Foley TP Jr, Kuller LH, Constantino JP, Buhari AM. 1995. Prevalence of thyroid antibodies among healthy middle-aged women. Findings from the thyroid study in healthy women. *Ann Epidemiol* 5:229–233.
- Mattsson S, Lindstrom S. 1995. Diuresis and voiding pattern in healthy schoolchildren. *Br J Urol* 76:783–789.
- Means LJ, Rescorla FJ, Grosfeld JL. 1990. Iodine toxicity: An unusual cause of cardiovascular collapse during anesthesia in an infant with Hirschsprung's disease. *J Pediatr Surg* 25:1278–1279.
- Missler U, Gutekunst R, Wood WG. 1994. Thyroglobulin is a more sensitive indicator of iodine deficiency than thyrotropin: Development and evaluation of dry blood spot assays for thyrotropin and thyroglobulin in iodine-deficient geographical areas. *Eur J Clin Chem* 32:137–143.
- Money WL, Rawson RW. 1950. The experimental production of thyroid tumors in the rat exposed to prolonged treatment with thiouracil. *Cancer* 3:321–335.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance Data, Vital and Health Statistics of the National Center for Health Statistics, Number 174. Hyattsville, MD: National Center for Health Statistics.
- Moulopoulos DS, Koutras DA, Mantzos J, Souvatzoglou A, Piperinos GD, Karaiskos KS, Makriyannis D, Sfontouris J, Moulopoulos SD. 1988. The relation of serum T4 and TSH with the urinary iodine excretion. *J Endocrinol Invest* 11:437–439.
- Nath SK, Moinier B, Thuillier F, Rongier M, Desjeux JF. 1992. Urinary excretion of iodide and fluoride from supplemented food grade salt. *Int J Vitam Nutr Res* 62:66–72.
- Nelson M, Phillips DI. 1985. Seasonal variations in dietary iodine intake and thyrotoxicosis. *Hum Nutr Appl Nutr* 39:213–216.
- Nilsson R, Ehrenberg L, Fedoresak I. 1987. Formation of potential antigens from radiographic contrast media. *Acta Radiol* 28:473–477.

- Oddie TH, Fisher DA, Long JM. 1964. Factors affecting the estimation of iodine entering the normal thyroid gland using short-term clearance studies. *J Clin Endocrinol* 24:924–933.
- Parsad D, Saini R. 1998. Acneform eruption with iodized salt. *Int J Dermatol* 37:478.
- Paul T, Meyers B, Witorsch RJ, Pino S, Chipkin S, Ingbar SH, Braverman LE. 1988. The effect of small increases in dietary iodine on thyroid function in euthyroid subjects. *Metabolism* 37:121–124.
- Pedersen KM, Laurberg P, Iversen E, Knudsen PR, Gregersen HE, Rasmussen OS, Larsen KR, Eriksen GM, Johannessen PL. 1993. Amelioration of some pregnancy-associated variations in thyroid function by iodine supplementation. *J Clin Endocrinol Metab* 77:1078–1083.
- Pennington JA. 1990. A review of iodine toxicity reports. *J Am Diet Assoc* 90:1571–1581.
- Pennington JAT, Schoen SA, Salmon GD, Young B, Johnson RD, Marts RW. 1995. Composition of core foods in the U.S. food supply, 1982–1991. *J Food Comp and Anal* 8:171–217.
- Pinchera A, MacGillivray MH, Crawford JD, Freeman AG. 1965. Thyroid refractoriness in an athyreotic cretin fed soybean formula. *N Engl J Med* 273:83–87.
- Riggs DS. 1952. Quantitative aspects of iodine metabolism in man. *Pharmacol Rev* 4:284–370.
- Romano R, Jannini EA, Pepe M, Grimaldi A, Olivieri M, Spennati P, Cappa F, D'Armiento M. 1991. The effects of iodoprophylaxis on thyroid size during pregnancy. *Am J Obstet Gynecol* 164:482–485.
- Schuppert F, Ehrenthal D, Frilling A, Suzuki K, Napolitano G, Kohn LD. 2000. Increased major histocompatibility complex (MHC) expression in nontoxic goiters is associated with iodine depletion, enhanced ability of the follicular thyroglobulin to increase MHC gene expression, and thyroid antibodies. *J Clin Endocrinol Metab* 85:858–867.
- Senior B, Chernoff HL. 1971. Iodide goiter in the newborn. *Pediatrics* 47:510–515.
- Shepard TH, Pyne GE, Kirschvink JF, McLean M. 1960. Soybean goiter: Report of three cases. *N Engl J Med* 262:1099–1103.
- Stanbury JB, Ermans AE, Bourdoux P, Todd C, Oken E, Tonglet R, Vidor G, Braverman LE, Medeiros-Neto G. 1998. Iodine-induced hyperthyroidism: Occurrence and epidemiology. *Thyroid* 8:83–100.
- Sulzberger MB, Witten VH. 1952. Allergic dermatoses due to drugs. *Postgrad Med* 11:549–557.
- Suzuki H, Mashimo K. 1973. Further studies of “endemic goiter” in Hokkaido, Japan. In: Mashimo K, Suzuki H, eds. *Iodine Metabolism and Thyroid Function*, Vol. 6. Sapporo, Japan: Hokkaido University School of Medicine. P. 143.
- Suzuki H, Higuchi T, Sawa K, Ohtaki S, Horiuchi Y. 1965. “Endemic coast goiter” in Hokkaido, Japan. *Acta Endocrinol* 50:161–176.
- Swanson EW, Miller JK, Mueller FJ, Patton CS, Bacon JA, Ramsey N. 1990. Iodine in milk and meat of dairy cows fed different amounts of potassium iodide or ethylenediamine dihydroiodide. *J Dairy Sci* 73:398–405.
- Tresch DD, Sweet DL, Keelan MH, Lange RL. 1974. Acute iodide intoxication with cardiac irritability. *Arch Intern Med* 134:760–762.
- Trowbridge FL, Hand KE., Nichaman MZ. 1975. Findings relating to goiter and iodine in the Ten-State Nutrition Survey. *Am J Clin Nutr* 28:712–716.
- Venturi S, Venturi A, Cimini D, Arduini C, Venturi M, Guidi A. 1993. A new hypothesis: Iodine and gastric cancer. *Eur J Cancer Prev* 2:17–23.
- Vought RL, London WT. 1967. Iodine intake, excretion and thyroidal accumulation in healthy subjects. *J Clin Endocrinol Metab* 27:913–919.

- Wayne EJ, Koutras DA, Alexander WD. 1964. *Clinical Aspects of Iodine Metabolism*. Oxford: Blackwell Scientific.
- Wexler P, Gad SC, Hartung R, Henderson RF, Krenzelok EP, Locey BJ, Mehendale HM, Plaa GL, Pope C, Witschi H. 1998. *Encyclopedia of Toxicology*, Vol. 2. San Diego: Academic Press. Pp. 186–187.
- WHO (World Health Organization) Nutrition Unit. 1994. *Indicators for Assessing Iodine Deficiency Disorders and their Control through Salt Iodization*. Geneva: WHO.
- WHO/UNICEF/ICCIDD (United Nations Childrens Fund/International Council for Control of Iodine Deficiency Disorders). 1993. *Indicators for Assessing Iodine Deficiency Disorders and their Control Programmes*. Report of a joint WHO/UNICEF/ICCIDD consultation (review version). Geneva: WHO.
- Wolff J. 1969. Iodide goiter and the pharmacologic effects of excess iodide. *Am J Med* 47:101–124.
- Xu F, Sullivan K, Houston R, Zhao J, May W, Maberly G. 1999. Thyroid volumes in U.S. and Bangladeshi schoolchildren: Comparison with European schoolchildren. *Eur J Endocrinol* 140: 498–504.

Ibid., Chapter 14, pp. 578–579.

- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Examination Survey: Under-reporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Gibson RS, Ferguson EL. 1998. Assessment of dietary zinc in a population. *Am J Clin Nutr* 68:430S–434S.
- Hallberg L, Hulthen L. 2000. Prediction of dietary iron absorption: An algorithm for calculating absorption and bioavailability of dietary iron. *Am J Clin Nutr* 71:1147–1160.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1980. *Recommended Dietary Allowances*, 9th ed. Washington, DC: National Academy Press.
- NRC. 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC. 1989. *Recommended Dietary Allowances*, 10th ed. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Schoeller DA. 1999. Recent advances from application of doubly labeled water to measurement of human energy expenditure. *J Nutr* 129:1765–1768.

USDA (U.S. Department of Agriculture). 1999. *USDA Nutrient Database for Standard Reference*, Release 13. [Online.] Available: <http://www.nal.usda.gov/fnic/foodcomp> [accessed February 2000].

WHO (World Health Organization). 1996. Zinc. In: *Trace Elements in Human Nutrition and Health*. Geneva: WHO. Pp. 72–104.

## IRON

*Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*  
(ISBN 0-309-07290-5), Chapter 9, pp. 378–393.

- AAP (American Academy of Pediatrics). 1999. Iron fortification of infant formulas. *Pediatrics* 104:119–123.
- Abma JC, Chandra A, Mosher WD, Peterson LS, Piccinino LJ. 1997. Fertility, family planning, and women's health: New data from the 1995 National Survey of Family Growth. *Vital Health Stat* 23:1–114.
- Abrams SA, Wen J, Stuff JE. 1997. Absorption of calcium, zinc, and iron from breast milk by five- to seven-month-old infants. *Pediatr Res* 41:384–390.
- Akesson A, Bjellerup P, Berglund M, Bremme K, Vahter M. 1998. Serum transferrin receptor: A specific marker of iron deficiency in pregnancy. *Am J Clin Nutr* 68:1241–1246.
- Alexander D, Ball MJ, Mann J. 1994. Nutrient intake and haematological status of vegetarians and age-sex matched omnivores. *Eur J Clin Nutr* 48:538–546.
- Allen LH. 1993. Iron-deficiency anemia increases risk of preterm delivery. *Nutr Rev* 51:49–52.
- Allen LH. 1997. Pregnancy and iron deficiency: Unresolved issues. *Nutr Rev* 55:91–101.
- Allen LH. 2000. Anemia and iron deficiency: Effects on pregnancy outcome. *Am J Clin Nutr* 71:1280S–1284S.
- Allen LH, Ahluwalia N. 1997. *Improving Iron Status through Diet. The Application of Knowledge Concerning Dietary Iron Bioavailability in Human Populations*. OMNI Technical Papers, No. 8. Arlington, VA: John Snow International.
- Ames SK, Gorham BM, Abrams SA. 1999. Effects of high compared with low calcium intake on calcium absorption and incorporation of iron by red blood cells in small children. *Am J Clin Nutr* 70:44–48.
- Anderson AC. 1994. Iron poisoning in children. *Curr Opin Pediatr* 6:289–294.
- Anderson RR. 1993. Longitudinal changes of trace elements in human milk during the first 5 months of lactation. *Nutr Res* 13:499–510.
- Andersson H, Navert B, Bingham SA, Englyst HN, Cummings JH. 1983. The effects of breads containing similar amounts of phytate but different amounts of wheat bran on calcium, zinc and iron balance in man. *Br J Nutr* 50:503–510.
- Ansell JE, Wheby MS. 1972. Pica: Its relation to iron deficiency. A review of the recent literature. *Va Med Mon* 99:951–954.
- Archer DF, Dorin MH, Heine W, Nanavati N, Arce JC. 1999. Uterine bleeding in postmenopausal women on continuous therapy with estradiol and norethindrone acetate. *Obstet Gynecol* 94:323–329.
- Aronow WS, Ahn C. 1996. Three-year follow-up shows no association of serum ferritin levels with incidence of new coronary events in 577 persons aged  $\geq 62$  years. *Am J Cardiol* 78:678–679.
- Bacon BR, Olynyk JK, Brunt EM, Britton RS, Wolff RK. 1999. HFE genotype in patients with hemochromatosis and other liver diseases. *Ann Intern Med* 130:953–962.
- Baer DM, Tekawa IS, Hurley LB. 1994. Iron stores are not associated with acute myocardial infarction. *Circulation* 89:2915–2918.

- Banner W Jr, Tong TG. 1986. Iron poisoning. *Pediatr Clin North Am* 33:393–409.
- Barrett JF, Whittaker PG, Williams JG, Lind T. 1994. Absorption of non-haem iron from food during normal pregnancy. *Br Med J* 309:79–82.
- Beaton GH. 1974. Epidemiology of iron deficiency. In: Jacobs A, Worwood M, eds. *Iron in Biochemistry and Medicine*. London: Academic Press. Pp. 477–528.
- Beaton GH. 2000. Iron needs during pregnancy: Do we need to rethink our targets? *Am J Clin Nutr* 72:265S–271S.
- Beaton GH, McCabe GP. 1999. *Efficacy of Intermittent Iron Supplementation in the Control of Iron Deficiency Anemia in Developing Countries: An Analysis of Experience*. Report to the Micronutrient Initiative and the Canadian International Development Agency. Ottawa: International Development Research Centre.
- Beaton GH, Thein M, Milne H, Veen MJ. 1970. Iron requirements of menstruating women. *Am J Clin Nutr* 23:275–283.
- Beaton GH, Corey PN, Steeles C. 1989. Conceptual and methodological issues regarding the epidemiology of iron deficiency and their implications for studies of the functional consequences of iron deficiency. *Am J Clin Nutr* 50:575–588.
- Behall KM, Scholfield DJ, Lee K, Powell AS, Moser PB. 1987. Mineral balance in adult men: Effect of four refined fibers. *Am J Clin Nutr* 46:307–314.
- Beutler E, Felitti V, Gelbart T, Ngoc H. 2000. The effect of HFE genotypes on measurements of iron overload in patients attending a health appraisal clinic. *Ann Intern Med* 133:329–337.
- Bjorn-Rasmussen E, Hallberg L, Isaksson B, Arvidsson B. 1974. Food iron absorption in man. Applications of the two-pool extrinsic tag method to measure heme and non-heme iron absorption from the whole diet. *J Clin Invest* 53:247–255.
- Blot I, Papiernik E, Kaltwasser JP, Werner E, Tchernia G. 1981. Influence of routine administration of folic acid and iron during pregnancy. *Gynecol Obstet Invest* 12:294–304.
- Bomford A, Williams R. 1976. Long term results of venesection therapy in idiopathic haemochromatosis. *Q J Med* 45:611–623.
- Bothwell TH. 2000. Iron requirements in pregnancy and strategies to meet them. *Am J Clin Nutr* 72:257S–264S.
- Bothwell TH, Charlton RW. 1981. *Iron Deficiency in Women*. Washington, DC: The Nutrition Foundation. Pp. 7–9.
- Bothwell TH, Finch CA. 1962. *Iron Metabolism*. Boston: Little, Brown.
- Bothwell TH, MacPhail AP. 1998. Hereditary hemochromatosis: Etiologic, pathologic, and clinical aspects. *Semin Hematol* 35:55–71.
- Bothwell TH, Seftel H, Jacobs P, Torrance JD, Baumslag N. 1964. Iron overload in Bantu subjects. Studies on the availability of iron in Bantu beer. *Am J Clin Nutr* 14:47–51.
- Bothwell TH, Charlton RW, Cook JD, Finch CA. 1979. *Iron Metabolism in Man*. Oxford: Blackwell Scientific.
- Braun J. 1999. Erythrocyte zinc protoporphyrin. *Kidney Int Suppl* 69:S57–S60.
- Brigham D, Beard J. 1996. Iron and thermoregulation: A review. *Crit Rev Food Sci Nutr* 36:747–763.
- Bro S, Sandstrom B, Heydorn K. 1990. Intake of essential and toxic trace elements in a random sample of Danish men as determined by the duplicate portion sampling technique. *J Trace Elem Electrolytes Health Dis* 4:147–155.

- Brock C, Curry H, Hanna C, Knipfer M, Taylor L. 1985. Adverse effects of iron supplementation: A comparative trial of wax-matrix iron preparation and conventional ferrous sulfate tablets. *Clin Ther* 7:568–573.
- Brune M, Rossander-Hulten L, Hallberg L, Gleerup A, Sandberg AS. 1992. Iron absorption from bread in humans: Inhibiting effects of cereal fiber, phytate and inositol phosphates with different numbers of phosphate groups. *J Nutr* 122:442–449.
- Bulaj ZJ, Griffen LM, Jorde LB, Edwards CQ, Kushner JP. 1996. Clinical and biochemical abnormalities in people heterozygous for hemochromatosis. *N Engl J Med* 335:1799–1805.
- Burman D. 1972. Haemoglobin levels in normal infants aged 3 to 24 months, and the effect of iron. *Arch Dis Child* 47:261–271.
- Butler NR, Bonham DB. 1963. *Perinatal Mortality*. The first report of the 1958 British Perinatal Mortality Survey. Edinburgh: Livingstone.
- Butte NF, Garza C, Smith EO, Wills C, Nichols BL. 1987. Macro- and trace-mineral intakes of exclusively breast-fed infants. *Am J Clin Nutr* 45:42–48.
- Canadian Paediatric Society. 1991. Meeting the iron needs of infants and young children: An update. *Canadian Med Assoc J* 144:1451–1454.
- Cannone-Hergaux F, Gruenheid S, Ponka P, Gros P. 1999. Cellular and subcellular localization of the Nramp2 iron transporter in the intestinal brush border and regulation by dietary iron. *Blood* 93:4406–4417.
- CDC (Centers for Disease Control). 1989. CDC criteria for anemia in children and childbearing-aged women. *Morbid Mortal Weekly Rpt* 38:400–404.
- Chalevelakis G, Tsirouannis K, Hatzioannou J, Arapakis G. 1984. Screening for thalassaemia and/or iron deficiency: Evaluation of some discrimination functions. *Scan J Clin Lab Invest* 44:1–6.
- Clarkson PM, Haymes EM. 1995. Exercise and mineral status of athletes: Calcium, magnesium, phosphorous, and iron. *Med Sci Sports Exerc* 27:831–843.
- Cole SK, Billewicz WZ, Thomson AM. 1971. Sources of variation in menstrual blood loss. *J Obstet Gynaecol Br Commonw* 78:933–939.
- Conrad ME. 1968. Intraluminal factors affecting iron absorption. *Isr J Med Sci* 4:917–931.
- Conrad ME, Umbreit JN. 2000. Iron absorption and transport—An update. *Am J Hematol* 64:287–298.
- Conrad ME, Benjamin B, Williams H, Foy A. 1967. Human absorption of hemoglobin-iron. *Gastroenterology* 53:5–10.
- Cook J. 1999. The nutritional assessment of iron status. *Arch Latinoam Nutr* 49:11S–14S.
- Cook JD, Lynch SR. 1986. The liabilities of iron deficiency. *Blood* 68:803–809.
- Cook JD, Lipschitz DA, Miles LE, Finch CA. 1974. Serum ferritin as a measure of iron stores in normal subjects. *Am J Clin Nutr* 27:681–687.
- Cook JD, Dassenko S, Skikne BS. 1990. Serum transferrin receptor as an index of iron absorption. *Br J Haematol* 75:603–609.
- Cook JD, Dassenko SA, Lynch SR. 1991. Assessment of the role of nonheme-iron availability in iron balance. *Am J Clin Nutr* 54:717–722.
- Cook JD, Reddy MB, Burri J, Juillerat MA, Hurrell RF. 1997. The influence of different cereal grains on iron absorption from infant cereal foods. *Am J Clin Nutr* 65:964–969.
- Coplin M, Schuette S, Leichtmann G, Lashner B. 1991. Tolerability of iron: A comparison of bis-glycino iron II and ferrous sulfate. *Clin Ther* 13:606–612.

- Coudray C, Bellanger J, Castiglia-Delavaud C, Remesy C, Vermorel M, Rayssignuier Y. 1997. Effect of soluble or partly soluble dietary fibres supplementation on absorption and balance of calcium, magnesium, iron and zinc in healthy young men. *Eur J Clin Nutr* 51:375–380.
- Dallman PR. 1986a. Biochemical basis for the manifestations of iron deficiency. *Annu Rev Nutr* 6:13–40.
- Dallman PR. 1986b. Iron deficiency in the weanling: A nutritional problem on the way to resolution. *Acta Paediatr Scand Suppl* 323:59–67.
- Dallman PR, Refino CA, Yland MJ. 1982. Sequence of development of iron deficiency in the rat. *Am J Clin Nutr* 35:671–677.
- Dalton MA, Sargent JD, O'Connor GT, Olmstead EM, Klein RZ. 1997. Calcium and phosphorous supplementation of iron-fortified infant formula: No effect on iron status of healthy full-term infants. *Am J Clin Nutr* 65:921–926.
- Danesh J, Appleby P. 1999. Coronary heart disease and iron status: Meta-analyses of prospective studies. *Circulation* 99:852–854.
- Davidsson L, Almgren A, Sandstrom B, Hurrell RF. 1995. Zinc absorption in adult humans: The effect of iron fortification. *Br J Nutr* 74:417–425.
- Davidsson L, Galan P, Cherouvrier F, Kastenmayer P, Juillerat MA, Hercberg S, Hurrell RF. 1997. Bioavailability in infants of iron from infant cereals: Effect of dephytinization. *Am J Clin Nutr* 65:916–920.
- Davidsson L, Kastenmayer P, Szajewska H, Hurrell RF, Barclay D. 2000. Iron bioavailability in infants from an infant cereal fortified with ferric pyrophosphate or ferrous fumarate. *Am J Clin Nutr* 71:1597–1602.
- Davies KJ, Donovan CM, Refino CJ, Brooks GA, Packer L, Dallman PR. 1984. Distinguishing effects of anemia and muscle iron deficiency on exercise bioenergetics in the rat. *Am J Physiol* 246:E535–E543.
- De Leeuw NK, Lowenstein L, Hsieh YS. 1966. Iron deficiency and hydremia in normal pregnancy. *Medicine* 45:291–315.
- Derman DP, Bothwell TH, MacPhail AP, Torrance JD, Bezwoda WR, Charlton RW, Mayet FG. 1980. Importance of ascorbic acid in the absorption of iron from infant foods. *Scand J Haematol* 25:193–201.
- Dewey KG, Lonnerdal B. 1983. Milk and nutrient intake of breast-fed infants from 1 to 6 months: Relation to growth and fatness. *J Pediatr Gastroenterol Nutr* 2:497–506.
- Dewey KG, Romero-Abal ME, Quan de Serrano J, Bulux J, Peerson JM, Engle P, Solomons NW. 1997. A randomized intervention study of the effects of discontinuing coffee intake on growth and morbidity of iron-deficient Guatemalan toddlers. *J Nutr* 127:306–313.
- Dibley MJ, Goldsby JB, Staehling NW, Trowbridge FL. 1987. Development of normalized curves for the international growth reference: Historical and technical considerations. *Am J Clin Nutr* 46:736–748.
- Dinneen SF, O'Mahony MS, O'Brien T, Cronin CC, Murray DM, O'Sullivan DJ. 1992. Serum ferritin in newly diagnosed and poorly controlled diabetes mellitus. *Ir J Med Sci* 161:636–638.
- Disler PB, Lynch SR, Charlton RW, Torrance JD, Bothwell TH, Walker RB, Mayet F. 1975. The effect of tea on iron absorption. *Gut* 16:193–200.
- Dwyer JT, Dietz WH, Andrews EM, Suskind RM. 1982. Nutritional status of vegetarian children. *Am J Clin Nutr* 35:204–216.
- Edlund M, Blomback M, von Schoultz B, Andersson O. 1996. On the value of menorrhagia as a predictor for coagulation disorders. *Am J Hematol* 53:234–238.

- Ehn L, Carlmark B, Hoglund S. 1980. Iron status in athletes involved in intense physical activity. *Med Sci Sports Exerc* 12:61–64.
- Eisenstein RS. 2000. Iron regulatory proteins and the molecular control of mammalian iron metabolism. *Annu Rev Nutr* 20:627–662.
- Eisenstein RS, Blehmings KP. 1998. Iron regulatory proteins, iron responsive elements and iron homeostasis. *J Nutr* 128:2295–2298.
- Expert Scientific Working Group. 1985. Summary of a report on assessment of the iron nutritional status of the United States population. *Am J Clin Nutr* 42:1318–1330.
- Fairbanks VF. 1999. Iron in medicine and nutrition. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th ed. Baltimore: Williams & Wilkins. Pp. 193–221.
- Fairweather-Tait S, Fox T, Wharf SG, Eagles J. 1995a. The bioavailability of iron in different weaning foods and the enhancing effect of a fruit drink containing ascorbic acid. *Pediatr Res* 37:389–394.
- Fairweather-Tait S, Wharf SG, Fox TE. 1995b. Zinc absorption in infants fed iron-fortified weaning food. *Am J Clin Nutr* 62:785–789.
- FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization). 1988. *Requirements of Vitamin A, Iron, Folate and Vitamin B<sub>12</sub>*. FAO Food and Nutrition Series No. 23. Rome: FAO. Pp. 33–50.
- Farquhar JD. 1963. Iron supplementation during first year of life. *Am J Dis Child* 106:201–206.
- FDA (Food and Drug Administration). 1997. *Preventing Iron Poisoning in Children*. FDA Backgrounder. [Online]. Available: <http://www.fda.gov/opacom/backgrounder/ironbg.html> [accessed July 1999].
- Feder JN. 1999. The hereditary hemochromatosis gene (HFE): A MHC class I-like gene that functions in the regulation of iron homeostasis. *Immunol Res* 20:175–185.
- Ferguson BJ, Skikne BS, Simpson KM, Baynes RD, Cook JD. 1992. Serum transferrin receptor distinguishes the anemia of chronic disease from iron deficiency anemia. *J Lab Clin Med* 119:385–390.
- Finch CA, Huebers H. 1982. Perspectives in iron metabolism. *N Engl J Med* 306:1520–1528.
- Finch CA, Miller LR, Inamdar AR, Person R, Seiler K, Mackler B. 1976. Iron deficiency in the rat. Physiological and biochemical studies of muscle dysfunction. *J Clin Invest* 58:447–453.
- Fleming AF. 1968. Hypoplastic anaemia in pregnancy. *J Obstet Gynaecol Br Commonw* 75:138–141.
- Fogelholm M. 1995. Inadequate iron status in athletes: An exaggerated problem? In: Kies CV, Driskell JA, eds. *Sports Nutrition: Minerals and Electrolytes*. Boca Raton: CRC Press. Pp. 81–95.
- Fomon SJ, Ziegler EE, Nelson SE. 1993. Erythrocyte incorporation of ingested <sup>58</sup>Fe by 56-day-old breast-fed and formula-fed infants. *Pediatr Res* 33:573–576.
- Ford ES, Cogswell ME. 1999. Diabetes and serum ferritin concentration among U.S. adults. *Diabetes Care* 22:1978–1983.
- Franco RF, Zago MA, Trip MD, ten Cate H, van den Ende A, Prins MH, Kastelein JJ, Reitsma PH. 1998. Prevalence of hereditary haemochromatosis in premature atherosclerotic vascular disease. *Br J Haematol* 102:1172–1175.
- Frey GH, Krider DW. 1994. Serum ferritin and myocardial infarct. *WV Med J* 90:13–15.

- Frisancho AR. 1990. *Anthropometric Standards for the Assessment of Growth and Nutritional Status*. Ann Arbor: University of Michigan Press.
- Frykman E, Bystrom M, Jansson U, Edberg A, Hansen T. 1994. Side effects of iron supplements in blood donors: Superior tolerance of heme iron. *J Lab Clin Med* 123:561–564.
- Fuerth JH. 1972. Iron supplementation of the diet in full-term infants: A controlled study. *J Pediatr* 80:974–979.
- Fung EB, Ritchie LD, Woodhouse LR, Roehl R, King JC. 1997. Zinc absorption in women during pregnancy and lactation: A longitudinal study. *Am J Clin Nutr* 66:80–88.
- Garby L, Sjolin S, Vuille JC. 1964. Studies on erythro-kinetics in infancy. IV. The long-term behaviour of radioiron in circulating foetal and adult haemoglobin and its faecal excretion. *Acta Paediatr Scand* 53:33–41.
- Garby L, Irnell L, Werner I. 1969. Iron deficiency in women of fertile age in a Swedish community. II. Efficiency of several laboratory tests to predict the response to iron supplementation. *Acta Med Scand* 185:107–111.
- Garn SM, Ridella SA, Petzold AS, Falkner F. 1981. Maternal hematologic levels and pregnancy outcomes. *Sem Perinatol* 5:155–162.
- Garry P, Koehler KM, Simon TL. 1995. Iron stores and iron absorption: Effects of repeated blood donations. *Am J Clin Nutr* 62:611–620.
- Garza C, Johnson CA, Smith EO, Nichols BL. 1983. Changes in the nutrient composition of human milk during gradual weaning. *Am J Clin Nutr* 37:61–65.
- Gillooly M, Bothwell TH, Torrance JD, MacPhail AP, Derman DP, Bezwoda WR, Mills W, Charlton RW, Mayet F. 1983. The effects of organic acids, phytates and polyphenols on the absorption of iron from vegetables. *Br J Nutr* 49:331–342.
- Gillooly M, Bothwell TH, Charlton RW, Torrance JD, Bezwoda WR, MacPhail AP, Derman DP, Novelli L, Morrall P, Mayet F. 1984. Factors affecting the absorption of iron from cereals. *Br J Nutr* 51:37–46.
- Goepel E, Ulmer HU, Neth RD. 1988. Premature labor contractions and the value of serum ferritin during pregnancy. *Gynecol Obstet Invest* 26:265–273.
- Gordeuk V, Mukiibi J, Hasstedt SJ, Samowitz W, Edwards CQ, West G, Ndambire S, Emmanuel J, Nkanza N, Chapanduka Z, Randall M, Boone P, Romano P, Martell RW, Yamashita T, Effler P, Brittenham G. 1992. Iron overload in Africa. Interaction between a gene and dietary iron content. *N Engl J Med* 326:95–100.
- Grasbeck R, Majuri R, Kouvonen I, Tenhunen R. 1982. Spectral and other studies on the intestinal haem receptor of the pig. *Biochim Biophys Acta* 700:137–142.
- Green R, Charlton R, Seftel H, Bothwell T, Mayet F, Adams B, Finch C, Layrisse M. 1968. Body iron excretion in man. *Am J Med* 45:336–353.
- Gunshin H, Mackenzie B, Berger UV, Gunshin Y, Romero MF, Boron WF, Nussberger S, Gollan JL, Hediger MA. 1997. Cloning and characterization of a mammalian proton-coupled metal-ion transporter. *Nature* 388:482–488.
- Gutierrez JA, Yu J, Rivera S, Wessling-Resnick M. 1997. Functional expression cloning and characterization of SFT, a stimulator of Fe transport. *J Cell Biol* 139:895–905.
- Hallberg L. 1992. Iron balance in pregnancy and lactation. In: Fomon SJ, Zlotkin S, eds. *Nutritional Anemias*. Nestle Nutrition Workshop Series, Vol. 30. New York: Raven Press. Pp. 13–28.

- Hallberg L, Hulthen L. 2000. Prediction of dietary iron absorption: An algorithm for calculating absorption and bioavailability of dietary iron. *Am J Clin Nutr* 71:1147–1160.
- Hallberg L, Rossander-Hulthen L. 1991. Iron requirements in menstruating women. *Am J Clin Nutr* 54:1047–1058.
- Hallberg L, Hogdahl AM, Nilsson L, Rybo G. 1966a. Menstrual blood loss and iron deficiency. *Acta Med Scand* 180:639–650.
- Hallberg L, Hogdahl AM, Nilsson L, Rybo G. 1966b. Menstrual blood loss: A population study. Variation at different ages and attempts to define normality *Acta Obstet Gynecol Scand* 45:320–351.
- Hallberg L, Ryttinger L, Solvell L. 1966c. Side-effects of oral iron therapy. A double-blind study of different iron compounds in tablet form. *Acta Med Scand Suppl* 459:3–10.
- Hallberg L, Brune M, Erlandsson M, Sandberg AS, Rossander-Hulthen L. 1991. Calcium: Effect of different amounts of nonheme- and heme-iron absorption in humans. *Am J Clin Nutr* 53:112–119.
- Hallberg L, Rossander-Hulthen L, Brune M, Gleerup A. 1993. Inhibition of haem-iron absorption in man by calcium. *Br J Nutr* 69:533–540.
- Hallfrisch J, Powell A, Carafelli C, Reiser S, Prather ES. 1987. Mineral balances of men and women consuming high fiber diets with complex or simple carbohydrate. *J Nutr* 117:48–55.
- Han O, Failla ML, Hill AD, Morris ER, Smith JC. 1995. Reduction of Fe(III) is required for uptake of nonheme iron by Caco-2 cells. *J Nutr* 125:1291–1299.
- Harland BF, Oberleas D. 1987. Phytate in foods. *World Rev Nutr Diet* 52:235–259.
- Hawkins WW. 1964. Iron, copper and cobalt. In: Beaton GH, McHenry EW, eds. *Nutrition: A Comprehensive Treatise*. New York: Academic Press. Pp. 309–372.
- Haycock GB, Schwartz GJ, Wisotsky DH. 1978. Geometric method for measuring body surface area: A height-weight formula validated in infants, children, and adults. *J Pediatr* 93:62–66.
- Hefnawi F, Yacout MM. 1978. Intrauterine contraception in developing countries. In: Ludwig H, Tauber PF, eds. *Human Fertilization*. Stuttgart: Georg Thieme. Pp. 249–253.
- Hefnawi F, el-Zayat AF, Yacout MM. 1980. Physiologic studies of menstrual blood loss. *Int J Gynaecol Obstet* 17:348–352.
- Hegenauer J, Saltman P, Ludwig D, Ripley L, Ley A. 1979. Iron-supplemented cow milk. Identification and spectral properties of iron bound to casein micelles. *J Agric Food Chem* 27:1294–1301.
- Hegsted DM. 1975. Balance studies. *J Nutr* 106:307–311.
- Higgs JM. 1973. Chromic mucocutaneous candidiasis: Iron deficiency and the effects of iron therapy. *Proc R Soc Med* 66:802–804.
- Hogan GR, Jones B. 1970. The relationship of koilonychia and iron deficiency in infants. *J Pediatr* 77:1054–1057.
- Holbrook JT, Smith JC, Reiser S. 1989. Dietary fructose or starch: Effects on copper, zinc, iron, manganese, calcium, and magnesium balances in humans. *Am J Clin Nutr* 49:1290–1294.
- Hsing AW, McLaughlin JK, Olsen JH, Mellemkjar L, Wacholder S, Fraumeni JF. 1995. Cancer risk following primary hemochromatosis: A population-based cohort study in Denmark. *Int J Cancer* 60:160–162.
- Hunt JR, Roughead ZK. 1999. Nonheme-iron absorption, fecal ferritin excretion, and blood indexes of iron status in women consuming controlled lactoovo-vegetarian diets for 8 weeks. *Am J Clin Nutr* 69:944–952.

- Hunt JR, Mullen LM, Lykken GI, Gallagher SK, Nielsen FH. 1990. Ascorbic acid: Effect on ongoing iron absorption and status in iron-depleted young women. *Am J Clin Nutr* 51:649–655.
- Hurrell RF, Juillerat MA, Reddy MB, Lynch SR, Dassenko SA, Cook JD. 1992. Soy protein, phytate and iron absorption in humans. *Am J Clin Nutr* 56:573–578.
- Hyttan FE, Leitch I. 1971. *The Physiology of Human Pregnancy*, 2nd ed. Oxford: Blackwell Scientific.
- Idjradinata P, Pollitt E. 1993. Reversal of developmental delays in iron-deficient anaemic infants treated with iron. *Lancet* 341:1–4.
- INACG (International Nutritional Anemia Consultative Group). 1985. *Measurements of Iron Status*. Washington, DC: Nutrition Foundation.
- IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Washington, DC: National Academy Press.
- IOM. 1993. *Iron Deficiency Anemia: Recommended Guidelines for the Prevention, Detection, and Management Among U.S. Children and Women of Childbearing Age*. Washington, DC: National Academy Press.
- Ivaturi R, Kies C. 1992. Mineral balances in humans as affected by fructose, high fructose corn syrup and sucrose. *Plant Foods Hum Nutr* 42:143–151.
- Jacobs A. 1971. The effect of iron deficiency on the tissues. *Gerontol Clin (Basel)* 13:61–68.
- Johnson MA, Baier MJ, Greger JL. 1982. Effects of dietary tin on zinc, copper, iron, manganese, and magnesium metabolism of adult males. *Am J Clin Nutr* 35:1332–1338.
- Kelly KA, Turnbull A, Cammock EE, Bombeck CT, Nyhus LM, Finch CA. 1967. Iron absorption after gastrectomy: An experimental study in the dog. *Surgery* 62:356–360.
- Kelsay JL, Behall KM, Prather ES. 1979. Effect of fiber from fruits and vegetables on metabolic responses of human subjects. *Am J Clin Nutr* 32:1876–1880.
- Kiechl S, Willeit J, Egger G, Poewe W, Oberholzer F. 1997. Body iron stores and the risk of carotid atherosclerosis: Prospective results from the Bruneck Study. *Circulation* 96:3300–3307.
- Klebanoff MA, Shiono PH, Selby JV, Trachtenberg AI, Graubard BI. 1991. Anemia and spontaneous preterm birth. *Am J Obstet Gynecol* 164:59–63.
- Konijn AM. 1994. Iron metabolism in inflammation. *Baillieres Clin Haematol* 7:829–849.
- Lampe JW, Slavin JL, Apple FS. 1991. Iron status of active women and the effect of running a marathon on bowel function and gastrointestinal blood loss. *Int J Sports Med* 12:173–179.
- Leggett BA, Brown NN, Bryant SJ, Duplock L, Powell LW, Halliday JW. 1990. Factors affecting the concentrations of ferritin in serum in a healthy Australian population. *Clin Chem* 36:1350–1355.
- Lemons JA, Moye L, Hall D, Simmons M. 1982. Differences in the composition of preterm and term human milk during early lactation. *Pediatr Res* 16:113–117.
- Liao Y, Cooper RS, McGee DL. 1994. Iron status and coronary heart disease: Negative findings from the NHANES I Epidemiologic Follow-Up Study. *Am J Epidemiol* 139:704–712.
- Lieberman E, Ryan KJ, Monson RR, Schoenbaum SC. 1988. Association of maternal hematocrit with premature labor. *Am J Obstet Gynecol* 159:107–114.
- Liguori L. 1993. Iron protein succinylate in the treatment of iron deficiency: Controlled, double-blind, multicenter clinical trial on over 1,000 patients. *Int J Clin Pharmacol Ther* 31:103–123.

- Lipsman S, Dewey KG, Lonnerdal B. 1985. Breast-feeding among teenage mothers: Milk composition, infant growth, and maternal dietary intake. *J Pediatr Gastroenterol Nutr* 4:426–434.
- Lokken P, Birkeland JM. 1979. Dental discolorations and side effects with iron and placebo tablets. *Scand J Dent Res* 87:275–278.
- Lonnerdal B, Keen CL, Hurley LS. 1981. Iron, copper, zinc and manganese in milk. *Ann Rev Nutr* 1:149–174.
- Lozoff B, Brittenham G, Viteri FE, Wolf AW, Urrutia JJ. 1982a. Developmental deficits in iron-deficient infants: Effects of age and severity of iron lack. *J Pediatr* 101:948–952.
- Lozoff B, Brittenham G, Viteri FE, Wolf AW, Urrutia JJ. 1982b. The effects of short-term oral iron therapy on developmental deficits in iron-deficient anemic infants. *J Pediatr* 100:351–357.
- Lozoff B, Wolf AW, Urrutia JJ, Viteri FE. 1985. Abnormal behavior and low developmental test scores in iron-deficient anemic infants. *J Dev Behav Pediatr* 6:69–75.
- Lozoff B, Klein NK, Prabucki KM. 1986. Iron-deficient anemic infants at play. *J Dev Behav Pediatr* 7:152–158.
- Lozoff B, Brittenham G, Wolf AW, McClish DK, Kuhnert PM, Jimenez E, Jimenez R, Mora LA, Gomez I, Krauskopf D. 1987. Iron deficiency anemia and iron therapy effects on infant developmental test performance. *Pediatrics* 79:981–995.
- Lozoff B, Jimenez E, Wolf AW. 1991. Long-term developmental outcome of infants with iron deficiency. *N Engl J Med* 325:687–694.
- Lozoff B, Wolf AW, Jimenez E. 1996. Iron-deficiency anemia and infant development: Effects of extended oral iron therapy. *J Pediatr* 129:382–389.
- Lozoff B, Jimenez E, Hagen J, Mollen E, Wolf AW. 2000. Poorer behavioral and developmental outcome more than 10 years after treatment for iron deficiency in infancy. *Pediatrics* 105:E51.
- Lynch SR, Beard JL, Dassenko SA, Cook JD. 1984. Iron absorption from legumes in humans. *Am J Clin Nutr* 40:42–47.
- Lynch SR, Dassenko SA, Cook JD, Juillerat MA, Hurrell RF. 1994. Inhibitory effect of a soybean-protein—Related moiety on iron absorption in humans. *Am J Clin Nutr* 60:567–572.
- MacLennan AH, MacLennan A, Wenzel S, Chambers HM, Eckert K. 1993. Continuous low-dose oestrogen and progestogen hormone replacement therapy: A randomised trial. *Med J Aust* 159:102–106.
- Magnusson B, Hallberg L, Rossander L, Swolin B. 1984. Iron metabolism and “sports anemia”. II. A hematological comparison of elite runners and control subjects. *Acta Med Scand* 216:157–164.
- Magnusson MK, Sigfusson N, Sigvaldason H, Johannesson GM, Magnusson S, Thorsteinsson G. 1994. Low iron-binding capacity as a risk factor for myocardial infarction. *Circulation* 89:102–108.
- Mahalko JR, Sandstead HH, Johnson L, Milne DB. 1983. Effect of moderate increase in dietary protein on the retention and excretion of Ca, Cu, Fe, Mg, P, and Zn by adult males. *Am J Clin Nutr* 37:8–14.
- Manttari M, Manninen V, Huttunen JK, Palosuo T, Ehnholm C, Heinonen OP, Frick MH. 1994. Serum ferritin and ceruloplasmin as coronary risk factors. *Eur Heart J* 15:1599–1603.
- McCord JM. 1996. Effects of positive iron status at a cellular level. *Nutr Rev* 54:85–88.

- McGuigan MA. 1996. Acute iron poisoning. *Pediatr Ann* 25:33–38.
- Meadows NJ, Grainger SL, Ruse W, Keeling PW, Thompson RP. 1983. Oral iron and the bioavailability of zinc. *Br Med J* 287:1013–1014.
- Mendelson RA, Anderson GH, Bryan MH. 1982. Zinc, copper and iron content of milk from mothers of preterm and full-term infants. *Early Hum Dev* 6:145–151.
- Mendoza C, Viteri FE, Lonnerdal B, Young KA, Raboy V, Brown KH. 1998. Effect of genetically modified, low-phytic acid maize on absorption of iron from tortillas. *Am J Clin Nutr* 68:1123–1127.
- Milman N, Kirchhoff M. 1991a. Iron stores in 1433, 30- to 60-year-old Danish males. Evaluation by serum ferritin and haemoglobin. *Scand J Clin Lab Invest* 51:635–641.
- Milman N, Kirchhoff M. 1991b. The influence of blood donation on iron stores assessed by serum ferritin and hemoglobin in a population survey of 1,359 Danish women. *Ann Hematol* 63:27–32.
- Minihane AM, Fairweather-Tait SJ. 1998. Effect of calcium supplementation on daily nonheme-iron absorption and long-term iron status. *Am J Clin Nutr* 68:96–102.
- Monsen ER, Hallberg L, Layrisse M, Hegsted DM, Cook JD, Mertz W, Finch CA. 1978. Estimation of available dietary iron. *Am J Clin Nutr* 31:134–141.
- Morrison HI, Semenciw RM, Mao Y, Wigle DT. 1994. Serum iron and risk of fatal acute myocardial infarction. *Epidemiology* 5:243–246.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance Data, Vital and Health Statistics of the National Center for Health Statistics, Number 174. Hyattsville, MD: National Center for Health Statistics.
- Muir A, Hopfer U. 1985. Regional specificity of iron uptake by small intestinal brush-border membranes from normal and iron-deficient mice. *Am J Physiol* 248:G376–G379.
- Murphy JF, O'Riordan J, Newcombe RG, Coles EC, Pearson JF. 1986. Relation of haemoglobin levels in first and second trimesters to outcome of pregnancy. *Lancet* 1:992–995.
- Nassar BA, Zayed EM, Title LM, O'Neill BJ, Bata IR, Kirkland SA, Dunn J, Dempsey GI, Tan MH, Johnstone DE. 1998. Relation of HFE gene mutations, high iron stores and early onset coronary artery disease. *Can J Cardiol* 14:215–220.
- Nelson RL, Davis FG, Sutter E, Sabin LH, Kikendall JW, Bowen P. 1994. Body iron stores and risk of colonic neoplasia. *J Natl Cancer Inst* 86:455–460.
- Nelson RL, Davis FG, Persky V, Becker E. 1995. Risk of neoplastic and other diseases among people with heterozygosity for hereditary hemochromatosis. *Cancer* 76:875–879.
- Newhouse IJ, Clement DB. 1995. The efficacy of iron supplementation in iron depleted women. In: Kies CV, Driskell JA, eds. *Sports Nutrition: Minerals and Electrolytes*. Boca Raton: CRC Press. Pp. 47–57.
- Niederau C, Fischer R, Sonnenberg A, Stremmel W, Trampisch HJ, Strohmeyer G. 1985. Survival and causes of death in cirrhotic and in noncirrhotic patients with primary hemochromatosis. *N Engl J Med* 313:1256–1262.
- Nilsson L, Solvell L. 1967. Clinical studies on oral contraceptives—A randomized, doubleblind, crossover study of 4 different preparations (Anovlar mite, Lyndiol mite, Ovulen, and Volidan). *Acta Obstet Gynecol Scand* 46:1–31.

- Nokes C, van den Bosch C, Bundy DAP. 1998. *The Effects of Iron Deficiency and Anemia on Mental and Motor Performance, Educational Achievement, and Behavior in Children*. The International Nutritional Anemia Consultative Group. Washington, DC: ILSI Press.
- NRC (National Research Council). 1979. *Iron*. Baltimore: University Park Press. Pp. 248.
- O'Brien KO, Zavaleta N, Caulfield LE, Wen J, Abrams SA. 2000. Prenatal iron supplements impair zinc absorption in pregnant Peruvian women. *J Nutr* 130:2251–2255.
- Olynik JK, Cullen DJ, Aquilia S, Rossi E, Summerville L, Powell LW. 1999. A population-based study of the clinical expression of the hemochromatosis gene. *N Engl J Med* 341:718–724.
- Oosterbaan HP, van Buuren AH, Schram JH, van Kempen PJ, Ubachs JM, van Leusden HA, Beyer GP. 1995. The effects of continuous combined transdermal oestrogen-progestogen treatment on bleeding patterns and the endometrium in postmenopausal women. *Maturitas* 21:211–219.
- Osaki S, Johnson DA, Frieden E. 1966. The possible significance of the ferrous oxidase activity of ceruloplasmin in normal human serum. *J Biol Chem* 241:2746–2751.
- Oski FA, Honig AS, Helu B, Howanitz P. 1983. Effect of iron therapy on behavior performance in nonanemic, iron-deficient infants. *Pediatrics* 71:877–880.
- Osler M, Milman N, Heitmann BL. 1998. Dietary and non-dietary factors associated with iron status in a cohort of Danish adults followed for six years. *Eur J Clin Nutr* 52:459–463.
- Picciano MF, Guthrie HA. 1976. Copper, iron, and zinc contents of mature human milk. *Am J Clin Nutr* 29:242–254.
- Pollitt E, Gorman KS, Engle PL, Martorell R, Rivera J. 1993. Early supplemental feeding and cognition: Effects over two decades. *Monogr Soc Res Child Dev* 58:1–99.
- Powell LW. 1970. Tissue damage in haemochromatosis: An analysis of the roles of iron and alcoholism. *Gut* 11:980.
- Preziosi P, Prual A, Galan P, Daouda H, Boureima H, Hercberg S. 1997. Effect of iron supplementation on the iron status of pregnant women: Consequences for newborns. *Am J Clin Nutr* 66:1178–1182.
- Raffin SB, Woo CH, Roost KT, Price DC, Schmid R. 1974. Intestinal absorption of hemoglobin iron-heme cleavage by mucosal heme oxygenase. *J Clin Invest* 54:1344–1352.
- Raja KB, Simpson RJ, Peters TJ. 1987. Comparison of  $^{59}\text{Fe}^{3+}$  uptake in vitro and in vivo by mouse duodenum. *Biochim Biophys Acta* 901:52–60.
- Raja KB, Simpson RJ, Peters TJ. 1993. Investigation of a role for reduction in ferric iron uptake by mouse duodenum. *Biochim Biophys Acta* 1135:141–146.
- Raper NR, Rosenthal JC, Wotecki CE. 1984. Estimates of available iron in diets of individuals 1 year old and older in the Nationwide Food Consumption Survey. *J Am Diet Assoc* 84:783–787.
- Raunikar RA, Sabio H. 1992. Anemia in the adolescent athlete. *Am J Dis Child* 146:1201–1205.
- Ravel R. 1989. *Clinical Laboratory Medicine: Clinical Application of Laboratory Data*. Chicago: Year Book Medical Publishers.
- Reddy MB, Hurrell RF, Cook JD. 2000. Estimation of nonheme-iron bioavailability from meal composition. *Am J Clin Nutr* 71:937–943.

- Reeves JD, Yip R. 1985. Lack of adverse side effects of oral ferrous sulfate therapy in 1-year-old infants. *Pediatrics* 75:352–355.
- Reunanen A, Takkunen H, Knekt P, Seppanen R, Aromaa A. 1995. Body iron stores, dietary iron intake and coronary heart disease mortality. *J Intern Med* 238:223–230.
- Roest M, van der Schouw YT, de Valk B, Marx JJ, Tempelman MJ, de Groot PG, Sixma JJ, Banga JD. 1999. Heterozygosity for a hereditary hemochromatosis gene is associated with cardiovascular death in women. *Circulation* 100:1268–1273.
- Roncagliolo M, Garrido M, Walter T, Peirano P, Lozoff B. 1998. Evidence of altered central nervous system development in infants with iron deficiency anemia at 6 months: Delayed maturation of auditory brainstem responses. *Am J Clin Nutr* 68:683–690.
- Rowland TW, Stagg L, Kelleher JF. 1991. Iron deficiency in adolescent girls. Are athletes at risk? *J Adolesc Health* 12:22–25.
- Rybo G, Solvell L. 1971. Side-effect studies on a new sustained release iron preparation. *Scand J Haematol* 8:257–264.
- Salonen JT, Nyssonnen K, Korpela H, Tuomilehto J, Seppanen R, Salonen R. 1992. High stored iron levels are associated with excess risk of myocardial infarction in eastern Finnish men. *Circulation* 86:803–811.
- Salonen JT, Nyssonnen K, Salonen R. 1994. Body iron stores and the risk of coronary heart disease. *N Engl J Med* 331:1159.
- Sandberg AS. 1991. The effect of food processing on phytate hydrolysis and availability of iron and zinc. *Adv Exp Med Biol* 289:499–508.
- Sandstrom B, Davidsson L, Cederblad A, Lonnerdal B. 1985. Oral iron, dietary ligands and zinc absorption. *J Nutr* 115:411–414.
- Scholl TO, Hediger ML, Fischer RL, Shearer JW. 1992. Anemia vs iron deficiency: Increased risk of preterm delivery in a prospective study. *Am J Clin Nutr* 55:985–988.
- Selby JV, Friedman GD. 1988. Epidemiologic evidence of an association between body iron stores and risk of cancer. *Int J Cancer* 41:677–682.
- Sempos CT, Looker AC, Gillum RF, Makuc DM. 1994. Body iron stores and the risk of coronary heart disease. *N Engl J Med* 330:1119–1124.
- Shaw NS, Chin CJ, Pan WH. 1995. A vegetarian diet rich in soybean products compromises iron status in young students. *J Nutr* 125:212–219.
- Siegel AJ, Hennekens CH, Solomon HS, Van Boeckel B. 1979. Exercise-related hematuria. Findings in a group of marathon runners. *J Am Med Assoc* 241:391–392.
- Siegenberg D, Baynes RD, Bothwell TH, Macfarlane BJ, Lamparelli RD, Car NG, MacPhail P, Schmidt U, Tal A, Mayet F. 1991. Ascorbic acid prevents the dose-dependent inhibitory effects of polyphenols and phytates on nonheme-iron absorption. *Am J Clin Nutr* 53:537–541.
- Siimes MA, Refino C, Dallman P. 1980a. Manifestation of iron deficiency at various levels of dietary iron intake. *Am J Clin Nutr* 33:570–574.
- Siimes MA, Refino C, Dallman P. 1980b. Physiological anemia of early development in the rat: Characterization of the iron-responsive component. *Am J Clin Nutr* 33:2601–2608.
- Simpson RJ, Raja KB, Peters TJ. 1986. Fe<sup>2+</sup> uptake by mouse intestinal musosa in vivo and by isolated intestinal brush-border membrane vesicles. *Biochim Biophys Acta* 860:229–235.

- Skinner JD, Carruth BR, Houck KS, Coletta F, Cotter R, Ott D, McLeod M. 1997. Longitudinal study of nutrient and food intakes of infants aged 2 to 24 months. *J Am Diet Assoc* 97:496–504.
- Smith NJ, Rios E. 1974. Iron metabolism and iron deficiency in infancy and childhood. *Adv Pediatr* 21:239–280.
- Snedeker SM, Smith SA, Greger JL. 1982. Effect of dietary calcium and phosphorus levels on the utilization of iron, copper, and zinc by adult males. *J Nutr* 112:136–143.
- Sokoll LJ, Dawson-Hughes B. 1992. Calcium supplementation and plasma ferritin concentrations in premenopausal women. *Am J Clin Nutr* 56:1045–1048.
- Solomons NW. 1986. Competitive interaction of iron and zinc in the diet: Consequences for human nutrition. *J Nutr* 116:927–935.
- Solomons NW, Jacob RA. 1981. Studies on the bioavailability of zinc in humans: Effects of heme and nonheme iron on the absorption of zinc. *Am J Clin Nutr* 34:475–482.
- Solomons NW, Pineda O, Viteri F, Sandstead H. 1983. Studies on the bioavailability of zinc in humans: Mechanism of the intestinal interaction of nonheme iron and zinc. *J Nutr* 113:337–349.
- Stampfer MJ, Grodstein F, Rosenberg I, Willett W, Hennekens C. 1993. A prospective study of plasma ferritin and risk of myocardial infarction in US physicians. *Circulation* 87:688.
- Stevens RG, Jones DY, Micozzi MS, Taylor PR. 1988. Body iron stores and the risk of cancer. *N Engl J Med* 319:1047–1052.
- Stevens RG, Graubard BI, Micozzi MS, Neriishi K, Blumberg BS. 1994. Moderate elevation of body iron level and increased risk of cancer occurrence and death. *Int J Cancer* 56:364–369.
- Stewart JG, Ahlquist DA, McGill DB, Ilstrup DM, Schwartz S, Owen RA. 1984. Gastrointestinal blood loss and anemia in runners. *Ann Intern Med* 100:843–845.
- Stoltzfus R, Dreyfuss M. 1998. *Guidelines for the Use of Iron Supplements to Prevent and Treat Iron Deficiency Anemia*. Washington, DC: ILSI Press.
- Strupp BJ, Levitsky DA. 1995. Enduring cognitive effects of early malnutrition: A theoretical reappraisal. *J Nutr* 125:2221S–2232S.
- Sullivan JL. 1981. Iron and the sex difference in heart disease risk. *Lancet* 1:1293–1294.
- Tanner JM, Whitehouse RH, Takaishi M. 1966. Standards from birth to maturity for height, weight, height velocity and weight velocity: British children, 1965. Part II. *Arch Dis Child* 41:613–635.
- Taylor D, Mallen C, McDougall N, Lind T. 1982. Effect of iron supplementation on serum ferritin levels during and after pregnancy. *Br J Obstet Gynecol* 89:1011–1017.
- Taylor PG, Martinz-Torres C, Romano EL, Layrisse M. 1986. The effect of cysteine-containing peptides released during meat digestion on iron absorption in humans. *Am J Clin Nutr* 43:68–71.
- Thompson CH, Green YS, Ledingham JG, Radda GK, Rajagopalan B. 1993. The effect of iron deficiency on skeletal muscle metabolism of the rat. *Acta Physiol Scand* 147:85–90.
- Tuntawiroon M, Sritongkul N, Brune M, Rossander-Hulten L, Pleehachinda R, Suwanik R, Hallberg L. 1991. Dose-dependent inhibitory effect of phenolic compounds in foods on nonheme-iron absorption in men. *Am J Clin Nutr* 53:554–557.

- Tuomainen TP, Nyssonnen K, Salonen R, Tervahauta A, Korpela H, Lakka T, Kaplan GA, Salonen JT. 1997. Body iron stores are associated with serum insulin and blood glucose concentrations. Population study in 1,013 eastern Finnish men. *Diabetes Care* 20:426–428.
- Tuomainen TP, Kontula K, Nyssonsen K, Lakka TA, Helio T, Salonen JT. 1999. Increased risk of acute myocardial infarction in carriers of the hemochromatosis gene Cys282Tyr mutation: A prospective cohort study in men in eastern Finland. *Circulation* 100:1274–1279.
- Turnlund JR, Keyes WR, Hudson CA, Betschart AA, Kretsch MJ, Sauberlich HE. 1991. A stable-isotope study of zinc, copper, and iron absorption and retention by young women fed vitamin B-6-deficient diets. *Am J Clin Nutr* 54:1059–1064.
- Valberg LS. 1980. Plasma ferritin concentration: Their clinical significance and relevance to patient care. *Can Med Assoc* 122:1240–1248.
- Valberg LS, Flanagan PR, Chamberlain MJ. 1984. Effects of iron, tin, and copper on zinc absorption in humans. *Am J Clin Nutr* 40:536–541.
- Van Asperen IA, Feskens EJ, Bowles CH, Kromhout D. 1995. Body iron stores and mortality due to cancer and ischaemic heart disease: A 17-year follow-up study of elderly men and women. *Int J Epidemiol* 24:665–670.
- Van de Vijver LP, Kardinaal AF, Charzewska J, Rotily M, Charles P, Maggiolini M, Ando S, Vaananen K, Wajszczyk B, Heikkinen J, Deloraine A, Schaafsma G. 1999. Calcium intake is weakly but consistently negatively associated with iron status in girls and women in six European countries. *J Nutr* 129:963–968.
- Van Dokkum W, Cloughley FA, Hulshof KF, Oosterveen LA. 1983. Effect of variations in fat and linoleic acid intake on the calcium, magnesium and iron balance of young men. *Ann Nutr Metab* 27:361–369.
- Vaughan LA, Weber CW, Kemberling SR. 1979. Longitudinal changes in the mineral content of human milk. *Am J Clin Nutr* 32:2301–2306.
- Viteri FE, Torun B. 1974. Anaemia and physical work capacity. *Clin Haematol* 3:609–626.
- Walker EM, Wolfe MD, Norton ML, Walker SM, Jones MM. 1998. Hereditary hemochromatosis. *Ann Clin Lab Sci* 28:300–312.
- Walsh CT, Sandstead HH, Prasad AS, Newberne PM, Fraker PJ. 1994. Zinc: Health effects and research priorities for the 1990s. *Environ Health Perspect* 102:5–46.
- Walter T, Kovalskys J, Stekel A. 1983. Effect of mild iron deficiency on infant mental developmental scores. *J Pediatr* 102:519–522.
- Walter T, de Andraca I, Chadud P, Perales CG. 1989. Iron deficiency anemia: Adverse effects on infant psychomotor development. *Pediatrics* 84:7–17.
- Weaver CM, Rajaram S. 1992. Exercise and iron status. *J Nutr* 122:782–787.
- Weight LM. 1993. Sports anemia. Does it exist? *Sports Med* 16:1–4.
- Weintraub LR, Conrad ME, Crosby WH. 1965. Absorption of hemoglobin iron by the rat. *Proc Soc Exp Biol Med* 120:840–843.
- Whiting SJ. 1995. The inhibitory effect of dietary calcium on iron bioavailability: A cause for concern? *Nutr Rev* 53:77–80.
- Whittaker P. 1998. Iron and zinc interactions in humans. *Am J Clin Nutr* 68:442S–446S.
- WHO (World Health Organization). 1992. *The Prevalence of Anaemia in Women. A Tabulation of Available Information*. Geneva: WHO.

- WHO. 1994. *An Evaluation of Infant Growth. A Summary of Analyses Performed in Preparation for the WHO Expert Committee on Physical Status: The Use and Interpretation of Anthropometry*. WHO Working Group on Infant Growth. WHO/NUT/94.8. Geneva: WHO.
- WHO/UNICEF/UNU (United Nations Children Fund/United Nations University). 1998. *IDA: Prevention, Assessment and Control*. Report of a joint WHO/UNICEF/UNU consultation. Geneva: WHO.
- Widdowson EM, Spray CM. 1951. Chemical development in utero. *Arch Dis Child* 26:205–214.
- Williams MD, Wheby MS. 1992. Anemia in pregnancy. *Med Clin North Am* 76:631–647.
- Willis WT, Dallman PR, Brooks GA. 1988. Physiological and biochemical correlates of increased work in trained iron-deficient rats. *J Appl Physiol* 65:256–263.
- Wollenberg P, Rummel W. 1987. Dependence of intestinal iron absorption on the valency state of iron. *Naunyn Schmiedebergs Arch Pharmacol* 336:578–582.
- Wollenberg P, Mahlberg R, Rummel W. 1990. The valency state of absorbed iron appearing in the portal blood and ceruloplasmin substitution. *Biometals* 3:1–7.
- Worwood M. 1999. Inborn errors of metabolism: Iron. *Br Med Bull* 55:556–567.
- Wurzelmann JI, Sliver A, Schreinemachers DM, Sandler RS, Everson RB. 1996. Iron intake and the risk of colorectal cancer. *Cancer Epidemiol Biomarkers Prev* 5:503–507.
- Yip R. 2000. Significance of an abnormally low or high hemoglobin concentration during pregnancy: Special consideration of iron nutrition. *Am J Clin Nutr* 72:272S–279S.
- Yip R, Reeves JD, Lonnerdal B, Keen CL, Dallman PR. 1985. Does iron supplementation compromise zinc nutrition in healthy infants? *Am J Clin Nutr* 42:683–687.

Ibid., Chapter 14, pp. 578–579.

- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Examination Survey: Under-reporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Gibson RS, Ferguson EL. 1998. Assessment of dietary zinc in a population. *Am J Clin Nutr* 68:430S–434S.
- Hallberg L, Hulthen L. 2000. Prediction of dietary iron absorption: An algorithm for calculating absorption and bioavailability of dietary iron. *Am J Clin Nutr* 71:1147–1160.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.

- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1980. *Recommended Dietary Allowances*, 9th ed. Washington, DC: National Academy Press.
- NRC. 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC. 1989. *Recommended Dietary Allowances*, 10th ed. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Schoeller DA. 1999. Recent advances from application of doubly labeled water to measurement of human energy expenditure. *J Nutr* 129:1765–1768.
- USDA (U.S. Department of Agriculture). 1999. *USDA Nutrient Database for Standard Reference*, Release 13. [Online.] Available: <http://www.nal.usda.gov/fnic/foodcomp> [accessed February 2000].
- WHO (World Health Organization). 1996. Zinc. In: *Trace Elements in Human Nutrition and Health*. Geneva: WHO. Pp. 72–104.

## MAGNESIUM

*Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride (ISBN 0-309-06350-7)*, pp. 325–374.

- Abbott L, Nadler J, Rude RK. 1994. Magnesium deficiency in alcoholism: Possible contribution to osteoporosis and cardiovascular disease in alcoholics. *Alcohol Clin Exp Res* 18:1976–1082.
- Abe E, Miyaura C, Sakagami H, Takeda M, Konno K, Yamazaki T, Yoshiki S, Suda T. 1981. Differentiation of mouse myeloid leukemia cells induced by 1 $\alpha$ 25-dihydroxyvitamin D<sub>3</sub>. *Proc Natl Acad Sci USA* 78:4990–4994.
- Abraham GE, Grewal H. 1990. A total dietary program emphasizing magnesium instead of calcium: Effect on the mineral density of calcaneous bone in postmenopausal women on hormonal therapy. *J Reprod Med* 35:503–507.
- Abrams SA, Stuff JE. 1994. Calcium metabolism in girls: Current dietary intakes lead to low rates of calcium absorption and retention during puberty. *Am J Clin Nutr* 60:739–743.
- Abrams SA, Sidbury JB, Muenzer J, Esteban NV, Vieira NE, Yerger AL. 1991. Stable isotopic measurement of endogenous fecal calcium excretion in children. *J Pediatr Gastroenterol Nutr* 12:469–473.
- Abrams SA, Esteban NV, Vieira NE, Sidbury JB, Specker BL, Yerger AL. 1992. Developmental changes in calcium kinetics in children assessed using stable isotopes. *J Bone Miner Res* 7:287–293.
- Abrams SA, Silber TJ, Esteban NV, Vieira NE, Stuff JE, Meyers R, Majd M, Yerger AL. 1993. Mineral balance and bone turnover in adolescents with anorexia nervosa. *J Pediatr* 123:326–331.
- Abrams SA, O'Brien KO, Stuff JE. 1996a. Changes in calcium kinetics associated with menarche. *J Clin Endocrinol Metab* 81:2017–2020.
- Abrams SA, O'Brien KO, Wen J, Liang LK, Stuff JE. 1996b. Absorption by 1-year-old children of an iron supplement given with cow's milk or juice. *Pediatr Res* 39:171–175.
- Abrams SA, Wen J, Stuff JE. 1997a. Absorption of calcium, zinc and iron from breast milk by 5- to 7-month-old infants. *Pediatr Res* 41:1–7.
- Abrams SA, Grusak MA, Stuff J, O'Brien KO. 1997b. Calcium and magnesium balance in 9- to 14-year-old children. *Am J Clin Nutr* 66:1172–1177.
- Abreo K, Adlakha A, Kilpatrick S, Flanagan R, Webb R, Shakamuri S. 1993. The Milk-Alkali Syndrome. A reversible form of acute renal failure. *Arch Intern Med* 153:1005–1010.
- Ackerman PG, Toro G. 1953. Calcium and phosphorus balance in elderly men. *J Gerontol* 8:298–300.
- ADA (American Dental Association Council on Dental Therapeutics). 1994. New fluoride guidelines proposed. *J Am Dent Assoc* 125:366.
- Adams JS. 1989. Vitamin D metabolite-mediated hypercalcemia. *Endocrinol Metab Clin North Am* 18:765–778.
- Adams JS, Beeker TG, Hongo T, Clemens TL. 1990. Constitutive expression of a vitamin D 1-hydroxylase in a myelomonocytic cell line: A model for studying 1,25-dihydroxyvitamin D production in vitro. *J Bone Miner Res* 5:1265–1269.
- Affinito P, Tommaselli GA, DiCarlo C, Guida F, Nappi C. 1996. Changes in bone mineral density and calcium metabolism in breast-feeding women: A one year follow-up study. *J Clin Endocrinol Metab* 81:2314–2318.

- Aksnes L, Aarskog D. 1982. Plasma concentrations of vitamin D metabolites in puberty: Effect of sexual maturation and implications for growth. *J Clin Endocrinol Metab* 55:94–101.
- Ala-Houhala M. 1985. 25-Hydroxyvitamin D levels during breast-feeding with or without maternal or infantile supplementation of vitamin D. *J Pediatr Gastroenterol Nutr* 4:220–226.
- Ala-Houhala M, Parvianinen MT, Pyyko K, Visakorpi JK. 1984. Serum 25-hydroxyvitamin D levels in Finnish children aged 2 to 17 years. *Acta Paediatr Scand* 73:232–236.
- Ala-Houhala M, Koskinen T, Terho A, Koivula T, Visakorpi J. 1986. Maternal compared with infant vitamin D supplementation. *Arch Dis Child* 61:1159–1163.
- Alaimo K, McDowell MA, Briefel RR, Bischof AM, Caughman CR, Loria CM, Johnson CL. 1994. *Dietary Intake of Vitamins, Minerals, and Fiber of Persons Ages 2 Months and Over in the United States: Third National Health and Nutrition Examination Survey, Phase I, 1988–91*. Advance data from vital and health statistics; no. 258. U.S. Department of Health and Human Services. Hyattsville, MD: National Center for Health Statistics.
- Albert DG, Morita Y, Iseri LT. 1958. Serum magnesium and plasma sodium levels in essential vascular hypertension. *Circulation* 17:761–764.
- Alderman BW, Weiss NS, Daling JR, Ure CL, Ballard JH. 1986. Reproductive history and postmenopausal risk of hip and forearm fracture. *Am J Epidemiol* 124:262–267.
- Alfrey AC, Miller NL, Butkus D. 1974. Evaluation of body magnesium stores. *J Lab Clin Med* 84:153–162.
- Allen JC, Keller RP, Archer P, Neville MC. 1991. Studies in human lactation: Milk composition and daily secretion rates of macronutrients in the first year of lactation. *Am J Clin Nutr* 54:69–80.
- Allen SH, Shah JH. 1992. Calcinosis and metastatic calcification due to vitamin D intoxication. A case report and review. *Horm Res* 37:68–77.
- Allender PS, Cutler JA, Follmann D, Cappuccio FP, Prysor J, Elliott P. 1996. Dietary calcium and blood pressure: A meta-analysis of randomized clinical trials. *Ann Intern Med* 124:825–831.
- Aloia JF, Vaswani AN, Yeh JK, Ross P, Ellis K, Cohn SH. 1983. Determinants of bone mass in postmenopausal women. *Arch Intern Med* 143:1700–1704.
- Aloia JF, Vaswani AN, Yeh JK, Ellis K, Cohn SH. 1984. Total body phosphorus in postmenopausal women. *Miner Electrolyte Metab* 10:73–76.
- Aloia JF, Vaswani A, Yeh JK, Ross PL, Flaster E, Dilmanian FA. 1994. Calcium supplementation with and without hormone replacement therapy to prevent postmenopausal bone loss. *Ann Intern Med* 120:97–103.
- Altura BT, Brust M, Bloom S, Barbour RL, Stempak JG, Altura BM. 1990. Magnesium dietary intake modulates blood lipid levels and atherogenesis. *Proc Natl Acad Sci USA* 87:1840–1844.
- Altura BT, Shirey TL, Hiti J, Dell'Orfano K, Handwerker SM, Altura BM. 1992. A new method for the rapid determination of ionized Mg<sup>2+</sup> in whole blood, serum and plasma. *Methods Find Exp Clin Pharmacol* 14:297–304.
- Altura BT, Wilimizig C, Trnovec T, Nyulassy S, Altura BM. 1994. Comparative effects of a Mg-enriched diet and different orally administered magnesium oxide preparations on ionized Mg, Mg metabolism and electrolytes in serum of human volunteers. *J Am Coll Nutr* 13:447–454.
- American Academy of Pediatrics. 1982. The promotion of breastfeeding: Policy statement based on task force report. *Pediatrics* 69:654–661.

- Anderson DM, Hollis BW, LeVine BR, Pittard WB III. 1988. Dietary assessment of maternal vitamin D intake and correlation with maternal and neonatal serum vitamin D concentrations at delivery. *J Perinatol* 8:46–48.
- Andon MB, Ilich JZ, Tzagournis MA, Matkovic V. 1996. Magnesium balance in adolescent females consuming a low- or high-calcium diet. *Am J Clin Nutr* 63:950–953.
- Angus RM, Sambrook PN, Pockock NA, Eisman JA. 1988. Dietary intake and bone mineral density. *Bone Miner* 4:265–277.
- Antman EM. 1996. Magnesium in acute myocardial infarction: Overview of available evidence. *Am Heart J* 132:487–495.
- Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin PH, Karanja N. 1997. A clinical trial of the effects of dietary patterns on blood pressure. *N Engl J Med* 336:1117–1124.
- Arnold FA Jr, Dean HT, Jay P, Knutson JW. 1956. Effect of fluoridated public water supplies on dental caries prevalence. Tenth year of the Grand Rapids-Muskegon Study. *Pub Hlth Rep* 71:652–658.
- Ascherio A, Rimm EB, Giovannucci EL, Colditz GA, Rosner B, Willett WC, Sacks F, Stampfer MJ. 1992. A prospective study of nutritional factors and hypertension among U.S. men. *Circulation* 86:1475–1484.
- Ashe JR, Schofield FA, Gram MR. 1979. The retention of calcium, iron, phosphorus, and magnesium during pregnancy: The adequacy of prenatal diets with and without supplementation. *Am J Clin Nutr* 32:286–291.
- Atkinson SA, Chappell JE, Clandinin MT. 1987. Calcium supplementation of mothers' milk for low birthweight infants: Problems related to absorption and excretion. *Nutr Res* 7:813–823.
- Atkinson SA, Alston-Mills BP, Lonnerdal B, Neville MC, Thompson MP. 1995. Major minerals and ionic constituents of human and bovine milk. In: Jensen RJ, ed. *Handbook of Milk Composition*. California: Academic Press. Pp. 593–619.
- Bainbridge RR, Mimouni FB, Landi T, Crossman M, Harris L, Tsang RC. 1996. Effect of rice cereal feedings on bone mineralization and calcium homeostasis in cow milk formula fed infants. *J Am Coll Nutr* 15:383–388.
- Baran D, Sorensen A, Grimes J, Lew R, Karella A, Johnson B, Roche J. 1990. Dietary modification with dairy products for preventing vertebral bone loss in premenopausal women: A three-year prospective study. *J Clin Endocrinol Metab* 70:264–270.
- Bardicef M, Bardicef O, Sorokin Y, Altura BM, Altura BT, Cotton DB, Resnick LM. 1995. Extracellular and intracellular magnesium depletion in pregnancy and gestational diabetes. *Am J Obstet Gynecol* 172:1009–1013.
- Barger-Lux MJ, Heaney RP. 1995. Caffeine and the calcium economy revisited. *Osteopor Int* 5:97–102.
- Barger-Lux MJ, Heaney RP, Stegman MR. 1990. Effects of moderate caffeine intake on the calcium economy of premenopausal women. *Am J Clin Nutr* 52:722–725.
- Barger-Lux MJ, Heaney RP, Lanspa SJ, Healy JC, DeLuca HF. 1995. An investigation of sources of variation in calcium absorption efficiency. *J Clin Endocrinol Metab* 80:406–411.
- Barger-Lux MJ, Heaney RP, Dowell S, Bierman J, Holick MF, Chen TC. 1996. Relative molar potency of 25-hydroxyvitamin D indicates a major role in calcium absorption. *J Bone Miner Res* 11:S423.

- Barnhart WE, Hiller LK, Leonard GJ, Michaels SE. 1974. Dentifrice usage and ingestion among four age groups. *J Dent Res* 53:1317–1322.
- Barragry JM, France MW, Corless D, Gupta SP, Switala S, Boucher BJ, Cohen RD. 1978. Intestinal cholecalciferol absorption in the elderly and in younger adults. *Clin Sci Molec Med* 55:213–220.
- Barrett-Connor E, Chang JC, Edelstein SL. 1994. Coffee-associated osteoporosis offset by daily milk consumption. The Rancho Bernardo Study. *J Am Med Assoc* 271:280–283.
- Bashir Y, Sneddon JF, Staunton HA, Haywood GA, Simpson IA, McKenna WJ, Camm AJ. 1993. Effects of long-term oral magnesium chloride replacement in congestive heart failure secondary to coronary artery disease. *Am J Cardiol* 72:1156–1162.
- Beall DP, Scofield RH. 1995. Milk-alkali syndrome associated with calcium carbonate consumption: Report of 7 patients with parathyroid hormone levels and an estimate of prevalence among patients hospitalized with hypercalcemia. *Medicine* 74:89–96.
- Beaton GH. 1994. Criteria of an adequate diet. In: Shils RE, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease, 8th edition*. Philadelphia: Lea & Febiger. Pp. 1491–1505.
- Beaton GH. 1996. Statistical approaches to establish mineral element recommendations. *J Nutr* 126:2302S–2328S.
- Begum A, Pereira SM. 1969. Calcium balance studies on children accustomed to low calcium intakes. *Br J Nutr* 23:905–911.
- Bell NH, Greene A, Epstein S, Oexmann MJ, Shaw S, Shary J. 1985. Evidence for alteration of the vitamin D-endocrine system in blacks. *J Clin Invest* 76:470–473.
- Bell NH, Shary J, Stevens J, Garza M, Gordon L, Edwards J. 1991. Demonstration that bone mass is greater in black than in white children. *J Bone Miner Res* 6:719–723.
- Bell NH, Yergey AL, Vieira NE, Oexmann MJ, Shary JR. 1993. Demonstration of a difference in urinary calcium, not calcium absorption, in black and white adolescents. *J Bone Miner Res* 8:1111–1115.
- Bell RA, Whitford GM, Barenie JT, Myers DR. 1985. Fluoride retention in children using self-applied topical fluoride products. *Clin Prev Dent* 7:22–27.
- Berkelhammer CH, Wood RJ, Sitrin MD. 1988. Acetate and hypercalciuria during total parenteral nutrition. *Am J Clin Nutr* 48:1482–1489.
- Bernstein DS, Sadowsky N, Hegsted DM, Guri CD, Stare FJ. 1966. Prevalence of osteoporosis in high- and low-fluoride areas in North Dakota. *J Am Med Assoc* 198:499–504.
- Bijvoet, OLM. 1969. Relation of plasma phosphate concentration to renal tubular reabsorption of phosphate. *Clin Sci* 37:23–26.
- Bikle DD, Gee E, Halloran B, Haddad JG. 1984. Free 1,25-dihydroxyvitamin D levels in serum from normal subjects, pregnant subjects, and subjects with liver disease. *J Clin Invest* 74:1966–1971.
- Birkeland JM, Charlton G. 1976. Effect of pH on the fluoride ion activity of plaque. *Caries Res* 10:72–80.
- Bishop NJ, Dahlenburg SL, Fewtrell MS, Morley R, Lucas A. 1996. Early diet of preterm infants and bone mineralization at age five years. *Acta Paediatr* 85:230–236.
- Bizik BK, Ding W, Cerklewski FL. 1996. Evidence that bone resorption of young men is not increased by high dietary phosphorus obtained from milk and cheese. *Nutr Res* 16:1143–1146.

- Black DM, Cummings SR, Genant HK, Nevitt MC, Palermo L, Browner W. 1992. Axial and appendicular bone density predict fractures in older women. *J Bone Miner Res* 7:633–638.
- Blank S, Scanlon KS, Sinks TH, Lett S, Falk H. 1995. An outbreak of hypervitaminosis D associated with the overfortification of milk from a home-delivery dairy. *Am J Publ Health* 85:656–659.
- Blayney JR, Hill IN. 1964. Evanston dental caries study XXIV. Prenatal fluorides—value of waterborne fluorides during pregnancy. *J Am Dent Assoc* 69:291–294.
- Bodanszky H, Leleiko N. 1985. Metabolic alkalosis with hypertonic dehydration in a patient with diarrhoea and magnesium oxide ingestion. *Acta Paediatr Hung* 26:241–246.
- Bogdonoff MD, Shock NW, Nichols MP. 1953. Calcium, phosphorus, nitrogen, and potassium balance studies in the aged male. *J Gerontol* 8:272–288.
- Bostick RM, Potter JD, Fosdick L, Grambsch P, Lampe JW, Wood JR, Louis TA, Ganz R, Grandits G. 1993. Calcium and colorectal epithelial cell proliferation: A preliminary randomized, double-blinded, placebo-controlled clinical trial. *J Natl Cancer Inst* 85:132–141.
- Boston JL, Beauchene RE, Cruikshank DP. 1989. Erythrocyte and plasma magnesium during teenage pregnancy: Relationship with blood pressure and pregnancy-induced hypertension. *Obstet Gynecol* 73:169–174.
- Bouillon R, Van Assche FA, Van Baelen H, Heuys W, De Moor P. 1981. Influence of the vitamin D-binding protein on the serum concentration of 1,25-dihydroxyvitamin D<sub>3</sub>. Significance of the free 1,25-dihydroxyvitamin D<sub>3</sub> concentration. *J Clin Invest* 67:589–596.
- Bour NJS, Soullier BA, Zemel MB. 1984. Effect of level and form of phosphorus and level of calcium intake on zinc, iron and copper bioavailability in man. *Nutr Res* 4:371–379.
- Bowden GH. 1990. Effects of fluoride on the microbial ecology of dental plaque. *J Dent Res* 69 (Spec Iss):653–659.
- Boyle DR, Chagnon M. 1995. An incidence of skeletal fluorosis associated with groundwaters of the maritime carboniferous basin, Gaspe Region, Quebec, Canada. *Environ Geochem Health* 17:5–12.
- BPA (British Paediatric Association). 1956. Hypercalcaemia in infants and Vitamin D. *Br Med J* 2:149.
- BPA (British Paediatric Association). 1964. Infantile hypercalcaemia, nutritional rickets, and infantile scurvy in Great Britain. *Br Med J* 1:1659–1661.
- Brambilla E, Belluomo G, Malerba A, Buscaglia M, Strohmenger L. 1994. Oral administration of fluoride in pregnant women, and the relation between concentration in maternal plasma and in amniotic fluid. *Arch Oral Biol* 39:991–994.
- Brandwein SL, Sigman, KM. 1994. Case report: Milk-alkali syndrome and pancreatitis. *Am J Med Sci* 308:173–176.
- Brannan PG, Vergne-Marini P, Pak CY, Hull AR, Fordtran JS. 1976. Magnesium absorption in the human small intestine. Results in normal subjects, patients with chronic renal disease, and patients with absorptive hypercalciuria. *J Clin Invest* 57:1412–1418.
- Bransby ER, Berry WTC, Taylor DM. 1964. Study of the vitamin-D intakes of infants in 1960. *Br Med J* 1:1661–1663.
- Brazier M, Kamel S, Maamer M, Agbomson F, Elesper I, Garabedian M, Desmet G, Sebert JL. 1995. Markers of bone remodeling in the elderly subject: Effects of vitamin D insufficiency and its correction. *J Bone Miner Res* 10:1753–1761.

- Brickman AS, Coburn JW, Massry SG. 1974. 1,25 dihydroxy-vitamin D<sub>3</sub> in normal man and patients with renal failure. *Ann Intern Med* 80:161–168.
- Brink EJ, Beynen AC. 1992. Nutrition and magnesium absorption: A review. *Prog Food Nutr Sci* 16:125–162.
- Brodehl J, Gellissen K, Weber H-P. 1982. Postnatal development of tubular phosphate reabsorption. *Clin Nephrol* 17:163–171.
- Brown WE, Gregory TM, Chow LC. 1977. Effects of fluoride on enamel solubility and cariostasis. *Caries Res* 11(Suppl 1):118–141.
- Brunelle JA, Carlos JP. 1990. Recent trends in dental caries in U.S. children and the effect of water fluoridation. *J Dent Res* 69(Spec Iss):723–727.
- Bruun C, Thylstrup A. 1988. Dentifrice usage among Danish children. *J Dent Res* 67:1114–1117.
- Bucher HC, Cook RJ, Guyatt GH, Lang JD, Cook DJ, Hatala R, Hunt DL. 1996. Effects of dietary calcium supplementation on blood pressure: A meta-analysis of randomized controlled trials. *J Am Med Assoc* 275:1016–1022.
- Bucuvalas JC, Heubi JE, Specker BL, Gregg DJ, Yerger AL, Vieira NE. 1990. Calcium absorption in bone disease associated with chronic cholestasis during childhood. *Hepatology* 12:1200–1205.
- Bullamore JR, Wilkinson R, Gallagher JC, Nordin BEC, Marshall DH. 1970. Effects of age on calcium absorption. *Lancet* 2:535–537.
- Bullimore DW, Miloszewski KJ. 1987. Raised parathyroid hormone levels in the milk-alkali syndrome: An appropriate response? *Postgrad Med J* 63:789–792.
- Burt BA. 1992. The changing patterns of systemic fluoride intake. *J Dent Res* 71:1228–1237.
- Burtis WJ, Gay L, Insogna KL, Ellison A, Broadus AE. 1994. Dietary hypercalciuria in patients with calcium oxalate kidney stones. *Am J Clin Nutr* 60:424–429.
- Bushe CJ. 1986. Profound hypophosphataemia in patients collapsing after a “fun run.” *Br Med J* 292:898–899.
- Butte NF, Garza C, Smith EO, Nichols BL. 1984. Human milk intake and growth in exclusively breast-fed infants. *J Pediatr* 104:187–195.
- Buzzard IM, Willett WC, eds. 1994. Dietary assessment methods. Proceedings of a conference held in St. Paul, MN. *Am J Clin Nutr* 59:143S–306S.
- Byrne J, Thomas MR, Chan GM. 1987. Calcium intake and bone density of lactating women in their late childbearing years. *J Am Diet Assoc* 87:883–887.
- Byrne PM, Freaney R, McKenna MJ. 1995. Vitamin D supplementation in the elderly: Review of safety and effectiveness of different regimens. *Calcif Tissue Int* 56:518–520.
- Caddell JL, Ratananon N, Trangratapit P. 1973. Parenteral magnesium load tests in postpartum Thai women. *Am J Clin Nutr* 26:612–615.
- Caddell JL, Saier FL, Thomason CA. 1975. Parenteral magnesium load tests in postpartum American women. *Am J Clin Nutr* 28:1099–1104.
- Calvo MS. 1993. Dietary phosphorus, calcium metabolism and bone. *J Nutr* 123:1627–1633.
- Calvo MS, Heath H III. 1988. Acute effects of oral phosphate-salt ingestion on serum phosphorus, serum ionized calcium, and parathyroid hormone in young adults. *Am J Clin Nutr* 47:1025–1029.
- Calvo MS, Park YK. 1996. Changing phosphorus content of the U.S. diet: Potential for adverse effects on bone. *J Nutr* 126:1168S–1180S.
- Calvo MS, Kumar R, Heath H III. 1988. Elevated secretion and action of serum parathyroid hormone in young adults consuming high phosphorus, low calcium diets assembled from common foods. *J Clin Endocrinol Metab* 66:823–829.

- Calvo MS, Kumar R, Heath H. 1990. Persistently elevated parathyroid hormone secretion and action in young women after four weeks of ingesting high phosphorus, low calcium diets. *J Clin Endocrinol Metab* 70:1334–1340.
- Campbell SB, MacFarlane DJ, Fleming SJ, Khafagi FA. 1994. Increased skeletal uptake of Tc-99m Methylene Disphosphonate in Milk-Alkali Syndrome. *Clin Nucl Med* 19:207–211.
- Canadian Paediatric Society (Nutrition Committee). 1991. Meeting the iron needs of infants and young children: An update. *Can Med Assoc J* 144:1451–1454.
- Canadian Paediatric Society. 1996. The use of fluoride in infants and children. *Paediatr Child Health* 1:131–134.
- Cappuccio FP, Markandu ND, Beynon GW, Shore AC, Sampson B, MacGregor GA. 1985. Lack of effect of oral magnesium on high blood pressure: A double blind study. *Br Med J Clin Res Ed* 291:235–238.
- Carlos JP, Gittelsohn AM, Haddon W Jr. 1962. Caries in deciduous teeth in relation to maternal ingestion of fluoride. *Pub Hlth Rep* 77:658–660.
- Carroll MD, Abraham S, Dresser CM. 1983. Dietary intake source data: United States, 1976–1980. Data from the National Health Survey. Vital and Health Statistics series 11, no. 231. DHHS Publ. No. (PHS) 83-1681. Hyattsville, MD: National Center for Health Statistics, Public Health Service, U.S. Department of Health and Human Services.
- Chan GM. 1991. Dietary calcium and bone mineral status of children and adolescents. *Am J Dis Child* 145:631–634.
- Chan GM, Roberts CC, Folland D, Jackson R. 1982a. Growth and bone mineralization of normal breast-fed infants and the effects of lactation on maternal bone mineral status. *Am J Clin Nutr* 36:438–443.
- Chan GM, Slater RN, Hollis J, Thomas MR. 1982b. Decreased bone mineral status in lactating adolescent mothers. *J Pediatr* 101:767–770.
- Chan GM, Leeper L, Book LS. 1987. Effects of soy formulas on mineral metabolism in term infants. *Am J Dis Child* 141:527–530.
- Chan GM, Hoffman K, McMurry M. 1995. Effects of dairy products on bone and body composition in pubertal girls. *J Pediatr* 126:551–556.
- Chan JT, Koh SH. 1996. Fluoride content in caffeinated, decaffeinated and herbal teas. *Caries Res* 30:88–92.
- Chan JT, Qui CC, Whitford GM, Weatherred JG. 1990. Influence of coffee on fluoride metabolism in rats. *Proc Soc Exp Biol Med* 194:43–47.
- Chandra RK. 1984. Physical growth of exclusively breast-fed infants. *Nutr Res* 2:275–276.
- Chapuy MC, Arlot ME, Duboeuf F, Brun J, Crouzet B, Arnaud S, Delmas PD, Meunier PJ. 1992. Vitamin D<sub>3</sub> and calcium to prevent hip fractures in elderly women. *N Engl J Med* 327:1637–1642.
- Charles P, Jensen FT, Mosekilde L, Hansen HH. 1983. Calcium metabolism evaluated by <sup>47</sup>Ca kinetics: Estimation of dermal calcium loss. *Clin Sci* 65:415–422.
- Chen TC, Castillo L, Korycka-Dahl M, DeLuca HF. 1974. Role of vitamin D metabolites in phosphate transport of rat intestine. *J Nutr* 104:1056–1060.
- Chen TC, Shao A, Heath H III, Holick MF. 1993. An update on the vitamin D content of fortified milk from the United States and Canada. *N Engl J Med* 329:1507.
- Chen X, Whitford GM. 1994. Lack of significant effect of coffee and caffeine on fluoride metabolism in rats. *J Dent Res* 73:1173–1179.
- Chesney RW. 1990. Requirements and upper limits of vitamin D intake in the term neonate, infant, and older child. *J Pediatr* 116:159–166.

- Chevalley T, Rizzoli R, Nydegger V, Slosman D, Rapin CH, Michel JP, Vasey H, Bonjour JP. 1994. Effects of calcium supplements on femoral bone mineral density and vertebral fracture rate in vitamin D-replete elderly patients. *Osteopor Int* 4:245–252.
- Chinn HI. 1981. Effects of dietary factors on skeletal integrity in adults: Calcium, phosphorus, vitamin D, and protein. Prepared for Bureau of Foods, Food and Drug Administration, U.S. Department of Health and Human Services, Washington, D.C.
- Cholak J. 1959. Fluorides: A critical review. I. The occurrence of fluoride in air, food and water. *J Occup Med* 1:501–511.
- Chow LC. 1990. Tooth-bound fluoride and dental caries. *J Dent Res* 69(Spec Iss):595–600.
- Clark DC, Hann HJ, Williamson MF, Berkowitz J. 1993. Aesthetic concerns of children and parents in relation to different classifications of the Tooth Surface Index of Fluorosis. *Community Dent Oral Epidemiol* 21:360–364.
- Clarkson EM, Warren RL, McDonald SJ, de Wardener HE. 1967. The effect of a high intake of calcium on magnesium metabolism in normal subjects and patients with chronic renal failure. *Clin Sci* 32:11–18.
- Clarkson PM, Haymes EM. 1995. Exercise and mineral status of athletes: Calcium, magnesium, phosphorus, and iron. *Med Sci Sports Exerc* 27:831–843.
- Clemens TL, Adams JS. 1996. Vitamin D metabolites. In: Favus MJ, Christakos S, eds. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 3rd edition*. Philadelphia, PA: Lippincott-Raven. Pp. 109–114.
- Clemens TL, Adams JS, Henderson SL, Holick MF. 1982. Increased skin pigment reduces the capacity of skin to synthesise vitamin D<sub>3</sub>. *Lancet* 1:74–76.
- Clemens TL, Zhou X, Myles M, Endres D, Lindsay R. 1986. Serum vitamin D<sub>2</sub> and vitamin D<sub>3</sub> metabolite concentrations and absorption of vitamin D<sub>2</sub> in elderly subjects. *J Clin Endocrinol Metab* 63:656–660.
- Cleveland LE, Goldman JD, Borrud LG. 1996. *Data Tables: Results from USDA's 1994 Continuing Survey of Food Intakes by Individuals and 1994 Diet and Health Knowledge Survey*. Beltsville, MD: Agricultural Research Service, U.S. Department of Agriculture.
- Clovis J, Hargreaves JA. 1988. Fluoride intake from beverage consumption. *Community Dent Oral Epidemiol* 16:11–15.
- CNPP, USDA (Center for Nutrition Policy and Promotion, U.S. Department of Agriculture). 1996. *Nutrient Content of the U.S. Food Supply, 1990–1994. Preliminary Data*. Washington, DC: U.S. Department of Agriculture.
- Cockburn F, Belton NR, Purvis RJ, Giles MM, Brown JK, Turner TL, Wilkinson EM, Forfar JO, Barrie WJM, McKay GS, Pocock SJ. 1980. Maternal vitamin D intake and mineral metabolism in mothers and their newborn infants. *Br Med J* 281:11–14.
- Coffin B, Azpiroz F, Guarner F, Malagelada JR. 1994. Selective gastric hypersensitivity and reflex hyporeactivity in functional dyspepsia. *Gastroenterology* 107:1345–1351.
- Cohen L. 1988. Recent data on magnesium and osteoporosis. *Magnes Res* 1:85–87.
- Cohen L, Laor A. 1990. Correlation between bone magnesium concentration and magnesium retention in the intravenous magnesium load test. *Magnes Res* 3:271–274.
- Cohn SH, Abesamis C, Yasumura S, Aloia JF, Zanzi I, Ellis KJ. 1977. Comparative skeletal mass and radial bone mineral content in black and white women. *Metabolism* 26:171–178.

- Colston K, Colston MJ, Feldman D. 1981. 1,25-dihydroxyvitamin D<sub>3</sub> and malignant melanoma: The presence of receptors and inhibition of cell growth in culture. *Endocrinol* 108:1083–1086.
- COMA (Committee on Medical Aspects of Food Policy). 1991. *Dietary Reference Values for Food Energy and Nutrients for the United Kingdom. Report on Health and Social Subjects, No. 41*. London: HMSO.
- Comstock GW. 1979. Water hardness and cardiovascular diseases. *Am J Epidemiol* 110:375–400.
- Conradt A, Weidinger H, Algayer H. 1984. On the role of magnesium in fetal hypotrophy, pregnancy induced hypertension and pre-eclampsia. *Magnes Bull* 2:68–76.
- Cooper C, Melton LJ III. 1992. Epidemiology of osteoporosis. *Trends Endocrinol Metab* 3:224–229.
- Cooper C, Campion G, Melton LJ III. 1992. Hip fractures in the elderly: A worldwide projection. *Osteopor Int* 2:285–289.
- Costello RB, Moser-Veillon PB, DiBianco R. 1997. Magnesium supplementation in patients with congestive heart failure. *J Am Coll Nutr* 16:22–31.
- Cowell DC, Taylor WH. 1981. Ionic fluoride: A study of its physiological variation in man. *Ann Clin Biochem* 18:76–83.
- Craig JM. 1959. Observations on the kidney after phosphate loading in the rat. *Arch Pathol* 68:306–315.
- Cramer CF. 1961. Progress and rate of absorption of radiophosphorus through the intestinal tract of rats. *Can J Biochem Physiol* 39:499–503.
- Cremer HD, Buttner W. 1970. *Absorption of Fluorides. Fluoride and Human Health*. Geneva, Switzerland: World Health Organization.
- Cross NA, Hillman LS, Allen SH, Krause GF, Vieira NE. 1995a. Calcium homeostasis and bone metabolism during pregnancy, lactation, and postweaning: A longitudinal study. *Am J Clin Nutr* 61:514–523.
- Cross NA, Hillman LS, Allen SH, Krasue GF. 1995b. Changes in bone mineral density and markers of bone remodeling during lactation and postweaning in women consuming high amounts of calcium. *J Bone Miner Res* 10:1312–1320.
- Cumming RG, Cummings SR, Nevitt MC, Scott J, Ensrud KE, Vogt TM, Fox K. 1997. Calcium intake and fracture risk: Results from the study of osteoporotic fractures. *Am J Epidemiol* 145:926–934.
- Cummings SR, Black DM, Nevitt MC, Browner W, Cauley J, Ensrud K, Genant HK, Palermo L, Scott J, Vogt TM. 1993. Bone density at various sites for prediction of hip fractures. The Study of Osteoporotic Fractures Research Group. *Lancet* 341:72–75.
- Cummings SR, Nevitt MC, Browner WS, Stone K, Fox KM, Ensrud KE, Cauley J, Black D, Vogt TM. 1995. Risk factors for hip fracture in white women: Study of Osteoporotic Fractures Research Group. *N Engl J Med* 332:767–773.
- Cunningham AS, Mazess RB. 1983. Bone mineral loss in lactating adolescents. *J Pediatr* 101:338–339.
- Curhan GC, Willett WC, Rimm EB, Stampfer MJ. 1993. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. *N Engl J Med* 328:833–838.
- Curhan GC, Willett WC, Speizer FE, Spiegelman D, Stampfer MJ. 1997. Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk for kidney stones in women. *Ann Intern Med* 126:497–504.

- Dabeka RW, McKenzie AD, Conacher HBS, Kirkpatrick DC. 1982. Determination of fluoride in Canadian infant foods and calculation of fluoride intakes by infants. *Can J Pub Hlth* 73:188–191.
- Dabeka RW, McKenzie AD, Lecroix GM. 1987. Dietary intakes of lead, cadmium, arsenic and fluoride by Canadian adults: A 24-hour duplicate diet study. *Food Addit Contam* 4:89–101.
- Dale G, Fleetwood JA, Inkster JS, Sainsbury JR. 1986. Profound hypophosphataemia in patients collapsing after a “fun run.” *Br Med J (Clin Res)* 292:447–448.
- Dalton MA, Sargent JD, O’Connor GT, Olmstead EM, Klein RZ. 1997. Calcium and phosphorus supplementation of iron-fortified infant formula: No effect on iron status of healthy full-term infants. *Am J Clin Nutr* 65:921–926.
- Davies M, Adams PH. 1978. The continuing risk of vitamin D intoxication. *Lancet* 2(8090):621–623.
- Davies M, Lawson DEM, Emberson C, Barnes JLC, Roberts GE, Barnes ND. 1982. Vitamin D from skin: Contribution to vitamin D status compared with oral vitamin D in normal and anti-convulsant-treated subjects. *Clin Sci* 63:461–472.
- Davies M, Hayes ME, Yin JA, Berry JL, Mawer EB. 1994. Abnormal synthesis of 1,25-dihydroxyvitamin D in patients with malignant lymphoma. *J Clin Endocrinol Metab* 78:1202–1207.
- Davis RH, Morgan DB, Rivlin RS. 1970. The excretion of calcium in the urine and its relation to calcium intake, sex and age. *Clin Sci* 39:1–12.
- Dawes C. 1989. Fluorides: Mechanisms of action and recommendations for use. *J Can Dent Assoc* 55:721–723.
- Dawson-Hughes B. 1996. Calcium. In: Marcus R, Feldman D, Kelsey J, eds. *Osteoporosis*. Orlando, FL: Academic Press, Inc. Pp. 1103, 1105.
- Dawson-Hughes B, Stern DT, Shipp CC, Rasmussen HM. 1988. Effect of lowering dietary calcium intake on fractional whole body calcium retention. *J Clin Endocrinol Metab* 67:62–68.
- Dawson-Hughes B, Dallal GE, Krall EA, Sadowski L, Sahyoun N, Tannenbaum S. 1990. A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women. *N Engl J Med* 323:878–883.
- Dawson-Hughes B, Dallal GE, Krall EA, Harris S, Sokoll LJ, Falconer G. 1991. Effect of vitamin D supplementation on wintertime and overall bone loss in healthy postmenopausal women. *Ann Intern Med* 115:505–512.
- Dawson-Hughes B, Harris S, Kramich C, Dallal G, Rasmussen HM. 1993. Calcium retention and hormone levels in black and white women on high- and low-calcium diets. *J Bone Miner Res* 8:779–787.
- Dawson-Hughes B, Harris SS, Krall EA, Dallal GE, Falconer G, Green CL. 1995. Rates of bone loss in postmenopausal women randomly assigned to one of two dosages of vitamin D. *Am J Clin Nutr* 61:1140–1145.
- Dawson-Hughes B, Fowler SE, Dalsky G, Gallagher C. 1996. Sodium excretion influences calcium homeostasis in elderly men and women. *J Nutr* 126:2107–2112.
- Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. 1997. Calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. *N Engl J Med* 337:670–676.
- Dean HT. 1942. The investigation of physiological effects by the epidemiological method. In: Moulton FR, ed. *Fluorine and Dental Health*. Washington, DC: American Association for the Advancement of Science. Pp. 23–31.
- Dean HT, Elvove E. 1937. Further studies on the minimal threshold of chronic endemic dental fluorosis. *Pub Hlth Rep* 52:1249–1264.

- Delmas PD. 1992. Clinical use of biochemical markers of bone remodeling in osteoporosis. *Bone* 13:S17–S21.
- Delmi M, Rapin CH, Bengoa JM, Delmas PD, Vasey H, Bonjour JP. 1990. Dietary supplementation in elderly patients with fractured neck of the femur. *Lancet* 335:1013–1016.
- DeLuca HF. 1984. The metabolism, physiology, and function of vitamin D. In: Kumar R, ed. *Vitamin D: Basic and Clinical Aspects*. Boston: M. Nijhoff Publishers.
- DeLuca HF. 1988. The vitamin D story: A collaborative effort of basic science and clinical medicine. *FASEB J* 2:224–236.
- Delvin EE, Salle BL, Glorieux FH, Adeleine P, David LS. 1986. Vitamin D supplementation during pregnancy: Effect on neonatal calcium homeostasis. *J Pediatr* 109:328–334.
- Demay MB. 1995. Hereditary defects in vitamin D metabolism and vitamin D receptor defects. In: DeGroot LJ, Besser M, Burger HG, Jameson JL, Loriaux DL, Marshall JC, O'Dell WD, Potts JT, Rubenstein AH, eds. *Endocrinology, Vol 2, Third edition*. Philadelphia, PA: WB Saunders. Pp. 1173–1178.
- Demirjian A. 1980. *Anthropometry Report. Height, Weight, and Body Dimensions: A Report from Nutrition Canada*. Ottawa: Minister of National Health and Welfare, Health and Promotion Directorate, Health Services and Promotion Branch.
- Dengel JL, Mangels AR, Moser-Veillon PB. 1994. Magnesium homeostasis: Conservation mechanism in lactating women consuming a controlled-magnesium diet. *Am J Clin Nutr* 59:990–994.
- Deurenberg P, Pieters JJ, Hautvast JG. 1990. The assessment of the body fat percentage by skinfold thickness measurements in childhood and young adolescence. *Br J Nutr* 63:293–303.
- Deuster PA, Singh A. 1993. Responses of plasma magnesium and other cations to fluid replacement during exercise. *J Am Coll Nutr* 12:286–293.
- Devine A, Criddle RA, Dick IM, Kerr DA, Prince RL. 1995. A longitudinal study of the effect of sodium and calcium intakes on regional bone density in postmenopausal women. *Am J Clin Nutr* 62:740–745.
- DeVizia B, Mansi A. 1992. Calcium and phosphorus metabolism in full-term infants. *Monatsschr Kinderheilkd* 140:S8–S12.
- DeVizia B, Fomon SJ, Nelson SE, Edwards BE, Zeigler EE. 1985. Effect of dietary calcium on metabolic balance of normal infants. *Pediatr Res* 19:800–806.
- Dewey KG, Finley DA, Lonnerdal B. 1984. Breast milk volume and composition during late lactation (7–20 months). *J Pediatr Gastroenterol Nutr* 3:713–720.
- DHHS (Department of Health and Human Services). 1988. *The Surgeon General's Report on Nutrition and Health*. Washington, DC: US Department of Health and Human Services, Public Health Service.
- DHHS (Department of Health and Human Services). 1990. *Healthy People 2000: National Health Promotion and Disease Prevention Objectives*. DHHS Publ. No. (PHS) 91-50212. Washington, DC: US Government Printing Office. Pp. 466–467.
- Diem K. 1970. *Documenta Geigy*. Ardsley, NY: Geigy Pharmaceuticals.
- Dobnig H, Kainer F, Stepan V, Winter R, Lipp R, Schaffer M, Kahr A, Nocnik S, Patterer G, Leb G. 1995. Elevated parathyroid hormone-related peptide levels after human gestation: Relationship to changes in bone and mineral metabolism. *J Clin Endocrinol Metab* 80:3699–3707.
- Dorsch TR. 1986. The milk-alkali syndrome, vitamin D, and parathyroid hormone. *Ann Intern Med* 105:800–801.

- Dorup I, Clausen T. 1993. Correlation between magnesium and potassium contents in muscle: Role of Na(+)-K<sup>+</sup> pump. *Am J Physiol* 264:C457–C463.
- Dourson ML, Stara JF. 1983. Regulatory history and experimental support of uncertainty (safety) factors. *Regul Toxicol Pharmacol* 3:224–238.
- Dowell TB. 1981. The use of toothpaste in infancy. *Br Dent J* 150:247–249.
- Drinkwater BL, Chesnut CH III. 1991. Bone density changes during pregnancy and lactation in active women: A longitudinal study. *Bone Miner* 14:153–160.
- Drinkwater B, Bruemner B, Chesnut C. 1990. Menstrual history as a determinant of current bone density in young athletes. *J Am Med Assoc* 263:545–548.
- Dwyer JT, Dietz WH, Hass G, Suskind R. 1979. Risk of nutritional rickets among vegetarian children. *Am J Dis Child* 133:134–140.
- Dyckner T, Wester PO. 1983. Effect of magnesium on blood pressure. *Br Med J (Clin Res)* 286:1847–1849.
- Dyckner T, Wester PO. 1985. Skeletal muscle magnesium and potassium determinations: Correlation with lymphocyte contents of magnesium and potassium. *J Am Coll Nutr* 4:619–625.
- Ebeling PR, Yergey AL, Vieira NE, Burritt MF, O'Fallon WM, Kumar R, Riggs BL. 1994. Influence of age on effects on endogenous 1,25-dihydroxy-vitamin D on calcium absorption in normal women. *Calcif Tissue Int* 55:330–334.
- Eble DM, Deaton TG, Wilson FC, Bawden JW. 1992. Fluoride concentrations in human and rat bone. *J Pub Hlth Dent* 52:288–291.
- Egsmose C, Lund B, McNair P, Lund B, Storm T, Sorensen OH. 1987. Low serum levels of 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D in institutionalized old people: Influence of solar exposure and vitamin D supplementation. *Age Ageing* 16:35–40.
- Eisman JA, Suva LJ, Sher E, Pearce PJ, Funder JW, Martin TJ. 1981. Frequency of 1,25-dihydroxyvitamin D<sub>3</sub> receptor in human breast cancer. *Cancer Res* 41:5121–5124.
- Ekstrand J, Ehrnebo M. 1979. Influence of milk products on fluoride bioavailability in man. *Eur J Clin Pharmacol* 16:211–215.
- Ekstrand J, Ehrnebo M. 1980. Absorption of fluoride from fluoride dentifrices. *Caries Res* 14:96–102.
- Ekstrand J, Boreus LO, de Chateau P. 1981. No evidence of transfer of fluoride from plasma to breast milk. *Br Med J* 283:761–762.
- Ekstrand J, Spak CJ, Falch J, Afseth J, Ulvestad H. 1984. Distribution of fluoride to human breast milk following intake of high doses of fluoride. *Caries Res* 18:93–95.
- Ekstrand J, Fomon SJ, Ziegler EE, Nelson SE. 1994a. Fluoride pharmacokinetics in infancy. *Pediatr Res* 35:157–163.
- Ekstrand J, Ziegler EE, Nelson SE, Fomon SJ. 1994b. Absorption and retention of dietary and supplemental fluoride by infants. *Adv Dent Res* 8:175–180.
- Elders PJ, Netelenbos JC, Lips P, van Ginkel FC, Khoe E, Leeuwenkamp OR, Hackeng WH, van der Stelt PF. 1991. Calcium supplementation reduces vertebral bone loss in perimenopausal women: A controlled trial in 248 women between 46 and 55 years of age. *J Clin Endocrinol Metab* 73:533–540.
- Elders PJ, Lips P, Netelenbos JC, van Ginkel FC, Khoe E, van der Vijgh WJ, van der Stelt PF. 1994. Long-term effect of calcium supplementation on bone loss in perimenopausal women. *J Bone Miner Res* 9:963–970.
- Elia M. 1992. Energy expenditure and the whole body. In: Kinney JM, Tucker HN, eds. *Energy Metabolism: Tissue Determinants and Cellular Corollaries*. New York: Raven Press Ltd. Pp. 19–59.

- Elin RJ. 1987. Assessment of magnesium status. *Clin Chem* 33:1965–1970.
- Elin RJ, Hosseini JM. 1985. Magnesium content of mononuclear blood cells. *Clin Chem* 31:377–380.
- Ellis KJ, Shypailo RJ, Hergenroeder A, Perez M, Abrams S. 1996. Total body calcium and bone mineral content: Comparison of dual-energy X-ray absorptiometry (DXA) with neutron activation analysis (NAA). *J Bone Miner Res* 11:843–848.
- Ellis KJ, Abrams SA, Wong WW. 1997. Body composition of a young, multiethnic female population. *Am J Clin Nutr* 65:724–731.
- EPA (U. S. Environmental Protection Agency). 1986. Guidelines for Carcinogen Risk Assessment. *Federal Register* 51(185):33992–34003.
- EPA (U. S. Environmental Protection Agency). 1996. Proposed Guidelines for Carcinogen Risk Assessment; Notice. *Federal Register* 61(79):17960–18011.
- Esala S, Vuori E, Helle A. 1982. Effect of maternal fluorine intake on breast milk fluorine content. *Br J Nutr* 48:201–204.
- Esveld RP, DeLuca HF. 1981. Calcitroic acid: Biological activity and tissue distribution studies. *Arch Biochem Biophys* 206:403–413.
- European Community. 1993. *Nutrient and Energy Intakes for the European Community*. Reports of the Scientific Committee for Food, Thirty-first Series.
- Evans RW. 1989. Changes in dental fluorosis following an adjustment to the fluoride concentration of Hong Kong's water supplies. *Adv Dent Res* 3:154–160.
- Evans RW, Darvell BW. 1995. Refining the estimate of the critical period for susceptibility to enamel fluorosis in human maxillary central incisors. *J Pub Hlth Dent* 55:238–249.
- Fairweather-Tait S, Prentice A, Heumann KG, Landing MAJ, Stirling DM, Wharf SG, Turnlund JR. 1995. Effect of calcium supplements and stage of lactation on the calcium absorption efficiency of lactating women accustomed to low calcium intakes. *Am J Clin Nutr* 62:1188–1192.
- FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization). 1982. *Evaluation of Certain Food Additives and Contaminants*. Twenty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives (WHO Technical Report Series No. 683).
- FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization, Expert Consultation). 1995. *The Application of Risk Analysis to Food Standard Issues*. Recommendations to the Codex Alimentarius Commission (ALINORM 95/9, Appendix 5).
- FAO/WHO/UNA (Food and Agriculture Organization of the United Nations/World Health Organization/United Nations). 1985. *Energy and Protein Requirements*. Report of a joint FAO/WHO/UNA Consultation Technical Report Series. No. 724. Geneva, Switzerland: World Health Organization.
- Fardellone P, Sebert JL, Garabedian M, Bellony R, Maamer M, Agbomson F, Brazier M. 1995. Prevalence and biological consequences of vitamin D deficiency in elderly institutionalized subjects. *Rev Rhum* 62:576–581.
- Farmer ME, White LR, Brody JA, Bailey KR. 1984. Race and sex differences in hip fracture incidence. *Am J Publ Health* 74:1374–1380.
- Fatemi S, Ryzen E, Flores J, Endres DB, Rude RK. 1991. Effect of experimental human magnesium depletion on parathyroid hormone secretion and 1,25-dihydroxyvitamin D metabolism. *J Clin Endocrinol Metab* 73:1067–1072.
- Faulkner KG, Cummings SR, Black D, Palermo L, Gluer CC, Genant HK. 1993. Simple measurement of femoral geometry predicts hip fracture: The study of osteoporotic fractures. *J Bone Miner Res* 8:1211–1217.

- Favus MJ, Christakos S. 1996. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 3rd Edition*. Philadelphia, PA: Lippincott-Raven.
- Featherstone JDB, Shields CP. 1988. *A Study of Fluoride in New York State Residents*. Final report to New York State Department of Health.
- Fehily AM, Coles RJ, Evans WD, Elwood PC. 1992. Factors affecting bone density in young adults. *Am J Clin Nutr* 56:579–586.
- Fejerskov O, Thylstrup A, Larsen MJ. 1977. Clinical and structural features and possible pathogenic mechanisms of dental fluorosis. *Scand J Dent Res* 85:510–534.
- Feldblum PJ, Zhang J, Rich LE, Fortney JA, Talmage RV. 1992. Lactation history and bone mineral density among perimenopausal women. *Epidemiology* 3:527–531.
- Feliciano ES, Ho ML, Specker BL, Falciglia G, Shui QM, Yin TA, Chen XC. 1994. Seasonal and geographical variations in the growth rate of infants in China receiving increasing dosages of vitamin D supplements. *J Trop Pediatr* 40:162–165.
- Feltman R, Kosel G. 1961. Prenatal and postnatal ingestion of fluorides—fourteen years of investigation. Final report. *J Dent Med* 16:190–198.
- Fieser LF, Fieser M. 1959. Vitamin D. In: *Steroids*. New York: Reinhold. Pp. 90–168.
- Filippo FA, Battistone GC. 1971. The fluoride content of a representative diet of the young adult male. *Clin Chim Acta* 31:453–457.
- Fine KD, Santa Ana CA, Porter JL, Fordtran JS. 1991a. Intestinal absorption of magnesium from food and supplements. *J Clin Invest* 88:396–402.
- Fine KD, Santa Ana CA, Fordtran JS. 1991b. Diagnosis of magnesium-induced diarrhea. *N Engl J Med* 324:1012–1017.
- Fink RI, Kolterman OG, Griffin J, Olefsky JM. 1983. Mechanisms of insulin resistance in aging. *J Clin Invest* 71:1523–1535.
- Fitzgerald MG, Fourman P. 1956. An experimental study of magnesium deficiency in man. *Clin Sci* 15:635.
- Fomon SJ, Nelson SE. 1993. Calcium, phosphorus, magnesium, and sulfur. In: Fomon SJ, ed. *Nutrition of Normal Infants*. St. Louis: Mosby-Year Book, Inc. Pp. 192–216.
- Fomon SJ, Younoszai MK, Thomas LN. 1966. Influence of vitamin D on linear growth of normal full-term infants. *J Nutr* 88:345–50.
- Fomon SJ, Haschke F, Ziegler EE, Nelson SE. 1982. Body composition of reference children from birth to age 10 years. *Am J Clin Nutr* 35:1169–1175.
- Franz KB. 1987. Magnesium intake during pregnancy. *Magnesium* 6:18–27.
- Franz KB. 1989. Influence of phosphorus on intestinal absorption of calcium and magnesium. In: Itokawa Y, Durlach J, eds. *Magnesium in Health and Disease*. London: John Libbey & Co. Pp. 71–78.
- Fraser DR. 1980. Regulation of the metabolism of vitamin D. *Physiol Rev* 60:551–613.
- Fraser DR. 1983. The physiological economy of vitamin D. *Lancet* 1:969–972.
- Freiman I, Pettifor JM, Moodley GM. 1982. Serum phosphorus in protein energy malnutrition. *J Pediatr Gastroenterol Nutr* 1:547–550.
- French JK, Koldaway IM, Williams LC. 1986. Milk-alkali syndrome following over-the-counter antacid self-medication. *N Zeal Med J* 99:322–323.
- Freudenheim JL, Johnson NE, Smith EL. 1986. Relationships between usual nutrient intake and bone-mineral content of women 35–65 years of age: Longitudinal and cross-sectional analysis. *Am J Clin Nutr* 44:863–876.

- Freyberg RH. 1942. Treatment of arthritis with vitamin and endocrine preparations. *J Am Med Assoc* 119:1165–1171.
- Frithz G, Wictorin B, Ronquist G. 1991. Calcium-induced constipation in a prepubescent boy. *Acta Paediatr Scand* 80:964–965.
- Frost HM. 1973. The origin and nature of transients in human bone remodeling dynamics. In: Frame B, Parfitt AM, Duncan H, eds. *Clinical Aspects of Metabolic Bone Disease*. Amsterdam: Excerpta Medica Series. Pp. 124–137.
- Frost HM. 1987. The mechanostat: A proposed pathogenic mechanism of osteoporosis and the bone mass effects of mechanical and nonmechanical agents. *Bone Miner* 2:73–85.
- Frost HM. 1997. Why do marathon runners have less bone than weight lifters? A vital-biomechanical view and explanation. *Bone* 20:183–189.
- Gadallah M, Massry SG, Bigazzi R, Horst RL, Eggema P, Campese VM. 1991. Intestinal absorption of calcium and calcium metabolism in patients with essential hypertension and normal renal function. *Am J Hypertens* 4:404–409.
- Galla JH, Booker BB, Luke RG. 1986. Role of the loop segment in the urinary concentrating defect of hypercalcemia. *Kidney Int* 29:977–982.
- Gallagher JC, Riggs BL, DeLuca HF. 1980. Effect of estrogen on calcium absorption and serum vitamin D metabolites in postmenopausal osteoporosis. *J Clin Endocrinol Metab* 51:1359–1364.
- Gallagher JC, Goldgar D, Moy A. 1987. Total bone calcium in women: Effect of age and menopause status. *J Bone Miner Res* 2:491–496.
- Garby L, Lammert O. 1984. Within-subjects between-days-and-weeks variation in energy expenditure at rest. *Human Nutr Clin Nutr* 38:395–397.
- Garfinkel L, Garfinkel D. 1985. Magnesium regulation of the glycolytic pathway and the enzymes involved. *Magnesium* 4:60–72.
- Garland C, Shekelle RB, Barrett-Connor E, Criqui MH, Rossof AH, Paul O. 1985. Dietary vitamin D and calcium and risk of colorectal cancer: A 19-year prospective study in men. *Lancet* 1:307–309.
- Garland FC, Garland CF, Gorham ED, Young JF. 1990. Geographic variation in breast cancer mortality in the United States: A hypothesis involving exposure to solar radiation. *Prev Med* 19:614–622.
- Garn SM. 1972. The course of bone gain and the phases of bone loss. *Orthop Clin North Am* 3:503–520.
- Gartside PS, Glueck CJ. 1995. The important role of modifiable dietary and behavioral characteristics in the causation and prevention of coronary heart disease hospitalization and mortality: The prospective NHANES I follow-up study. *J Am Coll Nutr* 14:71–79.
- Gedalia I, Brzezinski A, Portuguese N, Bercovici B. 1964. The fluoride content of teeth and bones of human foetuses. *Arch Oral Biol* 9:331–340.
- Geleijnse JM, Witteman JC, Bak AA, den Breeijen JH, Grobbee DE. 1994. Reduction in blood pressure with a low sodium, high potassium, high magnesium salt in older subjects with mild to moderate hypertension. *Br Med J* 309:436–440.
- German Society of Nutrition. 1991. *Recommendations on Nutrient Intake*. Abstract and Tables of the 157 Pages Booklet, 5th revised edition. Frankfurt: Druckerei Henrich.
- Gershoff SN, Legg MA, Hegsted DM. 1958. Adaptation to different calcium intakes in dogs. *J Nutr* 64:303–312.
- Gertner JM, Coustan DR, Kliger AS, Mallette LE, Ravin N, Broadus AE. 1986. Pregnancy as state of physiologic absorptive hypercalciuria. *Am J Med* 81:451–456.

- Gillman MW, Hood MY, Moore LL, Nguyen US, Singer MR, Andon MB. 1995. Effect of calcium supplementation on blood pressure in children. *J Pediatr* 127:186–192.
- Gilsanz V, Roe TF, Mora S, Costin G, Goodman WG. 1991. Changes in vertebral bone density in black girls and white girls during childhood and puberty. *N Engl J Med* 325:1597–1600.
- Glaser K, Parmelee AH, Hoffman WS. 1949. Comparative efficacy of vitamin D preparations in prophylactic treatment of premature infants. *Am J Dis Child* 77:1–14.
- Glass RL, Peterson JK, Zuckerberg DA, Naylor MN. 1975. Fluoride ingestion resulting from the use of a monofluorophosphate dentifrice by children. *Br Dent J* 138:423–426.
- Glenn FB. 1981. The rationale for the administration of a NaF tablet supplement during pregnancy and postnatally in a private practice setting. *J Dent Child* 48:118–122.
- Glenn FB, Glenn WD III, Duncan RC. 1984. Prenatal fluoride tablet supplementation and the fluoride content of teeth: Part VII. *J Dent Child* 51:344–351.
- Gloth FM III, Gundberg CM, Hollis BW, Haddad JG Jr, Tobin JD. 1995. Vitamin D deficiency in homebound elderly persons. *J Am Med Assoc* 274:1683–1686.
- Goeree R, O'Brien B, Pettitt D, Cuddy L, Ferraz M, Adachi J. 1996. An assessment of the burden of illness due to osteoporosis in Canada. *J SOGC*:15S–24S.
- Golden BE, Golden MH. 1981. Plasma zinc, rate of weight gain, and the energy cost of tissue deposition in children recovering from severe malnutrition on a cow's milk or soya protein-based diet. *Am J Clin Nutr* 34:892–899.
- Goldfarb S. 1994. Diet and nephrolithiasis. *Ann Rev Med* 45:235–243.
- Goldring SR, Krane SM, Avioli LV. 1995. Disorders of calcification: Osteomalacia and rickets. In: DeGroot LJ, ed. *Endocrinology*, Vol 2, *Third Edition*. Philadelphia: WB Saunders. Pp. 1204–1227.
- Golzarian J, Scott HW Jr, Richards WO. 1994. Hypermagnesemia-induced paralytic ileus. *Dig Dis Sci* 39:1138–1142.
- Gora ML, Seth SK, Bay WH, Visconti JA. 1989. Milk-alkali syndrome associated with use of chlorothiazide and calcium carbonate. *Clin Pharm* 8:227–229.
- Goren S, Silverstein LJ, Gonzales N. 1993. A survey of food service managers of Washington State boarding homes for the elderly. *J Nutr Elderly* 12:27–42.
- Graham S. 1959. Idiopathic hypercalcemia. *Postgraduate Med* 25:67–72.
- Gray TK, Lester GE, Lorenc RS. 1979. Evidence for extra-renal 1-hydroxylation of 25-hydroxyvitamin D<sub>3</sub> in pregnancy. *Science* 204:1311–1313.
- Greer FR. 1989. Calcium, phosphorus, and magnesium: How much is too much for infant formulas? *J Nutr* 119:1846–1851.
- Greer FR, Garn SM. 1982. Loss of bone mineral content in lactating adolescents. *J Pediatr* 101:718–719.
- Greer FR, Searcy JE, Levin RS, Steichen JJ, Steichen-Asche PS, Tsang RC. 1982a. Bone mineral content and serum 25-hydroxyvitamin D concentrations in breast-fed infants with and without supplemental vitamin D: One-year follow-up. *J Pediatr* 100:919–922.
- Greer FR, Tsang RC, Levin RS, Searcy JE, Wu R, Steichen JJ. 1982b. Increasing serum calcium and magnesium concentrations in breast-fed infants: Longitudinal studies of minerals in human milk and in sera of nursing mothers and their infants. *J Pediatr* 100:59–64.

- Greer FR, Steichen JJ, Tsang RC. 1982c. Effects of increased calcium, phosphorus, and vitamin D intake on bone mineralization in very low-birth-weight infants fed formulas with polycose and medium-chain triglycerides. *J Pediatr* 100:951–955.
- Greer FR, Lane J, Ho M. 1984. Elevated serum parathyroid hormone, calcitonin, and 1,25-dihydroxyvitamin D in lactating women nursing twins. *Am J Clin Nutr* 40:562–568.
- Greger JL, Baier MJ. 1983. Effect of dietary aluminum on mineral metabolism of adult males. *Am J Clin Nutr* 38:411–419.
- Greger JL, Baligar P, Abernathy RP, Bennett OA, Peterson T. 1978. Calcium, magnesium, phosphorus, copper, and manganese balance in adolescent females. *Am J Clin Nutr* 31:117–121.
- Greger JL, Huffman J, Abernathy RP, Bennett OA, Resnick SE. 1979. Phosphorus and magnesium balance of adolescent females fed two levels of zinc. *J Food Sci* 44:1765–1767.
- Greger JL, Smith SA, Snedeker SM. 1981. Effect of dietary calcium and phosphorus levels on the utilization of calcium, phosphorus, magnesium, manganese, and selenium by adult males. *Nutr Res* 1:315–325.
- Grill V, Martin TJ. 1993. Non-parathyroid hypercalcemias. In: Nordin BEC, Need AG, Morris HA, eds. *Metabolic Bone and Stone Disease*. Edinburgh: Churchill Livingstone. Pp. 133–145.
- Grimston SK, Morrison K, Harder JA, Hanley DA. 1992. Bone mineral density during puberty in Western Canadian children. *Bone Miner* 19:85–96.
- Groeneveld A, Van Eck AA, Backer-Dirks O. 1990. Fluoride in caries prevention: Is the effect pre- or post-eruptive? *J Dent Res* 69(Spec Iss):751–755.
- Gullestad L, Dolva LO, Waage A, Falch D, Fagerthun H, Kjekshus J. 1992. Magnesium deficiency diagnosed by an intravenous loading test. *Scan J Clin Lab Invest* 52:245–253.
- Gullestad L, Nes M, Ronneberg R, Midtveldt K, Falch D, Kjekshus J. 1994. Magnesium status in healthy free-living elderly Norwegians. *J Am Coll Nutr* 13:45–50.
- Gultekin A, Ozalp I, Hasanoglu A, Unal A. 1987. Serum-25-hydroxycholecalciferol levels in children and adolescents. *Turk J Pediatr* 29:155–162.
- Gunther T. 1993. Mechanisms and regulation of Mg<sup>2+</sup> efflux and Mg<sup>2+</sup> influx. *Miner Electrolyte Metab* 19:259–265.
- Guy WS. 1979. Inorganic and organic fluorine in human blood. In: Johansen E, Taves DR, Olsen TO, eds. *Continuing Evaluation of the Use of Fluorides*. AAAS Selected Symposium. Boulder, CO: Westview Press.
- Haddad JG, Jr. 1980. Competitive protein-binding radioassays for 25-OH-D; clinical applications. In: Norman, ed. *Vitamin D*, vol. 2. New York: Marcel Dekker, Inc., P. 587.
- Haddad JG, Hahn TJ. 1973. Natural and synthetic sources of circulating 25-hydroxyvitamin D in man. *Nature* 244:515–517.
- Hakim R, Tolis G, Goltzman D, Meltzer S, Friedman R. 1979. Severe hypercalcemia associated with hydrochlorothiazide and calcium carbonate therapy. *Can Med Assoc J* 21:591–594.
- Halioua L, Anderson JJ. 1989. Lifetime calcium intake and physical activity habits: Independent and combined effects on the radial bone of healthy premenopausal Caucasian women. *Am J Clin Nutr* 49:534–541.
- Hallberg L, Rossander-Hulten L, Brune M, Gleerup A. 1992. Calcium and iron absorption: Mechanism of action and nutritional importance. *Eur J Clin Nutr* 46:317–327.

- Hallfrisch J, Muller DC. 1993. Does diet provide adequate amounts of calcium, iron, magnesium, and zinc in a well-educated adult population? *Exper Gerontol* 28:473–483.
- Hamilton IR. 1990. Biochemical effects of fluoride on oral bacteria. *J Dent Res* 69(Spec Iss):660–667.
- Hammer DI, Heyden S. 1980. Water hardness and cardiovascular mortality. *J Am Med Assoc* 243:2399–2400.
- Hamuro Y, Shino A, Suzuki Z. 1970. Acute induction of soft tissue calcification with transient hyperphosphatemia in the KK mouse by modification in dietary contents of calcium, phosphorus, and magnesium. *J Nutr* 100:404–412.
- Handwerker SM, Altura BT, Altura BM. 1996. Serum ionized magnesium and other electrolytes in the antenatal period of human pregnancy. *J Am Coll Nutr* 15:36–43.
- Hardwick LL, Jones MR, Brautbar N, Lee DB. 1991. Magnesium absorption: Mechanisms and the influence of vitamin D, calcium and phosphate. *J Nutr* 121:13–23.
- Hargreaves JA. 1972. Fluoride content of deciduous tooth enamel from three different regions (Abstract). *J Dent Res* 51:274.
- Hargreaves JA. 1992. The level and timing of systemic exposure to fluoride with respect to caries resistance. *J Dent Res* 71:1244–1248.
- Hargreaves JA, Ingram GS, Wagg BJ. 1970. An extended excretion study on the ingestion of a monofluorophosphate toothpaste by children. *Acta Med Sci Hung* 27:413–419.
- Hargreaves JA, Ingram FF, Wagg BJ. 1972. A gravimetric based study of the ingestion of toothpaste by children. *Caries Res* 6:237–243.
- Hargreaves JA, Thompson GW, Pimlott JFL, Norbert LD. 1988. Commencement date of fluoride supplementation related to dental caries. *J Dent Res* 67:230.
- Harris SS, Dawson-Hughes B. 1994. Caffeine and bone loss in healthy postmenopausal women. *Am J Clin Nutr* 60:573–578.
- Hart M, Windle J, McHale M, Grissom R. 1982. Milk-alkali syndrome and hypercalcemia: A case report. *Nebr Med J* 67:128–130.
- Hasling C, Charles P, Jensen FT, Mosekilde L. 1990. Calcium metabolism in postmenopausal osteoporosis: The influence of dietary calcium and net absorbed calcium. *J Bone Miner Res* 5:939–946.
- Hayslip CC, Klein TA, Wray HL, Duncan WE. 1989. The effects of lactation on bone mineral content in healthy postpartum women. *Obstet Gynecol* 73:588–592.
- Health Canada. 1990. *Nutrition Recommendations. The Report of the Scientific Review Committee 1990*. Ottawa: Canadian Government Publishing Centre.
- Health Canada. 1993. *Health Risk Determination—The Challenge of Health Protection*. Health Canada, Health Protection Branch. Ottawa: Health Canada.
- Heaney RP. 1993. Protein intake and the calcium economy. *J Am Diet Assoc* 93:1259–1260.
- Heaney RP. 1997. Vitamin D: Role in the calcium economy. In: Feldman D, Glorieux FH, Pike JW, eds. *Vitamin D*. San Diego, CA: Academic Press. Pp. 485–497.
- Heaney RP, Recker RR. 1982. Effects of nitrogen, phosphorus, and caffeine on calcium balance in women. *J Lab Clin Med* 99:46–55.
- Heaney RP, Recker RR. 1987. Calcium supplements: Anion effects. *Bone Miner* 2:433–439.

- Heaney RP, Recker RR. 1994. Determinants of endogenous fecal calcium in healthy women. *J Bone Miner Res* 9:1621–1627.
- Heaney RP, Skillman TG. 1964. Secretion and excretion of calcium by the human gastrointestinal tract. *J Lab Clin Med* 64:29–41.
- Heaney RP, Skillman TG. 1971. Calcium metabolism in normal human pregnancy. *J Clin Endocrinol* 33:661–670.
- Heaney RP, Saville PD, Recker RR. 1975. Calcium absorption as a function of calcium intake. *J Lab Clin Med* 85:881–890.
- Heaney RP, Recker RR, Saville PD. 1977. Calcium balance and calcium requirements in middle-aged women. *Am J Clin Nutr* 30:1603–1611.
- Heaney RP, Recker RR, Saville PD. 1978. Menopausal changes in calcium balance performance. *J Lab Clin Med* 92:953–963.
- Heaney RP, Recker RR, Hinders SM. 1988. Variability of calcium absorption. *Am J Clin Nutr* 47:262–264.
- Heaney RP, Recker RR, Stegman MR, Moy AJ. 1989. Calcium absorption in women: Relationships to calcium intake, estrogen status, and age. *J Bone Miner Res* 4:469–475.
- Heaney RP, Recker RR, Weaver CM. 1990a. Absorbability of calcium sources: The limited role of solubility. *Calcif Tissue Int* 46:300–304.
- Heaney RP, Weaver CM, Fitzsimmons ML. 1990b. Influence of calcium load on absorption fraction. *J Bone Miner Res* 5:1135–1138.
- Heaney RP, Weaver CM, Fitzsimmons ML. 1991. Soybean phytate content: Effect on calcium absorption. *Am J Clin Nutr* 53:745–747.
- Heaton FW. 1969. The kidney and magnesium homeostasis. *Ann NY Acad Sci* 162:775–785.
- Hegsted DM. 1972. Problems in the use and interpretation of the Recommended Dietary Allowances. *Ecol Food Nutr* 1:255–265.
- Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. 1993. Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: The DARLING study. *Am J Clin Nutr* 58:152–161.
- Hemmingsen C, Staun M, Olgaard K. 1994. Effects of magnesium on renal and intestinal calbindin-D. *Miner Electrolyte Metab* 20:265–273.
- Herman-Giddens ME, Slora EJ, Wasserman RC, Bourdon CJ, Bhapkar MV, Koch GG, Hasemeier CM. 1997. Secondary sexual characteristics and menses in young girls seen in office practice: A study from the Pediatric Research in Office Settings Network. *Pediatrics* 99:505–512.
- Hill AB. 1971. *Principles of Medical Statistics, 9th Ed.* New York: Oxford University Press.
- Hillman LS. 1990. Mineral and vitamin D adequacy in infants fed human milk or formula between 6 and 12 months of age. *J Pediatr* 117:S134–S142.
- Hillman L, Sateesha S, Haussler M, Wiest W, Slatopolsky E, Haddad J. 1981. Control of mineral homeostasis during lactation: Interrelationships of 25-hydroxyvitamin D, 24,25-dihydroxyvitamin D, 1,25-dihydroxyvitamin D, parathyroid hormone, calcitonin, prolactin, and estradiol. *Am J Obstet Gynecol* 139:471–476.
- Hillman LS, Chow W, Salmons SJ, Weaver E, Erickson M, Hansen J. 1988. Vitamin D metabolism, mineral homeostasis and bone mineralization in term infants fed human milk, cow milk-based formula or soy-based formula. *J Pediatr* 112:864–874.
- Hodge HC, Smith FA. 1977. Occupational fluoride exposure. *J Occup Med* 19:12–39.

- Hodge HC. 1979. The safety of fluoride tablets or drops. In: Johansen E, Taves DR, Olson, TO, eds. *Continuing Evaluation of the Use of Fluorides, AAAS Selected Symposium 1*. Boulder, CO: Westview Press. Pp. 253–274.
- Hodgson E, Mailman RB, Chamber JE. 1988. *Dictionary of Toxicology*. New York: Van Nostrand Reinhold, Inc.
- Hoffman S, Grisso JA, Kelsey JL, Gammon MD, O'Brien LA. 1993. Parity, lactation and hip fracture. *Osteopor Int* 3:171–176.
- Hofvander Y, Hagman U, Hillervik C, Sjolin S. 1982. The amount of milk consumed by 1–3 months old breast- or bottle-fed infants. *Acta Pediatr Scand* 71:953–958.
- Holbrook TL, Barrett-Connor E, Wingard DL. 1988. Dietary calcium and risk of hip fracture: 14-year prospective population study. *Lancet* 2:1046–1049.
- Holick MF. 1986. Vitamin D requirements for the elderly. *Clin Nutr* 5:121–129.
- Holick MF. 1994. McCollum Award Lecture, 1994: Vitamin D: New horizons for the 21st century. *Am J Clin Nutr* 60:619–630.
- Holick MF. 1995. Vitamin D: Photobiology, metabolism, and clinical applications. In: DeGroot LJ, Besser M, Burger HG, Jameson JL, Loriaux DL, Marshall JC, O'Dell WD, Potts JL, Rubenstein AH, eds. *Endocrinology, 3rd Edition*. Philadelphia, PA: WB Saunders.
- Holick MF. 1996. Vitamin D: Photobiology, metabolism, mechanism of action, and clinical application. In: Favus MJ, ed. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 3rd Edition*. Philadelphia, PA: Lippincott-Raven. Pp. 74–81.
- Holick MF, Clark MB. 1978. The photobiogenesis and metabolism of vitamin D. *Fed Proc* 37:2567–2574.
- Holick MF, Schnoes HK, DeLuca HF. 1971. Identification of 1,25-dihydroxycholecalciferol, a form of vitamin D<sub>3</sub> metabolically active in the intestine. *Proc Natl Acad Sci USA* 68:803–804.
- Holick MF, Uskokovic M, Henley JW, MacLaughlin J, Holick SA, Potts JT Jr. 1980. The photoproduction of 1 $\alpha$ , 25-dihydroxyvitamin D<sub>3</sub> in skin: An approach to the therapy of vitamin-D-resistant syndromes. *N Engl J Med* 303:349–354.
- Holick MF, MacLaughlin JA, Doppelt SH. 1981. Regulation of cutaneous previtamin D<sub>3</sub> photosynthesis in man: Skin pigment is not an essential regulator. *Science* 211:590–593.
- Holick MF, Matsuoka LY, Wortsman J. 1989. Age, vitamin D, and solar ultraviolet. *Lancet* 2:1104–1105.
- Holick MF, Shao Q, Liu WW, Chen TC. 1992. The vitamin D content of fortified milk and infant formula. *N Engl J Med* 326:1178–1181.
- Hollifield JW. 1987. Magnesium depletion, diuretics, and arrhythmias. *Am J Med* 82(Suppl 3A):30–37.
- Hollis BW. 1996. Assessment of vitamin D nutritional and hormonal status: What to measure and how to do it. *Calcif Tissue Int* 58:4–5.
- Holmes RP, Kummerow FA. 1983. The relationship of adequate and excessive intake of vitamin D to health and disease. *J Am Coll Nutr* 2:173–199.
- Honkanen R, Alhava E, Parviainen M, Talasniemi S, Monkkonen R. 1990. The necessity and safety of calcium and vitamin D in the elderly. *J Am Geriatr Soc* 38:862–866.
- Hordon LD, Peacock M. 1987. Vitamin D metabolism in women with femoral neck fracture. *Bone Miner* 2:413–426.
- Horowitz HS. 1990. The future of water fluoridation and other systemic fluorides. *J Dent Res* 69(Spec Iss):760–764.

- Horowitz HS. 1996. The effectiveness of community water fluoridation in the United States. *J Pub Hlth Dent* 56:253–258.
- Horowitz HS, Heifetz SB. 1967. Effects of prenatal exposure to fluoridation on dental caries. *Pub Hlth Rep* 82:297–304.
- Horowitz M, Wishart J, Mundy L, Nordin BEC. 1987. Lactose and calcium absorption in postmenopausal osteoporosis. *Arch Intern Med* 147:534–536.
- Hoskova M. 1968. Fluoride tablets in the prevention of tooth decay. *Cesk Pediatr* 23:438–441.
- Howard JE, Hopkins TR, Connor TB. 1953. On certain physiologic responses to intravenous injection of calcium salts into normal, hyperparathyroid and hypoparathyroid persons. *J Clin Endocrinol Metab* 13:1–19.
- Hreshchyshyn MM, Hopkins A, Zylstra S, Anbar M. 1988. Associations of parity, breast-feeding, and birth control pills with lumbar spine and femoral neck bone densities. *Am J Obstet Gynecol* 159:318–322.
- Hua H, Gonzales J, Rude RK. 1995. Magnesium transport induced ex vivo by a pharmacological dose of insulin is impaired in non-insulin-dependent diabetes mellitus. *Magnes Res* 8:359–366.
- Huang Z, Himes JH, McGovern PG. 1996. Nutrition and subsequent hip fracture risk among a national cohort of white women. *Am J Epidemiol* 144:124–134.
- Hunt CD, Nielsen FH. 1981. Interaction between boron and cholecalciferol in the chick. In: McC Howell J, Gathorne JM, White CL, eds. *Trace Element Metabolism in Man and Animals, TEMA-4*. Canberra: Australian Academy of Science. Pp. 597–600.
- Hunt MS, Schofield FA. 1969. Magnesium balance and protein intake level in adult human female. *Am J Clin Nutr* 22:367–373.
- Hwang DL, Yen CF, Nadler JL. 1993. Insulin increases intracellular magnesium transport in human platelets. *J Clin Endocrinol Metab* 76:549–553.
- IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Report of the Subcommittee on Nutritional Status and Weight Gain During Pregnancy, Subcommittee on Dietary Intake and Nutrient Supplements During Pregnancy, Committee on Nutritional Status During Pregnancy and Lactation, Food and Nutrition Board. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1991. *Nutrition During Lactation*. Report of the Subcommittee on Nutrition During Lactation, Committee on Nutritional Status During Pregnancy and Lactation, Food and Nutrition Board. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Food and Nutrition Board. Washington, DC: National Academy Press.
- Ireland P, Fordtran JS. 1973. Effect of dietary calcium and age on jejunal calcium absorption in humans studied by intestinal perfusion. *J Clin Invest* 52:2672–2681.
- Irnell L. 1969. Metastatic calcification of soft tissue on overdose of vitamin D. *Acta Med Scand* 185:147–152.
- Iseri LT, French JH. 1984. Magnesium: Nature's physiologic calcium blocker. *Am Heart J* 108:188–193.
- ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. 1995. ISIS-4: A randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. *Lancet* 345:669–685.

- Ismail AI, Brodeur JM, Kavanagh M, Boisclair G, Tessier C, Picotte L. 1990. Prevalence of dental caries and dental fluorosis in students, 11–17 years of age, in fluoridated and non-fluoridated cities in Quebec. *Caries Res* 24:290–297.
- Jackman LA, Millane SS, Martin BR, Wood OB, McCabe GP, Peacock M, Weaver CM. 1997. Calcium retention in relation to calcium intake and postmenarcheal age in adolescent females. *Am J Clin Nutr* 66:327–333.
- Jackson D, Murray JJ, Fairpo CG. 1973. Life-long benefits of fluoride in drinking water. *Br Dent J* 134:419–422.
- Jacobus CH, Holick MF, Shao Q, Chen TC, Holm IA, Kolodny JM, Fuleihan GE, Seely EW. 1992. Hypervitaminosis D associated with drinking milk. *N Engl J Med* 326:1173–1177.
- Janas LM, Picone TA, Benson JD, MacLean WC. 1988. Influence of dietary calcium to phosphorus and parathormone during the first two weeks of life. *Pediatr Res* 23:485A.
- Janelle KC, Barr SI. 1995. Nutrient intakes and eating behavior scores of vegetarian and nonvegetarian women. *J Am Diet Assoc* 95:180–186.
- Jeans PC. 1950. Vitamin D. *J Am Med Assoc* 143:177–181.
- Jeans PC, Stearns G. 1938. The effect of vitamin D on linear growth in infancy. II. The effect of intakes above 1,800 USP units daily. *J Pediatr* 13:730–740.
- Joffres MR, Reed DM, Yano K. 1987. Relationship of magnesium intake and other dietary factors to blood pressure: The Honolulu heart study. *Am J Clin Nutr* 45:469–475.
- Johansson C, Mellström D, Milsom I. 1993. Reproductive factors as predictors of bone density and fractures in women at the age of 70. *Maturitas* 17:39–50.
- Johnson AO, Semenza JG, Buchowski MS, Enwonwu CO, Scrimshaw NS. 1993a. Correlation of lactose maldigestion, lactose intolerance, and milk intolerance. *Am J Clin Nutr* 57:399–401.
- Johnson AO, Semenza JG, Buchowski MS, Enwonwu CO, Scrimshaw NS. 1993b. Adaptation of lactose maldigesters to continued milk intakes. *Am J Clin Nutr* 58:879–881.
- Johnson CM, Wilson DM, O'Fallon WM, Malek RS, Kurland LT. 1979. Renal stone epidemiology: A 25-year study in Rochester, Minn. *Kidney Int* 16:624–631.
- Johnson J Jr, Bawden JW. 1987. The fluoride content of infant formulas available in 1985. *Pediatr Dent* 9:33–37.
- Johnson KR, Jobber J, Stonawski BJ. 1980. Prophylactic vitamin D in the elderly. *Age Ageing* 9:121–127.
- Johnston CC, Miller JZ, Slemenda CW, Reister TK, Hui S, Christian JC, Peacock M. 1992. Calcium supplementation and increases in bone mineral density in children. *N Engl J Med* 327:82–87.
- Jones JE, Manalo R, Flink EB. 1967. Magnesium requirements in adults. *Am J Clin Nutr* 20:632–635.
- Jowsey J, Balasubramaniam P. 1972. Effect of phosphate supplements on soft tissue calcification and bone turnover. *Clin Sci* 42:289–299.
- Junor JR, Catto GRD. 1976. Renal biopsy in the milk-alkali syndrome. *J Clin Path* 29:1074–1076.
- Kailis DG, Taylor SR, Davis GB, Bartlett LG, Fitzgerald DJ, Grose IJ, Newton PD. 1968. Fluoride and caries: Observations of the effects of prenatal and postnatal fluoride on some Perth pre-school children. *Med J Austral* 2:1037–1040.
- Kalkwarf HJ, Specker BL. 1995. Bone mineral loss during lactation and recovery after weaning. *Obstet Gynecol* 86:26–32.
- Kalkwarf HJ, Specker BL, Heubi JE, Vieira NE, Yergey AL. 1996. Intestinal calcium absorption of women during lactation and after weaning. *Am J Clin Nutr* 63:526–531.

- Kalkwarf HJ, Specker BL, Bianchi DC, Ranz J, Ho M. 1997. The effect of calcium supplementation on bone density during lactation and after weaning. *N Engl J Med* 337:523–528.
- Kallmeyer JC, Funston MR. 1983. The milk-alkali syndrome: A case report. *S Afr Med J* 64:287–288.
- Kamel S, Brazier M, Picard C, Boitte F, Samson L, Desmet G, Sebert JL. 1994. Urinary excretion of pyridinolines crosslinks measured by immunoassay and HPLC techniques in normal subjects and in elderly patients with vitamin D deficiency. *Bone Miner* 26:197–208.
- Kamel S, Brazier M, Rogez JC, Vincent O, Maamer M, Desmet G, Sebert JL. 1996. Different responses of free and peptide-bound cross-links to vitamin D and calcium supplementation in elderly women with vitamin D insufficiency. *J Clin Endocrinol Metab* 81:3717–3721.
- Kaminsky LS, Mahoney MC, Leach J, Melius J, Miller MJ. 1990. Fluoride: Benefits and risks of exposure. *Crit Rev Oral Biol Med* 1:261–281.
- Kanapka JA, Hamilton IR. 1971. Fluoride inhibition of enolase activity in vivo and its relationship to the inhibition of glucose-6-P formation in *Streptococcus salivarius*. *Arch Biochem Biophys* 146:167–174.
- Kanemitsu T, Koike A, Yamamoto S. 1985. Study of the cell proliferation kinetics in ulcerative colitis, adenomatous polyps, and cancer. *Cancer* 56:1094–1098.
- Kanis JA, Melton LJ III, Christiansen C, Johnston CC, Khaltaev N. 1994. The diagnosis of osteoporosis. *J Bone Miner Res* 9:1137–1141.
- Kapsner P, Langsdorf L, Marcus R, Kraemer FB, Hoffman AR. 1986. Milk-alkali syndrome in patients treated with calcium carbonate after cardiac transplantation. *Arch Intern Med* 146:1965–1968.
- Katzman DK, Bachrach LK, Carter DR, Marcus R. 1991. Clinical and anthropometric correlates of bone mineral acquisition in healthy adolescent girls. *J Clin Endocrinol Metab* 73:1332–1339.
- Kayne LH, Lee DB. 1993. Intestinal magnesium absorption. *Miner Electrolyte Metab* 19:210–217.
- Keddie KMG. 1987. Case report: Severe depressive illness in the context of hypervitaminosis D. *Br J Psych* 150:394–396.
- Kellie SE, Brody JA. 1990. Sex-specific and race-specific hip fracture rates. *Am J Pub Hlth* 80:326–328.
- Kelsay JL, Prather ES. 1983. Mineral balances of human subjects consuming spinach in a low-fiber diet and in a diet containing fruits and vegetables. *Am J Clin Nutr* 38:12–19.
- Kelsay JL, Behall KM, Prather ES. 1979. Effect of fiber from fruits and vegetables on metabolic responses of human subjects. II. Calcium, magnesium, iron, and silicon balances. *Am J Clin Nutr* 32:1876–1880.
- Kent GN, Price RI, Gutteridge DH, Smith M, Allen JR, Bhagat CI, Barnes MP, Hickling CJ, Retallack RW, Wilson SG, Devlin RD, Davies C, St. John A. 1990. Human lactation: Forearm trabecular bone loss, increased bone turnover, and renal conservation of calcium and inorganic phosphate with recovery of bone mass following weaning. *J Bone Miner Res* 5:361–369.
- Kent GN, Price RI, Gutteridge DH, Rosman KJ, Smith M, Allen JR, Hickling CJ, Blakeman SL. 1991. The efficiency of intestinal calcium absorption is increased in late pregnancy but not in established lactation. *Calcif Tissue Int* 48:293–295.
- Kesteloot H, Joossens JV. 1990. The relationship between dietary intake and urinary excretion of sodium, potassium, calcium and magnesium: Belgian Inter-university Research on Nutrition and Health. *J Hum Hypertension* 4:527–533.

- Kiel DP, Felson DT, Hannan MT, Anderson JJ, Wilson PW. 1990. Caffeine and the risk of hip fracture: The Framingham Study. *Am J Epidemiol* 132:675–684.
- Kinyamu HK, Gallagher JC, Balhorn KE, Petranick KM, Rafferty KA. 1997. Serum vitamin D metabolites and calcium absorption in normal young and elderly free-living women and in women living in nursing homes. *Am J Clin Nutr* 65:790–797.
- Klaassen CD, Amdur MO, Doull J. 1986. *Casarett and Doull's Toxicology: The Basic Science of Poisons, Third Edition*. New York: Macmillan Publishing Company.
- Kleerekoper M, Mendlovic DB. 1993. Sodium fluoride therapy of postmenopausal osteoporosis. *Endocrinol Rev* 14:312–323.
- Kleibeuker JH, Welberg JW, Mulder NH, van der Meer R, Cats A, Limburg AJ, Kreumer WM, Hardonk MJ, de Vries EG. 1993. Epithelial cell proliferation in the sigmoid colon of patients with adenomatous polyps increases during oral calcium supplementation. *Br J Cancer* 67:500–503.
- Klein CJ, Moser-Veillon PB, Douglass LW, Ruben KA, Trocki O. 1995. A longitudinal study of urinary calcium, magnesium, and zinc excretion in lactating and nonlactating postpartum women. *Am J Clin Nutr* 61:779–786.
- Kleiner SM, Bazzarre TL, Ainsworth BE. 1994. Nutritional status of nationally ranked elite bodybuilders. *Int J Sport Nutr* 4:54–69.
- Kleinman GE, Rodriguez H, Good MC, Caudle MR. 1991. Hypercalcemic crisis in pregnancy associated with excessive ingestion of calcium carbonate antacid (milk-alkali syndrome): Successful treatment with hemodialysis. *Obstet Gynecol* 73:496–499.
- Knochel JP. 1977. The pathophysiology and clinical characteristics of severe hypophosphatemia. *Arch Intern Med* 137:203–220.
- Knochel JP. 1985. The clinical status of hypophosphatemia: An update. *N Engl J Med* 313:447–449.
- Kobayashi A, Kawai S, Ohbe Y, Nagashima Y. 1975. Effects of dietary lactose and a lactase preparation on the intestinal absorption of calcium and magnesium in normal infants. *Am J Clin Nutr* 28:681–683.
- Kochersberger G, Westlund R, Lyles KW. 1991. The metabolic effects of calcium supplementation in the elderly. *J Am Geriatr Soc* 39:192–196.
- Koetting CA, Wardlaw GM. 1988. Wrist, spine, and hip bone density in women with variable histories of lactation. *Am J Clin Nutr* 48:1479–1481.
- Kohlmeier L, Mendez M, McDuffie J, Miller M. 1997. Computer-assisted self-interviewing: A multimedia approach to dietary assessment. *Am J Clin Nutr* 65:1275S–1281S.
- Koo W, Tsang R. 1997. Calcium, magnesium, phosphorus and vitamin D. In: *Nutrition During Infancy, 2nd Edition*. Cincinnati: Digital Education. Pp. 175–189.
- Koo W, Krug-Wispe S, Neylen M, Succop P, Oestreich AE, Tsang RC. 1995. Effect of three levels of vitamin D intake in preterm infants receiving high mineral-containing milk. *J Pediatr Gastroenterol Nutr* 21:182–189.
- Krall EA, Sahyoun N, Tannenbaum S, Dallal GE, Dawson-Hughes B. 1989. Effect of vitamin D intake on seasonal variations in parathyroid hormone secretion in postmenopausal women. *N Engl J Med* 321:1777–1783.
- Kramer L, Osis D, Wiatrowski E, Spenser H. 1974. Dietary fluoride in different areas of the United States. *Am J Clin Nutr* 27:590–594.
- Kreiger N, Kelsey JL, Holford TR, O'Connor T. 1982. An epidemiologic study of hip fracture in postmenopausal women. *Am J Epidemiol* 116:141–148.

- Krejs GJ, Nicar MJ, Zerwekh HE, Normal DA, Kane MG, Pak CY. 1983. Effect of 1,25-dihydroxyvitamin D<sub>3</sub> on calcium and magnesium absorption in the healthy human jejunum and ileum. *Am J Med* 75:973–976.
- Krishnamachari KA. 1986. Skeletal fluorosis in humans: A review of recent progress in the understanding of the disease. *Prog Food Nutr Sci* 10:279–314.
- Krook L, Whalen JP, Lesser GV, Berens DL. 1975. Experimental studies on osteoporosis. *Methods Achiev Exp Pathol* 7:72–108.
- Kröger H, Kotaniemi A, Vainio P, Alhava E. 1992. Bone densitometry of the spine and femur in children by dual-energy x-ray absorptiometry. *Bone Miner* 17:75–85.
- Kröger H, Kotaniemi A, Kröger L, Alhava E. 1993. Development of bone mass and bone density of the spine and femoral neck—a prospective study of 65 children and adolescents. *Bone Miner* 23:171–182.
- Kröger H, Alhava E, Honkanen R, Tuppurainen M, Saarikoski S. 1994. The effect of fluoridated drinking water on axial bone mineral density: A population-based study. *Bone Miner* 27:33–41.
- Kruse K, Bartels H, Kracht U. 1984. Parathyroid function in different stages of vitamin D deficiency rickets. *Eur J Pediatr* 141:158–162.
- Kumar JV, Green EL, Wallace W, Carnahan T. 1989. Trends in dental fluorosis and dental caries prevalences in Newburgh and Kingston, NY. *Am J Pub Hlth* 79:565–569.
- Kumar R. 1986. The metabolism and mechanism of action of 1,25-dihydroxyvitamin D<sub>3</sub>. *Kidney Int* 30:793–803.
- Kumar R, Cohen WR, Silva P, Epstein FH. 1979. Elevated 1,25-dihydroxyvitamin D plasma levels in normal human pregnancy and lactation. *J Clin Invest* 63:342–344.
- Kummerow FA, Simon Cho BH, Huang YT, Imai H, Kamio A, Deutsch MJ, Hooper WM. 1976. Additive risk factors in atherosclerosis. *Am J Clin Nutr* 29:579–584.
- Kurtz TW, Al-Bander HA, Morris RC. 1987. “Salt sensitive” essential hypertension in men. *N Engl J Med* 317:1043–1048.
- Kurzel RB. 1991. Serum magnesium levels in pregnancy and preterm labor. *Am J Perinatol* 8:119–127.
- Kuti V, Balazs M, Morvay F, Varenka Z, Szekely A, Szucs M. 1981. Effect of maternal magnesium supply on spontaneous abortion and premature birth and on intrauterine fetal development: Experimental epidemiological study. *Magnes Bull* 3:73–79.
- Ladizesky M, Lu Z, Oliveri B, San Roman N, Diaz S, Holick MF, Mautalen C. 1995. Solar ultraviolet B radiation and photoproduction of vitamin D<sub>3</sub> in central and southern areas of Argentina. *J Bone Miner Res* 10:545–549.
- Lafferty FW. 1991. Differential diagnosis of hypercalcemia. *J Bone Miner Res* 6:S51–S59.
- Lakshmanan LF, Rao RB, Kim WW, Kelsay JL. 1984. Magnesium intakes, balances, and blood levels of adults consuming self-selected diets. *Am J Clin Nutr* 40:1380–1389.
- Lamberg-Allardt C, von Knorring J, Slatis P, Holmstrom T. 1989. Vitamin D status and concentrations of serum vitamin D metabolites and osteocalcin in elderly patients with femoral neck fracture: A follow-up study. *Eur J Clin Nutr* 43:355–361.
- Lamberg-Allardt C, Karkkainen M, Seppanen R, Bistrom H. 1993. Low serum 25-hydroxyvitamin D concentrations and secondary hyperparathyroidism in middle-aged white strict vegetarians. *Am J Clin Nutr* 58:684–689.
- Largent EJ. 1952. Rates of elimination of fluoride stored in the tissues of man. *Arch Ind Hyg* 6:37–42.

- Larsen MJ, Senderovitz F, Kirkegaard E, Poulsen S, Fejerskov O. 1988. Dental fluorosis in the primary and permanent dentition in fluoridated areas with consumption of either powdered milk or natural cow's milk. *J Dent Res* 67:822–825.
- Lawson DE, Fraser DR, Kodicek E, Morris HR, Williams DH. 1971. Identification of 1,25-dihydroxycholecalciferol, a new kidney hormone controlling calcium metabolism. *Nature* 230:228–230.
- Lealman GT, Logan RW, Hutchison JH, Kerr MM, Fulton AM, Brown CA. 1976. Calcium, phosphorus, and magnesium concentrations in plasma during first week of life and their relation to type of milk feed. *Arch Dis Child* 51:377–384.
- LeBlanc A, Schneider V, Spector E, Evans H, Rowe R, Lane H, Demers L, Lipton A. 1995. Calcium absorption, endogenous excretion, and endocrine changes during and after long-term bed rest. *Bone* 16:301S–304S.
- Lebrun JB, Moffatt ME, Mundy RJ, Sangster RK, Postl BD, Dooley JP, Dilling LA, Godel JC, Haworth JC. 1993. Vitamin D deficiency in a Manitoba community. *Can J Pub Hlth* 84:394–396.
- Lee WT, Leung SS, Wang SH, Xu YC, Zeng WP, Lau J, Oppenheimer SJ, Cheng JC. 1994. Double-blind, controlled calcium supplementation and bone mineral accretion in children accustomed to a low-calcium diet. *Am J Clin Nutr* 60:744–750.
- Lee WT, Leung SS, Leung DM, Tsang HS, Lau J, Cheng JC. 1995. A randomized double-blind controlled calcium supplementation trial, and bone and height acquisition in children. *Br J Nutr* 74:125–139.
- Lee WT, Leung SS, Leung DM, Cheng JC. 1996. A follow-up study on the effects of calcium-supplement withdrawal and puberty on bone acquisition of children. *Am J Clin Nutr* 64:71–77.
- LeGeros RZ, Glenn FB, Lee DD, Glenn WD. 1985. Some physico-chemical properties of deciduous enamel with and without pre-natal fluoride supplementation (PNF). *J Dent Res* 64:465–469.
- Lechner NDM, Bullock BC, Clarkson TB, Lofland HB. 1967. Biologic activities of vitamin D<sub>2</sub> and D<sub>3</sub> for growing squirrel monkeys. *Lab Anim Care* 17:483.
- Leitch I, Aitken FC. 1959. The estimation of calcium requirement: A re-examination. *Nutr Abs Rev* 29:393–409.
- Lemann J Jr. 1996. Calcium and phosphate metabolism: An overview in health and in calcium stone formers. In: Coe FL, Favus MJ, Pak CY, Parks JH, Preminger GM, eds. *Kidney Stones: Medical and Surgical Management*. Philadelphia, PA: Lippincott-Raven. Pp. 259–288.
- Lemann J Jr, Worcester EM, Gray RW. 1991. Hypercalciuria and stones. *Am J Kidney Dis* 17:386–391.
- Lemke CW, Doherty JM, Arra MC. 1970. Controlled fluoridation: The dental effects of discontinuation in Antigo, Wisconsin. *J Am Dent Assoc* 80:782–786.
- Leone NC, Shimkin MB, Arnold FA, Stevenson CA, Zimmerman ER, Geiser PB, Lieberman JE. 1954. Medical aspects of excessive fluoride in a water supply. *Pub Hlth Rep* 69:925–936.
- Leone NC, Stevenson CA, Hilbush TF, Sosman MC. 1955. A roentgenologic study of a human population exposed to high-fluoride domestic water: A ten-year study. *Am J Roentg* 74:874–885.
- Leone NC, Stevenson CA, Besse B, Hawes, LE, Dawber TA. 1960. The effects of the absorption of fluoride. II. A radiological investigation of 546 human residents of an area in which the drinking water contained only a minute trace of fluoride. *Archs Ind Hlth* 21:326–327.

- Leoni V, Fabiani L, Ticchiarelli L. 1985. Water hardness and cardiovascular mortality rate in Abruzzo, Italy. *Arch Environ Health* 40:274–278.
- Leung SSF, Lui S, Swaminathan R. 1989. Vitamin D status of Hong Kong Chinese infants. *Acta Paediatr Scand* 78:303–306.
- Leverett DH. 1986. Prevalence of dental fluorosis in fluoridated and nonfluoridated communities—a preliminary investigation. *J Pub Hlth Dent* 46:184–187.
- Leverett DH, Adair SM, Vaughan BW, Proskin HM, Moss ME. 1997. Randomized clinical trial of the effect of prenatal fluoride supplements in preventing dental caries. *Caries Res* 31:174–179.
- Levine RJ, Hauth JC, Curet LB, Sibai BM, Catalano PM, Morris CD, DerSimonian R, Esterlitz JR, Raymond EG, Bild DE, Clemens JD, Cutler JA. 1997. Trial of calcium to prevent preeclampsia. *N Engl J Med* 337:69–76.
- Levy SM, Muchow G. 1992. Provider compliance with recommended dietary fluoride supplement protocol. *Am J Pub Hlth* 82:281–283.
- Levy SM, Kohout FJ, Kiritsy MC, Heilman JR, Wefel JS. 1995. Infants' fluoride ingestion from water, supplements and dentifrice. *J Am Dent Assoc* 126:1625–1632.
- Lewis DW. 1976. *An Evaluation of the Effects of Water Fluoridation, City of Toronto, 1963–1975*. Toronto, Canada: The Corporation of the City of Toronto.
- Lewis NM, Marcus MSK, Behling AR, Greger JL. 1989. Calcium supplements and milk: Effects on acid-base balance and on retention of calcium, magnesium, and phosphorus. *Am J Clin Nutr* 49:527–533.
- Liel Y, Edwards J, Shary J, Spicer KM, Gordon L, Bell NH. 1988. The effects of race and body habitus on bone mineral density of the radius, hip, and spine in premenopausal women. *J Clin Endocrinol Metab* 66:1247–1250.
- Lin S-H, Lin Y-F, Shieh S-D. 1996. Milk-alkali syndrome in an aged patient with osteoporosis and fractures. *Nephron* 73:496–497.
- Linden V. 1974. Vitamin D and myocardial infarction. *Br Med J* 3:647–650.
- Linkswiler HM, Zemel MB, Hegsted M, Schuette S. 1981. Protein-induced hypercalciuria. *Fed Proc* 40:2429–2433.
- Lips P, Wiersinga A, vanGinkel FC, Jongen MJ, Netelenbos JC, Hackeng WH, Delmas PD, vanderVijgh WJ. 1988. The effect of vitamin D supplementation on vitamin D status and parathyroid function in elderly subjects. *J Clin Endocrinol Metab* 67:644–650.
- Lips P, Graafmans WC, Ooms ME, Bezemer D, Bouter LM. 1996. Vitamin D supplementation and fracture incidence in elderly persons: A randomized, placebo-controlled clinical trial. *Ann Intern Med* 124:400–406.
- Lipski PS, Torrance A, Kelly PJ, James OF. 1993. A study of nutritional deficits of long-stay geriatric patients. *Age Aging* 22:244–255.
- Lissner L, Bengtsson C, Hansson T. 1991. Bone mineral content in relation to lactation history in pre- and postmenopausal women. *Calcif Tissue Int* 48:319–325.
- Livingstone MB, Prentice AM, Coward WA, Strain JJ, Black AE, Davies PS, Stewart CM, McKenna PG, Whitehead RG. 1992. Validation estimates of energy intake by weighted dietary record and diet history in children and adolescents. *Am J Clin Nutr* 56:29–35.
- Lloyd T, Schaeffer JM, Walker MA, Demers LM. 1991. Urinary hormonal concentrations and spinal bone densities of premenopausal vegetarian and nonvegetarian women. *Am J Clin Nutr* 54:1005–1010.

- Lloyd T, Andon MB, Rollings N, Martel JK, Landis R, Demers LM, Eggli DF, Kieselhorst K, Kulin HE. 1993. Calcium supplementation and bone mineral density in adolescent girls. *J Am Med Assoc* 270:841–844.
- Lo CW, Paris PW, Clemens TL, Nolan J, Holick MF. 1985. Vitamin D absorption in healthy subjects and in patients with intestinal malabsorption syndromes. *Am J Clin Nutr* 42:644–649.
- Lonnerdal B. 1997. Effects of milk and milk components on calcium, magnesium, and trace element absorption during infancy. *Physiol Rev* 77:643–669.
- Looker AC, Harris TB, Madans JH, Sempers CT. 1993. Dietary calcium and hip fracture risk: The NHANES I Epidemiology Follow-Up Study. *Osteopor Int* 3:177–184.
- Looker AC, Johnston CC Jr, Wahner HW, Dunn WL, Calvo MS, Harris TB, Heyse SP, Lindsay RL. 1995. Prevalence of low femoral bone density in older US women from NHANES III. *J Bone Miner Res* 10:796–802.
- Lopez JM, Gonzalez G, Reyes V, Campino C, Diaz S. 1996. Bone turnover and density in healthy women during breastfeeding and after weaning. *Osteopor Int* 6:153–159.
- Lotz M, Zisman E, Bartter FC. 1968. Evidence for a phosphorus-depletion syndrome in man. *N Engl J Med* 278:409–415.
- Lowenstein FW, Stanton MF. 1986. Serum magnesium levels in the United States, 1971–1974. *J Am Coll Nutr* 5:399–414.
- Lowik MR, van Dokkum W, Kistemaker C, Schaafsma G, Ockhuizen T. 1993. Body composition, health status and urinary magnesium excretion among elderly people (Dutch Nutrition Surveillance System). *Magnes Res* 6:223–232.
- LSRO/FASEB (Life Sciences Research Office/Federation of American Societies for Experimental Biology). 1986. *Guidelines for Use of Dietary Intake Data*. Anderson SA, ed. Bethesda, MD: LSRO/FASEB.
- Lu PW, Briody JN, Ogle GD, Morley K, Humphries IR, Allen J, Howman-Giles R, Sillence D, Cowell CT. 1994. Bone mineral density of total body, spine, and femoral neck in children and young adults: A cross-sectional and longitudinal study. *J Bone Miner Res* 9:1451–1458.
- Luckey MM, Meier DE, Mandeli JP, DaCosta MC, Hubbard ML, Goldsmith SJ. 1989. Radial and vertebral bone density in white and black women: Evidence for racial differences in premenopausal bone homeostasis. *J Clin Endocrinol Metab* 69:762–770.
- Lukert BP, Raisz LG. 1990. Glucocorticoid-induced osteoporosis: Pathogenesis and management. *Ann Intern Med* 112:352–364.
- Lund B, Sorensen OH. 1979. Measurement of 25-hydroxyvitamin D in serum and its relation to sunshine, age and vitamin D intake in the Danish population. *Scand J Clin Lab Invest* 39:23–30.
- Luoma H, Aromaa A, Helminen S, Murtomaa H, Kiviluoto L, Punstar S, Knekt P. 1983. Risk of myocardial infarction in Finnish men in relation to fluoride, magnesium and calcium concentration in drinking water. *Acta Med Scand* 213:171–176.
- Lutwak L, Lester L, Gitelman HJ, Fox M, Whedon GD. 1964. Effects of high dietary calcium and phosphorus on calcium, phosphorus, nitrogen and fat metabolism in children. *Am J Clin Nutr* 14:76–82.

- Ma J, Folsom AR, Melnick SL, Eckfeldt JH, Sharrett AR, Nabulsi AA, Hutchinson RG, Metcalf PA. 1995. Associations of serum and dietary magnesium with cardiovascular disease, hypertension, diabetes, insulin, and carotid arterial wall thickness: The ARIC study. *Atherosclerosis Risk in Community Study. J Clin Epidemiol* 48:927–940.
- MacLaughlin J, Holick MF. 1985. Aging decreases the capacity of human skin to produce vitamin D<sub>3</sub>. *J Clin Invest* 76:1536–1538.
- MacLaughlin JA, Anderson RR, Holick MF. 1982. Spectral character of sunlight modulates photosynthesis of previtamin D<sub>3</sub> and its photoisomers in human skin. *Science* 216:1001–1003.
- Maguire ME. 1984. Hormone-sensitive magnesium transport and magnesium regulation of adenylate cyclase. *Trends Pharmacol Sci* 5:73–77.
- Mahalko JR, Sandstead HH, Johnson LK, Milne DB. 1983. Effect of a moderate increase in dietary protein on the retention and excretion of Ca, Cu, Fe, Mg, P, and Zn by adult males. *Am J Clin Nutr* 37:8–14.
- Maheshwari UR, McDonald JT, Schneider VS, Brunetti AJ, Leybin L, Newbrun E, Hodge HC. 1981. Fluoride balance studies in ambulatory healthy men with and without fluoride supplements. *Am J Clin Nutr* 34:2679–2684.
- Maheshwari UR, King JC, Leybin L, Newbrun E, Hodge HC. 1983. Fluoride balances during early and late pregnancy. *J Occup Med* 25:587–590.
- Mallet E, Gugi B, Brunelle P, Henocq A, Basuyau JP, Lemeur H. 1986. Vitamin D supplementation in pregnancy: A controlled trial of two methods. *Obstet Gynecol* 68:300–304.
- Malm OJ. 1958. Calcium requirement and adaptation in adult men. *Scand J Clin Lab Invest* 10(Suppl 36):1–280.
- Malone DNS, Horn DB. 1971. Acute hypercalcemia and renal failure after antacid therapy. *Br Med J* 1:709–710.
- Manz F. 1992. Why is the phosphorus content of human milk exceptionally low? *Monatsschr Kinderheilkd* 140:S35–S39.
- Marcus R, Cann C, Madvig P, Minkoff J, Goddard M, Bayer M, Martin M, Gaudiani L, Haskell W, Genant H. 1985. Menstrual function and bone mass in elite women distance runners. Endocrine and metabolic features. *Ann Intern Med* 102:158–163.
- Margen S, Chu JY, Kaufmann NA, Calloway DH. 1974. Studies in calcium metabolism I. The calciuretic effect of dietary protein. *Am J Clin Nutr* 27:584–589.
- Margolis HC, Moreno EC. 1990. Physicochemical perspectives on the cariostatic mechanisms of systemic and topical fluorides. *J Dent Res* 69(Spec Iss):606–613.
- Marier JR. 1986. Magnesium content of the food supply in the modern-day world. *Magnesium* 5:1–8.
- Marken PA, Weart CW, Carson DS, Gums JG, Lopes-Virella MF. 1989. Effects of magnesium oxide on the lipid profile of healthy volunteers. *Atherosclerosis* 77:37–42.
- Markestad T, Elzouki AY. 1991. Vitamin-D deficiency rickets in northern Europe and Libya. In: Glorieux FH, ed. *Rickets: Nestle Nutrition Workshop Series, Vol 21*. New York, NY: Raven Press.
- Markestad T, Ulstein M, Bassoe HH, Aksnes L, Aarskog D. 1983. Vitamin D metabolism in normal and hypoparathyroid pregnancy and lactation. Case report. *Br J Obstet Gynaecol* 90:971–976.
- Markestad T, Ulstein M, Aksnes L, Aarskog D. 1986. Serum concentrations of vitamin D metabolites in vitamin D supplemented pregnant women. A longitudinal study. *Acta Obstet Gynecol Scand* 65:63–67.

- Marquis RE. 1995. Antimicrobial actions of fluoride for oral bacteria. *Can J Microbiol* 41:955–964.
- Marsh AG, Sanchez TV, Midkelsen O, Keiser J, Mayor G. 1980. Cortical bone density of adult lacto-ovo-vegetarian and omnivorous women. *J Am Diet Assoc* 76:148–151.
- Marshall DH, Nordin BEC, Speed R. 1976. Calcium, phosphorus and magnesium requirement. *Proc Nutr Soc* 35:163–173.
- Martin AD, Bailey DA, McKay HA. 1997. Bone mineral and calcium accretion during puberty. *Am J Clin Nutr* 66:611–615.
- Martin BJ. 1990. The magnesium load test: Experience in elderly subjects. *Aging (Milano)* 2:291–296.
- Martin TJ, Grill V. 1995. Hypercalcemia. *Clin Endocrinol* 42:535–538.
- Martinez ME, Salinas M, Miguel JL, Herrero E, Gomez P, Garcia J, Sanchez-Sicilia L, Montero A. 1985. Magnesium excretion in idiopathic hypercalciuria. *Nephron* 40: 446–450.
- Massey LK, Wise KJ. 1984. The effect of dietary caffeine on urinary excretion of calcium, magnesium, sodium and potassium in healthy young females. *Nutr Res* 4:43–50.
- Massey LK, Roman-Smith H, Sutton RA. 1993. Effect of dietary oxalate and calcium on urinary oxalate and risk of formation of calcium oxalate kidney stones. *J Am Diet Assoc* 93:901–906.
- Matkovic V. 1991. Calcium metabolism and calcium requirements during skeletal modeling and consolidation of bone mass. *Am J Clin Nutr* 54:245S–260S.
- Matkovic V, Heaney RP. 1992. Calcium balance during human growth: Evidence for threshold behavior. *Am J Clin Nutr* 55:992–996.
- Matkovic V, Fontana D, Tominac C, Goel P, Chesnut CH III. 1990. Factors that influence peak bone mass formation: A study of calcium balance and the inheritance of bone mass in adolescent females. *Am J Clin Nutr* 52:878–888.
- Matkovic V, Jelic T, Wardlaw GM, Illich JZ, Goel PK, Wright JK, Andon MB, Smith KT, Heaney RP. 1994. Timing of peak bone mass in Caucasian females and its implication for the prevention of osteoporosis. *J Clin Invest* 93:799–808.
- Matkovic V, Illich JZ, Andon MB, Hsieh LC, Tzagournis MA, Lagger BJ, Goel PK. 1995. Urinary calcium, sodium, and bone mass of young females. *Am J Clin Nutr* 62:417–425.
- Matsuda H. 1991. Magnesium gating of the inwardly rectifying K<sup>+</sup> channel. *Ann Rev Physiol* 53:289–298.
- Matsuoka LY, Ide L, Wortsman J, MacLaughlin JA, Holick MF. 1987. Sunscreens suppress cutaneous vitamin D<sub>3</sub> synthesis. *J Clin Endocrinol Metab* 64:1165–1168.
- Matsuoka LY, Wortsman J, Dannenberg MJ, Hollis BW, Lu Z, Holick MF. 1992. Clothing prevents ultraviolet-B radiation-dependent photosynthesis of vitamin D<sub>3</sub>. *J Clin Endocrinol Metab* 75:1099–1103.
- Mawer EB, Schaefer K, Lumb GA, Stanbury SW. 1971. The metabolism of isotopically labelled vitamin D<sub>3</sub> in man: The influence of the state of vitamin D nutrition. *Clin Sci* 40:39–53.
- Mawer EB, Backhouse J, Holman CA, Lumb GA, Stanbury DW. 1972. The distribution and storage of vitamin D and its metabolites in human tissues. *Clin Sci* 43:413–431.
- Mazariegos-Ramos E, Guerrero-Romero F, Rodriguez-Moran M, Lazcano-Burciaga G, Paniagua R, Amato D. 1995. Consumption of soft drinks with phosphoric acid as a risk factor for the development of hypocalcemia in children: A case-control study. *J Pediatr* 126:940–942.

- McCarron DA. 1983. Calcium and magnesium nutrition in human hypertension. *Ann Int Med* 98:800–805.
- McCarron DA, Morris CD. 1985. Blood pressure response to oral calcium in persons with mild to moderate hypertension: A randomized, double-blind, placebo-controlled, crossover trial. *Ann Intern Med* 103:825–831.
- McCarron DA, Morris CD, Young E, Roullet C, Drüeke T. 1991. Dietary calcium and blood pressure: Modifying factors in specific populations. *Am J Clin Nutr* 54:215S–219S.
- McCauley HB, McClure FJ. 1954. Effect of fluoride in drinking water on the osseous development of the hand and wrist in children. *Pub Hlth Rep* 69:671–683.
- McClure FJ. 1943. Ingestion of fluoride and dental caries. Quantitative relations based on food and water requirements of children one to twelve years old. *Am J Dis Child* 66:362–369.
- McClure FJ, Zipkin I. 1958. Physiologic effects of fluoride as related to water fluoridation. *Dent Clin North Am* 2:441–458.
- McCrory WW, Forman CW, McNamara H, Barnett HL. 1950. Renal excretion of phosphate in newborn infants: Observations in normal infants and in infants with hypocalcemic tetany. *Am J Dis Child* 80:512–513.
- McFarlane D. 1941. Experimental phosphate nephritis in the rat. *J Pathol* 52:17–24.
- McGrath N, Singh V, Cundy T. 1993. Severe vitamin D deficiency in Auckland. *N Zel Med J* 106:524–526.
- McKenna MJ. 1992. Differences in vitamin D status between countries in young adults and the elderly. *Am J Med* 93:69–77.
- McKnight-Hanes MC, Leverett DH, Adair SM, Shields CP. 1988. Fluoride content of infant formulas: Soy-based formulas as a potential factor in dental fluorosis. *Pediatr Dent* 10:189–194.
- Meier DE, Luckey MM, Wallenstein S, Clemens TL, Orwoll ES, Waslien CI. 1991. Calcium, vitamin D, and parathyroid hormone status in young white and black women: Association with racial differences in bone mass. *J Clin Endocrinol Metab* 72:703–710.
- Melton LJ III, Chrischilles EA, Cooper C, Lane AW, Riggs, BL. 1992. Perspective. How many women have osteoporosis? *J Bone Miner Res* 7:1005–1010.
- Melton LJ III, Atkinson EJ, O'Fallon WM, Wahner HW, Riggs BL. 1993a. Long-term fracture prediction by bone mineral assessed at different skeletal sites. *J Bone Miner Res* 8:1227–1233.
- Melton LJ III, Bryant SC, Wahner HW, O'Fallon WM, Malkasian GD, Judd HL, Riggs BL. 1993b. Influence of breastfeeding and other reproductive factors on bone mass later in life. *Osteopor Int* 3:76–83.
- Merke J, Klaus G, Hugel U, Waldherr R, Ritz E. 1986. No 1,25-dihydroxyvitamin D<sub>3</sub> receptors on osteoclasts of calcium-deficient chicken despite demonstrable receptors on circulating monocytes. *J Clin Invest* 77:312–314.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- Mertz W, Abernathy CO, Olin SS. 1994. *Risk Assessment of Essential Elements*. Washington, DC: ILSI Press.
- Meulmeester JF, vandenBerg H, Wedel M, Boshuis PG, Hulshof KF, Luyken R. 1990. Vitamin D status, parathyroid hormone and sunlight in Turkish, Moroccan and Caucasian children in The Netherlands. *Eur J Clin Nutr* 44:461–470.

- Meyer F, White E. 1993. Alcohol and nutrients in relation to colon cancer in middle-aged adults. *Am J Epidemiol* 138:225–236.
- Miller JZ, Smith DL, Flora L, Slemenda C, Jiang X, Johnston CC Jr. 1988. Calcium absorption from calcium carbonate and a new form of calcium (CCM) in healthy male and female adolescents. *Am J Clin Nutr* 48:1291–1294.
- Mimouni FB. 1996. The ion-selective magnesium electrode: A new tool for clinicians and investigators. *J Am College Nutr* 15:4–5.
- Mimouni F, Tsang RC, Hertzberg VS, Miodovnik M. 1986. Polycythemia hypomagnesemia and hypocalcemia infants of diabetic mothers. *Am J Dis Child* 140:798–800.
- Mimouni F, Campaigne B, Neylan M, Tsang RC. 1993. Bone mineralization in the first year of life in infants fed human milk, cow-milk formula, or soy-based formula. *J Pediatr* 122:348–354.
- Moncrief MW, Chance GW. 1969. Nephrotoxic effect of vitamin D therapy in vitamin D refractory rickets. *Arch Dis Child* 44:571–579.
- Montaldo MB, Benson JD. 1986. Nutrient intakes of older infants: Effect of different milk feedings. *J Am Coll Nutr* 5:331–341.
- Mordes JP, Wacker WEC. 1978. Excessive magnesium. *Pharmacol Rev* 29:273–300.
- Moser PB, Issa CF, Reynolds RD. 1983. Dietary magnesium intake and the concentration of magnesium in plasma and erythrocytes of postpartum women. *J Am Coll Nutr* 2:387–396.
- Moser PB, Reynolds RD, Acharya S, Howard MP, Andon MB. 1988. Calcium and magnesium dietary intakes and plasma and milk concentrations of Nepalese lactating women. *Am J Clin Nutr* 47:735–739.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance data from vital and health statistics, No. 174. Hyattsville, MD: National Center for Health Statistics.
- Motoyama T, Sano H, Fukuzaki H. 1989. Oral magnesium supplementation in patients with essential hypertension. *Hypertension* 13:227–232.
- Mountokalakis TD. 1987. Effects of aging, chronic disease, and multiple supplements on magnesium requirements. *Magnesium* 6:5–11.
- Moya M, Cortes E, Ballester MI, Vento M, Juste M. 1992. Short-term polycose substitution for lactose reduces calcium absorption in healthy term babies. *J Pediatr Gastroenterol Nutr* 14:57–61.
- Muhler JC. 1970. Ingestion from foods. In: Adler P, ed. *Fluorides and Human Health*. Monograph series no. 59. Geneva: World Health Organization. Pp. 32–40.
- Muldowney WP, Mazbar SA. 1996. Rolaids-yogurt syndrome: A 1990s version of milk-alkali syndrome. *Am J Kidney Dis* 27:270–272.
- Murphy SP, Calloway DH. 1986. Nutrient intakes of women in NHANES II, emphasizing trace minerals, fiber, and phytate. *J Am Diet Assoc* 86:1366–1372.
- Naccache H, Simard PL, Trahan L, Demers M, Lapointe C, Brodeur JM. 1990. Variability in the ingestion of toothpaste by preschool children. *Caries Res* 24:359–363.
- Naccache H, Simard PL, Trahan L, Brodeur JM, Demers M, Lachapelle D, Bernard PM. 1992. Factors affecting the ingestion of fluoride dentifrice by children. *J Pub Hlth Dent* 52:222–226.
- Nadler JL, Malayan S, Luong H, Shaw S, Natarajan RD, Rude RK. 1992. Intracellular free magnesium deficiency plays a key role in increased platelet reactivity in type II diabetes mellitus. *Diabetes Care* 15:835–841.

- Nadler JL, Buchanan T, Natarajan R, Antonipillai I, Bergman R, Rude RK. 1993. Magnesium deficiency produces insulin resistance and increased thromboxane synthesis. *Hypertension* 21:1024–1029.
- Nagubandi S, Kumar R, Londowski JM, Corradino RA, Tietz PS. 1980. Role of vitamin D glucosiduronate in calcium homeostasis. *J Clin Invest* 66:1274–1280.
- Nagy L, Tarnok F, Past T, Mozsik GY, Deak G, Tapsonyi Z, Fendler K, Javor T. 1988. Human tolerability and pharmacodynamic study of TISACID tablet in duodenal ulcer patients. A prospective, randomized, self-controlled clinico-pharmacological study. *Acta Medica Hung* 45:231–246.
- Nakamura T, Turner CH, Yoshikawa T, Slemenda CW, Peacock M, Burr DB, Mizuno Y, Orimo H, Ouchi Y, Johnston CC Jr. 1994. Do variations in hip geometry explain differences in hip fracture risk between Japanese and white Americans? *J Bone Miner Res* 9:1071–1076.
- Nakao H. 1988. Nutritional significance of human milk vitamin D in neonatal period. *Kobe J Med Sci* 34:121–128.
- Narang NK, Gupta RC, Jain MK. 1984. Role of vitamin D in pulmonary tuberculosis. *J Assoc Physicians India* 32:185–188.
- National Council for Nutrition (Conseil National de la Nutrition). 1994. *Recommendations nutritionnelles pour la Belgique*. Bruxelles, Belgium: Ministère des Affaires Sociales de la Santé Publique et de l’Environnement.
- National Food Administration. 1989. *Swedish Nutrition Recommendations, 2nd edition*. Uppsala, Sweden: National Food Administration.
- Need AG, Morris HA, Horowitz M, Nordin C. 1993. Effects of skin thickness, age, body fat, and sunlight on serum 25-hydroxyvitamin D. *Am J Clin Nutr* 58:882–885.
- Neri LC, Johansen HL. 1978. Water hardness and cardiovascular mortality. *Ann NY Acad Sci* 304:203–219.
- Neri LC, Johansen HL, Hewitt D, Marier J, Langner N. 1985. Magnesium and certain other elements and cardiovascular disease. *Sci Total Environ* 42:49–75.
- Netherlands Food and Nutrition Council. 1992. *Report on the Age Limit to be Adopted in Connection with “Guidelines for a Healthy Diet.”* The Hague: Netherlands Food and Nutrition Council.
- Neville MC, Keller R, Seacat J, Lutes V, Neifert M, Casey C, Allen J, Archer P. 1988. Studies in human lactation: Milk volumes in lactating women during the onset of lactation and full lactation. *Am J Clin Nutr* 48:1375–1386.
- Newmark K, Nugent P. 1993. Milk-alkali syndrome: A consequence of chronic antacid abuse. *Postgrad Med* 93:149–156.
- Ng K, St John A, Bruce DG. 1994. Secondary hyperparathyroidism, vitamin D deficiency and hip fracture: Importance of sampling times after fracture. *Bone Miner* 25:103–109.
- Niekamp RA, Baer JT. 1995. In-season dietary adequacy of trained male cross-country runners. *Int J Sport Nutr* 5:45–55.
- Nielsen FH. 1990. Studies on the relationship between boron and magnesium which possibly affects the formation and maintenance of bones. *Magnes Trace Elem* 9:61–69.
- Nielsen FH, Hunt CD, Mullen LM, Hunt JR. 1987. Effect of dietary boron on mineral, estrogen, and testosterone metabolism in postmenopausal women. *FASEB J* 1:394–397.
- Nieves JW, Golden AL, Siris E, Kelsey JL, Lindsay R. 1995. Teenage and current calcium intake are related to bone mineral density of the hip and forearm in women aged 30–39 years. *Am J Epidemiol* 141:342–351.

- NIH (National Institutes of Health). 1994. *Optimal Calcium Intake*. NIH Consensus Statement 12:4. Bethesda, MD: NIH.
- NIN (National Institute of Nutrition). 1995. Dairy products in the Canadian diet. NIN Review No. 24. Ontario, Canada: NIN.
- Nordin BEC. 1976. *Calcium, Phosphate and Magnesium Metabolism*. Edinburgh: Churchill Livingstone.
- Nordin BEC. 1989. Phosphorus. *J Food Nutr* 45:62–75.
- Nordin BEC, Polley KJ. 1987. Metabolic consequences of the menopause. A cross-sectional, longitudinal, and intervention study on 557 normal postmenopausal women. *Calcif Tissue Int* 41:S1–S59.
- Nose O, Iida Y, Kai H, Harada T, Ogawa M, Yabuuchi H. 1979. Breath hydrogen test for detecting lactose malabsorption in infants and children: Prevalence of lactose malabsorption in Japanese children and adults. *Arch Dis Child* 54:436–440.
- NRC (National Research Council). 1980. *Recommended Dietary Allowances, 9th Edition*. Committee on Dietary Allowances, Food and Nutrition Board. Washington, DC: National Academy Press.
- NRC (National Research Council). 1982. *Diet, Nutrition, and Cancer*. Report of the Committee on Diet, Nutrition, and Cancer, Assembly of Life Sciences. Washington, DC: National Academy Press.
- NRC (National Research Council). 1983. *Risk Assessment in the Federal Government: Managing the Process*. Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC (National Research Council). 1989a. *Recommended Dietary Allowances: 10th Edition*. Report of the Subcommittee on the Tenth Edition of the RDAs, Food and Nutrition Board, and the Commission on Life Sciences. Washington, DC: National Academy Press.
- NRC (National Research Council). 1989b. *Diet and Health: Implications for Reducing Chronic Disease Risk*. Report of the Committee on Diet and Health, Food and Nutrition Board, Commission on Life Sciences. Washington, DC: National Academy Press.
- NRC (National Research Council). 1993. *Health Effects of Ingested Fluoride*. Subcommittee on Health Effects of Ingested Fluoride. Washington, DC: National Academy Press.
- NRC (National Research Council). 1994. *Science and Judgment in Risk Assessment. Committee on Risk Assessment of Hazardous Air Pollutants*. Board on Environmental Studies and Toxicology. Washington, DC: National Academy Press.
- NRC (National Research Council). 1995. *Nutrient Requirements of Laboratory Animals*. Committee on Animal Nutrition, Board on Agriculture. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- O'Brien KO, Abrams SA, Stuff JE, Liang LK, Welch TR. 1996. Variables related to urinary calcium excretion in young girls. *J Pediatr Gastroenterol Nutr* 23:8–12.
- O'Dowd KJ, Clemens TL, Kelsey JL, Lindsay R. 1993. Exogenous calciferol (vitamin D) and vitamin D endocrine status among elderly nursing home residents in the New York City area. *J Am Geriatr Soc* 41:414–421.

- Ohlson MA, Brewer WD, Jackson L, Swanson PP, Roberts PH, Mangel M, Leverton RM, Chaloupka M, Gram MR, Reynolds MS, Lutz R. 1952. Intakes and retentions of nitrogen, calcium and phosphorus by 136 women between 30 and 85 years of age. *Fed Proc* 11:775–783.
- Oliveri MB, Ladizesky M, Mautalen CA, Alonso A, Martinez L. 1993. Seasonal variations of 25 hydroxyvitamin D and parathyroid hormone in Ushuaia (Argentina), the southernmost city in the world. *Bone Miner* 20:99–108.
- Ooms ME, Roos JC, Bezemer PD, VanDerVijgh WJ, Bouter LM, Lips P. 1995. Prevention of bone loss by vitamin D supplementation in elderly women: A randomized double-blind trial. *J Clin Endocrinol Metab* 80:1052–1058.
- Ophaug RH, Singer L, Harland BF. 1980a. Estimated fluoride intake of 6-month-old infants in four dietary regions of the United States. *Am J Clin Nutr* 33:324–327.
- Ophaug RH, Singer L, Harland BF. 1980b. Estimated fluoride intake of average two-year-old children in four dietary regions of the United States. *J Dent Res* 59:777–781.
- Ophaug RH, Singer L, Harland BF. 1985. Dietary fluoride intake of 6-month and 2-year-old children in four dietary regions of the United States. *Am J Clin Nutr* 42:701–707.
- Orimo H, Ouchi Y. 1990. The role of calcium and magnesium in the development of atherosclerosis. Experimental and clinical evidence. *Ann NY Acad Sci* 598:444–457.
- Orwoll ES. 1982. The milk-alkali syndrome: Current concepts. *Ann Intern Med* 97:242–248.
- Orwoll ES, Oviatt SK, McClung MR, Deftos LJ, Sexton G. 1990. The rate of bone mineral loss in normal men and the effects of calcium and cholecalciferol supplementation. *Ann Intern Med* 112:29–34.
- Osis D, Kramer L, Wiatrowski E, Spencer H. 1974. Dietary fluoride intake in man. *J Nutr* 104:1313–1318.
- Osteoporosis Society of Canada. 1993. Consensus on calcium nutrition. Official position of the Osteoporosis Society of Canada. *Nutr Quart* 18:62–69.
- Osuji OO, Leake JL, Chipman ML, Nikiforuk G, Locker D, Levine N. 1988. Risk factors for dental fluorosis in a fluoridated community. *J Dent Res* 67:1488–1492.
- OTA (Office of Technology Assessment). 1993. *Researching Health Risks*. Washington, DC: Office of Technology Assessment.
- Outhouse J, Kinsman G, Sheldon D, Tworney I, Smith J. 1939. The calcium requirements of five pre-school girls. *J Nutr* 17:199–211.
- Outhouse J, Breiter H, Rutherford E, Dwight J, Mills R, Armstrong W. 1941. The calcium requirement of man: Balance studies on seven adults. *J Nutr* 21:565–575.
- Paganini-Hill A, Chao A, Ross RK, Henderson BE. 1991. Exercise and other factors in the prevention of hip fracture: The Leisure World Study. *Epidemiology* 2:16–25.
- Pak CY. 1988. Medical management of nephrolithiasis in Dallas: Update 1987. *J Urol* 140:461–467.
- Pak CY, Sakhaei K, Rubin CD, Zerwekh JE. 1997. Sustained-release sodium fluoride in the management of established menopausal osteoporosis. *Am J Med Sci* 313:23–32.
- Pang DT, Phillips CL, Bawden JW. 1992. Fluoride intake from beverage consumption in a sample of North Carolina children. *J Dent Res* 71:1382–1388.

- Paolisso G, Passariello N, Pizza G, Marrazzo G, Giunta R, Sgambato S, Varricchio M, D'Onofrio F. 1989. Dietary magnesium supplements improve B-cell response to glucose and arginine in elderly non-insulin-dependent diabetic subjects. *Acta Endocrinol Copenh* 121:16–20.
- Paolisso G, Scheen A, D'Onofrio FD, Lefebvre P. 1990. Magnesium and glucose homeostasis. *Diabetologia* 33:511–514.
- Paolisso G, Sgambato S, Gambardella A, Pizza G, Tesauro P, Varricchio M, D'Onofrio F. 1992. Daily magnesium supplements improve glucose handling in elderly subjects. *Am J Clin Nutr* 55:1161–1167.
- Parfitt AM. 1977. Metacarpal cortical dimensions in hypoparathyroidism, primary hyperparathyroidism and chronic renal failure. *Calcif Tiss Res Suppl* 22:329–331.
- Parfitt AM. 1988. Bone remodeling: Relationship to the amount and structure of bone, and the pathogenesis and prevention of fractures. In: Riggs BL, Melton LJ III eds. *Osteoporosis: Etiology, Diagnosis, and Management*. New York, NY: Raven Press.
- Parfitt AM, Higgins BA, Nassim JR, Collins JA, Hilb A. 1964. Metabolic studies in patients with hypercalciuria. *Clin Sci* 27:463–482.
- Parfitt AM, Chir B, Gallagher JC, Heaney RP, Johnston CC, Neer R, Whedon GD. 1982. Vitamin D and bone health in the elderly. *Am J Clin Nutr* 36:1014–1031.
- Paunier L, Lacourt G, Pilloud P, Schlaeppi P, Sizomenko PC. 1978. 25-hydroxyvitamin D and calcium levels in maternal, cord and infant serum in relation to maternal vitamin D intake. *Helv Paediatr Acta* 33:95–103.
- Peace H, Beattie JH. 1991. No effect of boron on bone mineral excretion and plasma sex steroid levels in healthy postmenopausal women. Monography, proceedings, roundtables, and discussions of the Seventh International Symposium on Trace Elements in Man and Animals, held May 20–25, 1990, in Dubrovnik, Croatia, Yugoslavia.
- Peacock M. 1991. Calcium absorption efficiency and calcium requirements in children and adolescents. *Am J Clin Nutr* 54:261S–265S.
- Pedersen AB, Bartholomew MJ, Dolence LA, Aljadir LP, Netteburg KL, Lloyd T. 1991. Menstrual differences due to vegetarian and nonvegetarian diets. *Am J Clin Nutr* 53:879–885.
- Pendrys DG, Katz RV. 1989. Risk of enamel fluorosis associated with fluoride supplementation, infant formula, and fluoride dentifrice use. *Am J Epidemiol* 130:1199–1208.
- Pendrys DG, Morse DE. 1990. Use of fluoride supplementation by children living in fluoridated communities. *J Dent Child* 57:343–347.
- Pendrys DG, Stamm JW. 1990. Relationship of total fluoride intake to beneficial effects and enamel fluorosis. *J Dent Res* 69(Spec Iss):529–538.
- Peng SK, Taylor CB. 1980. Editorial: Probable role of excesses of vitamin D in genesis of arteriosclerosis. *Arterial Wall* 6:63–68.
- Peng SK, Taylor CB, Tham P, Mikkelsen B. 1978. Role of mild excesses of vitamin D in arteriosclerosis. A study in squirrel monkeys. *Arterial Wall* 4:229.
- Pennington JA. 1994. *Bowes and Church's Food Values of Portions Commonly Used*. Philadelphia, PA: JB Lippincott.
- Pennington JA, Wilson DB. 1990. Daily intakes of nine nutritional elements: Analyzed vs. calculated values. *J Am Diet Assoc* 90:375–381.
- Pennington JA, Young BE. 1991. Total diet study nutritional elements, 1982–1989. *J Am Diet Assoc* 91:179–183.

- Perloff BP, Rizek RL, Haytowitz DB, Reid PR. 1990. Dietary intake methodology. II. USDA's Nutrient Data Base for Nationwide Dietary Intake Surveys. *J Nutr* 120:1530–1534.
- Petley A, Macklin B, Renwick AG, Wilkin TJ. 1995. The pharmacokinetics of niacinamide in humans and rodents. *Diabetes* 44:152–155.
- Pett LB, Ogilvie GH. 1956. The Canadian Weight-Height Survey. *Hum Biol* 28:177–188.
- Pettifor JM, Ross FP, Moodley G, Wang J, Marco G, Skjolde C. 1978a. Serum calcium, magnesium, phosphorus, alkaline phosphatase and 25-hydroxyvitamin D concentrations in children. *S Afr Med J* 53:751–754.
- Pettifor JM, Ross P, Wang J, Moodley G, Couper-Smith J. 1978b. Rickets in children of rural origin in South Africa: Is low dietary calcium a factor? *J Pediatr* 92:320–324.
- Pettifor JM, Bikle DD, Cavaleros M, Zachen D, Kamdar MC, Ross FP. 1995. Serum levels of free 1,25-dihydroxyvitamin D in vitamin D toxicity. *Ann Intern Med* 122:511–513.
- Pietschmann P, Woloszczuk W, Pietschmann H. 1990. Increased serum osteocalcin levels in elderly females with vitamin D deficiency. *Exp Clin Endocrinol* 95:275–278.
- Pillai S, Bikle DD, Elias PM. 1987. 1,25-Dihydroxyvitamin D production and receptor binding in human keratinocytes varies with differentiation. *J Biol Chem* 263:5390–5395.
- Pitkin RM, Reynolds WA, Williams GA, Hargis GK. 1979. Calcium metabolism in normal pregnancy: A longitudinal study. *Am J Obstet Gynecol* 133:781–787.
- Pittard WB III, Geddes KM, Sutherland SE, Miller MC, Hollis BW. 1990. Longitudinal changes in the bone mineral content of term and premature infants. *Am J Dis Child* 144:36–40.
- Pluckebaum JM, Chavez N. 1994. Nutritional status of Northwest Indiana Hispanics in a congregate meal program. *J Nutr Elderly* 13:1–22.
- PNUN (Standing Nordic Committee on Food). 1989. *Nordic Nutrition Recommendations*, 2nd Edition. Oslo: Nordic Council of Ministers.
- Ponder SW, McCormick DP, Fawcett HD, Palmer JL, McKernan MG, Brouhard BH. 1990. Spinal bone mineral density in children aged 5.00 through 11.99 years. *Am J Dis Child* 144:1346–1348.
- Ponz de Leon M, Roncucci L, Di Donato P, Tassi L, Smerieri O, Amorico MG, Malagoli G, De Maria D, Antonioli A, Chahin NJ. 1988. Pattern of epithelial cell proliferation in colorectal mucosa of normal subjects and of patients with adenomatous polyps or cancer of the large bowel. *Cancer Res* 48:4121–4126.
- Portale AA, Booth BE, Halloran BP, Morris RC Jr. 1984. Effect of dietary phosphorus on circulating concentrations of 1,25-dihydroxyvitamin D and immunoreactive parathyroid hormone in children with moderate renal insufficiency. *J Clin Invest* 73:1580–1589.
- Portale AA, Halloran BP, Murphy MM, Morris RC. 1986. Oral intake of phosphorus can determine the serum concentration of 1,25-dihydroxyvitamin D by determining its production rate in humans. *J Clin Invest* 77:7–12.
- Portale AA, Halloran BP, Morris RC Jr. 1987. Dietary intake of phosphorus modulates the circadian rhythm in serum concentration of phosphorus. Implications for the renal production of 1,25-dihydroxyvitamin D. *J Clin Invest* 80:1147–1154.

- Portale AA, Halloran BP, Morris RC Jr. 1989. Physiologic regulation of the serum concentration of 1,25-dihydroxyvitamin D by phosphorus in normal men. *J Clin Invest* 83:1494–1499.
- Prentice A, Laskey MA, Shaw J, Cole TJ, Fraser DR. 1990. Bone mineral content of Gambian and British children aged 0–36 months. *Bone Miner* 10:211–214.
- Prentice A, Jarjou LM, Cole TJ, Stirling DM, Dibba B, Fairweather-Tait S. 1995. Calcium requirements of lactating Gambian mothers: Effects of a calcium supplement on breast-milk calcium concentration, maternal bone mineral content, and urinary calcium excretion. *Am J Clin Nutr* 62:58–67.
- Prichard JL. 1969. The prenatal and postnatal effects of fluoride supplements on West Australian school children, aged 6, 7 and 8, Perth, 1967. *Austral Dent J* 14:335–338.
- Prince RL, Smith M, Dick IM, Price RI, Webb PG, Henderson NK, Harris MM. 1991. Prevention of postmenopausal osteoporosis. A comparative study of exercise, calcium supplementation, and hormone-replacement therapy. *N Engl J Med* 325:1189–1195.
- Prince R, Devine A, Dick I, Criddle A, Kerr D, Kent N, Price R, Randell A. 1995. The effects of calcium supplementation (milk powder or tablets) and exercise on bone density in postmenopausal women. *J Bone Miner Res* 10:1068–1075.
- Purdie DW, Aaron JE, Selby PL. 1988. Bone histology and mineral homeostasis in human pregnancy. *Br J Obstet Gynecol* 95:849–854.
- Quamme GA. 1989. Control of magnesium transport in the thick ascending limb. *Am J Physiol* 256:F197–F210.
- Quamme GA. 1993. Laboratory evaluation of magnesium status. Renal function and free intracellular magnesium concentration. *Clin Lab Med* 13:209–223.
- Quamme GA, Dirks JH. 1986. The physiology of renal magnesium handling. *Renal Physiol* 9:257–269.
- Raisz LG, Niemann I. 1969. Effect of phosphate, calcium and magnesium on bone resorption and hormonal responses in tissue culture. *Endocrinology* 85:446–452.
- Rajalakshmi K, Srikantia SG. 1980. Copper, zinc, and magnesium content of breast milk of Indian women. *Am J Clin Nutr* 33:664–669.
- Raman L, Rajalakshmi K, Krishnamachari KA, Sastry JG. 1978. Effect of calcium supplementation to undernourished mothers during pregnancy on the bone density of the neonates. *Am J Clin Nutr* 31:466–469.
- Randall RE, Cohen D, Spray CC, Rossmeisl EC. 1964. Hypermagnesemia in renal failure. *Ann Intern Med* 61:73–88.
- Rao DR, Bello H, Warren AP, Brown GE. 1994. Prevalence of lactose maldigestion. Influence and interaction of age, race, and sex. *Dig Dis Sci* 39:1519–1524.
- Rasmussen HS, McNair P, Goransson L, Balslev S, Larsen OG, Aurup P. 1988. Magnesium deficiency in patients with ischemic heart disease with and without acute myocardial infarction uncovered by an intravenous loading test. *Arch Intern Med* 148:329–332.
- Ray NF, Chan JK, Thamer M, Melton LJ III. 1997. Medical expenditures for the treatment of osteoporotic fractures in the United States in 1995: Report from the National Osteoporosis Foundation. *J Bone Miner Res* 12:24–35.
- Reasner CA II, Dunn JF, Fetchick DA, Liel Y, Hollis BW, Epstein S, Shary J, Mundy GR, Bell NH. 1990. Alteration of vitamin D metabolism in Mexican-Americans. *J Bone Miner Res* 5:13–17.
- Recker RR. 1985. Calcium absorption and achlorhydria. *N Engl J Med* 313:70–73.

- Recker RR, Hassing GS, Lau JR, Saville PD. 1973. The hyperphosphatemic effect of disodium ethane-1-hydroxy-1, 1-diphosphonate (EHDP): Renal handling of phosphorus and the renal response to parathyroid hormone. *J Lab Clin Med* 81:258–266.
- Recker RR, Davies KM, Hinders SM, Heaney RP, Stegman MR, Kimmel DB. 1992. Bone gain in young adult women. *J Am Med Assoc* 268:2403–2408.
- Recker RR, Hinders S, Davies KM, Heaney RP, Stegman MR, Lappe JM, Kimmel DB. 1996. Correcting calcium nutritional deficiency prevents spine fractures in elderly women. *J Bone Miner Res* 11:1961–1966.
- Reddy GS, Norman AW, Willis DM, Goltzman D, Guyda H, Solomon S, Philips DR, Bishop JE, Mayer E. 1983. Regulation of vitamin D metabolism in normal human pregnancy. *J Clin Endocrinol Metab* 56:363–370.
- Reed A, Haugen M, Pachman LM, Langman CB. 1990. Abnormalities in serum osteocalcin values in children with chronic rheumatic diseases. *J Pediatr* 116:574–580.
- Reed JA, Anderson JJ, Tylavsky FA, Gallagher PN Jr. 1994. Comparative changes in radial-bone density of elderly female lacto-ovovegetarians and omnivores. *Am J Clin Nutr* 59:1197S–1202S.
- Reginster JY, Strause L, Deroisy R, Lecart MP, Saltman P, Franchimont P. 1989. Preliminary report of decreased serum magnesium in postmenopausal osteoporosis. *Magnesium* 8:106–109.
- Reichel H, Koeffler HP, Norman AW. 1989. The role of vitamin D endocrine system in health and disease. *N Engl J Med* 320:980–991.
- Reid IR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. 1995. Long-term effects of calcium supplementation on bone loss and fractures in postmenopausal women: A randomized controlled trial. *Am J Med* 98:331–335.
- Reinhart RA. 1988. Magnesium metabolism. A review with special reference to the relationship between intracellular content and serum levels. *Arch Intern Med* 148:2415–2420.
- Reinhold JG, Fardadji B, Abadi P, Ismail-Beigi F. 1991. Decreased absorption of calcium, magnesium, zinc and phosphorus by humans due to increased fiber and phosphorus consumption as wheat bread. *Am J Clin Nutr* 49:204–206.
- Resnick LM, Gupta RK, Laragh JH. 1984. Intracellular free magnesium in erythrocytes of essential hypertension: Relation to blood pressure and serum divalent cations. *Proc Natl Acad Sci USA* 81:6511–6515.
- Resnick L, Gupta R, and Bhargava KK, Gruenspan H, Alderman MH, Laragh JH. 1991. Cellular ions in hypertension, diabetes and obesity: A nuclear magnetic resonance spectroscopic study. *Hypertension* 17:951–957.
- Riancho JA, delArco C, Arteaga R, Herranz JL, Albajar M, Macias JG. 1989. Influence of solar irradiation on vitamin D levels in children on anticonvulsant drugs. *Acta Neurol Scand* 79:296–299.
- Ricci JM, Hariharan S, Helfott A, Reed K, O'Sullivan MJ. 1991. Oral tocolysis with magnesium chloride: A randomized controlled prospective clinical trial. *Am J Obstet Gynecol* 165:603–610.
- Richards A, Mosekilde L, Søgaard CH. 1994. Normal age-related changes in fluoride content of vertebral trabecular bone—relation to bone quality. *Bone* 15:21–26.
- Riggs BL, Melton LJ III. 1995. The worldwide problem of osteoporosis: Insights afforded by epidemiology. *Bone* 17:505S–511S.

- Riggs BL, O'Fallon WM, Muse J, O'Conner MK, Melton LJ III. 1996. Long-term effects of calcium supplementation on serum PTH, bone turnover, and bone loss in elderly women. *J Bone Miner Res* 11:S118.
- Rigo J, Salle BL, Picaud JC, Putet G, Senterre J. 1995. Nutritional evaluation of protein hydrolysate formulas. *Eur J Clin Nutr* 49:S26–S38.
- Riis B, Thomsen K, Christiansen C. 1987. Does calcium supplementation prevent postmenopausal bone loss? *N Engl J Med* 316:173–177.
- Ritz E. 1982. Acute hypophosphatemia. *Kidney Int* 22:84–94.
- Rizzoli R, Stoermann C, Ammann P, Bonjour J-P. 1994. Hypercalcemia and hyperosteolysis in vitamin D intoxication: Effects of clodronate therapy. *Bone* 15:193–198.
- Robertson, WG. 1985. Dietary factors important in calcium stone formation. In: Schwillie PO, Smith LH, Robertson WG, Vahlensieck W, eds. *Urolithiasis and Related Clinical Research*. New York: Plenum Press. Pp. 61–68.
- Romani A, Marfella C, Scarpa A. 1993. Cell magnesium transport and homeostasis: Role of intracellular compartments. *Miner Electrolyte Metab* 19:282–289.
- Roncucci L, Scalmati A, Ponz de Leon M. 1991. Pattern of cell kinetics in colorectal mucosa of patients with different types of adenomatous polyps of the large bowel. *Cancer* 68:873–878.
- Ronis DL, Lang WP, Farghaly MM, Passow E. 1993. Tooth brushing, flossing, and preventive dental visits by Detroit-area residents in relation to demographic and socioeconomic factors. *J Pub Hlth Dent* 53:138–145.
- Rosado JL, Lopez P, Morales M, Munoz E, Allen LH. 1992. Bioavailability of energy, nitrogen, fat, zinc, iron and calcium from rural and urban Mexican diets. *Br J Nutr* 68:45–58.
- Rowe JW, Minaker KL, Pallotta JA, Flier JS. 1983. Characterization of the insulin resistance of aging. *J Clin Invest* 71:1581–1587.
- Rubenowitz E, Axelsson G, Rylander R. 1996. Magnesium in drinking water and death from acute myocardial infarction. *Am J Epidemiol* 143:456–462.
- Rubin H. 1975. Central role for magnesium in coordinate control of metabolism and growth in animal cells. *Proc Natl Acad Sci USA* 72:3551–3555.
- Rude RK. 1993. Magnesium metabolism and deficiency. *Endocrinol Metab Clin North Am* 22:377–395.
- Rude RK, Olerich M. 1996. Magnesium deficiency: Possible role in osteoporosis associated with gluten-sensitive enteropathy. *Osteopor Int* 6:453–461.
- Rude RK, Singer FR. 1980. Magnesium deficiency and excess. *Ann Rev Med* 32:245–259.
- Rude RK, Oldham SB, Singer FR. 1976. Functional hypoparathyroidism and parathyroid hormone end-organ resistance in human magnesium deficiency. *Clin Endocrinol* 5:209–224.
- Rude RK, Bethune JE, Singer FR. 1980. Renal tubular maximum for magnesium in normal, hyperparathyroid and hypoparathyroid man. *J Clin Endocrinol Metab* 51:1425–1431.
- Rude RK, Manoogian C, Ehrlich L, DeRusso P, Ryzen E, Nadler J. 1989. Mechanisms of blood pressure regulation by magnesium in man. *Magnesium* 8:266–278.
- Rude RK, Stephen A, Nadler J. 1991. Determination of red blood cell intracellular free magnesium by nuclear magnetic resonance as an assessment of magnesium depletion. *Magnes Trace Elem* 10:117–121.

- Rudloff S, Lonnerdal B. 1990. Calcium retention from milk-based infant formulas, whey-hydrolysate formula, and human milk in weanling rhesus monkeys. *Am J Dis Child* 144:360–363.
- Rudnicki M, Frolich A, Rasmussen WF, McNair P. 1991. The effect of magnesium on maternal blood pressure in pregnancy-induced hypertension. A randomized double-blind placebo-controlled trial. *Acta Obstet Gynecol Scand* 70:445–450.
- Ruiz JC, Mandel C, Garabedian M. 1995. Influence of spontaneous calcium intake and physical exercise on the vertebral and femoral bone mineral density of children and adolescents. *J Bone Miner Res* 10:675–682.
- Russell AL. 1949. Dental effects of exposure to fluoride-bearing Dakota sandstone waters at various ages and for various lengths of time. II. Patterns of dental caries inhibition as related to exposure span, to elapsed time since exposure, and to periods of calcification and eruption. *J Dent Res* 28:600–612.
- Russell AL, Elvove E. 1951. Domestic water and dental caries. VII. A study of the fluoride-dental caries relationship in an adult population. *Pub Hlth Rep* 66:1389–1401.
- Ryan MP. 1987. Diuretics and potassium/magnesium depletion. Directions for treatment. *Am J Med* 82:38–47.
- Ryzen E, Elbaum N, Singer FR, Rude RK. 1985. Parenteral magnesium tolerance testing in the evaluation of magnesium deficiency. *Magnesium* 4:137–147.
- Ryzen E, Elkayam U, Rude RK. 1986. Low blood mononuclear cell magnesium in intensive cardiac care unit patients. *Am Heart J* 111:475–480.
- Sacks FM, Brown LE, Appel L, Borhani NO, Evans D, Whelton P. 1995. Combinations of potassium, calcium, and magnesium supplements in hypertension. *Hypertension* 26:950–956.
- Sakhaee K, Baker S, Zerwekh J, Poindexter J, Garcia-Hernandez PA, Pak CY. 1994. Limited risk of kidney stone formation during long-term calcium citrate supplementation in nonstone forming subjects. *J Urol* 152:324–327.
- Salama F, Whitford GM, Barenie JT. 1989. Fluoride retention by children from toothbrushing. *J Dent Res* 68(Spec Issue):335.
- Salle BL, Delvin E, Glorieux F, David L. 1990. Human neonatal hypocalcemia. *Biol Neonate* 58:S22–S31.
- Sandberg AS, Larsen T, Sandstrom B. 1993. High dietary calcium level decreases colonic phytate degradation in pigs fed a rapeseed diet. *J Nutr* 123:559–566.
- Sanders TA, Purves R. 1981. An anthropometric and dietary assessment of the nutritional status of vegan preschool children. *J Human Nutr* 35:349–357.
- Sandler RB, Slemenda CW, LaPorte RE, Cauley JA, Schramm MM, Barresi ML, Kriska AM. 1985. Postmenopausal bone density and milk consumption in childhood and adolescence. *Am J Clin Nutr* 42:270–274.
- Saunders D, Sillery J, Chapman R. 1988. Effect of calcium carbonate and aluminum hydroxide on human intestinal function. *Dig Dis Sci* 33:409–412.
- Schanler RJ, Garza C, Smith EO. 1985. Fortified mothers' milk for very low birth weight infants: Results of macromineral balance studies. *J Pediatr* 107:767–774.
- Schendel DE, Berg CJ, Yeargin-Allsopp M, Boyle CA, Decoufle P. 1996. Prenatal magnesium sulfate exposure and the risk for cerebral palsy or mental retardation among very low-birth-weight children aged 3 to 5 years. *J Am Med Assoc* 276:1805–1810.
- Schiffl H, Binswanger U. 1982. Renal handling of fluoride in healthy man. *Renal Physiol* 5:192–196.

- Schiller L, Santa Ana C, Sheikh M, Emmett M, Fordtran J. 1989. Effect of the time of administration of calcium acetate on phosphorus binding. *N Engl J Med* 320:1110–1113.
- Schlesinger ES, Overton DE, Riverhead LI, Chase HC, Cantwell KT. 1956. Newburgh-Kingston caries-fluorine study XIII. Pediatric findings after ten years. *J Am Dent Assoc* 52:296–306.
- Schlesinger L, Arevalo M, Arredondo S, Diaz M, Lonnerdal B, Stekel A. 1992. Effect of a zinc-fortified formula on immunocompetence and growth of malnourished infants. *Am J Clin Nutr* 56:491–498.
- Schmidt LE, Arfken CL, Heins JM. 1994. Evaluation of nutrient intake in subjects with non-insulin-dependent diabetes mellitus. *J Am Diet Assoc* 94:773–774.
- Schmidt-Gayk H, Goossen J, Lendle F, Seidel D. 1977. Serum 25-hydroxycholecalciferol in myocardial infarction. *Atherosclerosis* 26:55–58.
- Schneider EL, Guralnik JM. 1990. The aging of America. Impact on health care costs. *J Am Med Assoc* 263:2335–2340.
- Schofield FA, and Morrell E. 1960. Calcium, phosphorus and magnesium. *Fed Proc* 19:1014–1016.
- Schuman CA, Jones HW III. 1985. The “milk-alkali” syndrome: Two case reports with discussion of pathogenesis. *Quart J Med (New Series)* 55:119–126.
- Schutzmansky G. 1971. Fluoride tablet application in pregnant females. *Dtsch Stomatol* 21:122–129.
- Schwartz E, Chokas WV, Panariello VA. 1964. Metabolic balance studies of high calcium intake in osteoporosis. *Am J Med* 36:233–249.
- Schwartz GG, Hulka BS. 1990. Is vitamin D deficiency a risk factor for prostate cancer? *Anticancer Res* 10:1307–1312.
- Schwartz R, Walker G, Linz MD, MacKellar I. 1973. Metabolic responses of adolescent boys to two levels of dietary magnesium and protein. I. Magnesium and nitrogen retention. *Am J Clin Nutr* 26:510–518.
- Schwartz R, Spencer H, Welsh JJ. 1984. Magnesium absorption in human subjects from leafy vegetables, intrinsically labeled with stable  $^{26}\text{Mg}$ . *Am J Clin Nutr* 39:571–576.
- Schwartz R, Apgar BJ, Wien EM. 1986. Apparent absorption and retention of Ca, Cu, Mg, Mn, and Zn from a diet containing bran. *Am J Clin Nutr* 43:444–455.
- Schwartzman MS, Franck WA. 1987. Vitamin D toxicity complicating the treatment of senile, postmenopausal, and glucocorticoid-induced osteoporosis: Four case reports and a critical commentary on the use of vitamin D in these disorders. *Am J Med* 82:224–229.
- Sebastian A, Harris ST, Ottaway JH, Todd KM, Morris RC Jr. 1994. Improved mineral balance and skeletal metabolism in postmenopausal women treated with potassium bicarbonate. *N Engl J Med* 330:1776–1781.
- Sebert JL, Garabedian M, Chauvenet M, Maamer M, Agbomson F, Brazier M. 1995. Evaluation of a new solid formulation of calcium and vitamin D in institutionalized elderly subjects: A randomized comparative trial versus separate administration of both constituents. *Rev Rhum* 62:288–294.
- Seelig MS. 1981. Magnesium requirements in human nutrition. *Magnes Bull* 3(suppl):26–47.
- Seelig MS. 1993. Interrelationship of magnesium and estrogen in cardiovascular and bone disorders, eclampsia, migraine and premenstrual syndrome. *J Am Coll Nutr* 12:442–458.
- Seelig MS, Elin RJ. 1996. Is there a place for magnesium in the treatment of acute myocardial infarction? *Am Heart J* 132:471–477.

- Seki K, Makimura N, Mitsui C, Hirata J, Nagata I. 1991. Calcium-regulating hormones and osteocalcin levels during pregnancy: A longitudinal study. *Am J Obstet Gynecol* 164:1248–1252.
- Selby PL. 1994. Calcium requirement—A reappraisal of the methods used in its determination and their application to patients with osteoporosis. *Am J Clin Nutr* 60:944–948.
- Selby PL, Davies M, Marks JS, Mawer EB. 1995. Vitamin D intoxication causes hypercalcemia by increased bone resorption which responds to pamidronate. *Clin Endocrinol* 43:531–536.
- Sentipal JM, Wardlaw GM, Mahan J, Matkovic V. 1991. Influence of calcium intake and growth indexes on vertebral bone mineral density in young females. *Am J Clin Nutr* 54:425–428.
- Seydoux J, Girardin E, Paunier L, Beguin F. 1992. Serum and intracellular magnesium during normal pregnancy and in patients with pre-eclampsia. *Br J Obstet Gynecol* 99:207–211.
- Shapses SA, Robins SP, Schwartz EI, Chowdhury H. 1995. Short-term changes in calcium but not protein intake alter the rate of bone resorption in healthy subjects as assessed by urinary pyridinium cross-link excretion. *J Nutr* 125:2814–2821.
- Sharma OP. 1996. Vitamin D, calcium, and sarcoidosis. *Chest* 109:535–539.
- Shen YW, Taves DR. 1974. Fluoride concentrations in the human placenta and maternal and cord blood. *Am J Obstet Gynecol* 119:205–207.
- Sherman HC, Hawley E. 1922. Calcium and phosphorus metabolism in childhood. *J Biol Chem* 52:375–399.
- Shils ME. 1969. Experimental human magnesium depletion. *Medicine* 46:61–85.
- Shils ME. 1994. Magnesium. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*. Philadelphia, PA: Lea & Febiger. Pp. 164–184.
- Shils ME, Rude RK. 1996. Deliberations and evaluations of the approaches, endpoints and paradigms for magnesium dietary recommendations. *J Nutr* 126:2398S–2403S.
- Sibai BM, Villar MA, Bray E. 1989. Magnesium supplementation during pregnancy: A double-blind randomized controlled clinical trial. *Am J Obstet Gynecol* 161:115–119.
- Siener R, Hesse A. 1995. Influence of a mixed and a vegetarian diet on urinary magnesium excretion and concentration. *Br J Nutr* 73:783–790.
- Silverberg SJ, Shane E, Clemens TL, Dempster DW, Segre GV, Lindsay R, Bilezikian JP. 1986. The effect of oral phosphate administration on major indices of skeletal metabolism in normal subjects. *J Bone Miner Res* 1:383–388.
- Silvis SE, Paragas PD Jr. 1972. Paresthesias, weakness, seizures, and hypophosphatemia in patients receiving hyperalimentation. *Gastroenterology* 62:513–520.
- Simard PL, Lachapelle C, Trahan L, Naccache H, Demers M, Broduer JM. 1989. The ingestion of fluoride dentifrice by young children. *J Dent Child* 56:177–181.
- Simard PL, Naccache H, Lachapelle D, Brodeur JM. 1991. Ingestion of fluoride from dentifrices by children aged 12 to 24 months. *Clin Pediatr Phila* 30:614–617.
- Simmer K, Khanum S, Carlsson L, Thompson RP. 1988. Nutritional rehabilitation in Bangladesh—the importance of zinc. *Am J Clin Nutr* 47:1036–1040.
- Singer L, Ophaug R. 1979. Total fluoride intake of infants. *Pediatrics* 63:460–466.
- Singer L, Ophaug RH, Harland BF. 1980. Fluoride intakes of young male adults in the United States. *Am J Clin Nutr* 33:328–332.
- Singer L, Ophaug RH, Harland BF. 1985. Dietary fluoride intake of 15–19-year-old male adults residing in the United States. *J Dent Res* 64:1302–1305.

- Singh A, Jolly SS. 1970. Chronic toxic effects on the skeletal system. In: *Fluorides and Human Health*. Geneva: World Health Organization. Pp 238–249.
- Skajaa K, Dorup I, Sandstrom BM. 1991. Magnesium intake and status and pregnancy outcome in a Danish population. *Br J Obstet Gynecol* 98:919–928.
- Slattery ML, Sorenson AW, Ford MH. 1988. Dietary calcium intake as a mitigating factor in colon cancer. *Am J Epidemiol* 128:504–514.
- Slemenda CW, Reister TK, Hui SL, Miller JZ, Christian JC, Johnston CC Jr. 1994. Influences on skeletal mineralization in children and adolescents: Evidence for varying effects of sexual maturation and physical activity. *J Pediatr* 125:201–207.
- Slemenda CW, Peacock M, Hui S, Zhou L, Johnston CC Jr. 1997. Reduced rates of skeletal remodeling are associated with increased bone mineral density during the development of peak skeletal mass. *J Bone Miner Res* 12:676–682.
- Slesinski MJ, Subar AF, Kahle LL. 1996. Dietary intake of fat, fiber, and other nutrients is related to the use of vitamin and mineral supplements in the United States: The 1992 National Health Interview Survey. *J Nutr* 126:3001–3008.
- Smilkstein MJ, Smolinske SC, Kulig KW, Rumack, BH. 1988. Severe hypermagnesemia due to multiple-dose cathartic therapy. *West J Med* 148:208–211.
- Smith EL, Gilligan C, Smith PE, Sempos CT. 1989. Calcium supplementation and bone loss in middle-aged women. *Am J Clin Nutr* 50:833–842.
- Smith KT, Heaney RP, Flora L, Hinders SM. 1987. Calcium absorption from a new calcium delivery system (CCM). *Calcif Tissue Int* 41:351–352.
- Smith R, Dent CE. 1969. Vitamin D requirements in adults. Clinical and metabolic studies on seven patients with nutritional osteomalacia. *Bibl Nutr Dieta* 13:44–45.
- Snedeker SM, Smith SA, Greger JL. 1982. Effect of dietary calcium and phosphorus levels on the utilization of iron, copper, and zinc by adult males. *J Nutr* 112:136–143.
- Sojka JE, Wastney ME, Abrams S, Froese S, Martin BR, Weaver CM. 1997. Magnesium kinetics in adolescent girls determined using stable isotopes: Effects of high and low calcium intakes. *Am J Physiol* 273:R170–R175.
- Sojka JE, Weaver CM. 1995. Magnesium supplementation and osteoporosis. *Nutr Rev* 53:71–74.
- Sokoll LJ, Dawson-Hughes B. 1992. Calcium supplementation and plasma ferritin concentrations in premenopausal women. *Am J Clin Nutr* 56:1045–1048.
- Sorva A, Risteli J, Risteli L, Valimaki M, Tilvis R. 1991. Effects of vitamin D and calcium on markers of bone metabolism in geriatric patients with low serum 25-hydroxyvitamin D levels. *Calcif Tissue Int* 49:S88–S89.
- Southgate DAT, Widdowson EM, Smits BJ, Cooke WT, Walker CHM, Mathers NP. 1969. Absorption and excretion of calcium and fat by young infants. *Lancet* 1:487–489.
- Sowers M, Wallace RB, Lemke JH. 1985. Correlates of forearm bone mass among women during maximal bone mineralization. *Prev Med* 14:585–596.
- Sowers M, Wallace RB, Lemke JH. 1986. The relationship of bone mass and fracture history to fluoride and calcium intake: A study of three communities. *Am J Clin Nutr* 44:889–898.
- Sowers M, Clark MK, Jannausch ML, Wallace RB. 1991. A prospective study of bone mineral content and fracture in communities with differential fluoride exposure. *Am J Epidemiol* 133:649–660.
- Sowers M, Corton G, Shapiro B, Jannausch ML, Crutchfield M, Smith ML, Randolph JF, Hollis B. 1993. Changes in bone density with lactation. *J Am Med Assoc* 269:3130–3135.

- Sowers M, Randolph J, Shapiro B, Jannaush M. 1995a. A prospective study of bone density and pregnancy after an extended period of lactation with bone loss. *Obstet Gynecol* 85:285–289.
- Sowers M, Eyre D, Hollis BW, Randolph JF, Shapiro B, Jannausch ML, Crutchfield M. 1995b. Biochemical markers of bone turnover in lactating and nonlactating postpartum women. *J Clin Endocrinol Metab*. 80:2210–2216.
- Spak CJ, Ekstrand J, Zylberstein D. 1982. Bioavailability of fluoride added by baby formula and milk. *Caries Res* 16:249–256.
- Spak CJ, Hardell LI, De Chateau P. 1983. Fluoride in human milk. *Acta Paediatr Scand* 72:699–701.
- Spatling L, Spatling G. 1988. Magnesium supplementation in pregnancy. A double blind study. *Br J Obstet Gynecol* 95:120–125.
- Specker BL. 1996. Evidence for an interaction between calcium intake and physical activity on changes in bone mineral density. *J Bone Miner Res* 11:1539–1544.
- Specker BL, Tsang RC. 1987. Cyclical serum 25-hydroxyvitamin D concentrations paralleling sunshine exposure in exclusively breast-fed infants. *J Pediatr* 110:744–747.
- Specker BL, Tsang RC, Hollis BW. 1985a. Effect of race and diet on human-milk vitamin D and 25-hydroxyvitamin D. *Am J Dis Child* 139:1134–1137.
- Specker BL, Valanis B, Hertzberg V, Edwards N, Tsang RC. 1985b. Sunshine exposure and serum 25-hydroxyvitamin D concentrations in exclusively breast-fed infants. *J Pediatr* 107:372–376.
- Specker BL, Lichtenstein P, Mimouni F, Gormley C, Tsang RC. 1986. Calcium-regulating hormones and minerals from birth to 18 months of age: A cross-sectional study. II. Effects of sex, race, age, season, and diet on serum minerals, parathyroid hormone, and calcitonin. *Pediatrics* 77:891–896.
- Specker BL, Tsang RC, Ho ML, Miller D. 1987. Effect of vegetarian diet on serum 1,25-dihydroxyvitamin D concentrations during lactation. *Obstet Gynecol* 70:870–874.
- Specker BL, Tsang RC, Ho ML. 1991a. Changes in calcium homeostasis over the first year postpartum: Effect of lactation and weaning. *Obstet Gynecol* 78:56–62.
- Specker BL, Tsang RC, Ho ML, Landi TM, Gratton TL. 1991b. Low serum calcium and high parathyroid hormone levels in neonates fed “humanized” cow’s milk-based formula. *Am J Dis Child* 145:941–945.
- Specker BL, Ho ML, Oestreich A, Yin TA, Shui QM, Chen XC, Tsang RC. 1992. Prospective study of vitamin D supplementation and rickets in China. *J Pediatr* 120:733–739.
- Specker BL, Vieira NE, O’Brien KO, Ho ML, Heubi JE, Abrams SA, Yerger AL. 1994. Calcium kinetics in lactating women with low and high calcium intakes. *Am J Clin Nutr* 59:593–599.
- Specker BL, Beck A, Kalkwarf H, Ho M. 1997. Randomized trial of varying mineral intake on total body bone mineral accretion during the first year of life. *Pediatrics* 99:e12.
- Spencer H, Menczel J, Lewin I, Samachson J. 1965. Effect of high phosphorus intake on calcium and phosphorus metabolism in man. *J Nutr* 86:125–132.
- Spencer H, Lewin I, Fowler J, Samachson J. 1969. Influence of dietary calcium intake on  $\text{Ca}^{47}$  absorption in man. *Am J Med* 46:197–205.
- Spencer H, Kramer L, Osis D, Norris C. 1978a. Effect of phosphorus on the absorption of calcium and on the calcium balance in man. *J Nutr* 108:447–457.
- Spencer H, Lesniak M, Gatzka CA, Kramer L, Norris C, Coffey J. 1978b. Magnesium–calcium interrelationships in man. *Trace Substances Environ Hlth* 12:241–247.

- Spencer H, Kramer L, Lesniak M, DeBartolo M, Norris C, Osis D. 1984. Calcium requirements in humans. Report of original data and a review. *Clin Orthop Relat Res* 184:270–280.
- Spencer H, Fuller H, Norris C, Williams D. 1994. Effect of magnesium on the intestinal absorption of calcium in man. *J Am Coll Nutr* 13:485–492.
- Spencer H, Osis D, Lender M. 1981. Studies of fluoride metabolism in man. A review and report of original data. *Sci Total Environ* 17:1–12.
- Stamp TCB, Haddad JG, Twigg CA. 1977. Comparison of oral 25-hydroxycholecalciferol, vitamin D, and ultraviolet light as determinants of circulating 25-hydroxyvitamin D. *Lancet* 1:1341–1343.
- Stanbury SW. 1971. The phosphate ion in chronic renal failure. In: Hioco DJ, ed. *Phosphate et Metabolisme Phosphocalcique*. Paris: Sandoz Laboratories.
- Stapleton FB. 1994. Hematuria associated with hypercalciuria and hyperuricosuria: A practical approach. *Pediatr Nephrol* 8:756–761.
- Stearns G. 1968. Early studies of vitamin D requirement during growth. *Am J Pub Hlth* 58:2027–2035.
- Steenbock H, Black A. 1924. The reduction of growth-promoting and calcifying properties in a ration by exposure to ultraviolet light. *J Biol Chem* 61:408–422.
- Steichen JJ, Tsang RC. 1987. Bone mineralization and growth in term infants fed soy-based or cow milk-based formula. *J Pediatr* 110:687–692.
- Stein JH, Smith WO, Ginn HE. 1966. Hypophosphatemia in acute alcoholism. *Am J Med Sci* 252:78–83.
- Stendig-Lindberg G, Tepper R, Leichter I. 1993. Trabecular bone density in a two year controlled trial of peroral magnesium in osteoporosis. *Magnes Res* 6:155–163.
- Stephen KW, McCall DR, Tullis JI. 1987. Caries prevalence in northern Scotland before, and 5 years after, water defluoridation. *Br Dent J* 163:324–326.
- Stevenson CA, Watson AR. 1957. Fluoride osteosclerosis. *Am J Roentg Rad Ther Nucl Med* 78:13–18.
- Stumpf WE, Sar M, Reid FA, Tanakay Y, DeLuca HF. 1979. Target cells for 1,25-dihydroxyvitamin D<sub>3</sub> in intestinal tract, stomach, kidney, skin, pituitary, and parathyroid. *Science* 206:1188–1190.
- Suarez FL, Savaiano DA, Levitt MD. 1995. A comparison of symptoms after the consumption of milk or lactose-hydrolyzed milk by people with self-reported severe lactose intolerance. *N Engl J Med* 333:1–4.
- Svenningsen NW, Lindquist B. 1974. Postnatal development of renal hydrogen ion excretion capacity in relation to age and protein intake. *Acta Paediatr Scand* 63:721–731.
- Switzer RL. 1971. Regulation and mechanism of phosphoribosylpyrophosphate synthetase. III. Kinetic studies of the reaction mechanism. *J Biol Chem* 246:2447–2458.
- Tanner JT, Smith J, Defibaugh P, Angyal G, Villalobos M, Bueno MP, McGarrahan ET, Wehr HM, Muniz JF, Hollis BW. 1988. Survey of vitamin content of fortified milk. *J Assoc Off Anal Chem* 71: 607–610.
- Tanner JM. 1990. *Growth at Adolescence*. Oxford: Oxford University Press.
- Tatevossian A. 1990. Fluoride in dental plaque and its effects. *J Dent Res* 69(Spec Iss): 645–652.
- Taves DR. 1978. Fluoridation and mortality due to heart disease. *Nature* 272:361–362.
- Taves DR. 1983. Dietary intake of fluoride ashed (total fluoride) v. unashed (inorganic fluoride) analysis of individual foods. *Br J Nutr* 49:295–301.

- Taves DR, Neuman WF. 1964. Factors controlling calcification in vitro: Fluoride and magnesium. *Arch Biochem Biophys* 108:390–397.
- Taylor AF, Norman ME. 1984. Vitamin D metabolite levels in normal children. *Pediatr Res* 18: 886–890.
- Taylor CB, Hass GM, Ho KJ, Liu LB. 1972. Risk factors in the pathogenesis of arteriosclerotic heart disease and generalized atherosclerosis. *Ann Clin Lab Sci* 2:239.
- Teegarden D, Proulx WR, Martin BR, Zhao J, McCabe GP, Lyle RM, Peacock M, Slemenda C, Johnston CC, Weaver CM. 1995. Peak bone mass in young women. *J Bone Miner Res* 10:711–715.
- Ten Cate JM. 1990. In vitro studies on the effects of fluoride on de- and remineralization. *J Dent Res* 69(Spec Iss):614–619.
- Terblanche S, Noakes TD, Dennis SC, Marais D, Eckert M. 1992. Failure of magnesium supplementation to influence marathon running performance or recovery in magnesium-replete subjects. *Int J Sport Nutr* 2:154–164.
- Tesar R, Notelovitz M, Shim E, Kauwell G, Brown J. 1992. Axial and peripheral bone density and nutrient intakes of postmenopausal vegetarian and omnivorous women. *Am J Clin Nutr* 56:699–704.
- Thatcher HS, Rock L. 1928. Clinical notes, suggestions and new instruments. *J Am Med Assoc* 91:1185–1186.
- Theintz G, Buchs B, Rizzoli R, Slosman D, Clavien H, Sizonenko PC, Bonjour JP. 1992. Longitudinal monitoring of bone mass accumulation in healthy adolescents: Evidence for a marked reduction after 16 years of age at the levels of lumbar spine and femoral neck in female subjects. *J Clin Endocrinol Metab* 75:1060–1065.
- Thompson FE, Byers T. 1994. Dietary assessment resource manual. *J Nutr* 124:224S–231S.
- Thys-Jacobs S, Ceccarelli S, Bierman A, Weisman H, Cohen M-A, Alvir J. 1989. Calcium supplementation in premenstrual syndrome: A randomized cross-over trial. *J Gen Intern Med* 4:183–189.
- Tillman DM, Semple PF. 1988. Calcium and magnesium in essential hypertension. *Clin Sci* 75:395–402.
- Touitou Y, Godard JP, Ferment O, Chastang C, Proust J, Bogdan A, Auzeby A, Touitou C. 1987. Prevalence of magnesium and potassium deficiencies in the elderly. *Clin Chem* 33:518–523.
- Travis SF, Sugerman HJ, Ruberg RL, Dudrick SJ, Delivoria-Papadopoulos M, Miller L, Osaki FA. 1971. Alterations of red cell glycolytic intermediates and oxygen transport as a consequence of hypophosphatemia in patients receiving intravenous hyperalimentation. *N Engl J Med* 285:763–768.
- Tremaine WJ, Newcomer AD, Riggs BL, McGill DB. 1986. Calcium absorption from milk in lactase-deficient and lactase-sufficient adults. *Dig Dis Sci* 31:376–378.
- Tsang RC, Strub R, Brown DR, Steichen J, Hartman C, Chen IW. 1976. Hypomagnesemia in infants of diabetic mothers: Perinatal studies. *J Pediatr* 89:115–119.
- Tucker K. 1996. The use of epidemiological approaches and meta-analysis to determine mineral element requirements. *J Nutr* 126:2365S–2372S.
- Tucker K, Kiel DP, Hannan MT, Felson DT. 1995. Magnesium intake is associated with bone-mineral density (BMD) in elderly women. *J Bone Miner Res* 10:S466.
- Tylavsky FA, Anderson JJ. 1988. Dietary factors in bone health of elderly lacto-ovo vegetarian and omnivorous women. *Am J Clin Nutr* 48:842–849.

- Urakabe S, Nakata K, Ando A, Orita Y, Abe Y. 1975. Hypokalemia and metabolic acidosis from overuse of magnesium oxide. *Jpn Circ J* 39:1135–1137.
- USDA (US Department of Agriculture). 1985. *Nationwide Food Consumption Survey. Continuing Survey of Food Intakes of Individuals*. Women 19–50 years and their children 1–5 years, 1 day, 1985. Report No. 85-1. Hyattsville, MD: Nutrition Monitoring Division, Human Nutrition Information Service, USDA.
- USDA (US Department of Agriculture). 1991. *Provisional Table on the Vitamin D Content of Foods*. Hyattsville, MD: Nutrient Data Research Branch, USDA.
- USDA (US Department of Agriculture), Center for Nutrition Policy and Promotion. 1997. *Nutrient Content of the U.S. Food Supply, 1909–1994*. Washington DC: Center for Nutrition Policy and Promotion, USDA.
- USPHS (US Public Health Service). 1991. *Ad Hoc Subcommittee on Fluoride: Review of Fluoride Benefits and Risks*. Bethesda, MD: Department of Health and Human Services.
- Venkataraman PS, Tsang RC, Greer FR, Noguchi A, Laskarzewski P, Steichen JJ. 1985. Late infantile tetany and secondary hyperparathyroidism in infants fed humanized cow milk formula. Longitudinal follow-up. *Am J Dis Child* 139:664–668.
- Vicchio D, Yergey A, O'Brien K, Allen L, Ray R, Holick MF. 1993. Quantification and kinetics of 25-hydroxyvitamin D<sub>3</sub> by isotope dilution liquid chromatography/thermospray mass spectrometry. *Biol Mass Spectrom* 22:53–58.
- Vik T, Try K, Thelle DS, Forde OH. 1979. Tromso heart study: Vitamin D metabolism and myocardial infarction. *Br Med J* 2:176.
- Villar J, Repke JT. 1990. Calcium supplementation during pregnancy may reduce preterm delivery in high-risk populations. *Am J Obstet Gynecol* 163:1124–1131.
- Villareal DT, Civitelli R, Chines A, Avioli LV. 1991. Subclinical vitamin D deficiency in postmenopausal women with low vertebral bone mass. *J Clin Endocrinol Metab* 72: 628–634.
- Wacker WE, Parisi AF. 1968. Magnesium metabolism. *N Engl J Med* 45:658–663, 712–717, 772–776.
- Wagener DK, Novrjah P, Horowitz AM. 1995. *Trends in Childhood Use of Dental Care Products Containing Fluoride: United States, 1983–1989*. Advance data from Vital Health Statistics of the Center for Disease Control. National Center for Health Statistics #219; Nov. 20, 1992. Hyattsville, MD: National Center for Health Statistics.
- Walker AR, Richardson B, Walker F. 1972. The influence of numerous pregnancies and lactations on bone dimensions in South African Bantu and Caucasian mothers. *Clin Sci* 42:189–196.
- Walker RM, Linkswiler HM. 1972. Calcium retention in the adult human male as affected by protein intake. *J Nutr* 102:1297–1302.
- Wallach S, Verch RL. 1986. Tissue magnesium in spontaneously hypertensive rats. *Magnesium* 5:33–38.
- Wang CC, Kern R, Kaucher M. 1930. Minimum requirement of calcium and phosphorus in children. *Am J Dis Child* 39:768–773.
- Wardlaw GM, Pike AM. 1986. The effect of lactation on peak adult shaft and ultra-distal forearm bone mass in women. *Am J Clin Nutr* 44:283–286.
- Wasnich R, Yano K, Vogel J. 1983. Postmenopausal bone loss at multiple skeletal sites: Relationship to estrogen use. *J Chron Dis* 36:781–790.
- Wastney ME, Ng J, Smith D, Martin BR, Peacock M, Weaver CM. 1996. Differences in calcium kinetics between adolescent girls and young women. *Am J Physiol* 271:R208–R216.

- Waterhouse C, Taves D, Munzer A. 1980. Serum inorganic fluoride: Changes related to previous fluoride intake, renal function and bone resorption. *Clin Sci* 58:145–152.
- Weaver CM. 1994. Age-related calcium requirements due to changes in absorption and utilization. *J Nutr* 124:1418S–1425S.
- Weaver CM, Martin BR, Plawecki KL, Peacock M, Wood OB, Smith DL, Wastney ME. 1995. Differences in calcium metabolism between adolescent and adult females. *Am J Clin Nutr* 61:577–581.
- Webb AR, Kline L, Holick MF. 1988. Influence of season and latitude on the cutaneous synthesis of vitamin D<sub>3</sub>: Exposure to winter sunlight in Boston and Edmonton will not promote vitamin D<sub>3</sub> synthesis in human skin. *J Clin Endocrinol Metab* 67:373–378.
- Webb AR, De Costa BR, Holick MF. 1989. Sunlight regulates the cutaneous production of vitamin D<sub>3</sub> by causing its photodegradation. *J Clin Endocrinol Metab* 68:882–887.
- Webb AR, Pilbeam C, Hanafin N, Holick MF. 1990. An evaluation of the relative contributions of exposure to sunlight and of diet to the circulating concentrations of 25-hydroxyvitamin D in an elderly nursing home population in Boston. *Am J Clin Nutr* 51:1075–1081.
- Wei SH, Hattab FN, Mellberg JR. 1989. Concentration of fluoride and selected other elements in teas. *Nutrition* 5:237–240.
- Weinsier RL, Krumdieck CL. 1981. Death resulting from overzealous total parenteral nutrition: The refeeding syndrome revisited. *Am J Clin Nutr* 34:393–399.
- Weisman Y, Harell A, Edelstein S, Spirer Z, Golander A. 1979. 1,25-dihydroxyvitamin D<sub>3</sub> and 24,25-dihydroxyvitamin D<sub>3</sub> in vitro synthesis by human decidua and placenta. *Nature* 281:317–319.
- Weissberg N, Schwartz G, Shemesh O, Brooks BA, Algur N, Eylath U, Abraham AS. 1992. Serum and mononuclear cell potassium, magnesium, sodium and calcium in pregnancy and labour and their relation to uterine muscle contraction. *Magnes Res* 5:173–177.
- Wester PO, Dyckner T. 1980. Diuretic treatment and magnesium losses. *Acta Med Scand* 647:145–152.
- Whitford GM. 1994. Effects of plasma fluoride and dietary calcium concentrations on GI absorption and secretion of fluoride in the rat. *Calcif Tissue Int* 54:421–425.
- Whitford GM. 1996. The metabolism and toxicity of fluoride. In Myers HM, ed. *Monographs in Oral Science*, 2nd Revised Edition. Basel, Switzerland: Karger.
- Whitford GM, Allmann DW, Shahed AR. 1987. Topical fluorides: Effects on physiologic and biochemical processes. *J Dent Res* 66:1072–1078.
- Whiting SJ, Pluhator MM. 1992. Comparison of in vitro and in vivo tests for determination of availability of calcium from calcium carbonate tablets. *J Am Coll Nutr* 11:553–560.
- Whiting SJ, Wood RJ. 1997. Adverse effects of high-calcium diets in humans. *Nutr Rev* 55:1–9.
- WHO (World Health Organization). 1984. *Fluorine and Fluorides*. Environmental Health Criteria 36. Geneva: World Health Organization. Pp. 77–79.
- WHO (World Health Organization). 1987. *Principles for the Safety Assessment of Food Additives and Contaminants in Food*. Environmental Health Criteria 70. Geneva: World Health Organization.

- WHO (World Health Organization). 1994. *Assessment of Fracture Risk and its Application to Screening for Postmenopausal Osteoporosis*. Technical Report Series 843. Geneva: World Health Organization.
- WHO (World Health Organization). 1996. *Trace Elements in Human Nutrition and Health*. Prepared in collaboration with the Food and Agriculture Organization of the United Nations and the International Atomic Energy Agency. Geneva: World Health Organization.
- Wickham CA, Walsh K, Cooper C, Barker DJ, Margetts BM, Morris J, Bruce SA. 1989. Dietary calcium, physical activity, and risk of hip fracture: A prospective study. *Br Med J* 299:889–892.
- Widdowson EM. 1965. Absorption and excretion of fat, nitrogen, and minerals from “filled” milks by babies one week old. *Lancet* 2:1099–1105.
- Widdowson EM, Dickerson JWT. 1964. The chemical composition of the body. In: Comar CL, Bronner F, eds. *Mineral Metabolism: An Advanced Treatise, Vol. II. The Elements, Part A*. New York: Academic Press.
- Widdowson EM, McCance RA, Spray CM. 1951. The chemical composition of the human body. *Clin Sci* 10:113–125.
- Widman L, Wester PO, Stegmayr BK, Wirell M. 1993. The dose-dependent reduction in blood pressure through administration of magnesium. A double blind placebo controlled cross-over study. *Am J Hypertens* 6:41–45.
- Wiktorsson AM, Martinsson T, Zimmerman M. 1992. Caries prevalence among adults in communities with optimal and low water fluoride concentrations. *Community Dent Oral Epidemiol* 20:359–363.
- Wilkinson R. 1976. Absorption of calcium, phosphorus, and magnesium. In: Nor din BEC, ed. *Calcium, Phosphate and Magnesium Metabolism*. Edinburgh: Churchill Livingstone. Pp. 36–112.
- Willett W. 1990. *Nutritional Epidemiology*. New York, NY: Oxford University Press.
- Willett WC, Sampson L, eds. 1997. Dietary assessment methods. *Am J Clin Nutr* 65:1097S–1368S.
- Williams JE, Zwemer JD. 1990. Community water fluoride levels, preschool dietary patterns, and the occurrence of fluoride dental opacities. *J Pub Hlth Dent* 50:276–281.
- Williams ML, Rose CS, Morrow G, Sloan SE, Barness LA. 1970. Calcium and fat absorption in neonatal period. *Am J Clin Nutr* 23:1322–1330.
- Wilson SG, Retallack RW, Kent JC, Worth GK, Gutteridge DH. 1990. Serum free 1,25-dihydroxyvitamin D and the free 1,25-dihydroxyvitamin D index during a longitudinal study of human pregnancy and lactation. *Clin Endocrinol* 32:613–622.
- Wise A, Gilbert DJ. 1982. Phytate hydrolysis by germfree and conventional rats. *Appl Environ Microbiol* 43:753–756.
- Wisker E, Nagel R, Tanudjaja TK, Feldheim W. 1991. Calcium, magnesium, zinc, and iron balances in young women: Effects of a low-phytate barley-fiber concentrate. *Am J Clin Nutr* 54:553–559.
- Witteman JC, Willett WC, Stampfer MJ, Colditz GA, Sacks FM, Speizer FE, Rosner B, Hennekens CH. 1989. A prospective study of nutritional factors and hypertension among U.S. women. *Circulation* 80:1320–1327.
- Witteman JC, Grobbee DE, Derkx FH, Bouillon R, de Brujin AM, Hofman A. 1994. Reduction of blood pressure with oral magnesium supplementation in women with mild to moderate hypertension. *Am J Clin Nutr* 60:129–135.
- Wong NL, Quamme GA, Dirks JH. 1986. Effects of acid-base disturbances on renal handling of magnesium in the dog. *Clin Sci* 70:277–284.

- Wood RJ, Zheng JJ. 1990. Milk consumption and zinc retention in postmenopausal women. *J Nutr* 120:398–403.
- Wood RJ, Sitrin MD, Rosenberg IH. 1988. Effect of phosphorus on endogenous calcium losses during total parenteral nutrition. *Am J Clin Nutr* 48:632–636.
- Woods KL, Fletcher S. 1994. Long-term outcome after intravenous magnesium sulphate in suspected acute myocardial infarction: The second Leicester Intravenous Magnesium Intervention Trial (LIMIT-2). *Lancet* 343:816–819.
- Workshop Reports. 1992. *J Dent Res* 71:1218–1227.
- Yamagata Z, Miyamura T, Iijima S, Asaka A, Sasaki M, Kato J, Koizumi K. 1994. Vitamin D receptor gene polymorphism and bone mineral density in healthy Japanese women. *Lancet* 344:1027.
- Yamamoto ME, Applegate WB, Klag MJ, Borhani NO, Cohen JD, Kirchner KA, Lakatos E, Sacks FM, Taylor JO, Hennekens CH. 1995. Lack of blood pressure effect with calcium and magnesium supplementation in adults with high-normal blood pressure. Results from Phase I of the Trials of Hypertension Prevention (TOHP). Trials of Hypertension Prevention (TOHP) Collaborative Research Group. *Ann Epidemiol* 5:96–107.
- Yano K, Heilbrun LK, Wasnich RD, Hankin JH, Vogel JM. 1985. The relationship between diet and bone mineral content of multiple skeletal sites in elderly Japanese men and women living in Hawaii. *Am J Clin Nutr* 42:877–888.
- Young GP, Thomas RJ, Bourne DW, Russell DM. 1985. Parenteral nutrition. *Med J Aust* 143:597–601.
- Zeghoud F, Vervel C, Guillozo H, Walrant-Debray O, Boutignon H, Garabedian M. 1997. Subclinical vitamin D deficiency in neonates: Definition and response to vitamin D supplements. *Am J Clin Nutr* 65:771–778.
- Zemel PC, Zemel MB, Urberg M, Douglas FL, Geiser R, Sower JR. 1990. Metabolic and hemodynamic effects of magnesium supplementation in patients with essential hypertension. *Am J Clin Nutr* 51:665–669.
- Ziegler EE, Fomon SJ. 1983. Lactose enhances mineral absorption in infancy. *J Pediatr Gastroenterol Nutr* 2:228–294.
- Zielhuis RL, van der Kreek FW. 1979. The use of a safety factor in setting health-based permissible levels for occupational exposure. *Int Arch Occup Environ Health* 42:191–201.
- Zipkin I, Zucas SM, Lavender DR, Fullmer HM, Schiffmann E, Corcoran BA. 1970. Fluoride and calcification of rat aorta. *Calcif Tissue Res* 6:173–182.

## MANGANESE

*Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*  
(ISBN 0-309-07290-5), Chapter 10, pp. 415–419.

- Anderson RR. 1992. Comparison of trace elements in milk of four species. *J Dairy Sci* 75:3050–3055.
- Aquilio E, Spagnoli R, Seri S, Bottone G, Spennati G. 1996. Trace element content in human milk during lactation of preterm newborns. *Biol Trace Elem Res* 51:63–70.
- Aschner M, Vrana KE, Zheng W. 1999. Manganese uptake and distribution in the central nervous system (CNS). *Neurotoxicology* 20:173–180.
- Barceloux DG. 1999. Manganese. *J Toxicol Clin Toxicol* 37:293–307.
- Behall KM, Scholfield DJ, Lee K, Powell AS, Moser PB. 1987. Mineral balance in adult men: Effect of four refined fibers. *Am J Clin Nutr* 46:307–314.
- Bell JG, Keen CL, Lonnerdal BJ. 1989. Higher retention of manganese in suckling than in adult rats is not due to maturational differences in manganese uptake by rat small intestine. *J Toxicol Environ Health* 26:387–398.
- Bonilla E. 1984. Chronic manganese intake induces changes in the motor activity of rats. *Exp Neurol* 84:696–700.
- Bonilla E, Prasad ALN. 1984. Effects of chronic manganese intake on the levels of biogenic amines in rat brain regions. *Neurobehav Toxicol Teratol* 6:341–344.
- Britton AA, Cotzias GC. 1966. Dependence of manganese turnover on intake. *Am J Physiol* 211:203–206.
- Brock AA, Chapman SA, Ulman EA, Wu G. 1994. Dietary manganese deficiency decreases rat hepatic arginase activity. *J Nutr* 124:340–344.
- Butterworth RF, Spahr L, Fontaine S, Layrargues GP. 1995. Manganese toxicity, dopaminergic dysfunction and hepatic encephalopathy. *Metab Brain Dis* 10:259–267.
- Carmichael S, Abrams B, Selvin S. 1997. The pattern of maternal weight gain in women with good pregnancy outcomes. *Am J Public Health* 87:1984–1988.
- Casey CE, Robinson MF. 1978. Copper, manganese, zinc, nickel, cadmium and lead in human foetal tissues. *Br J Nutr* 39:639–646.
- Casey CE, Hambidge KM, Neville MC. 1985. Studies in human lactation: Zinc, copper, manganese and chromium in human milk in the first month of lactation. *Am J Clin Nutr* 41:1193–1200.
- Casey CE, Neville MC, Hambidge KM. 1989. Studies in human lactation: Secretion of zinc, copper, and manganese in human milk. *Am J Clin Nutr* 49:773–785.
- Cotzias GC, Miller ST, Papavasiliou PS, Tang LC. 1976. Interactions between manganese and brain dopamine. *Med Clin North Am* 60:729–738.
- Davidsson L, Cederblad A, Hagebo E, Lonnerdal B, Sandstrom B. 1988. Intrinsic and extrinsic labeling for studies of manganese absorption in humans. *J Nutr* 118:1517–1521.
- Davidsson L, Cederblad A, Lonnerdal B, Sandstrom B. 1989a. Manganese absorption from human milk, cow's milk, and infant formulas in humans. *Am J Dis Child* 143:823–827.

- Davidsson L, Cederblad A, Lonnerdal B, Sandstrom B. 1989b. Manganese retention in man: A method for estimating manganese absorption in man. *Am J Clin Nutr* 49:170–179.
- Davidsson L, Lonnerdal B, Sandstrom B, Kunz C, Keen CL. 1989c. Identification of transferrin as the major plasma carrier protein for manganese introduced orally or intravenously or after in vitro addition in the rat. *J Nutr* 119:1461–1464.
- Davidsson L, Cederblad A, Lonnerdal B, Sandstrom B. 1991. The effect of individual dietary components on manganese absorption in humans. *Am J Clin Nutr* 54:1065–1070.
- Davidsson L, Almgren A, Juillerat MA, Hurrell RF. 1995. Manganese absorption in humans: The effect of phytic acid and ascorbic acid in soy formula. *Am J Clin Nutr* 62:984–987.
- Davis CD, Greger JL. 1992. Longitudinal changes of manganese-dependent superoxide dismutase and other indexes of manganese and iron status in women. *Am J Clin Nutr* 55:747–752.
- Davis CD, Ney DM, Greger JL. 1990. Manganese, iron and lipid interactions in rats. *J Nutr* 120:507–513.
- Davis CD, Wolf TL, Greger JL. 1992. Varying levels of manganese and iron affect absorption and gut endogenous losses of manganese by rats. *J Nutr* 122:1300–1308.
- Davis CD, Zech L, Greger JL. 1993. Manganese metabolism in rats: An improved methodology for assessing gut endogenous losses. *Proc Soc Exp Biol Med* 202:103–108.
- Doisy EA Jr. 1973. Micronutrient controls on biosynthesis of clotting proteins and cholesterol. In: Hemphill DD, ed. *Trace Substances in Environmental Health*, VI. Columbia, MO: University of Missouri. Pp. 193–199.
- Dreosti IE, Manuel SJ, Buckley RA. 1982. Superoxide dismutase (EC 1.15.1.1), manganese and the effect of ethanol in adult and foetal rats. *Br J Nutr* 48:205–210.
- Fechter LD. 1999. Distribution of manganese in development. *Neurotoxicology* 20:197–201.
- Finley JW. 1999. Manganese absorption and retention by young women is associated with serum ferritin concentration. *Am J Clin Nutr* 70:37–43.
- Finley JW, Johnson PE, Johnson LK. 1994. Sex affects manganese absorption and retention by humans from a diet adequate in manganese. *Am J Clin Nutr* 60:949–955.
- Freeland-Graves J. 1994. Derivation of manganese estimated safe and adequate daily dietary intakes. In: Mertz W, Abernathy CO, Olin SS, eds. *Risk Assessment of Essential Elements*. Washington, DC: ILSI Press. Pp. 237–252.
- Freeland-Graves J, Lin PH. 1991. Plasma uptake of manganese as affected by oral loads of manganese, calcium, milk, phosphorous, copper and zinc. *J Am Coll Nutr* 10:38–43.
- Freeland-Graves J, Turnlund JR. 1996. Deliberations and evaluations of the approaches, endpoints and paradigms for manganese and molybdenum dietary recommendations. *J Nutr* 126:243S–244S.
- Freeland-Graves J, Behmardi F, Bales CW, Dougherty V, Lin PH, Crosby JB, Trickett PC. 1988. Metabolic balance of manganese in young men consuming diets containing five levels of dietary manganese. *J Nutr* 118:764–773.

- Friedman BJ, Freeland-Graves JH, Bales CW, Behmardi F, Shorey-Kutschke RL, Willis RA, Crosby JB, Trickett PC, Houston SD. 1987. Manganese balance and clinical observations in young men fed a manganese-deficient diet. *J Nutr* 117:133–143.
- Garcia-Aranda JA, Wapnir RA, Lifshitz F. 1983. In vivo intestinal absorption of manganese in the rat. *J Nutr* 113:2601–2607.
- Gibson RS. 1994. Content and bioavailability of trace elements in vegetarian diets. *Am J Clin Nutr* 59:1223S–1232S.
- Gibson RS, De Wolfe MS. 1980. The dietary trace metal intake of some Canadian full-term and low birthweight infants during the first twelve months of infancy. *J Can Diet Assoc* 41:206–215.
- Greger JL. 1998. Dietary standards for manganese: Overlap between nutritional and toxicological studies. *J Nutr* 128:368S–371S.
- Greger JL. 1999. Nutrition versus toxicology of manganese in humans: Evaluation of potential biomarkers. *Neurotoxicology* 20:205–212.
- Greger JL, Baligar P, Abernathy RP, Bennett OA, Peterson T. 1978a. Calcium, magnesium, phosphorous, copper, and manganese balance in adolescent females. *Am J Clin Nutr* 31:117–121.
- Greger JL, Zaikis SC, Abernathy RP, Bennett OA, Huffman J. 1978b. Zinc, nitrogen, copper, iron, and manganese balance in adolescent females fed two levels of zinc. *J Nutr* 108:1449–1456.
- Greger JL, Davis CD, Suttie JW, Lyle BJ. 1990. Intake, serum concentrations, and urinary excretion of manganese by adult males. *Am J Clin Nutr* 51:457–461.
- Hallfrisch J, Powell A, Carafelli C, Reiser S, Prather ES. 1987. Mineral balances of men and women consuming high fiber diets with complex or simple carbohydrate. *J Nutr* 117:48–55.
- Hauser RA, Zesiewicz TA, Rosemurgy AS, Martinez C, Olanow CW. 1994. Manganese intoxication and chronic liver failure. *Ann Neurol* 36:871–875.
- Holbrook JT, Smith JC Jr, Reiser S. 1989. Dietary fructose or starch: Effects on copper, zinc, iron, manganese, calcium, and magnesium balances in humans. *Am J Clin Nutr* 49:1290–1294.
- Hunt JR, Matthys LA, Johnson LK. 1998. Zinc absorption, mineral balance, and blood lipids in women consuming controlled lactoovovegetarian and omnivorous diets for 8 weeks. *Am J Clin Nutr* 67:421–430.
- Hurley LS, Keen CL. 1987. Manganese. In: Mertz W, ed. *Trace Elements in Human and Animal Nutrition*, 5th ed. San Diego: Academic Press. Pp. 185–223.
- IOM (Institute of Medicine) 1990. *Nutrition During Pregnancy*. Washington, DC: National Academy Press.
- Ivaturi R, Kies C. 1992. Mineral balances in humans as affected by fructose, high fructose corn syrup and sucrose. *Plant Foods Hum Nutr* 42:143–151.
- Johnson MA, Baier MJ, Greger JL. 1982. Effects of dietary tin on zinc, copper, iron, manganese, and magnesium metabolism of adult males. *Am J Clin Nutr* 35:1332–1338.
- Johnson P, Lykken G. 1991. Manganese and calcium absorption and balance in young women fed diets with varying amounts of manganese and calcium. *J Trace Elem Exp Med* 4:19–35.
- Johnson PE, Lykken GI, Korynta ED. 1991. Absorption and biological half-life in humans of intrinsic and extrinsic  $^{54}\text{Mn}$  tracers from foods of plant origin. *J Nutr* 121:711–717.

## ONLINE REFERENCES

## 1187

- Kawamura R, Ikuta H, Fukuzumi S, Yamada R, Tsubaki S, Kodama T, Kurata S. 1941. Intoxication by manganese in well water. *Kitasato Arch Exp Med* 18:145–169.
- Keen CL, Zidenberg-Cherr S, Lonnerdal B. 1994. Nutritional and toxicological aspects of manganese intake: An overview. In: Mertz W, Abernathy CO, Olin SS, eds. *Risk Assessment of Essential Elements*. Washington, DC: ILSI Press. Pp. 221–235.
- Keen CL, Ensunsa JL, Watson MH, Baly DL, Donovan SM, Monaco MH, Clegg MS. 1999. Nutritional aspects of manganese from experimental studies. *Neurotoxicology* 20:213–223.
- Kelly DA. 1998. Liver complications of pediatric parenteral nutrition—epidemiology. *Nutrition* 14:153–157.
- Komura J, Sakamoto M. 1992. Effects of manganese forms on biogenic amines in the brain and behavioral alterations in the mouse: Long-term oral administration of several manganese compounds. *Environ Res* 57:34–44.
- Kondakis XG, Makris N, Leotsinidis M, Prinou M, Papapetropoulos T. 1989. Possible health effects of high manganese concentration in drinking water. *Arch Environ Health* 44:175–178.
- Krishna G, Whitlock HW Jr, Feldbruegge DH, Porter JW. 1966. Enzymatic conversion of farnesyl pyrophosphate to squalene. *Arch Biochem Biophys* 114: 200–215.
- Lonnerdal B, Keen CL, Hurley LS. 1981. Iron, copper, zinc and manganese in milk. *Ann Rev Nutr* 1:149–174.
- Lutz TA, Schroff A, Scharrer E. 1993. Effects of calcium and sugars on intestinal manganese absorption. *Biol Trace Elem Res* 39:221–227.
- Malecki EA, Huttner DL, Greger JL. 1994. Manganese status, gut endogenous losses of manganese, and antioxidant enzyme activity in rats fed varying levels of manganese and fat. *Biol Trace Elem Res* 42:17–29.
- McLeod BE, Robinson MF. 1972. Metabolic balance of manganese in young women. *Br J Nutr* 27:221–227.
- Morris SM Jr. 1992. Regulation of enzymes of urea and arginine synthesis. *Ann Rev Nutr* 12:81–101.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance Data, Vital and Health Statistics of the National Center for Health Statistics, Number 174. Hyattsville, MD: National Center for Health Statistics.
- Murthy GK. 1974. Trace elements in milk. *Crit Rev Environ Control* 4:1–38.
- Newland MC. 1999. Animal models of manganese's neurotoxicity. *Neurotoxicology* 20:415–432.
- Pappas BA, Zhang D, Davidson CM, Crowder T, Park GAS, Fortin T. 1997. Perinatal manganese exposure: Behavioral, neurochemical, and histopathological effects in the rat. *Neurotoxicol Teratol* 19:17–25.
- Patterson KY, Holbrook JT, Bodner JE, Kelsay JL, Smith JC Jr, Veillon C. 1984. Zinc, copper, and manganese intake and balance for adults consuming self-selected diets. *Am J Clin Nutr* 40:1397–1403.
- Paynter DI. 1980. Changes in activity of the manganese superoxide dismutase enzyme in tissues of the rat with changes in dietary manganese. *J Nutr* 110:437–447.
- Penland JG, Johnson PE. 1993. Dietary calcium and manganese effects on menstrual cycle symptoms. *Am J Obstet Gynecol* 168:1417–1423.
- Pennington JA, Young BE. 1991. Total Diet Study nutritional elements, 1982–1989. *J Am Diet Assoc* 91:179–183.

- Rabin O, Hegedus L, Bourre JM, Smith QR. 1993. Rapid brain uptake of manganese (II) across the blood-brain barrier. *J Neurochem* 61:509–517.
- Rossander-Hulten L, Brune M, Sandstrom B, Lonnerdal B, Hallberg L. 1991. Competitive inhibition of iron absorption by manganese and zinc in humans. *Am J Clin Nutr* 54:152–156.
- Sandstrom B, Davidsson L, Cederblad A, Eriksson R, Lonnerdal B. 1986. Manganese absorption and metabolism in man. *Acta Pharmacol Toxicol* 59:60–62.
- Sandstrom B, Davidsson L, Eriksson R, Alpsten M, Bogentoft C. 1987. Retention of selenium (75Se), Zinc (65Zn) and manganese (54Mn) in humans after intake of a labelled vitamin and mineral supplement. *J Trace Elem Electrolytes Health Dis* 1:33–38.
- Sandstrom B, Davidsson L, Erickson RA, Alpsten M. 1990. Effects of long-term trace element supplementation on blood trace element levels and absorption of (75Se), (54Mn), and (65Zn). *J Trace Elem Electrolytes Health Dis* 4:65–72.
- Schroeder HA, Balassa JJ, Tipton IH. 1966. Essential trace metals in man: Manganese. A study in homeostasis. *J Chron Dis* 19:545–571.
- Senturk UK, Oner G. 1996. The effect of manganese-induced hypercholesterolemia on learning in rats. *Biol Trace Elem Res* 51:249–257.
- Spahr L, Butterworth RF, Fontaine S, Bui L, Therrien G, Milette PC, Lebrun LH, Zayed J, LeBlanc A, Pomier-Layrargues G. 1996. Increased blood manganese in cirrhotic patients: Relationship to pallidal magnetic resonance signal hyperintensity and neurological symptoms. *Hepatology* 24:1116–1120.
- Spencer H, Asmussen CR, Holtzman RB, Kramer L. 1979. Metabolic balances of cadmium, copper, manganese, and zinc in man. *Am J Clin Nutr* 32:1867–1875.
- Stastny D, Vogel RS, Picciano MF. 1984. Manganese intake and serum manganese concentration of human milk-fed and formula-fed infants. *Am J Clin Nutr* 39:872–878.
- Strause L, Saltman P. 1987. Role of manganese in bone metabolism. In: Kies C, ed. *Nutritional Bioavailability of Manganese*. Washington, DC: American Chemical Society. Pp. 46–55.
- Strause L, Hegenauer J, Saltman P, Cone R, Resnick D. 1986. Effects of long-term dietary manganese and copper deficiency on rat skeleton. *J Nutr* 116:135–141.
- Strause L, Saltman P, Glowacki J. 1987. The effect of deficiencies of manganese and copper on osteoinduction and on resorption of bone particles in rats. *Calcif Tissue Int* 41:145–150.
- Velazquez SF, Du JT. 1994. Derivation of the reference dose for manganese. In: Mertz W, Abernathy CO, Olin SS, eds. *Risk Assessment of Essential Elements*. Washington, DC: ILSI Press. Pp. 253–266.
- Vieregge P, Heinzw B, Korf G, Teichert HM, Schleifenbaum P, Mosinger HU. 1995. Long term exposure to manganese in rural well water has no neurological effects. *Can J Neurol Sci* 22:286–289.
- Zidenberg-Cherr S, Keen CL, Lonnerdal B, Hurley LS. 1983. Superoxide dismutase activity and lipid peroxidation in the rat: Developmental correlations affected by manganese deficiency. *J Nutr* 113:2498–2504.

Ibid., Chapter 14, pp. 578–579.

Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.

- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Examination Survey: Under-reporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Gibson RS, Ferguson EL. 1998. Assessment of dietary zinc in a population. *Am J Clin Nutr* 68:430S–434S.
- Hallberg L, Hulthen L. 2000. Prediction of dietary iron absorption: An algorithm for calculating absorption and bioavailability of dietary iron. *Am J Clin Nutr* 71:1147–1160.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1980. *Recommended Dietary Allowances*, 9th ed. Washington, DC: National Academy Press.
- NRC. 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC. 1989. *Recommended Dietary Allowances*, 10th ed. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Schoeller DA. 1999. Recent advances from application of doubly labeled water to measurement of human energy expenditure. *J Nutr* 129:1765–1768.
- USDA (U.S. Department of Agriculture). 1999. *USDA Nutrient Database for Standard Reference*, Release 13. [Online.] Available: <http://www.nal.usda.gov/fnic/foodcomp> [accessed February 2000].
- WHO (World Health Organization). 1996. Zinc. In: *Trace Elements in Human Nutrition and Health*. Geneva: WHO. Pp. 72–104.

## MOLYBDENUM

*Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*  
 (ISBN 0-309-07290-5), Chapter 11, pp. 439–441.

- Abumrad NN, Schneider AJ, Steel D, Rogers LS. 1981. Amino acid intolerance during prolonged total parenteral nutrition reversed by molybdate therapy. *Am J Clin Nutr* 34:2551–2559.
- Anderson RR. 1992. Comparison of trace elements in milk of four species. *J Dairy Sci* 75:3050–3055.
- Anke M, Groppel B, Kronemann H, Grun M. 1985. Molybdenum supply and status in animals and human beings. *Nutr Res* 1:S180–S186.
- Aquilio E, Spagnoli R, Seri S, Bottone G, Spennati G. 1996. Trace element content in human milk during lactation of preterm newborns. *Biol Trace Elem Res* 51:63–70.
- Arrington LR, Davis GK. 1953. Molybdenum toxicity in the rabbit. *J Nutr* 51:295–304.
- Arthur D. 1965. Interrelationships of molybdenum and copper in the diet of the guinea pig. *J Nutr* 87:69–76.
- Asmangulyan TA. 1965. The maximum permissible concentration of molybdenum in the water of surface water basins. *Gig Sanit* 30:6–11.
- Biego GH, Joyeux M, Hartemann P, Debry G. 1998. Determination of mineral contents in different kinds of milk and estimation of dietary intake in infants. *Food Addit Contam* 15:775–781.
- Bompart G, Pecher C, Prevot D, Girolami JP. 1990. Mild renal failure induced by subchronic exposure to molybdenum: Urinary kallikrein excretion as a marker of distal tubular effect. *Toxicol Lett* 52:293–300.
- Bougle D, Bureau F, Foucault P, Duhamel J-F, Muller G, Drosdowsky M. 1988. Molybdenum content of term and preterm human milk during the first 2 months of lactation. *Am J Clin Nutr* 48:652–654.
- Bremner I. 1979. The toxicity of cadmium, zinc and molybdenum and their effects on copper metabolism. *Proc Nutr Soc* 38:235–242.
- Cantone MC, de Bartolo D, Gambarini G, Giussani A, Ottolenghi A, Pirola L. 1995. Proton activation analysis of stable isotopes for a molybdenum biokinetics study in humans. *Med Phys* 22:1293–1298.
- Carmichael S, Abrams B, Selvin S. 1997. The pattern of maternal weight gain in women with good pregnancy outcomes. *Am J Public Health* 87:1984–1988.
- Casey CE, Neville MC. 1987. Studies in human lactation 3: Molybdenum and nickel in human milk during the first month of lactation. *Am J Clin Nutr* 45:921–926.
- Chappell WR, Meglen RR, Moure-Eraso R, Solomons CC, Tsongas TA, Walravens PA, Winston PW. 1979. *Human Health Effects of Molybdenum in Drinking Water*. EPA-600/1-79-006. Cincinnati, OH: U.S. Environmental Protection Agency, Health Effects Research Laboratory.
- Deosthale YG, Gopalan C. 1974. The effect of molybdenum levels in sorghum (*Sorghum vulgare Pers.*) on uric acid and copper excretion in man. *Br J Nutr* 31:351–355.
- Engel RW, Price NO, Miller RF. 1967. Copper, manganese, cobalt, and molybdenum balance in preadolescent girls. *J Nutr* 92:197–204.

- Friel JK, MacDonald AC, Mercer CN, Belkhode SL, Downton G, Kwa PG, Aziz K, Andrews WL. 1999. Molybdenum requirements in low-birth-weight infants receiving parenteral and enteral nutrition. *J Parenter Enteral Nutr* 23:155–159.
- Fungwe TV, Buddingh F, Demick DS, Lox CD, Yang MT, Yang SP. 1990. The role of dietary molybdenum on estrous activity, fertility, reproduction and molybdenum and copper enzyme activities of female rats. *Nutr Res* 10:515–524.
- Hurrell RF, Juillerat MA, Reddy MB, Lynch SR, Dassenko SA, Cook JD. 1992. Soy protein, phytate and iron absorption in humans. *Am J Clin Nutr* 56:573–578.
- IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Washington, DC: National Academy Press.
- Jeter MA, Davis GK. 1954. The effect of dietary molybdenum upon growth, hemoglobin, reproduction and lactation of rats. *J Nutr* 54:215–220.
- Johnson JL. 1997. Molybdenum. In: O'Dell BL, Sunde RA, eds. *Handbook of Nutritionally Essential Mineral Elements. Clinical Nutrition in Health and Disease*. New York: Marcel Dekker. Pp. 413–438.
- Johnson JL, Rajagopalan KV, Wadman SK. 1993. Human molybdenum cofactor deficiency. In: Ayling JE, Nair GM, Baugh CM, eds. *Chemistry and Biology of Pteridines and Folates*. New York: Plenum Press. Pp. 373–378.
- Kovalsky VV, Yarovaya GA, Shmavonyan DM. 1961. The change in purine metabolism of humans and animals under the conditions of molybdenum biogeochemical provinces. *Zh Obshch Biol* 22:179–191.
- Krachler M, Li FS, Rossipal E, Irgolic KJ. 1998. Changes in the concentrations of trace elements in human milk during lactation. *J Trace Elem Med Biol* 12:159–176.
- McCarter A, Riddell PE, Robinson GA. 1962. Molybdenosis induced in laboratory rabbits. *Can J Biochem Physiol* 40:1415–1425.
- Miller RF, Price NO, Engel RW. 1956. Added dietary inorganic sulfate and its effect upon rats fed molybdenum. *J Nutr* 60:539–547.
- Mills CF, Davis GK. 1987. Molybdenum. In: Mertz W, ed. *Trace Elements in Human and Animal Nutrition*, Vol. 1. San Diego: Academic Press. Pp. 429–463.
- Nielsen FH. 1999. Ultratrace minerals. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th ed. Baltimore: Williams & Wilkins. Pp. 283–303.
- O'Dell BL. 1989. Mineral interactions relevant to nutrient requirements. *J Nutr* 119:1832–1838.
- Ostrom CA, Van Reen R, Miller CW. 1961. Changes in the connective tissue of rats fed toxic diets containing molybdenum salts. *J Dent Res* 40:520–528.
- Paschal DC, Ting BG, Morrow JC, Pirkle JL, Jackson RJ, Sampson EJ, Miller DT, Caldwell KL. 1998. Trace metals of United States residents: reference range concentrations. *Environ Res* 76:53–59.
- Pennington JAT, Jones JW. 1987. Molybdenum, nickel, cobalt, vanadium, and strontium in total diets. *J Am Diet Assoc* 87:1644–1650.
- Rajagopalan KV. 1988. Molybdenum: An essential trace element in human nutrition. *Ann Rev Nutr* 8:401–427.
- Rosoff B, Spencer H. 1964. Fate of molybdenum-99 in man. *Nature* 202:410–411.
- Rossipal E, Krachler M. 1998. Pattern of trace elements in human milk during the course of lactation. *Nutr Res* 18:11–24.
- Schroeder HA, Mitchener M. 1971. Toxic effects of trace elements on the reproduction of mice and rats. *Arch Environ Health* 23:102–106.

- Tsongas TA, Meglen RR, Walravens PA, Chappell WR. 1980. Molybdenum in the diet: An estimate of average daily intake in the United States. *Am J Clin Nutr* 33:1103–1107.
- Turnlund JR, Keyes WR. 2000. Dietary molybdenum: Effect on copper absorption, excretion, and status in young men. In: Roussel AM, Anderson RA, Favier A, eds. *Trace Elements in Man and Animals 10*. New York: Kluwer Academic.
- Turnlund JR, Keyes WR, Peiffer GL. 1995a. Molybdenum absorption, excretion, and retention studied with stable isotopes in young men at five intakes of dietary molybdenum. *Am J Clin Nutr* 62:790–796.
- Turnlund JR, Keyes WR, Peiffer GL, Chiang G. 1995b. Molybdenum absorption, excretion, and retention studied with stable isotopes in young men during depletion and repletion. *Am J Clin Nutr* 61:1102–1109.
- Turnlund JR, Weaver CM, Kim SK, Keyes WR, Gizaw Y, Thompson KH, Peiffer GL. 1999. Molybdenum absorption and utilization in humans from soy and kale intrinsically labeled with stable isotopes of molybdenum. *Am J Clin Nutr* 69:1217–1223.
- Valli VE, McCarter A, McSherry BJ, Robinson GA. 1969. Hematopoiesis and epiphyseal growth zones in rabbits with molybdenosis. *Am J Vet Res* 30:435–445.
- Versieck J, Hoste J, Barbier F, Vanballenberghe L, De Rudder J, Cornelis R. 1978. Determination of molybdenum in human serum by neutron activation analysis. *Clin Chim Acta* 87:135–140.
- Vyskocil A, Viau C. 1999. Assessment of molybdenum toxicity in humans. *J Appl Toxicol* 19:185–192.
- WHO (World Health Organization). 1996. *Trace Elements in Human Nutrition and Health*. Geneva: WHO. Pp. 144–154.

Ibid., Chapter 14, pp. 578–579.

- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Examination Survey: Under-reporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Gibson RS, Ferguson EL. 1998. Assessment of dietary zinc in a population. *Am J Clin Nutr* 68:430S–434S.
- Hallberg L, Hulthen L. 2000. Prediction of dietary iron absorption: An algorithm for calculating absorption and bioavailability of dietary iron. *Am J Clin Nutr* 71:1147–1160.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.

## ONLINE REFERENCES

1193

- NRC (National Research Council). 1980. *Recommended Dietary Allowances*, 9th ed. Washington, DC: National Academy Press.
- NRC. 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC. 1989. *Recommended Dietary Allowances*, 10th ed. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Schoeller DA. 1999. Recent advances from application of doubly labeled water to measurement of human energy expenditure. *J Nutr* 129:1765–1768.
- USDA (U.S. Department of Agriculture). 1999. *USDA Nutrient Database for Standard Reference*, Release 13. [Online.] Available: <http://www.nal.usda.gov/fnic/foodcomp> [accessed February 2000].
- WHO (World Health Organization). 1996. Zinc. In: *Trace Elements in Human Nutrition and Health*. Geneva: WHO. Pp. 72–104.

## PHOSPHORUS

*Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride (ISBN 0-309-06350-7), pp. 325–374.*

- Abbott L, Nadler J, Rude RK. 1994. Magnesium deficiency in alcoholism: Possible contribution to osteoporosis and cardiovascular disease in alcoholics. *Alcohol Clin Exp Res* 18:1976–1082.
- Abe E, Miyaura C, Sakagami H, Takeda M, Konno K, Yamazaki T, Yoshiki S, Suda T. 1981. Differentiation of mouse myeloid leukemia cells induced by 1 $\alpha$ 25-dihydroxyvitamin D<sub>3</sub>. *Proc Natl Acad Sci USA* 78:4990–4994.
- Abraham GE, Grewal H. 1990. A total dietary program emphasizing magnesium instead of calcium: Effect on the mineral density of calcaneous bone in postmenopausal women on hormonal therapy. *J Reprod Med* 35:503–507.
- Abrams SA, Stuff JE. 1994. Calcium metabolism in girls: Current dietary intakes lead to low rates of calcium absorption and retention during puberty. *Am J Clin Nutr* 60:739–743.
- Abrams SA, Sidbury JB, Muenzer J, Esteban NV, Vieira NE, Yerger AL. 1991. Stable isotopic measurement of endogenous fecal calcium excretion in children. *J Pediatr Gastroenterol Nutr* 12:469–473.
- Abrams SA, Esteban NV, Vieira NE, Sidbury JB, Specker BL, Yerger AL. 1992. Developmental changes in calcium kinetics in children assessed using stable isotopes. *J Bone Miner Res* 7:287–293.
- Abrams SA, Silber TJ, Esteban NV, Vieira NE, Stuff JE, Meyers R, Majd M, Yerger AL. 1993. Mineral balance and bone turnover in adolescents with anorexia nervosa. *J Pediatr* 123:326–331.
- Abrams SA, O'Brien KO, Stuff JE. 1996a. Changes in calcium kinetics associated with menarche. *J Clin Endocrinol Metab* 81:2017–2020.
- Abrams SA, O'Brien KO, Wen J, Liang LK, Stuff JE. 1996b. Absorption by 1-year-old children of an iron supplement given with cow's milk or juice. *Pediatr Res* 39:171–175.
- Abrams SA, Wen J, Stuff JE. 1997a. Absorption of calcium, zinc and iron from breast milk by 5- to 7-month-old infants. *Pediatr Res* 41:1–7.
- Abrams SA, Grusak MA, Stuff J, O'Brien KO. 1997b. Calcium and magnesium balance in 9- to 14-year-old children. *Am J Clin Nutr* 66:1172–1177.
- Abreo K, Adlakha A, Kilpatrick S, Flanagan R, Webb R, Shakamuri S. 1993. The Milk-Alkali Syndrome. A reversible form of acute renal failure. *Arch Intern Med* 153:1005–1010.
- Ackerman PG, Toro G. 1953. Calcium and phosphorus balance in elderly men. *J Gerontol* 8:298–300.
- ADA (American Dental Association Council on Dental Therapeutics). 1994. New fluoride guidelines proposed. *J Am Dent Assoc* 125:366.
- Adams JS. 1989. Vitamin D metabolite-mediated hypercalcemia. *Endocrinol Metab Clin North Am* 18:765–778.
- Adams JS, Beeker TG, Hongo T, Clemens TL. 1990. Constitutive expression of a vitamin D 1-hydroxylase in a myelomonocytic cell line: A model for studying 1,25-dihydroxyvitamin D production in vitro. *J Bone Miner Res* 5:1265–1269.
- Affinito P, Tommaselli GA, DiCarlo C, Guida F, Nappi C. 1996. Changes in bone mineral density and calcium metabolism in breast-feeding women: A one year follow-up study. *J Clin Endocrinol Metab* 81:2314–2318.

- Aksnes L, Aarskog D. 1982. Plasma concentrations of vitamin D metabolites in puberty: Effect of sexual maturation and implications for growth. *J Clin Endocrinol Metab* 55:94–101.
- Ala-Houhala M. 1985. 25-Hydroxyvitamin D levels during breast-feeding with or without maternal or infantile supplementation of vitamin D. *J Pediatr Gastroenterol Nutr* 4:220–226.
- Ala-Houhala M, Parvianinen MT, Pyyko K, Visakorpi JK. 1984. Serum 25-hydroxyvitamin D levels in Finnish children aged 2 to 17 years. *Acta Paediatr Scand* 73:232–236.
- Ala-Houhala M, Koskinen T, Terho A, Koivula T, Visakorpi J. 1986. Maternal compared with infant vitamin D supplementation. *Arch Dis Child* 61:1159–1163.
- Alaimo K, McDowell MA, Briefel RR, Bischof AM, Caughman CR, Loria CM, Johnson CL. 1994. *Dietary Intake of Vitamins, Minerals, and Fiber of Persons Ages 2 Months and Over in the United States: Third National Health and Nutrition Examination Survey, Phase I, 1988–91*. Advance data from vital and health statistics; no. 258. U.S. Department of Health and Human Services. Hyattsville, MD: National Center for Health Statistics.
- Albert DG, Morita Y, Iseri LT. 1958. Serum magnesium and plasma sodium levels in essential vascular hypertension. *Circulation* 17:761–764.
- Alderman BW, Weiss NS, Daling JR, Ure CL, Ballard JH. 1986. Reproductive history and postmenopausal risk of hip and forearm fracture. *Am J Epidemiol* 124:262–267.
- Alfrey AC, Miller NL, Butkus D. 1974. Evaluation of body magnesium stores. *J Lab Clin Med* 84:153–162.
- Allen JC, Keller RP, Archer P, Neville MC. 1991. Studies in human lactation: Milk composition and daily secretion rates of macronutrients in the first year of lactation. *Am J Clin Nutr* 54:69–80.
- Allen SH, Shah JH. 1992. Calcinosis and metastatic calcification due to vitamin D intoxication. A case report and review. *Horm Res* 37:68–77.
- Allender PS, Cutler JA, Follmann D, Cappuccio FP, Pryer J, Elliott P. 1996. Dietary calcium and blood pressure: A meta-analysis of randomized clinical trials. *Ann Intern Med* 124:825–831.
- Aloia JF, Vaswani AN, Yeh JK, Ross P, Ellis K, Cohn SH. 1983. Determinants of bone mass in postmenopausal women. *Arch Intern Med* 143:1700–1704.
- Aloia JF, Vaswani AN, Yeh JK, Ellis K, Cohn SH. 1984. Total body phosphorus in postmenopausal women. *Miner Electrolyte Metab* 10:73–76.
- Aloia JF, Vaswani A, Yeh JK, Ross PL, Flaster E, Dilmanian FA. 1994. Calcium supplementation with and without hormone replacement therapy to prevent postmenopausal bone loss. *Ann Intern Med* 120:97–103.
- Altura BT, Brust M, Bloom S, Barbour RL, Stempak JG, Altura BM. 1990. Magnesium dietary intake modulates blood lipid levels and atherogenesis. *Proc Natl Acad Sci USA* 87:1840–1844.
- Altura BT, Shirey TL, Hiti J, Dell'Orfano K, Handwerker SM, Altura BM. 1992. A new method for the rapid determination of ionized Mg<sup>2+</sup> in whole blood, serum and plasma. *Methods Find Exp Clin Pharmacol* 14:297–304.
- Altura BT, Wilimizig C, Trnovec T, Nyulassy S, Altura BM. 1994. Comparative effects of a Mg-enriched diet and different orally administered magnesium oxide preparations on ionized Mg, Mg metabolism and electrolytes in serum of human volunteers. *J Am Coll Nutr* 13:447–454.
- American Academy of Pediatrics. 1982. The promotion of breastfeeding: Policy statement based on task force report. *Pediatrics* 69:654–661.

- Anderson DM, Hollis BW, LeVine BR, Pittard WB III. 1988. Dietary assessment of maternal vitamin D intake and correlation with maternal and neonatal serum vitamin D concentrations at delivery. *J Perinatol* 8:46–48.
- Andon MB, Ilich JZ, Tzagournis MA, Matkovic V. 1996. Magnesium balance in adolescent females consuming a low- or high-calcium diet. *Am J Clin Nutr* 63:950–953.
- Angus RM, Sambrook PN, Pockock NA, Eisman JA. 1988. Dietary intake and bone mineral density. *Bone Miner* 4:265–277.
- Antman EM. 1996. Magnesium in acute myocardial infarction: Overview of available evidence. *Am Heart J* 132:487–495.
- Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin PH, Karanja N. 1997. A clinical trial of the effects of dietary patterns on blood pressure. *N Engl J Med* 336:1117–1124.
- Arnold FA Jr, Dean HT, Jay P, Knutson JW. 1956. Effect of fluoridated public water supplies on dental caries prevalence. Tenth year of the Grand Rapids-Muskegon Study. *Pub Hlth Rep* 71:652–658.
- Ascherio A, Rimm EB, Giovannucci EL, Colditz GA, Rosner B, Willett WC, Sacks F, Stampfer MJ. 1992. A prospective study of nutritional factors and hypertension among U.S. men. *Circulation* 86:1475–1484.
- Ashe JR, Schofield FA, Gram MR. 1979. The retention of calcium, iron, phosphorus, and magnesium during pregnancy: The adequacy of prenatal diets with and without supplementation. *Am J Clin Nutr* 32:286–291.
- Atkinson SA, Chappell JE, Clandinin MT. 1987. Calcium supplementation of mothers' milk for low birthweight infants: Problems related to absorption and excretion. *Nutr Res* 7:813–823.
- Atkinson SA, Alston-Mills BP, Lonnerdal B, Neville MC, Thompson MP. 1995. Major minerals and ionic constituents of human and bovine milk. In: Jensen RJ, ed. *Handbook of Milk Composition*. California: Academic Press. Pp. 593–619.
- Bainbridge RR, Mimouni FB, Landi T, Crossman M, Harris L, Tsang RC. 1996. Effect of rice cereal feedings on bone mineralization and calcium homeostasis in cow milk formula fed infants. *J Am Coll Nutr* 15:383–388.
- Baran D, Sorensen A, Grimes J, Lew R, Karella A, Johnson B, Roche J. 1990. Dietary modification with dairy products for preventing vertebral bone loss in premenopausal women: A three-year prospective study. *J Clin Endocrinol Metab* 70:264–270.
- Bardicef M, Bardicef O, Sorokin Y, Altura BM, Altura BT, Cotton DB, Resnick LM. 1995. Extracellular and intracellular magnesium depletion in pregnancy and gestational diabetes. *Am J Obstet Gynecol* 172:1009–1013.
- Barger-Lux MJ, Heaney RP. 1995. Caffeine and the calcium economy revisited. *Osteopor Int* 5:97–102.
- Barger-Lux MJ, Heaney RP, Stegman MR. 1990. Effects of moderate caffeine intake on the calcium economy of premenopausal women. *Am J Clin Nutr* 52:722–725.
- Barger-Lux MJ, Heaney RP, Lanspa SJ, Healy JC, DeLuca HF. 1995. An investigation of sources of variation in calcium absorption efficiency. *J Clin Endocrinol Metab* 80:406–411.
- Barger-Lux MJ, Heaney RP, Dowell S, Bierman J, Holick MF, Chen TC. 1996. Relative molar potency of 25-hydroxyvitamin D indicates a major role in calcium absorption. *J Bone Miner Res* 11:S423.

- Barnhart WE, Hiller LK, Leonard GJ, Michaels SE. 1974. Dentifrice usage and ingestion among four age groups. *J Dent Res* 53:1317–1322.
- Barragry JM, France MW, Corless D, Gupta SP, Switala S, Boucher BJ, Cohen RD. 1978. Intestinal cholecalciferol absorption in the elderly and in younger adults. *Clin Sci Molec Med* 55:213–220.
- Barrett-Connor E, Chang JC, Edelstein SL. 1994. Coffee-associated osteoporosis offset by daily milk consumption. The Rancho Bernardo Study. *J Am Med Assoc* 271:280–283.
- Bashir Y, Sneddon JF, Staunton HA, Haywood GA, Simpson IA, McKenna WJ, Camm AJ. 1993. Effects of long-term oral magnesium chloride replacement in congestive heart failure secondary to coronary artery disease. *Am J Cardiol* 72:1156–1162.
- Beall DP, Scofield RH. 1995. Milk-alkali syndrome associated with calcium carbonate consumption: Report of 7 patients with parathyroid hormone levels and an estimate of prevalence among patients hospitalized with hypercalcemia. *Medicine* 74:89–96.
- Beaton GH. 1994. Criteria of an adequate diet. In: Shils RE, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease, 8th edition*. Philadelphia: Lea & Febiger. Pp. 1491–1505.
- Beaton GH. 1996. Statistical approaches to establish mineral element recommendations. *J Nutr* 126:2302S–2328S.
- Begum A, Pereira SM. 1969. Calcium balance studies on children accustomed to low calcium intakes. *Br J Nutr* 23:905–911.
- Bell NH, Greene A, Epstein S, Oexmann MJ, Shaw S, Shary J. 1985. Evidence for alteration of the vitamin D-endocrine system in blacks. *J Clin Invest* 76:470–473.
- Bell NH, Shary J, Stevens J, Garza M, Gordon L, Edwards J. 1991. Demonstration that bone mass is greater in black than in white children. *J Bone Miner Res* 6:719–723.
- Bell NH, Yergey AL, Vieira NE, Oexmann MJ, Shary JR. 1993. Demonstration of a difference in urinary calcium, not calcium absorption, in black and white adolescents. *J Bone Miner Res* 8:1111–1115.
- Bell RA, Whitford GM, Barenie JT, Myers DR. 1985. Fluoride retention in children using self-applied topical fluoride products. *Clin Prev Dent* 7:22–27.
- Berkelhammer CH, Wood RJ, Sitrin MD. 1988. Acetate and hypercalciuria during total parenteral nutrition. *Am J Clin Nutr* 48:1482–1489.
- Bernstein DS, Sadowsky N, Hegsted DM, Guri CD, Stare FJ. 1966. Prevalence of osteoporosis in high- and low-fluoride areas in North Dakota. *J Am Med Assoc* 198:499–504.
- Bijvoet, OLM. 1969. Relation of plasma phosphate concentration to renal tubular reabsorption of phosphate. *Clin Sci* 37:23–26.
- Bikle DD, Gee E, Halloran B, Haddad JG. 1984. Free 1,25-dihydroxyvitamin D levels in serum from normal subjects, pregnant subjects, and subjects with liver disease. *J Clin Invest* 74:1966–1971.
- Birkeland JM, Charlton G. 1976. Effect of pH on the fluoride ion activity of plaque. *Caries Res* 10:72–80.
- Bishop NJ, Dahlenburg SL, Fewtrell MS, Morley R, Lucas A. 1996. Early diet of preterm infants and bone mineralization at age five years. *Acta Paediatr* 85:230–236.
- Bizik BK, Ding W, Cerklewski FL. 1996. Evidence that bone resorption of young men is not increased by high dietary phosphorus obtained from milk and cheese. *Nutr Res* 16:1143–1146.

- Black DM, Cummings SR, Genant HK, Nevitt MC, Palermo L, Browner W. 1992. Axial and appendicular bone density predict fractures in older women. *J Bone Miner Res* 7:633–638.
- Blank S, Scanlon KS, Sinks TH, Lett S, Falk H. 1995. An outbreak of hypervitaminosis D associated with the overfortification of milk from a home-delivery dairy. *Am J Publ Health* 85:656–659.
- Blayney JR, Hill IN. 1964. Evanston dental caries study XXIV. Prenatal fluorides—value of waterborne fluorides during pregnancy. *J Am Dent Assoc* 69:291–294.
- Bodanszky H, Leleiko N. 1985. Metabolic alkalosis with hypertonic dehydration in a patient with diarrhoea and magnesium oxide ingestion. *Acta Paediatr Hung* 26:241–246.
- Bogdonoff MD, Shock NW, Nichols MP. 1953. Calcium, phosphorus, nitrogen, and potassium balance studies in the aged male. *J Gerontol* 8:272–288.
- Bostick RM, Potter JD, Fosdick L, Grambsch P, Lampe JW, Wood JR, Louis TA, Ganz R, Grandits G. 1993. Calcium and colorectal epithelial cell proliferation: A preliminary randomized, double-blinded, placebo-controlled clinical trial. *J Natl Cancer Inst* 85:132–141.
- Boston JL, Beauchene RE, Cruikshank DP. 1989. Erythrocyte and plasma magnesium during teenage pregnancy: Relationship with blood pressure and pregnancy-induced hypertension. *Obstet Gynecol* 73:169–174.
- Bouillon R, Van Assche FA, Van Baelen H, Heyns W, De Moor P. 1981. Influence of the vitamin D-binding protein on the serum concentration of 1,25-dihydroxyvitamin D<sub>3</sub>. Significance of the free 1,25-dihydroxyvitamin D<sub>3</sub> concentration. *J Clin Invest* 67:589–596.
- Bour NJS, Soullier BA, Zemel MB. 1984. Effect of level and form of phosphorus and level of calcium intake on zinc, iron and copper bioavailability in man. *Nutr Res* 4:371–379.
- Bowden GH. 1990. Effects of fluoride on the microbial ecology of dental plaque. *J Dent Res* 69 (Spec Iss):653–659.
- Boyle DR, Chagnon M. 1995. An incidence of skeletal fluorosis associated with groundwaters of the maritime carboniferous basin, Gaspe Region, Quebec, Canada. *Environ Geochem Health* 17:5–12.
- BPA (British Paediatric Association). 1956. Hypercalcaemia in infants and Vitamin D. *Br Med J* 2:149.
- BPA (British Paediatric Association). 1964. Infantile hypercalcaemia, nutritional rickets, and infantile scurvy in Great Britain. *Br Med J* 1:1659–1661.
- Brambilla E, Belluomo G, Malerba A, Buscaglia M, Strohmenger L. 1994. Oral administration of fluoride in pregnant women, and the relation between concentration in maternal plasma and in amniotic fluid. *Arch Oral Biol* 39:991–994.
- Brandwein SL, Sigman, KM. 1994. Case report: Milk-alkali syndrome and pancreatitis. *Am J Med Sci* 308:173–176.
- Brannan PG, Vergne-Marini P, Pak CY, Hull AR, Fordtran JS. 1976. Magnesium absorption in the human small intestine. Results in normal subjects, patients with chronic renal disease, and patients with absorptive hypercalciuria. *J Clin Invest* 57:1412–1418.
- Bransby ER, Berry WTC, Taylor DM. 1964. Study of the vitamin-D intakes of infants in 1960. *Br Med J* 1:1661–1663.
- Brazier M, Kamel S, Maamer M, Agbomson F, Elesper I, Garabedian M, Desmet G, Sebert JL. 1995. Markers of bone remodeling in the elderly subject: Effects of vitamin D insufficiency and its correction. *J Bone Miner Res* 10:1753–1761.

- Brickman AS, Coburn JW, Massry SG. 1974. 1,25 dihydroxy-vitamin D<sub>3</sub> in normal man and patients with renal failure. *Ann Intern Med* 80:161–168.
- Brink EJ, Beynen AC. 1992. Nutrition and magnesium absorption: A review. *Prog Food Nutr Sci* 16:125–162.
- Brodehl J, Gellissen K, Weber H-P. 1982. Postnatal development of tubular phosphate reabsorption. *Clin Nephrol* 17:163–171.
- Brown WE, Gregory TM, Chow LC. 1977. Effects of fluoride on enamel solubility and cariostasis. *Caries Res* 11(Suppl 1):118–141.
- Brunelle JA, Carlos JP. 1990. Recent trends in dental caries in U.S. children and the effect of water fluoridation. *J Dent Res* 69(Spec Iss):723–727.
- Bruun C, Thylstrup A. 1988. Dentifrice usage among Danish children. *J Dent Res* 67:1114–1117.
- Bucher HC, Cook RJ, Guyatt GH, Lang JD, Cook DJ, Hatala R, Hunt DL. 1996. Effects of dietary calcium supplementation on blood pressure: A meta-analysis of randomized controlled trials. *J Am Med Assoc* 275:1016–1022.
- Bucuvalas JC, Heubi JE, Specker BL, Gregg DJ, Yerger AL, Vieira NE. 1990. Calcium absorption in bone disease associated with chronic cholestasis during childhood. *Hepatology* 12:1200–1205.
- Bullamore JR, Wilkinson R, Gallagher JC, Nordin BEC, Marshall DH. 1970. Effects of age on calcium absorption. *Lancet* 2:535–537.
- Bullimore DW, Miloszewski KJ. 1987. Raised parathyroid hormone levels in the milk-alkali syndrome: An appropriate response? *Postgrad Med J* 63:789–792.
- Burt BA. 1992. The changing patterns of systemic fluoride intake. *J Dent Res* 71:1228–1237.
- Burtis WJ, Gay L, Insogna KL, Ellison A, Broadus AE. 1994. Dietary hypercalciuria in patients with calcium oxalate kidney stones. *Am J Clin Nutr* 60:424–429.
- Bushe CJ. 1986. Profound hypophosphataemia in patients collapsing after a “fun run.” *Br Med J* 292:898–899.
- Butte NF, Garza C, Smith EO, Nichols BL. 1984. Human milk intake and growth in exclusively breast-fed infants. *J Pediatr* 104:187–195.
- Buzzard IM, Willett WC, eds. 1994. Dietary assessment methods. Proceedings of a conference held in St. Paul, MN. *Am J Clin Nutr* 59:143S–306S.
- Byrne J, Thomas MR, Chan GM. 1987. Calcium intake and bone density of lactating women in their late childbearing years. *J Am Diet Assoc* 87:883–887.
- Byrne PM, Freaney R, McKenna MJ. 1995. Vitamin D supplementation in the elderly: Review of safety and effectiveness of different regimens. *Calcif Tissue Int* 56:518–520.
- Caddell JL, Ratananon N, Trangratapit P. 1973. Parenteral magnesium load tests in postpartum Thai women. *Am J Clin Nutr* 26:612–615.
- Caddell JL, Saier FL, Thomason CA. 1975. Parenteral magnesium load tests in postpartum American women. *Am J Clin Nutr* 28:1099–1104.
- Calvo MS. 1993. Dietary phosphorus, calcium metabolism and bone. *J Nutr* 123:1627–1633.
- Calvo MS, Heath H III. 1988. Acute effects of oral phosphate-salt ingestion on serum phosphorus, serum ionized calcium, and parathyroid hormone in young adults. *Am J Clin Nutr* 47:1025–1029.
- Calvo MS, Park YK. 1996. Changing phosphorus content of the U.S. diet: Potential for adverse effects on bone. *J Nutr* 126:1168S–1180S.
- Calvo MS, Kumar R, Heath H III. 1988. Elevated secretion and action of serum parathyroid hormone in young adults consuming high phosphorus, low calcium diets assembled from common foods. *J Clin Endocrinol Metab* 66:823–829.

- Calvo MS, Kumar R, Heath H. 1990. Persistently elevated parathyroid hormone secretion and action in young women after four weeks of ingesting high phosphorus, low calcium diets. *J Clin Endocrinol Metab* 70:1334–1340.
- Campbell SB, MacFarlane DJ, Fleming SJ, Khafagi FA. 1994. Increased skeletal uptake of Tc-99m Methylene Disphosphonate in Milk-Alkali Syndrome. *Clin Nucl Med* 19:207–211.
- Canadian Paediatric Society (Nutrition Committee). 1991. Meeting the iron needs of infants and young children: An update. *Can Med Assoc J* 144:1451–1454.
- Canadian Paediatric Society. 1996. The use of fluoride in infants and children. *Paediatr Child Health* 1:131–134.
- Cappuccio FP, Markandu ND, Beynon GW, Shore AC, Sampson B, MacGregor GA. 1985. Lack of effect of oral magnesium on high blood pressure: A double blind study. *Br Med J Clin Res Ed* 291:235–238.
- Carlos JP, Gittelsohn AM, Haddon W Jr. 1962. Caries in deciduous teeth in relation to maternal ingestion of fluoride. *Pub Hlth Rep* 77:658–660.
- Carroll MD, Abraham S, Dresser CM. 1983. Dietary intake source data: United States, 1976–1980. Data from the National Health Survey. Vital and Health Statistics series 11, no. 231. DHHS Publ. No. (PHS) 83-1681. Hyattsville, MD: National Center for Health Statistics, Public Health Service, U.S. Department of Health and Human Services.
- Chan GM. 1991. Dietary calcium and bone mineral status of children and adolescents. *Am J Dis Child* 145:631–634.
- Chan GM, Roberts CC, Folland D, Jackson R. 1982a. Growth and bone mineralization of normal breast-fed infants and the effects of lactation on maternal bone mineral status. *Am J Clin Nutr* 36:438–443.
- Chan GM, Slater RN, Hollis J, Thomas MR. 1982b. Decreased bone mineral status in lactating adolescent mothers. *J Pediatr* 101:767–770.
- Chan GM, Leeper L, Book LS. 1987. Effects of soy formulas on mineral metabolism in term infants. *Am J Dis Child* 141:527–530.
- Chan GM, Hoffman K, McMurry M. 1995. Effects of dairy products on bone and body composition in pubertal girls. *J Pediatr* 126:551–556.
- Chan JT, Koh SH. 1996. Fluoride content in caffeinated, decaffeinated and herbal teas. *Caries Res* 30:88–92.
- Chan JT, Qui CC, Whitford GM, Weatherred JG. 1990. Influence of coffee on fluoride metabolism in rats. *Proc Soc Exp Biol Med* 194:43–47.
- Chandra RK. 1984. Physical growth of exclusively breast-fed infants. *Nutr Res* 2:275–276.
- Chapuy MC, Arlot ME, Duboeuf F, Brun J, Crouzet B, Arnaud S, Delmas PD, Meunier PJ. 1992. Vitamin D<sub>3</sub> and calcium to prevent hip fractures in elderly women. *N Engl J Med* 327:1637–1642.
- Charles P, Jensen FT, Mosekilde L, Hansen HH. 1983. Calcium metabolism evaluated by <sup>47</sup>Ca kinetics: Estimation of dermal calcium loss. *Clin Sci* 65:415–422.
- Chen TC, Castillo L, Korycka-Dahl M, DeLuca HF. 1974. Role of vitamin D metabolites in phosphate transport of rat intestine. *J Nutr* 104:1056–1060.
- Chen TC, Shao A, Heath H III, Holick MF. 1993. An update on the vitamin D content of fortified milk from the United States and Canada. *N Engl J Med* 329:1507.
- Chen X, Whitford GM. 1994. Lack of significant effect of coffee and caffeine on fluoride metabolism in rats. *J Dent Res* 73:1173–1179.
- Chesney RW. 1990. Requirements and upper limits of vitamin D intake in the term neonate, infant, and older child. *J Pediatr* 116:159–166.

- Chevalley T, Rizzoli R, Nydegger V, Slosman D, Rapin CH, Michel JP, Vasey H, Bonjour JP. 1994. Effects of calcium supplements on femoral bone mineral density and vertebral fracture rate in vitamin D-replete elderly patients. *Osteopor Int* 4:245–252.
- Chinn HI. 1981. Effects of dietary factors on skeletal integrity in adults: Calcium, phosphorus, vitamin D, and protein. Prepared for Bureau of Foods, Food and Drug Administration, U.S. Department of Health and Human Services, Washington, D.C.
- Cholak J. 1959. Fluorides: A critical review. I. The occurrence of fluoride in air, food and water. *J Occup Med* 1:501–511.
- Chow LC. 1990. Tooth-bound fluoride and dental caries. *J Dent Res* 69(Spec Iss):595–600.
- Clark DC, Hann HJ, Williamson MF, Berkowitz J. 1993. Aesthetic concerns of children and parents in relation to different classifications of the Tooth Surface Index of Fluorosis. *Community Dent Oral Epidemiol* 21:360–364.
- Clarkson EM, Warren RL, McDonald SJ, de Wardener HE. 1967. The effect of a high intake of calcium on magnesium metabolism in normal subjects and patients with chronic renal failure. *Clin Sci* 32:11–18.
- Clarkson PM, Haymes EM. 1995. Exercise and mineral status of athletes: Calcium, magnesium, phosphorus, and iron. *Med Sci Sports Exerc* 27:831–843.
- Clemens TL, Adams JS. 1996. Vitamin D metabolites. In: Favus MJ, Christakos S, eds. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 3rd edition*. Philadelphia, PA: Lippincott-Raven. Pp. 109–114.
- Clemens TL, Adams JS, Henderson SL, Holick MF. 1982. Increased skin pigment reduces the capacity of skin to synthesise vitamin D<sub>3</sub>. *Lancet* 1:74–76.
- Clemens TL, Zhou X, Myles M, Endres D, Lindsay R. 1986. Serum vitamin D<sub>2</sub> and vitamin D<sub>3</sub> metabolite concentrations and absorption of vitamin D<sub>2</sub> in elderly subjects. *J Clin Endocrinol Metab* 63:656–660.
- Cleveland LE, Goldman JD, Borrud LG. 1996. *Data Tables: Results from USDA's 1994 Continuing Survey of Food Intakes by Individuals and 1994 Diet and Health Knowledge Survey*. Beltsville, MD: Agricultural Research Service, U.S. Department of Agriculture.
- Clovis J, Hargreaves JA. 1988. Fluoride intake from beverage consumption. *Community Dent Oral Epidemiol* 16:11–15.
- CNPP, USDA (Center for Nutrition Policy and Promotion, U.S. Department of Agriculture). 1996. *Nutrient Content of the U.S. Food Supply, 1990–1994. Preliminary Data*. Washington, DC: U.S. Department of Agriculture.
- Cockburn F, Belton NR, Purvis RJ, Giles MM, Brown JK, Turner TL, Wilkinson EM, Forfar JO, Barrie WJM, McKay GS, Pocock SJ. 1980. Maternal vitamin D intake and mineral metabolism in mothers and their newborn infants. *Br Med J* 281:11–14.
- Coffin B, Azpiroz F, Guarner F, Malagelada JR. 1994. Selective gastric hypersensitivity and reflex hyporeactivity in functional dyspepsia. *Gastroenterology* 107:1345–1351.
- Cohen L. 1988. Recent data on magnesium and osteoporosis. *Magnes Res* 1:85–87.
- Cohen L, Laor A. 1990. Correlation between bone magnesium concentration and magnesium retention in the intravenous magnesium load test. *Magnes Res* 3:271–274.
- Cohn SH, Abesamis C, Yasumura S, Aloia JF, Zanzi I, Ellis KJ. 1977. Comparative skeletal mass and radial bone mineral content in black and white women. *Metabolism* 26:171–178.

- Colston K, Colston MJ, Feldman D. 1981. 1,25-dihydroxyvitamin D<sub>3</sub> and malignant melanoma: The presence of receptors and inhibition of cell growth in culture. *Endocrinol* 108:1083–1086.
- COMA (Committee on Medical Aspects of Food Policy). 1991. *Dietary Reference Values for Food Energy and Nutrients for the United Kingdom. Report on Health and Social Subjects, No. 41*. London: HMSO.
- Comstock GW. 1979. Water hardness and cardiovascular diseases. *Am J Epidemiol* 110:375–400.
- Conradt A, Weidinger H, Algayer H. 1984. On the role of magnesium in fetal hypotrophy, pregnancy induced hypertension and pre-eclampsia. *Magnes Bull* 2:68–76.
- Cooper C, Melton LJ III. 1992. Epidemiology of osteoporosis. *Trends Endocrinol Metab* 3:224–229.
- Cooper C, Campion G, Melton LJ III. 1992. Hip fractures in the elderly: A worldwide projection. *Osteopor Int* 2:285–289.
- Costello RB, Moser-Veillon PB, DiBianco R. 1997. Magnesium supplementation in patients with congestive heart failure. *J Am Coll Nutr* 16:22–31.
- Cowell DC, Taylor WH. 1981. Ionic fluoride: A study of its physiological variation in man. *Ann Clin Biochem* 18:76–83.
- Craig JM. 1959. Observations on the kidney after phosphate loading in the rat. *Arch Pathol* 68:306–315.
- Cramer CF. 1961. Progress and rate of absorption of radiophosphorus through the intestinal tract of rats. *Can J Biochem Physiol* 39:499–503.
- Cremer HD, Buttner W. 1970. *Absorption of Fluorides. Fluoride and Human Health*. Geneva, Switzerland: World Health Organization.
- Cross NA, Hillman LS, Allen SH, Krause GF, Vieira NE. 1995a. Calcium homeostasis and bone metabolism during pregnancy, lactation, and postweaning: A longitudinal study. *Am J Clin Nutr* 61:514–523.
- Cross NA, Hillman LS, Allen SH, Krasue GF. 1995b. Changes in bone mineral density and markers of bone remodeling during lactation and postweaning in women consuming high amounts of calcium. *J Bone Miner Res* 10:1312–1320.
- Cumming RG, Cummings SR, Nevitt MC, Scott J, Ensrud KE, Vogt TM, Fox K. 1997. Calcium intake and fracture risk: Results from the study of osteoporotic fractures. *Am J Epidemiol* 145:926–934.
- Cummings SR, Black DM, Nevitt MC, Browner W, Cauley J, Ensrud K, Genant HK, Palermo L, Scott J, Vogt TM. 1993. Bone density at various sites for prediction of hip fractures. The Study of Osteoporotic Fractures Research Group. *Lancet* 341:72–75.
- Cummings SR, Nevitt MC, Browner WS, Stone K, Fox KM, Ensrud KE, Cauley J, Black D, Vogt TM. 1995. Risk factors for hip fracture in white women: Study of Osteoporotic Fractures Research Group. *N Engl J Med* 332:767–773.
- Cunningham AS, Mazess RB. 1983. Bone mineral loss in lactating adolescents. *J Pediatr* 101:338–339.
- Curhan GC, Willett WC, Rimm EB, Stampfer MJ. 1993. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. *N Engl J Med* 328:833–838.
- Curhan GC, Willett WC, Speizer FE, Spiegelman D, Stampfer MJ. 1997. Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk for kidney stones in women. *Ann Intern Med* 126:497–504.

- Dabeka RW, McKenzie AD, Conacher HBS, Kirkpatrick DC. 1982. Determination of fluoride in Canadian infant foods and calculation of fluoride intakes by infants. *Can J Pub Hlth* 73:188–191.
- Dabeka RW, McKenzie AD, Lecroix GM. 1987. Dietary intakes of lead, cadmium, arsenic and fluoride by Canadian adults: A 24-hour duplicate diet study. *Food Addit Contam* 4:89–101.
- Dale G, Fleetwood JA, Inkster JS, Sainsbury JR. 1986. Profound hypophosphataemia in patients collapsing after a “fun run.” *Br Med J (Clin Res)* 292:447–448.
- Dalton MA, Sargent JD, O’Connor GT, Olmstead EM, Klein RZ. 1997. Calcium and phosphorus supplementation of iron-fortified infant formula: No effect on iron status of healthy full-term infants. *Am J Clin Nutr* 65:921–926.
- Davies M, Adams PH. 1978. The continuing risk of vitamin D intoxication. *Lancet* 2(8090):621–623.
- Davies M, Lawson DEM, Emberson C, Barnes JLC, Roberts GE, Barnes ND. 1982. Vitamin D from skin: Contribution to vitamin D status compared with oral vitamin D in normal and anti-convulsant-treated subjects. *Clin Sci* 63:461–472.
- Davies M, Hayes ME, Yin JA, Berry JL, Mawer EB. 1994. Abnormal synthesis of 1,25-dihydroxyvitamin D in patients with malignant lymphoma. *J Clin Endocrinol Metab* 78:1202–1207.
- Davis RH, Morgan DB, Rivlin RS. 1970. The excretion of calcium in the urine and its relation to calcium intake, sex and age. *Clin Sci* 39:1–12.
- Dawes C. 1989. Fluorides: Mechanisms of action and recommendations for use. *J Can Dent Assoc* 55:721–723.
- Dawson-Hughes B. 1996. Calcium. In: Marcus R, Feldman D, Kelsey J, eds. *Osteoporosis*. Orlando, FL: Academic Press, Inc. Pp. 1103, 1105.
- Dawson-Hughes B, Stern DT, Shipp CC, Rasmussen HM. 1988. Effect of lowering dietary calcium intake on fractional whole body calcium retention. *J Clin Endocrinol Metab* 67:62–68.
- Dawson-Hughes B, Dallal GE, Krall EA, Sadowski L, Sahyoun N, Tannenbaum S. 1990. A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women. *N Engl J Med* 323:878–883.
- Dawson-Hughes B, Dallal GE, Krall EA, Harris S, Sokoll LJ, Falconer G. 1991. Effect of vitamin D supplementation on wintertime and overall bone loss in healthy postmenopausal women. *Ann Intern Med* 115:505–512.
- Dawson-Hughes B, Harris S, Kramich C, Dallal G, Rasmussen HM. 1993. Calcium retention and hormone levels in black and white women on high- and low-calcium diets. *J Bone Miner Res* 8:779–787.
- Dawson-Hughes B, Harris SS, Krall EA, Dallal GE, Falconer G, Green CL. 1995. Rates of bone loss in postmenopausal women randomly assigned to one of two dosages of vitamin D. *Am J Clin Nutr* 61:1140–1145.
- Dawson-Hughes B, Fowler SE, Dalsky G, Gallagher C. 1996. Sodium excretion influences calcium homeostasis in elderly men and women. *J Nutr* 126:2107–2112.
- Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. 1997. Calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. *N Engl J Med* 337:670–676.
- Dean HT. 1942. The investigation of physiological effects by the epidemiological method. In: Moulton FR, ed. *Fluorine and Dental Health*. Washington, DC: American Association for the Advancement of Science. Pp. 23–31.
- Dean HT, Elvove E. 1937. Further studies on the minimal threshold of chronic endemic dental fluorosis. *Pub Hlth Rep* 52:1249–1264.

- Delmas PD. 1992. Clinical use of biochemical markers of bone remodeling in osteoporosis. *Bone* 13:S17–S21.
- Delmi M, Rapin CH, Bengoa JM, Delmas PD, Vasey H, Bonjour JP. 1990. Dietary supplementation in elderly patients with fractured neck of the femur. *Lancet* 335:1013–1016.
- DeLuca HF. 1984. The metabolism, physiology, and function of vitamin D. In: Kumar R, ed. *Vitamin D: Basic and Clinical Aspects*. Boston: M. Nijhoff Publishers.
- DeLuca HF. 1988. The vitamin D story: A collaborative effort of basic science and clinical medicine. *FASEB J* 2:224–236.
- Delvin EE, Salle BL, Glorieux FH, Adeleine P, David LS. 1986. Vitamin D supplementation during pregnancy: Effect on neonatal calcium homeostasis. *J Pediatr* 109:328–334.
- Demay MB. 1995. Hereditary defects in vitamin D metabolism and vitamin D receptor defects. In: DeGroot LJ, Besser M, Burger HG, Jameson JL, Loriaux DL, Marshall JC, O'Dell WD, Potts JT, Rubenstein AH, eds. *Endocrinology, Vol 2, Third edition*. Philadelphia, PA: WB Saunders. Pp. 1173–1178.
- Demirjian A. 1980. *Anthropometry Report. Height, Weight, and Body Dimensions: A Report from Nutrition Canada*. Ottawa: Minister of National Health and Welfare, Health and Promotion Directorate, Health Services and Promotion Branch.
- Dengel JL, Mangels AR, Moser-Veillon PB. 1994. Magnesium homeostasis: Conservation mechanism in lactating women consuming a controlled-magnesium diet. *Am J Clin Nutr* 59:990–994.
- Deurenberg P, Pieters JJ, Hautvast JG. 1990. The assessment of the body fat percentage by skinfold thickness measurements in childhood and young adolescence. *Br J Nutr* 63:293–303.
- Deuster PA, Singh A. 1993. Responses of plasma magnesium and other cations to fluid replacement during exercise. *J Am Coll Nutr* 12:286–293.
- Devine A, Criddle RA, Dick IM, Kerr DA, Prince RL. 1995. A longitudinal study of the effect of sodium and calcium intakes on regional bone density in postmenopausal women. *Am J Clin Nutr* 62:740–745.
- DeVizia B, Mansi A. 1992. Calcium and phosphorus metabolism in full-term infants. *Monatsschr Kinderheilkd* 140:S8–S12.
- DeVizia B, Fomon SJ, Nelson SE, Edwards BE, Zeigler EE. 1985. Effect of dietary calcium on metabolic balance of normal infants. *Pediatr Res* 19:800–806.
- Dewey KG, Finley DA, Lonnerdal B. 1984. Breast milk volume and composition during late lactation (7–20 months). *J Pediatr Gastroenterol Nutr* 3:713–720.
- DHHS (Department of Health and Human Services). 1988. *The Surgeon General's Report on Nutrition and Health*. Washington, DC: US Department of Health and Human Services, Public Health Service.
- DHHS (Department of Health and Human Services). 1990. *Healthy People 2000: National Health Promotion and Disease Prevention Objectives*. DHHS Publ. No. (PHS) 91-50212. Washington, DC: US Government Printing Office. Pp. 466–467.
- Diem K. 1970. *Documenta Geigy*. Ardsley, NY: Geigy Pharmaceuticals.
- Dobnig H, Kainer F, Stepan V, Winter R, Lipp R, Schaffer M, Kahr A, Nocnik S, Patterer G, Leb G. 1995. Elevated parathyroid hormone-related peptide levels after human gestation: Relationship to changes in bone and mineral metabolism. *J Clin Endocrinol Metab* 80:3699–3707.
- Dorsch TR. 1986. The milk-alkali syndrome, vitamin D, and parathyroid hormone. *Ann Intern Med* 105:800–801.

- Dorup I, Clausen T. 1993. Correlation between magnesium and potassium contents in muscle: Role of Na(+)-K<sup>+</sup> pump. *Am J Physiol* 264:C457–C463.
- Dourson ML, Stara JF. 1983. Regulatory history and experimental support of uncertainty (safety) factors. *Regul Toxicol Pharmacol* 3:224–238.
- Dowell TB. 1981. The use of toothpaste in infancy. *Br Dent J* 150:247–249.
- Drinkwater BL, Chesnut CH III. 1991. Bone density changes during pregnancy and lactation in active women: A longitudinal study. *Bone Miner* 14:153–160.
- Drinkwater B, Bruemner B, Chesnut C. 1990. Menstrual history as a determinant of current bone density in young athletes. *J Am Med Assoc* 263:545–548.
- Dwyer JT, Dietz WH, Hass G, Suskind R. 1979. Risk of nutritional rickets among vegetarian children. *Am J Dis Child* 133:134–140.
- Dyckner T, Wester PO. 1983. Effect of magnesium on blood pressure. *Br Med J (Clin Res)* 286:1847–1849.
- Dyckner T, Wester PO. 1985. Skeletal muscle magnesium and potassium determinations: Correlation with lymphocyte contents of magnesium and potassium. *J Am Coll Nutr* 4:619–625.
- Ebeling PR, Yergey AL, Vieira NE, Burritt MF, O'Fallon WM, Kumar R, Riggs BL. 1994. Influence of age on effects on endogenous 1,25-dihydroxy-vitamin D on calcium absorption in normal women. *Calcif Tissue Int* 55:330–334.
- Eble DM, Deaton TG, Wilson FC, Bawden JW. 1992. Fluoride concentrations in human and rat bone. *J Pub Hlth Dent* 52:288–291.
- Egsmose C, Lund B, McNair P, Lund B, Storm T, Sorensen OH. 1987. Low serum levels of 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D in institutionalized old people: Influence of solar exposure and vitamin D supplementation. *Age Ageing* 16:35–40.
- Eisman JA, Suva LJ, Sher E, Pearce PJ, Funder JW, Martin TJ. 1981. Frequency of 1,25-dihydroxyvitamin D<sub>3</sub> receptor in human breast cancer. *Cancer Res* 41:5121–5124.
- Ekstrand J, Ehrnebo M. 1979. Influence of milk products on fluoride bioavailability in man. *Eur J Clin Pharmacol* 16:211–215.
- Ekstrand J, Ehrnebo M. 1980. Absorption of fluoride from fluoride dentifrices. *Caries Res* 14:96–102.
- Ekstrand J, Boreus LO, de Chateau P. 1981. No evidence of transfer of fluoride from plasma to breast milk. *Br Med J* 283:761–762.
- Ekstrand J, Spak CJ, Falch J, Afseth J, Ulvestad H. 1984. Distribution of fluoride to human breast milk following intake of high doses of fluoride. *Caries Res* 18:93–95.
- Ekstrand J, Fomon SJ, Ziegler EE, Nelson SE. 1994a. Fluoride pharmacokinetics in infancy. *Pediatr Res* 35:157–163.
- Ekstrand J, Ziegler EE, Nelson SE, Fomon SJ. 1994b. Absorption and retention of dietary and supplemental fluoride by infants. *Adv Dent Res* 8:175–180.
- Elders PJ, Netelenbos JC, Lips P, van Ginkel FC, Khoe E, Leeuwenkamp OR, Hackeng WH, van der Stelt PF. 1991. Calcium supplementation reduces vertebral bone loss in perimenopausal women: A controlled trial in 248 women between 46 and 55 years of age. *J Clin Endocrinol Metab* 73:533–540.
- Elders PJ, Lips P, Netelenbos JC, van Ginkel FC, Khoe E, van der Vijgh WJ, van der Stelt PF. 1994. Long-term effect of calcium supplementation on bone loss in perimenopausal women. *J Bone Miner Res* 9:963–970.
- Elia M. 1992. Energy expenditure and the whole body. In: Kinney JM, Tucker HN, eds. *Energy Metabolism: Tissue Determinants and Cellular Corollaries*. New York: Raven Press Ltd. Pp. 19–59.

- Elin RJ. 1987. Assessment of magnesium status. *Clin Chem* 33:1965–1970.
- Elin RJ, Hosseini JM. 1985. Magnesium content of mononuclear blood cells. *Clin Chem* 31:377–380.
- Ellis KJ, Shypailo RJ, Hergenroeder A, Perez M, Abrams S. 1996. Total body calcium and bone mineral content: Comparison of dual-energy X-ray absorptiometry (DXA) with neutron activation analysis (NAA). *J Bone Miner Res* 11:843–848.
- Ellis KJ, Abrams SA, Wong WW. 1997. Body composition of a young, multiethnic female population. *Am J Clin Nutr* 65:724–731.
- EPA (U. S. Environmental Protection Agency). 1986. Guidelines for Carcinogen Risk Assessment. *Federal Register* 51(185):33992–34003.
- EPA (U. S. Environmental Protection Agency). 1996. Proposed Guidelines for Carcinogen Risk Assessment; Notice. *Federal Register* 61(79):17960–18011.
- Esala S, Vuori E, Helle A. 1982. Effect of maternal fluorine intake on breast milk fluorine content. *Br J Nutr* 48:201–204.
- Esveld RP, DeLuca HF. 1981. Calcitroic acid: Biological activity and tissue distribution studies. *Arch Biochem Biophys* 206:403–413.
- European Community. 1993. *Nutrient and Energy Intakes for the European Community*. Reports of the Scientific Committee for Food, Thirty-first Series.
- Evans RW. 1989. Changes in dental fluorosis following an adjustment to the fluoride concentration of Hong Kong's water supplies. *Adv Dent Res* 3:154–160.
- Evans RW, Darvell BW. 1995. Refining the estimate of the critical period for susceptibility to enamel fluorosis in human maxillary central incisors. *J Pub Hlth Dent* 55:238–249.
- Fairweather-Tait S, Prentice A, Heumann KG, Landing MAJ, Stirling DM, Wharf SG, Turnlund JR. 1995. Effect of calcium supplements and stage of lactation on the calcium absorption efficiency of lactating women accustomed to low calcium intakes. *Am J Clin Nutr* 62:1188–1192.
- FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization). 1982. *Evaluation of Certain Food Additives and Contaminants*. Twenty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives (WHO Technical Report Series No. 683).
- FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization, Expert Consultation). 1995. *The Application of Risk Analysis to Food Standard Issues*. Recommendations to the Codex Alimentarius Commission (ALINORM 95/9, Appendix 5).
- FAO/WHO/UNA (Food and Agriculture Organization of the United Nations/World Health Organization/United Nations). 1985. *Energy and Protein Requirements*. Report of a joint FAO/WHO/UNA Consultation Technical Report Series. No. 724. Geneva, Switzerland: World Health Organization.
- Fardellone P, Sebert JL, Garabedian M, Bellony R, Maamer M, Agbomson F, Brazier M. 1995. Prevalence and biological consequences of vitamin D deficiency in elderly institutionalized subjects. *Rev Rhum* 62:576–581.
- Farmer ME, White LR, Brody JA, Bailey KR. 1984. Race and sex differences in hip fracture incidence. *Am J Publ Health* 74:1374–1380.
- Fatemi S, Ryzen E, Flores J, Endres DB, Rude RK. 1991. Effect of experimental human magnesium depletion on parathyroid hormone secretion and 1,25-dihydroxyvitamin D metabolism. *J Clin Endocrinol Metab* 73:1067–1072.
- Faulkner KG, Cummings SR, Black D, Palermo L, Gluer CC, Genant HK. 1993. Simple measurement of femoral geometry predicts hip fracture: The study of osteoporotic fractures. *J Bone Miner Res* 8:1211–1217.

- Favus MJ, Christakos S. 1996. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 3rd Edition*. Philadelphia, PA: Lippincott-Raven.
- Featherstone JDB, Shields CP. 1988. *A Study of Fluoride in New York State Residents*. Final report to New York State Department of Health.
- Fehily AM, Coles RJ, Evans WD, Elwood PC. 1992. Factors affecting bone density in young adults. *Am J Clin Nutr* 56:579–586.
- Fejerskov O, Thylstrup A, Larsen MJ. 1977. Clinical and structural features and possible pathogenic mechanisms of dental fluorosis. *Scand J Dent Res* 85:510–534.
- Feldblum PJ, Zhang J, Rich LE, Fortney JA, Talmage RV. 1992. Lactation history and bone mineral density among perimenopausal women. *Epidemiology* 3:527–531.
- Feliciano ES, Ho ML, Specker BL, Falciglia G, Shui QM, Yin TA, Chen XC. 1994. Seasonal and geographical variations in the growth rate of infants in China receiving increasing dosages of vitamin D supplements. *J Trop Pediatr* 40:162–165.
- Feltman R, Kosel G. 1961. Prenatal and postnatal ingestion of fluorides—fourteen years of investigation. Final report. *J Dent Med* 16:190–198.
- Fieser LF, Fieser M. 1959. Vitamin D. In: *Steroids*. New York: Reinhold. Pp. 90–168.
- Filippo FA, Battistone GC. 1971. The fluoride content of a representative diet of the young adult male. *Clin Chim Acta* 31:453–457.
- Fine KD, Santa Ana CA, Porter JL, Fordtran JS. 1991a. Intestinal absorption of magnesium from food and supplements. *J Clin Invest* 88:396–402.
- Fine KD, Santa Ana CA, Fordtran JS. 1991b. Diagnosis of magnesium-induced diarrhea. *N Engl J Med* 324:1012–1017.
- Fink RI, Kolterman OG, Griffin J, Olefsky JM. 1983. Mechanisms of insulin resistance in aging. *J Clin Invest* 71:1523–1535.
- Fitzgerald MG, Fourman P. 1956. An experimental study of magnesium deficiency in man. *Clin Sci* 15:635.
- Fomon SJ, Nelson SE. 1993. Calcium, phosphorus, magnesium, and sulfur. In: Fomon SJ, ed. *Nutrition of Normal Infants*. St. Louis: Mosby-Year Book, Inc. Pp. 192–216.
- Fomon SJ, Younoszai MK, Thomas LN. 1966. Influence of vitamin D on linear growth of normal full-term infants. *J Nutr* 88:345–50.
- Fomon SJ, Haschke F, Ziegler EE, Nelson SE. 1982. Body composition of reference children from birth to age 10 years. *Am J Clin Nutr* 35:1169–1175.
- Franz KB. 1987. Magnesium intake during pregnancy. *Magnesium* 6:18–27.
- Franz KB. 1989. Influence of phosphorus on intestinal absorption of calcium and magnesium. In: Itokawa Y, Durlach J, eds. *Magnesium in Health and Disease*. London: John Libbey & Co. Pp. 71–78.
- Fraser DR. 1980. Regulation of the metabolism of vitamin D. *Physiol Rev* 60:551–613.
- Fraser DR. 1983. The physiological economy of vitamin D. *Lancet* 1:969–972.
- Freiman I, Pettifor JM, Moodley GM. 1982. Serum phosphorus in protein energy malnutrition. *J Pediatr Gastroenterol Nutr* 1:547–550.
- French JK, Koldaway IM, Williams LC. 1986. Milk-alkali syndrome following over-the-counter antacid self-medication. *N Zeal Med J* 99:322–323.
- Freudenheim JL, Johnson NE, Smith EL. 1986. Relationships between usual nutrient intake and bone-mineral content of women 35–65 years of age: Longitudinal and cross-sectional analysis. *Am J Clin Nutr* 44:863–876.

- Freyberg RH. 1942. Treatment of arthritis with vitamin and endocrine preparations. *J Am Med Assoc* 119:1165–1171.
- Frithz G, Wictorin B, Ronquist G. 1991. Calcium-induced constipation in a prepubescent boy. *Acta Paediatr Scand* 80:964–965.
- Frost HM. 1973. The origin and nature of transients in human bone remodeling dynamics. In: Frame B, Parfitt AM, Duncan H, eds. *Clinical Aspects of Metabolic Bone Disease*. Amsterdam: Excerpta Medica Series. Pp. 124–137.
- Frost HM. 1987. The mechanostat: A proposed pathogenic mechanism of osteoporosis and the bone mass effects of mechanical and nonmechanical agents. *Bone Miner* 2:73–85.
- Frost HM. 1997. Why do marathon runners have less bone than weight lifters? A vital-biomechanical view and explanation. *Bone* 20:183–189.
- Gadallah M, Massry SG, Bigazzi R, Horst RL, Eggema P, Campese VM. 1991. Intestinal absorption of calcium and calcium metabolism in patients with essential hypertension and normal renal function. *Am J Hypertens* 4:404–409.
- Galla JH, Booker BB, Luke RG. 1986. Role of the loop segment in the urinary concentrating defect of hypercalcemia. *Kidney Int* 29:977–982.
- Gallagher JC, Riggs BL, DeLuca HF. 1980. Effect of estrogen on calcium absorption and serum vitamin D metabolites in postmenopausal osteoporosis. *J Clin Endocrinol Metab* 51:1359–1364.
- Gallagher JC, Goldgar D, Moy A. 1987. Total bone calcium in women: Effect of age and menopause status. *J Bone Miner Res* 2:491–496.
- Garby L, Lammert O. 1984. Within-subjects between-days-and-weeks variation in energy expenditure at rest. *Human Nutr Clin Nutr* 38:395–397.
- Garfinkel L, Garfinkel D. 1985. Magnesium regulation of the glycolytic pathway and the enzymes involved. *Magnesium* 4:60–72.
- Garland C, Shekelle RB, Barrett-Connor E, Criqui MH, Rossof AH, Paul O. 1985. Dietary vitamin D and calcium and risk of colorectal cancer: A 19-year prospective study in men. *Lancet* 1:307–309.
- Garland FC, Garland CF, Gorham ED, Young JF. 1990. Geographic variation in breast cancer mortality in the United States: A hypothesis involving exposure to solar radiation. *Prev Med* 19:614–622.
- Garn SM. 1972. The course of bone gain and the phases of bone loss. *Orthop Clin North Am* 3:503–520.
- Gartside PS, Glueck CJ. 1995. The important role of modifiable dietary and behavioral characteristics in the causation and prevention of coronary heart disease hospitalization and mortality: The prospective NHANES I follow-up study. *J Am Coll Nutr* 14:71–79.
- Gedalia I, Brzezinski A, Portuguese N, Bercovici B. 1964. The fluoride content of teeth and bones of human foetuses. *Arch Oral Biol* 9:331–340.
- Geleijnse JM, Witteman JC, Bak AA, den Breeijen JH, Grobbee DE. 1994. Reduction in blood pressure with a low sodium, high potassium, high magnesium salt in older subjects with mild to moderate hypertension. *Br Med J* 309:436–440.
- German Society of Nutrition. 1991. *Recommendations on Nutrient Intake*. Abstract and Tables of the 157 Pages Booklet, 5th revised edition. Frankfurt: Druckerei Henrich.
- Gershoff SN, Legg MA, Hegsted DM. 1958. Adaptation to different calcium intakes in dogs. *J Nutr* 64:303–312.
- Gertner JM, Coustan DR, Kliger AS, Mallette LE, Ravin N, Broadus AE. 1986. Pregnancy as state of physiologic absorptive hypercalciuria. *Am J Med* 81:451–456.

- Gillman MW, Hood MY, Moore LL, Nguyen US, Singer MR, Andon MB. 1995. Effect of calcium supplementation on blood pressure in children. *J Pediatr* 127:186–192.
- Gilsanz V, Roe TF, Mora S, Costin G, Goodman WG. 1991. Changes in vertebral bone density in black girls and white girls during childhood and puberty. *N Engl J Med* 325:1597–1600.
- Glaser K, Parmelee AH, Hoffman WS. 1949. Comparative efficacy of vitamin D preparations in prophylactic treatment of premature infants. *Am J Dis Child* 77:1–14.
- Glass RL, Peterson JK, Zuckerberg DA, Naylor MN. 1975. Fluoride ingestion resulting from the use of a monofluorophosphate dentifrice by children. *Br Dent J* 138:423–426.
- Glenn FB. 1981. The rationale for the administration of a NaF tablet supplement during pregnancy and postnatally in a private practice setting. *J Dent Child* 48:118–122.
- Glenn FB, Glenn WD III, Duncan RC. 1984. Prenatal fluoride tablet supplementation and the fluoride content of teeth: Part VII. *J Dent Child* 51:344–351.
- Gloth FM III, Gundberg CM, Hollis BW, Haddad JG Jr, Tobin JD. 1995. Vitamin D deficiency in homebound elderly persons. *J Am Med Assoc* 274:1683–1686.
- Goeree R, O'Brien B, Pettitt D, Cuddy L, Ferraz M, Adachi J. 1996. An assessment of the burden of illness due to osteoporosis in Canada. *J SOGC*:15S–24S.
- Golden BE, Golden MH. 1981. Plasma zinc, rate of weight gain, and the energy cost of tissue deposition in children recovering from severe malnutrition on a cow's milk or soya protein-based diet. *Am J Clin Nutr* 34:892–899.
- Goldfarb S. 1994. Diet and nephrolithiasis. *Ann Rev Med* 45:235–243.
- Goldring SR, Krane SM, Avioli LV. 1995. Disorders of calcification: Osteomalacia and rickets. In: DeGroot LJ, ed. *Endocrinology*, Vol 2, *Third Edition*. Philadelphia: WB Saunders. Pp. 1204–1227.
- Golzarian J, Scott HW Jr, Richards WO. 1994. Hypermagnesemia-induced paralytic ileus. *Dig Dis Sci* 39:1138–1142.
- Gora ML, Seth SK, Bay WH, Visconti JA. 1989. Milk-alkali syndrome associated with use of chlorothiazide and calcium carbonate. *Clin Pharm* 8:227–229.
- Goren S, Silverstein LJ, Gonzales N. 1993. A survey of food service managers of Washington State boarding homes for the elderly. *J Nutr Elderly* 12:27–42.
- Graham S. 1959. Idiopathic hypercalcemia. *Postgraduate Med* 25:67–72.
- Gray TK, Lester GE, Lorenc RS. 1979. Evidence for extra-renal 1-hydroxylation of 25-hydroxyvitamin D<sub>3</sub> in pregnancy. *Science* 204:1311–1313.
- Greer FR. 1989. Calcium, phosphorus, and magnesium: How much is too much for infant formulas? *J Nutr* 119:1846–1851.
- Greer FR, Garn SM. 1982. Loss of bone mineral content in lactating adolescents. *J Pediatr* 101:718–719.
- Greer FR, Searcy JE, Levin RS, Steichen JJ, Steichen-Asche PS, Tsang RC. 1982a. Bone mineral content and serum 25-hydroxyvitamin D concentrations in breast-fed infants with and without supplemental vitamin D: One-year follow-up. *J Pediatr* 100:919–922.
- Greer FR, Tsang RC, Levin RS, Searcy JE, Wu R, Steichen JJ. 1982b. Increasing serum calcium and magnesium concentrations in breast-fed infants: Longitudinal studies of minerals in human milk and in sera of nursing mothers and their infants. *J Pediatr* 100:59–64.

- Greer FR, Steichen JJ, Tsang RC. 1982c. Effects of increased calcium, phosphorus, and vitamin D intake on bone mineralization in very low-birth-weight infants fed formulas with polycose and medium-chain triglycerides. *J Pediatr* 100:951–955.
- Greer FR, Lane J, Ho M. 1984. Elevated serum parathyroid hormone, calcitonin, and 1,25-dihydroxyvitamin D in lactating women nursing twins. *Am J Clin Nutr* 40:562–568.
- Greger JL, Baier MJ. 1983. Effect of dietary aluminum on mineral metabolism of adult males. *Am J Clin Nutr* 38:411–419.
- Greger JL, Baligar P, Abernathy RP, Bennett OA, Peterson T. 1978. Calcium, magnesium, phosphorus, copper, and manganese balance in adolescent females. *Am J Clin Nutr* 31:117–121.
- Greger JL, Huffman J, Abernathy RP, Bennett OA, Resnick SE. 1979. Phosphorus and magnesium balance of adolescent females fed two levels of zinc. *J Food Sci* 44:1765–1767.
- Greger JL, Smith SA, Snedeker SM. 1981. Effect of dietary calcium and phosphorus levels on the utilization of calcium, phosphorus, magnesium, manganese, and selenium by adult males. *Nutr Res* 1:315–325.
- Grill V, Martin TJ. 1993. Non-parathyroid hypercalcemias. In: Nordin BEC, Need AG, Morris HA, eds. *Metabolic Bone and Stone Disease*. Edinburgh: Churchill Livingstone. Pp. 133–145.
- Grimston SK, Morrison K, Harder JA, Hanley DA. 1992. Bone mineral density during puberty in Western Canadian children. *Bone Miner* 19:85–96.
- Groeneveld A, Van Eck AA, Backer-Dirks O. 1990. Fluoride in caries prevention: Is the effect pre- or post-eruptive? *J Dent Res* 69(Spec Iss):751–755.
- Gullestad L, Dolva LO, Waage A, Falch D, Fagerthun H, Kjekshus J. 1992. Magnesium deficiency diagnosed by an intravenous loading test. *Scan J Clin Lab Invest* 52:245–253.
- Gullestad L, Nes M, Ronneberg R, Midtveldt K, Falch D, Kjekshus J. 1994. Magnesium status in healthy free-living elderly Norwegians. *J Am Coll Nutr* 13:45–50.
- Gultekin A, Ozalp I, Hasanoglu A, Unal A. 1987. Serum-25-hydroxycholecalciferol levels in children and adolescents. *Turk J Pediatr* 29:155–162.
- Gunther T. 1993. Mechanisms and regulation of Mg<sup>2+</sup> efflux and Mg<sup>2+</sup> influx. *Miner Electrolyte Metab* 19:259–265.
- Guy WS. 1979. Inorganic and organic fluorine in human blood. In: Johansen E, Taves DR, Olsen TO, eds. *Continuing Evaluation of the Use of Fluorides*. AAAS Selected Symposium. Boulder, CO: Westview Press.
- Haddad JG, Jr. 1980. Competitive protein-binding radioassays for 25-OH-D; clinical applications. In: Norman, ed. *Vitamin D*, vol. 2. New York: Marcel Dekker, Inc., P. 587.
- Haddad JG, Hahn TJ. 1973. Natural and synthetic sources of circulating 25-hydroxyvitamin D in man. *Nature* 244:515–517.
- Hakim R, Tolis G, Goltzman D, Meltzer S, Friedman R. 1979. Severe hypercalcemia associated with hydrochlorothiazide and calcium carbonate therapy. *Can Med Assoc J* 21:591–594.
- Halioua L, Anderson JJ. 1989. Lifetime calcium intake and physical activity habits: Independent and combined effects on the radial bone of healthy premenopausal Caucasian women. *Am J Clin Nutr* 49:534–541.
- Hallberg L, Rossander-Hulten L, Brune M, Gleerup A. 1992. Calcium and iron absorption: Mechanism of action and nutritional importance. *Eur J Clin Nutr* 46:317–327.

- Hallfrisch J, Muller DC. 1993. Does diet provide adequate amounts of calcium, iron, magnesium, and zinc in a well-educated adult population? *Exper Gerontol* 28:473–483.
- Hamilton IR. 1990. Biochemical effects of fluoride on oral bacteria. *J Dent Res* 69(Spec Iss):660–667.
- Hammer DI, Heyden S. 1980. Water hardness and cardiovascular mortality. *J Am Med Assoc* 243:2399–2400.
- Hamuro Y, Shino A, Suzuki Z. 1970. Acute induction of soft tissue calcification with transient hyperphosphatemia in the KK mouse by modification in dietary contents of calcium, phosphorus, and magnesium. *J Nutr* 100:404–412.
- Handwerker SM, Altura BT, Altura BM. 1996. Serum ionized magnesium and other electrolytes in the antenatal period of human pregnancy. *J Am Coll Nutr* 15:36–43.
- Hardwick LL, Jones MR, Brautbar N, Lee DB. 1991. Magnesium absorption: Mechanisms and the influence of vitamin D, calcium and phosphate. *J Nutr* 121:13–23.
- Hargreaves JA. 1972. Fluoride content of deciduous tooth enamel from three different regions (Abstract). *J Dent Res* 51:274.
- Hargreaves JA. 1992. The level and timing of systemic exposure to fluoride with respect to caries resistance. *J Dent Res* 71:1244–1248.
- Hargreaves JA, Ingram GS, Wagg BJ. 1970. An extended excretion study on the ingestion of a monofluorophosphate toothpaste by children. *Acta Med Sci Hung* 27:413–419.
- Hargreaves JA, Ingram FF, Wagg BJ. 1972. A gravimetric based study of the ingestion of toothpaste by children. *Caries Res* 6:237–243.
- Hargreaves JA, Thompson GW, Pimlott JFL, Norbert LD. 1988. Commencement date of fluoride supplementation related to dental caries. *J Dent Res* 67:230.
- Harris SS, Dawson-Hughes B. 1994. Caffeine and bone loss in healthy postmenopausal women. *Am J Clin Nutr* 60:573–578.
- Hart M, Windle J, McHale M, Grissom R. 1982. Milk-alkali syndrome and hypercalcemia: A case report. *Nebr Med J* 67:128–130.
- Hasling C, Charles P, Jensen FT, Mosekilde L. 1990. Calcium metabolism in postmenopausal osteoporosis: The influence of dietary calcium and net absorbed calcium. *J Bone Miner Res* 5:939–946.
- Hayslip CC, Klein TA, Wray HL, Duncan WE. 1989. The effects of lactation on bone mineral content in healthy postpartum women. *Obstet Gynecol* 73:588–592.
- Health Canada. 1990. *Nutrition Recommendations. The Report of the Scientific Review Committee 1990*. Ottawa: Canadian Government Publishing Centre.
- Health Canada. 1993. *Health Risk Determination—The Challenge of Health Protection*. Health Canada, Health Protection Branch. Ottawa: Health Canada.
- Heaney RP. 1993. Protein intake and the calcium economy. *J Am Diet Assoc* 93:1259–1260.
- Heaney RP. 1997. Vitamin D: Role in the calcium economy. In: Feldman D, Glorieux FH, Pike JW, eds. *Vitamin D*. San Diego, CA: Academic Press. Pp. 485–497.
- Heaney RP, Recker RR. 1982. Effects of nitrogen, phosphorus, and caffeine on calcium balance in women. *J Lab Clin Med* 99:46–55.
- Heaney RP, Recker RR. 1987. Calcium supplements: Anion effects. *Bone Miner* 2:433–439.

- Heaney RP, Recker RR. 1994. Determinants of endogenous fecal calcium in healthy women. *J Bone Miner Res* 9:1621–1627.
- Heaney RP, Skillman TG. 1964. Secretion and excretion of calcium by the human gastrointestinal tract. *J Lab Clin Med* 64:29–41.
- Heaney RP, Skillman TG. 1971. Calcium metabolism in normal human pregnancy. *J Clin Endocrinol* 33:661–670.
- Heaney RP, Saville PD, Recker RR. 1975. Calcium absorption as a function of calcium intake. *J Lab Clin Med* 85:881–890.
- Heaney RP, Recker RR, Saville PD. 1977. Calcium balance and calcium requirements in middle-aged women. *Am J Clin Nutr* 30:1603–1611.
- Heaney RP, Recker RR, Saville PD. 1978. Menopausal changes in calcium balance performance. *J Lab Clin Med* 92:953–963.
- Heaney RP, Recker RR, Hinders SM. 1988. Variability of calcium absorption. *Am J Clin Nutr* 47:262–264.
- Heaney RP, Recker RR, Stegman MR, Moy AJ. 1989. Calcium absorption in women: Relationships to calcium intake, estrogen status, and age. *J Bone Miner Res* 4:469–475.
- Heaney RP, Recker RR, Weaver CM. 1990a. Absorbability of calcium sources: The limited role of solubility. *Calcif Tissue Int* 46:300–304.
- Heaney RP, Weaver CM, Fitzsimmons ML. 1990b. Influence of calcium load on absorption fraction. *J Bone Miner Res* 5:1135–1138.
- Heaney RP, Weaver CM, Fitzsimmons ML. 1991. Soybean phytate content: Effect on calcium absorption. *Am J Clin Nutr* 53:745–747.
- Heaton FW. 1969. The kidney and magnesium homeostasis. *Ann NY Acad Sci* 162:775–785.
- Hegsted DM. 1972. Problems in the use and interpretation of the Recommended Dietary Allowances. *Ecol Food Nutr* 1:255–265.
- Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. 1993. Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: The DARLING study. *Am J Clin Nutr* 58:152–161.
- Hemmingsen C, Staun M, Olgaard K. 1994. Effects of magnesium on renal and intestinal calbindin-D. *Miner Electrolyte Metab* 20:265–273.
- Herman-Giddens ME, Slora EJ, Wasserman RC, Bourdon CJ, Bhapkar MV, Koch GG, Hasemeier CM. 1997. Secondary sexual characteristics and menses in young girls seen in office practice: A study from the Pediatric Research in Office Settings Network. *Pediatrics* 99:505–512.
- Hill AB. 1971. *Principles of Medical Statistics, 9th Ed.* New York: Oxford University Press.
- Hillman LS. 1990. Mineral and vitamin D adequacy in infants fed human milk or formula between 6 and 12 months of age. *J Pediatr* 117:S134–S142.
- Hillman L, Sateesha S, Haussler M, Wiest W, Slatopolsky E, Haddad J. 1981. Control of mineral homeostasis during lactation: Interrelationships of 25-hydroxyvitamin D, 24,25-dihydroxyvitamin D, 1,25-dihydroxyvitamin D, parathyroid hormone, calcitonin, prolactin, and estradiol. *Am J Obstet Gynecol* 139:471–476.
- Hillman LS, Chow W, Salmons SJ, Weaver E, Erickson M, Hansen J. 1988. Vitamin D metabolism, mineral homeostasis and bone mineralization in term infants fed human milk, cow milk-based formula or soy-based formula. *J Pediatr* 112:864–874.
- Hodge HC, Smith FA. 1977. Occupational fluoride exposure. *J Occup Med* 19:12–39.

- Hodge HC. 1979. The safety of fluoride tablets or drops. In: Johansen E, Taves DR, Olson, TO, eds. *Continuing Evaluation of the Use of Fluorides, AAAS Selected Symposium 1*. Boulder, CO: Westview Press. Pp. 253–274.
- Hodgson E, Mailman RB, Chamber JE. 1988. *Dictionary of Toxicology*. New York: Van Nostrand Reinhold, Inc.
- Hoffman S, Grisso JA, Kelsey JL, Gammon MD, O'Brien LA. 1993. Parity, lactation and hip fracture. *Osteopor Int* 3:171–176.
- Hofvander Y, Hagman U, Hillervik C, Sjolin S. 1982. The amount of milk consumed by 1–3 months old breast- or bottle-fed infants. *Acta Pediatr Scand* 71:953–958.
- Holbrook TL, Barrett-Connor E, Wingard DL. 1988. Dietary calcium and risk of hip fracture: 14-year prospective population study. *Lancet* 2:1046–1049.
- Holick MF. 1986. Vitamin D requirements for the elderly. *Clin Nutr* 5:121–129.
- Holick MF. 1994. McCollum Award Lecture, 1994: Vitamin D: New horizons for the 21st century. *Am J Clin Nutr* 60:619–630.
- Holick MF. 1995. Vitamin D: Photobiology, metabolism, and clinical applications. In: DeGroot LJ, Besser M, Burger HG, Jameson JL, Loriaux DL, Marshall JC, O'Dell WD, Potts JL, Rubenstein AH, eds. *Endocrinology, 3rd Edition*. Philadelphia, PA: WB Saunders.
- Holick MF. 1996. Vitamin D: Photobiology, metabolism, mechanism of action, and clinical application. In: Favus MJ, ed. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 3rd Edition*. Philadelphia, PA: Lippincott-Raven. Pp. 74–81.
- Holick MF, Clark MB. 1978. The photobiogenesis and metabolism of vitamin D. *Fed Proc* 37:2567–2574.
- Holick MF, Schnoes HK, DeLuca HF. 1971. Identification of 1,25-dihydroxycholecalciferol, a form of vitamin D<sub>3</sub> metabolically active in the intestine. *Proc Natl Acad Sci USA* 68:803–804.
- Holick MF, Uskokovic M, Henley JW, MacLaughlin J, Holick SA, Potts JT Jr. 1980. The photoproduction of 1 $\alpha$ , 25-dihydroxyvitamin D<sub>3</sub> in skin: An approach to the therapy of vitamin-D-resistant syndromes. *N Engl J Med* 303:349–354.
- Holick MF, MacLaughlin JA, Doppelt SH. 1981. Regulation of cutaneous previtamin D<sub>3</sub> photosynthesis in man: Skin pigment is not an essential regulator. *Science* 211:590–593.
- Holick MF, Matsuoka LY, Wortsman J. 1989. Age, vitamin D, and solar ultraviolet. *Lancet* 2:1104–1105.
- Holick MF, Shao Q, Liu WW, Chen TC. 1992. The vitamin D content of fortified milk and infant formula. *N Engl J Med* 326:1178–1181.
- Hollifield JW. 1987. Magnesium depletion, diuretics, and arrhythmias. *Am J Med* 82(Suppl 3A):30–37.
- Hollis BW. 1996. Assessment of vitamin D nutritional and hormonal status: What to measure and how to do it. *Calcif Tissue Int* 58:4–5.
- Holmes RP, Kummerow FA. 1983. The relationship of adequate and excessive intake of vitamin D to health and disease. *J Am Coll Nutr* 2:173–199.
- Honkanen R, Alhava E, Parviainen M, Talasniemi S, Monkkonen R. 1990. The necessity and safety of calcium and vitamin D in the elderly. *J Am Geriatr Soc* 38:862–866.
- Hordon LD, Peacock M. 1987. Vitamin D metabolism in women with femoral neck fracture. *Bone Miner* 2:413–426.
- Horowitz HS. 1990. The future of water fluoridation and other systemic fluorides. *J Dent Res* 69(Spec Iss):760–764.

- Horowitz HS. 1996. The effectiveness of community water fluoridation in the United States. *J Pub Hlth Dent* 56:253–258.
- Horowitz HS, Heifetz SB. 1967. Effects of prenatal exposure to fluoridation on dental caries. *Pub Hlth Rep* 82:297–304.
- Horowitz M, Wishart J, Mundy L, Nordin BEC. 1987. Lactose and calcium absorption in postmenopausal osteoporosis. *Arch Intern Med* 147:534–536.
- Hoskova M. 1968. Fluoride tablets in the prevention of tooth decay. *Cesk Pediatr* 23:438–441.
- Howard JE, Hopkins TR, Connor TB. 1953. On certain physiologic responses to intravenous injection of calcium salts into normal, hyperparathyroid and hypoparathyroid persons. *J Clin Endocrinol Metab* 13:1–19.
- Hreshchyshyn MM, Hopkins A, Zylstra S, Anbar M. 1988. Associations of parity, breast-feeding, and birth control pills with lumbar spine and femoral neck bone densities. *Am J Obstet Gynecol* 159:318–322.
- Hua H, Gonzales J, Rude RK. 1995. Magnesium transport induced ex vivo by a pharmacological dose of insulin is impaired in non-insulin-dependent diabetes mellitus. *Magnes Res* 8:359–366.
- Huang Z, Himes JH, McGovern PG. 1996. Nutrition and subsequent hip fracture risk among a national cohort of white women. *Am J Epidemiol* 144:124–134.
- Hunt CD, Nielsen FH. 1981. Interaction between boron and cholecalciferol in the chick. In: McC Howell J, Gathorne JM, White CL, eds. *Trace Element Metabolism in Man and Animals, TEMA-4*. Canberra: Australian Academy of Science. Pp. 597–600.
- Hunt MS, Schofield FA. 1969. Magnesium balance and protein intake level in adult human female. *Am J Clin Nutr* 22:367–373.
- Hwang DL, Yen CF, Nadler JL. 1993. Insulin increases intracellular magnesium transport in human platelets. *J Clin Endocrinol Metab* 76:549–553.
- IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Report of the Subcommittee on Nutritional Status and Weight Gain During Pregnancy, Subcommittee on Dietary Intake and Nutrient Supplements During Pregnancy, Committee on Nutritional Status During Pregnancy and Lactation, Food and Nutrition Board. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1991. *Nutrition During Lactation*. Report of the Subcommittee on Nutrition During Lactation, Committee on Nutritional Status During Pregnancy and Lactation, Food and Nutrition Board. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Food and Nutrition Board. Washington, DC: National Academy Press.
- Ireland P, Fordtran JS. 1973. Effect of dietary calcium and age on jejunal calcium absorption in humans studied by intestinal perfusion. *J Clin Invest* 52:2672–2681.
- Irnell L. 1969. Metastatic calcification of soft tissue on overdose of vitamin D. *Acta Med Scand* 185:147–152.
- Iseri LT, French JH. 1984. Magnesium: Nature's physiologic calcium blocker. *Am Heart J* 108:188–193.
- ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. 1995. ISIS-4: A randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. *Lancet* 345:669–685.

- Ismail AI, Brodeur JM, Kavanagh M, Boisclair G, Tessier C, Picotte L. 1990. Prevalence of dental caries and dental fluorosis in students, 11–17 years of age, in fluoridated and non-fluoridated cities in Quebec. *Caries Res* 24:290–297.
- Jackman LA, Millane SS, Martin BR, Wood OB, McCabe GP, Peacock M, Weaver CM. 1997. Calcium retention in relation to calcium intake and postmenarcheal age in adolescent females. *Am J Clin Nutr* 66:327–333.
- Jackson D, Murray JJ, Fairpo CG. 1973. Life-long benefits of fluoride in drinking water. *Br Dent J* 134:419–422.
- Jacobus CH, Holick MF, Shao Q, Chen TC, Holm IA, Kolodny JM, Fuleihan GE, Seely EW. 1992. Hypervitaminosis D associated with drinking milk. *N Engl J Med* 326:1173–1177.
- Janas LM, Picone TA, Benson JD, MacLean WC. 1988. Influence of dietary calcium to phosphorus and parathormone during the first two weeks of life. *Pediatr Res* 23:485A.
- Janelle KC, Barr SI. 1995. Nutrient intakes and eating behavior scores of vegetarian and nonvegetarian women. *J Am Diet Assoc* 95:180–186.
- Jeans PC. 1950. Vitamin D. *J Am Med Assoc* 143:177–181.
- Jeans PC, Stearns G. 1938. The effect of vitamin D on linear growth in infancy. II. The effect of intakes above 1,800 USP units daily. *J Pediatr* 13:730–740.
- Joffres MR, Reed DM, Yano K. 1987. Relationship of magnesium intake and other dietary factors to blood pressure: The Honolulu heart study. *Am J Clin Nutr* 45:469–475.
- Johansson C, Mellström D, Milsom I. 1993. Reproductive factors as predictors of bone density and fractures in women at the age of 70. *Maturitas* 17:39–50.
- Johnson AO, Semenza JG, Buchowski MS, Enwonwu CO, Scrimshaw NS. 1993a. Correlation of lactose maldigestion, lactose intolerance, and milk intolerance. *Am J Clin Nutr* 57:399–401.
- Johnson AO, Semenza JG, Buchowski MS, Enwonwu CO, Scrimshaw NS. 1993b. Adaptation of lactose maldigesters to continued milk intakes. *Am J Clin Nutr* 58:879–881.
- Johnson CM, Wilson DM, O'Fallon WM, Malek RS, Kurland LT. 1979. Renal stone epidemiology: A 25-year study in Rochester, Minn. *Kidney Int* 16:624–631.
- Johnson J Jr, Bawden JW. 1987. The fluoride content of infant formulas available in 1985. *Pediatr Dent* 9:33–37.
- Johnson KR, Jobber J, Stonawski BJ. 1980. Prophylactic vitamin D in the elderly. *Age Ageing* 9:121–127.
- Johnston CC, Miller JZ, Slemenda CW, Reister TK, Hui S, Christian JC, Peacock M. 1992. Calcium supplementation and increases in bone mineral density in children. *N Engl J Med* 327:82–87.
- Jones JE, Manalo R, Flink EB. 1967. Magnesium requirements in adults. *Am J Clin Nutr* 20:632–635.
- Jowsey J, Balasubramaniam P. 1972. Effect of phosphate supplements on soft tissue calcification and bone turnover. *Clin Sci* 42:289–299.
- Junor JR, Catto GRD. 1976. Renal biopsy in the milk-alkali syndrome. *J Clin Path* 29:1074–1076.
- Kailis DG, Taylor SR, Davis GB, Bartlett LG, Fitzgerald DJ, Grose IJ, Newton PD. 1968. Fluoride and caries: Observations of the effects of prenatal and postnatal fluoride on some Perth pre-school children. *Med J Austral* 2:1037–1040.
- Kalkwarf HJ, Specker BL. 1995. Bone mineral loss during lactation and recovery after weaning. *Obstet Gynecol* 86:26–32.
- Kalkwarf HJ, Specker BL, Heubi JE, Vieira NE, Yerger AL. 1996. Intestinal calcium absorption of women during lactation and after weaning. *Am J Clin Nutr* 63:526–531.

- Kalkwarf HJ, Specker BL, Bianchi DC, Ranz J, Ho M. 1997. The effect of calcium supplementation on bone density during lactation and after weaning. *N Engl J Med* 337:523–528.
- Kallmeyer JC, Funston MR. 1983. The milk-alkali syndrome: A case report. *S Afr Med J* 64:287–288.
- Kamel S, Brazier M, Picard C, Boitte F, Samson L, Desmet G, Sebert JL. 1994. Urinary excretion of pyridinolines crosslinks measured by immunoassay and HPLC techniques in normal subjects and in elderly patients with vitamin D deficiency. *Bone Miner* 26:197–208.
- Kamel S, Brazier M, Rogez JC, Vincent O, Maamer M, Desmet G, Sebert JL. 1996. Different responses of free and peptide-bound cross-links to vitamin D and calcium supplementation in elderly women with vitamin D insufficiency. *J Clin Endocrinol Metab* 81:3717–3721.
- Kaminsky LS, Mahoney MC, Leach J, Melius J, Miller MJ. 1990. Fluoride: Benefits and risks of exposure. *Crit Rev Oral Biol Med* 1:261–281.
- Kanapka JA, Hamilton IR. 1971. Fluoride inhibition of enolase activity in vivo and its relationship to the inhibition of glucose-6-P formation in *Streptococcus salivarius*. *Arch Biochem Biophys* 146:167–174.
- Kanemitsu T, Koike A, Yamamoto S. 1985. Study of the cell proliferation kinetics in ulcerative colitis, adenomatous polyps, and cancer. *Cancer* 56:1094–1098.
- Kanis JA, Melton LJ III, Christiansen C, Johnston CC, Khaltaev N. 1994. The diagnosis of osteoporosis. *J Bone Miner Res* 9:1137–1141.
- Kapsner P, Langsdorf L, Marcus R, Kraemer FB, Hoffman AR. 1986. Milk-alkali syndrome in patients treated with calcium carbonate after cardiac transplantation. *Arch Intern Med* 146:1965–1968.
- Katzman DK, Bachrach LK, Carter DR, Marcus R. 1991. Clinical and anthropometric correlates of bone mineral acquisition in healthy adolescent girls. *J Clin Endocrinol Metab* 73:1332–1339.
- Kayne LH, Lee DB. 1993. Intestinal magnesium absorption. *Miner Electrolyte Metab* 19:210–217.
- Keddie KMG. 1987. Case report: Severe depressive illness in the context of hypervitaminosis D. *Br J Psych* 150:394–396.
- Kellie SE, Brody JA. 1990. Sex-specific and race-specific hip fracture rates. *Am J Pub Hlth* 80:326–328.
- Kelsay JL, Prather ES. 1983. Mineral balances of human subjects consuming spinach in a low-fiber diet and in a diet containing fruits and vegetables. *Am J Clin Nutr* 38:12–19.
- Kelsay JL, Behall KM, Prather ES. 1979. Effect of fiber from fruits and vegetables on metabolic responses of human subjects. II. Calcium, magnesium, iron, and silicon balances. *Am J Clin Nutr* 32:1876–1880.
- Kent GN, Price RI, Gutteridge DH, Smith M, Allen JR, Bhagat CI, Barnes MP, Hickling CJ, Retallack RW, Wilson SG, Devlin RD, Davies C, St. John A. 1990. Human lactation: Forearm trabecular bone loss, increased bone turnover, and renal conservation of calcium and inorganic phosphate with recovery of bone mass following weaning. *J Bone Miner Res* 5:361–369.
- Kent GN, Price RI, Gutteridge DH, Rosman KJ, Smith M, Allen JR, Hickling CJ, Blakeman SL. 1991. The efficiency of intestinal calcium absorption is increased in late pregnancy but not in established lactation. *Calcif Tissue Int* 48:293–295.
- Kesteloot H, Joossens JV. 1990. The relationship between dietary intake and urinary excretion of sodium, potassium, calcium and magnesium: Belgian Inter-university Research on Nutrition and Health. *J Hum Hypertension* 4:527–533.

- Kiel DP, Felson DT, Hannan MT, Anderson JJ, Wilson PW. 1990. Caffeine and the risk of hip fracture: The Framingham Study. *Am J Epidemiol* 132:675–684.
- Kinyamu HK, Gallagher JC, Balhorn KE, Petranick KM, Rafferty KA. 1997. Serum vitamin D metabolites and calcium absorption in normal young and elderly free-living women and in women living in nursing homes. *Am J Clin Nutr* 65:790–797.
- Klaassen CD, Amdur MO, Doull J. 1986. *Casarett and Doull's Toxicology: The Basic Science of Poisons, Third Edition*. New York: Macmillan Publishing Company.
- Kleerekoper M, Mendlovic DB. 1993. Sodium fluoride therapy of postmenopausal osteoporosis. *Endocrinol Rev* 14:312–323.
- Kleibeuker JH, Welberg JW, Mulder NH, van der Meer R, Cats A, Limburg AJ, Kreumer WM, Hardonk MJ, de Vries EG. 1993. Epithelial cell proliferation in the sigmoid colon of patients with adenomatous polyps increases during oral calcium supplementation. *Br J Cancer* 67:500–503.
- Klein CJ, Moser-Veillon PB, Douglass LW, Ruben KA, Trocki O. 1995. A longitudinal study of urinary calcium, magnesium, and zinc excretion in lactating and nonlactating postpartum women. *Am J Clin Nutr* 61:779–786.
- Kleiner SM, Bazzarre TL, Ainsworth BE. 1994. Nutritional status of nationally ranked elite bodybuilders. *Int J Sport Nutr* 4:54–69.
- Kleinman GE, Rodriguez H, Good MC, Caudle MR. 1991. Hypercalcemic crisis in pregnancy associated with excessive ingestion of calcium carbonate antacid (milk-alkali syndrome): Successful treatment with hemodialysis. *Obstet Gynecol* 73:496–499.
- Knochel JP. 1977. The pathophysiology and clinical characteristics of severe hypophosphatemia. *Arch Intern Med* 137:203–220.
- Knochel JP. 1985. The clinical status of hypophosphatemia: An update. *N Engl J Med* 313:447–449.
- Kobayashi A, Kawai S, Ohbe Y, Nagashima Y. 1975. Effects of dietary lactose and a lactase preparation on the intestinal absorption of calcium and magnesium in normal infants. *Am J Clin Nutr* 28:681–683.
- Kochersberger G, Westlund R, Lyles KW. 1991. The metabolic effects of calcium supplementation in the elderly. *J Am Geriatr Soc* 39:192–196.
- Koetting CA, Wardlaw GM. 1988. Wrist, spine, and hip bone density in women with variable histories of lactation. *Am J Clin Nutr* 48:1479–1481.
- Kohlmeier L, Mendez M, McDuffie J, Miller M. 1997. Computer-assisted self-interviewing: A multimedia approach to dietary assessment. *Am J Clin Nutr* 65:1275S–1281S.
- Koo W, Tsang R. 1997. Calcium, magnesium, phosphorus and vitamin D. In: *Nutrition During Infancy, 2nd Edition*. Cincinnati: Digital Education. Pp. 175–189.
- Koo W, Krug-Wispe S, Neylen M, Succop P, Oestreich AE, Tsang RC. 1995. Effect of three levels of vitamin D intake in preterm infants receiving high mineral-containing milk. *J Pediatr Gastroenterol Nutr* 21:182–189.
- Krall EA, Sahyoun N, Tannenbaum S, Dallal GE, Dawson-Hughes B. 1989. Effect of vitamin D intake on seasonal variations in parathyroid hormone secretion in postmenopausal women. *N Engl J Med* 321:1777–1783.
- Kramer L, Osis D, Wiatrowski E, Spenser H. 1974. Dietary fluoride in different areas of the United States. *Am J Clin Nutr* 27:590–594.
- Kreiger N, Kelsey JL, Holford TR, O'Connor T. 1982. An epidemiologic study of hip fracture in postmenopausal women. *Am J Epidemiol* 116:141–148.

- Krejs GJ, Nicar MJ, Zerwekh HE, Normal DA, Kane MG, Pak CY. 1983. Effect of 1,25-dihydroxyvitamin D<sub>3</sub> on calcium and magnesium absorption in the healthy human jejunum and ileum. *Am J Med* 75:973–976.
- Krishnamachari KA. 1986. Skeletal fluorosis in humans: A review of recent progress in the understanding of the disease. *Prog Food Nutr Sci* 10:279–314.
- Krook L, Whalen JP, Lesser GV, Berens DL. 1975. Experimental studies on osteoporosis. *Methods Achiev Exp Pathol* 7:72–108.
- Kröger H, Kotaniemi A, Vainio P, Alhava E. 1992. Bone densitometry of the spine and femur in children by dual-energy x-ray absorptiometry. *Bone Miner* 17:75–85.
- Kröger H, Kotaniemi A, Kröger L, Alhava E. 1993. Development of bone mass and bone density of the spine and femoral neck—a prospective study of 65 children and adolescents. *Bone Miner* 23:171–182.
- Kröger H, Alhava E, Honkanen R, Tuppurainen M, Saarikoski S. 1994. The effect of fluoridated drinking water on axial bone mineral density: A population-based study. *Bone Miner* 27:33–41.
- Kruse K, Bartels H, Kracht U. 1984. Parathyroid function in different stages of vitamin D deficiency rickets. *Eur J Pediatr* 141:158–162.
- Kumar JV, Green EL, Wallace W, Carnahan T. 1989. Trends in dental fluorosis and dental caries prevalences in Newburgh and Kingston, NY. *Am J Pub Hlth* 79:565–569.
- Kumar R. 1986. The metabolism and mechanism of action of 1,25-dihydroxyvitamin D<sub>3</sub>. *Kidney Int* 30:793–803.
- Kumar R, Cohen WR, Silva P, Epstein FH. 1979. Elevated 1,25-dihydroxyvitamin D plasma levels in normal human pregnancy and lactation. *J Clin Invest* 63:342–344.
- Kummerow FA, Simon Cho BH, Huang YT, Imai H, Kamio A, Deutsch MJ, Hooper WM. 1976. Additive risk factors in atherosclerosis. *Am J Clin Nutr* 29:579–584.
- Kurtz TW, Al-Bander HA, Morris RC. 1987. “Salt sensitive” essential hypertension in men. *N Engl J Med* 317:1043–1048.
- Kurzel RB. 1991. Serum magnesium levels in pregnancy and preterm labor. *Am J Perinatol* 8:119–127.
- Kuti V, Balazs M, Morvay F, Varenka Z, Szekely A, Szucs M. 1981. Effect of maternal magnesium supply on spontaneous abortion and premature birth and on intrauterine fetal development: Experimental epidemiological study. *Magnes Bull* 3:73–79.
- Ladizesky M, Lu Z, Oliveri B, San Roman N, Diaz S, Holick MF, Mautalen C. 1995. Solar ultraviolet B radiation and photoproduction of vitamin D<sub>3</sub> in central and southern areas of Argentina. *J Bone Miner Res* 10:545–549.
- Lafferty FW. 1991. Differential diagnosis of hypercalcemia. *J Bone Miner Res* 6:S51–S59.
- Lakshmanan LF, Rao RB, Kim WW, Kelsay JL. 1984. Magnesium intakes, balances, and blood levels of adults consuming self-selected diets. *Am J Clin Nutr* 40:1380–1389.
- Lamberg-Allardt C, von Knorring J, Slatis P, Holmstrom T. 1989. Vitamin D status and concentrations of serum vitamin D metabolites and osteocalcin in elderly patients with femoral neck fracture: A follow-up study. *Eur J Clin Nutr* 43:355–361.
- Lamberg-Allardt C, Karkkainen M, Seppanen R, Bistrom H. 1993. Low serum 25-hydroxyvitamin D concentrations and secondary hyperparathyroidism in middle-aged white strict vegetarians. *Am J Clin Nutr* 58:684–689.
- Largent EJ. 1952. Rates of elimination of fluoride stored in the tissues of man. *Arch Ind Hyg* 6:37–42.

- Larsen MJ, Senderovitz F, Kirkegaard E, Poulsen S, Fejerskov O. 1988. Dental fluorosis in the primary and permanent dentition in fluoridated areas with consumption of either powdered milk or natural cow's milk. *J Dent Res* 67:822–825.
- Lawson DE, Fraser DR, Kodicek E, Morris HR, Williams DH. 1971. Identification of 1,25-dihydroxycholecalciferol, a new kidney hormone controlling calcium metabolism. *Nature* 230:228–230.
- Lealman GT, Logan RW, Hutchison JH, Kerr MM, Fulton AM, Brown CA. 1976. Calcium, phosphorus, and magnesium concentrations in plasma during first week of life and their relation to type of milk feed. *Arch Dis Child* 51:377–384.
- LeBlanc A, Schneider V, Spector E, Evans H, Rowe R, Lane H, Demers L, Lipton A. 1995. Calcium absorption, endogenous excretion, and endocrine changes during and after long-term bed rest. *Bone* 16:301S–304S.
- Lebrun JB, Moffatt ME, Mundy RJ, Sangster RK, Postl BD, Dooley JP, Dilling LA, Godel JC, Haworth JC. 1993. Vitamin D deficiency in a Manitoba community. *Can J Pub Hlth* 84:394–396.
- Lee WT, Leung SS, Wang SH, Xu YC, Zeng WP, Lau J, Oppenheimer SJ, Cheng JC. 1994. Double-blind, controlled calcium supplementation and bone mineral accretion in children accustomed to a low-calcium diet. *Am J Clin Nutr* 60:744–750.
- Lee WT, Leung SS, Leung DM, Tsang HS, Lau J, Cheng JC. 1995. A randomized double-blind controlled calcium supplementation trial, and bone and height acquisition in children. *Br J Nutr* 74:125–139.
- Lee WT, Leung SS, Leung DM, Cheng JC. 1996. A follow-up study on the effects of calcium-supplement withdrawal and puberty on bone acquisition of children. *Am J Clin Nutr* 64:71–77.
- LeGeros RZ, Glenn FB, Lee DD, Glenn WD. 1985. Some physico-chemical properties of deciduous enamel with and without pre-natal fluoride supplementation (PNF). *J Dent Res* 64:465–469.
- Lechner NDM, Bullock BC, Clarkson TB, Lofland HB. 1967. Biologic activities of vitamin D<sub>2</sub> and D<sub>3</sub> for growing squirrel monkeys. *Lab Anim Care* 17:483.
- Leitch I, Aitken FC. 1959. The estimation of calcium requirement: A re-examination. *Nutr Abs Rev* 29:393–409.
- Lemann J Jr. 1996. Calcium and phosphate metabolism: An overview in health and in calcium stone formers. In: Coe FL, Favus MJ, Pak CY, Parks JH, Preminger GM, eds. *Kidney Stones: Medical and Surgical Management*. Philadelphia, PA: Lippincott-Raven. Pp. 259–288.
- Lemann J Jr, Worcester EM, Gray RW. 1991. Hypercalciuria and stones. *Am J Kidney Dis* 17:386–391.
- Lemke CW, Doherty JM, Arra MC. 1970. Controlled fluoridation: The dental effects of discontinuation in Antigo, Wisconsin. *J Am Dent Assoc* 80:782–786.
- Leone NC, Shimkin MB, Arnold FA, Stevenson CA, Zimmerman ER, Geiser PB, Lieberman JE. 1954. Medical aspects of excessive fluoride in a water supply. *Pub Hlth Rep* 69:925–936.
- Leone NC, Stevenson CA, Hilbush TF, Sosman MC. 1955. A roentgenologic study of a human population exposed to high-fluoride domestic water: A ten-year study. *Am J Roentg* 74:874–885.
- Leone NC, Stevenson CA, Besse B, Hawes, LE, Dawber TA. 1960. The effects of the absorption of fluoride. II. A radiological investigation of 546 human residents of an area in which the drinking water contained only a minute trace of fluoride. *Archs Ind Hlth* 21:326–327.

- Leoni V, Fabiani L, Ticchiarelli L. 1985. Water hardness and cardiovascular mortality rate in Abruzzo, Italy. *Arch Environ Health* 40:274–278.
- Leung SSF, Lui S, Swaminathan R. 1989. Vitamin D status of Hong Kong Chinese infants. *Acta Paediatr Scand* 78:303–306.
- Leverett DH. 1986. Prevalence of dental fluorosis in fluoridated and nonfluoridated communities—a preliminary investigation. *J Pub Hlth Dent* 46:184–187.
- Leverett DH, Adair SM, Vaughan BW, Proskin HM, Moss ME. 1997. Randomized clinical trial of the effect of prenatal fluoride supplements in preventing dental caries. *Caries Res* 31:174–179.
- Levine RJ, Hauth JC, Curet LB, Sibai BM, Catalano PM, Morris CD, DerSimonian R, Esterlitz JR, Raymond EG, Bild DE, Clemens JD, Cutler JA. 1997. Trial of calcium to prevent preeclampsia. *N Engl J Med* 337:69–76.
- Levy SM, Muchow G. 1992. Provider compliance with recommended dietary fluoride supplement protocol. *Am J Pub Hlth* 82:281–283.
- Levy SM, Kohout FJ, Kiritsy MC, Heilman JR, Wefel JS. 1995. Infants' fluoride ingestion from water, supplements and dentifrice. *J Am Dent Assoc* 126:1625–1632.
- Lewis DW. 1976. *An Evaluation of the Effects of Water Fluoridation, City of Toronto, 1963–1975*. Toronto, Canada: The Corporation of the City of Toronto.
- Lewis NM, Marcus MSK, Behling AR, Greger JL. 1989. Calcium supplements and milk: Effects on acid-base balance and on retention of calcium, magnesium, and phosphorus. *Am J Clin Nutr* 49:527–533.
- Liel Y, Edwards J, Shary J, Spicer KM, Gordon L, Bell NH. 1988. The effects of race and body habitus on bone mineral density of the radius, hip, and spine in premenopausal women. *J Clin Endocrinol Metab* 66:1247–1250.
- Lin S-H, Lin Y-F, Shieh S-D. 1996. Milk-alkali syndrome in an aged patient with osteoporosis and fractures. *Nephron* 73:496–497.
- Linden V. 1974. Vitamin D and myocardial infarction. *Br Med J* 3:647–650.
- Linkswiler HM, Zemel MB, Hegsted M, Schuette S. 1981. Protein-induced hypercalciuria. *Fed Proc* 40:2429–2433.
- Lips P, Wiersinga A, vanGinkel FC, Jongen MJ, Netelenbos JC, Hackeng WH, Delmas PD, vanderVijgh WJ. 1988. The effect of vitamin D supplementation on vitamin D status and parathyroid function in elderly subjects. *J Clin Endocrinol Metab* 67:644–650.
- Lips P, Graafmans WC, Ooms ME, Bezemer D, Bouter LM. 1996. Vitamin D supplementation and fracture incidence in elderly persons: A randomized, placebo-controlled clinical trial. *Ann Intern Med* 124:400–406.
- Lipski PS, Torrance A, Kelly PJ, James OF. 1993. A study of nutritional deficits of long-stay geriatric patients. *Age Aging* 22:244–255.
- Lissner L, Bengtsson C, Hansson T. 1991. Bone mineral content in relation to lactation history in pre- and postmenopausal women. *Calcif Tissue Int* 48:319–325.
- Livingstone MB, Prentice AM, Coward WA, Strain JJ, Black AE, Davies PS, Stewart CM, McKenna PG, Whitehead RG. 1992. Validation estimates of energy intake by weighted dietary record and diet history in children and adolescents. *Am J Clin Nutr* 56:29–35.
- Lloyd T, Schaeffer JM, Walker MA, Demers LM. 1991. Urinary hormonal concentrations and spinal bone densities of premenopausal vegetarian and nonvegetarian women. *Am J Clin Nutr* 54:1005–1010.

- Lloyd T, Andon MB, Rollings N, Martel JK, Landis R, Demers LM, Eggli DF, Kieselhorst K, Kulin HE. 1993. Calcium supplementation and bone mineral density in adolescent girls. *J Am Med Assoc* 270:841–844.
- Lo CW, Paris PW, Clemens TL, Nolan J, Holick MF. 1985. Vitamin D absorption in healthy subjects and in patients with intestinal malabsorption syndromes. *Am J Clin Nutr* 42:644–649.
- Lonnerdal B. 1997. Effects of milk and milk components on calcium, magnesium, and trace element absorption during infancy. *Physiol Rev* 77:643–669.
- Looker AC, Harris TB, Madans JH, Sempers CT. 1993. Dietary calcium and hip fracture risk: The NHANES I Epidemiology Follow-Up Study. *Osteopor Int* 3:177–184.
- Looker AC, Johnston CC Jr, Wahner HW, Dunn WL, Calvo MS, Harris TB, Heyse SP, Lindsay RL. 1995. Prevalence of low femoral bone density in older US women from NHANES III. *J Bone Miner Res* 10:796–802.
- Lopez JM, Gonzalez G, Reyes V, Campino C, Diaz S. 1996. Bone turnover and density in healthy women during breastfeeding and after weaning. *Osteopor Int* 6:153–159.
- Lotz M, Zisman E, Bartter FC. 1968. Evidence for a phosphorus-depletion syndrome in man. *N Engl J Med* 278:409–415.
- Lowenstein FW, Stanton MF. 1986. Serum magnesium levels in the United States, 1971–1974. *J Am Coll Nutr* 5:399–414.
- Lowik MR, van Dokkum W, Kistemaker C, Schaafsma G, Ockhuizen T. 1993. Body composition, health status and urinary magnesium excretion among elderly people (Dutch Nutrition Surveillance System). *Magnes Res* 6:223–232.
- LSRO/FASEB (Life Sciences Research Office/Federation of American Societies for Experimental Biology). 1986. *Guidelines for Use of Dietary Intake Data*. Anderson SA, ed. Bethesda, MD: LSRO/FASEB.
- Lu PW, Briody JN, Ogle GD, Morley K, Humphries IR, Allen J, Howman-Giles R, Sillence D, Cowell CT. 1994. Bone mineral density of total body, spine, and femoral neck in children and young adults: A cross-sectional and longitudinal study. *J Bone Miner Res* 9:1451–1458.
- Luckey MM, Meier DE, Mandeli JP, DaCosta MC, Hubbard ML, Goldsmith SJ. 1989. Radial and vertebral bone density in white and black women: Evidence for racial differences in premenopausal bone homeostasis. *J Clin Endocrinol Metab* 69:762–770.
- Lukert BP, Raisz LG. 1990. Glucocorticoid-induced osteoporosis: Pathogenesis and management. *Ann Intern Med* 112:352–364.
- Lund B, Sorensen OH. 1979. Measurement of 25-hydroxyvitamin D in serum and its relation to sunshine, age and vitamin D intake in the Danish population. *Scand J Clin Lab Invest* 39:23–30.
- Luoma H, Aromaa A, Helminen S, Murtomaa H, Kiviluoto L, Punstar S, Knekt P. 1983. Risk of myocardial infarction in Finnish men in relation to fluoride, magnesium and calcium concentration in drinking water. *Acta Med Scand* 213:171–176.
- Lutwak L, Lester L, Gitelman HJ, Fox M, Whedon GD. 1964. Effects of high dietary calcium and phosphorus on calcium, phosphorus, nitrogen and fat metabolism in children. *Am J Clin Nutr* 14:76–82.

- Ma J, Folsom AR, Melnick SL, Eckfeldt JH, Sharrett AR, Nabulsi AA, Hutchinson RG, Metcalf PA. 1995. Associations of serum and dietary magnesium with cardiovascular disease, hypertension, diabetes, insulin, and carotid arterial wall thickness: The ARIC study. *Atherosclerosis Risk in Community Study. J Clin Epidemiol* 48:927–940.
- MacLaughlin J, Holick MF. 1985. Aging decreases the capacity of human skin to produce vitamin D<sub>3</sub>. *J Clin Invest* 76:1536–1538.
- MacLaughlin JA, Anderson RR, Holick MF. 1982. Spectral character of sunlight modulates photosynthesis of previtamin D<sub>3</sub> and its photoisomers in human skin. *Science* 216:1001–1003.
- Maguire ME. 1984. Hormone-sensitive magnesium transport and magnesium regulation of adenylate cyclase. *Trends Pharmacol Sci* 5:73–77.
- Mahalko JR, Sandstead HH, Johnson LK, Milne DB. 1983. Effect of a moderate increase in dietary protein on the retention and excretion of Ca, Cu, Fe, Mg, P, and Zn by adult males. *Am J Clin Nutr* 37:8–14.
- Maheshwari UR, McDonald JT, Schneider VS, Brunetti AJ, Leybin L, Newbrun E, Hodge HC. 1981. Fluoride balance studies in ambulatory healthy men with and without fluoride supplements. *Am J Clin Nutr* 34:2679–2684.
- Maheshwari UR, King JC, Leybin L, Newbrun E, Hodge HC. 1983. Fluoride balances during early and late pregnancy. *J Occup Med* 25:587–590.
- Mallet E, Gugi B, Brunelle P, Henocq A, Basuyau JP, Lemeur H. 1986. Vitamin D supplementation in pregnancy: A controlled trial of two methods. *Obstet Gynecol* 68:300–304.
- Malm OJ. 1958. Calcium requirement and adaptation in adult men. *Scand J Clin Lab Invest* 10(Suppl 36):1–280.
- Malone DNS, Horn DB. 1971. Acute hypercalcemia and renal failure after antacid therapy. *Br Med J* 1:709–710.
- Manz F. 1992. Why is the phosphorus content of human milk exceptionally low? *Monatsschr Kinderheilkd* 140:S35–S39.
- Marcus R, Cann C, Madvig P, Minkoff J, Goddard M, Bayer M, Martin M, Gaudiani L, Haskell W, Genant H. 1985. Menstrual function and bone mass in elite women distance runners. Endocrine and metabolic features. *Ann Intern Med* 102:158–163.
- Margen S, Chu JY, Kaufmann NA, Calloway DH. 1974. Studies in calcium metabolism I. The calciuretic effect of dietary protein. *Am J Clin Nutr* 27:584–589.
- Margolis HC, Moreno EC. 1990. Physicochemical perspectives on the cariostatic mechanisms of systemic and topical fluorides. *J Dent Res* 69(Spec Iss):606–613.
- Marier JR. 1986. Magnesium content of the food supply in the modern-day world. *Magnesium* 5:1–8.
- Marken PA, Weart CW, Carson DS, Gums JG, Lopes-Virella MF. 1989. Effects of magnesium oxide on the lipid profile of healthy volunteers. *Atherosclerosis* 77:37–42.
- Markestad T, Elzouki AY. 1991. Vitamin-D deficiency rickets in northern Europe and Libya. In: Glorieux FH, ed. *Rickets: Nestle Nutrition Workshop Series, Vol 21*. New York, NY: Raven Press.
- Markestad T, Ulstein M, Bassoe HH, Aksnes L, Aarskog D. 1983. Vitamin D metabolism in normal and hypoparathyroid pregnancy and lactation. Case report. *Br J Obstet Gynaecol* 90:971–976.
- Markestad T, Ulstein M, Aksnes L, Aarskog D. 1986. Serum concentrations of vitamin D metabolites in vitamin D supplemented pregnant women. A longitudinal study. *Acta Obstet Gynecol Scand* 65:63–67.

- Marquis RE. 1995. Antimicrobial actions of fluoride for oral bacteria. *Can J Microbiol* 41:955–964.
- Marsh AG, Sanchez TV, Midkelsen O, Keiser J, Mayor G. 1980. Cortical bone density of adult lacto-ovo-vegetarian and omnivorous women. *J Am Diet Assoc* 76:148–151.
- Marshall DH, Nordin BEC, Speed R. 1976. Calcium, phosphorus and magnesium requirement. *Proc Nutr Soc* 35:163–173.
- Martin AD, Bailey DA, McKay HA. 1997. Bone mineral and calcium accretion during puberty. *Am J Clin Nutr* 66:611–615.
- Martin BJ. 1990. The magnesium load test: Experience in elderly subjects. *Aging (Milano)* 2:291–296.
- Martin TJ, Grill V. 1995. Hypercalcemia. *Clin Endocrinol* 42:535–538.
- Martinez ME, Salinas M, Miguel JL, Herrero E, Gomez P, Garcia J, Sanchez-Sicilia L, Montero A. 1985. Magnesium excretion in idiopathic hypercalciuria. *Nephron* 40: 446–450.
- Massey LK, Wise KJ. 1984. The effect of dietary caffeine on urinary excretion of calcium, magnesium, sodium and potassium in healthy young females. *Nutr Res* 4:43–50.
- Massey LK, Roman-Smith H, Sutton RA. 1993. Effect of dietary oxalate and calcium on urinary oxalate and risk of formation of calcium oxalate kidney stones. *J Am Diet Assoc* 93:901–906.
- Matkovic V. 1991. Calcium metabolism and calcium requirements during skeletal modeling and consolidation of bone mass. *Am J Clin Nutr* 54:245S–260S.
- Matkovic V, Heaney RP. 1992. Calcium balance during human growth: Evidence for threshold behavior. *Am J Clin Nutr* 55:992–996.
- Matkovic V, Fontana D, Tominac C, Goel P, Chesnut CH III. 1990. Factors that influence peak bone mass formation: A study of calcium balance and the inheritance of bone mass in adolescent females. *Am J Clin Nutr* 52:878–888.
- Matkovic V, Jelic T, Wardlaw GM, Illich JZ, Goel PK, Wright JK, Andon MB, Smith KT, Heaney RP. 1994. Timing of peak bone mass in Caucasian females and its implication for the prevention of osteoporosis. *J Clin Invest* 93:799–808.
- Matkovic V, Illich JZ, Andon MB, Hsieh LC, Tzagournis MA, Lagger BJ, Goel PK. 1995. Urinary calcium, sodium, and bone mass of young females. *Am J Clin Nutr* 62:417–425.
- Matsuda H. 1991. Magnesium gating of the inwardly rectifying K<sup>+</sup> channel. *Ann Rev Physiol* 53:289–298.
- Matsuoka LY, Ide L, Wortsman J, MacLaughlin JA, Holick MF. 1987. Sunscreens suppress cutaneous vitamin D<sub>3</sub> synthesis. *J Clin Endocrinol Metab* 64:1165–1168.
- Matsuoka LY, Wortsman J, Dannenberg MJ, Hollis BW, Lu Z, Holick MF. 1992. Clothing prevents ultraviolet-B radiation-dependent photosynthesis of vitamin D<sub>3</sub>. *J Clin Endocrinol Metab* 75:1099–1103.
- Mawer EB, Schaefer K, Lumb GA, Stanbury SW. 1971. The metabolism of isotopically labelled vitamin D<sub>3</sub> in man: The influence of the state of vitamin D nutrition. *Clin Sci* 40:39–53.
- Mawer EB, Backhouse J, Holman CA, Lumb GA, Stanbury DW. 1972. The distribution and storage of vitamin D and its metabolites in human tissues. *Clin Sci* 43:413–431.
- Mazariegos-Ramos E, Guerrero-Romero F, Rodriguez-Moran M, Lazcano-Burciaga G, Paniagua R, Amato D. 1995. Consumption of soft drinks with phosphoric acid as a risk factor for the development of hypocalcemia in children: A case-control study. *J Pediatr* 126:940–942.

- McCarron DA. 1983. Calcium and magnesium nutrition in human hypertension. *Ann Int Med* 98:800–805.
- McCarron DA, Morris CD. 1985. Blood pressure response to oral calcium in persons with mild to moderate hypertension: A randomized, double-blind, placebo-controlled, crossover trial. *Ann Intern Med* 103:825–831.
- McCarron DA, Morris CD, Young E, Roullet C, Drüeke T. 1991. Dietary calcium and blood pressure: Modifying factors in specific populations. *Am J Clin Nutr* 54:215S–219S.
- McCauley HB, McClure FJ. 1954. Effect of fluoride in drinking water on the osseous development of the hand and wrist in children. *Pub Hlth Rep* 69:671–683.
- McClure FJ. 1943. Ingestion of fluoride and dental caries. Quantitative relations based on food and water requirements of children one to twelve years old. *Am J Dis Child* 66:362–369.
- McClure FJ, Zipkin I. 1958. Physiologic effects of fluoride as related to water fluoridation. *Dent Clin North Am* 2:441–458.
- McCrory WW, Forman CW, McNamara H, Barnett HL. 1950. Renal excretion of phosphate in newborn infants: Observations in normal infants and in infants with hypocalcemic tetany. *Am J Dis Child* 80:512–513.
- McFarlane D. 1941. Experimental phosphate nephritis in the rat. *J Pathol* 52:17–24.
- McGrath N, Singh V, Cundy T. 1993. Severe vitamin D deficiency in Auckland. *N Zel Med J* 106:524–526.
- McKenna MJ. 1992. Differences in vitamin D status between countries in young adults and the elderly. *Am J Med* 93:69–77.
- McKnight-Hanes MC, Leverett DH, Adair SM, Shields CP. 1988. Fluoride content of infant formulas: Soy-based formulas as a potential factor in dental fluorosis. *Pediatr Dent* 10:189–194.
- Meier DE, Luckey MM, Wallenstein S, Clemens TL, Orwoll ES, Waslien CI. 1991. Calcium, vitamin D, and parathyroid hormone status in young white and black women: Association with racial differences in bone mass. *J Clin Endocrinol Metab* 72:703–710.
- Melton LJ III, Chrischilles EA, Cooper C, Lane AW, Riggs, BL. 1992. Perspective. How many women have osteoporosis? *J Bone Miner Res* 7:1005–1010.
- Melton LJ III, Atkinson EJ, O'Fallon WM, Wahner HW, Riggs BL. 1993a. Long-term fracture prediction by bone mineral assessed at different skeletal sites. *J Bone Miner Res* 8:1227–1233.
- Melton LJ III, Bryant SC, Wahner HW, O'Fallon WM, Malkasian GD, Judd HL, Riggs BL. 1993b. Influence of breastfeeding and other reproductive factors on bone mass later in life. *Osteopor Int* 3:76–83.
- Merke J, Klaus G, Hugel U, Waldherr R, Ritz E. 1986. No 1,25-dihydroxyvitamin D<sub>3</sub> receptors on osteoclasts of calcium-deficient chicken despite demonstrable receptors on circulating monocytes. *J Clin Invest* 77:312–314.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- Mertz W, Abernathy CO, Olin SS. 1994. *Risk Assessment of Essential Elements*. Washington, DC: ILSI Press.
- Meulmeester JF, vandenBerg H, Wedel M, Boshuis PG, Hulshof KF, Luyken R. 1990. Vitamin D status, parathyroid hormone and sunlight in Turkish, Moroccan and Caucasian children in The Netherlands. *Eur J Clin Nutr* 44:461–470.

- Meyer F, White E. 1993. Alcohol and nutrients in relation to colon cancer in middle-aged adults. *Am J Epidemiol* 138:225–236.
- Miller JZ, Smith DL, Flora L, Slemenda C, Jiang X, Johnston CC Jr. 1988. Calcium absorption from calcium carbonate and a new form of calcium (CCM) in healthy male and female adolescents. *Am J Clin Nutr* 48:1291–1294.
- Mimouni FB. 1996. The ion-selective magnesium electrode: A new tool for clinicians and investigators. *J Am College Nutr* 15:4–5.
- Mimouni F, Tsang RC, Hertzberg VS, Miodovnik M. 1986. Polycythemia hypomagnesemia and hypocalcemia infants of diabetic mothers. *Am J Dis Child* 140:798–800.
- Mimouni F, Campaigne B, Neylan M, Tsang RC. 1993. Bone mineralization in the first year of life in infants fed human milk, cow-milk formula, or soy-based formula. *J Pediatr* 122:348–354.
- Moncrief MW, Chance GW. 1969. Nephrotoxic effect of vitamin D therapy in vitamin D refractory rickets. *Arch Dis Child* 44:571–579.
- Montaldo MB, Benson JD. 1986. Nutrient intakes of older infants: Effect of different milk feedings. *J Am Coll Nutr* 5:331–341.
- Mordes JP, Wacker WEC. 1978. Excessive magnesium. *Pharmacol Rev* 29:273–300.
- Moser PB, Issa CF, Reynolds RD. 1983. Dietary magnesium intake and the concentration of magnesium in plasma and erythrocytes of postpartum women. *J Am Coll Nutr* 2:387–396.
- Moser PB, Reynolds RD, Acharya S, Howard MP, Andon MB. 1988. Calcium and magnesium dietary intakes and plasma and milk concentrations of Nepalese lactating women. *Am J Clin Nutr* 47:735–739.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance data from vital and health statistics, No. 174. Hyattsville, MD: National Center for Health Statistics.
- Motoyama T, Sano H, Fukuzaki H. 1989. Oral magnesium supplementation in patients with essential hypertension. *Hypertension* 13:227–232.
- Mountokalakis TD. 1987. Effects of aging, chronic disease, and multiple supplements on magnesium requirements. *Magnesium* 6:5–11.
- Moya M, Cortes E, Ballester MI, Vento M, Juste M. 1992. Short-term polycose substitution for lactose reduces calcium absorption in healthy term babies. *J Pediatr Gastroenterol Nutr* 14:57–61.
- Muhler JC. 1970. Ingestion from foods. In: Adler P, ed. *Fluorides and Human Health*. Monograph series no. 59. Geneva: World Health Organization. Pp. 32–40.
- Muldowney WP, Mazbar SA. 1996. Rolaids-yogurt syndrome: A 1990s version of milk-alkali syndrome. *Am J Kidney Dis* 27:270–272.
- Murphy SP, Calloway DH. 1986. Nutrient intakes of women in NHANES II, emphasizing trace minerals, fiber, and phytate. *J Am Diet Assoc* 86:1366–1372.
- Naccache H, Simard PL, Trahan L, Demers M, Lapointe C, Brodeur JM. 1990. Variability in the ingestion of toothpaste by preschool children. *Caries Res* 24:359–363.
- Naccache H, Simard PL, Trahan L, Brodeur JM, Demers M, Lachapelle D, Bernard PM. 1992. Factors affecting the ingestion of fluoride dentifrice by children. *J Pub Hlth Dent* 52:222–226.
- Nadler JL, Malayan S, Luong H, Shaw S, Natarajan RD, Rude RK. 1992. Intracellular free magnesium deficiency plays a key role in increased platelet reactivity in type II diabetes mellitus. *Diabetes Care* 15:835–841.

- Nadler JL, Buchanan T, Natarajan R, Antonipillai I, Bergman R, Rude RK. 1993. Magnesium deficiency produces insulin resistance and increased thromboxane synthesis. *Hypertension* 21:1024–1029.
- Nagubandi S, Kumar R, Londowski JM, Corradino RA, Tietz PS. 1980. Role of vitamin D glucosiduronate in calcium homeostasis. *J Clin Invest* 66:1274–1280.
- Nagy L, Tarnok F, Past T, Mozsik GY, Deak G, Tapsonyi Z, Fendler K, Javor T. 1988. Human tolerability and pharmacodynamic study of TISACID tablet in duodenal ulcer patients. A prospective, randomized, self-controlled clinico-pharmacological study. *Acta Medica Hung* 45:231–246.
- Nakamura T, Turner CH, Yoshikawa T, Slemenda CW, Peacock M, Burr DB, Mizuno Y, Orimo H, Ouchi Y, Johnston CC Jr. 1994. Do variations in hip geometry explain differences in hip fracture risk between Japanese and white Americans? *J Bone Miner Res* 9:1071–1076.
- Nakao H. 1988. Nutritional significance of human milk vitamin D in neonatal period. *Kobe J Med Sci* 34:121–128.
- Narang NK, Gupta RC, Jain MK. 1984. Role of vitamin D in pulmonary tuberculosis. *J Assoc Physicians India* 32:185–188.
- National Council for Nutrition (Conseil National de la Nutrition). 1994. *Recommendations nutritionnelles pour la Belgique*. Bruxelles, Belgium: Ministère des Affaires Sociales de la Santé Publique et de l’Environnement.
- National Food Administration. 1989. *Swedish Nutrition Recommendations, 2nd edition*. Uppsala, Sweden: National Food Administration.
- Need AG, Morris HA, Horowitz M, Nordin C. 1993. Effects of skin thickness, age, body fat, and sunlight on serum 25-hydroxyvitamin D. *Am J Clin Nutr* 58:882–885.
- Neri LC, Johansen HL. 1978. Water hardness and cardiovascular mortality. *Ann NY Acad Sci* 304:203–219.
- Neri LC, Johansen HL, Hewitt D, Marier J, Langner N. 1985. Magnesium and certain other elements and cardiovascular disease. *Sci Total Environ* 42:49–75.
- Netherlands Food and Nutrition Council. 1992. *Report on the Age Limit to be Adopted in Connection with “Guidelines for a Healthy Diet.”* The Hague: Netherlands Food and Nutrition Council.
- Neville MC, Keller R, Seacat J, Lutes V, Neifert M, Casey C, Allen J, Archer P. 1988. Studies in human lactation: Milk volumes in lactating women during the onset of lactation and full lactation. *Am J Clin Nutr* 48:1375–1386.
- Newmark K, Nugent P. 1993. Milk-alkali syndrome: A consequence of chronic antacid abuse. *Postgrad Med* 93:149–156.
- Ng K, St John A, Bruce DG. 1994. Secondary hyperparathyroidism, vitamin D deficiency and hip fracture: Importance of sampling times after fracture. *Bone Miner* 25:103–109.
- Niekamp RA, Baer JT. 1995. In-season dietary adequacy of trained male cross-country runners. *Int J Sport Nutr* 5:45–55.
- Nielsen FH. 1990. Studies on the relationship between boron and magnesium which possibly affects the formation and maintenance of bones. *Magnes Trace Elem* 9:61–69.
- Nielsen FH, Hunt CD, Mullen LM, Hunt JR. 1987. Effect of dietary boron on mineral, estrogen, and testosterone metabolism in postmenopausal women. *FASEB J* 1:394–397.
- Nieves JW, Golden AL, Siris E, Kelsey JL, Lindsay R. 1995. Teenage and current calcium intake are related to bone mineral density of the hip and forearm in women aged 30–39 years. *Am J Epidemiol* 141:342–351.

- NIH (National Institutes of Health). 1994. *Optimal Calcium Intake*. NIH Consensus Statement 12:4. Bethesda, MD: NIH.
- NIN (National Institute of Nutrition). 1995. Dairy products in the Canadian diet. NIN Review No. 24. Ontario, Canada: NIN.
- Nordin BEC. 1976. *Calcium, Phosphate and Magnesium Metabolism*. Edinburgh: Churchill Livingstone.
- Nordin BEC. 1989. Phosphorus. *J Food Nutr* 45:62–75.
- Nordin BEC, Polley KJ. 1987. Metabolic consequences of the menopause. A cross-sectional, longitudinal, and intervention study on 557 normal postmenopausal women. *Calcif Tissue Int* 41:S1–S59.
- Nose O, Iida Y, Kai H, Harada T, Ogawa M, Yabuuchi H. 1979. Breath hydrogen test for detecting lactose malabsorption in infants and children: Prevalence of lactose malabsorption in Japanese children and adults. *Arch Dis Child* 54:436–440.
- NRC (National Research Council). 1980. *Recommended Dietary Allowances, 9th Edition*. Committee on Dietary Allowances, Food and Nutrition Board. Washington, DC: National Academy Press.
- NRC (National Research Council). 1982. *Diet, Nutrition, and Cancer*. Report of the Committee on Diet, Nutrition, and Cancer, Assembly of Life Sciences. Washington, DC: National Academy Press.
- NRC (National Research Council). 1983. *Risk Assessment in the Federal Government: Managing the Process*. Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC (National Research Council). 1989a. *Recommended Dietary Allowances: 10th Edition*. Report of the Subcommittee on the Tenth Edition of the RDAs, Food and Nutrition Board, and the Commission on Life Sciences. Washington, DC: National Academy Press.
- NRC (National Research Council). 1989b. *Diet and Health: Implications for Reducing Chronic Disease Risk*. Report of the Committee on Diet and Health, Food and Nutrition Board, Commission on Life Sciences. Washington, DC: National Academy Press.
- NRC (National Research Council). 1993. *Health Effects of Ingested Fluoride*. Subcommittee on Health Effects of Ingested Fluoride. Washington, DC: National Academy Press.
- NRC (National Research Council). 1994. *Science and Judgment in Risk Assessment. Committee on Risk Assessment of Hazardous Air Pollutants*. Board on Environmental Studies and Toxicology. Washington, DC: National Academy Press.
- NRC (National Research Council). 1995. *Nutrient Requirements of Laboratory Animals*. Committee on Animal Nutrition, Board on Agriculture. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- O'Brien KO, Abrams SA, Stuff JE, Liang LK, Welch TR. 1996. Variables related to urinary calcium excretion in young girls. *J Pediatr Gastroenterol Nutr* 23:8–12.
- O'Dowd KJ, Clemens TL, Kelsey JL, Lindsay R. 1993. Exogenous calciferol (vitamin D) and vitamin D endocrine status among elderly nursing home residents in the New York City area. *J Am Geriatr Soc* 41:414–421.

- Ohlson MA, Brewer WD, Jackson L, Swanson PP, Roberts PH, Mangel M, Leverton RM, Chaloupka M, Gram MR, Reynolds MS, Lutz R. 1952. Intakes and retentions of nitrogen, calcium and phosphorus by 136 women between 30 and 85 years of age. *Fed Proc* 11:775–783.
- Oliveri MB, Ladizesky M, Mautalen CA, Alonso A, Martinez L. 1993. Seasonal variations of 25 hydroxyvitamin D and parathyroid hormone in Ushuaia (Argentina), the southernmost city in the world. *Bone Miner* 20:99–108.
- Ooms ME, Roos JC, Bezemer PD, VanDerVijgh WJ, Bouter LM, Lips P. 1995. Prevention of bone loss by vitamin D supplementation in elderly women: A randomized double-blind trial. *J Clin Endocrinol Metab* 80:1052–1058.
- Ophaug RH, Singer L, Harland BF. 1980a. Estimated fluoride intake of 6-month-old infants in four dietary regions of the United States. *Am J Clin Nutr* 33:324–327.
- Ophaug RH, Singer L, Harland BF. 1980b. Estimated fluoride intake of average two-year-old children in four dietary regions of the United States. *J Dent Res* 59:777–781.
- Ophaug RH, Singer L, Harland BF. 1985. Dietary fluoride intake of 6-month and 2-year-old children in four dietary regions of the United States. *Am J Clin Nutr* 42:701–707.
- Orimo H, Ouchi Y. 1990. The role of calcium and magnesium in the development of atherosclerosis. Experimental and clinical evidence. *Ann NY Acad Sci* 598:444–457.
- Orwoll ES. 1982. The milk-alkali syndrome: Current concepts. *Ann Intern Med* 97:242–248.
- Orwoll ES, Oviatt SK, McClung MR, Deftos LJ, Sexton G. 1990. The rate of bone mineral loss in normal men and the effects of calcium and cholecalciferol supplementation. *Ann Intern Med* 112:29–34.
- Osis D, Kramer L, Wiatrowski E, Spencer H. 1974. Dietary fluoride intake in man. *J Nutr* 104:1313–1318.
- Osteoporosis Society of Canada. 1993. Consensus on calcium nutrition. Official position of the Osteoporosis Society of Canada. *Nutr Quart* 18:62–69.
- Osuji OO, Leake JL, Chipman ML, Nikiforuk G, Locker D, Levine N. 1988. Risk factors for dental fluorosis in a fluoridated community. *J Dent Res* 67:1488–1492.
- OTA (Office of Technology Assessment). 1993. *Researching Health Risks*. Washington, DC: Office of Technology Assessment.
- Outhouse J, Kinsman G, Sheldon D, Tworney I, Smith J. 1939. The calcium requirements of five pre-school girls. *J Nutr* 17:199–211.
- Outhouse J, Breiter H, Rutherford E, Dwight J, Mills R, Armstrong W. 1941. The calcium requirement of man: Balance studies on seven adults. *J Nutr* 21:565–575.
- Paganini-Hill A, Chao A, Ross RK, Henderson BE. 1991. Exercise and other factors in the prevention of hip fracture: The Leisure World Study. *Epidemiology* 2:16–25.
- Pak CY. 1988. Medical management of nephrolithiasis in Dallas: Update 1987. *J Urol* 140:461–467.
- Pak CY, Sakhaei K, Rubin CD, Zerwekh JE. 1997. Sustained-release sodium fluoride in the management of established menopausal osteoporosis. *Am J Med Sci* 313:23–32.
- Pang DT, Phillips CL, Bawden JW. 1992. Fluoride intake from beverage consumption in a sample of North Carolina children. *J Dent Res* 71:1382–1388.

- Paolisso G, Passariello N, Pizza G, Marrazzo G, Giunta R, Sgambato S, Varricchio M, D'Onofrio F. 1989. Dietary magnesium supplements improve B-cell response to glucose and arginine in elderly non-insulin-dependent diabetic subjects. *Acta Endocrinol Copenh* 121:16–20.
- Paolisso G, Scheen A, D'Onofrio FD, Lefebvre P. 1990. Magnesium and glucose homeostasis. *Diabetologia* 33:511–514.
- Paolisso G, Sgambato S, Gambardella A, Pizza G, Tesauro P, Varricchio M, D'Onofrio F. 1992. Daily magnesium supplements improve glucose handling in elderly subjects. *Am J Clin Nutr* 55:1161–1167.
- Parfitt AM. 1977. Metacarpal cortical dimensions in hypoparathyroidism, primary hyperparathyroidism and chronic renal failure. *Calcif Tiss Res Suppl* 22:329–331.
- Parfitt AM. 1988. Bone remodeling: Relationship to the amount and structure of bone, and the pathogenesis and prevention of fractures. In: Riggs BL, Melton LJ III eds. *Osteoporosis: Etiology, Diagnosis, and Management*. New York, NY: Raven Press.
- Parfitt AM, Higgins BA, Nassim JR, Collins JA, Hilb A. 1964. Metabolic studies in patients with hypercalciuria. *Clin Sci* 27:463–482.
- Parfitt AM, Chir B, Gallagher JC, Heaney RP, Johnston CC, Neer R, Whedon GD. 1982. Vitamin D and bone health in the elderly. *Am J Clin Nutr* 36:1014–1031.
- Paunier L, Lacourt G, Pilloud P, Schlaepi P, Sizomenko PC. 1978. 25-hydroxyvitamin D and calcium levels in maternal, cord and infant serum in relation to maternal vitamin D intake. *Helv Paediatr Acta* 33:95–103.
- Peace H, Beattie JH. 1991. No effect of boron on bone mineral excretion and plasma sex steroid levels in healthy postmenopausal women. Monography, proceedings, roundtables, and discussions of the Seventh International Symposium on Trace Elements in Man and Animals, held May 20–25, 1990, in Dubrovnik, Croatia, Yugoslavia.
- Peacock M. 1991. Calcium absorption efficiency and calcium requirements in children and adolescents. *Am J Clin Nutr* 54:261S–265S.
- Pedersen AB, Bartholomew MJ, Dolence LA, Aljadir LP, Netteburg KL, Lloyd T. 1991. Menstrual differences due to vegetarian and nonvegetarian diets. *Am J Clin Nutr* 53:879–885.
- Pendrys DG, Katz RV. 1989. Risk of enamel fluorosis associated with fluoride supplementation, infant formula, and fluoride dentifrice use. *Am J Epidemiol* 130:1199–1208.
- Pendrys DG, Morse DE. 1990. Use of fluoride supplementation by children living in fluoridated communities. *J Dent Child* 57:343–347.
- Pendrys DG, Stamm JW. 1990. Relationship of total fluoride intake to beneficial effects and enamel fluorosis. *J Dent Res* 69(Spec Iss):529–538.
- Peng SK, Taylor CB. 1980. Editorial: Probable role of excesses of vitamin D in genesis of arteriosclerosis. *Arterial Wall* 6:63–68.
- Peng SK, Taylor CB, Tham P, Mikkelsen B. 1978. Role of mild excesses of vitamin D in arteriosclerosis. A study in squirrel monkeys. *Arterial Wall* 4:229.
- Pennington JA. 1994. *Bowes and Church's Food Values of Portions Commonly Used*. Philadelphia, PA: JB Lippincott.
- Pennington JA, Wilson DB. 1990. Daily intakes of nine nutritional elements: Analyzed vs. calculated values. *J Am Diet Assoc* 90:375–381.
- Pennington JA, Young BE. 1991. Total diet study nutritional elements, 1982–1989. *J Am Diet Assoc* 91:179–183.

- Perloff BP, Rizek RL, Haytowitz DB, Reid PR. 1990. Dietary intake methodology. II. USDA's Nutrient Data Base for Nationwide Dietary Intake Surveys. *J Nutr* 120:1530–1534.
- Petley A, Macklin B, Renwick AG, Wilkin TJ. 1995. The pharmacokinetics of niacinamide in humans and rodents. *Diabetes* 44:152–155.
- Pett LB, Ogilvie GH. 1956. The Canadian Weight-Height Survey. *Hum Biol* 28:177–188.
- Pettifor JM, Ross FP, Moodley G, Wang J, Marco G, Skjolde C. 1978a. Serum calcium, magnesium, phosphorus, alkaline phosphatase and 25-hydroxyvitamin D concentrations in children. *S Afr Med J* 53:751–754.
- Pettifor JM, Ross P, Wang J, Moodley G, Couper-Smith J. 1978b. Rickets in children of rural origin in South Africa: Is low dietary calcium a factor? *J Pediatr* 92:320–324.
- Pettifor JM, Bikle DD, Cavaleros M, Zachen D, Kamdar MC, Ross FP. 1995. Serum levels of free 1,25-dihydroxyvitamin D in vitamin D toxicity. *Ann Intern Med* 122:511–513.
- Pietschmann P, Woloszczuk W, Pietschmann H. 1990. Increased serum osteocalcin levels in elderly females with vitamin D deficiency. *Exp Clin Endocrinol* 95:275–278.
- Pillai S, Bikle DD, Elias PM. 1987. 1,25-Dihydroxyvitamin D production and receptor binding in human keratinocytes varies with differentiation. *J Biol Chem* 263:5390–5395.
- Pitkin RM, Reynolds WA, Williams GA, Hargis GK. 1979. Calcium metabolism in normal pregnancy: A longitudinal study. *Am J Obstet Gynecol* 133:781–787.
- Pittard WB III, Geddes KM, Sutherland SE, Miller MC, Hollis BW. 1990. Longitudinal changes in the bone mineral content of term and premature infants. *Am J Dis Child* 144:36–40.
- Pluckebaum JM, Chavez N. 1994. Nutritional status of Northwest Indiana Hispanics in a congregate meal program. *J Nutr Elderly* 13:1–22.
- PNUN (Standing Nordic Committee on Food). 1989. *Nordic Nutrition Recommendations*, 2nd Edition. Oslo: Nordic Council of Ministers.
- Ponder SW, McCormick DP, Fawcett HD, Palmer JL, McKernan MG, Brouhard BH. 1990. Spinal bone mineral density in children aged 5.00 through 11.99 years. *Am J Dis Child* 144:1346–1348.
- Ponz de Leon M, Roncucci L, Di Donato P, Tassi L, Smerieri O, Amorico MG, Malagoli G, De Maria D, Antonioli A, Chahin NJ. 1988. Pattern of epithelial cell proliferation in colorectal mucosa of normal subjects and of patients with adenomatous polyps or cancer of the large bowel. *Cancer Res* 48:4121–4126.
- Portale AA, Booth BE, Halloran BP, Morris RC Jr. 1984. Effect of dietary phosphorus on circulating concentrations of 1,25-dihydroxyvitamin D and immunoreactive parathyroid hormone in children with moderate renal insufficiency. *J Clin Invest* 73:1580–1589.
- Portale AA, Halloran BP, Murphy MM, Morris RC. 1986. Oral intake of phosphorus can determine the serum concentration of 1,25-dihydroxyvitamin D by determining its production rate in humans. *J Clin Invest* 77:7–12.
- Portale AA, Halloran BP, Morris RC Jr. 1987. Dietary intake of phosphorus modulates the circadian rhythm in serum concentration of phosphorus. Implications for the renal production of 1,25-dihydroxyvitamin D. *J Clin Invest* 80:1147–1154.

- Portale AA, Halloran BP, Morris RC Jr. 1989. Physiologic regulation of the serum concentration of 1,25-dihydroxyvitamin D by phosphorus in normal men. *J Clin Invest* 83:1494–1499.
- Prentice A, Laskey MA, Shaw J, Cole TJ, Fraser DR. 1990. Bone mineral content of Gambian and British children aged 0–36 months. *Bone Miner* 10:211–214.
- Prentice A, Jarjou LM, Cole TJ, Stirling DM, Dibba B, Fairweather-Tait S. 1995. Calcium requirements of lactating Gambian mothers: Effects of a calcium supplement on breast-milk calcium concentration, maternal bone mineral content, and urinary calcium excretion. *Am J Clin Nutr* 62:58–67.
- Prichard JL. 1969. The prenatal and postnatal effects of fluoride supplements on West Australian school children, aged 6, 7 and 8, Perth, 1967. *Austral Dent J* 14:335–338.
- Prince RL, Smith M, Dick IM, Price RI, Webb PG, Henderson NK, Harris MM. 1991. Prevention of postmenopausal osteoporosis. A comparative study of exercise, calcium supplementation, and hormone-replacement therapy. *N Engl J Med* 325:1189–1195.
- Prince R, Devine A, Dick I, Criddle A, Kerr D, Kent N, Price R, Randell A. 1995. The effects of calcium supplementation (milk powder or tablets) and exercise on bone density in postmenopausal women. *J Bone Miner Res* 10:1068–1075.
- Purdie DW, Aaron JE, Selby PL. 1988. Bone histology and mineral homeostasis in human pregnancy. *Br J Obstet Gynecol* 95:849–854.
- Quamme GA. 1989. Control of magnesium transport in the thick ascending limb. *Am J Physiol* 256:F197–F210.
- Quamme GA. 1993. Laboratory evaluation of magnesium status. Renal function and free intracellular magnesium concentration. *Clin Lab Med* 13:209–223.
- Quamme GA, Dirks JH. 1986. The physiology of renal magnesium handling. *Renal Physiol* 9:257–269.
- Raisz LG, Niemann I. 1969. Effect of phosphate, calcium and magnesium on bone resorption and hormonal responses in tissue culture. *Endocrinology* 85:446–452.
- Rajalakshmi K, Srikantia SG. 1980. Copper, zinc, and magnesium content of breast milk of Indian women. *Am J Clin Nutr* 33:664–669.
- Raman L, Rajalakshmi K, Krishnamachari KA, Sastry JG. 1978. Effect of calcium supplementation to undernourished mothers during pregnancy on the bone density of the neonates. *Am J Clin Nutr* 31:466–469.
- Randall RE, Cohen D, Spray CC, Rossmeisl EC. 1964. Hypermagnesemia in renal failure. *Ann Intern Med* 61:73–88.
- Rao DR, Bello H, Warren AP, Brown GE. 1994. Prevalence of lactose maldigestion. Influence and interaction of age, race, and sex. *Dig Dis Sci* 39:1519–1524.
- Rasmussen HS, McNair P, Goransson L, Balslev S, Larsen OG, Aurup P. 1988. Magnesium deficiency in patients with ischemic heart disease with and without acute myocardial infarction uncovered by an intravenous loading test. *Arch Intern Med* 148:329–332.
- Ray NF, Chan JK, Thamer M, Melton LJ III. 1997. Medical expenditures for the treatment of osteoporotic fractures in the United States in 1995: Report from the National Osteoporosis Foundation. *J Bone Miner Res* 12:24–35.
- Reasner CA II, Dunn JF, Fetchick DA, Liel Y, Hollis BW, Epstein S, Shary J, Mundy GR, Bell NH. 1990. Alteration of vitamin D metabolism in Mexican-Americans. *J Bone Miner Res* 5:13–17.
- Recker RR. 1985. Calcium absorption and achlorhydria. *N Engl J Med* 313:70–73.

- Recker RR, Hassing GS, Lau JR, Saville PD. 1973. The hyperphosphatemic effect of disodium ethane-1-hydroxy-1, 1-diphosphonate (EHDP): Renal handling of phosphorus and the renal response to parathyroid hormone. *J Lab Clin Med* 81:258–266.
- Recker RR, Davies KM, Hinders SM, Heaney RP, Stegman MR, Kimmel DB. 1992. Bone gain in young adult women. *J Am Med Assoc* 268:2403–2408.
- Recker RR, Hinders S, Davies KM, Heaney RP, Stegman MR, Lappe JM, Kimmel DB. 1996. Correcting calcium nutritional deficiency prevents spine fractures in elderly women. *J Bone Miner Res* 11:1961–1966.
- Reddy GS, Norman AW, Willis DM, Goltzman D, Guyda H, Solomon S, Philips DR, Bishop JE, Mayer E. 1983. Regulation of vitamin D metabolism in normal human pregnancy. *J Clin Endocrinol Metab* 56:363–370.
- Reed A, Haugen M, Pachman LM, Langman CB. 1990. Abnormalities in serum osteocalcin values in children with chronic rheumatic diseases. *J Pediatr* 116:574–580.
- Reed JA, Anderson JJ, Tylavsky FA, Gallagher PN Jr. 1994. Comparative changes in radial-bone density of elderly female lacto-ovovegetarians and omnivores. *Am J Clin Nutr* 59:1197S–1202S.
- Reginster JY, Strause L, Deroisy R, Lecart MP, Saltman P, Franchimont P. 1989. Preliminary report of decreased serum magnesium in postmenopausal osteoporosis. *Magnesium* 8:106–109.
- Reichel H, Koeffler HP, Norman AW. 1989. The role of vitamin D endocrine system in health and disease. *N Engl J Med* 320:980–991.
- Reid IR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. 1995. Long-term effects of calcium supplementation on bone loss and fractures in postmenopausal women: A randomized controlled trial. *Am J Med* 98:331–335.
- Reinhart RA. 1988. Magnesium metabolism. A review with special reference to the relationship between intracellular content and serum levels. *Arch Intern Med* 148:2415–2420.
- Reinhold JG, Fardadji B, Abadi P, Ismail-Beigi F. 1991. Decreased absorption of calcium, magnesium, zinc and phosphorus by humans due to increased fiber and phosphorus consumption as wheat bread. *Am J Clin Nutr* 49:204–206.
- Resnick LM, Gupta RK, Laragh JH. 1984. Intracellular free magnesium in erythrocytes of essential hypertension: Relation to blood pressure and serum divalent cations. *Proc Natl Acad Sci USA* 81:6511–6515.
- Resnick L, Gupta R, and Bhargava KK, Gruenspan H, Alderman MH, Laragh JH. 1991. Cellular ions in hypertension, diabetes and obesity: A nuclear magnetic resonance spectroscopic study. *Hypertension* 17:951–957.
- Riancho JA, delArco C, Arteaga R, Herranz JL, Albajar M, Macias JG. 1989. Influence of solar irradiation on vitamin D levels in children on anticonvulsant drugs. *Acta Neurol Scand* 79:296–299.
- Ricci JM, Hariharan S, Helfott A, Reed K, O'Sullivan MJ. 1991. Oral tocolysis with magnesium chloride: A randomized controlled prospective clinical trial. *Am J Obstet Gynecol* 165:603–610.
- Richards A, Mosekilde L, Søgaard CH. 1994. Normal age-related changes in fluoride content of vertebral trabecular bone—relation to bone quality. *Bone* 15:21–26.
- Riggs BL, Melton LJ III. 1995. The worldwide problem of osteoporosis: Insights afforded by epidemiology. *Bone* 17:505S–511S.

- Riggs BL, O'Fallon WM, Muse J, O'Conner MK, Melton LJ III. 1996. Long-term effects of calcium supplementation on serum PTH, bone turnover, and bone loss in elderly women. *J Bone Miner Res* 11:S118.
- Rigo J, Salle BL, Picaud JC, Putet G, Senterre J. 1995. Nutritional evaluation of protein hydrolysate formulas. *Eur J Clin Nutr* 49:S26–S38.
- Riis B, Thomsen K, Christiansen C. 1987. Does calcium supplementation prevent postmenopausal bone loss? *N Engl J Med* 316:173–177.
- Ritz E. 1982. Acute hypophosphatemia. *Kidney Int* 22:84–94.
- Rizzoli R, Stoermann C, Ammann P, Bonjour J-P. 1994. Hypercalcemia and hyperosteolysis in vitamin D intoxication: Effects of clodronate therapy. *Bone* 15:193–198.
- Robertson, WG. 1985. Dietary factors important in calcium stone formation. In: Schwillie PO, Smith LH, Robertson WG, Vahlensieck W, eds. *Urolithiasis and Related Clinical Research*. New York: Plenum Press. Pp. 61–68.
- Romani A, Marfella C, Scarpa A. 1993. Cell magnesium transport and homeostasis: Role of intracellular compartments. *Miner Electrolyte Metab* 19:282–289.
- Roncucci L, Scalmati A, Ponz de Leon M. 1991. Pattern of cell kinetics in colorectal mucosa of patients with different types of adenomatous polyps of the large bowel. *Cancer* 68:873–878.
- Ronis DL, Lang WP, Farghaly MM, Passow E. 1993. Tooth brushing, flossing, and preventive dental visits by Detroit-area residents in relation to demographic and socioeconomic factors. *J Pub Hlth Dent* 53:138–145.
- Rosado JL, Lopez P, Morales M, Munoz E, Allen LH. 1992. Bioavailability of energy, nitrogen, fat, zinc, iron and calcium from rural and urban Mexican diets. *Br J Nutr* 68:45–58.
- Rowe JW, Minaker KL, Pallotta JA, Flier JS. 1983. Characterization of the insulin resistance of aging. *J Clin Invest* 71:1581–1587.
- Rubenowitz E, Axelsson G, Rylander R. 1996. Magnesium in drinking water and death from acute myocardial infarction. *Am J Epidemiol* 143:456–462.
- Rubin H. 1975. Central role for magnesium in coordinate control of metabolism and growth in animal cells. *Proc Natl Acad Sci USA* 72:3551–3555.
- Rude RK. 1993. Magnesium metabolism and deficiency. *Endocrinol Metab Clin North Am* 22:377–395.
- Rude RK, Olerich M. 1996. Magnesium deficiency: Possible role in osteoporosis associated with gluten-sensitive enteropathy. *Osteopor Int* 6:453–461.
- Rude RK, Singer FR. 1980. Magnesium deficiency and excess. *Ann Rev Med* 32:245–259.
- Rude RK, Oldham SB, Singer FR. 1976. Functional hypoparathyroidism and parathyroid hormone end-organ resistance in human magnesium deficiency. *Clin Endocrinol* 5:209–224.
- Rude RK, Bethune JE, Singer FR. 1980. Renal tubular maximum for magnesium in normal, hyperparathyroid and hypoparathyroid man. *J Clin Endocrinol Metab* 51:1425–1431.
- Rude RK, Manoogian C, Ehrlich L, DeRusso P, Ryzen E, Nadler J. 1989. Mechanisms of blood pressure regulation by magnesium in man. *Magnesium* 8:266–278.
- Rude RK, Stephen A, Nadler J. 1991. Determination of red blood cell intracellular free magnesium by nuclear magnetic resonance as an assessment of magnesium depletion. *Magnes Trace Elem* 10:117–121.

- Rudloff S, Lonnerdal B. 1990. Calcium retention from milk-based infant formulas, whey-hydrolysate formula, and human milk in weanling rhesus monkeys. *Am J Dis Child* 144:360–363.
- Rudnicki M, Frolich A, Rasmussen WF, McNair P. 1991. The effect of magnesium on maternal blood pressure in pregnancy-induced hypertension. A randomized double-blind placebo-controlled trial. *Acta Obstet Gynecol Scand* 70:445–450.
- Ruiz JC, Mandel C, Garabedian M. 1995. Influence of spontaneous calcium intake and physical exercise on the vertebral and femoral bone mineral density of children and adolescents. *J Bone Miner Res* 10:675–682.
- Russell AL. 1949. Dental effects of exposure to fluoride-bearing Dakota sandstone waters at various ages and for various lengths of time. II. Patterns of dental caries inhibition as related to exposure span, to elapsed time since exposure, and to periods of calcification and eruption. *J Dent Res* 28:600–612.
- Russell AL, Elvove E. 1951. Domestic water and dental caries. VII. A study of the fluoride-dental caries relationship in an adult population. *Pub Hlth Rep* 66:1389–1401.
- Ryan MP. 1987. Diuretics and potassium/magnesium depletion. Directions for treatment. *Am J Med* 82:38–47.
- Ryzen E, Elbaum N, Singer FR, Rude RK. 1985. Parenteral magnesium tolerance testing in the evaluation of magnesium deficiency. *Magnesium* 4:137–147.
- Ryzen E, Elkayam U, Rude RK. 1986. Low blood mononuclear cell magnesium in intensive cardiac care unit patients. *Am Heart J* 111:475–480.
- Sacks FM, Brown LE, Appel L, Borhani NO, Evans D, Whelton P. 1995. Combinations of potassium, calcium, and magnesium supplements in hypertension. *Hypertension* 26:950–956.
- Sakhaee K, Baker S, Zerwekh J, Poindexter J, Garcia-Hernandez PA, Pak CY. 1994. Limited risk of kidney stone formation during long-term calcium citrate supplementation in nonstone forming subjects. *J Urol* 152:324–327.
- Salama F, Whitford GM, Barenie JT. 1989. Fluoride retention by children from toothbrushing. *J Dent Res* 68(Spec Issue):335.
- Salle BL, Delvin E, Glorieux F, David L. 1990. Human neonatal hypocalcemia. *Biol Neonate* 58:S22–S31.
- Sandberg AS, Larsen T, Sandstrom B. 1993. High dietary calcium level decreases colonic phytate degradation in pigs fed a rapeseed diet. *J Nutr* 123:559–566.
- Sanders TA, Purves R. 1981. An anthropometric and dietary assessment of the nutritional status of vegan preschool children. *J Human Nutr* 35:349–357.
- Sandler RB, Slemenda CW, LaPorte RE, Cauley JA, Schramm MM, Barresi ML, Kriska AM. 1985. Postmenopausal bone density and milk consumption in childhood and adolescence. *Am J Clin Nutr* 42:270–274.
- Saunders D, Sillery J, Chapman R. 1988. Effect of calcium carbonate and aluminum hydroxide on human intestinal function. *Dig Dis Sci* 33:409–412.
- Schanler RJ, Garza C, Smith EO. 1985. Fortified mothers' milk for very low birth weight infants: Results of macromineral balance studies. *J Pediatr* 107:767–774.
- Schendel DE, Berg CJ, Yeargin-Allsopp M, Boyle CA, Decoufle P. 1996. Prenatal magnesium sulfate exposure and the risk for cerebral palsy or mental retardation among very low-birth-weight children aged 3 to 5 years. *J Am Med Assoc* 276:1805–1810.
- Schiffl H, Binswanger U. 1982. Renal handling of fluoride in healthy man. *Renal Physiol* 5:192–196.

- Schiller L, Santa Ana C, Sheikh M, Emmett M, Fordtran J. 1989. Effect of the time of administration of calcium acetate on phosphorus binding. *N Engl J Med* 320:1110–1113.
- Schlesinger ES, Overton DE, Riverhead LI, Chase HC, Cantwell KT. 1956. Newburgh-Kingston caries-fluorine study XIII. Pediatric findings after ten years. *J Am Dent Assoc* 52:296–306.
- Schlesinger L, Arevalo M, Arredondo S, Diaz M, Lonnerdal B, Stekel A. 1992. Effect of a zinc-fortified formula on immunocompetence and growth of malnourished infants. *Am J Clin Nutr* 56:491–498.
- Schmidt LE, Arfken CL, Heins JM. 1994. Evaluation of nutrient intake in subjects with non-insulin-dependent diabetes mellitus. *J Am Diet Assoc* 94:773–774.
- Schmidt-Gayk H, Goossen J, Lendle F, Seidel D. 1977. Serum 25-hydroxycholecalciferol in myocardial infarction. *Atherosclerosis* 26:55–58.
- Schneider EL, Guralnik JM. 1990. The aging of America. Impact on health care costs. *J Am Med Assoc* 263:2335–2340.
- Schofield FA, and Morrell E. 1960. Calcium, phosphorus and magnesium. *Fed Proc* 19:1014–1016.
- Schuman CA, Jones HW III. 1985. The “milk-alkali” syndrome: Two case reports with discussion of pathogenesis. *Quart J Med (New Series)* 55:119–126.
- Schutzmansky G. 1971. Fluoride tablet application in pregnant females. *Dtsch Stomatol* 21:122–129.
- Schwartz E, Chokas WV, Panariello VA. 1964. Metabolic balance studies of high calcium intake in osteoporosis. *Am J Med* 36:233–249.
- Schwartz GG, Hulka BS. 1990. Is vitamin D deficiency a risk factor for prostate cancer? *Anticancer Res* 10:1307–1312.
- Schwartz R, Walker G, Linz MD, MacKellar I. 1973. Metabolic responses of adolescent boys to two levels of dietary magnesium and protein. I. Magnesium and nitrogen retention. *Am J Clin Nutr* 26:510–518.
- Schwartz R, Spencer H, Welsh JJ. 1984. Magnesium absorption in human subjects from leafy vegetables, intrinsically labeled with stable  $^{26}\text{Mg}$ . *Am J Clin Nutr* 39:571–576.
- Schwartz R, Apgar BJ, Wien EM. 1986. Apparent absorption and retention of Ca, Cu, Mg, Mn, and Zn from a diet containing bran. *Am J Clin Nutr* 43:444–455.
- Schwartzman MS, Franck WA. 1987. Vitamin D toxicity complicating the treatment of senile, postmenopausal, and glucocorticoid-induced osteoporosis: Four case reports and a critical commentary on the use of vitamin D in these disorders. *Am J Med* 82:224–229.
- Sebastian A, Harris ST, Ottaway JH, Todd KM, Morris RC Jr. 1994. Improved mineral balance and skeletal metabolism in postmenopausal women treated with potassium bicarbonate. *N Engl J Med* 330:1776–1781.
- Sebert JL, Garabedian M, Chauvenet M, Maamer M, Agbomson F, Brazier M. 1995. Evaluation of a new solid formulation of calcium and vitamin D in institutionalized elderly subjects: A randomized comparative trial versus separate administration of both constituents. *Rev Rhum* 62:288–294.
- Seelig MS. 1981. Magnesium requirements in human nutrition. *Magnes Bull* 3(suppl):26–47.
- Seelig MS. 1993. Interrelationship of magnesium and estrogen in cardiovascular and bone disorders, eclampsia, migraine and premenstrual syndrome. *J Am Coll Nutr* 12:442–458.
- Seelig MS, Elin RJ. 1996. Is there a place for magnesium in the treatment of acute myocardial infarction? *Am Heart J* 132:471–477.

- Seki K, Makimura N, Mitsui C, Hirata J, Nagata I. 1991. Calcium-regulating hormones and osteocalcin levels during pregnancy: A longitudinal study. *Am J Obstet Gynecol* 164:1248–1252.
- Selby PL. 1994. Calcium requirement—A reappraisal of the methods used in its determination and their application to patients with osteoporosis. *Am J Clin Nutr* 60:944–948.
- Selby PL, Davies M, Marks JS, Mawer EB. 1995. Vitamin D intoxication causes hypercalcemia by increased bone resorption which responds to pamidronate. *Clin Endocrinol* 43:531–536.
- Sentipal JM, Wardlaw GM, Mahan J, Matkovic V. 1991. Influence of calcium intake and growth indexes on vertebral bone mineral density in young females. *Am J Clin Nutr* 54:425–428.
- Seydoux J, Girardin E, Paunier L, Beguin F. 1992. Serum and intracellular magnesium during normal pregnancy and in patients with pre-eclampsia. *Br J Obstet Gynecol* 99:207–211.
- Shapses SA, Robins SP, Schwartz EI, Chowdhury H. 1995. Short-term changes in calcium but not protein intake alter the rate of bone resorption in healthy subjects as assessed by urinary pyridinium cross-link excretion. *J Nutr* 125:2814–2821.
- Sharma OP. 1996. Vitamin D, calcium, and sarcoidosis. *Chest* 109:535–539.
- Shen YW, Taves DR. 1974. Fluoride concentrations in the human placenta and maternal and cord blood. *Am J Obstet Gynecol* 119:205–207.
- Sherman HC, Hawley E. 1922. Calcium and phosphorus metabolism in childhood. *J Biol Chem* 52:375–399.
- Shils ME. 1969. Experimental human magnesium depletion. *Medicine* 46:61–85.
- Shils ME. 1994. Magnesium. In: Shils ME, Olson JA, Shike M, eds. *Modern Nutrition in Health and Disease*. Philadelphia, PA: Lea & Febiger. Pp. 164–184.
- Shils ME, Rude RK. 1996. Deliberations and evaluations of the approaches, endpoints and paradigms for magnesium dietary recommendations. *J Nutr* 126:2398S–2403S.
- Sibai BM, Villar MA, Bray E. 1989. Magnesium supplementation during pregnancy: A double-blind randomized controlled clinical trial. *Am J Obstet Gynecol* 161:115–119.
- Siener R, Hesse A. 1995. Influence of a mixed and a vegetarian diet on urinary magnesium excretion and concentration. *Br J Nutr* 73:783–790.
- Silverberg SJ, Shane E, Clemens TL, Dempster DW, Segre GV, Lindsay R, Bilezikian JP. 1986. The effect of oral phosphate administration on major indices of skeletal metabolism in normal subjects. *J Bone Miner Res* 1:383–388.
- Silvis SE, Paragas PD Jr. 1972. Paresthesias, weakness, seizures, and hypophosphatemia in patients receiving hyperalimentation. *Gastroenterology* 62:513–520.
- Simard PL, Lachapelle C, Trahan L, Naccache H, Demers M, Broduer JM. 1989. The ingestion of fluoride dentifrice by young children. *J Dent Child* 56:177–181.
- Simard PL, Naccache H, Lachapelle D, Brodeur JM. 1991. Ingestion of fluoride from dentifrices by children aged 12 to 24 months. *Clin Pediatr Phila* 30:614–617.
- Simmer K, Khanum S, Carlsson L, Thompson RP. 1988. Nutritional rehabilitation in Bangladesh—the importance of zinc. *Am J Clin Nutr* 47:1036–1040.
- Singer L, Ophaug R. 1979. Total fluoride intake of infants. *Pediatrics* 63:460–466.
- Singer L, Ophaug RH, Harland BF. 1980. Fluoride intakes of young male adults in the United States. *Am J Clin Nutr* 33:328–332.
- Singer L, Ophaug RH, Harland BF. 1985. Dietary fluoride intake of 15–19-year-old male adults residing in the United States. *J Dent Res* 64:1302–1305.

## ONLINE REFERENCES

## 1237

- Singh A, Jolly SS. 1970. Chronic toxic effects on the skeletal system. In: *Fluorides and Human Health*. Geneva: World Health Organization. Pp 238–249.
- Skajaa K, Dorup I, Sandstrom BM. 1991. Magnesium intake and status and pregnancy outcome in a Danish population. *Br J Obstet Gynecol* 98:919–928.
- Slattery ML, Sorenson AW, Ford MH. 1988. Dietary calcium intake as a mitigating factor in colon cancer. *Am J Epidemiol* 128:504–514.
- Slemenda CW, Reister TK, Hui SL, Miller JZ, Christian JC, Johnston CC Jr. 1994. Influences on skeletal mineralization in children and adolescents: Evidence for varying effects of sexual maturation and physical activity. *J Pediatr* 125:201–207.
- Slemenda CW, Peacock M, Hui S, Zhou L, Johnston CC Jr. 1997. Reduced rates of skeletal remodeling are associated with increased bone mineral density during the development of peak skeletal mass. *J Bone Miner Res* 12:676–682.
- Slesinski MJ, Subar AF, Kahle LL. 1996. Dietary intake of fat, fiber, and other nutrients is related to the use of vitamin and mineral supplements in the United States: The 1992 National Health Interview Survey. *J Nutr* 126:3001–3008.
- Smilkstein MJ, Smolinske SC, Kulig KW, Rumack, BH. 1988. Severe hypermagnesemia due to multiple-dose cathartic therapy. *West J Med* 148:208–211.
- Smith EL, Gilligan C, Smith PE, Sempos CT. 1989. Calcium supplementation and bone loss in middle-aged women. *Am J Clin Nutr* 50:833–842.
- Smith KT, Heaney RP, Flora L, Hinders SM. 1987. Calcium absorption from a new calcium delivery system (CCM). *Calcif Tissue Int* 41:351–352.
- Smith R, Dent CE. 1969. Vitamin D requirements in adults. Clinical and metabolic studies on seven patients with nutritional osteomalacia. *Bibl Nutr Dieta* 13:44–45.
- Snedeker SM, Smith SA, Greger JL. 1982. Effect of dietary calcium and phosphorus levels on the utilization of iron, copper, and zinc by adult males. *J Nutr* 112:136–143.
- Sojka JE, Wastney ME, Abrams S, Froese S, Martin BR, Weaver CM. 1997. Magnesium kinetics in adolescent girls determined using stable isotopes: Effects of high and low calcium intakes. *Am J Physiol* 273:R170–R175.
- Sojka JE, Weaver CM. 1995. Magnesium supplementation and osteoporosis. *Nutr Rev* 53:71–74.
- Sokoll LJ, Dawson-Hughes B. 1992. Calcium supplementation and plasma ferritin concentrations in premenopausal women. *Am J Clin Nutr* 56:1045–1048.
- Sorva A, Risteli J, Risteli L, Valimaki M, Tilvis R. 1991. Effects of vitamin D and calcium on markers of bone metabolism in geriatric patients with low serum 25-hydroxyvitamin D levels. *Calcif Tissue Int* 49:S88–S89.
- Southgate DAT, Widdowson EM, Smits BJ, Cooke WT, Walker CHM, Mathers NP. 1969. Absorption and excretion of calcium and fat by young infants. *Lancet* 1:487–489.
- Sowers M, Wallace RB, Lemke JH. 1985. Correlates of forearm bone mass among women during maximal bone mineralization. *Prev Med* 14:585–596.
- Sowers M, Wallace RB, Lemke JH. 1986. The relationship of bone mass and fracture history to fluoride and calcium intake: A study of three communities. *Am J Clin Nutr* 44:889–898.
- Sowers M, Clark MK, Jannausch ML, Wallace RB. 1991. A prospective study of bone mineral content and fracture in communities with differential fluoride exposure. *Am J Epidemiol* 133:649–660.
- Sowers M, Corton G, Shapiro B, Jannausch ML, Crutchfield M, Smith ML, Randolph JF, Hollis B. 1993. Changes in bone density with lactation. *J Am Med Assoc* 269:3130–3135.

- Sowers M, Randolph J, Shapiro B, Jannaush M. 1995a. A prospective study of bone density and pregnancy after an extended period of lactation with bone loss. *Obstet Gynecol* 85:285–289.
- Sowers M, Eyre D, Hollis BW, Randolph JF, Shapiro B, Jannausch ML, Crutchfield M. 1995b. Biochemical markers of bone turnover in lactating and nonlactating postpartum women. *J Clin Endocrinol Metab*. 80:2210–2216.
- Spak CJ, Ekstrand J, Zylberstein D. 1982. Bioavailability of fluoride added by baby formula and milk. *Caries Res* 16:249–256.
- Spak CJ, Hardell LI, De Chateau P. 1983. Fluoride in human milk. *Acta Paediatr Scand* 72:699–701.
- Spatling L, Spatling G. 1988. Magnesium supplementation in pregnancy. A double blind study. *Br J Obstet Gynecol* 95:120–125.
- Specker BL. 1996. Evidence for an interaction between calcium intake and physical activity on changes in bone mineral density. *J Bone Miner Res* 11:1539–1544.
- Specker BL, Tsang RC. 1987. Cyclical serum 25-hydroxyvitamin D concentrations paralleling sunshine exposure in exclusively breast-fed infants. *J Pediatr* 110:744–747.
- Specker BL, Tsang RC, Hollis BW. 1985a. Effect of race and diet on human-milk vitamin D and 25-hydroxyvitamin D. *Am J Dis Child* 139:1134–1137.
- Specker BL, Valanis B, Hertzberg V, Edwards N, Tsang RC. 1985b. Sunshine exposure and serum 25-hydroxyvitamin D concentrations in exclusively breast-fed infants. *J Pediatr* 107:372–376.
- Specker BL, Lichtenstein P, Mimouni F, Gormley C, Tsang RC. 1986. Calcium-regulating hormones and minerals from birth to 18 months of age: A cross-sectional study. II. Effects of sex, race, age, season, and diet on serum minerals, parathyroid hormone, and calcitonin. *Pediatrics* 77:891–896.
- Specker BL, Tsang RC, Ho ML, Miller D. 1987. Effect of vegetarian diet on serum 1,25-dihydroxyvitamin D concentrations during lactation. *Obstet Gynecol* 70:870–874.
- Specker BL, Tsang RC, Ho ML. 1991a. Changes in calcium homeostasis over the first year postpartum: Effect of lactation and weaning. *Obstet Gynecol* 78:56–62.
- Specker BL, Tsang RC, Ho ML, Landi TM, Gratton TL. 1991b. Low serum calcium and high parathyroid hormone levels in neonates fed “humanized” cow’s milk-based formula. *Am J Dis Child* 145:941–945.
- Specker BL, Ho ML, Oestreich A, Yin TA, Shui QM, Chen XC, Tsang RC. 1992. Prospective study of vitamin D supplementation and rickets in China. *J Pediatr* 120:733–739.
- Specker BL, Vieira NE, O’Brien KO, Ho ML, Heubi JE, Abrams SA, Yerger AL. 1994. Calcium kinetics in lactating women with low and high calcium intakes. *Am J Clin Nutr* 59:593–599.
- Specker BL, Beck A, Kalkwarf H, Ho M. 1997. Randomized trial of varying mineral intake on total body bone mineral accretion during the first year of life. *Pediatrics* 99:e12.
- Spencer H, Menczel J, Lewin I, Samachson J. 1965. Effect of high phosphorus intake on calcium and phosphorus metabolism in man. *J Nutr* 86:125–132.
- Spencer H, Lewin I, Fowler J, Samachson J. 1969. Influence of dietary calcium intake on  $\text{Ca}^{47}$  absorption in man. *Am J Med* 46:197–205.
- Spencer H, Kramer L, Osis D, Norris C. 1978a. Effect of phosphorus on the absorption of calcium and on the calcium balance in man. *J Nutr* 108:447–457.
- Spencer H, Lesniak M, Gatzka CA, Kramer L, Norris C, Coffey J. 1978b. Magnesium–calcium interrelationships in man. *Trace Substances Environ Hlth* 12:241–247.

- Spencer H, Kramer L, Lesniak M, DeBartolo M, Norris C, Osis D. 1984. Calcium requirements in humans. Report of original data and a review. *Clin Orthop Relat Res* 184:270–280.
- Spencer H, Fuller H, Norris C, Williams D. 1994. Effect of magnesium on the intestinal absorption of calcium in man. *J Am Coll Nutr* 13:485–492.
- Spencer H, Osis D, Lender M. 1981. Studies of fluoride metabolism in man. A review and report of original data. *Sci Total Environ* 17:1–12.
- Stamp TCB, Haddad JG, Twigg CA. 1977. Comparison of oral 25-hydroxycholecalciferol, vitamin D, and ultraviolet light as determinants of circulating 25-hydroxyvitamin D. *Lancet* 1:1341–1343.
- Stanbury SW. 1971. The phosphate ion in chronic renal failure. In: Hioco DJ, ed. *Phosphate et Metabolisme Phosphocalcique*. Paris: Sandoz Laboratories.
- Stapleton FB. 1994. Hematuria associated with hypercalciuria and hyperuricosuria: A practical approach. *Pediatr Nephrol* 8:756–761.
- Stearns G. 1968. Early studies of vitamin D requirement during growth. *Am J Pub Hlth* 58:2027–2035.
- Steenbock H, Black A. 1924. The reduction of growth-promoting and calcifying properties in a ration by exposure to ultraviolet light. *J Biol Chem* 61:408–422.
- Steichen JJ, Tsang RC. 1987. Bone mineralization and growth in term infants fed soy-based or cow milk-based formula. *J Pediatr* 110:687–692.
- Stein JH, Smith WO, Ginn HE. 1966. Hypophosphatemia in acute alcoholism. *Am J Med Sci* 252:78–83.
- Stendig-Lindberg G, Tepper R, Leichter I. 1993. Trabecular bone density in a two year controlled trial of peroral magnesium in osteoporosis. *Magnes Res* 6:155–163.
- Stephen KW, McCall DR, Tullis JI. 1987. Caries prevalence in northern Scotland before, and 5 years after, water defluoridation. *Br Dent J* 163:324–326.
- Stevenson CA, Watson AR. 1957. Fluoride osteosclerosis. *Am J Roentg Rad Ther Nucl Med* 78:13–18.
- Stumpf WE, Sar M, Reid FA, Tanakay Y, DeLuca HF. 1979. Target cells for 1,25-dihydroxyvitamin D<sub>3</sub> in intestinal tract, stomach, kidney, skin, pituitary, and parathyroid. *Science* 206:1188–1190.
- Suarez FL, Savaiano DA, Levitt MD. 1995. A comparison of symptoms after the consumption of milk or lactose-hydrolyzed milk by people with self-reported severe lactose intolerance. *N Engl J Med* 333:1–4.
- Svenningsen NW, Lindquist B. 1974. Postnatal development of renal hydrogen ion excretion capacity in relation to age and protein intake. *Acta Paediatr Scand* 63:721–731.
- Switzer RL. 1971. Regulation and mechanism of phosphoribosylpyrophosphate synthetase. III. Kinetic studies of the reaction mechanism. *J Biol Chem* 246:2447–2458.
- Tanner JT, Smith J, Defibaugh P, Angyal G, Villalobos M, Bueno MP, McGarrahan ET, Wehr HM, Muniz JF, Hollis BW. 1988. Survey of vitamin content of fortified milk. *J Assoc Off Anal Chem* 71: 607–610.
- Tanner JM. 1990. *Growth at Adolescence*. Oxford: Oxford University Press.
- Tatevossian A. 1990. Fluoride in dental plaque and its effects. *J Dent Res* 69(Spec Iss): 645–652.
- Taves DR. 1978. Fluoridation and mortality due to heart disease. *Nature* 272:361–362.
- Taves DR. 1983. Dietary intake of fluoride ashed (total fluoride) v. unashed (inorganic fluoride) analysis of individual foods. *Br J Nutr* 49:295–301.

- Taves DR, Neuman WF. 1964. Factors controlling calcification in vitro: Fluoride and magnesium. *Arch Biochem Biophys* 108:390–397.
- Taylor AF, Norman ME. 1984. Vitamin D metabolite levels in normal children. *Pediatr Res* 18: 886–890.
- Taylor CB, Hass GM, Ho KJ, Liu LB. 1972. Risk factors in the pathogenesis of arteriosclerotic heart disease and generalized atherosclerosis. *Ann Clin Lab Sci* 2:239.
- Teegarden D, Proulx WR, Martin BR, Zhao J, McCabe GP, Lyle RM, Peacock M, Slemenda C, Johnston CC, Weaver CM. 1995. Peak bone mass in young women. *J Bone Miner Res* 10:711–715.
- Ten Cate JM. 1990. In vitro studies on the effects of fluoride on de- and remineralization. *J Dent Res* 69(Spec Iss):614–619.
- Terblanche S, Noakes TD, Dennis SC, Marais D, Eckert M. 1992. Failure of magnesium supplementation to influence marathon running performance or recovery in magnesium-replete subjects. *Int J Sport Nutr* 2:154–164.
- Tesar R, Notelovitz M, Shim E, Kauwell G, Brown J. 1992. Axial and peripheral bone density and nutrient intakes of postmenopausal vegetarian and omnivorous women. *Am J Clin Nutr* 56:699–704.
- Thatcher HS, Rock L. 1928. Clinical notes, suggestions and new instruments. *J Am Med Assoc* 91:1185–1186.
- Theintz G, Buchs B, Rizzoli R, Slosman D, Clavien H, Sizonenko PC, Bonjour JP. 1992. Longitudinal monitoring of bone mass accumulation in healthy adolescents: Evidence for a marked reduction after 16 years of age at the levels of lumbar spine and femoral neck in female subjects. *J Clin Endocrinol Metab* 75:1060–1065.
- Thompson FE, Byers T. 1994. Dietary assessment resource manual. *J Nutr* 124:224S–231S.
- Thys-Jacobs S, Ceccarelli S, Bierman A, Weisman H, Cohen M-A, Alvir J. 1989. Calcium supplementation in premenstrual syndrome: A randomized cross-over trial. *J Gen Intern Med* 4:183–189.
- Tillman DM, Semple PF. 1988. Calcium and magnesium in essential hypertension. *Clin Sci* 75:395–402.
- Touitou Y, Godard JP, Ferment O, Chastang C, Proust J, Bogdan A, Auzeby A, Touitou C. 1987. Prevalence of magnesium and potassium deficiencies in the elderly. *Clin Chem* 33:518–523.
- Travis SF, Sugerman HJ, Ruberg RL, Dudrick SJ, Delivoria-Papadopoulos M, Miller L, Osaki FA. 1971. Alterations of red cell glycolytic intermediates and oxygen transport as a consequence of hypophosphatemia in patients receiving intravenous hyperalimentation. *N Engl J Med* 285:763–768.
- Tremaine WJ, Newcomer AD, Riggs BL, McGill DB. 1986. Calcium absorption from milk in lactase-deficient and lactase-sufficient adults. *Dig Dis Sci* 31:376–378.
- Tsang RC, Strub R, Brown DR, Steichen J, Hartman C, Chen IW. 1976. Hypomagnesemia in infants of diabetic mothers: Perinatal studies. *J Pediatr* 89:115–119.
- Tucker K. 1996. The use of epidemiological approaches and meta-analysis to determine mineral element requirements. *J Nutr* 126:2365S–2372S.
- Tucker K, Kiel DP, Hannan MT, Felson DT. 1995. Magnesium intake is associated with bone-mineral density (BMD) in elderly women. *J Bone Miner Res* 10:S466.
- Tylavsky FA, Anderson JJ. 1988. Dietary factors in bone health of elderly lacto-ovo vegetarian and omnivorous women. *Am J Clin Nutr* 48:842–849.

- Urakabe S, Nakata K, Ando A, Orita Y, Abe Y. 1975. Hypokalemia and metabolic acidosis from overuse of magnesium oxide. *Jpn Circ J* 39:1135–1137.
- USDA (US Department of Agriculture). 1985. *Nationwide Food Consumption Survey. Continuing Survey of Food Intakes of Individuals*. Women 19–50 years and their children 1–5 years, 1 day, 1985. Report No. 85-1. Hyattsville, MD: Nutrition Monitoring Division, Human Nutrition Information Service, USDA.
- USDA (US Department of Agriculture). 1991. *Provisional Table on the Vitamin D Content of Foods*. Hyattsville, MD: Nutrient Data Research Branch, USDA.
- USDA (US Department of Agriculture), Center for Nutrition Policy and Promotion. 1997. *Nutrient Content of the U.S. Food Supply, 1909–1994*. Washington DC: Center for Nutrition Policy and Promotion, USDA.
- USPHS (US Public Health Service). 1991. *Ad Hoc Subcommittee on Fluoride: Review of Fluoride Benefits and Risks*. Bethesda, MD: Department of Health and Human Services.
- Venkataraman PS, Tsang RC, Greer FR, Noguchi A, Laskarzewski P, Steichen JJ. 1985. Late infantile tetany and secondary hyperparathyroidism in infants fed humanized cow milk formula. Longitudinal follow-up. *Am J Dis Child* 139:664–668.
- Vicchio D, Yergey A, O'Brien K, Allen L, Ray R, Holick MF. 1993. Quantification and kinetics of 25-hydroxyvitamin D<sub>3</sub> by isotope dilution liquid chromatography/thermospray mass spectrometry. *Biol Mass Spectrom* 22:53–58.
- Vik T, Try K, Thelle DS, Forde OH. 1979. Tromso heart study: Vitamin D metabolism and myocardial infarction. *Br Med J* 2:176.
- Villar J, Repke JT. 1990. Calcium supplementation during pregnancy may reduce preterm delivery in high-risk populations. *Am J Obstet Gynecol* 163:1124–1131.
- Villareal DT, Civitelli R, Chines A, Avioli LV. 1991. Subclinical vitamin D deficiency in postmenopausal women with low vertebral bone mass. *J Clin Endocrinol Metab* 72: 628–634.
- Wacker WE, Parisi AF. 1968. Magnesium metabolism. *N Engl J Med* 45:658–663, 712–717, 772–776.
- Wagener DK, Novrjah P, Horowitz AM. 1995. *Trends in Childhood Use of Dental Care Products Containing Fluoride: United States, 1983–1989*. Advance data from Vital Health Statistics of the Center for Disease Control. National Center for Health Statistics #219; Nov. 20, 1992. Hyattsville, MD: National Center for Health Statistics.
- Walker AR, Richardson B, Walker F. 1972. The influence of numerous pregnancies and lactations on bone dimensions in South African Bantu and Caucasian mothers. *Clin Sci* 42:189–196.
- Walker RM, Linkswiler HM. 1972. Calcium retention in the adult human male as affected by protein intake. *J Nutr* 102:1297–1302.
- Wallach S, Verch RL. 1986. Tissue magnesium in spontaneously hypertensive rats. *Magnesium* 5:33–38.
- Wang CC, Kern R, Kaucher M. 1930. Minimum requirement of calcium and phosphorus in children. *Am J Dis Child* 39:768–773.
- Wardlaw GM, Pike AM. 1986. The effect of lactation on peak adult shaft and ultra-distal forearm bone mass in women. *Am J Clin Nutr* 44:283–286.
- Wasnich R, Yano K, Vogel J. 1983. Postmenopausal bone loss at multiple skeletal sites: Relationship to estrogen use. *J Chron Dis* 36:781–790.
- Wastney ME, Ng J, Smith D, Martin BR, Peacock M, Weaver CM. 1996. Differences in calcium kinetics between adolescent girls and young women. *Am J Physiol* 271:R208–R216.

- Waterhouse C, Taves D, Munzer A. 1980. Serum inorganic fluoride: Changes related to previous fluoride intake, renal function and bone resorption. *Clin Sci* 58:145–152.
- Weaver CM. 1994. Age-related calcium requirements due to changes in absorption and utilization. *J Nutr* 124:1418S–1425S.
- Weaver CM, Martin BR, Plawecki KL, Peacock M, Wood OB, Smith DL, Wastney ME. 1995. Differences in calcium metabolism between adolescent and adult females. *Am J Clin Nutr* 61:577–581.
- Webb AR, Kline L, Holick MF. 1988. Influence of season and latitude on the cutaneous synthesis of vitamin D<sub>3</sub>: Exposure to winter sunlight in Boston and Edmonton will not promote vitamin D<sub>3</sub> synthesis in human skin. *J Clin Endocrinol Metab* 67:373–378.
- Webb AR, De Costa BR, Holick MF. 1989. Sunlight regulates the cutaneous production of vitamin D<sub>3</sub> by causing its photodegradation. *J Clin Endocrinol Metab* 68:882–887.
- Webb AR, Pilbeam C, Hanafin N, Holick MF. 1990. An evaluation of the relative contributions of exposure to sunlight and of diet to the circulating concentrations of 25-hydroxyvitamin D in an elderly nursing home population in Boston. *Am J Clin Nutr* 51:1075–1081.
- Wei SH, Hattab FN, Mellberg JR. 1989. Concentration of fluoride and selected other elements in teas. *Nutrition* 5:237–240.
- Weinsier RL, Krumdieck CL. 1981. Death resulting from overzealous total parenteral nutrition: The refeeding syndrome revisited. *Am J Clin Nutr* 34:393–399.
- Weisman Y, Harell A, Edelstein S, Spirer Z, Golander A. 1979. 1,25-dihydroxyvitamin D<sub>3</sub> and 24,25-dihydroxyvitamin D<sub>3</sub> in vitro synthesis by human decidua and placenta. *Nature* 281:317–319.
- Weissberg N, Schwartz G, Shemesh O, Brooks BA, Algur N, Eylath U, Abraham AS. 1992. Serum and mononuclear cell potassium, magnesium, sodium and calcium in pregnancy and labour and their relation to uterine muscle contraction. *Magnes Res* 5:173–177.
- Wester PO, Dyckner T. 1980. Diuretic treatment and magnesium losses. *Acta Med Scand* 647:145–152.
- Whitford GM. 1994. Effects of plasma fluoride and dietary calcium concentrations on GI absorption and secretion of fluoride in the rat. *Calcif Tissue Int* 54:421–425.
- Whitford GM. 1996. The metabolism and toxicity of fluoride. In Myers HM, ed. *Monographs in Oral Science*, 2nd Revised Edition. Basel, Switzerland: Karger.
- Whitford GM, Allmann DW, Shahed AR. 1987. Topical fluorides: Effects on physiologic and biochemical processes. *J Dent Res* 66:1072–1078.
- Whiting SJ, Pluhator MM. 1992. Comparison of in vitro and in vivo tests for determination of availability of calcium from calcium carbonate tablets. *J Am Coll Nutr* 11:553–560.
- Whiting SJ, Wood RJ. 1997. Adverse effects of high-calcium diets in humans. *Nutr Rev* 55:1–9.
- WHO (World Health Organization). 1984. *Fluorine and Fluorides*. Environmental Health Criteria 36. Geneva: World Health Organization. Pp. 77–79.
- WHO (World Health Organization). 1987. *Principles for the Safety Assessment of Food Additives and Contaminants in Food*. Environmental Health Criteria 70. Geneva: World Health Organization.

- WHO (World Health Organization). 1994. *Assessment of Fracture Risk and its Application to Screening for Postmenopausal Osteoporosis*. Technical Report Series 843. Geneva: World Health Organization.
- WHO (World Health Organization). 1996. *Trace Elements in Human Nutrition and Health*. Prepared in collaboration with the Food and Agriculture Organization of the United Nations and the International Atomic Energy Agency. Geneva: World Health Organization.
- Wickham CA, Walsh K, Cooper C, Barker DJ, Margetts BM, Morris J, Bruce SA. 1989. Dietary calcium, physical activity, and risk of hip fracture: A prospective study. *Br Med J* 299:889–892.
- Widdowson EM. 1965. Absorption and excretion of fat, nitrogen, and minerals from “filled” milks by babies one week old. *Lancet* 2:1099–1105.
- Widdowson EM, Dickerson JWT. 1964. The chemical composition of the body. In: Comar CL, Bronner F, eds. *Mineral Metabolism: An Advanced Treatise, Vol. II. The Elements, Part A*. New York: Academic Press.
- Widdowson EM, McCance RA, Spray CM. 1951. The chemical composition of the human body. *Clin Sci* 10:113–125.
- Widman L, Wester PO, Stegmayr BK, Wirell M. 1993. The dose-dependent reduction in blood pressure through administration of magnesium. A double blind placebo controlled cross-over study. *Am J Hypertens* 6:41–45.
- Wiktorsson AM, Martinsson T, Zimmerman M. 1992. Caries prevalence among adults in communities with optimal and low water fluoride concentrations. *Community Dent Oral Epidemiol* 20:359–363.
- Wilkinson R. 1976. Absorption of calcium, phosphorus, and magnesium. In: Nor din BEC, ed. *Calcium, Phosphate and Magnesium Metabolism*. Edinburgh: Churchill Livingstone. Pp. 36–112.
- Willett W. 1990. *Nutritional Epidemiology*. New York, NY: Oxford University Press.
- Willett WC, Sampson L, eds. 1997. Dietary assessment methods. *Am J Clin Nutr* 65:1097S–1368S.
- Williams JE, Zwemer JD. 1990. Community water fluoride levels, preschool dietary patterns, and the occurrence of fluoride dental opacities. *J Pub Hlth Dent* 50:276–281.
- Williams ML, Rose CS, Morrow G, Sloan SE, Barness LA. 1970. Calcium and fat absorption in neonatal period. *Am J Clin Nutr* 23:1322–1330.
- Wilson SG, Retallack RW, Kent JC, Worth GK, Gutteridge DH. 1990. Serum free 1,25-dihydroxyvitamin D and the free 1,25-dihydroxyvitamin D index during a longitudinal study of human pregnancy and lactation. *Clin Endocrinol* 32:613–622.
- Wise A, Gilbert DJ. 1982. Phytate hydrolysis by germfree and conventional rats. *Appl Environ Microbiol* 43:753–756.
- Wisker E, Nagel R, Tanudjaja TK, Feldheim W. 1991. Calcium, magnesium, zinc, and iron balances in young women: Effects of a low-phytate barley-fiber concentrate. *Am J Clin Nutr* 54:553–559.
- Witterman JC, Willett WC, Stampfer MJ, Colditz GA, Sacks FM, Speizer FE, Rosner B, Hennekens CH. 1989. A prospective study of nutritional factors and hypertension among U.S. women. *Circulation* 80:1320–1327.
- Witterman JC, Grobbee DE, Derkx FH, Bouillon R, de Brujin AM, Hofman A. 1994. Reduction of blood pressure with oral magnesium supplementation in women with mild to moderate hypertension. *Am J Clin Nutr* 60:129–135.
- Wong NL, Quamme GA, Dirks JH. 1986. Effects of acid-base disturbances on renal handling of magnesium in the dog. *Clin Sci* 70:277–284.

- Wood RJ, Zheng JJ. 1990. Milk consumption and zinc retention in postmenopausal women. *J Nutr* 120:398–403.
- Wood RJ, Sitrin MD, Rosenberg IH. 1988. Effect of phosphorus on endogenous calcium losses during total parenteral nutrition. *Am J Clin Nutr* 48:632–636.
- Woods KL, Fletcher S. 1994. Long-term outcome after intravenous magnesium sulphate in suspected acute myocardial infarction: The second Leicester Intravenous Magnesium Intervention Trial (LIMIT-2). *Lancet* 343:816–819.
- Workshop Reports. 1992. *J Dent Res* 71:1218–1227.
- Yamagata Z, Miyamura T, Iijima S, Asaka A, Sasaki M, Kato J, Koizumi K. 1994. Vitamin D receptor gene polymorphism and bone mineral density in healthy Japanese women. *Lancet* 344:1027.
- Yamamoto ME, Applegate WB, Klag MJ, Borhani NO, Cohen JD, Kirchner KA, Lakatos E, Sacks FM, Taylor JO, Hennekens CH. 1995. Lack of blood pressure effect with calcium and magnesium supplementation in adults with high-normal blood pressure. Results from Phase I of the Trials of Hypertension Prevention (TOHP). Trials of Hypertension Prevention (TOHP) Collaborative Research Group. *Ann Epidemiol* 5:96–107.
- Yano K, Heilbrun LK, Wasnich RD, Hankin JH, Vogel JM. 1985. The relationship between diet and bone mineral content of multiple skeletal sites in elderly Japanese men and women living in Hawaii. *Am J Clin Nutr* 42:877–888.
- Young GP, Thomas RJ, Bourne DW, Russell DM. 1985. Parenteral nutrition. *Med J Aust* 143:597–601.
- Zeghoud F, Vervel C, Guillozo H, Walrant-Debray O, Boutignon H, Garabedian M. 1997. Subclinical vitamin D deficiency in neonates: Definition and response to vitamin D supplements. *Am J Clin Nutr* 65:771–778.
- Zemel PC, Zemel MB, Urberg M, Douglas FL, Geiser R, Sower JR. 1990. Metabolic and hemodynamic effects of magnesium supplementation in patients with essential hypertension. *Am J Clin Nutr* 51:665–669.
- Ziegler EE, Fomon SJ. 1983. Lactose enhances mineral absorption in infancy. *J Pediatr Gastroenterol Nutr* 2:228–294.
- Zielhuis RL, van der Kreek FW. 1979. The use of a safety factor in setting health-based permissible levels for occupational exposure. *Int Arch Occup Environ Health* 42:191–201.
- Zipkin I, Zucas SM, Lavender DR, Fullmer HM, Schiffmann E, Corcoran BA. 1970. Fluoride and calcification of rat aorta. *Calcif Tissue Res* 6:173–182.

## POTASSIUM

*Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate* (ISBN 0-309-09158-6), Chapter 5, pp. 255–268.

- Agarwal R, Afzalpurkur R, Fordtran JS. 1994. Pathophysiology of potassium absorption and secretion by the human intestine. *Gastroenterol* 107:548–571.
- Alon US, Berenbom A. 2000. Idiopathic hypercalciuria of childhood: 4- to 11-year outcome. *Pediatric Nephrol* 14:1011–1015.
- Alpern RJ. 1995. Trade-offs in the adaptation to acidosis. *Kidney Int* 47:1205–1215.
- Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin PH, Karanja N. 1997. A clinical trial of the effects of dietary patterns on blood pressure. *N Engl J Med* 336:1117–1124.
- Armstrong LE, Hubbard RW, Szlyk PC, Matthew WT, Sils IV. 1985. Voluntary dehydration and electrolyte losses during prolonged exercise in the heat. *Aviat Space Environ Med* 56:765–770.
- Ascherio A, Rimm EB, Giovannucci EL, Colditz GA, Rosner B, Willet WC, Sacks F, Stampfer MJ. 1992. A prospective study of nutritional factors and hypertension among US men. *Circulation* 86:1475–1484.
- Ascherio A, Rimm EB, Hernan MA, Giovannucci EL, Kawachi I, Stampfer MJ, Willett WC. 1998. Intake of potassium, magnesium, calcium, and fiber and risk of stroke among US men. *Circulation* 98:1198–1204.
- August P, Lindheimer MD. 1999. Chronic hypertension and pregnancy. In: Lindheimer MD, Roberts JM, Cunningham FG, eds. *Hypertensive Disorders in Pregnancy*, 2nd ed. Stamford, CT: Appleton & Lange. Pp. 605–633.
- Barcelo P, Wuhl O, Servitge E, Rousaud A, Pak CY. 1993. Randomized double-blind study of potassium citrate in idiopathic hypocitraturic calcium nephro lithiasis. *J Urol* 150:1761–1764.
- Barden AE, Vandongen R, Beilin LJ, Margetts B, Rogers P. 1986. Potassium supplementation does not lower blood pressure in normotensive women. *J Hypertens* 4:339–343.
- Barden AE, Beilin LJ, Vandongen R, Puddey IB. 1991. A double-blind placebo-controlled trial of the effects of short-term potassium supplementation on blood pressure and atrial natriuretic peptide in normotensive women. *Am J Hypertens* 4:206–213.
- Barzel US. 1995. The skeleton as an ion exchange system: Implications for the role of acid-base imbalance in the genesis of osteoporosis. *J Bone Miner Res* 10:1431–1436.
- Barzel US, Jowsey J. 1969. The effects of chronic acid and alkali administration on bone turnover in adult rats. *Clin Sci* 36:517–524.
- Bazzano LA, He J, Ogden LG, Loria C, Vuppuluri S, Myers L, Whelton PK. 2001. Dietary potassium intake and risk of stroke in US men and women. *Stroke* 32:1473–1480.
- Berenson GS, Voors AW, Dalferes ER, Webber LS, Shuler SE. 1979. Creatinine clearance, electrolytes, and plasma renin activity related to the blood pressure of white and black children—The Bogalusa Heart Study. *J Lab Clin Med* 93:535–548.
- Berliner RW. 1961. Renal mechanisms for potassium excretion. In: *Harvey Lectures Series 55*. New York: Academic Press. Pp. 141–171.
- Bisaz S, Feliz R, Neuman WF, Fleisch H. 1978. Quantitative determination of in-

- hibitors of calcium phosphate precipitation in whole urine. *Miner Electrolyte Metab* 1:74–83.
- Brancati FL, Appel LJ, Seidler AJ, Whelton PK. 1996. Effect of potassium supplementation on blood pressure in African Americans on a low-potassium diet. A randomized, double-blind, placebo-controlled trial. *Arch Intern Med* 156:61–67.
- Brandis M, Keyes J, Windhager EE. 1972. Potassium-induced inhibition of proximal tubular fluid reabsorption in rats. *Am J Physiol* 222:421–427.
- Breslau NA, Brinkley L, Hill KD, Pak CYC. 1988. Relationship of animal protein-rich diet to kidney stone formation and calcium metabolism. *J Clin Endocrinol Metab* 66:140–146.
- Brown MA, Sinosich MJ, Saunders DM, Gallery EDM. 1986. Potassium regulation and progesterone-aldosterone interrelationships in human pregnancy: A prospective study. *Am J Obstet Gynecol* 155:349–353.
- Brunette MG, Mailloux J, Lajeunesse D. 1992. Calcium transport through the luminal membrane of the distal tubule. I. Interrelationship with sodium. *Kidney Int* 41:281–288.
- Bruun NE, Skott P, Damkjaer Nielsen M, Rasmussen S, Schutten HJ, Leth A, Pedersen EB, Giese J. 1990. Normal renal tubular response to changes of sodium intake in hypertensive man. *J Hypertens* 8:219–227.
- Bulpitt CJ, Ferrier G, Lewis PJ, Daymond M, Bulpitt PF, Dollery CT. 1985. Potassium supplementation fails to lower blood pressure in hypertensive patients receiving a potassium lowering diuretic. *Ann Clin Res* 17:126–130.
- Bushinsky DA. 1998. Acid-base imbalance and the skeleton. In: Burckhardt PB, Dawson-Hughes B, Heaney RP, eds. *Nutritional Aspects of Osteoporosis*. New York: Springer-Verlag. Pp. 208–217.
- Bushinsky DA, Frick KK. 2000. The effects of acid on bone. *Curr Opin Nephrol Hypertens* 9:369–379.
- Cappuccio FP, MacGregor GA. 1991. Does potassium supplementation lower blood pressure? A meta-analysis of published trials. *J Hypertens* 9:465–473.
- Castenmiller JJM, Mensink RP, van der Heijden L, Kouwenhoven T, Hautvast J, de Leeuw PW, Schaafsma G. 1985. The effect of dietary sodium on urinary calcium and potassium excretion in normotensive men with different calcium intakes. *Am J Clin Nutr* 41:52–60.
- Chalmers J, Morgan T, Doyle A, Dickson B, Hopper J, Mathews J, Matthews G, Moulds R, Myers J, Nowson C, Scoggins B, Stebbing M. 1986. Australian National Health and Medical Research Council dietary salt study in mild hypertension. *J Hypertens* 4:S629–S637.
- Cirillo M, Laurenzi M, Panarelli W, Stamler J. 1994. Urinary sodium to potassium ratio and urinary stone disease. *Kidney Int* 46:1133–1139.
- Clinkingbeard C, Lawrence D, Shenker Y. 1991. Effect of varying potassium intake on atrial natriuretic hormone-induced suppression of aldosterone. *Am J Hypertens* 4:456–459.
- Coe FL, Parks JH, Asplin JR. 1992. The pathogenesis and treatment of kidney stones. *N Engl J Med* 327:1141–1152.
- Consolazio CF, Matoushi LO, Nelsom RS, Harding RS, Canham JR. 1963. Excretion of sodium, potassium, magnesium and iron in human sweat and the relation of each to balance and requirements. *J Nutr* 79:407–415.
- Coruzzi P, Brambilla L, Brambilla V, Gualerzi M, Rossi M, Parati G, Di Renzo M, Tadonio J, Novarini A. 2001. Potassium depletion and salt sensitivity in essential hypertension. *J Clin Endocrinol Metab* 86:2857–2862.

- Costill DL, Cote R, Fink W. 1982. Dietary potassium and heavy exercise: Effects of muscle water and electrolyte. *Am J Clin Nutr* 36:266–275.
- Culleton BF, Larson MG, Evans JC, Wilson PWF, Barrett BJ, Parfrey P, Levy D. 1999. Prevalence and correlates of elevated serum creatinine levels. *Arch Intern Med* 159:1785–1790.
- Cummings JH, Hill MJ, Jenkins DJA, Pearson JR, Wiggins HS. 1976. Changes in fecal composition and colonic function due to cereal fiber. *Am J Clin Nutr* 29:1468–1473.
- Curhan GC, Willett WC, Rimm ER, Stampfer MJ. 1993. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. *N Engl J Med* 328:833–838.
- Curhan GC, Willett WC, Speizer FE, Spiegelman D, Stampfer MJ. 1997. Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk of kidney stones in women. *Ann Intern Med* 126:497–504.
- Cushman WC, Langford HG. 1988. Randomized controlled trial of potassium chloride versus placebo in mildly hypertensive blacks and whites. *Circulation* 78:II-370.
- Dai WS, Kuller LH, Miller G. 1984. Arterial blood pressure and urinary electrolytes. *J Chron Dis* 37:75–84.
- Davis KM, Fish LC, Ten Cate AJ, Bonis P, Fields D, Clark BA, Elahi D, Minaker KL. 1989. Determinants of basal atrial natriuretic peptide (ANP) in the institutionalized elderly. *Gerontologist* 29:A6.
- Deriaz O, Theriault G, Lavallee N, Fournier G, Nadeau A, Bouchard C. 1991. Human resting energy expenditure in relation to dietary potassium. *Am J Clin Nutr* 54:628–634.
- Devine A, Criddle RA, Dick IM, Kerr DA, Prince RL. 1995. A longitudinal study of the effect of sodium and calcium intakes on regional bone density in postmenopausal women. *Am J Clin Nutr* 62:740–745.
- Dewey KG, Lonnerdal B. 1983. Milk and nutrient intake of breast-fed infants from 1 to 6 months: Relation to growth and fatness. *J Pediatr Gastroenterol Nutr* 2:497–506.
- Dluhy RG, Axelrod L, Underwood RH, Williams GH. 1972. Studies of the control of plasma aldosterone concentration in normal man. II. Effect of dietary potassium and acute potassium infusion. *J Clin Invest* 51:1950–1957.
- Dyer AR, Elliott P, Shipley M. 1994. Urinary electrolyte excretion in 24 hours and blood pressure in the INTERSALT study. II. Estimates of electrolyte blood pressure associations corrected for regression dilution bias. *Am J Epidemiol* 139:941–951.
- Eaton SB, Eaton SBI, Konner MJ. 1999. Paleolithic nutrition revisited. In: Trevathan WR, Smith EO, McKenna JJ, eds. *Evolutionary Medicine*. New York: Oxford University Press. Pp. 313–332.
- Ehrlich EN, Lindheimer MD. 1972. Effects of administered mineralocorticoids or ACTH in pregnant women: Attenuation of the kaliuretic influence of mineralocorticoids during pregnancy. *J Clin Invest* 51:1301–1309.
- Fang J, Madhavan S, Alderman MH. 2000. Dietary potassium intake and stroke mortality. *Stroke* 31:1532–1537.
- Fisch C, Knoebel SB, Feigenbaum H, Greenspan K. 1966. Potassium and the monophasic action potential, electrocardiogram, conduction and arrhythmias. *Prog Cardiovasc Dis* 8:387–418.

- Follenius M, Brandenberger G, Reinhardt B, Simeoni M. 1979. Plasma aldosterone, renin activity, and cortisol responses to heat exposure in sodium depleted and repleted subjects. *Eur J Appl Physiol* 41:41–50.
- Forsum E, Sadurkis A, Wager J. 1988. Resting metabolic rate and body composition of healthy Swedish women during pregnancy. *Am J Clin Nutr* 47:942–947.
- Fotherby MD, Potter JF. 1992. Potassium supplementation reduces clinic and ambulatory blood pressure in elderly hypertensive patients. *J Hypertens* 10:1403–1408.
- Franse LV, Pahor M, Di Bari M, Somes GW, Cushman WC, Applegate WB. 2000. Hypokalemia associated with diuretic use and cardiovascular events in the Systolic Hypertension in the Elderly Program. *Hypertension* 35:1025–1030.
- Frassetto LA, Morris RC Jr, Sebastian A. 1996. Effect of age on blood acid-base composition in adult humans: Role of age-related renal functional decline. *Am J Physiol* 271:F1114–F1122.
- Frassetto LA, Morris RC Jr, Sebastian A. 1997. Potassium bicarbonate reduces urinary nitrogen excretion in postmenopausal women. *J Clin Endocrinol Metab* 82:254–259.
- Frassetto LA, Todd KM, Morris RC, Sebastian A. 1998. Estimation of the net endogenous noncarbonic acid production in humans from diet potassium and protein contents. *Am J Clin Nutr* 68:576–583.
- Friedman SA, Friedman CL. 1957. Salt and water balance in ageing rats. *Gerontologia* 1:107–121.
- Frisancho AR, Leonard WR, Bollettino LA. 1984. Blood pressure in blacks and whites and its relationship to dietary sodium and potassium intake. *J Chron Dis* 37:515–519.
- Fukumoto T, Tanaka T, Fujioka H, Yoshihara S, Ochi T, Kuroiwa A. 1988. Differences in composition of sweat induced by thermal exposure and by running exercise. *Clin Cardiol* 11:707–709.
- Furberg CD, Wright JT Jr, Davis BR, Cutler JA, Alderman M, Black H, Cushman W, Grimm R, Haywood LJ, Leenen F, Oparil S, Probstfield J, Whelton P, Nwachuku C, Gordon D, Proschan M, Einhom P, Ford CE, Piller LB, Dunn IK, Goff D, Pressel S, Bettencourt J, DeLeon B, Simpson LM, Blanton J, Geraci T, Walsh SM, Nelson C, Rahman M, Juratovac A, Pospisil R, Carroll L, Sullivan S, Russo J, Barone G, Christian R, Feldman S, Lucente T, Calhoun D, Jenkins K, McDowell P, Johnson J, Kingry C, Alzate J, Margolis KL, Holland-Klemme LA, Jaeger B, Williamson J, Louis G, Ragusa P, Williard A, Ferguson RLS, Tanner J, Eckfeldt J, Crow R, Pelosi J. 2002. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *J Am Med Assoc* 288:2981–2997.
- Gallen IW, Rosa RM, Esparaz DY, Young JB, Robertson GL, Batlle D, Epstein FH, Landsberg L. 1998. On the mechanism of the effects of potassium restriction on blood pressure and renal sodium retention. *Am J Kidney Dis* 31:19–27.
- Geleijnse JM, Grobbee DE, Hofman A. 1990. Sodium and potassium intake and blood pressure change in childhood. *Br Med J* 300:899–902.
- Geleijnse JM, Witteman J, den Breeijen JH, Hofman A, de Jong, TVM, Pols H, Grobbee DE. 1996. Dietary electrolyte intake and blood pressure in older subjects: The Rotterdam Study. *J Hypertens* 14:737–741.

- Geleijnse JM, Kok FJ, Grobbee DE. 2003. Blood pressure response to changes in sodium and potassium intake: A metaregression analysis of randomised trials. *J Hum Hypertens* 17:471–480.
- Gennari FJ, Segal AS. 2002. Hyperkalemia: An adaptive response in chronic renal insufficiency. *Kidney Int* 62:1–9.
- Gilliland FD, Berhane KT, Li YF, Kim DH, Margolis HG. 2002. Dietary magnesium, potassium, sodium, and children's lung function. *Am J Epidemiol* 155:125–131.
- Godfrey BE, Wordsworth GR. 1970. Total body potassium in pregnant women. *J Obstet Gynaecol Br Commw* 77:244–246.
- Green DM, Ropper AH, Kronmal RA, Psaty BM, Burke GL. 2002. Serum potassium level and dietary potassium intake as risk factors for stroke. *Neurology* 59:314–320.
- Grim CE, Luft FC, Miller JZ, Meneely GR, Battarbee HD, Hames CG, Dahl LK. 1980. Racial differences in blood pressure in Evans County, Georgia: Relationship to sodium and potassium intake and plasma renin activity. *J Chron Dis* 33:87–94.
- Grimm RH, Kofron PM, Neaton JD, Svendsen KH, Elmer PJ, Holland L, Witte L, Clearman D, Prineas RJ. 1988. Effect of potassium supplementation combined with dietary sodium reduction on blood pressure in men taking antihypertensive medication. *J Hypertens* 6:S591–S593.
- Grimm RH, Neaton JD, Elmer PJ, Svendsen KH, Levin J, Segal M, Holland L, Witte LJ, Clearman DR, Kofron P, LaBounty RK, Crow R, Prineas RJ. 1990. The influence of oral potassium chloride on blood pressure in hypertensive men on a low-sodium diet. *N Engl J Med* 322:569–574.
- Grobbee DE, Hofman A, Roelandt JT, Boomsma F, Schalekamp MA, Valkenburg HA. 1987. Sodium restriction and potassium supplementation in young people with mildly elevated blood pressure. *J Hypertens* 5:115–119.
- Gross SJ, David RJ, Bauman L, Tomarelli RM. 1980. Nutritional composition of milk produced by mothers delivering preterm. *J Pediatr* 96:641–644.
- Gu D, He J, Wu X, Duan X, Whelton PK. 2001. Effect of potassium supplementation on blood pressure in Chinese: A randomized, placebo-controlled trial. *J Hypertens* 19:1325–1331.
- Haddad A, Strong E. 1975. Potassium in salt substitutes. *N Engl J Med* 292:1082.
- Hajjar IM, Grim CE, George V, Kotchen TA. 2001. Impact of diet on blood pressure and age-related changes in blood pressure in the US population. *Arch Intern Med* 161:589–593.
- Hamm LL. 1990. Renal handling of citrate. *Kidney Int* 38:728–735.
- Hay E, Derazon H, Bukish N, Katz L, Kruglyakov I, Armoni M. 2002. Fatal hyperkalemia related to combined therapy with a cox-2 inhibitor, ace inhibitor and potassium rich diet. *J Emerg Med* 22:349–352.
- Helderman JH, Elahi D, Andersen DK, Raizes GS, Tobin JD, Shocket D, Andres R. 1983. Prevention of the glucose intolerance of thiazide diuretics by maintenance of body potassium. *Diabetes* 32:106–111.
- Hene RJ, Koomans HA, Boer P, Dorhout Mees EJ. 1986. Adaptation to chronic potassium loading in normal man. *Miner Electrolyte Metab* 12:165–172.
- Hirvonen T, Pietinen P, Virtanen M, Albanes D, Virtamo J. 1999. Nutrient intake and use of beverages and the risk of kidney stones among male smokers. *Am J Epidemiol* 150:187–194.
- Holbrook JT, Patterson KY, Bodner JE, Douglas LW, Veillon C, Kelsay JL, Mertz W, Smith JC. 1984. Sodium and potassium intake and balance in adults consuming self-selected diets. *Am J Clin Nutr* 40:786–793.

- Hypertension Prevention Trial Research Group. 1990. The Hypertension Prevention Trial: Three-year effects of dietary changes on blood pressure. *Arch Intern Med* 150:153–162.
- Hyttén FE, Leitch I. 1971. *The Physiology of Human Pregnancy*, 2nd ed. Philadelphia: FA Davis.
- Imura O, Kijima T, Kikuchi K, Miyama A, Ando T, Nakao T, Takigami Y. 1981. Studies on the hypotensive effect of high potassium intake in patients with essential hypertension. *Clin Sci* 61:77S–80S.
- IOM (Institute of Medicine). 2000. *The Role of Nutrition in Maintaining Health in the Nation's Elderly*. Washington, DC: National Academy Press.
- IOM. 2002/2005. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*. Washington, DC: The National Academies Press.
- Iso H, Stampfer MJ, Manson JE, Rexrode K, Hennekens CH, Colditz GA, Speizer FE, Willett WC. 1999. Prospective study of calcium, potassium, and magnesium intake and risk of stroke in women. *Stroke* 30:1772–1779.
- John JH, Ziebland S, Yudkin P, Roe LS, Neil HA. 2002. Effects of fruit and vegetable consumption on plasma antioxidant concentration and blood pressure: A randomised controlled trial. *Lancet* 359:1969–1974.
- Jones G, Riley MD, Whiting S. 2001. Association between urinary potassium, urinary sodium, current diet, and bone density in prepubertal children. *Am J Clin Nutr* 73:839–844.
- Kallen RJ, Rieger CHL, Cohen HS, Suter MA, Ong RT. 1976. Near-fatal hyperkalemia due to ingestion of salt substitute by an infant. *J Am Med Assoc* 235:2125–2126.
- Kamel KS, Halperin ML, Faber MD, Steigerwalt SP, Heilig CW, Narins RG. 1996. Disorders of potassium balance. In: Brenner BM, ed. *Brenner and Rector's The Kidney*, 5th ed., vol. 1. Philadelphia: WB Saunders. Pp. 999–1037.
- Kaplan NM, Carnegie A, Raskin P, Heller JA, Simmons M. 1985. Potassium supplementation in hypertensive patients with diuretic-induced hypokalemia. *N Engl J Med* 312:746–749.
- Keenan BS, Buzek SW, Garza C, Potts E, Nichols BL. 1982. Diurnal and longitudinal variations in human milk sodium and potassium: Implication for nutrition and physiology. *Am J Clin Nutr* 35:527–534.
- Kesteloot H, Joossens JV. 1988. Relationship of dietary sodium, potassium, calcium, and magnesium with blood pressure. *Hypertension* 12:594–599.
- Khaw KT, Barrett-Connor E. 1984. Dietary potassium and blood pressure in a population. *Am J Clin Nutr* 39:963–968.
- Khaw KT, Barrett-Connor E. 1987. Dietary potassium and stroke-associated mortality. *N Engl J Med* 316:235–240.
- Khaw KT, Barrett-Connor E. 1988. The association between blood pressure, age, and dietary sodium and potassium: A population study. *Circulation* 77:53–61.
- Khaw KT, Barrett-Connor E. 1990. Increasing sensitivity of blood pressure to dietary sodium and potassium with increasing age. A population study using casual urine specimens. *Am J Hypertens* 6:505–511.
- Khaw KT, Thom S. 1982. Randomised double-blind cross-over trial of potassium on blood-pressure in normal subjects. *Lancet* 2:1127–1129.
- Kirkendall WM, Conner EW, Abboud F, Rastogi SP, Anderson TA, Fry M. 1976. The effect of dietary sodium chloride on blood pressure, body fluids, electrolytes, renal function, and serum lipids of normotensive man. *J Lab Clin Med* 87:418–434.

- Knochel JP. 1984. Diuretic-induced hypokalemia. *Am J Med* 77:18–27.
- Kok FJ, Vandenbroucke JP, van der Heide-Wessel C, van der Heide RM. 1986. Dietary sodium, calcium, and potassium, and blood pressure. *Am J Epidemiol* 123:1043–1048.
- Krishna GG, Kapoor SC. 1991. Potassium depletion exacerbates essential hypertension. *Ann Intern Med* 115:77–83.
- Krishna GG, Miller E, Kapoor S. 1989. Increased blood pressure during potassium depletion in normotensive men. *N Engl J Med* 320:1177–1182.
- Kurtz I, Maher T, Hulter HN, Schambelan M, Sebastian A. 1983. Effect of diet on plasma acid-base composition in normal humans. *Kidney Int* 24:570–580.
- Lambert JR, Newman A. 1980. Ulceration and stricture of the esophagus due to oral potassium chloride (slow release tablet) therapy. *Am J Gastroenterol* 73:508–511.
- Langford HG. 1983. Dietary potassium and hypertension: Epidemiologic data. *Ann Intern Med* 98:770–772.
- Lawton WJ, Fitz AE, Anderson EA, Sinkey CA, Coleman RA. 1990. Effect of dietary potassium on blood pressure, renal function, muscle sympathetic nerve activity, and forearm vascular resistance and flow in normotensive and borderline hypertensive humans. *Circulation* 81:173–184.
- Lee CN, Reed DM, MacLean CJ, Yano K, Chiu D. 1988. Dietary potassium and stroke. *N Engl J Med* 318:995–996.
- Leijonmarck CE, Raf L. 1985. Gastrointestinal lesions and potassium chloride supplements. *Lancet* 1:56–57.
- Lemann J. 1999. Relationship between urinary calcium and net acid excretion as determined by dietary protein and potassium: A review. *Nephron* 81:18S–25S.
- Lemann J, Litzow JR, Lennon EJ. 1966. The effects of chronic acid loads in normal man: Further evidence for participation of bone mineral in the defense against chronic metabolic acidosis. *J Clin Invest* 45:1608–1614.
- Lemann J, Pleuss JA, Gray RW. 1989. Potassium bicarbonate, but not sodium bicarbonate, reduces urinary calcium excretion and improves calcium balances in healthy men. *Kidney Int* 35:688–695.
- Lemann J, Pleuss JA, Gray RW, Hoffmann RG. 1991. Potassium administration reduces and potassium deprivation increases urinary calcium excretion in healthy adults. *Kidney Int* 39: 973–983.
- Lemann J, Pleuss JA, Gray RW. 1993. Potassium causes calcium retention in healthy adults. *J Nutr* 123:1623–1626.
- Lemann J, Bushinsky DA, Hamm LL. 2003. Bone buffering of acid and base in humans. *Am J Physiol* 285:F811–F832.
- Lemons JA, Moye L, Hall D, Simmons M. 1982. Differences in the composition of preterm and term human milk during early lactation. *Pediatr Res* 16:113–117.
- Lennon EJ, Lemann Jr, Litzow JR. 1966. The effects of diet and stool composition on the net external acid balance of normal subjects. *J Clin Invest* 45:1601–1607.
- Lindheimer MD, Katz AI. 1985. Fluid and electrolyte metabolism in normal and abnormal pregnancy. In: Arieff AI, DeFronzo RA, eds. *Fluid, Electrolyte, and Acid-Base Disorders*. New York: Churchill Livingstone. Pp. 1041–1086.
- Lindheimer MD, Katz AI. 2000. Renal physiology and disease in pregnancy. In: Seldin DW, Geibisch G, eds. *The Kidney: Physiology and Pathophysiology*, 3rd ed. New York: Lippincott Williams & Wilkins. Pp. 2597–2644.
- Lindheimer MD, Richardson DA, Ehrlich EN, Katz AI. 1987. Potassium homeostasis in pregnancy. *J Reprod Med* 32:517–522.

- Liu K, Ruth KJ, Flack JM, Jones-Webb R, Burke G, Savage PJ, Hulley SB. 1996. Blood pressure in young blacks and whites: Relevance of obesity and lifestyle factors in determining differences. *Circulation* 93:60–66.
- Liu LS, Xie J, Fang WQ. 1988. Urinary cations and blood pressure: A collaborative study of 16 districts in China. *J Hypertens* 6:587S–590S.
- Loria CM, Obarzanek E, Ernst ND. 2001. Choose and prepare foods with less salt: Dietary advice for all Americans. *J Nutr* 131:536S–551S.
- Luft FC, Rankin LI, Bloch R, Weyman AE, Willis LR, Murray RH, Grim CE, Weinberger MH. 1979. Cardiovascular and humoral responses to extremes of sodium intake in normal black and white men. *Circulation* 60:697–706.
- Luft FC, Weinberger MH, Grim CE. 1982. Sodium sensitivity and resistance in normotensive humans. *Am J Med* 72:726–736.
- Macdonald HM, New SA, Golden MH, Campbell MK, Reid DM. 2004. Nutritional associations with bone loss during the menopausal transition: Evidence of a beneficial effect of calcium, alcohol, and fruit and vegetable nutrients and of a detrimental effect of fatty acids. *Am J Clin Nutr* 79:155–165.
- MacGillivray L, Buchanan TJ. 1958. Total exchangeable sodium and potassium in non-pregnant women and in normal and preeclamptic pregnancy. *Lancet* 2: 1090–1093.
- MacGregor GA, Cappuccio FP. 1993. The kidney and essential hypertension: A link to osteoporosis? *J Hypertens* 11:781–785.
- MacGregor GA, Smith SJ, Markandu ND, Banks RA, Sagnella GA. 1982. Moderate potassium supplementation in essential hypertension. *Lancet* 2:567–570.
- Malhotra MS, Sridharan K, Venkataswamy Y. 1976. Potassium losses in sweat under heat stress. *Aviat Space Environ Med* 47:503–504.
- Matkovic V, Ilich JZ, Andon MB, Hsieh LC, Tzagournis MA, Lagger BJ, Goel PK. 1995. Urinary calcium, sodium and bone mass of young females. *Am J Clin Nutr* 62:417–425.
- Matlou SM, Isles CG, Higgs A, Milne FJ, Murray GD, Schultz E, Starke IF. 1986. Potassium supplementation in blacks with mild to moderate essential hypertension. *J Hypertens* 4:61–64.
- Maurer M, Riesen W, Muser J, Hulter HN, Krapf R. 2003. Neutralization of Western diet inhibits bone resorption independently of K intake and reduces cortisol secretion in humans. *Am J Physiol* 284:F32–F40.
- McGarvey ST, Zinner SH, Willett WC, Rosner B. 1991. Maternal prenatal dietary potassium, calcium magnesium, and infant blood pressure. *Hypertension* 17: 218–224.
- Medical Economics. 2001. *Physicians' Desk Reference for Nutritional Supplements*, 1st ed. Montvale, NJ: Medical Economics.
- Meyer JL, Smith LH. 1975. Growth of calcium oxalate monohydrate. *J Cryst Growth* 21:267–276.
- Miller JZ, Weinberger MH, Christian JC. 1987. Blood pressure response to potassium supplementation in normotensive adults and children. *Hypertension* 10: 437–442.
- Minaker KL, Rowe JW. 1982. Potassium homeostasis during hyperinsulinemia: Effect of insulin level,  $\beta$ -blockade, and age. *Am J Physiol* E378–E377.
- Modan M, Halkin H, Fuch Z, Lusky A, Cherit A, Segal P, Eshkol A, Almog S, Shefi M. 1987. Hyperinsulinemia: A link between glucose intolerance, obesity, hypertension, dyslipoproteinemia, elevated serum uric acid and internal cation imbalance. *Diabete Metab* 13:375–380.

- Morgan T, Myers J, Teow B. 1984. The role of sodium and potassium in the control of blood pressure. *Aust N Z J Med* 14:458–462.
- Morimoto A, Uzu T, Fujii T, Nishimura M, Kuroda S, Nakamura S, Inenaga T, Kimura G. 1997. Sodium sensitivity and cardiovascular events in patients with essential hypertension. *Lancet* 350:1734–1737.
- Morris CD, Jacobson SL, Anand R, Ewell MG, Hauth JC, Curet LB, Catalano PM, Sibai BM, Levine RJ. 2001. Nutrient intake and hypertensive disorders of pregnancy: Evidence from a large prospective cohort. *Am J Obstet Gynecol* 184:643–651.
- Morris RC, Sebastian A. 1995. Potassium-responsive hypertension. In: Laragh J, Brenner B, eds. *Hypertension: Pathophysiology, Diagnosis, and Management*, 2nd ed. New York: Raven Press. Pp. 2715–2726.
- Morris RC Jr, Schmidlin O, Tanaka M, Forman A, Frassetto L, Sebastian A. 1999a. Differing effects of supplemental KCl and KHCO<sub>3</sub>: Pathophysiological and clinical implications. *Sem Nephrol* 19:487–493.
- Morris RC Jr, Sebastian A, Forman A, Tanaka M, Schmidlin O. 1999b. Normotensive salt-sensitivity: Effects of race and dietary potassium. *Hypertension* 33:18–23.
- Morris RC Jr, Frassetto LA, Schmidlin O, Forman A, Sebastian A. 2001. Expression of osteoporosis as determined by diet-disordered electrolyte and acid-base metabolism. In: Burckhardt PB, Dawson-Hughes B, Heaney RP, eds. *Nutritional Aspects of Osteoporosis*. San Diego: Academic Press. Pp. 357–378.
- Mujais SK, Nora NA, Chen Y. 1993. Regulation of the renal Na:K pump: Role of progesterone. *J Am Soc Nephrol* 3:1488–1495.
- Mullen JT, O'Connor DT. 1990. Potassium effects on blood pressure: Is the conjugate anion important? *J Hum Hypertens* 4:589–596.
- Naismith DJ, Braschi A. 2003. The effect of low-dose potassium supplementation on blood pressure in apparently healthy volunteers. *Br J Nutr* 90:53–60.
- New SA, Bolton-Smith C, Grubb DA, Reid DM. 1997. Nutritional influences on bone mineral density: A cross-sectional study in premenopausal women. *Am J Clin Nutr* 65:1831–1839.
- New SA, Robins SP, Campbell MK, Martin JC, Garton MJ, Bolton-Smith C, Grubb DA, Lee SJ, Reid DM. 2000. Dietary influences on bone mass and bone metabolism: Further evidence of a positive link between fruit and vegetable consumption and bone health. *Am J Clin Nutr* 71:142–151.
- New SA, MacDonald HM, Campbell MK, Martin JC, Garton MJ, Robins SP, Reid DM. 2004. Lower estimates of net endogenous noncarbonic acid production are positively associated with indexes of bone health in premenopausal and perimenopausal women. *Am J Clin Nutr* 79:131–138.
- Norbiato G, Bevilacqua M, Meroni R, Raggi U, Dagani R, Scorza D, Frigeni G, Vago T. 1984. Effects of potassium supplementation on insulin binding and insulin action in human obesity: Protein-modified fast and refeeding. *Eur J Clin Invest* 14:414–419.
- Obel AO. 1989. Placebo-controlled trial of potassium supplements in black patients with mild essential hypertension. *J Cardiovasc Pharmacol* 14:294–296.
- Oster JR, Singer I, Fishman LM. 1995. Heparin-induced aldosterone suppression and hyperkalemia. *Am J Med* 98:575–586.
- Overlack A, Conrad H, Stumpe KO. 1991. The influence of oral potassium citrate/bicarbonate on blood pressure in essential hypertension during unrestricted salt intake. *Klin Wochenschr* 69:79–83.

- Overlack A, Ruppert M, Kolloch R, Gobel B, Kraft K, Diehl J, Schmitt W, Stumpe K. 1993. Divergent hemodynamic and hormonal responses to varying salt intake in normotensive subjects. *Hypertension* 22:331–338.
- Pak CY. 1987. Citrate and renal calculi. *Miner Electrolyte Metab* 13:257–266.
- Pak CY, Fuller C. 1986. Idiopathic hypocitraturic calcium-oxalate nephrolithiasis successfully treated with potassium citrate. *Ann Intern Med* 104:33–37.
- Pak CY, Fuller C, Sakhaei K, Preminger GM, Britton F. 1985. Long-term treatment of calcium nephrolithiasis with potassium citrate. *J Urol* 134:11–19.
- Pak CY, Sakhaei K, Fuller C. 1986. Successful management of uric acid nephrolithiasis with potassium citrate. *Kidney Int* 30:422–428.
- Pak CY, Peterson RD, Poindexter J. 2002. Prevention of spinal bone loss by potassium citrate in cases of calcium urolithiasis. *J Urol* 168:31–34.
- Patki PS, Singh J, Gokhale SV, Bulakh PM, Shrotri DS, Patwardhan B. 1990. Efficacy of potassium and magnesium in essential hypertension: A double blind, placebo controlled, crossover study. *Br Med J* 301:521–523.
- Peart S, Barnes GR, Broughton PMG, Dollery CT, Green KG, Hudson MF, Lever AF, Meade TW, Miall WE, Rose GA, Greenberg G. 1987. Comparison of the antihypertensive efficacy and adverse reactions to two doses of bendrofluazide and hydrochlorothiazide and the effect of potassium supplementation on the hypotensive action of bendrofluazide: Substudies of the Medical Research Council's Trials of Treatment of Mild Hypertension: Medical Research Council Working Party. *J Clin Pharmacol* 27:271–277.
- Pennington JAT. 1998. *Bowes and Church's Food Values of Portions Commonly Used*, 17th ed. Philadelphia: Lippincott.
- Peraino RA, Suki WN. 1980. Urine HCO<sub>3</sub> augments renal Ca<sup>2+</sup> absorption independent of systemic acid-base changes. *Am J Physiol* 238:F394–F398.
- Picciano MF, Calkins EJ, Garrick JR, Deering RH. 1981. Milk and mineral intakes of breastfed infants. *Acta Paediatr Scand* 70:189–194.
- Pietinen P. 1982. Estimating sodium intake from food consumption data. *Ann Nutr Metab* 26: 90–99.
- Pietro DA, Davidson L. 1990. Evaluation of patients' preference of two potassium chloride supplements: Slow-K and K-Dur. *Clin Ther* 12:431–435.
- Pistelli R, Forastiere F, Corbo GM, Dell'Orco V, Brancato G, Agabiti N, Pizzaboloca A, Perucci CA. 1993. Respiratory symptoms and bronchial responsiveness are related to dietary salt intake and urinary potassium excretion in male children. *Eur Respir J* 6:517–522.
- Plavinik FL, Rodrigues CIS, Zanella MT, Ribeiro AB. 1992. Hypokalemia, glucose intolerance, and hyperinsulinemia during diuretic therapy. *Hypertension* 19: II26S–II29S.
- Pollare T, Lithell H, Berne C. 1989. A comparison of the effects of hydrochlorothiazide and captopril on glucose and lipid metabolism in patients with hypertension. *N Engl J Med* 321: 868–873.
- Poulter NR, Sever PS. 1986. Moderate potassium supplementation: Ineffective in black normotensives. *East Afr Med J* 63:798–802.
- Preminger GM, Sakhaei K, Skurla C, Pak CY. 1985. Prevention of recurrent calcium stone formation with potassium citrate therapy in patients with distal renal tubular acidosis. *J Urol* 134:20–23.
- Price DA, Fisher NDL, Lansang MC, Stevanovic R, Williams GH, Hollenberg NK. 2002. Renal perfusion in blacks. Alterations caused by insuppressibility of intrarenal renin with salt. *Hypertension* 40:186–189.

- Rabelink TJ, Koomans HA, Hene RJ, Dorhout Mees EJ. 1990. Early and late adjustment to potassium loading in humans. *Kidney Int* 38:942–947.
- Ray KK, Dorman S, Watson RDS. 1999. Severe hyperkalemia due to the concomitant use of salt substitutes and ACE inhibitors in hypertension: A potentially life threatening interaction. *J Hum Hypertens* 13:717–720.
- Reardon LC, Macpherson DS. 1998. Hyperkalemia in outpatients using angiotensin-converting enzyme inhibitors. How much should we worry? *Arch Intern Med* 158:26–32.
- Reddy ST, Wang C-Y, Sakhaee K, Brinkley L, Pak CYC. 2002. Effect of low-carbohydrate high-protein diets on acid-base balance, stone-forming propensity, and calcium metabolism. *Am J Kidney Dis* 40:265–274.
- Riccardella D, Dwyer J. 1985. Salt substitutes and medicinal potassium sources: Risks and benefits. *J Am Diet Assoc* 85:471–474.
- Richards AM, Nicholls MG, Espiner EA, Akram H, Maslowski AH, Hamilton EJ, Wells JE. 1984. Blood-pressure response to moderate sodium restriction and to potassium supplementation in mild essential hypertension. *Lancet* 1:757–761.
- Robertson JI. 1984. Diuretics, potassium depletion and the risk of arrhythmias. *Eur Heart J* 5:25S–28S.
- Rosa RM, Silva P, Young JB, Landsberg L, Brown RS, Rowe JW, Epstein FH. 1980. Adrenergic modulation of extrarenal potassium disposal. *N Engl J Med* 302:431–433.
- Rose G, Stamler J, Stamler R, Elliott P, Marmot M, Pyorala K, Kesteloot H, Joossens J, Hansson L, Mancia G, Dyer A, Kromhout D, Laaser U, Sans S. 1988. Intersalt: An international study of electrolyte excretion and blood pressure. Results for 24 hour urinary sodium and potassium excretion. *Br Med J* 297:319–328.
- Rowe JW, Minaker KL, Levi M. 1992. Pathophysiology and management of electrolyte disturbances in the elderly. In: Martinez-Maldonado M, ed. *Hypertension and Renal Disease in the Elderly*. Boston: Blackwell Scientific Publications. Pp. 170–184.
- Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, Obarzanek E, Conlin PR, Miller ER, Simons-Morton DG, Karanja N, Lin PH. 2001. Effects of blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. *N Engl J Med* 344:3–10.
- Sakhaee K, Alpern R, Jacobson HR, Pak CYC. 1991. Contrasting effects of various potassium salts on renal citrate excretion. *J Clin Endocrinol Metab* 72:396–400.
- Sasaki S, Zhang X, Kesteloot H. 1995. Dietary sodium, potassium, saturated fat, alcohol, and stroke mortality. *Stroke* 26:783–789.
- Schmidlin O, Forman A, Tanaka M, Sebastian A, Morris RC. 1999. NaCl-induced renal vasoconstriction in salt-sensitive African-Americans: Antipressor and hemodynamic effects of potassium bicarbonate. *Hypertension* 33:633–639.
- Schoolwerth AC, Sica DA, Ballermann BJ, Wilcox CS. 2001. Renal considerations in angiotensin converting enzyme inhibitor therapy: A statement for healthcare professionals from the Council on the Kidney in Cardiovascular Disease and the Council for High Blood Pressure Research of the American Heart Association. *Circulation* 104:1985–1991.
- Schultze RG. 1973. Recent advances in the physiology and pathophysiology of potassium excretion. *Arch Intern Med* 131:885–897.
- Sebastian A, McSherry E, Morris RC Jr. 1971. Renal potassium wasting in renal tubular acidosis (RTA): Its occurrence in types 1 and 2 RTA despite sustained correction of systemic acidosis. *J Clin Invest* 50:667–678.

- Sebastian A, Harris ST, Ottaway JH, Todd KM, Morris RC Jr. 1994. Improved mineral balance and skeletal metabolism in postmenopausal women treated with potassium bicarbonate. *N Engl J Med* 330:1776–1781.
- Sebastian A, Frassetto LA, Sellmeyer DE, Merriam RL, Morris RC Jr. 2002. Estimation of the net acid load of the diet ancestral preagricultural *Homo sapiens* and their hominid ancestors. *Am J Clin Nutr* 76:1308–1316.
- Sellmeyer DE, Schlotter M, Sebastian A. 2002. Potassium citrate prevents increased urine calcium excretion and bone resorption induced by high sodium chloride diet. *J Clin Endocrinol Metab* 87:2008–2012.
- Sharma AM, Arntz HR, Kribben A, Schattenfroh S, Distler A. 1990. Dietary sodium restriction: Adverse effect on plasma lipids. *Klin Wochenschr* 68:664–668.
- Siani A, Strazzullo P, Russo L, Guglielmi S, Iacoviello L, Ferrara LA, Mancini M. 1987. Controlled trial of long term oral potassium supplements in patients with mild hypertension. *Br Med J* 294:1453–1456.
- Simpson DP. 1983. Citrate excretion: A window on renal metabolism. *Am J Physiol* 244:F223–F234.
- Sinaiko AR, Gomez-Marin O, Prineas RJ. 1993. Effect of low sodium diet or potassium supplementation on adolescent blood pressure. *Hypertension* 21:989–994.
- Sinar DR, Bozymski EM, Blackshear JL. 1986. Effects of oral potassium supplements on upper gastrointestinal mucosa: A multicenter clinical comparison of three formulations and placebo. *Clin Ther* 8:157–163.
- Skrabal F, Aubock J, Hortnagl H. 1981. Low sodium/high potassium diet for prevention of hypertension: Probable mechanisms of action. *Lancet* 2:895–900.
- Smith SJ, Markandu ND, Sagnella GA, MacGregor GA. 1985. Moderate potassium chloride supplementation in essential hypertension: Is it additive to moderate sodium restriction? *Br Med J* 290:110–113.
- Smith SR, Klotman PE, Svetkey LP. 1992. Potassium chloride lowers blood pressure and causes natriuresis in older patients with hypertension. *J Am Soc Nephrol* 2:1302–1309.
- Snyder EL, Dixon T, Bresnitz E. 1975. Abuse of salt “substitute”. *New Engl J Med* 292:320.
- Souhrada JF, Souhrada M. 1983. Significance of the sodium pump for airway smooth muscle. *Eur J Respir Dis Suppl* 128:196–205.
- Souhrada M, Souhrada JF. 1984. Immunologically induced alterations of airway smooth muscle cell membrane. *Science* 225:723–725.
- Squires RD, Huth EJ. 1959. Experimental potassium depletion in normal human subjects. I. Relation of ionic intakes to the renal conservation of potassium. *J Clin Invest* 38:1134–1148.
- Stamler J, Cirillo M. 1997. Dietary salt and renal stone disease. *Lancet* 349:506–507.
- Stokes JBI, Lee I, Williams A. 1982. Consequences of potassium recycling in the renal medulla: Effects on ion transport by the medullary thick ascending limb of Henle's loop. *J Clin Invest* 70:219–229.
- Su M, Stork C, Ravuri S, Lavoie T, Anguish D, Nelson LS, Hoffman RS. 2001. Sustained-release potassium chloride overdose. *J Toxicol Clin Toxicol* 39:641–648.
- Subar AF, Thompson FE, Kipnis V, Midthune D, Hurwitz P, McNutt S, McIntosh A, Rosenfeld S. 2001. Comparative validation of the Block, Willett, and National Cancer Institute food frequency questionnaires. *Am J Epidemiol* 154:1089–1099.
- Sudhir K, Forman A, Yi S-L, Sorof J, Schmidlin O, Sebastian A, Morris RC Jr. 1997. Reduced dietary potassium reversibly enhances vasopressor response to stress in African-Americans. *Hypertension* 29:1083–1090.

- Sullivan JM, Ratts TE, Taylor JC, Kraus DH, Barton BR, Patrick DR, Reed SW. 1980. Hemodynamic effects of dietary sodium in man. *Hypertension* 2:506–514.
- Svetkey LP, Yarger WE, Feussner JR, DeLong E, Klotman PE. 1987. Double-blind, placebo-controlled trial of potassium chloride in the treatment of mild hypertension. *Hypertension* 9:444–450.
- Szwed JJ, Clarke M. 1982. Renal tubular acidosis in pregnancy. *Am J Med Sci* 384: 32–36.
- Takemori K, Mikami S, Nihira S, Sasaki N. 1989. Relationship of blood pressure to sodium and potassium excretion in Japanese women. *Tohoku J Exp Med* 158: 269–281.
- Tanaka M, Schmidlin O, Yi S-L, Bollen AW, Morris RC Jr. 1997. Genetically determined chloride-sensitive hypertension and stroke. *Proc Natl Acad Sci USA* 94: 14748–14752.
- Tanaka M, Schmidlin O, Olson JL, Yi S-L, Morris RC Jr. 2001. Chloride-sensitive renal microangiopathy in the stroke-prone spontaneously hypertensive rat. *Kidney Int* 59:1066–1076.
- Tannen RL. 1986. Drug interactions causing hyperkalemia. In: Whelton P, Whelton A, Walker WG, eds. *Potassium in Cardiovascular and Renal Medicine*. New York: Marcel Dekker. Pp. 467–476.
- Textor SC, Bravo EL, Fouad FM, Tarazi RC. 1982. Hyperkalemia in azotemic patients during angiotensin-converting enzyme inhibition and aldosterone reduction with captopril. *Am J Med* 73:719–725.
- Tobian L. 1986. High-potassium diets markedly protect against stroke deaths and kidney disease in hypertensive rats, an echo from prehistoric days. *J Hypertens Suppl* 4:S67–S76.
- Tobian L, Lange JM, Ulm KM, Wold LJ, Iwai J. 1984. Potassium prevents death from strokes in hypertensive rats without lowering blood pressure. *J Hypertens* 2:363S–366S.
- Tribe RM, Barton JR, Poston L, Burney PGJ. 1994. Dietary sodium intake, airway responsiveness, and cellular sodium transport. *Am J Respir Crit Care Med* 149: 1426–1433.
- Tucker KL, Hannan MT, Chen H, Cupples LA, Wilson PWF, Kiel DP. 1999. Potassium, magnesium, and fruit and vegetable intakes are associated with greater bone mineral density in elderly men and women. *Am J Clin Nutr* 69:727–736.
- Tunstall-Pedoe H. 1999. Does dietary potassium lower blood pressure and protect against coronary heart disease and death? Findings from the Scottish Heart Health Study. *Semin Nephrol* 19:500–502.
- Tunstall-Pedoe H, Woodward M, Tavendale R, Brook RA, McCluskey MK. 1997. Comparison of the prediction of 27 different factors of coronary heart disease and death in men and women of Scottish heart health study: Cohort study. *Br Med J* 315:722–729.
- Valdes G, Vio CP, Montero J, Avendano R. 1991. Potassium supplementation lowers blood pressure and increases urinary kallikrein in essential hypertensives. *J Hum Hypertens* 5:91–96.
- van Buren M, Rabelink TJ, Van Rijn HJM, Koomans HA. 1992. Effects of acute NaCl, KCl and KHCO<sub>3</sub> loads on renal electrolyte excretion in humans. *Clin Sci* 83:567–574.
- Wachman A, Bernstein DS. 1968. Diet and osteoporosis. *Lancet* 2:958–959.

- Walker WG, Whelton PK, Saito H, Russell RP, Hermann J. 1979. Relation between blood pressure and renin, renin substrate, angiotensin II, aldosterone and urinary sodium and potassium in 574 ambulatory subjects. *Hypertension* 1:287–291.
- Weinberger MH. 1996. Salt sensitivity of blood pressure in humans. *Hypertension* 27:481–490.
- Weinberger MH, Luft FC, Bloch R, Henry DP, Pratt JH, Weyman AE, Rankin LI, Murray RH, Willis LR, Grim CE. 1982. The blood pressure-raising effects of high dietary sodium intake: Racial differences and the role of potassium. *J Am Coll Nutr* 1:139–148.
- Weinberger MH, Fineberg NS, Fineberg SE, Weinberger M. 2001. Salt sensitivity, pulse pressure, and death in normal and hypertensive humans. *Hypertension* 37:429–432.
- Wells CL, Schrader TA, Stern JR, Krahenbuhl GS. 1985. Physiological responses to a 20-mile run under three fluid replacement treatments. *Med Sci Sports Exerc* 17:364–369.
- Westman EC, Yancy WS, Edman JS, Tomlin KF, Perkins CE. 2002. Effect of 6-month adherence to a very low carbohydrate diet program. *Am J Med* 113: 30–36.
- Wetli CV, Davis JH. 1978. Fatal hyperkalemia from accidental overdose of potassium chloride. *J Am Med Assoc* 240:1339.
- Whelton PK, Buring J, Borhani NO, Cohen JD, Cook N, Cutler JA, Kiley JE, Kuller LH, Satterfield S, Sacks FM, Taylor JO. 1995. The effect of potassium supplementation in persons with a high-normal blood pressure. Results from phase I of the Trials of Hypertension Prevention (TOHP). *Ann Epidemiol* 5:85–95.
- Whelton PK, He J, Cutler JA, Brancati FL, Appel LJ, Follmann D, Klag MJ. 1997. Effects of oral potassium on blood pressure. Meta-analysis of randomized controlled clinical trials. *J Am Med Assoc* 277:1624–1632.
- Wilson M, Morganti AA, Zervoudakis I, Letcher RL, Romney BM, Von Oeyen P, Papera S, Sealey JE, Laragh JH. 1980. Blood pressure, the renin-aldosterone system and sex steroids throughout normal pregnancy. *Am J Med* 68:97–104.
- Witterman JC, Willett WC, Stampfer MJ, Colditz GA, Sacks FM, Speizer FE, Rosner B, Hennekens CH. 1989. A prospective study of nutritional factors and hypertension among US women. *Circulation* 80:1320–1327.
- Witzgall H, Behr J. 1986. Effects of potassium loading in normal man on dopaminergic control of mineralocorticoids and renin release. *J Hypertens* 4:201–205.
- Xie JX, Sasaki S, Joossens JV, Kesteloot H. 1992. The relationship between urinary anions obtained from the INTERSALT study and cerebrovascular mortality. *J Hum Hypertens* 6:17–21.
- Yamori Y, Nara Y, Misushima S, Sawamura M, Horie R. 1994. Nutritional factors for stroke and major cardiovascular diseases: International epidemiological comparison of dietary prevention. *Health Prev* 6:22–27.
- Young DB. 1985. Analysis of long-term potassium regulation. *Endocr Rev* 6:24–44.
- Young DB. 2001. *Role of Potassium in Preventive Cardiovascular Medicine*. Boston: Kluwer Academic Publishers.
- Young DB, McCabe RD. 2000. Endocrine control of potassium balance. In: Fray JCS, Goodman HM, eds. *Handbook of Physiology: Section 7, The Endocrine System*. New York: Oxford University Press. Pp. 306–330.
- Zhou B, Zhang X, Zhu A, Zhao L, Ruan L, Zhu L, Liang S. 1994. The relationship of dietary animal protein and electrolytes to blood pressure: A study on three Chinese populations. *Int J Epidemiol* 23:716–722.

- Zoccali C, Cumming AMM, Hutcheson MJ, Barnett P, Semple PF. 1985. Effects of potassium on sodium balance, renin, noradrenaline and arterial pressure. *J Hypertens* 3:67–72.
- Zoia MC, Fanfulla F, Bruschi C, Basso O, De Marco R, Casali L, Cerveri I. 1995. Chronic respiratory symptoms, bronchial responsiveness and dietary sodium and potassium: A population based study. *Monaldi Arch Chest Dis* 50:104–108.
- Ibid., Chapter 8, pp. 462–464.
- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- IOM. 2001. *Caffeine for the Sustainment of Mental Task Performance*. Washington, DC: National Academy Press.
- IOM. 2002/2005. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*. Washington, DC: The National Academies Press.
- IOM. 2003. *Dietary Reference Intakes: Applications in Dietary Planning*. Washington, DC: The National Academies Press.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Schoeller DA. 1995. Limitations in the assessment of dietary energy by self-report. *Metabolism* 44:18–22.
- Schoeller DA, Bandini LG, Dietz WH. 1990. Inaccuracies in self-reported intake identified by comparison with the doubly labelled water method. *Can J Physiol Pharmacol* 68:941–949.
- Taivainen H, Laitinen R, Tahtela R, Kiianmaa K, Valimaki MJ. 1995. Role of plasma vasopressin in changes of water balance accompanying acute alcohol intoxication. *Alcohol Clin Exp Res* 19:759–762.
- Vasan RS, Beiser A, Seshadri S, Larson MG, Kannel WB, D'Agostino RB, Levey D. 2002. Residual lifetime risk for developing hypertension in middle-aged women and men: The Framingham Heart Study. *J Am Med Assoc* 287:1003–1010.

## SELENIUM

*Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids* (ISBN 0-309-06949-1), Chapter 7, pp. 319–324.

- Allen JC, Keller RP, Archer P, Neville MC. 1991. Studies in human lactation: Milk composition and daily secretion rates of macronutrients in the first year of lactation. *Am J Clin Nutr* 54:69–80.
- Arteel GE, Mostert V, Oubrahim H, Briviba K, Abel J, Sies H. 1998. Protection by selenoprotein P in human plasma against peroxynitrite-mediated oxidation and nitration. *Biol Chem* 379:1201–1205.
- Avissar N, Slemmon JR, Palmer IS, Cohen HJ. 1991. Partial sequence of human plasma glutathione peroxidase and immunologic identification of milk glutathione peroxidase as the plasma enzyme. *J Nutr* 121:1243–1249.
- Beck MA, Levander OA. 1998. Dietary oxidative stress and the potentiation of viral infection. *Annu Rev Nutr* 18:93–116.
- Behne D, Wolters W. 1983. Distribution of selenium and glutathione peroxidase in the rat. *J Nutr* 113:456–461.
- Behne D, Kyriakopoulos A, Kalcklosch M, Weiss-Nowak C, Pfeifer H, Gessner H, Hammel C. 1997. Two new selenoproteins found in the prostatic glandular epithelium and in the spermatid nuclei. *Biomed Environ Sci* 10:340–345.
- Berry MJ, Larsen PR. 1992. The role of selenium in thyroid hormone action. *Endocr Rev* 13:207–219.
- Blot WJ, Li JY, Taylor PR, Guo W, Dawsey SM, Li B. 1995. The Linxian trials: Mortality rates by vitamin-mineral intervention group. *Am J Clin Nutr* 62:1424S–1426S.
- Bösl MR, Takaku K, Oshima M, Nishimura S, Taketo MM. 1997. Early embryonic lethality caused by targeted disruption of the mouse selenocysteine tRNA gene (Trsp). *Proc Natl Acad Sci USA* 94:5531–5534.
- Bratakos MS, Zafiropoulos TF, Siskos PA, Ioannou PV. 1988. Total selenium concentration in tap and bottled drinking water and coastal waters of Greece. *Sci Total Environ* 76:49–54.
- Brätter P, Negretti de Brätter VE. 1996. Influence of high dietary selenium intake on the thyroid hormone level in human serum. *J Trace Elem Med Biol* 10:163–166.
- Brätter P, Negretti de Brätter VE, Jaffe WG, Mendez Castellano H. 1991. Selenium status of children living in seleniferous areas of Venezuela. *J Trace Elem Electrolytes Health Dis* 5:269–270.
- Burk RF, Brown DG, Seely RJ, Scaief CC III. 1972. Influence of dietary and injected selenium on whole-body retention, route of excretion, and tissue retention of  $^{75}\text{SeO}_3^{2-}$  in the rat. *J Nutr* 102:1049–1055.
- Burk RF, Hill KE, Awad JA, Morrow JD, Kato T, Cockell KA, Lyons PR. 1995. Pathogenesis of diquat-induced liver necrosis in selenium-deficient rats. Assessment of the roles of lipid peroxidation and selenoprotein P. *Hepatology* 21:561–569.
- Burk RF, Levander OA. 1999. Selenium. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th edition. Baltimore, MD: Williams & Wilkins. Pp. 265–276.
- Burk RF, Pearson WN, Wood RP II, Viteri F. 1967. Blood selenium levels and in vitro red blood cell uptake of  $^{75}\text{Se}$  in kwashiorkor. *Am J Clin Nutr* 20:723–733.

- Butte NF, Garza C, Smith EO, Nichols BL. 1984. Human milk intake and growth in exclusively breast-fed infants. *J Pediatr* 104:187–195.
- Cantor AH, Tarino JZ. 1982. Comparative effects of inorganic and organic dietary sources of selenium on selenium levels and selenium-dependent glutathione peroxidase activity in blood of young turkeys. *J Nutr* 112:2187–2196.
- Carter RF. 1966. Acute selenium poisoning. *Med J Aust* 1:525–528.
- CDC (Centers for Disease Control and Prevention). 1984. Selenium intoxication—New York. *Morbid Mortal Wkly Rep* 33:157–158.
- Cheng YY, Qian P-C. 1990. The effect of selenium-fortified table salt in the prevention of Keshan disease on a population of 1.05 million. *Biomed Environ Sci* 3:422–428.
- Clark LC, Cantor KP, Allaway WH. 1991. Selenium in forage crops and cancer mortality in U.S. counties. *Arch Environ Health* 46:37–42.
- Clark LC, Combs GF, Turnbull BW, Slate EH, Chalker DK, Chow J, Davis LS, Glover RA, Graham GF, Gross EG, Krongrad A, Lesher JL, Park HK, Sanders BB, Smith CL, Taylor JR. 1996. Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin. A randomized controlled trial. *J Am Med Assoc* 276:1957–1963.
- Cohen HJ, Chovaniec ME, Mistretta D, Baker SS. 1985. Selenium repletion and glutathione peroxidase—Differential effects on plasma and red blood cell enzyme activity. *Am J Clin Nutr* 41:735–747.
- Cumming FJ, Fardy JJ, Woodward DR. 1992. Selenium and human lactation in Australia: Milk and blood selenium levels in lactating women, and selenium intakes of their breast-fed infants. *Acta Paediatr* 81:292–295.
- Debski B, Finley DA, Picciano MF, Lonnerdal B, Milner J. 1989. Selenium content and glutathione peroxidase activity of milk from vegetarian and nonvegetarian women. *J Nutr* 119:215–220.
- Dewey KG, Finley DA, Lonnerdal B. 1984. Breast milk volume and composition during late lactation (7–20 months). *J Pediatr Gastroenterol Nutr* 3:713–720.
- Duffield AJ, Thomson CD, Hill KE, Williams S. 1999. An estimation of selenium requirements for New Zealanders. *Am J Clin Nutr* 70:896–903.
- Ehrenreich A, Forchhammer K, Tormay P, Veprek B, Böck A. 1992. Selenoprotein synthesis in *E. coli*. Purification and characterization of the enzyme catalysing selenium activation. *Eur J Biochem* 206:767–773.
- Ellis L, Picciano MF, Smith AM, Hamosh M, Mehta NR. 1990. The impact of gestational length on human milk selenium concentration and glutathione peroxidase activity. *Pediatr Res* 27:32–35.
- Esaki N, Nakamura T, Tanaka H, Soda K. 1982. Selenocysteine lyase, a novel enzyme that specifically acts on selenocysteine. Mammalian distribution and purification and properties of pig liver enzyme. *J Biol Chem* 257:4386–4391.
- Flohe L. 1988. Glutathione peroxidase. *Basic Life Sci* 49:663–668.
- Fomon SJ, Anderson TA. 1974. *Infant Nutrition*, 2nd edition. Philadelphia: WB Saunders. Pp. 104–111.
- Funk MA, Hamlin L, Picciano MF, Prentice A, Milner JA. 1990. Milk selenium of rural African women: Influence of maternal nutrition, parity, and length of lactation. *Am J Clin Nutr* 51:220–224.
- Ge K, Xue A, Bai J, Wang S. 1983. Keshan disease—An endemic cardiomyopathy in China. *Virchows Arch A Pathol Anat Histopathol* 401:1–15.
- Griffiths NM. 1973. Dietary intake and urinary excretion of selenium in some New Zealand women. *Proc Univ Otago Med Sch* 51:8–9.

- Guimaraes MJ, Peterson D, Vicari A, Cocks BG, Copeland NG, Gilbert DJ, Jenkins NA, Ferrick DA, Kastelein RA, Bazan JF, Zlotnik A. 1996. Identification of a novel selenoD homolog from eukaryotes, bacteria, and archaea: Is there an auto-regulatory mechanism in selenocysteine metabolism? *Proc Natl Acad Sci USA* 93:15086–15091.
- Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. 1993. Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: The DARLING Study. *Am J Clin Nutr* 58:152–161.
- Helzlsouer K, Jacobs R, Morris S. 1985. Acute selenium intoxication in the United States. *Fed Proc* 44:1670.
- Higashi A, Tamari H, Kuroki Y, Matsuda I. 1983. Longitudinal changes in selenium content of breast milk. *Acta Paediatr Scand* 72:433–436.
- Hill KE, Xia Y, Åkesson B, Boeglin ME, Burk RF. 1996. Selenoprotein P concentration in plasma is an index of selenium status in selenium-deficient and selenium-supplemented Chinese subjects. *J Nutr* 126:138–145.
- Hojo Y. 1986. Sequential study on glutathione peroxidase and selenium contents of human milk. *Sci Total Environ* 52:83–91.
- IOM (Institute of Medicine). 1991. *Nutrition During Lactation*. Washington, DC: National Academy Press.
- Ip C. 1998. Lessons from basic research in selenium and cancer prevention. *J Nutr* 128:1845–1854.
- Jensen R, Closson W, Rothenberg R. 1984. Selenium intoxication—New York. *Morbid Mortal Wkly Rep* 33:157–158.
- Jochum F, Fuchs A, Cser A, Menzel H, Lombeck I. 1995. Trace mineral status of full-term infants fed human milk, milk-based formula or partially hydrolysed whey protein formula. *Analyst* 120:905–909.
- Keshan Disease Research Group. 1979. Observations on effect of sodium selenite in prevention of Keshan disease. *Chin Med J* 92:471–476.
- Kumpulainen J, Vuori E, Kuitunen P, Makinen S, Kara R. 1983. Longitudinal study on the dietary selenium intake of exclusively breast-fed infants and their mothers in Finland. *Int J Vitam Nutr Res* 53:420–426.
- Kumpulainen J, Vuori E, Siimes MA. 1984. Effect of maternal dietary selenium intake on selenium levels in breast milk. *Int J Vitam Nutr Res* 54:251–255.
- Kumpulainen J, Salmenpera L, Siimes MA, Koivistoinen P, Perheentupa J. 1985. Selenium status of exclusively breast-fed infants as influenced by maternal organic or inorganic selenium supplementation. *Am J Clin Nutr* 42:829–835.
- Lacourciere GM, Stadtman TC. 1998. The NIFS protein can function as a selenide delivery protein in the biosynthesis of selenophosphate. *J Biol Chem* 273:30921–30926.
- Levander OA. 1976. Selenium in foods. In: *Proceedings of the Symposium on Selenium-Tellurium in the Environment*. South Bend, IN: University of Notre Dame.
- Levander OA. 1989. Upper limit of selenium in infant formulas. *J Nutr* 119:1869–1873.
- Levander OA, Moser PB, Morris VC. 1987. Dietary selenium intake and selenium concentrations of plasma, erythrocytes, and breast milk in pregnant and post-partum lactating and nonlactating women. *Am J Clin Nutr* 46:694–698.
- Lombeck I, Ebert KH, Kasperek K, Feinendegen LE, Bremer HJ. 1984. Selenium intake of infants and young children, healthy children and dietetically treated patients with phenylketonuria. *Eur J Pediatr* 143:99–102.

- Lombeck I, Menzel H, Frosch D. 1987. Acute selenium poisoning of a 2-year old child. *Eur J Pediatr* 146:308–312.
- Longnecker MP, Taylor PR, Levander OA, Howe M, Veillon C, McAdam PA, Patterson KY, Holden JM, Stampfer MJ, Morris JS, Willett WC. 1991. Selenium in diet, blood, and toenails in relation to human health in a seleniferous area. *Am J Clin Nutr* 53:1288–1294.
- Mannan S, Picciano MF. 1987. Influence of maternal selenium status on human milk selenium concentration and glutathione peroxidase activity. *Am J Clin Nutr* 46:95–100.
- Matoba R, Kimura H, Uchima E, Abe T, Yamada T, Mitsukuni Y, Shikata I. 1986. An autopsy case of acute selenium (selenious acid) poisoning and selenium levels in human tissues. *Forensic Sci Int* 31:87–92.
- May JM, Cobb CE, Mendiratta S, Hill KE, Burk RF. 1998. Reduction of the ascorbyl free radical to ascorbate by thioredoxin reductase. *J Biol Chem* 273:23039–23045.
- McConnell KP, Portman OW. 1952. Excretion of dimethyl selenide by the rat. *J Biol Chem* 195:277–282.
- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance Data, Vital and Health Statistics of the National Center for Health Statistics. Number 174. Hyattsville, MD: National Center for Health Statistics.
- Mozier NM, McConnell KP, Hoffman JL. 1988. S-Adenosyl-L-methionine:thioether S-methyltransferase, a new enzyme in sulfur and selenium metabolism. *J Biol Chem* 263:4527–4531.
- Nantel AJ, Brown M, Dery P, Lefebvre M. 1985. Acute poisoning by selenious acid. *Vet Hum Toxicol* 27:531–533.
- NRC (National Research Council). 1976. *Selenium*. Washington, DC: National Academy of Sciences.
- NRC (National Research Council). 1980a. *Drinking Water and Health*, Volume 3. Washington, DC: National Academy Press.
- NRC (National Research Council). 1980b. *Recommended Dietary Allowances*, 9th edition. Washington, DC: National Academy Press.
- Pennington JA, Schoen SA. 1996. Total diet study: Estimated dietary intakes of nutritional elements, 1982–1991. *Int J Vitam Nutr Res* 66:350–362.
- Pentel P, Fletcher D, Jentzen J. 1985. Fatal acute selenium toxicity. *J Forensic Sci* 30:556–562.
- Robberecht H, Van Grieken R, Van Sprundel M, Vanden Berghe D, Deelstra H. 1983. Selenium in environmental and drinking waters of Belgium. *Sci Total Environ* 26:163–172.
- Ruta DA, Haider S. 1989. Attempted murder by selenium poisoning. *Br Med J* 299:316–317.
- Saito Y, Hayashi T, Tanaka A, Watanabe Y, Suzuki M, Saito E, Takahashi K. 1999. Selenoprotein P in human plasma as an extracellular phospholipid hydroperoxide glutathione peroxidase. Isolation and enzymatic characterization of human selenoprotein P. *J Biol Chem* 274:2866–2871.
- Salbe AD, Levander OA. 1990. Effect of various dietary factors on the deposition of selenium in the hair and nails of rats. *J Nutr* 120:200–206.
- Schroeder HA, Frost DV, Balassa JJ. 1970. Essential trace metals in man: Selenium. *J Chronic Dis* 23:227–243.
- Shearer RR, Hadjimarkos DM. 1975. Geographic distribution of selenium in human milk. *Arch Environ Hlth* 30:230–233.

- Smith AM, Picciano MF, Milner JA. 1982. Selenium intakes and status of human milk and formula fed infants. *Am J Clin Nutr* 35:521–526.
- Stadtman TC. 1991. Biosynthesis and function of selenocysteine-containing enzymes. *J Biol Chem* 266:16257–16260.
- Sun QA, Wu Y, Zappacosta F, Jeang KT, Lee BJ, Hatfield DL, Gladyshev VN. 1999. Redox regulation of cell signaling by selenocysteine in mammalian thioredoxin reductases. *J Biol Chem* 274:24522–24530.
- Sunde RA. 1994. Intracellular glutathione peroxidases—Structure, regulation, and function. In: Burk RF, ed. *Selenium in Biology and Human Health*. New York: Springer Verlag. Pp. 45–78.
- Swanson CA, Reamer DC, Veillon C, King JC, Levander OA. 1983. Quantitative and qualitative aspects of selenium utilization in pregnant and nonpregnant women: An application of stable isotope methodology. *Am J Clin Nutr* 38:169–180.
- Swanson CA, Patterson BH, Levander OA, Veillon C, Taylor PR, Helzlsouer K, McAdam PA, Zech LA. 1991. Human [<sup>74</sup>Se]selenomethionine metabolism: A kinetic model. *Am J Clin Nutr* 54:917–926.
- Thompson JN, Erdody P, Smith DC. 1975. Selenium content of food consumed by Canadians. *J Nutr* 105:274–277.
- Thomson CD, Robinson MF. 1980. Selenium in human health and disease with emphasis on those aspects peculiar to New Zealand. *Am J Clin Nutr* 33:303–323.
- Thomson CD, Robinson MF. 1986. Urinary and fecal excretions and absorption of a large supplement of selenium: Superiority of selenate over selenite. *Am J Clin Nutr* 44:659–663.
- Valentine JL, Kang HK, Spivey GH. 1978. Selenium levels in human blood, urine, and hair in response to exposure via drinking water. *Environ Res* 17:347–355.
- Vanderpas JB, Dumont JE, Contempre B, Diplock AT. 1992. Iodine and selenium deficiency in northern Zaire. *Am J Clin Nutr* 56:957–958.
- Van Vleet JF. 1980. Current knowledge of selenium-vitamin E deficiency in domestic animals. *J Am Vet Med Assoc* 176:321–325.
- Varo P, Alftan G, Huttunen JK, Aro A. 1994. Nationwide selenium supplementation in Finland—Effects on diet, blood and tissue levels, and health. In: Burk RF, ed. *Selenium in Biology and Human Health*. New York: Springer Verlag. Pp. 197–218.
- Veres Z, Tsai L, Scholz TD, Politino M, Balaban RS, Stadtman TC. 1992. Synthesis of 5-methylaminomethyl-2-selenouridine in tRNAs: <sup>31</sup>P NMR studies show the labile selenium donor synthesized by the selD gene product contains selenium bonded to phosphorus. *Proc Natl Acad Sci USA* 89:2975–2979.
- Waschulewski IH, Sunde RA. 1988. Effect of dietary methionine on tissue selenium and glutathione peroxidase (EC 1.11.1.9) activity in rats given selenomethionine. *Br J Nutr* 60:57–68.
- Welsh SO, Holden JM, Wolf WR, Levander OA. 1981. Selenium in self-selected diets of Maryland residents. *J Am Diet Assoc* 79:277–285.
- WHO (World Health Organization). 1987. *Selenium. A Report of the International Programme on Chemical Safety*. Environmental Health Criteria 58. Geneva: WHO.
- Wright PL, Bell MC. 1963. Selenium and vitamin E influence upon the in vitro uptake of Se<sup>75</sup> by ovine blood cells. *Proc Soc Exp Biol Med* 114:379–382.
- Xia YM, Hill KE, Burk RF. 1989. Biochemical studies of a selenium-deficient population in China: Measurement of selenium, glutathione peroxidase, and other oxidant defense indices in blood. *J Nutr* 119:1318–1326.

- Yang G-Q, Xia YM. 1995. Studies on human dietary requirements and safe range of dietary intakes of selenium in China and their application in the prevention of related endemic diseases. *Biomed Environ Sci* 8:187–201.
- Yang G-Q, Zhou R-H. 1994. Further observations on the human maximum safe dietary selenium intake in a seleniferous area of China. *J Trace Elem Electrolytes Hlth Dis* 8:159–165.
- Yang G-Q, Wang S-Z, Zhou R-H, Sun S-Z. 1983. Endemic selenium intoxication of humans in China. *Am J Clin Nutr* 37:872–881.
- Yang G-Q, Zhu L-Z, Liu S-J, Gu L-Z, Qian P-C, Huang J-H, Lu M-D. 1987. Human selenium requirements in China. In: Combs GF Jr, Levander OA, Spallholz JE, Oldfield JE, eds. *Selenium in Biology and Medicine*. New York: Avi. Pp. 589–607.
- Yang G-Q, Ge K, Chen J, Chen X. 1988. Selenium-related endemic diseases and the daily selenium requirement of humans. *World Rev Nutr Diet* 55:98–152.
- Yang G-Q, Yin S, Zhou R-H, Gu L, Yan B, Liu Y, Liu Y. 1989a. Studies of safe maximal daily dietary Se-intake in a seleniferous area in China. II. Relation between Se-intake and the manifestation of clinical signs and certain biochemical alterations in blood and urine. *J Trace Elem Electrolytes Hlth Dis* 3:123–130.
- Yang G-Q, Zhou R, Yin S, Gu L, Yan B, Liu Y, Liu Y, Li X. 1989b. Studies of safe maximal daily dietary selenium intake in a seleniferous area in China. I. Selenium intake and tissue selenium levels of the inhabitants. *J Trace Elem Electrolytes Hlth Dis* 3:77–87.
- Yang JG, Hill KE, Burk RF. 1989. Dietary selenium intake controls rat plasma selenoprotein P concentration. *J Nutr* 119:1010–1012.
- Yoshizawa K, Willett WC, Morris SJ, Stampfer MJ, Spiegelman D, Rimm EB, Giovannucci E. 1999. Study of prediagnostic selenium level in toenails and the risk of advanced prostate cancer. *J Natl Cancer Inst* 90:1219–1224.

Ibid., Chapter 9, 399–400.

- AIN (American Institute of Nutrition). 1990. Nomenclature policy: Generic descriptors and trivial names for vitamins and related compounds. *J Nutr* 120:12–19.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the third National Health and Nutrition Examination Survey: Underreporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- Horwitt MK. 1976. Vitamin E: A reexamination. *Am J Clin Nutr* 29:569–578.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances be Revised?* Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1997. *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. Washington, DC: National Academy Press.
- IOM (Institute of Medicine). 1998. *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B<sub>6</sub>, Folate, Vitamin B<sub>12</sub>, Pantothenic Acid, Biotin, and Choline*. Washington, DC: National Academy Press.
- IUPAC-IUB Commission on Biochemical Nomenclature. 1974. Nomenclature of tocopherols and related compounds. Recommendations 1973. *Eur J Biochem* 46:217–219.

- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1980. *Drinking Water and Health*, Volume 3. Washington, DC: National Academy Press.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Swanson CA, Patterson BH, Levander OA, Veillon C, Taylor PR, Helzlsouer K, McAdam PA, Zech LA. 1991. Human [ $^{74}\text{Se}$ ]selenomethionine metabolism: A kinetic model. *Am J Clin Nutr* 54:917–926.
- Thomson CD, Robinson MF. 1986. Urinary and fecal excretions and absorption of a large supplement of selenium: Superiority of selenate over selenite. *Am J Clin Nutr* 44:659–663.
- USDA (U.S. Department of Agriculture). 1999. USDA Nutrient Database for Standard Reference, Release, [Online]. Available: <http://www.nal.usda.gov/fnic/foodcomp>.
- Weiser H, Vecchi M, Schlachter M. 1986. Stereoisomers of alpha-tocopherol acetate. IV. USP units and alpha-tocopherol equivalents of all-rac-, 2-ambo- and RRR-alpha-tocopherol evaluated by simultaneous determination of resorption-gestation, myopath and liver storage capacity in rats. *Int J Vitam Nutr Res* 56:45–56.
- Williams AW, Erdman JW Jr. 1999. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*. Baltimore, MD: Williams and Wilkins. P. 181.

## SODIUM AND CHLORIDE

*Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate* (ISBN 0-309-09158-6), Chapter 6, pp. 397–423.

- Alam S, Johnson AG. 1999. A meta-analysis of randomized controlled trials (RCT) among healthy normotensive and essential hypertensive elderly patients to determine the effect of high salt (NaCl) diet of blood pressure. *J Hum Hypertens* 13:367–374.
- Alcantara PF, Hanson LE, Smith JD. 1980. Sodium requirements, balance and tissue composition of growing pigs. *J Animal Sci* 50:1092–1101.
- Al-Dahhan J, Haycock GB, Chantler C, Stimmller L. 1984. Sodium homeostasis in term and preterm neonates. III. Effect of salt supplementation. *Arch Dis Child* 59:945–950.
- Alderman MH. 2002. Salt, blood pressure and health: A cautionary tale. *Int J Epidemiol* 31:311–315.
- Alderman MH, Laragh JH. 1996. Low urinary sodium and myocardial infarction. *Hypertension* 27:156–157.
- Alderman MH, Madhavan S, Ooi WL, Cohen H, Sealey JE, Laragh JH. 1991. Association of the renin-sodium profile with the risk of myocardial infarction in patients with hypertension. *N Engl J Med* 324:1098–1104.
- Alderman MH, Madhavan S, Cohen H, Sealey JE, Laragh JH. 1995. Low urinary sodium is associated with greater risk of myocardial infarction among treated hypertensive men. *Hypertension* 25:1144–1152.
- Alderman M, Sealey J, Cohen H, Madahavan S, Laragh J. 1997. Urinary sodium excretion and myocardial infarction in hypertensive patients: A prospective cohort study. *Am J Clin Nutr* 65:682S–686S.
- Alderman MH, Cohen H, Madhavan S. 1998a. Dietary sodium intake and mortality: NHANES. *Lancet* 352:987–988.
- Alderman MH, Cohen H, Madhavan S. 1998b. Dietary sodium intake and mortality: The National Health and Nutrition Examination Survey (NHANES I). *Lancet* 351:781–785.
- Allan JR, Wilson CG. 1971. Influence of acclimatization on sweat sodium concentration. *J Appl Physiol* 30:708–712.
- Allender PS, Cutler JA, Follmann D, Cappuccio FP, Pryer J, Elliott P. 1996. Dietary calcium and blood pressure: A meta-analysis of randomized trials. *Ann Intern Med* 124:825–831.
- Allikmets K, Parik T, Teesalu R. 1996. Association between plasma renin activity and metabolic cardiovascular risk factors in essential hypertension. *J Intern Med* 239:49–55.
- Allsopp AJ, Sutherland R, Wood P, Wootton SA. 1998. The effect of sodium balance on sweat sodium secretion and plasma aldosterone concentration. *Eur J Applied Physiol* 78:516–521.
- Altschul AM, Ayers WR, Grommet JK, Slotkoff L. 1981. Salt sensitivity in experimental animals and man. *Int J Obes* 5:27S–38S.
- Ames RP. 2001. The effect of sodium supplementation on glucose tolerance and insulin concentrations in patients with hypertension and diabetes mellitus. *Am J Hypertens* 14:I653–I659.
- Anderson G, Springer J, Randall P, Streeten DH, Blakeman N. 1980. Effect of age on diagnostic usefulness of stimulated plasma renin activity and saralasin test in detection of renovascular hypertension. *Lancet* 2:821–824.

- Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin PH, Karanja N. 1997. A clinical trial of the effects of dietary patterns on blood pressure. *N Engl J Med* 336:1117–1124.
- Appel LJ, Espeland MA, Easter L, Wilson AC, Folmar S, Lacy CR. 2001. Effects of reduced sodium intake on hypertension control in older individuals. *Arch Intern Med* 161:685–693.
- Aronow WS, Ahn C, Kronzon I, Gutstein H. 1997. Association of plasma renin activity and echocardiographic left ventricular hypertrophy with frequency of new coronary events and new atherothrombotic brain infarction in older persons with systemic hypertension. *Am J Cardiol* 79:1543–1545.
- Ascherio A, Rimm EB, Giovannucci EL, Colditz GA, Rosner B, Willett WC, Sacks F, Stampfer MJ. 1992. A prospective study of nutritional factors and hypertension among US men. *Circulation* 86:1475–1484.
- Bao W, Threepoint SA, Srinivasan SR, Berenson GS. 1995. Essential hypertension predicted by tracking of elevated blood pressure from childhood to adulthood: The Bogalusa Heart Study. *Am J Hypertens* 8:657–665.
- Barden AE, Vandongen R, Beilin LJ, Margetts B, Rogers P. 1986. Potassium supplementation does not lower blood pressure in normotensive women. *J Hypertens* 4:339–343.
- Barden A, Beilin LJ, Vandongen R, Pudsey IB. 1991. A double-blind placebo-controlled trial of the effects of short-term potassium supplementation on blood pressure and atrial natriuretic peptide in normotensive women. *Am J Hypertens* 4:206–213.
- Barr SB, Costill DL, Fink WJ. 1991. Fluid replacement during prolonged exercise: Effects of water, saline, or no fluid. *Med Sci Sports Exerc* 23:811–817.
- Bartter FC, Pronove P, Gill JR, MacCardle RC. 1962. Hyperplasia of the juxtaglomerular complex with hyperaldosteronism and hypokalemic alkalosis. A new syndrome. *Am J Med* 33:811–828.
- Bay WH, Ferris TF. 1979. Factors controlling plasma renin and aldosterone during pregnancy. *Hypertension* 1:410–415.
- Beil AH, Schmieder RE, Messerli FH. 1994. Salt intake, blood pressure, and cardiovascular structure. *Cardiovasc Drugs Ther* 8:425–432.
- Benetos A, Yang-Yan X, Cuche JL, Hannaert P, Safar M. 1992. Arterial effects of salt restriction in hypertensive patients. A 9-week, randomized, double-blind, crossover study. *J Hypertens* 10:355–360.
- Bernstein HM, Cooper PA, Turner MJ. 1990. Dynamic skinfold thickness measurement in infants fed breast milk, low or high sodium formula. *S Afr Med J* 78:644–646.
- Bernstein L, Henderson BE. 1985. Studies comparing population differences in sodium intake and gastric cancer rates. *J Cancer Res Clin Oncol* 110:184.
- Bikkina M, Levy D, Evans JC, Larson MG, Benjamin EJ, Wolf PA, Castelli WP. 1994. Left ventricular mass and risk of stroke in an elderly cohort: The Framingham Heart Study. *J Am Med Assoc* 272:33–36.
- Boeing H, Jedrychowski W, Wahrendorf J, Popiela T, Tobiasz-Adamczyk B, Kulig A. 1991. Dietary risk factors in intestinal and diffuse types of stomach cancer: A multicenter case-control study in Poland. *Cancer Causes Control* 2:227–233.
- Boero R, Pignataro A, Bancale E, Campo A, Morelli E, Nigra M, Novarese M, Possamai D, Prodi E, Quarello F. 2000. Metabolic effects of changes in dietary sodium intake in patients with essential hypertension. *Minerva Urol Nefrol* 52:13–16.

- Bomsztyk K, Calalb MB. 1988. Bicarbonate absorption stimulates active calcium absorption in the rat proximal tubule. *J Clin Invest* 81:1455–1461.
- Bower TR, Pringle KC, Soper RT. 1988. Sodium deficit causing decreased weight gain and metabolic acidosis in infants with ileostomy. *J Pediatr Sur* 23:567–572.
- Brancati FL, Appel LJ, Seidler AJ, Whelton PK. 1996. Effect of potassium supplementation on blood pressure in African Americans on a low-potassium diet: A randomized, double-blind, placebo-controlled trial. *Arch Intern Med* 156: 61–67.
- Breslau NA, McGuire JL, Zerwekh JE, Pak CYC. 1982. The role of dietary sodium on renal excretion and intestinal absorption of calcium and on vitamin D metabolism. *J Clin Endocrinol Metab* 55:369–373.
- Britton J, Pavord I, Richards K, Knox A, Wisniewski A, Weiss S, Tattersfield A. 1994. Dietary sodium intake and the risk of airway hyperreactivity in a random adult population. *Thorax* 49:875–880.
- Brouns F. 1991. Heat-sweat-dehydration-rehydration: A praxis oriented approach. *J Sports Sci* 9:143–152.
- Brown JE, Toma RB. 1986. Taste changes during pregnancy. *Am J Clin Nutr* 43: 414–418.
- Brown MA, Gallery EDM. 1994. Volume homeostasis in normal pregnancy and pre-eclampsia: Physiology and clinical implications. *Clin Obstet Gynaecol (Bailleres)* 8:287–310.
- Brown MA, Gallery EDM, Ross MR, Esber RP. 1988. Sodium excretion in normal and hypertensive pregnancy: A prospective study. *Am J Obstet Gynecol* 159:297–307.
- Brunette MG, Mailloux J, Lajeunesse D. 1992. Calcium transport through the luminal membrane of the distal tubule. I. Interrelationship with sodium. *Kidney Int* 41:281–288.
- Brunner E, White I, Thorogood M, Bristow A, Curle D, Marmot M. 1997. Can dietary interventions change diet and cardiovascular risk factors? A meta-analysis of randomized controlled trials. *Am J Public Health* 87:1415–1422.
- Bruun NE, Skott P, Nielsen MD, Rasmussen S, Schutten HJ, Leth A, Pedersen EB, Giese J. 1990. Normal renal tubular response to changes of sodium intake in hypertensive man. *J Hypertens* 8:219–227.
- Bucher HC, Cook RJ, Guyatt GH, Lang JD, Cook DJ, Hatala R, Hunt D. 1996. Effects of dietary calcium supplementation on blood pressure. A meta-analysis of randomized clinical trials. *J Am Med Assoc* 275:1016–1022.
- Buckley MG, Markandu ND, Sagnella GA, MacGregor GA. 1994. Brain and atrial natriuretic peptides: A dual peptide system of potential importance in sodium balance and blood pressure regulation in patients with essential hypertension. *J Hypertens* 12:809–813.
- Burney PG, Britton JR, Chinn S, Tattersfield AE, Platt HS, Papacosta AO, Kelson MC. 1986. Response to inhaled histamine and 24 hour sodium excretion. *Br Med J* 292:1483–1486.
- Burnier M, Rutschmann B, Nussberger J, Versaggi J, Shahinfar S, Waeber B, Brunner HR. 1993. Salt-dependent renal effects of an angiotensin II antagonist in healthy subjects. *Hypertension* 22:339–347.
- Burt VL, Whelton P, Roccella EJ, Brown C, Cutler JA, Higgins M, Horan MJ, Labarthe D. 1995. Prevalence of hypertension in the United States adult population. *Hypertension* 25:305–313.
- Burtis WJ, Gay L, Insogna KL, Ellison A, Broadus AE. 1994. Dietary hypercalcemia in patients with calcium oxalate kidney stones. *Am J Clin Nutr* 60:424–429.

- Bushinsky DA. 1998. Acid-base imbalance and the skeleton. In: Burckhardt PB, Dawson-Hughes B, Heaney RP, eds. *Nutritional Aspects of Osteoporosis*. New York: Springer-Verlag. Pp. 208–217.
- Calabrese EJ, Tuthill RW. 1985. The Massachusetts Blood Pressure Study, Part 3. Experimental reduction of sodium in drinking water: Effects on blood pressure. *Toxicol Ind Health* 1:19–34.
- Cappuccio FP, Markandu ND, Sagnella GA, MacGregor GA. 1985. Sodium restriction lowers high blood pressure through a decreased response of the renin system—Direct evidence using saralasin. *J Hypertens* 3:243–247.
- Cappuccio FP, Markandu ND, Beynon GW, Shore AC, MacGregor GA. 1986. Effect of increasing calcium intake on urinary sodium excretion in normotensive subjects. *Clin Sci* 71:453–456.
- Cappuccio FP, Markandu ND, Carney C, Sagnella GA, MacGregor GA. 1997. Double-blind randomized trial of modest salt restriction in older people. *Lancet* 350:850–854.
- Carey OJ, Locke C, Cookson JB. 1993. Effect of alterations of dietary sodium on the severity of asthma in men. *Thorax* 48:714–718.
- Carmichael S, Abrams B, Selvin S. 1997. The pattern of maternal weight gain in women with good pregnancy outcomes. *Am J Public Health* 87:1984–1988.
- Carter EP, Barrett AD, Heeley AF, Kuzemko JA. 1984. Improved sweat test method for the diagnosis of cystic fibrosis. *Arch Dis Child* 59:919–922.
- Casale PN, Devereux RB, Milner M, Zullo G, Harshfield GA, Pickering TG, Laragh JH. 1986. Value of echocardiographic measurement of left ventricular mass in predicting cardiovascular morbid events in hypertensive men. *Ann Intern Med* 105:173–178.
- Castenmiller JJM, Mensink RP, van der Heijden L, Kouwenhoven T, Hautvast J, de Leeuw PW, Schaafsma G. 1985. The effect of dietary sodium on urinary calcium and potassium excretion in normotensive men with different calcium intakes. *Am J Clin Nutr* 41:52–60.
- CDC (Centers for Disease Control and Prevention). 1979. Infant metabolic alkalosis and soy-based formula. *Morb Mortal Wkly Rep* 28:358–359.
- CDC. 1980. Follow-up on formula-associated illness in children. *Morb Mortal Wkly Rep* 29:124–129.
- CDC. 2002. *Iodine Level, United States, 2000*. Online. Available at <http://www.cdc.gov/nchs/products/pubs/pubd/hestats/iodine.htm>. Accessed February 2, 2004.
- CFSAN (Center for Food Safety and Applied Nutrition). 2001. *Fish and Fisheries Products Hazards and Controls Guidance*, 3rd ed. Rockville, MD: Food and Drug Administration.
- Chan ELP, Ho CS, MacDonald D, Ho SC, Chan TYK, Swaminathan R. 1992. Interrelationships between urinary sodium, calcium, hydroxyproline and serum PTH in healthy subjects. *Acta Endocrinol* 127:242–245.
- Chance GW, Radde IC, Willis DM, Roy RN, Park E, Ackerman I. 1977. Postnatal growth of infants of <1.3 kg birth weight: Effects of metabolic acidosis, of caloric intake, and of calcium, sodium, and phosphate supplementation. *J Pediatr* 91:787–793.
- Chen J, Delaney KH, Kwieciens JM, Lee RM. 1997. The effects of dietary sodium on hypertension and stroke development in female stroke-prone spontaneously hypertensive rats. *Exp Mol Pathol* 64:173–183.
- Chesley LC. 1978. *Hypertensive Disorders in Pregnancy*. New York: Appleton-Century-Crofts.
- Chesley LC, Velenti C, Rein H. 1958. Excretion of water loads by nonpregnant and

- pregnant normal, hypertensive, and pre-eclamptic women. *Metabolism* 7:575–588.
- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ, National High Blood Pressure Education Program Coordinating Committee. 2003. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 42:1206–1252.
- Churchill D, Beevers DG. 1999. *Hypertension in Pregnancy*. London: British Medical Association.
- Clapp JF. 1991. The changing thermal response to endurance exercise during pregnancy. *Am J Obstet Gynecol* 165:1684–1689.
- Cobiac L, Nestel PJ, Wing LMH, Howe PRC. 1992. A low-sodium diet supplemented with fish oil lowers blood pressure in the elderly. *J Hypertens* 10:87–92.
- Coggon D, Barker DJP, Cole RB, Nelson M. 1989. Stomach cancer and food storage. *J Natl Cancer Inst* 81:1178–1182.
- Cohen AJ, Roe FJC. 1997. Evaluation of the aetiological role of dietary salt exposure in gastric and other cancers in humans. *Food Chem Toxicol* 35:271–293.
- Cohen JD, Grandits G, Cutler J, Neaton JD, Kuller LH, Stamler J. 1999. Dietary sodium intake and mortality: MRFIT follow up study results. *Circulation* 100: 2758.
- Collins R, Yusuf S, Peto R. 1985. Overview of randomized trials of diuretics in pregnancy. *Br Med J* 290:17–23.
- Conn JW. 1949. The mechanism of acclimatization to heat. *Adv Intern Med* 3:373–393.
- Consolazio CF, Matoush LO, Nelson RG, Harding RS, Canham JE. 1963. Excretion of sodium, potassium, magnesium and iron in human sweat and the relation of each to balance and requirements. *J Nutr* 79:407–415.
- Cook NR, Cutler JA, Hennekens CH. 1995a. An unexpected result from sodium—Causal or casual? *Hypertension* 25:1153–1154.
- Cook NR, Cohen J, Hebert PR, Taylor JO, Hennekens CH. 1995b. Implications of small reductions in diastolic blood pressure for primary prevention. *Arch Intern Med* 155:701–709.
- Cook NR, Kumanyika SK, Cutler JA. 1998. Effect of change in sodium excretion on change in blood pressure corrected for measurement error: The Trials of Hypertension Prevention, Phase I. *Am J Epidemiol* 148:431–444.
- Cooper R, Liu K, Trevisan M, Miller W, Stamler J. 1983. Urinary sodium excretion and blood pressure in children: Absence of a reproducible association. *Hypertension* 5:135–139.
- Cooper R, Van Horn L, Liu K, Trevisan M, Nanas S, Ueshima H, Larbi E, Yu CS, Sempos C, LeGrady D, Stamler J. 1984. A randomized trial on the effect of decreased dietary sodium intake on blood pressure in adolescents. *J Hypertens* 2:361–366.
- Correa P, Haenszel W, Cuello C, Tannenbaum S, Archer M. 1975. A model for gastric cancer epidemiology. *Lancet* 2:58–60.
- Coyle P. 1988. High NaCl predisposes Dahl rats to cerebral infarction after middle cerebral artery occlusion. *Hypertension* 12:96–101.
- Craddick SR, Elmer PJ, Obarzanek E, Vollmer WM, Svetkey LP, Swain MC. 2003. The DASH diet and blood pressure. *Curr Atheroscler Rep* 5:484–491.
- Crane MG, Harris JJ. 1976. Effect of aging on renin activity and aldosterone excretion. *J Lab Clin Med* 87:947–959.
- Crocco SC. 1982. The role of sodium in food processing. *J Am Diet Assoc* 80:36–39.

- Cugini P, Murano G, Lucia P, Letizia C, Scavo D, Halberg F, Schramm H. 1987. The gerontologic decline of the renin-aldosterone system: A chronobiological approach extended to essential hypertension. *J Gerontol* 42:461–465.
- Curhan GC, Willett WC, Speizer FE, Spiegelman D, Stampfer MJ. 1997. Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk of kidney stones in women. *Ann Intern Med* 126:497–504.
- Cutler JA, Brittain E. 1990. Calcium and blood pressure. An epidemiologic perspective. *Am J Hypertens* 3:137S–146S.
- Cutler JA, Follmann D, Elliott P, Suh I. 1991. An overview of randomized trials of sodium reduction and blood pressure. *Hypertension* 17:I34S–I35S.
- Cutler JA, Follmann D, Allender PS. 1997. Randomized trials of sodium reduction: An overview. *Am J Clin Nutr* 65:643S–651S.
- Dahl LK. 1958. Salt intake and salt need. *N Engl J Med* 258:1152–1156.
- Dahl LK. 1960. Possible role of salt intake in the development of essential hypertension. In: Block KD, Cottier PT, eds. *Essential Hypertension, an International Symposium*. Berlin: Springer-Verlag. Pp. 53–65.
- Dahl LK. 1968. Salt in processed baby foods. *Am J Clin Nutr* 21:787–792.
- Dahl LK, Stall BG, Cotzias GC. 1955. Metabolic effects of marked sodium restriction in hypertensive patients: Skin electrolyte losses. *J Clin Invest* 34:462–470.
- Daniels SD, Meyer RA, Loggie JM. 1990 Determinants of cardiac involvement in children and adolescents with essential hypertension. *Circulation* 82:1243–1248.
- Dawson-Hughes B, Fowler SE, Dalsky G, Gallagher C. 1996. Sodium excretion influences calcium homeostasis in elderly men and women. *J Nutr* 126:2107–2112.
- de Chatel R, Weidmann P, Flammer J, Ziegler WH, Beretta-Piccoli C, Vetter W, Reubi FC. 1977. Sodium, renin, aldosterone, catecholamines, and blood pressure in diabetes mellitus. *Kidney Int* 12:412–421.
- Dekkers JC, Snieder H, Van Den Oord EJ, Treiber FA. 2002. Moderators of blood pressure development from childhood to adulthood: A 10-year longitudinal study. *J Pediatr* 141:770–779.
- Del Rio A, Rodriguez-Villamil JL. 1993. Metabolic effects of strict salt restriction in essential hypertensive patients. *J Intern Med* 233:409–414.
- de Simone G, Devereux RB, Roman MJ, Alderman MH, Laragh JH. 1994. Relation of obesity and gender to left ventricular hypertrophy in normotensive and hypertensive adults. *Hypertension* 23:600–606.
- Devine A, Criddle AR, Dick IM, Kerr DA, Prince RL. 1995. A longitudinal study of the effect of sodium and calcium intakes on regional bone density in postmenopausal women. *Am J Clin Nutr* 62:740–745.
- de Wardener HE. 1999. Salt reduction and cardiovascular risk: The anatomy of a myth. *J Hum Hypertens* 13:1–4.
- de Wardener HE, MacGregor GA. 1980. Dahl's hypothesis that a saluretic substance may be responsible for a sustained rise in arterial pressure: Its possible role in essential hypertension. *Kidney Int* 18:1–9.
- Dewey KG, Lonnerdal B. 1983. Milk and nutrient intake of breast-fed infants from 1 to 6 months: Relation to growth and fatness. *J Pediatr Gastroenterol Nutr* 2:497–506.
- Dodson PM, Beevers M, Hallworth R, Webberley MJ, Fletcher RF, Taylor KG. 1989. Sodium restriction and blood pressure in hypertensive type II diabetics: Randomized blind controlled and crossover studies of moderate sodium restriction and sodium supplementation. *Br Med J* 298:227–230.
- Dole VP, Dahl LK, Cotzias GC, Eder HA, Krebs ME. 1950. Dietary treatment of

- hypertension: Clinical and metabolic studies of patients on the rice-fruit diet. *J Clin Invest* 39:1189–1206.
- du Cailar G, Ribstein J, Grolleau R, Mimran A. 1989. Influence of sodium intake on left ventricular structure in untreated essential hypertensives. *J Hypertens* 7:S258–S289.
- du Cailar GD, Ribstein J, Daures JP, Mimran A. 1992. Sodium and left ventricular mass in untreated hypertensive and normotensive subjects. *Heart Circ Physiol* 32:H177–H181.
- du Cailar G, Ribstein J, Mimran A. 2002. Dietary sodium and target organ damage in essential hypertension. *Am J Hypertens* 15:222–229.
- Durr JA, Lindheimer MD. 1999. Control of volume and body tonicity. In: Lindheimer, MD, Roberts JM, Cunningham FG, eds. *Chesley's Hypertensive Disorders in Pregnancy*, 2nd ed. Stamford, CT: Appleton & Lange. Pp. 103–166.
- Duvekot JJ, Cheriex EC, Peters FAA, Menheere PP, Peeters LH. 1993. Early pregnancy changes in hemodynamics and volume homeostasis are consecutive adjustments triggered by a primary fall in systemic vasculature tone. *Am J Obstet Gynecol* 169:1382–1392.
- Egan BM, Stepniakowski KT. 1997. Adverse effects of short-term, very-low-salt diets in subjects with risk-factor clustering. *Am J Clin Nutr* 65:671S–677S.
- Egan BM, Weder AB, Petrin J, Hoffman RG. 1991. Neurohormonal and metabolic effects of short-term dietary NaCl restriction in men. *Am J Hypertens* 4:416–421.
- Egan BM, Stepniakowski K, Goodfriend TL. 1994. Renin and aldosterone are higher and the hyperinsulinemic effect of salt restriction greater in subjects with risk factors clustering. *Am J Hypertens* 7:886–893.
- Elliott P. 1991. Observational studies of salt and blood pressure. *Hypertension* 17:I3S–I8S.
- Elliott P, Stamler J, Nichols R, Dyer AR, Stamler R, Kesteloot H, Marmot M. 1996. Intersalt revisited: Further analyses of 24 hour sodium excretion and blood pressure within and across populations. *Br Med J* 312:1249–1253.
- Ellison RC, Capper AL, Stephenson WP, Goldberg RJ, Hosmer DW Jr, Humphrey KF, Ockene JK, Gamble WJ, Witschi JC, Stare FJ. 1989. Effects on blood pressure of a decrease in sodium use in institutional food preparation: The Exeter-Andover Project. *J Clin Epidemiol* 42:201–208.
- Epstein M, Hollenberg NK. 1976. Age as a determinant of renal sodium conservation in normal man. *J Lab Clin Med* 87:411–417.
- Eurogast Study Group. 1993. An international association between *Helicobacter pylori* infection and gastric cancer. *Lancet* 341:1359–1362.
- Evans CEL, Chughtai AY, Blumsohn A, Giles M, Eastell R. 1997. The effect of dietary sodium on calcium metabolism in premenopausal and postmenopausal women. *Eur J Clin Nutr* 51:393–399.
- Fagerberg B, Berglund A, Andersson OK, Berglund G, Wikstrand J. 1991. Cardiovascular effects of weight reduction versus antihypertensive drug treatment: A comparative, randomized, 1-year study of obese men with mild hypertension. *J Hypertens* 9:431–439.
- FDA (Food and Drug Administration). 1985. Nutrient requirements for infant formula. *Fed Regis* 50:45106–45108.
- Feldman RD, Schmidt ND. 1999. Moderate dietary salt restriction increases vascular and systemic insulin resistance. *Am J Hypertens* 12:643–647.
- Feldman RD, Logan AG, Schmidt ND. 1996. Dietary salt restriction increases vascular insulin resistance. *Clin Pharmacol Ther* 60:444–451.
- Ferrara LA, de Simone G, Pasanisi F, Mancini M, Mancini M. 1984. Left ventricular

- mass reduction during salt depletion in arterial hypertension. *Hypertension* 6:755–759.
- Ferri C, Bellini C, Carluomagno A, Desideri G, Santucci A. 1996. Active kallikrein response to changes in sodium-chloride intake in essential hypertensive patients. *J Am Soc Nephrol* 7:443–453.
- Fine BP, Ty A, Lestrage N, Levine OR. 1987. Sodium deprivation growth failure in the rat: Alterations in tissue composition and fluid spaces. *J Nutr* 117:1623–1628.
- Fliser D, Nowack R, Allendorf-Ostwald N, Kohl B, Hubinger A, Ritz E. 1993. Serum lipid changes on low salt diet. Effects of  $\alpha_1$ -adrenergic blockade. *Am J Hypertens* 6:320–324.
- Fotherby MD, Potter JF. 1992. Potassium supplementation reduces clinic and ambulatory blood pressure in elderly hypertensive patients. *J Hypertens* 10:1403–1408.
- Fotherby MD, Potter JF. 1993. Effects of moderate sodium restriction on clinic and twenty-four-hour ambulatory blood pressure in elderly hypertensive subjects. *J Hypertens* 11:657–663.
- Franx A, Steegers EAP, de Boo T, Thien T, Merkus JMWM. 1999. Sodium-blood pressure interrelationship in pregnancy. *J Hum Hypertens* 13:159–166.
- Fregly MJ. 1984. Sodium and potassium. In: *Nutrition Reviews' Present Knowledge in Nutrition*, 5th ed. Washington, DC: The Nutrition Foundation. Pp. 439–458.
- Frost CD, Law MR, Wald NJ. 1991. By how much does dietary salt reduction lower blood pressure? II. Analysis of observational data within populations. *Br Med J* 302:815–818.
- Fuchs FD, Wannmacher CM, Wannmacher L, Guimaraes FS, Rosito GA, Gastaldo G, Hoeffel CP, Wagner EM. 1987. Effect of sodium intake on blood pressure, serum levels and renal excretion of sodium and potassium in normotensives with and without familial predisposition to hypertension. *Braz J Med Biol Res* 20:25–34.
- Fukumoto T, Tanaka T, Fujioka H, Yoshihara S, Ochi T, Kuroiwa A. 1988. Differences in composition of sweat induced by thermal exposure and by running exercise. *Clin Cardiol* 11:707–709.
- Gardenswartz MH, Berl T. 1981. Drug-induced changes in water excretion. *Kidney* 14:19–26.
- Garzon P, Eisenberg MJ. 1998. Variation in the mineral content of commercially available bottled waters: Implications for health and disease. *Am J Med* 105:125–130.
- Geleijnse JM, Grobbee DE, Hofman A. 1990. Sodium and potassium intake and blood pressure change in childhood. *Br Med J* 300:899–902.
- Geleijnse JM, Witteman JC, Bak AA, den Breejen JH, Grobbee DE. 1995. Long-term moderate sodium restriction does not adversely affect the serum HDL/total cholesterol ratio. *J Hum Hypertens* 9:975–979.
- Geleijnse JM, Hofman A, Witteman JCM, Hazebroek AAJM, Valenburg HA, Grobbee DE. 1997. Long-term effects of neonatal sodium restriction on blood pressure. *Hypertension* 29:913–917.
- Geleijnse JM, Kok FJ, Grobbee DE. 2003. Blood pressure response to changes in sodium and potassium intake: A metaregression analysis of randomised trials. *J Hum Hypertens* 17:471–480.
- Gerdts E, Myking OL, Omvik P. 1996. Factors influencing left ventricular mass in hypertensive type-1 diabetic patients. *Am J Hypertens* 9:65A.
- Ghali JK III, Liao Y, Cooper RS. 1997. Left ventricular hypertrophy in the elderly.

- Am J Geriatr Cardiol* 6:38–49.
- Gillman MW, Cook NR, Rosner B, Evans DA, Keough ME, Taylor JO, Hennekens CH. 1993. Identifying children at high risk for the development of essential hypertension. *J Pediatr* 122:837–846.
- Gillum RF, Elmer PJ, Prineas RJ. 1981. Changing sodium intake in children. The Minneapolis Children's Blood Pressure Study. *Hypertension* 3:698–703.
- Ginty F, Flynn A, Cashman KD. 1998. The effects of dietary sodium intake on biochemical markers of bone metabolism in young women. *Br J Nutr* 79:343–350.
- Gleibermann L. 1973. Blood pressure and dietary salt in human populations. *Ecol Food Nutr* 2:143–156.
- Gotshall RW, Mickleborough TD, Cordain L. 2000. Dietary salt restriction improves pulmonary function in exercise-induced asthma. *Med Sci Sports Exerc* 32:1815–1819.
- Graham S, Haughey B, Marshall J, Brasuré J, Zielezny M, Freudenheim J, West D, Nolan J, Wilkinson G. 1990. Diet in the epidemiology of gastric cancer. *Nutr Cancer* 13:19–34.
- Graudal NA, Galloé AM, Garred P. 1998. Effects of sodium restriction on blood pressure, renin, aldosterone, catecholamines, cholesterol, and triglyceride. A meta-analysis. *J Am Med Assoc* 279:1383–1391.
- Greendale GA, Barrett-Connor E, Edelstein S, Ingles, Haile R. 1994. Dietary sodium and bone mineral density: Results of a 16 year follow-up. *J Am Geriatr Soc* 42:1050–1055.
- Grey A, Braatvedt G, Holdaway I. 1996. Moderate dietary salt restriction does not alter insulin resistance or serum lipids in normal men. *Am J Hypertens* 9:317–322.
- Griffith LE, Guyatt GH, Cook RJ, Bucher HC, Cook DJ. 1999. The influence of dietary and nondietary calcium supplementation on blood pressure: An updated metaanalysis of randomized controlled trials. *Am J Hypertens* 12:84–92.
- Grim CE, Weinberger MH, Higgins JT Jr, Kramer NJ. 1977. Diagnosis of secondary forms of hypertension: A comprehensive protocol. *J Am Med Assoc* 237:1331–1335.
- Grobbee DE, Hofman A, Roelandt JT, Boomsma F, Schalekamp MA, Valkenburg HA. 1987. Sodium restriction and potassium supplementation in young people with mildly elevated blood pressure. *J Hypertens* 5:115–119.
- Gross P, Ketteler M, Hausmann C, Reinhard C, Schomig A, Hackenthal E, Ritz E, Rascher W. 1988. Role of diuretics, hormonal derangements, and clinical setting of hyponatremia in medical patients. *Klin Wochenschr* 66:662–669.
- Gross SJ, David RJ, Bauman L, Tomarelli RM. 1980. Nutritional composition of milk produced by mothers delivering preterm. *J Pediatr* 96:641–644.
- Grossman H, Duggan E, McCamman S. 1980. The dietary chloride deficiency syndrome. *Pediatrics* 66:366–374.
- Gu D, He J, Wu X, Duan X, Whelton PK. 2001. Effect of potassium supplementation on blood pressure in Chinese: A randomized, placebo-controlled trial. *J Hypertens* 19:1325–1331.
- Hajjar I, Kotchen TA. 2003. Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988–2000. *J Am Med Assoc* 290:199–206.
- Hajjar IM, Grim CE, George V, Kotchen TA. 2001. Impact of diet on blood pressure and age-related changes in blood pressure in the US population. *Arch Intern Med* 161:589–593.

- Hall JE, Coleman TG, Guyton AC. 1989. The renin–angiotensin system: Normal physiology and changes in older hypertensives. *J Am Geront Soc* 37:801–813.
- Hall JE, Kuo JJ, da Silva AA, de Paula RB, Liu J, Tallam L. 2003. Obesity-associated hypertension and kidney disease. *Curr Opin Nephrol Hypertens* 12:195–200.
- Hamet P, Mongeau E, Lambert J, Bellavance F, Daignault-Gelinas M, Ledoux M, Whissell-Cambiotti L. 1991. Interactions among calcium, sodium, and alcohol intake as determinants of blood pressure. *Hypertension* 17:I150–I154.
- Hargreaves M, Morgan TO, Snow R, Guerin M. 1989. Exercise tolerance in the heat on low and normal salt intakes. *Clin Sci* 76:553–557.
- Harsha DW, Sacks FM, Obarzanek E, Svetkey LP, Lin PH, Bray GA, Aickin M, Colin PR, Miller ER III, Appel LJ. 2004. Effect of dietary sodium intake on blood lipids. Results from the DASH-Sodium Trial. *Hypertension* 43:393–398.
- Harshfield GA, Alpert BS, Becker JA. 1992. Correlates of LV mass index in healthy adolescents. *Hypertension* 20:422.
- Harshfield GA, Koelsch DW, Pulliam DA, Alpert BS, Richey PA, Becker JA. 1994. Racial differences in the age-related increase in left ventricular mass in youths. *Hypertension* 24:747–751.
- He FJ, MacGregor GA. 2002. Effects of modest salt reduction on blood pressure: A meta-analysis of randomized trials. Implications for public health. *J Hum Hypertens* 16:761–770.
- He FJ, Markandu ND, Sagnella GA, MacGregor GA. 1998. Importance of the renin system in determining blood pressure fall with salt restriction in black and white hypertensives. *Hypertension* 32:820–824.
- He FJ, Markandu ND, MacGregor GA. 2001. Importance of the renin system in determining blood pressure fall with acute salt restriction in hypertensive and normotensive whites. *Hypertension* 38:321–325.
- He J, Klag MJ, Coresh J, Whelton PK. 1994. Age, body mass, and dietary intake of protein and fiber modify the salt-blood pressure relationship. *Circulation* 90: I503.
- He J, Ogden LG, Vupputuri S, Bazzano L, Loria C, Whelton PK. 1999. Dietary sodium intake and subsequent risk of cardiovascular disease in overweight adults. *J Am Med Assoc* 282:2027–2034.
- He J, Whelton PK, Appel LJ, Charleston J, Klang MJ. 2000. Long-term effects of weight loss and dietary sodium reductions on incidence of hypertension. *Hypertension* 35:544–549.
- He J, Ogden LG, Bazzano LA, Vupputuri S, Loria C, Whelton PK. 2002. Dietary sodium intake and incidence of congestive heart failure in overweight US men and women: First National Health and Nutrition Examination Survey Epidemiologic Follow-up study. *Arch Intern Med* 162:1619–1624.
- Health Canada. 2003. *Food Program. Consolidation of the Food and Drug Act and the Food and Drug Regulations. Division 25 Infant Foods, Infant Formula*. Online. Available at [http://www.hc-sc.gc.ca/food-aliment/friia-raaif/food\\_drugs-aliments\\_drogues/act-loi/e\\_index.html](http://www.hc-sc.gc.ca/food-aliment/friia-raaif/food_drugs-aliments_drogues/act-loi/e_index.html). Accessed January 13, 2004.
- Henneman PH, Dempsey EF. 1956. Factors determining fecal electrolyte excretion. *J Clin Invest* 35:711.
- Hoffman CJ. 1988. Does the sodium level in drinking water affect blood pressure levels? *J Am Diet Assoc* 88:1432–1435.
- Hofman A, Hazebroek A, Valkenburg HA. 1983. A randomized trial of sodium intake and blood pressure in newborn infants. *J Am Med Assoc* 250:370–373.
- Holbrook JT, Patterson KY, Bodner JE, Douglas LW, Veillon C, Kelsay JL, Mertz W, Smith JC. 1984. Sodium and potassium intake and balance in adults consum-

- ing self-selected diets. *Am J Clin Nutr* 40:786–793.
- Honjo S, Kono S, Yamaguchi M. 1994. Salt and geographic variation in stomach cancer mortality in Japan. *Cancer Causes Control* 5:285–286.
- Hooper L, Bartlett C, Smith GD, Ebrahim S. 2002. Systematic review of long term effects of advice to reduce dietary salt in adults. *Br Med J* 325:628–637.
- Hooper L, Bartlett C, Davey SM, Ebrahim S. 2003. Reduced dietary salt for prevention of cardiovascular disease. *Cochrane Database Syst Rev* 1: CD003656.
- Hoshiyama Y, Sasaba T. 1992. A case-control study of single and multiple stomach cancers in Saitama Prefecture, Japan. *Jpn J Cancer Res* 83:937–947.
- Houlihan CA, Allen TJ, Baxter AL, Panangiotopoulos S, Casley DJ, Cooper ME, Jerums G. 2002. A low-sodium diet potentiates the effects of Losartan in type 2 diabetes. *Diabetes Care* 25:663–671.
- Howe PR, Cobiac L, Smith RM. 1991. Lack of effect of short-term changes in sodium intake on blood pressure in adolescent schoolchildren. *J Hypertens* 9:181–186.
- Howe PRC, Jureidini KF, Smith RM. 1985. Sodium and blood pressure in children—A short term dietary intervention study. *Proc Nutr Soc Aust* 10:121–124.
- Hunt SC, Cook NR, Oberman A, Cutler JA, Hennekens CH, Allender PS, Walker WG, Whelton PK, Williams RR. 1998. Angiotensinogen genotype, sodium reduction, weight loss, and prevention of hypertension: Trials of Hypertension Prevention, Phase II. *Hypertension* 32:393–401.
- Hunt SC, Geleijnse JM, Wu LL, Witteman JCM, Williams RR, Grobbee DE. 1999. Enhanced blood pressure response to mild sodium reduction in subjects with the 235T variant of the angiotensinogen gene. *Am J Hypertens* 12:460–466.
- Hypertension Prevention Trial Research Group. 1990. The Hypertension Prevention Trial: Three-year effects of dietary changes on blood pressure. *Arch Intern Med* 150:153–162.
- Hyttén FE. 1980. Weight gain in pregnancy. In: Hyttén FE, Chamberlain G, eds. *Clinical Physiology in Obstetrics*. Oxford: Blackwell Scientific. Pp. 193–230.
- Ikeda M, Kasahara M, Koizumi A, Watanabe T. 1986. Correlation of cerebrovascular disease standardized mortality ratios with dietary sodium and the sodium/potassium ratio among the Japanese population. *Prev Med* 15:46–59.
- Ikeda M, Nakatsuka H, Watanabe T. 1988. The absence of correlation between Na in diet duplicates and stomach cancer mortality in Japan. *Tohoku J Exp Med* 155:285–294.
- Inoue Y, Havenith G, Kenney WL, Loomis JL, Buskirk ER. 1999. Exercise- and methylcholine-induced sweating responses in older and younger men: Effect of heat acclimation and aerobic fitness. *Int J Biometeorol* 42:210–216.
- IOM (Institute of Medicine). 1997. *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. Washington, DC: National Academy Press.
- IOM. 1998. *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline*. Washington, DC: National Academy Press.
- IOM. 2000a. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- IOM. 2000b. *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*. Washington, DC: National Academy Press.
- IOM. 2001. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Washington, DC: National Academy Press.

- IOM. 2002/2005. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*. Washington, DC: The National Academies Press.
- IOM. 2003. *Food Chemicals Codex*, 5th ed. Washington, DC: The National Academies Press.
- Itoh R, Suyama Y. 1996. Sodium excretion in relation to calcium and hydroxyproline excretion in a healthy Japanese population. *Am J Clin Nutr* 63:735–740.
- Jay JM. 1996. *Modern Food Microbiolog*. 5th ed. New York: Chapman and Hall.
- Jee SH, Miller ER, Guallar E, Singh VK, Appel LJ, Klag MJ. 2002. The effect of magnesium supplementation on blood pressure: A meta-analysis of randomized clinical trials. *Am J Hypertens* 15:691–696.
- JNC (Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure). 1997. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Arch Intern Med* 157:2413–2446.
- Joffres MR, Hamet P, MacLean DR, L'italien GJ, Fodor G. 2001. Distribution of blood pressure and hypertension in Canada and the United States. *Am J Hypertens* 14:1099–1105.
- Johnson AG, Nguyen TV, Davis D. 2001. Blood pressure is linked to salt intake and modulated by the angiotensinogen gene in normotensive and hypertensive elderly subjects. *J Hypertens* 19:1053–1060.
- Johnson RJ, Herrera-Acosta J, Schreiner GF, Rodriguez-Iturbe B. 2002. Subtle acquired renal injury as a mechanism of salt-sensitive hypertension. *N Engl J Med* 346:913–923.
- Jones G, Beard T, Parameswaran V, Greenaway T, von Witt R. 1997. A population-based study of the relationship between salt intake, bone resorption and bone mass. *Eur J Clin Nutr* 51:561–565.
- Joossens JV, Hill ML, Elliott P, Stamler R, Stamler J, Lesaffre E, Dyer A, Nichols R, Kesteloot H. 1996. Dietary salt, nitrate and stomach cancer mortality in 24 countries. *Int J Epidemiol* 25:494–504.
- Jula AM, Karanko HM. 1994. Effects on left ventricular hypertrophy of long-term nonpharmacological treatment with sodium restriction in mild to moderate essential hypertension. *Circulation* 89:1023–1031.
- Kagan A, Popper JS, Rhoads GG, Yano K. 1985. Dietary and other risk factors for stroke in Hawaiian Japanese men. *Stroke* 16:390–396.
- Kalksma R, Leemhuis MP. 2002. Hyponatremia caused by thiazide diuretics: Be aware of drug combinations which enhance this effect. *Ned Tijdschr Geneeskde* 146:1521–1525.
- Kannel WB. 1991. Left ventricular hypertrophy as a risk factor: The Framingham experience. *J Hypertens* 9:3S–8S.
- Karanja NM, Obarzanek E, Lin PH, McCullough ML, Phillips KM, Swain JF, Champagne CM, Hoben KP. 1999. Descriptive characteristics of the dietary patterns used in the Dietary Approaches to Stop Hypertension Trial. *J Am Diet Assoc* 99:19S–27S.
- Kawasaki T, Delea CS, Bartter FC, Smith H. 1978. The effect of high sodium and low sodium intakes on blood pressure and other related variables in human subjects with idiopathic hypertension. *Am J Med* 64:193–198.
- Keenan BS, Buzek SW, Garza C, Potts E, Nichols BL. 1982. Diurnal and longitudinal variations in human milk sodium and potassium: Implication for nutrition and physiology. *Am J Clin Nutr* 35:527–534.

- Kempner W. 1948. Treatment of hypertensive vascular disease with rice diet. *Am J Med* 4:545–577.
- Kesteloot H, Joossens JV. 1988. Relationship of dietary sodium, potassium, calcium, and magnesium with blood pressure. *Hypertension* 12:594–599.
- Khaw KT, Barrett-Connor E. 1988. The association between blood pressure, age, and dietary sodium and potassium: A population study. *Circulation* 77:53–61.
- Khaw KT, Barrett-Connor E. 1990. Increasing sensitivity of blood pressure to dietary sodium and potassium with increasing age: A population study using casual urine specimens. *Am J Hypertens* 3:505–511.
- Kini N, Zahn S, Werlin SL. 1995. Hypernatremic dehydration in breast-fed infants. *Wis Med J* 94:143–145.
- Kirby CR, Convertino VA. 1986. Plasma aldosterone and sweat sodium concentrations after exercise and heat acclimation. *J Appl Physiol* 61:967–970.
- Kirkendall WM, Conner EW, Abboud F, Rastogi SP, Anderson TA, Fry M. 1976. The effect of dietary sodium chloride on blood pressure, body fluids, electrolytes, renal function, and serum lipids of normotensive man. *J Lab Clin Med* 87:418–434.
- Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Ford CE, Shulman NB, Stamler J. 1996. Blood pressure and end-stage renal disease in men. *N Engl J Med* 334:13–18.
- Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Stamler J. 1997. End-stage renal disease in African-American and white men: 16-year MR-FIT findings. *J Am Med Assoc* 277:1293–1298.
- Klahr S, Levey AS, Beck GJ, Caggiula AW, Hunsicker L, Kusek JW, Striker G. 1994. The effects of dietary protein restriction and blood pressure control on the progression of chronic renal disease. *N Engl J Med* 330:877–884.
- Klingbeil AU, Schneider M, Martus P, Messerli FH, Schmieder RE. 2003. A meta-analysis of the effects of treatment on left ventricular mass in essential hypertension. *Am J Med* 115:41–46.
- Kneller RW, Guo WD, Hsing AW, Chen JS, Blot WJ, Li JY, Forman D, Fraumeni JF. 1992. Risk factors for stomach cancer in sixty-five Chinese counties. *Cancer Epidemiol Biomarkers Prev* 1:113–118.
- Knuist M, Bonsel GJ, Zondervan HA, Treffers PE. 1998. Low sodium diet and pregnancy-induced hypertension: A multi-centre randomized controlled trial. *Br J Obstet Gynaecol* 105:430–434.
- Koga M, Sasaguri M, Miura S, Tashiro E, Kinoshita A, Ideishi M, Arakawa K. 1998. Plasma renin activity could be a useful predictor of left ventricular hypertrophy in essential hypertensives. *J Hum Hypertens* 12:455–461.
- Koolen MI, van Brummelen P. 1984. Sodium sensitivity in essential hypertension: Role of the renin-angiotensin-aldosterone system and predictive value of an intravenous frusemide test. *J Hypertens* 2:55–59.
- Koren MJ, Devereux RB, Casale PN, Savage DD, Laragh JH. 1991. Relation of left ventricular mass and geometry to morbidity and mortality in uncomplicated essential hypertension. *Ann Intern Med* 114:345–352.
- Korhonen MH, Jarvinen MK, Sarkkinen ES, Uusitupa MJ. 2000. Effects of a salt-restricted diet on the intake of other nutrients. *Am J Clin Nutr* 72:414–420.
- Kotchen TA. 1999. To salt, or not to salt? *Am J Physiol* 276:H1807–H1810.
- Kriemler S, Wilk B, Schurer W, Wilson WM, Bar-Or O. 1999. Preventing dehydration in children with cystic fibrosis who exercise in the heat. *Med Sci Sports Exerc* 31:774–779.

- Krishna GG, Miller E, Kapoor S. 1989. Increased blood pressure during potassium depletion in normotensive men. *N Engl J Med* 320:1177–1182.
- Kumanyika SK, Hebert PR, Cutler JA, Lasser VI, Sugars CP, Steffen-Batey L, Brewer AA, Cameron M, Shepak LD, Cook NR, Miller ST. 1993. Feasibility and efficacy of sodium reduction in the Trials of Hypertension Prevention, Phase I. *Hypertension* 22:502–512.
- Kupari M, Koskinen P, Virolainen J. 1994. Correlates of left ventricular mass in a population sample aged 36 to 37 years: Focus on lifestyle and salt intake. *Circulation* 89:1041–1050.
- Kurtz TW, Al-Bander HA, Morris RC. 1987. “Salt-sensitive” essential hypertension in men. *N Engl J Med* 317:1043–1048.
- Langenfeld MRW, Schobel H, Veelken R, Weihprecht H, Schmieder RE. 1998. Impact of dietary sodium intake on left ventricular diastolic filling in early essential hypertension. *Eur Heart J* 19:951–958.
- La Vecchia C, Negri E, Franceschi S, Decarli A. 1997. Case-control study on influence of methionine, nitrate, and salt on gastric carcinogenesis in Northern Italy. *Nutr Cancer* 27:65–68.
- Law MR, Frost CD, Wald NJ. 1991a. By how much does dietary salt reduction lower blood pressure? I—Analysis of observational data among populations. *Br Med J* 302:811–815.
- Law MR, Frost CD, Wald NJ. 1991b. By how much does dietary salt reduction lower blood pressure? III—Analysis of data from trials of salt reduction. *Br Med J* 302:819–824.
- Lawton WJ, Sinkey CA, Fitz AE, Mark AL. 1988. Dietary salt produces abnormal renal vasoconstrictor responses to upright posture in borderline hypertensive subjects. *Hypertension* 11:529–536.
- Lawton WJ, Fitz AE, Anderson EA, Sinkey CA, Coleman RA. 1990. Effect of dietary potassium on blood pressure, renal function, muscle sympathetic nerve activity, and forearm vascular resistance and flow in normotensive and borderline hypertensive humans. *Circulation* 81:173–184.
- Lee JK, Park BJ, Yoo KY, Ahn YO. 1995. Dietary factors and stomach cancer: A case-control study in Korea. *Int J Epidemiol* 24:33–41.
- Lemann J Jr, Gray RW, Pleuss JA. 1989. Potassium bicarbonate, but not sodium bicarbonate, reduces urinary calcium excretion and improves calcium balance in healthy men. *Kidney Int* 35:688–695.
- Lemons JA, Moye L, Hall D, Simmons M. 1982. Differences in the composition of preterm and term human milk during early lactation. *Pediatr Res* 16:113–117.
- Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. 1990. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *N Engl J Med* 322:1561–1566.
- Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. 2002. Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 360:1903–1913.
- Liddle GW, Bennett LL, Forsham PH. 1953. The prevention of ACTH-induced sodium retention by the use of potassium salts: A quantitative study. *J Clin Invest* 32:1197–1207.
- Liebson PR, Grandits G, Prineas R, Dianzumba S, Flack JM, Cutler JA, Grimm R, Stamler J. 1993. Echocardiographic correlates of left ventricular structure among 844 mildly hypertensive men and women in the Treatment of Mild Hypertension Study (TOMHS). *Circulation* 87:476–486.

- Liebson PR, Grandits GA, Dianzumba S, Prineas RJ, Grimm Jr RH, Neaton JD, Stamler J. 1995. Comparison of five antihypertensive monotherapies and placebo for change in left ventricular mass in patients receiving nutritional-hygienic therapy in the treatment of mild hypertension study (TOMHS). *Circulation* 91:698–706.
- Lietz G, Avenell A, Robins S. 1997. Short-term effects of dietary sodium intake on bone metabolism in postmenopausal women measured using urinary deoxypyridinoline excretion. *Br J Nutr* 78:73–82.
- Lifton RP, Wilson FH, Choate KA, Geller DS. 2002. Salt and blood pressure: New insight from human genetic studies. *Cold Spring Harb Symp Quant Biol* 67:445–450.
- Lijnen P, M'Buyamba-Kabangu JR, Fagard R, Staessen J, Lissens W, Goossens W, Amery A. 1987. Dietary sodium variation, erythrocyte cationic transport and plasma rennin-aldosterone in men. *Methods Find Exp Clin Pharmacol* 9:55–62.
- Lin PH, Ginty F, Appel LJ, Aickin M, Bohnannon A, Garner P, Barclay D, Svetkey L. 2003. The DASH diet and sodium reduction improve markers of bone turnover and calcium metabolism in adults. *J Nutr* 133:3130–3136.
- Lindheimer MD, Katz AI. 1985. Fluid and electrolyte metabolism in normal and abnormal pregnancy. In: Arieff AI, DeFronzo RA, eds. *Fluid, Electrolyte, and Acid-Base Disorders*. New York: Churchill Livingstone. Pp. 1041–1086.
- Lindheimer MD, Katz AI. 2000. Renal physiology and disease in pregnancy. In: Seldin DW, Giebisch G, eds. *The Kidney: Physiology and Pathophysiology*, 3rd ed. New York: Lippincott Williams & Wilkins. Pp. 2597–2644.
- Liu K, Cooper R, McKeever J, McKeever P, Byington R, Soltero I, Stamler R, Gosch F, Stevens E, Stamler J. 1979. Assessment of the association between habitual salt intake and high blood pressure: Methodological problems. *Am J Epidemiol* 110:219–226.
- Liu L, Mizushima S, Ikeda K, Hattori H, Miura A, Gao M, Nara Y, Yamori Y. 2000. Comparative studies of diet-related factors and blood pressure among Chinese and Japanese: Results from the China-Japan cooperative research of the WHO-Cardiac study. *Hypertens Res* 23:413–420.
- Longworth DL, Drayer JI, Weber MA, Laragh JH. 1980. Divergent blood pressure responses during short-term sodium restriction in hypertension. *Clin Pharmacol Ther* 27:544–546.
- LSRO (Life Sciences Research Office). 1998. Assessment of nutrient requirements for infant formulas. *J Nutr* 128:2059S–2293S.
- Luft FC, Rankin LI, Bloch R, Grim CE, Weyman AE, Murray RH, Weinberger MH. 1979a. Plasma and urinary norepinephrine values at extremes of sodium intake in normal man. *Hypertension* 1:261–266.
- Luft FC, Rankin LI, Bloch R, Weyman AE, Willis LR, Murray RH, Grim CE, Weinberger MH. 1979b. Cardiovascular and humoral responses to extremes of sodium intake in normal black and white men. *Circulation* 60:697–706.
- Luft FC, Fineberg NS, Miller JZ, Rankin LI, Grim CE, Weinberger MH. 1980. The effects of age, race, and heredity on glomerular filtration rate following volume expansion and contraction in normal man. *Am J Med Sci* 279:15–24.
- Luft FC, Weinberger MH, Grim CE. 1982. Sodium sensitivity and resistance in normotensive humans. *Am J Med* 72:726–736.
- Luft FC, Weinberger MH, Fineberg MS, Miller JZ, Grim CE. 1987. Effect of age on renal sodium homeostasis and its relevance to sodium sensitivity. *Am J Med* 82:9S–15S.

- Luft FC, Zemel MB, Sowers JA, Fineberg NS, Weinberger MH. 1990. Sodium bicarbonate and sodium chloride: Effects on blood pressure and electrolyte homeostasis in normal and hypertensive man. *J Hypertens* 8:663–670.
- Lutz J. 1984. Calcium balance and acid-base status of women as affected by increased protein intake and by sodium bicarbonate ingestion. *Am J Clin Nutr* 39:281–288.
- MacGregor GA. 1996. Low urinary sodium and myocardial infarction. *Hypertension* 127:I56.
- MacGregor GA, Markandu ND, Best FE, Elder DM, Cam JM, Sagnella GA, Squires M. 1982a. Double-blind randomized crossover trial of moderate sodium restriction in essential hypertension. *Lancet* 1:351–355.
- MacGregor GA, Markandu ND, Singer DR, Cappuccio FP, Shore AC, Sagnella GA. 1982b. Moderate potassium supplementation in essential hypertension. *Lancet* 2:567–570.
- MacGregor GA, Markandu ND, Sagnella GA, Singer DRJ, Cappuccio FP. 1989. Double-blind study of three sodium intakes and long-term effects of sodium restriction in essential hypertension. *Lancet* 2:1244–1247.
- Macias-Nuñez JF, García-Iglesias C, Bonda-Roman A, Rodriguez-Commes JL, Corbacho-Becerra L, Tabernero-Romo JM, De Castro-De Pozo S. 1978. Renal handling of sodium in old people: A functional study. *Age Ageing* 7:178–181.
- Macias-Nuñez JF, García Iglesias C, Tabernero-Romo JM, Rodriguez Commes JL, Corbacho Bercerra L, Sanchez Tomero JA. 1980. Renal management of sodium under indomethacin and aldosterone in the elderly. *Age Ageing* 9:165–172.
- MacMahon S, Peto R, Cutler J, Collins R, Sorlie P, Neaton J, Abbott R, Godwin J, Dyer A, Stamler J. 1990. Blood pressure, stroke, and coronary heart disease. Part 1, prolonged differences in blood pressure: Prospective observational studies corrected for the regression dilution bias. *Lancet* 335:765–774.
- Malloy MH, Graubard B, Moss H, McCarthy M, Gwyn S, Vietze P, Willoughby A, Rhoads GG, Berendes H. 1991. Hypochloremic metabolic alkalosis from ingestion of a chloride-deficient infant formula: Outcome 9 and 10 years later. *Pediatrics* 87:811–822.
- Mancilha-Carvalho JdeJ, Souza e Silva NA. 2003. The Yanomami Indians in the INTERSALT Study. *Arg Bras Cardiol* 80:289–300.
- Mao IF, Chen ML, Ko YC. 2001. Electrolyte loss in sweat and iodine deficiency in a hot environment. *Arch Environ Health* 56:271–277.
- Mark AL, Lawton WJ, Abboud FM, Fitz AE, Connor WE, Heistad DD. 1975. Effects of high and low sodium intake on arterial pressure and forearm vascular resistance in borderline hypertension. *Circ Res* 36:I194–I198.
- Marsden JL. 1980. Sodium-containing additives in processed meats: A technological overview. In: White PL, Crocco SC, eds. *Sodium and Potassium in Food and Drugs*. Chicago: American Medical Association.
- Martini LA, Cuppari L, Cunha MA, Schor N, Heilberg IP. 1998. Potassium and sodium intake and excretion in calcium stone forming patients. *J Ren Nutr* 8:127–131.
- Martini LA, Cuppari L, Colugnati FAB, Sigulem DM, Szejnfeld VL, Schor N, Heilberg IP. 2000. High sodium chloride intake is associated with low density in calcium in stone-forming patients. *Clin Nephrol* 54:85–93.
- Mascioli S, Grimm R, Launer C, Svendsen K, Flack J, Gonzalez N, Elmer P, Neaton J. 1991. Sodium chloride raises blood pressure in normotensive subjects. *Hypertension* 17:I21–I26.

- Masugi F, Ogihara T, Hashizume K, Hasegawa T, Sakaguchi K, Kumahara Y. 1988. Changes in plasma lipids and uric acid with sodium loading and sodium depletion in patients with essential hypertension. *J Hum Hypertens* 1:293–298.
- Matkovic V, Ilich JZ, Andon MB, Hsieh LC, Tzagournis MA, Lagger BJ, Goel PK. 1995. Urinary calcium, sodium, and bone mass of young females. *Am J Clin Nutr* 62:417–425.
- Matlou SM, Isles CG, Higgs A, Milne FJ, Murray GD, Schultz E, Starke IF. 1986. Potassium supplementation in blacks with mild to moderate essential hypertension. *J Hypertens* 4:61–64.
- Mattes RD, Donnelly D. 1991. Relative contributions of dietary sodium sources. *J Am Coll Nutr* 10:383–393.
- McCarron DA, Rankin LI, Bennett WM, Krutzik S, McClung MR, Luft F. 1981. Urinary calcium excretion at extremes of sodium intake in normal man. *Am J Nephrol* 1:84–90.
- McParland BE, Goulding A, Campbell AJ. 1989. Dietary salt affect biochemical markers of resorption and formation of bone in elderly women. *Br Med J* 299:834–835.
- Meade TW, Cooper JA, Peart WS. 1993. Plasma renin activity and ischemic heart disease. *N Engl J Med* 329:616–619.
- Medici TC, Schmid AZ, Hacki M, Vetter W. 1993. Are asthmatics salt-sensitive? A preliminary controlled study. *Chest* 104:1138–1143.
- Messerli FH, Soria F. 1994. Ventricular dysrhythmias, left ventricular hypertrophy, and sudden death. *Cardiovasc Drugs Ther* 8:557S–5563S.
- Meyer F, Bar-Or O, MacDougall D, Heigenhauser GJF. 1992. Sweat electrolyte loss during exercise in the heat: Effects of gender and maturation. *Med Sci Sports Exerc* 24:776–781.
- Midgley JP, Matthew AG, Greenwood CMT, Logan AG. 1996. Effect of reduced dietary sodium on blood pressure: A meta-analysis of randomized controlled trials. *J Am Med Assoc* 275:1590–1597.
- Miller JZ, Weinberger MH. 1986. Blood pressure response to sodium restriction and potassium supplementation in healthy normotensive children. *Clin Exp Hypertens* 8:823–827.
- Miller JZ, Daugherty SA, Weinberger MH, Grim CE, Christian JC, Lang CL. 1983. Blood pressure response to dietary sodium restriction in normotensive adults. *Hypertension* 5:790–795.
- Miller JZ, Weinberger MH, Daugherty SA, Fineberg NS, Christian JC, Grim CE. 1987. Heterogeneity of blood pressure response to dietary sodium restriction in normotensive adults. *J Chronic Dis* 40:245–250.
- Miller JZ, Weinberger MH, Daugherty SA, Fineberg NS, Christian JC, Grim CE. 1988. Blood pressure response to dietary sodium restriction on healthy normotensive children. *Am J Clin Nutr* 47:113–119.
- Mitch WE. 1998. Robert H. Herman Memorial Award in Clinical Nutrition Lecture, 1997. Mechanisms causing loss of lean body mass in kidney disease. *Am J Clin Nutr* 67:359–366.
- Mizushima S, Cappuccio FP, Nichols R, Elliott P. 1998. Dietary magnesium intake and blood pressure: A qualitative overview of the observational studies. *J Hum Hypertens* 12:447–453.
- Montes G, Cuello C, Correa P, Zarama G, Liuzza G, Zavala D, de Marin E, Haenszel W. 1985. Sodium intake and gastric cancer. *J Cancer Res Clin Oncol* 109:42–45.

- Morgan T, Anderson A. 1987. Sodium restriction can delay the return of hypertension in patients previously well-controlled on drug therapy. *Can J Physiol Pharmacol* 65:1752–1755.
- Morgan TO. 1982. The effect of potassium and bicarbonate ions on the rise in blood pressure caused by sodium. *Clin Sci* 63:407S–409S.
- Morimoto A, Uzu T, Fujii T, Nishimura M, Kuroda S, Nakamura S, Inenaga T, Kimura G. 1997. Sodium sensitivity and cardiovascular events in patients with essential hypertension. *Lancet* 350:1734–1737.
- Morris CD, Jacobson S-L, Anand R, Ewell MG, Hauth JC, Curet LB, Catalano PM, Sibai DM, Levine RJ. 2001. Nutrient intake and hypertensive disorders of pregnancy: Evidence from a large prospective cohort. *Am J Obstet Gynecol* 184:643–651.
- Morris RC Jr, Sebastian A, Forman A, Tanaka M, Schmidlin O. 1999. Normotensive salt-sensitivity: Effects of race and dietary potassium. *Hypertension* 33:18–23.
- Morriss FH, Brewer ED, Spedale SB, Riddle L, Temple DM, Caprioli RM, West MS. 1986. Relationship of human milk pH during course of lactation to concentrations of citrate and fatty acids. *Pediatrics* 78:458–464.
- Mulhauser I, Prange K, Sawicki PT, Bender R, Dworschak A, Schaden W, Berger M. 1996. Effects of dietary sodium on blood pressure in IDDM patients with nephropathy. *Diabetologia* 39:212–219.
- Murakami K, Hirayama T. 1964. Study of sweat electrolytes in Japanese children. *Paediatr Indones* 4:161S–168S.
- Murayama T, Taguchi H. 1988. Clinical studies of the recurrence of urolithiasis. Influence of sodium intake on urinary excretion of calcium, uric acid, oxalate, phosphate and magnesium. *Hinyokika Kiyo* 34:1537–1541.
- Nazario CM, Szklo M, Diamond E, Roman-Franco A, Climent C, Suarez E, Conde JG. 1993. Salt and gastric cancer: A case-control study in Puerto Rico. *Int J Epidemiol* 22:790–797.
- Neter JE, Stam BE, Kok FJ, Grobbee DE, Geleijnse JM. 2003. Influence of weight reduction on blood pressure: A meta-analysis of randomized controlled trials. *Hypertension* 42:878–884.
- NHBPEP (National High Blood Pressure Education Program). 1993. National High Blood Pressure Education Program Working Group report on primary prevention of hypertension. *Arch Intern Med* 153:186–208.
- Niarchos AP, Weinstein DL, Laragh JH. 1984. Comparison of the effects of diuretic therapy and low sodium intake in isolated systolic hypertension. *Am J Med* 77:1061–1068.
- Niven CF. 1980. Technology of sodium in processed foods: General bacteriological principles, with emphasis on canned fruits and vegetables, and dairy foods. In: White PL, Crocco SC, eds. *Sodium and Potassium in Food and Drugs*. Chicago: American Medical Association.
- Nordin BEC, Need AG, Morris HA, Horowitz M. 1993. The nature and significance of the relationship between urinary sodium and urinary calcium in women. *J Nutr* 123:1615–1622.
- Obarzanek E, Proschan MA, Vollmer WM, Moore TJ, Sacks FM, Appel LJ, Svetkey LP, Most-Windhauser MM, Cutler JA. 2003. Individual blood pressure responses to changes in salt intake: Results from the DASH-Sodium Trial. *Hypertension* 42:459–467.
- Oh MS, Uribarri J. 1999. Electrolytes, water, and acid-base balance. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th ed. Baltimore: Williams and Wilkins. Pp. 105–139.

- Oles KS, Denham JW. 1984. Hyponatremia induced by thiazide-like diuretics in the elderly. *South Med J* 77:1314–1315.
- Oliver WJ, Cohen EL, Neel JV. 1975. Blood pressure, sodium intake, and sodium related hormones in the Yanomamo Indians, a “no-salt” culture. *Circulation* 52:146–151.
- Oliver WJ, Neel JV, Grekin RJ, Cohen EL. 1981. Hormonal adaptation to the stress imposed on sodium balance by pregnancy and lactation in Yanomama Indians, a culture without salt. *Circulation* 63:1210–1216.
- Orent-Keiles E, McCollum EV. 1940. Mineral metabolism of rats on an extremely sodium-deficient diet. *J Biol Chem* 133:75–81.
- Orinius E. 1984. Hyponatremia in congestive heart failure treated with diuretics. *Acta Pharmacol Toxicol* 54:S115–S117.
- Overlack A, Conrad H, Stumpe KO. 1991. The influence of oral potassium citrate/bicarbonate on blood pressure in essential hypertension during unrestricted salt intake. *Klin Wochenschr* 69:79–83.
- Overlack A, Ruppert M, Kolloch R, Gobel B, Kraft K, Diehl J, Schmitt W, Stumpe K. 1993. Divergent hemodynamic and hormonal responses to varying salt intake in normotensive subjects. *Hypertension* 22:331–338.
- Overlack A, Ruppert M, Kolloch R, Kraft K, Stumpe KO. 1995. Age is a major determinant of the divergent blood pressure responses to varying salt intake in essential hypertension. *Am J Hypertens* 8:829–836.
- Palli D, Russo A, Decarli A. 2001. Dietary patterns, nutrient intake and gastric cancer in a high-risk area of Italy. *Cancer Causes Control* 12:163–172.
- Parijs J, Joossens JV, Van der Linden L, Verstreken G, Amery AK. 1973. Moderate sodium restriction and diuretics in the treatment of hypertension. *Am Heart J* 85:22–34.
- PCG (PROGRESS Collaborative Group). 2001. Randomized trial of perindopril-based blood pressure lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. *Lancet* 358:1033–1041.
- Pearson AM, Wolzak AM. 1982. Salt—Its use in animal products—A human health dilemma. *J Anim Sci* 54:1263–1278.
- Perry IJ. 2003. Salt, science and politics. *J Hum Hypertens* 17:1–3.
- Perry IJ, Beavers DG. 1992. Salt intake and stroke: A possible direct effect. *J Hum Hypertens* 6:23–25.
- Peters JM. 1989. Hypernatremia in breast-fed infants due to elevated breast milk sodium. *J Am Osteopath Assoc* 89:1165–1170.
- Peterson JC, Adler S, Burkart JM, Greene T, Hebert LA, Hunsicker LG, King AJ, Klahr S, Massry SG, Seifter JL. 1995. Blood pressure control, proteinuria, and the progression of renal disease. *Ann Intern Med* 123:754–762.
- Picciano MF, Calkins EJ, Garrick JR, Deering RH. 1981. Milk and mineral intakes of breastfed infants. *Acta Paediatr Scand* 70:189–194.
- Pietinen P. 1982. Estimating sodium intake from food consumption data. *Ann Nutr Metab* 26:90–99.
- Pillion DJ, Meezan E. 1985. Liquid-chromatographic determination of chloride in sweat from cystic fibrosis patients and normal persons. *Clin Chem* 31:1155–1157.
- Pitts RF. 1974. *Physiology of the Kidney and Body Fluids*. 3rd ed. Chicago: Year Book Medical Publishers.

- Psaty BM, Lumley T, Furberg CD, Schellenbaum G, Pahor M, Alderman MH, Weiss NS. 2003. Health outcomes associated with various antihypertensive therapies used as first-line agents. A network meta-analysis. *J Am Med Assoc* 289:2534–2544.
- Rastenye D, Tuomilehto J, Moltchanov V, Lindström J, Pietinen P, Nissinen A. 1997. Association between salt intake, heart rate and blood pressure. *J Hum Hypertens* 11:57–62.
- Resnick LM, Nicholson JP, Laragh JH. 1985. Alterations in calcium metabolism mediate dietary salt sensitivity in essential hypertension. *Trans Assoc Am Physicians* 98:313–321.
- Rich GM, McCullough M, Olmedo A, Malarick C, Moore TJ. 1991. Blood pressure and renal blood flow responses to dietary calcium and sodium intake in humans. *Am J Hypertens* 4:642S–645S.
- Richards AM, Nicholls MG, Espiner EA, Ikram H, Maslowski AH, Hamilton EJ, Wells JE. 1984. Blood-pressure response to moderate sodium restriction and to potassium supplementation in mild essential hypertension. *Lancet* 1:757–761.
- Robertson JS. 1984. Water sodium, urinary electrolytes, and blood pressure of adolescents. *J Epidemiol Community Health* 38:186–194.
- Robinson MR. 1958. Salt in pregnancy. *Lancet* 1:178–181.
- Rocchini AP, Key J, Bondie D, Chico R, Moorehead C, Katch V, Martin M. 1989. The effect of weight loss on the sensitivity of blood pressure to sodium in obese adolescents. *N Engl J Med* 32:580–585.
- Roland JM, O'Hare JP, Walters G, Corrall RJ. 1986. Sodium retention in response to saline infusion in uncomplicated diabetes mellitus. *Diabetes Res* 3:213–215.
- Roos JC, Koomans HA, Dorhout-Meess EJ, Delawi IMK. 1985. Renal sodium handling in normal humans subjected to low, normal, and extremely high sodium supplies. *Am J Physiol* 249:F941–F947.
- Rose G. 1985. Sick individuals and sick populations. *Int J Epidemiol* 14:32–38.
- Rose G, Stamler J, Stamler R, Elliott P, Marmot M, Pyorala K, Kesteloot H, Joossens J, Hansson L, Mancia G, Dyer A, Kromhout D, Laaser U, Sans S. 1988. Intersalt: An international study of electrolyte excretion and blood pressure. Results for 24 hour urinary sodium and potassium excretion. *Br Med J* 297:319–328.
- Rosler A. 1984. The natural history of salt-wasting disorders of adrenal and renal origin. *J Clin Endocrinol Metab* 59:689–700.
- Roy S. 1984. The chloride depletion syndrome. *Adv Pediatr* 31:235–257.
- Roy S, Arant B. 1979. Alkalosis from chloride-deficient Neo-Mull-Soy. *N Engl J Med* 301:615.
- Roy S, Arant B. 1981. Hypokalemic metabolic alkalosis in normotensive infants with elevated plasma rennin activity and hyperaldosteronism: Role of dietary chloride deficiency. *Pediatrics* 79:851–857.
- Ruppert M, Diehl J, Kolloch R, Overlack A, Kraft K, Gobel B, Hittel N, Stumpe KO. 1991. Short-term dietary sodium restriction increases serum lipids and insulin in salt-sensitive and salt-resistant normotensive adults. *Klin Wochenschr* 69:51–57.
- Ruppert M, Overlack A, Kolloch R, Kraft K, Gobel B, Stumpe KO. 1993. Neurohormonal and metabolic effects of severe and moderate salt restriction in non-obese normotensive adults. *J Hypertens* 11:743–749.
- Ruppert M, Overlack A, Kolloch R, Kraft K, Lennarz M, Stumpe KO. 1994. Effects of severe and moderate salt restriction on serum lipid in nonobese normotensive adults. *Am J Med Sci* 307:87S–90S.

- Sacks FM, Rosner B, Kass EH. 1974. Blood pressure in vegetarians. *Am J Epidemiol* 100:390–398.
- Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, Obarzanek E, Conlin PR, Miller ER, Simons-Morton DG, Karanja N, Lin PH. 2001. Effects of blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. *N Engl J Med* 344:3–10.
- Sagnella GA, Markandu ND, Buckley MG, Miller MA, Singer DRJ, MacGregor GA. 1990. Plasma atrial natriuretic peptide, aldosterone, and plasma renin activity responses to gradual changes in dietary sodium intake. *Am J Hypertens* 3:863–865.
- Saito K, Sano H, Furuta Y, Fukuzaki H. 1989. Effect of oral calcium on blood pressure response in salt-loaded borderline hypertensive patients. *Hypertension* 13:219–226.
- Sakhaee K, Harvey JA, Padalino PK, Whitson P, Pak CYC. 1993. The potential role of salt abuse on the risk for kidney stone formation. *J Urol* 150:310–312.
- Sanchez-Castillo CP, Warrender S, Whitehead TP, James WP. 1987. An assessment of the sources of dietary salt in a British population. *Clin Sci* 72:95–102.
- Sasaki N. 1964. The relationship of salt intake to hypertension in the Japanese. *Geriatrics* 19:735–744.
- Sasaki S, Zhang X-H, Kesteloot HK. 1995. Dietary sodium, potassium, saturated fat, alcohol, and stroke mortality. *Stroke* 26:783–789.
- Sawka MN, Montain SJ. 2000. Fluid and electrolyte supplementation for exercise heat stress. *Am J Clin Nutr* 72:564S–572S.
- Schambelan M, Stockigt JR, Biglieri EG. 1972. Isolated hypoaldosteronism in adults. A renin-deficiency syndrome. *N Engl J Med* 287:573–578.
- Schmid M, Mann JFE, Stein G, Herter M, Nussberger J, Klingbeil A, Ritz E. 1990. Natriuresis-pressure relationship in polycystic kidney disease. *J Hypertens* 8:277–283.
- Schmieder RE, Messerli FH. 1993. Does obesity influence early target organ damage in hypertensive patient? *Circulation* 87:1482–1488.
- Schmieder RE, Grube E, Impelmann V, Ruddel H, Schulte W. 1990. Determinants of myocardial hypertrophy in mild essential hypertension. Impact of dietary salt intake on left ventricular hypertrophy. *Z Kardiol* 79:557–564.
- Schmieder RE, Langenfeld MR, Friedrich A, Schobel HP, Gatzka CD, Weihprecht H. 1996. Angiotensin II Related to sodium excretion modulates left ventricular structure in human essential hypertension. *Circulation* 94:1304–1309.
- Schmieder RE, Messerli FH, Ruddel H, Garavaglia GG, Grube E, Nunez BD, Schulte W. 1988. Sodium intake modulates left ventricular hypertrophy in essential hypertension. *J Hypertens* 6:S148–S150.
- Schorr U, Distler A, Sharma AM. 1996. Effect of sodium chloride- and sodium bicarbonate-rich mineral water on blood pressure and metabolic parameters in elderly normotensive individuals: A randomized double-blind crossover trial. *J Hypertens* 14:131–135.
- Schrier RW, Briner VA. 1991. Peripheral vasodilation hypothesis of sodium and water retention in pregnancy: Implications for the pathogenesis of preeclampsia. *Obstet Gynecol* 77:632–639.
- Schwartz GL, Turner ST, Sing CF. 1992. Twenty-four-hour blood pressure profiles in normotensive sons of hypertensive parents. *Hypertension* 20:834–840.
- Schwartz J, Weiss ST. 1990. Dietary factors and their relation to respiratory symptoms. *Am J Epidemiol* 132:67–76.

- Seikaly MG, Arant BS. 1992. Development of renal hemodynamics: Glomerular filtration and renal blood flow. *Clin Perinatol* 19:1–13.
- Sharma AM, Arntz HR, Kribben A, Schattenfroh S, Distler A. 1990. Dietary sodium restriction: Adverse effect on plasma lipids. *Klin Wochenschr* 68:664–668.
- Sharma AM, Ruland K, Spies KP, Distler A. 1991. Salt sensitivity in young normotensive subjects is associated with a hyperinsulinemic response to oral glucose. *J Hypertens* 9:329–335.
- Sharma AM, Schattenfroh S, Thiede H-M, Oelkers W, Distler A. 1992. Effects of sodium salts on pressor reactivity in salt-sensitive men. *Hypertension* 19:541–548.
- Sharma AM, Schorr U, Thiede HM, Distler A. 1993. Effect of dietary salt restriction on urinary serotonin and 5-hydroxyindolacetic acid excretion in man. *J Hypertens* 11:1381–1386.
- Shore AC, Markandu ND, MacGregor GA. 1988. A randomized crossover study to compare the blood pressure response to sodium loading with and without chloride in patients with essential hypertension. *J Hypertens* 6:613–617.
- Shortt C, Madden A, Flynn A, Morrissey PA. 1988. Influence of dietary sodium intake on urinary calcium excretion in selected Irish individuals. *Eur J Clin Nutr* 42:595–603.
- Simon JA, Obarzanek E, Daniels SR, Frederick MM. 1994. Dietary cation intake and blood pressure in black girls and white girls. *Am J Epidemiol* 139:130–140.
- Simons-Morton DG, Obarzanek E. 1997. Diet and blood pressure in children and adolescents. *Pediatr Nephrol* 11:244–249.
- Sinaiko AR, Gomez-Marin O, Prineas RJ. 1993. Effect of low sodium diet or potassium supplementation on adolescent blood pressure. *Hypertension* 21:989–994.
- Skrabal F, Aubock J, Hortnagl H. 1981. Low sodium/high potassium diet for prevention of hypertension: Probable mechanisms of action. *Lancet* 2:895–900.
- Skrabal F, Gasser RW, Finkenstedt G, Rhomberg HP, Lochs A. 1984a. Low-sodium diet versus low-sodium/high-potassium diet for treatment of hypertension. *Klin Wochenschr* 62:124–128.
- Skrabal F, Herholz H, Neumayr M, Hamberger L, Ledochowski M, Sporer H, Hortngal H, Schwarz S, Schonitzer D. 1984b. Salt sensitivity in humans is linked to enhanced sympathetic responsiveness and to enhanced proximal tubular reabsorption. *Hypertension* 6:152–158.
- Skrabal F, Hamberger L, Cerny E. 1985. Salt sensitivity in normotensive with and salt resistance in normotensives without heredity of hypertension. *Scan J Clin Lab Invest* 176:47–57.
- Smith SR, Klotman PE, Svetkey LP. 1992. Potassium chloride lowers blood pressure and causes natriuresis in older patients with hypertension. *J Am Soc Nephrol* 2:1302–1309.
- Sofer S, Ben-Ezer D, Dagan R. 1993. Early severe dehydration in young breast-fed newborn infants. *Isr J Med Sci* 29:85–89.
- Sowers JR, Zemel MB, Zemel P, Beck FW, Walsh MF, Zawada ET. 1988. Salt sensitivity in blacks: Salt intake and natriuretic substances. *Hypertension* 12:485–490.
- Stamler R. 1991. Implications of the INTERSALT Study. *Hypertension* 17:I16S–I20S.
- Stamler J, Cirillo M. 1997. Dietary salt and renal stone disease. *Lancet* 349:506–507.
- Stamler J, Rose G, Stamler R, Elliott P, Dyer A, Marmot M. 1989. Intersalt study findings. Public health and medical care implications. *Hypertension* 14:570–577.

- Stamler J, Rose G, Elliott P, Dyer A, Marmot M, Kesteloot H, Stamler R. 1991. Findings of the international cooperative INTERSALT study. *Hypertension* 17: I9S–I15S.
- Stamler J, Stamler R, Neaton JD. 1993. Blood pressure, systolic and diastolic, and cardiovascular risks: U.S. population data. *Arch Intern Med* 153:598–615.
- Stamler J, Caggiula AW, Grandits GA. 1997. Relation of body mass and alcohol, nutrient, fiber, and caffeine intakes to blood pressure in the special intervention and usual care groups in the Multiple Risk Factor Intervention Trial. *Am J Clin Nutr* 65:338S–365S.
- Steegers EAP, Eskes TKAB, Jongsma HW, Hein PR. 1991a. Dietary sodium restriction during pregnancy: An historical review. *Eur J Obstet Gynecol Reprod Biol* 40:83–90.
- Steegers EAP, Van Lakwijk HPJM, Jongsma HW, Fast JH, DeBoo T, Eskes TK, Hein PR. 1991b. (Patho)physiological implications of chronic dietary sodium restriction during pregnancy: A longitudinal prospective randomized study. *Br J Obstet Gynaecol* 98:980–987.
- Strauss AL, Coe FL, Deutsch L, Parks JH. 1982. Factors that predict relapse of calcium nephrolithiasis during treatment. *Am J Med* 72:17–24.
- Strazzullo P, Galletti F, Barba G. 2003. Altered renal handling of sodium in human hypertension: Short review of the evidence. *Hypertension* 41:1000–1005.
- Sullivan JM, Ratts TE, Taylor JC, Kraus DH, Barton BR, Patrick DR, Reed SW. 1980. Hemodynamic effects of dietary sodium in man. *Hypertension* 2:506–514.
- Svetkey LP, Simons-Morton D, Vollmer WM, Appel LJ, Conlin PR, Ryan DH, Ard J, Kennedy BM. 1999. Effects of dietary patterns on blood pressure: Subgroup analysis of the Dietary Approaches to Stop Hypertension (DASH) randomized clinical trial. *Arch Int Med* 159:285–293.
- Svetkey LP, Moore TJ, Simons-Morton DG, Appel LJ, Bray GA, Sacks FM, Ard JD, Mortensen RM, Mitchell SR, Conlin PR, Kesari M. 2001. Angiotensinogen genotype and blood pressure response in the Dietary Approaches to Stop Hypertension (DASH) study. *J Hypertens* 19:1949–1956.
- Takahashi M, Hasegawa R. 1986. Enhancing effects of dietary salt on both initiation and promotion stages of rat gastric carcinogenesis. In: Hayashi Y, Nagao M, Sugimura T. *Diet, Nutrition, and Cancer*. Tokyo: Japan Scientific Societies Press. Pp. 169–182.
- TOHP (Trials of Hypertension Prevention) Collaborative Research Group. 1992a. The effects of nonpharmacologic interventions on blood pressure of persons with high normal levels. Results of the Trials of Hypertension Prevention, Phase I. *J Am Med Assoc* 267:1213–1220.
- TOHP Collaborative Research Group. 1992b. Erratum. The effects of nonpharmacologic interventions on blood pressure of persons with high normral levels. Results of the Trials of Hypertension Prevention, Phase I. *J Am Med Assoc* 267:2330.
- TOHP Collaborative Research Group. 1997. Effects of weight loss and sodium reduction intervention on blood pressure and hypertension incidence in overweight people with high-normal blood pressure. The Trials of Hypertension Prevention, Phase II. *Arch Intern Med* 157:657–667.
- Townsend RR, Zhao H. 1994. Plasma renin activity and insulin sensitivity in normotensive subjects. *Am J Hypertens* 7:894–898.
- Tracy RE, MacLean CJ, Reed DM, Hayashi T, Gandia M, Strong JP. 1988. Blood pressure, nephrosclerosis, and age autopsy findings from the Honolulu Heart Program. *Mod Pathol* 1:420–427.

- Tribe RM, Barton JR, Poston L, Burney P. 1994. Dietary sodium intake, airway responsiveness and cellular sodium transport. *J Respir Crit Care Med* 149:1426–1433.
- Tsubono Y, Takahashi T, Iwase Y, Itoi Y, Akabane M, Tsugane S. 1997. Nutrient consumption and gastric cancer mortality in five regions of Japan. *Nutr Cancer* 27:310–315.
- Tsugane S, Akabane M, Inami T, Matsushima S, Ishibashi T, Ichinowatari Y, Miyajima Y, Watanabe S. 1991. Urinary salt excretion and stomach cancer mortality among four Japanese populations. *Cancer Causes Control* 2:165–168.
- Tsugane S, Tei Y, Takahashi T, Watanabe S, Sugano K. 1994. Salty food intake and risk of *Helicobacter pylori* infection. *Jpn J Cancer Res* 85:474–478.
- Tsugane S, Sasazuki S, Kobayashi M, Sasaki S. 2004. Salt and salted food intake and subsequent risk of gastric cancer among middle-aged Japanese men and women. *Br J Cancer* 90:128–134.
- Tsunoda K, Abe K, Goto T, Yasujima M, Sato M, Omata K, Seino M, Yoshinaga K. 1986. Effect of age on the renin-angiotensin-aldosterone system in normal subjects: Simultaneous measurement of active and inactive renin, renin substrate, and aldosterone in plasma. *J Clin Endocrinol Metab* 62:384–389.
- Tuck M, Corry D, Trujillo A. 1990. Salt-sensitive blood pressure and exaggerated vascular reactivity in the hypertension of diabetes mellitus. *Am J Med* 88:210–216.
- Tucker DT, Smothers M, Lewis C, Feldman H. 1989. Effects of decreased dietary salt intake on blood pressure in preschool children. *J Natl Med Assoc* 81:299–302.
- Tunstall-Pedoe H. 1999. Does dietary potassium lower blood pressure and protect against coronary heart disease? Findings from the Scottish Heart Health Study. *Semin Nephrol* 19:500–502.
- Tunstall-Pedoe H, Woodward M, Tavendale R, A'Brook R, McCluskey MK. 1997. Comparison of the prediction by 27 different factors of coronary heart disease and death in men and women of the Scottish Heart Health Study: Cohort study. *Br Med J* 315:722–729.
- Tuomilehto J, Jousilahti P, Rastenyte D, Moltchanov V, Tanskanen A, Pietinen P, Nissinen A. 2001. Urinary sodium excretion and cardiovascular mortality in Finland: A prospective study. *Lancet* 357:848–851.
- Tuyns AJ. 1983. Sodium chloride and cancer of the digestive tract. *Nutr Cancer* 4:198–205.
- USDA/ARS (U.S. Department of Agriculture/Agricultural Research Service). 2002. *USDA National Nutrient Database for Standard Reference, Release 15*. Online. Available at <http://www.nal.usda.gov/fnic/foodcomp>. Accessed June 30, 2003.
- USRDS (U.S. Renal Data System). 1999. *USRDS 1999 Annual Data Report*. Online. National Institute of Diabetes and Digestive and Kidney Diseases. Available at [http://www.usrds.org/adr\\_1999.htm](http://www.usrds.org/adr_1999.htm). Accessed September 1, 2004.
- Valtin H, Schafer JA. 1995. *Renal Function: Mechanisms Preserving Fluid and Solute Balance in Health*. 3rd ed. Boston: Little Brown.
- van Buren M, Rabelink TJ, van Rijn HJ, Koomans HA. 1992. Effects of acute NaCl, KCl and KHCO<sub>3</sub> loads on renal electrolyte excretion in humans. *Clin Sci* 83:567–574.
- Vander AJ. 1970. Direct effects of potassium on renin secretion and renal function. *Am J Physiol* 219:455–459.

- van der Maten GD, van Raaij JM, Visman L, van der Heijden LJ, Oosterbaan HP, de Boer R, Eskes TK, Hautvast JG. 1997. Low-sodium diet in pregnancy: Effects on blood pressure and maternal nutritional status. *Br J Nutr* 77:703–720.
- Van Goidsenhoven GMT, Gray OV, Price AV, Sanderson PH. 1954. The effect of prolonged administration of large doses of sodium bicarbonate in man. *Clin Sci* 13:383–401.
- Van Lenthe FJ, Kemper HCG, Twisk JWR. 1994. Tracking of blood pressure in children and youth. *Am J Hum Biol* 6:389–399.
- Vasan RS, Beiser A, Seshadri S, Larson MG, Kannel WB, D'Agostino RB, Levey D. 2002. Residual lifetime risk for developing hypertension in middle-aged women and men: The Framingham Heart Study. *J Am Med Assoc* 287:1003–1010.
- Verde T, Shephard RJ, Corey P, Moore R. 1982. Sweat composition in exercise and in heat. *J Appl Physiol* 53:1540–1545.
- Vollmer WM, Sacks FM, Ard J, Appel LJ, Bray GA, Simons-Morton DG, Conlin PR, Svetkey LP, Erlinger TP, Moore TJ, Karanja N. 2001. Effects of diet and sodium intake on blood pressure: Subgroup analysis of the DASH-sodium trial. *Ann Intern Med* 135:1019–1028.
- Watt GCM, Edwards C, Hart JT, Hart M, Walton P, Foy CJW. 1983. Dietary sodium restriction for mild hypertension in general practice. *Br Med J* 286:432–436.
- Weder AN, Egan BM. 1991. Potential deleterious impact of dietary salt restriction on cardiovascular risk factors. *Klin Wochenschr* 69:45–50.
- Weidmann P, De Myttenaere-Bursztein S, Maxwell MH, de Lima J. 1975. Effect of aging on plasma renin and aldosterone in normal man. *Kidney Int* 8:325–333.
- Weidmann P, de Chatel R, Schiffmann A, Bachmann E, Beretta-Piccoli C, Reubi FC, Ziegler WH, Vetter W. 1977. Interrelations between age and plasma renin, aldosterone and cortisol, urinary catecholamines, and the body sodium/volume state in normal man. *Klin Wochenschr* 55:725–733.
- Weinberger MH. 1993. Racial differences in renal sodium excretion: Relationship to hypertension. *Am J Kidney Dis* 21:41–45.
- Weinberger MH. 1996. Salt sensitivity of blood pressure in humans. *Hypertension* 27:II481–II490.
- Weinberger MH, Fineberg NS. 1991. Sodium and volume sensitivity of blood pressure. Age and pressure change over time. *Hypertension* 18:67–71.
- Weinberger MH, Kramer NJ, Grim CE, Petersen LP. 1977. The effect of posture and saline loading on plasma renin activity and aldosterone concentration in pregnant, non-pregnant and estrogen-treated women. *J Clin Endocrinol Metab* 44:69–77.
- Weinberger MH, Luft FC, Bloch R, Henry DP, Pratt JH, Weyman AE, Rankin LI, Murray RH, Willis LR, Grim CE. 1982. The blood pressure-raising effects of high dietary sodium intake: Racial differences and the role of potassium. *J Am Coll Nutr* 1:139–148.
- Weinberger MH, Miller JZ, Luft FC, Grim CE, Fineberg NS. 1986. Definitions and characteristics of sodium sensitivity and blood pressure resistance. *Hypertension* 8:II127–II134.
- Weinberger MH, Cohen SJ, Miller JZ, Lift FC, Grim CE, Fineberg NS. 1988. Dietary sodium restriction as adjunctive treatment of hypertension. *J Am Med Assoc* 259:2561–2565.
- Weinberger MH, Stegner JE, Fineberg NS. 1993a. A comparison of two tests for the assessment of blood pressure responses to sodium. *Am J Hypertens* 6:I179–I184.

- Weinberger MH, Wagner UL, Fineberg NS. 1993b. The blood pressure effects of calcium supplementation in humans of known sodium responsiveness. *Am J Hypertens* 6:799–805.
- Weinberger MH, Fineberg NS, Fineberg SE, Weinberger M. 2001. Salt sensitivity, pulse pressure, and death in normal and hypertensive humans. *Hypertension* 37:II429–II432.
- Weir MR, Dengel DR, Behrens T, Goldberg AP. 1995. Salt-induced increases in systolic blood pressure affect renal hemodynamics and proteinuria. *Hypertension* 25:1339–1344.
- Whelton PK, Buring J, Borhani NO, Cohen JD, Cook N, Cutler JA, Kiley JE, Kuller LH, Satterfield S, Sacks FM, Taylor JO. 1995. The effect of potassium supplementation in persons with a high-normal blood pressure: Results from phase I of the Trials of Hypertension Prevention (TOHP). *Ann Epidemiol* 5:85–95.
- Whelton PK, Perneger TV, He J, Klag MJ. 1996. The role of blood pressure as a risk factor for renal disease: A review of the epidemiological evidence. *J Hum Hypertens* 10:683–689.
- Whelton PK, He J, Appel LJ, Cutler JA, Havas S, Kotchen TA, Roccella EJ, Stout R, Vallbona C, Winston MC, Karimbakas J. 2002. Primary prevention of hypertension: Clinical and public health advisory from the National High Blood Pressure Education Program. *J Am Med Assoc* 288:1882–1888.
- Willoughby A, Graubard BI, Hocker A, Storr C, Vietze P, Thackaberry JM, Gerry MA, McCarthy M, Gist NF, Magenheim M, Berendes H, Rhoads GG. 1990. Population-based study of the developmental outcome of children exposed to chloride-deficient infant formula. *Pediatrics* 85:485–490.
- Wilson M, Morganti AA, Zervoudakis J, Letcher RL, Romney BM, Von Oeyen P, Papera S, Sealey JE, Laragh JH. 1980. Blood pressure, the renin-aldosterone system and sex steroids throughout normal pregnancy. *Am J Med* 68:97–104.
- Witterman JC, Willett WC, Stampfer MJ, Colditz GA, Sacks FM, Speizer FE, Rosner B, Hennekens CH. 1989. A prospective study of nutritional factors and hypertension among us women. *Circulation* 8:1320–1327.
- Wolf-Maier K, Cooper RS, Banegas JR, Giampaoli S, Hense HW, Joffres M, Kastarinen M, Poulter N, Primatesta P, Rodriguez-Artalejo F, Stegmayr B, Thamm M, Tuomilehto J, Vanuzzo D, Vescio F. 2003. Hypertension prevalence and blood pressure levels in 6 European countries, Canada, and the United States. *J Am Med Assoc* 289:2363–2369.
- Yamori Y, Horie R. 1994. Community-based prevention of stroke: Nutritional improvement in Japan. *Health Rep* 6:181–188.
- Yamori Y, Nara Y, Mizushima S, Mano M, Sawamura M, Kihara M, Horie R. 1990. International cooperative study on the relationship between dietary factors and blood pressure: A report from the Cardiovascular Diseases and Alimentary Comparison (CARDIAC) study. *J Cardiovasc Pharmacol* 16:43S–47S.
- Yamori Y, Nara Y, Mizushima S, Sawamura M, Horie R. 1994. Nutritional factors for stroke and major cardiovascular diseases: International epidemiological comparison of dietary prevention. *Health Rep* 6:22–27.
- Yamori Y, Liu L, Ikeda K, Mizushima S, Nara Y, Simpson FO. 2001. Different associations of blood pressure with 24-hour urinary sodium excretion among pre- and post-menopausal women. *J Hypertens* 19:535–538.
- Yang J, Zhang H, Zhao L, Zhou B, Wu Y, Zhang X. 1997. Protein, salt and stroke mortality. *Can J Cardiol* 13:44B.

- You WC, Blot WJ, Chang YS, Ershow AG, Yang ZT, An Q, Henderson B, Xu GW, Fraumeni JF, Wang TG. 1988. Diet and high risk of stomach cancer in Shandong, China. *Cancer Res* 48:3518–3523.
- Young DB, McCaa RE, Pan YJ, Guyton AC. 1976. The natriuretic and hypotensive effects of potassium. *Circ Res* 38:84S–89S.
- Zarkadas M, Gougeon-Reyburn R, Marliss EB, Block E, Alton-Mackey M. 1989. Sodium chloride supplementation and urinary calcium excretion in postmenopausal women. *Am J Clin Nutr* 50:1088–1094.
- Zemel MB, Gualdoni SM, Sowers JR. 1986. Sodium excretion and plasma rennin activity in normotensive and hypertensive black adults as affected by dietary calcium and sodium. *J Hypertens* 4:343S–345S.
- Zhou BF, Stamler J, Dennis B, Moag-Stahlberg A, Okuda N, Robertson C, Zhao L, Chan Q, Elliott P. 2003. Nutrient intakes of middle-aged men and women in China, Japan, United Kingdom, and United States in the late 1990s: The INTERMAP Study. *J Hum Hypertens* 17: 623–630.
- Zoccali C, Mallamaci F, Parlongo S. 1994. The influence of salt intake on plasma calcitonin gene-related peptide in subjects with mild essential hypertension. *J Hypertens* 12:1249–1253.
- Zoia MC, Fanfulla F, Bruschi C, Basso O, De Marco R, Casali L, Cerveri I. 1995. Chronic respiratory symptoms, bronchial responsiveness and dietary sodium and potassium: A population based study. *Monaldi Arch Chest Dis* 50:104–108.

Ibid., Chapter 8, pp. 462–464.

- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- IOM. 2001. *Caffeine for the Sustainment of Mental Task Performance*. Washington, DC: National Academy Press.
- IOM. 2002/2005. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*. Washington, DC: The National Academies Press.
- IOM. 2003. *Dietary Reference Intakes: Applications in Dietary Planning*. Washington, DC: The National Academies Press.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Schoeller DA. 1995. Limitations in the assessment of dietary energy by self-report. *Metabolism* 44:18–22.

- Schoeller DA, Bandini LG, Dietz WH. 1990. Inaccuracies in self-reported intake identified by comparison with the doubly labelled water method. *Can J Physiol Pharmacol* 68:941–949.
- Taivainen H, Laitinen R, Tahtela R, Kiianmaa K, Valimaki MJ. 1995. Role of plasma vasopressin in changes of water balance accompanying acute alcohol intoxication. *Alcohol Clin Exp Res* 19:759–762.
- Vasan RS, Beiser A, Seshadri S, Larson MG, Kannel WB, D'Agostino RB, Levey D. 2002. Residual lifetime risk for developing hypertension in middle-aged women and men: The Framingham Heart Study. *J Am Med Assoc* 287:1003–1010.

## SULFATE

*Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate (ISBN 0-309-09158-6)*, Chapter 7, pp. 443–448.

- Ahearn GA, Murer H. 1984. Functional roles of  $\text{Na}^+$  and  $\text{H}^+$  in  $\text{SO}_4^{2-}$  transport by rabbit ileal brush border membrane vesicles. *J Membr Biol* 78:177–186.
- Ahmed A, Hamza HM. 1989. Barium sulfate absorption and sensitivity. *Radiology* 172:213–214.
- Allen HE, Halley-Henderson MA, Hass CN. 1989. Chemical composition of bottled mineral water. *Arch Environ Health* 44:102–116.
- Anast C, Kennedy R, Volk G, Adamson L. 1965. In vitro studies of sulfate transport by the small intestine of the rat, rabbit, and hamster. *J Lab Clin Med* 65:903–911.
- Anderson JO, Warnick RE, Dalai RK. 1975. Replacing dietary methionine and cysteine in chick diets with sulfate or other sulfur compounds. *Poultry Sci* 54:1122–1128.
- AWWA (American Water Works Association). 1995. AWWA *Comments on USEPA's Proposed Sulfate Rule*. Online. Available at <http://www.awwa.org/Advocacy/govtaff/sulfate.cfm>. Accessed February 25, 2003.
- Backer LC. 2000. Assessing the acute gastrointestinal effects of ingesting naturally occurring, high levels of sulfate in drinking water. *Crit Rev Clin Lab Sci* 37:389–400.
- Baker DH, Wood RJ. 1992. Cellular antioxidant status and human immunodeficiency virus replication. *Nutr Rev* 50:15–18.
- Batt ER. 1969. Sulfate accumulation by mouse intestine: Influence of age and other factors. *Am J Physiol* 217:1101–1104.
- Bauer JH. 1976. Oral administration of radioactive sulfate to measure extracellular fluid space in man. *J Appl Physiol* 40:648–650.
- Blum JE, Coe FL. 1977. Metabolic acidosis after sulfur ingestion. *N Engl J Med* 297:869–870.
- Byington MH, Howe JM, Clark HE. 1972. Effect of different levels of and proportions of methionine, cystine, choline, and inorganic sulfur on growth and body composition of young rats. *J Nutr* 102:219–227.
- Cardin CJ, Mason J. 1975. Sulphate transport by rat ileum. Effect of molybdate and other anions. *Biochim Biophys Acta* 394:46–54.
- Cardin CJ, Mason J. 1976. Molybdate and tungstate transfer by rat ileum. Competitive inhibition by sulphate. *Biochim Biophys Acta* 455:937–946.
- Carrier J, Aghdassi E, Cullen J, Allard JP. 2002. Iron supplementation increases disease activity and vitamin E ameliorates the effect in rats with dextran sulfate sodium-induced colitis. *J Nutr* 132:3146–3150.
- Chien L, Robertson H, Gerrard JW. 1968. Infantile gastroenteritis due to water with high sulfate content. *Can Med Assoc J* 99:102–104.
- Christl SU, Gibson GR, Cummings JH. 1992. Role of dietary sulphate in the regulation of methanogenesis in the human large intestine. *Gut* 33:1234–1238.
- Cocchetto DM, Levy G. 1981. Absorption of orally administered sodium sulfate in humans. *J Pharm Sci* 70:331–333.
- Cole DEC, Evrovski J. 2000. The clinical chemistry of inorganic sulfate. *Crit Rev Clin Lab Sci* 37:299–344.
- Cole DEC, Oulton M, Stirk LJ, Magor B. 1992. Increased inorganic sulfate concentrations in amniotic fluid. *J Perinat Med* 20:443–447.

- Drever JI. 1988. The hydrologic cycle. In: *The Geochemistry of Natural Waters*. 2nd ed. Englewood Cliffs, NJ: Prentice Hall. Pp. 1–14.
- EPA (U.S. Environmental Protection Agency). 1990. National primary and secondary drinking water regulations; Synthetic organic chemicals and inorganic; Proposed rule. *Fed Regist* 55:30370.
- EPA. 1999a. *Health Effects from Exposure to High Levels of Sulfate in Drinking Water Study*. EPA 815/R/99/001. Washington, DC: Office of Water, EPA.
- EPA. 1999b. *Health Effects from Exposure to Sulfate in Drinking Water Workshop*. EPA 815/R/99/002. Washington, DC: Office of Water, EPA.
- EPA. 2001. *Contaminant Candidate List Preliminary Regulatory Determination Support Document for Sulfate*. EPA 815/01/015. Washington, DC: Office of Water, EPA.
- EPA. 2002a. Announcement of preliminary regulatory determinations for priority contaminants on the drinking water contaminant candidate list. *Fed Regist* 67:38222–38244.
- EPA. 2002b. *2002 Edition of the Drinking Water Standards and Health Advisories*. EPA 822/R/02/038. Washington, DC: Office of Water, EPA.
- Esteban E, Rubin CH, McGeehin MA, Flanders WD, Baker MJ, Sinks TH. 1997. Evaluation of infant diarrhea associated with elevated levels of sulfate in drinking water: A case-control investigation in South Dakota. *Int J Occup Environ Health* 3:171–176.
- Field CW. 1972. Sulfur: Element and geochemistry. In: Fairbridge RW, ed. *The Encyclopedia of Geochemistry and Environmental Sciences*. New York: Van Nostrand Reinhold. Pp. 1142–1148.
- Florin THJ, Gibson GR, Neale G, Cummings JH. 1990. A role for sulfate reducing bacteria in ulcerative colitis? *Gastroenterology* 98:A170.
- Florin T, Neale G, Gibson GR, Christl SU, Cummings JH. 1991. Metabolism of dietary sulphate: Absorption and excretion in humans. *Gut* 32:766–773.
- Florin THJ, Neale G, Goretski S, Cummings JH. 1993. The sulfate content of foods and beverages. *J Food Comp Anal* 6:140–151.
- Garcia RAG, Stipanuk MH. 1992. The splanchnic organs, liver and kidney have unique roles in the metabolism of sulfur amino acids and their metabolites in rats. *J Nutr* 122:1693–1701.
- Gomez GG, Sandler RS, Seal E. 1995. High levels of inorganic sulfate cause diarrhea in neonatal piglets. *J Nutr* 125:2325–2332.
- Gordon RS, Sizer IW. 1955. Ability of sodium sulfate to stimulate growth of the chicken. *Science* 122:1270–1271.
- Greer FR, McCormick A, Loker J. 1986. Increased urinary excretion of inorganic sulfate in premature infants fed bovine milk protein. *J Pediatr* 109:692–697.
- Hamadeh MJ, Hoffer LJ. 2001. Use of sulfate production as a measure of short-term sulfur amino acid catabolism in humans. *Am J Physiol Endocrinol Metab* 280:E857–E866.
- Health Canada. 2002. *Summary Guidelines for Canadian Drinking Water Quality*. Online. Available at <http://www.hc-sc.gc.ca/waterquality>. Accessed February 25, 2003.
- Heizer WD, Sandler RS, Seal E Jr, Murray SC, Busby MG, Schliebe BG, Pusek SN. 1997. Intestinal effects of sulfate in drinking water on normal human subjects. *Dig Dis Sci* 42:1055–1061.
- Hoffer LJ. 2002. Methods for measuring sulfur amino acid metabolism. *Curr Opin Clin Nutr Metab Care* 5:511–517.
- Hoffer LJ, Kaplan LN, Hamadeh MJ, Grigoriu AC, Baron M. 2001. Sulfate could mediate the therapeutic effect of glucosamine sulfate. *Metabolism* 50:767–770.

- Holmes JH, Miller ES, Hlad CJ. 1960. Serum and urine sulfate changes in uremia. *Trans Am Soc Artif Intern Organs* 6:163–175.
- Hoppe B, Roth B, Bauerfeld C, Langman CB. 1998. Oxalate, citrate, and sulfate concentration in human milk compared with formula preparations: Influence on urinary anion excretion. *J Pediatr Gastroenterol Nutr* 27:383–386.
- Houterman S, van Faassen A, Ocke MC, Habets LHM, van Diejen-Visser MP, Bueno-de-Mesquita BH, Janknegt RA. 1997. Is urinary sulfate a biomarker for the intake of animal protein and meat? *Cancer Lett* 114:295–296.
- Ikem A, Odueyungbo S, Egiebor NO, Nyavor K. 2002. Chemical quality of bottled waters from three cities in eastern Alabama. *Sci Total Environ* 285:165–175.
- IOM (Institute of Medicine). 2002/2005. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*. Washington, DC: The National Academies Press.
- Izzo AA, Gaginella TS, Capasso F. 1996. The osmotic and intrinsic mechanisms of the pharmacological laxative action of oral high doses of magnesium sulphate. Importance of the release of digestive polypeptides and nitric oxide. *Magnes Res* 9:133–138.
- Kandylis K. 1983. Transfer of plasma from blood to rumen. A review. *J Dairy Sci* 66:2263–2270.
- Kaneko-Mohammed S, Hogben CAM. 1964. Ionic fluxes of *Rana pipens* stomach bathed by sulfate solutions. *Am J Physiol* 207:1173–1176.
- Kelly GS. 1998. Clinical applications of N-acetylcysteine. *Altern Med Rev* 3:114–127.
- Kirschbaum B. 1998. Effect of hemodialysis on the hypersulfatemia of chronic renal failure. *ASAIO J* 44:314–318.
- Kovatscheva EG, Popova JG. 1977. S-methylmethionine content in plant and animal tissues and stability during storage. *Nahrung* 21:465–472.
- Kuczmarski RJ, Ogden CL, Grummer-Strawn LM, Flegal KM, Guo SS, Wei R, Mei Z, Curtin LR, Roche AF, Johnson CL. 2000. CDC growth charts: United States. *Adv Data* 314:1–28.
- Langridge-Smith JE, Sellin JH, Field M. 1983. Sulfate influx across the rabbit ileal brush border membrane: Sodium and proton dependence, and substrate specificities. *J Membr Biol* 72:131–139.
- Machlin LJ, Pearson PB. 1956. Studies on utilization of sulfate sulfur for growth of the chicken. *Proc Soc Exp Biol Med* 93:204–206.
- Magee EA, Richardson CJ, Hughes R, Cummings JH. 2000. Contribution of dietary protein to sulfide production in the large intestine: An in vitro and a controlled feeding study in humans. *Am J Clin Nutr* 72:1488–1494.
- Marcus R, Watt J. 1969. Seaweeds and ulcerative colitis in laboratory animals. *Lancet* 2:489–490.
- Marcus R, Watt J. 1974. Ulcerative disease of the colon in laboratory animals induced by pepsin inhibitors. *Gastroenterology* 67:473–483.
- Michalk D, Tschope W, Bohles HJ, Mehls O. 1981. Possible role of inorganic sulphate in the pathogenesis of hyperparathyroidism in chronic renal failure. *Proc Eur Dial Transplant Assoc* 18:561–566.
- Miller EL, Huang YX, Kasinathan S, Rayner B, Luzzana U, Moretti VM, Valfr F, Torrisen KR, Jensen HB, Opstredt J. 2001. Heat damaged protein has reduced ileal true digestibility of cystine and aspartic acid in chickens. *J Anim Sci* 79:65.
- Moore EW. 1952. Physiological effects of the consumption of saline drinking water. *Bulletin of the Subcommittee on Water Supply, Appendix B*. Washington, DC: National Academy of Sciences. Pp. 221–227.

- Moore JW. 1991. Sulfur. In: DeSanto RS, ed. *Inorganic Contaminants of Surface Water, Research and Monitoring Priorities*. New York: Springer-Verlag. Pp. 266–277.
- Mordes JP. 1978. Excess magnesium. *Pharmacol Rev* 29:273–300.
- Morris ME, Levy G. 1983. Serum concentration and renal excretion by normal adults of inorganic sulfate after acetaminophen, ascorbic acid, or sodium sulfate. *Clin Pharmacol Ther* 33:529–536.
- Morris ME, LeRoy S, Sutton SC. 1987. Absorption of magnesium from orally administered magnesium sulfate in man. *Clin Toxicol* 25:371–382.
- Nakanishi T, Otaki Y, Hasuike Y, Nanami M, Itahana R, Miyagawa K, Nishikage H, Izumi M, Takamitsu Y. 2002. Association of hyperhomocysteinemia with plasma sulfate and urine sulfate excretion in patients with progressive renal disease. *Am J Kidney Dis* 40:909–915.
- NRC (National Research Council). 1980. *Mineral Tolerance of Domestic Animals*. Washington, DC: National Academy Press.
- NRC. 1994. *Nutrient Requirements of Poultry*. 9th ed. Washington, DC: National Academy Press.
- Ohkusa T. 1985. Production of experimental ulcerative colitis in hamsters by dextran sulfate sodium and change in intestinal microflora. *Jpn J Gastroenterol* 82:1327–1336.
- Okayasu I, Hatakeyama S, Yamada M, Ohkusa T, Inagaki Y, Nakaya R. 1990. A novel method in the induction of reliable experimental acute and chronic ulcerative colitis in mice. *Gastroenterology* 98:694–702.
- Parsons CM, Hashimoto K, Wedekind KJ, Han Y, Baker DH. 1992. Effect of overprocessing on availability of amino acids and energy in soybean meal. *Poultry Sci* 71:133–140.
- Paterson DW, Wahlstrom RC, Libal GW, Olson OE. 1979. Effects of sulfate in water on swine reproduction and young pig performance. *J Anim Sci* 49:664–667.
- Pitcher MCL, Cummings JH. 1996. Hydrogen sulfide: A bacterial toxin in ulcerative colitis? *Gut* 39:1–4.
- Pitcher MCL, Gibson GR, Neale G, Cummings JH. 1994. Gentamicin kills multiple drug-resistant sulfate-reducing bacteria in patients with ulcerative colitis. *Gastroenterology* 106:A753.
- Pitcher MCL, Beatty ER, Cummings JH. 1995. Salicylates inhibit bacterial sulphide production within the colonic lumen in ulcerative colitis. *Gut* 37:A15S.
- Ricci J, Oster JR, Gutierrez R, Schlessinger FB, Rietberg B, O'Sullivan MJ, Clerch AR, Vaamonde CA. 1990. Influence of magnesium sulfate-induced hypermagnesemia on the anion gap: Role of hypersulfatemia. *Am J Nephrol* 10:409–411.
- Roediger WEW, Duncan A. 1996. 5-ASA decreases colonic sulfide formation: Implications for ulcerative colitis. *Med Sci Res* 24:27–29.
- Roediger WEW, Moore J, Babidge W. 1997. Colonic sulfide in pathogenesis and treatment of ulcerative colitis. *Dig Dis Sci* 42:1571–1579.
- Sabry ZI, Shadarevian SB, Cowan JW, Campbell JA. 1965. Relationship of dietary intake of sulphur amino-acids to urinary excretion of inorganic sulphate in man. *Nature* 206:931–933.
- Sasse CE, Baker DH. 1974a. Factors affecting sulfate-sulfur utilization by the young chick. *Poultry Sci* 53:652–662.
- Sasse CE, Baker DH. 1974b. Sulfur utilization by the chick with emphasis on the effect of inorganic sulfate on the cystine-methionine interrelationship. *J Nutr* 104:244–251.

- Schwartz SM, Carroll HM, Scharschmidt LA. 1986. Sublimed (inorganic) sulfur ingestion: A cause of life-threatening metabolic acidosis with a high anion gap. *Arch Intern Med* 146:1437–1438.
- Shils ME, Olson JA, Shike M, Ross AC. 1999. *Modern Nutrition in Health and Disease*. 9th ed. Baltimore, MD: Williams and Wilkins.
- Smith JT. 1973. An optimal level of inorganic sulfate for the diet of a rat. *J Nutr* 103:1008–1011.
- Smithgall JM. 1985. The copper controlled diet: Current aspects of dietary copper restriction in management of copper metabolism disorders. *J Am Diet Assoc* 85:609–611.
- Soares JH. 1974. Experiments on the requirement of inorganic sulfate by the chick. *Poultry Sci* 53:246–252.
- Tallgren LG. 1980. Inorganic sulfates in relation to serum thyroxin level and in renal failure. *Acta Med Scand* 640:1S–100S.
- Til HP, Feron VJ. 1992. Toxicology of sulphiting agents. I: Animal studies. *Food Addit Contam* 9:587–595.
- Truelove SC. 1961. Ulcerative colitis provoked by milk. *Br Med J* 1:154–160.
- Wedzicha BL. 1992. Chemistry of sulphiting agents in food. *Food Addit Contam* 9:449–459.
- WHO (World Health Organization). 1984. *Guidelines for Drinking Water Quality. Volume 1. Recommendations*. Geneva: WHO.
- Wierzbicka GT, Hagen TM, Jones DP. 1989. Glutathione in food. *J Food Comp Anal* 2:327–337.
- Zezulka AY, Calloway DH. 1976. Nitrogen retention in men fed isolated soybean protein supplemented with L-methionine, D-methionine, N-acetyl-L-methionine, or inorganic sulfate. *J Nutr* 106:1286–1291.

Ibid., Chapter 8, pp. 462–464.

- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances Be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- IOM. 2001. *Caffeine for the Sustainment of Mental Task Performance*. Washington, DC: National Academy Press.
- IOM. 2002/2005. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*. Washington, DC: The National Academies Press.
- IOM. 2003. *Dietary Reference Intakes: Applications in Dietary Planning*. Washington, DC: The National Academies Press.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.

- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Schoeller DA. 1995. Limitations in the assessment of dietary energy by self-report. *Metabolism* 44:18–22.
- Schoeller DA, Bandini LG, Dietz WH. 1990. Inaccuracies in self-reported intake identified by comparison with the doubly labelled water method. *Can J Physiol Pharmacol* 68:941–949.
- Taivainen H, Laitinen R, Tahtela R, Kianmaa K, Valimaki MJ. 1995. Role of plasma vasopressin in changes of water balance accompanying acute alcohol intoxication. *Alcohol Clin Exp Res* 19:759–762.
- Vasan RS, Beiser A, Seshadri S, Larson MG, Kannel WB, D'Agostino RB, Levey D. 2002. Residual lifetime risk for developing hypertension in middle-aged women and men: The Framingham Heart Study. *J Am Med Assoc* 287:1003–1010.

## ZINC

*Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*  
(ISBN 0-309-07290-5), Chapter 12, pp. 489–501.

- Abrams SA, Wen J, Stuff JE. 1997. Absorption of calcium, zinc, and iron from breast milk by five- to seven-month-old infants. *Pediatr Res* 41:384–390.
- Aggett PJ. 1989. Severe zinc deficiency. In: Mills CF, ed. *Zinc in Human Biology*. New York: Springer-Verlag. Pp. 259–279.
- Alexander D, Ball MJ, Mann J. 1994. Nutrient intake and haematological status of vegetarians and age-sex matched omnivores. *Eur J Clin Nutr* 48:538–546.
- Alexander FW, Clayton BE, Delves HT. 1974. Mineral and trace-metal balances in children receiving normal and synthetic diets. *Quart J Med* 169:89–111.
- Allen JC, Keller RP, Archer P, Neville MC. 1991. Studies in human lactation: Milk composition and daily secretion rates of macronutrients in the first year of lactation. *Am J Clin Nutr* 54:69–80.
- Anderson BM, Gibson RS, Sabry JH. 1981. The iron and zinc status of long-term vegetarian women. *Am J Clin Nutr* 34:1042–1048.
- Anderson RR. 1993. Longitudinal changes of trace elements in human milk during the first 5 months of lactation. *Nutr Res* 13:499–510.
- Aquilio E, Spagnoli R, Seri S, Bottone G, Spennati G. 1996. Trace element content in human milk during lactation of preterm newborns. *Biol Trace Elem Res* 51:63–70.
- Artacho R, Ruiz-Lopez MD, Gamez C, Puerta A, Lopez MC. 1997. Serum concentration and dietary intake of Zn in healthy institutionalized elderly subjects. *Sci Total Environment* 205:159–165.
- August D, Janghorbani M, Young VR. 1989. Determination of zinc and copper absorption at three dietary Zn-Cu ratios by using stable isotope methods in young adult and elderly subjects. *Am J Clin Nutr* 50:1457–1463.
- Baer MT, King JC. 1984. Tissue zinc levels and zinc excretion during experimental zinc depletion in young men. *Am J Clin Nutr* 39:556–570.
- Bales CW, DiSilvestro RA, Currie KL, Plaisted CS, Joung H, Galanos AN, Lin PH. 1994. Marginal zinc deficiency in older adults: Responsiveness of zinc status indicators. *J Am Coll Nutr* 13:455–462.
- Beck FW, Kaplan J, Fine N, Handschu W, Prasad AS. 1997a. Decreased expression of CD73 (ecto-5'-nucleotidase) in the CD8+ subset is associated with zinc deficiency in human patients. *J Lab Clin Med* 130:147–156.
- Beck FW, Prasad AS, Kaplan J, Fitzgerald JT, Brewer GJ. 1997b. Changes in cytokine production and T cell subpopulations in experimentally induced zinc-deficient humans. *Am J Physiol* 272:E1002–E1007.
- Behall KM, Scholfield DJ, Lee K, Powell AS, Moser PB. 1987. Mineral balance in adult men: Effect of four refined fibers. *Am J Clin Nutr* 46:307–314.
- Berg JM, Shi Y. 1996. The galvanization of biology: A growing appreciation for the roles of zinc. *Science* 271:1081–1085.
- Berglund M, Akesson A, Nermell B, Vahter M. 1994. Intestinal absorption of dietary cadmium in women depends on body iron stores and fiber intake. *Environ Health Perspect* 102:1058–1066.

- Bhutta ZA, Nizami SQ, Isani Z. 1999. Zinc supplementation in malnourished children with persistent diarrhea in Pakistan. *Pediatrics* 103:e42. [Online]. Available: <http://www.pediatrics.org/cgi/content/full/103/4/e42> [accessed June 5, 2000].
- Biego GH, Joyeux M, Hartemann P, Debry G. 1998. Determination of mineral contents in different kinds of milk and estimation of dietary intake in infants. *Food Addit Contam* 15:775–781.
- Black MR, Medeiros DM, Brunett E, Welke R. 1988. Zinc supplements and serum lipids in young adult white males. *Am J Clin Nutr* 47:970–975.
- Bogden JD, Oleske JM, Munves EM, Lavenhar MA, Bruening KS, Kemp FW, Holding KJ, Denny TN, Louria DB. 1987. Zinc and immunocompetence in the elderly: Baseline data on zinc nutriture and immunity in supplemented subjects. *Am J Clin Nutr* 46:101–109.
- Botash AS, Nasca J, Dubowy R, Weinberger HL, Oliphant M. 1992. Zinc-induced copper deficiency in an infant. *Am J Dis Child* 146:709–711.
- Boukaiba N, Flament C, Acher S, Chappuis P, Piau A, Fusselier M, Dardenne M, Lemonnier D. 1993. A physiological amount of zinc supplementation: Effects on nutritional, lipid, and thymic status in an elderly population. *Am J Clin Nutr* 57:566–572.
- Brants HA, Lowik MR, Westenbrink S, Hulshof KF, Kistemaker C. 1990. Adequacy of a vegetarian diet at old age (Dutch Nutrition Surveillance System). *J Am Coll Nutr* 9:292–302.
- Brewer GJ, Yuzbasiyan-Gurkan V, Johnson V, Dick RD, Wang Y. 1993. Treatment of Wilson's Disease with zinc XII: Dose regimen requirements. *Am J Med Sci* 305:199–202.
- Brown KH, Peerson JM, Allen LH. 1998. Effect of zinc supplementation on children's growth: A meta-analysis of intervention trials. *Bibl Nutr Dieta* 54:76–83.
- Bunker VW, Lawson MS, Delves HT, Clayton BE. 1982. Metabolic balance studies for zinc and nitrogen in healthy elderly subjects. *Hum Nutr Clin Nutr* 36:213–221.
- Burke DM, DeMicco FJ, Taper LJ, Ritchey SJ. 1981. Copper and zinc utilization in elderly adults. *J Gerontol* 36:558–563.
- Butte NF, Garza C, Smith EO, Nichols BL. 1984. Human milk intake and growth in exclusively breast-fed infants. *J Pediatr* 104:187–195.
- Cakman I, Kirchner H, Rink L. 1997. Zinc supplementation reconstitutes the production of interferon- $\alpha$  by leukocytes from elderly persons. *J Interferon Cytokine Res* 17:469–472.
- Casey CE, Hambidge KM, Neville MC. 1985. Studies in human lactation: Zinc, copper, manganese and chromium in human milk in the first month of lactation. *Am J Clin Nutr* 41:1193–1200.
- Casey CE, Neville MC, Hambidge KM. 1989. Studies in human lactation: Secretion of zinc, copper, and manganese in human milk. *Am J Clin Nutr* 49:773–785.
- Caulfield LE, Zavaleta N, Figueroa A. 1999a. Adding zinc to prenatal iron and folate supplements improves maternal and neonatal zinc status in a Peruvian population. *Am J Clin Nutr* 69:1257–1263.
- Caulfield LE, Zavaleta N, Figueroa A, Leon Z. 1999b. Maternal zinc supplementation does not affect size at birth or pregnancy duration in Peru. *J Nutr* 129:1563–1568.
- Chandra RK. 1984. Excessive intake of zinc impairs immune responses. *J Am Med Assoc* 252:1443–1446.

- Cheek DB, Reba RC, Woodward K. 1968. Cell growth and the possible role of trace minerals. In: Cheek DB, ed. *Human Growth; Body Composition, Cell Growth, Energy, and Intelligence*. Philadelphia: Lea and Febiger. Pp. 424–439.
- Chen W, Chiang TP, Chen TC. 1991. Serum zinc and copper during long-term total parenteral nutrition. *J Formos Med Assoc* 90:1075–1080.
- Chesters JK. 1997. Zinc. In: O'Dell BL, Sunde RA, eds. *Handbook of Nutritionally Essential Mineral Elements*. New York: Marcel Dekker. Pp. 185–230.
- Cole TB, Wenzel HJ, Kafer KE, Schwartzkroin PA, Palmiter RD. 1999. Elimination of zinc from synaptic vesicles in the intact mouse brain by disruption of the ZnT3 gene. *Proc Natl Acad Sci USA* 96:1716–1721.
- Colin MA, Taper LJ, Ritchey SJ. 1983. Effect of dietary zinc and protein levels on the utilization of zinc and copper by adult females. *J Nutr* 113:1480–1488.
- Coudray C, Bellanger J, Castiglia-Delavaud C, Remesy C, Vermorel M, Rayssignuier Y. 1997. Effect of soluble or partly soluble dietary fibres supplementation on absorption and balance of calcium, magnesium, iron and zinc in healthy young men. *Eur J Clin Nutr* 51:375–380.
- Cousins RJ. 1985. Absorption, transport, and hepatic metabolism of copper and zinc: Special reference to metallothionein and ceruloplasmin. *Physiol Rev* 65:238–309.
- Cousins RJ. 1989a. Systemic transport of zinc. In: Mills CF, ed. *Zinc in Human Biology*. New York: Springer-Verlag. Pp. 79–93.
- Cousins RJ. 1989b. Theoretical and practical aspects of zinc uptake and absorption. *Adv Exp Med Biol* 249:3–12.
- Cousins RJ. 1994. Metal elements and gene expression. *Ann Rev Nutr* 14:449–469.
- Cousins RJ. 1996. Zinc. In: Filer LJ, Ziegler EE, eds. *Present Knowledge in Nutrition*, 7th ed. Washington, DC: International Life Science Institute-Nutrition Foundation. Pp. 293–306.
- Couzy F, Kastenmayer P, Mansourian R, Guinchard S, Munoz-Box R, Dirren H. 1993. Zinc absorption in healthy elderly humans and the effect of diet. *Am J Clin Nutr* 58:690–694.
- Dalton TP, Bittel D, Andrews GK. 1997. Reversible activation of mouse metal response element-binding transcription factor 1 DNA binding involves zinc interaction with the zinc finger domain. *Molec Cell Biol* 17:2781–2789.
- Davidsson L, Mackenzie J, Kastenmayer P, Aggett PJ, Hurrell RF. 1996. Zinc and calcium apparent absorption from an infant cereal: A stable isotope study in healthy infants. *Br J Nutr* 75:291–300.
- Davis CD, Milne DB, Nielsen FH. 2000. Changes in dietary zinc and copper affect zinc-status indicators of postmenopausal women, notably extracellular superoxide dismutase and amyloid precursor proteins. *Am J Clin Nutr* 71:781–788.
- Devine A, Rosen C, Mohan S, Baylink D, Prince RL. 1998. Effects of zinc and other nutritional factors on insulin-like growth factor I and insulin-like growth factor binding proteins in postmenopausal women. *Am J Clin Nutr* 68:200–206.
- Dewey KG, Cohen RJ, Brown KH, Rivera LL. 1999. Age of introduction of complementary foods and growth of term, low-birth-weight, breast-fed infants: A randomized intervention study in Honduras. *Am J Clin Nutr* 69:679–686.
- Donovan UM, Gibson RS. 1995. Iron and zinc status of young women aged 14 to 19 years consuming vegetarian and omnivorous diets. *J Am Coll Nutr* 14:463–472.
- Donovan UM, Gibson RS. 1996. Dietary intakes of adolescent females consuming vegetarian, semi-vegetarian, and omnivorous diets. *J Adolesc Health* 18:292–300.

- Duchateau J, Delepesse G, Vrijens R, Collet H. 1981. Beneficial effects of oral zinc supplementation on the immune response of old people. *Am J Med* 70:1001–1004.
- Ellis R, Kelsay JL, Reynolds RD, Morris ER, Moser PB, Frazier CW. 1987. Phytate:zinc and phytate × calcium:zinc millimolar ratios in self-selected diets of Americans, Asian Indians, and Nepalese. *J Am Diet Assoc* 87:1043–1047.
- Faber M, Gouws E, Spinnler Benade AJ, Labadarios D. 1986. Anthropometric measurements, dietary intake and biochemical data of South African lacto-ovo vegetarians. *S Afr Med J* 69:733–738.
- Failla ML. 1999. Considerations for determining “optimal nutrition” for copper, zinc, manganese and molybdenum. *Proc Nutr Soc* 58:497–505.
- Fairweather-Tait SJ, Wharf SG, Fox TE. 1995. Zinc absorption in infants fed iron-fortified weaning food. *Am J Clin Nutr* 62:785–789.
- Ferguson EL, Gibson RS, Opare-Obisaw C, Ounpuu S, Thompson LU, Lehrfeld J. 1993. The zinc nutriture of preschool children living in two African countries. *J Nutr* 123:1487–1496.
- Festa MD, Anderson HL, Dowdy RP, Ellersieck MR. 1985. Effect of zinc intake on copper excretion and retention in men. *Am J Clin Nutr* 41:285–292.
- Fischer PWF, Giroux A, L’Abbe MR. 1984. Effect of zinc supplementation on copper status in adult man. *Am J Clin Nutr* 40:743–746.
- Fortes C, Forastiere F, Agabiti N, Fano V, Pacifici R, Virgili F, Piras G, Guidi L, Bartoloni C, Tricerri A, Zuccaro P, Ebrahim S, Perucci CA. 1998. The effect of zinc and vitamin A supplementation on immune response in an older population. *J Am Geriatr Soc* 46:19–26.
- Fosmire CJ. 1990. Zinc toxicity. *Am J Clin Nutr* 51:225–227.
- Fransson GB, Lonnerdal B. 1982. Zinc, copper, calcium, and magnesium in human milk. *J Pediatr* 101:504–508.
- Freeland-Graves JH, Bodzy PW, Eppright MA. 1980a. Zinc status of vegetarians. *J Am Diet Assoc* 77:655–661.
- Freeland-Graves JH, Ebangit ML, Hendrikson PJ. 1980b. Alterations in zinc absorption and salivary sediment zinc after a lacto-ovo-vegetarian diet. *Am J Clin Nutr* 33:1757–1766.
- Freeland-Graves JH, Friedman BJ, Han WH, Shorey RL, Young R. 1982. Effect of zinc supplementation on plasma high-density lipoprotein cholesterol and zinc. *Am J Clin Nutr* 35:988–992.
- Fung EB, Ritchie LD, Woodhouse LR, Roehl R, King JC. 1997. Zinc absorption in women during pregnancy and lactation: A longitudinal study. *Am J Clin Nutr* 66:80–88.
- Ganapathy SN, Booker LK, Craven R, Edwards CH. 1981. Trace minerals, amino acids, and plasma proteins in adult men fed wheat diets. *J Am Diet Assoc* 78:490–497.
- Gibson RS. 1994. Content and bioavailability of trace elements in vegetarian diets. *Am J Clin Nutr* 59:1223S–1232S.
- Gibson RS, Vanderkooy PD, MacDonald AC, Goldman A, Ryan BA, Berry M. 1989. A growth-limiting, mild zinc-deficiency syndrome in some southern Ontario boys with low height percentiles. *Am J Clin Nutr* 49:1266–1273.
- Gibson RS, Donovan UM, Heath AL. 1997. Dietary strategies to improve the iron and zinc nutriture of young women following a vegetarian diet. *Plant Foods Hum Nutr* 51:1–16.

- Gibson RS, Heath AL, Prosser N, Parnell W, Donovan UM, Green T, McLaughlin KE, O'Connor DL, Bettger W, Skeaff CM. 2000. Are young women with low iron stores at risk of zinc as well as iron deficiency? In: Roussel AM, Anderson RA, Favrier A, eds. *Trace Elements in Man and Animals 10*. New York: Kluwer Academic. Pp. 323–328.
- Goldenberg RL, Tamura T, Neggers Y, Copper RL, Johnston KE, DuBard MB, Hauth JC. 1995. The effect of zinc supplementation on pregnancy outcome. *J Am Med Assoc* 274:463–468.
- Greger JL, Snedeker SM. 1980. Effect of dietary protein and phosphorus levels on the utilization of zinc, copper and manganese by adult males. *J Nutr* 110:2243–2253.
- Greger JL, Baligar P, Abernathy RP, Bennett OA, Peterson T. 1978. Calcium, magnesium, phosphorus, copper, and manganese balance in adolescent females. *Am J Clin Nutr* 31:117–121.
- Grider A, Bailey LB, Cousins RJ. 1990. Erythrocyte metallothionein as an index of zinc status in humans. *Proc Natl Acad Sci USA* 87:1259–1262.
- Günes C, Heuchel R, Georgiev O, Müller K-H, Lichtlen P, Blüthmann H, Marino S, Aguzzi A, Schaffner W. 1998. Embryonic lethality and liver degeneration in mice lacking the metal-responsive transcriptional activator MTF-1. *Embo J* 17:2846–2854.
- Gunshin H, Mackenzie B, Berger UV, Gunshin Y, Romero MF, Boron WF, Nussberger S, Gollan JL, Hediger MA. 1997. Cloning and characterization of a mammalian proton-coupled metal-ion transporter. *Nature* 388:482–488.
- Hallfrisch J, Powell A, Carafelli C, Reiser S, Prather ES. 1987. Mineral balances of men and women consuming high fiber diets with complex or simple carbohydrate. *J Nutr* 117:48–55.
- Hambidge KM. 1989. Mild zinc deficiency in human subjects. In: Mills CF, ed. *Zinc in Human Biology*. New York: Springer-Verlag. Pp. 281–296.
- Hambidge KM, Hambidge C, Jacobs M, Baum JD. 1972. Low levels of zinc in hair, anorexia, poor growth, and hypoguesia in children. *Pediatr Res* 6:868–874.
- Hambidge KM, Chavez MN, Brown RM, Walravens PA. 1979a. Zinc nutritional status of young middle-income children and effects of consuming zinc-fortified breakfast cereals. *Am J Clin Nutr* 32:2532–2539.
- Hambidge KM, Walravens PA, Casey CE, Brown RM, Bender C. 1979b. Plasma zinc concentrations of breast-fed infants. *J Pediatr* 94:607–608.
- Hambidge KM, Krebs NF, Jacobs MA, Favier A, Guyette L, Ikle DN. 1983. Zinc nutritional status during pregnancy: A longitudinal study. *Am J Clin Nutr* 37:429–442.
- Han O, Failla ML, Hill AD, Morris ER, Smith JC Jr. 1994. Inositol phosphates inhibit uptake and transport of iron and zinc by a human intestinal cell line. *J Nutr* 124:580–587.
- Harland BF, Peterson M. 1978. Nutritional status of lacto-ovo vegetarian Trappist monks. *J Am Diet Assoc* 72:259–264.
- Harland BF, Smith SA, Howard MP, Ellis R, Smith JC Jr. 1988. Nutritional status and phytate:zinc and phytate x calcium:zinc dietary molar ratios of lacto-ovo vegetarian Trappist monks: 10 years later. *J Am Diet Assoc* 88:1562–1566.
- Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. 1993. Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: The DARLING Study. *Am J Clin Nutr* 58:152–161.

- Hess FM, King JC, Margen S. 1977. Zinc excretion in young women on low zinc intakes and oral contraceptive agents. *J Nutr* 107:1610–1620.
- Holbrook JT, Smith JC Jr, Reiser S. 1989. Dietary fructose or starch: Effects on copper, zinc, iron, manganese, calcium, and magnesium balances in humans. *Am J Clin Nutr* 49:1290–1294.
- Hooper PL, Visconti L, Garry PJ, Johnson GE. 1980. Zinc lowers high-density lipoprotein-cholesterol levels. *J Am Med Assoc* 244:1960–1961.
- Hunt CD, Johnson PE, Herbel J, Mullen LK. 1992. Effects of dietary zinc depletion on seminal volume and zinc loss, serum testosterone concentrations, and sperm morphology in young men. *Am J Clin Nutr* 56:148–157.
- Hunt IF, Murphy NJ, Henderson C. 1988. Food and nutrient intake of Seventh-day Adventist women. *Am J Clin Nutr* 48:850–851.
- Hunt JR. 1996. Bioavailability algorithms in setting recommended dietary allowances: Lessons from iron, applications to zinc. *J Nutr* 126:2345S–2353S.
- Hunt JR, Mullen LK, Lykken GI. 1992. Zinc retention from an experimental diet based on the US FDA Total Diet Study. *Nutr Res* 12:1335–1344.
- Hunt JR, Gallagher SK, Johnson LK, Lykken GI. 1995. High- versus low-meat diets: Effects on zinc absorption, iron status, and calcium, copper, iron, magnesium, manganese, nitrogen, phosphorus, and zinc balance in postmenopausal women. *Am J Clin Nutr* 62:621–632.
- Hunt JR, Matthys LA, Johnson LK. 1998. Zinc absorption, mineral balance, and blood lipids in women consuming controlled lactoovovegetarian and omnivorous diets for 8 weeks. *Am J Clin Nutr* 67:421–430.
- Huse M, Eck MJ, Harrison SC. 1998. A Zn<sup>2+</sup> ion links the cytoplasmic tail of CD4 and the N-terminal region of Lck. *J Biol Chem* 273:18729–18733.
- Jackson JL, Lesho E, Peterson C. 2000. Zinc and the common cold: A meta-analysis revisited. *J Nutr* 130:1512S–1515S.
- Jackson MJ, Jones DA, Edwards RH, Swainbank IG, Coleman ML. 1984. Zinc homeostasis in man: Studies using a new stable isotope-dilution technique. *Br J Nutr* 51:199–208.
- Jacob C, Maret W, Vallee BL. 1998. Control of zinc transfer between thionein, metallothionein, and zinc proteins. *Proc Natl Acad Sci USA* 95:3489–3494.
- Janelle KC, Barr SI. 1995. Nutrient intakes and eating behavior scores of vegetarian and nonvegetarian women. *J Am Diet Assoc* 95:180–186, 189.
- Johansson G, Widerstrom L. 1994. Change from mixed diet to lactovegetarian diet: Influence on IgA levels in blood and saliva. *Scand J Dent Res* 102:350–354.
- Johnson MA, Baier MJ, Greger JL. 1982. Effects of dietary tin on zinc, copper, iron, manganese, and magnesium metabolism of adult males. *Am J Clin Nutr* 35:1332–1338.
- Johnson PE, Evans GW. 1978. Relative zinc availability in human breast milk, infant formulas, and cow's milk. *Am J Clin Nutr* 31:416–421.
- Johnson PE, Hunt CD, Milne DB, Mullen LK. 1993. Homeostatic control of zinc metabolism in men: Zinc excretion and balance in men fed diets low in zinc. *Am J Clin Nutr* 57:557–565.
- Kadrabova J, Madaric A, Kovacikova Z, Ginter E. 1995. Selenium status, plasma zinc, copper, and magnesium in vegetarians. *Biol Trace Elem Res* 50:13–24.
- Kaji M, Gotoh M, Takagi Y, Masuda H, Kimura Y, Uenoyama Y. 1998. Studies to determine the usefulness of the zinc clearance test to diagnose marginal zinc deficiency and the effects of oral zinc supplementation for short children. *J Am Coll Nutr* 17:388–391.

- Kant AK, Moser-Veillon PB, Reynolds RD. 1989. Dietary intakes and plasma concentrations of zinc, copper, iron, magnesium, and selenium of young, middle aged, and older men. *Nutr Res* 9:717–724.
- Kauwell GP, Bailey LB, Gregory JF 3rd, Bowling DW, Cousins RJ. 1995. Zinc status is not adversely affected by folic acid supplementation and zinc intake does not impair folate utilization in human subjects. *J Nutr* 125:66–72.
- Kelsay JL, Frazier CW, Prather ES, Canary JJ, Clark WM, Powell AS. 1988. Impact of variation in carbohydrate intake on mineral utilization by vegetarians. *Am J Clin Nutr* 48:875–879.
- Kies CV. 1988. Mineral utilization of vegetarians: Impact of variation in fat intake. *Am J Clin Nutr* 48: 884–887.
- King JC. 1990. Assessment of zinc status. *J Nutr* 120:1474–1479.
- King JC, Keen CL. 1999. Zinc. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th ed. Baltimore: Williams & Wilkins. Pp. 223–239.
- King JC, Turnlund JR. 1989. Human zinc requirements. In: Mills CF, ed. *Zinc in Human Biology*. London: Springer-Verlag. Pp. 335–350.
- King JC, Stein T, Doyle M. 1981. Effect of vegetarianism on the zinc status of pregnant women. *Am J Clin Nutr* 34:1049–1055.
- King JC, Hambidge KM, Westcott JL, Kern DL, Marshall G. 1994. Daily variation in plasma zinc concentrations in women fed meals at six-hour intervals. *J Nutr* 124:508–516.
- Kirksey A, Ernst JA, Roepke JL, Tsai TL. 1979. Influence of mineral intake and use of oral contraceptives before pregnancy on the mineral content of human colostrum and of more mature milk. *Am J Clin Nutr* 32:30–39.
- Klug A, Schwabe JWR. 1995. Zinc fingers. *FASEB J* 9:597–604.
- Krajcovicova-Kudlackova M, Simoncic R, Babinska K, Bederova A, Brtkova A, Magalova T, Grancicova E. 1995. Selected vitamins and trace elements in blood of vegetarians. *Ann Nutr Metab* 39:334–339.
- Krebs NF, Hambidge KM. 1986. Zinc requirements and zinc intakes of breast-fed infants. *Am J Clin Nutr* 43:288–292.
- Krebs NF, Hambidge KM, Jacobs MA, Rasbach JO. 1985. The effects of a dietary zinc supplement during lactation on longitudinal changes in maternal zinc status and milk zinc concentrations. *Am J Clin Nutr* 41:560–570.
- Krebs NF, Reidinger CJ, Robertson AD, Hambidge KM. 1994. Growth and intakes of energy and zinc in infants fed human milk. *J Pediatr* 124:32–39.
- Krebs NF, Reidinger CJ, Hartley S, Robertson AD, Hambidge KM. 1995. Zinc supplementation during lactation: Effects on maternal status and milk zinc concentrations. *Am J Clin Nutr* 61:1030–1036.
- Krebs NF, Reidinger CJ, Miller LV, Hambidge KM. 1996. Zinc homeostasis in breast-fed infants. *Pediatr Res* 39:661–665.
- Kuczmarski RJ, Ogden CL, Grummer-Strawn LM, Flegal KM, Guo SS, Wei R, Mei Z, Curtin LR, Roche AF, Johnson CL. 2000. *CDC Growth Charts: United States*. Advance data from vital health statistics. No. 314. Hyattsville, MD: National Center for Health Statistics.
- Kumar S. 1976. Effect of zinc supplementation on rats during pregnancy. *Nutr Rpts Intl* 13:33–36.
- Lee DY, Prasad AS, Hydrick-Adair C, Brewer G, Johnson PE. 1993. Homeostasis of zinc in marginal human zinc deficiency: Role of absorption and endogenous excretion of zinc. *J Lab Clin Med* 122:549–556.

- Lee HH, Prasad AS, Brewer GJ, Owyang C. 1989. Zinc absorption in human small intestine. *Am J Physiol* 256:G87–G91.
- Levin N, Rattan J, Gilat T. 1986. Mineral intake and blood levels in vegetarians. *Isr J Med Sci* 22:105–108.
- Lin RS, Rodriguez C, Veillette A, Lodish HF. 1998. Zinc is essential for binding of p56<sup>lck</sup> to CD4 and CD8α. *J Biol Chem* 273:32878–32882.
- Lonnerdal B. 1989. Intestinal absorption of zinc. In: Mills CF, ed. *Zinc in Human Biology*. New York: Springer-Verlag. Pp. 33–55.
- Lonnerdal B, Keen CL, Hurley LS. 1981. Iron, copper, zinc and manganese in milk. *Ann Rev Nutr* 1:149–174.
- Lonnerdal B, Bell JG, Hendrickx AG, Burns RA, Keen CL. 1988. Effect of phytate removal on zinc absorption from soy formula. *Am J Clin Nutr* 48:1301–1306.
- Lowik MR, Schrijver J, Odink J, van den Berg H, Wedel M. 1990. Long-term effects of a vegetarian diet on the nutritional status of elderly people (Dutch Nutrition Surveillance System). *J Am Coll Nutr* 9:600–609.
- Mahalko JR, Sandstead HH, Johnson LK, Milne DB. 1983. Effect of a moderate increase in dietary protein on the retention and excretion of Ca, Cu, Fe, Mg, P, and Zn by adult males. *Am J Clin Nutr* 37:8–14.
- Mares-Perlman JA, Subar AF, Block G, Greger JL, Luby MH. 1995. Zinc intake and sources in the US adult population: 1976–1980. *J Am Coll Nutr* 14:349–357.
- McCabe MJ Jr, Jiang SA, Orrenius S. 1993. Chelation of intracellular zinc triggers apoptosis in mature thymocytes. *Lab Invest* 69:101–110.
- McKenna AA, Ilich JZ, Andon MB, Wang C, Matkovic V. 1997. Zinc balance in adolescent females consuming a low- or high-calcium diet. *Am J Clin Nutr* 65:1460–1464.
- McMahon RJ, Cousins RJ. 1998. Mammalian zinc transporters. *J Nutr* 128:667–670.
- Merialdi M, Caulfield LE, Zavaleta N, Figueroa A, DiPietro JA. 1998. Adding zinc to prenatal iron and folate tablets improves fetal neurobehavioral development. *Am J Obstet Gynecol* 180:483–490.
- Miller LV, Hambidge KM, Naake VL, Hong Z, Westcott JL, Fennessey PV. 1994. Size of the zinc pools that exchange rapidly with plasma zinc in humans: Alternative techniques for measuring and relation to dietary zinc intake. *J Nutr* 124:268–276.
- Miller LV, Krebs NF, Hambidge KM. 1998. Human zinc metabolism: Advances in the modeling of stable isotope data. *Adv Exp Med Biol* 445:253–269.
- Milne DB, Canfield WK, Mahalko JR, Sandstead HH. 1983. Effect of dietary zinc on whole body surface loss of zinc: Impact on estimation of zinc retention by balance method. *Am J Clin Nutr* 38:181–186.
- Milne DB, Canfield WK, Mahalko JR, Sandstead HH. 1984. Effect of oral folic acid supplements on zinc, copper, and iron absorption and excretion. *Am J Clin Nutr* 39:535–539.
- Milne DB, Canfield WK, Gallagher SK, Hunt JR, Klevay LM. 1987. Ethanol metabolism in postmenopausal women fed a diet marginal in zinc. *Am J Clin Nutr* 46:688–693.
- Moser PB, Reynolds RD. 1983. Dietary zinc intake and zinc concentrations of plasma, erythrocytes, and breast milk in antepartum and postpartum lactating and nonlactating women: A longitudinal study. *Am J Clin Nutr* 38:101–108.
- Moser-Veillon PB, Reynolds RD. 1990. A longitudinal study of pyridoxine and zinc supplementation of lactating women. *Am J Clin Nutr* 52:135–141.

- Moss AJ, Levy AS, Kim I, Park YK. 1989. *Use of Vitamin and Mineral Supplements in the United States: Current Users, Types of Products, and Nutrients*. Advance Data, Vital and Health Statistics of the National Center for Health Statistics, Number 174. Hyattsville, MD: National Center for Health Statistics.
- Nakamura T, Nishiyama S, Futagoishi-Suginohara Y, Matsuda I, Higashi A. 1993. Mild to moderate zinc deficiency in short children: Effect of zinc supplementation on linear growth velocity. *J Pediatr* 123:65–69.
- Neggers YH, Goldenberg RL, Tamura T, Johnston KE, Copper RL, DuBard M. 1997. Plasma and erythrocyte zinc concentrations and their relationship to dietary zinc intake and zinc supplementation during pregnancy in low-income African-American women. *J Am Diet Assoc* 97:1269–1274.
- Ninh NX, Thissen JP, Collette L, Gerard G, Khoi HH, Ketelslegers JM. 1996. Zinc supplementation increases growth and circulating insulin-like growth factor I (IGF-I) in growth-retarded Vietnamese children. *Am J Clin Nutr* 63:514–519.
- Oberleas D, Muhrer ME, O'Dell BL. 1966. Dietary metal-complexing agents and zinc availability in the rat. *J Nutr* 90:56–62.
- O'Brien KO, Zavaleta N, Caulfield LE, Wen J, Abrams SA. 2000. Prenatal iron supplements impair zinc absorption in pregnant Peruvian women. *J Nutr* 130:2251–2255.
- Ortega RM, Andres P, Martinez RM, Lopez-Sobaler AM, Quintas ME. 1997. Zinc levels in maternal milk: The influence of nutritional status with respect to zinc during the third trimester of pregnancy. *Eur J Clin Nutr* 51:253–258.
- Paik HY, Joung H, Lee JY, Lee HK, King JC, Keen CL. 1999. Serum extracellular superoxide dismutase activity as an indicator of zinc status in humans. *Biol Trace Elem Res* 69:45–57.
- Payette H, Gray-Donald K. 1991. Dietary intake and biochemical indices of nutritional status in an elderly population, with estimates of the precision of the 7-d food record. *Am J Clin Nutr* 54:478–488.
- Picciano MF, Guthrie HA. 1976. Copper, iron, and zinc contents of mature human milk. *Am J Clin Nutr* 29:242–254.
- Pironi L, Miglioli M, Cornia GL, Ursitti MA, Tolomelli M, Piazzi S, Barbara L. 1987. Urinary zinc excretion in Crohn's disease. *Dig Dis Sci* 32:358–362.
- Prasad AS. 1976. Deficiency of zinc in man and its toxicity. In: Prasad AS, Oberleas D, eds. *Trace Elements in Human Health and Disease, Volume 1. Zinc and Copper*. New York: Academic Press. Pp. 1–20.
- Prasad AS. 1991. Discovery of human zinc deficiency and studies in an experimental human model. *Am J Clin Nutr* 53:403–412.
- Prasad AS, Brewer GJ, Schoomaker EB, Rabbani P. 1978. Hypocupremia induced by zinc therapy in adults. *J Am Med Assoc* 240:2166–2168.
- Prasad AS, Fitzgerald JT, Hess JW, Kaplan J, Pelen F, Dardenne M. 1993. Zinc deficiency in elderly patients. *Nutrition* 9:218–224.
- Prasad AS, Mantzoros CS, Beck FW, Hess JW, Brewer GJ. 1996. Zinc status and serum testosterone levels of healthy adults. *Nutrition* 12:344–348.
- Roesijadi G, Bogumil R, Vasak M, Kagi JH. 1998. Modulation of DNA binding of a tramtrack zinc finger peptide by the metallothionein-thionein conjugate pair. *J Biol Chem* 273:17425–17432.
- Rossander-Hulten L, Brune M, Sandstrom B, Lonnerdal B, Hallberg L. 1991. Competitive inhibition of iron absorption by manganese and zinc in humans. *Am J Clin Nutr* 54:152–156.
- Roth HP, Kirchgessner M. 1985. Utilization of zinc from picolinic or citric acid complexes in relation to dietary protein source in rats. *J Nutr* 115:1641–1649.

- Ruz M, Cavan KR, Bettger WJ, Gibson RS. 1992. Erythrocytes, erythrocyte membranes, neutrophils and platelets as biopsy materials for the assessment of zinc status in humans. *Br J Nutr* 68:515–527.
- Samman S, Roberts DCK. 1987. The effect of zinc supplements on plasma zinc and copper levels and the reported symptoms in healthy volunteers. *Med J Aust* 146:246–249.
- Samman S, Roberts DCK. 1988. The effect of zinc supplements on lipoproteins and copper status. *Atherosclerosis* 70:247–252.
- Samman S, Soto S, Cooke L, Ahmad Z, Farmakalidis E. 1996. Is erythrocyte alkaline phosphatase activity a marker of zinc status in humans? *Biol Trace Elem Res* 51:285–291.
- Sandstead HH, Penland JG, Alcock NW, Dayal HH, Chen XC, Li JS, Zhao F, Yang JJ. 1998. Effects of repletion with zinc and other micronutrients on neuro-psychologic performance and growth of Chinese children. *Am J Clin Nutr* 68:470S–475S.
- Sandstrom B, Lonnerdal B. 1989. Promoters and antagonists of zinc absorption. In: Mills CF, ed. *Zinc in Human Biology*. New York: Springer-Verlag. Pp. 57–78.
- Sandstrom B, Cederblad A, Lonnerdal B. 1983. Zinc absorption from human milk, cow's milk, and infant formulas. *Am J Dis Child* 137:726–729.
- Scholl TO, Hediger ML, Schall JI, Fischer RL, Khoo CS. 1993. Low zinc intake during pregnancy: Its association with preterm and very preterm delivery. *Am J Epidemiol* 137:1115–1124.
- Seal CJ, Heaton FW. 1985. Effect of dietary picolinic acid on the metabolism of exogenous and endogenous zinc in the rat. *J Nutr* 115:986–993.
- Shankar AH, Prasad AS. 1998. Zinc and immune function: The biological basis of altered resistance to infection. *Am J Clin Nutr* 68:447S–463S.
- Sian L, Mingyan X, Miller LV, Tong L, Krebs NF, Hambidge KM. 1996. Zinc absorption and intestinal losses of endogenous zinc in young Chinese women with marginal zinc intakes. *Am J Clin Nutr* 63:348–353.
- Sievers E, Oldigs HD, Dorner K, Schaub J. 1992. Longitudinal zinc balances in breast-fed and formula-fed infants. *Acta Paediatr* 81:1–6.
- Singh H, Flynn A, Fox PF. 1989. Zinc binding in bovine milk. *J Dairy Res* 56:249–263.
- Smit-Vanderkooy PD, Gibson RS. 1987. Food consumption patterns of Canadian preschool children in relation to zinc and growth status. *Am J Clin Nutr* 45:609–616.
- Snedecker SM, Smith SA, Greger JL. 1982. Effect of dietary calcium and phosphorus levels on the utilization of iron, copper, and zinc by adult males. *J Nutr* 112:136–143.
- Solomons NW, Jacob RA. 1981. Studies on the bioavailability of zinc in humans: Effects of heme and nonheme iron on the absorption of zinc. *Am J Clin Nutr* 34:475–482.
- Spencer H, Asmussen CR, Holtzman RB, Kramer L. 1979. Metabolic balances of cadmium, copper, manganese, and zinc in man. *Am J Clin Nutr* 32:1867–1875.
- Spencer H, Kramer L, Norris C, Osis D. 1984. Effect of calcium and phosphorus on zinc metabolism in man. *Am J Clin Nutr* 40:1213–1218.
- Srikumar TS, Johansson GK, Ockerman PA, Gustafsson JA, Akesson B. 1992. Trace element status in healthy subjects switching from a mixed to a lactovegetarian diet for 12 months. *Am J Clin Nutr* 55:885–890.

- Sullivan VK, Burnett FR, Cousins RJ. 1998. Metallothionein expression is increased in monocytes and erythrocytes of young men during zinc supplementation. *J Nutr* 128:707–713.
- Swanson CA, King JC. 1982. Zinc utilization in pregnant and nonpregnant women fed controlled diets providing the zinc RDA. *J Nutr* 112:697–707.
- Swanson CA, King JC. 1987. Zinc and pregnancy outcome. *Am J Clin Nutr* 46:763–771.
- Swanson CA, Mansourian R, Dirren H, Rapin CH. 1988. Zinc status of healthy elderly adults: Response to supplementation. *Am J Clin Nutr* 48:343–349.
- Taper LJ, Hinnens ML, Ritchey SJ. 1980. Effects of zinc intake on copper balance in adult females. *Am J Clin Nutr* 33:1077–1082.
- Taylor CM, Bacon JR, Aggett PJ, Bremner I. 1991. Homeostatic regulation of zinc absorption and endogenous losses in zinc-deprived men. *Am J Clin Nutr* 53:755–763.
- Telford WG, Fraker PJ. 1995. Preferential induction of apoptosis in mouse CD4<sup>+</sup>CD8<sup>+</sup> $\alpha\beta$ TCR<sup>lo</sup>CD3 $\varepsilon$ <sup>lo</sup> thymocytes by zinc. *J Cell Physiol* 164:259–270.
- Thomas AJ, Bunker VW, Hinks LJ, Sodha N, Mullee MA, Clayton BE. 1988. Energy, protein, zinc and copper status of twenty-one elderly inpatients: Analysed dietary intake and biochemical indices. *Br J Nutr* 59:181–191.
- Thomas EA, Bailey LB, Kauwell GA, Lee D-Y, Cousins RJ. 1992. Erythrocyte metallothionein response to dietary zinc in humans. *J Nutr* 122:2408–2414.
- Turnlund JR, Michel MC, Keyes WR, King JC, Margen S. 1982. Use of enriched stable isotopes to determine zinc and iron absorption in elderly men. *Am J Clin Nutr* 35:1033–1040.
- Turnlund JR, King JC, Keyes WR, Gong B, Michel MC. 1984. A stable isotope study of zinc absorption in young men: Effects of phytate and alpha-cellulose. *Am J Clin Nutr* 40:1071–1077.
- Turnlund JR, Durkin N, Costa F, Margen S. 1986. Stable isotope studies of zinc absorption and retention in young and elderly men. *J Nutr* 116:1239–1247.
- Turnlund JR, Keyes WR, Hudson CA, Betschart AA, Kretsch MJ, Sauberlich HE. 1991. A stable-isotope study of zinc, copper, and iron absorption and retention by young women fed vitamin B-6-deficient diets. *Am J Clin Nutr* 54:1059–1064.
- Udomkesmalee E, Dhanamitta S, Yhoun-Aree J, Rojroongwasinkul N, Smith JC Jr. 1990. Biochemical evidence suggestive of suboptimal zinc and vitamin A status in schoolchildren in northeast Thailand. *Am J Clin Nutr* 52:564–567.
- Umeta M, West CE, Haidar J, Deurenberg P, Hautvast JGAJ. 2000. Zinc supplementation and stunted infants in Ethiopia: A randomised controlled trial. *Lancet* 355:2021–2026.
- Valberg LS, Flanagan PR, Chamberlain MJ. 1984. Effects of iron, tin, and copper on zinc absorption in humans. *Am J Clin Nutr* 40:536–541.
- Valberg LS, Flanagan PR, Kertesz A, Bondy DC. 1986. Zinc absorption in inflammatory bowel disease. *Dig Dis Sci* 31:724–731.
- Vallee BL, Galdes A. 1984. The metallobiochemistry of zinc enzymes. *Adv Enzymol* 56:283–429.
- Vuori E, Makinen SM, Kara R, Kuitunen P. 1980. The effects of the dietary intakes of copper, iron, manganese, and zinc on the trace element content of human milk. *Am J Clin Nutr* 33:227–231.
- Wada L, King JC. 1986. Effect of low zinc intakes on basal metabolic rate, thyroid hormones and protein utilization in adult men. *J Nutr* 116:1045–1053.

- Wada L, Turnlund JR, King JC. 1985. Zinc utilization in young men fed adequate and low zinc intakes. *J Nutr* 115:1345–1354.
- Walling A, Householder M, Walling A. 1989. Acrodermatitis enteropathica. *Am Fam Physician* 39:151–154.
- Walravens PA, Hambidge KM. 1976. Growth of infants fed a zinc supplemented formula. *Am J Clin Nutr* 29:1114–1121.
- Walravens PA, Krebs NF, Hambidge KM. 1983. Linear growth of low income preschool children receiving a zinc supplement. *Am J Clin Nutr* 38:195–201.
- Walravens PA, Hambidge KM, Koepfer DM. 1989. Zinc supplementation in infants with a nutritional pattern of failure to thrive: A double-blind, controlled study. *Pediatrics* 83:532–538.
- Walravens PA, Chakar A, Mokni R, Denise J, Lemonnier D. 1992. Zinc supplements in breastfed infants. *Lancet* 340:683–685.
- Wastney ME, Aamodt RL, Rumble WF, Henkin RI. 1986. Kinetic analysis of zinc metabolism and its regulation in normal humans. *Am J Physiol* 251:R398–R408.
- Whittaker P. 1998. Iron and zinc interactions in humans. *Am J Clin Nutr* 68:442S–446S.
- WHO (World Health Organization). 1996. *Trace Elements in Human Nutrition and Health*. Geneva: WHO. Pp. 72–104.
- Widdowson EM, Dickerson JWT. 1964. Chemical composition of the body. In: Comar CL, Bronner F, eds. *Mineral Metabolism. An Advanced Treatise, Vol. II. The Elements, Part A*. New York: Academic Press. Pp. 1–247.
- Williams AW, Erdman JW Jr. 1999. Food processing: Nutrition, safety, and quality balances. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease*, 9th ed. Baltimore: Williams & Wilkins. Pp. 1813–1821.
- Wisker E, Nagel R, Tanudjaja TK, Feldheim W. 1991. Calcium, magnesium, zinc, and iron balances in young women: Effects of a low-phytate barley-fiber concentrate. *Am J Clin Nutr* 54:553–559.
- Wood RJ, Zheng JJ. 1997. High dietary calcium intakes reduce zinc absorption and balance in humans. *Am J Clin Nutr* 65:1803–1809.
- Yadrick MK, Kenney MA, Winterfeldt EA. 1989. Iron, copper, and zinc status: Response to supplementation with zinc or zinc and iron in adult females. *Am J Clin Nutr* 49:145–150.
- Yokoi K, Alcock NW, Sandstead HH. 1994. Iron and zinc nutriture of premenopausal women: Associations of diet with serum ferritin and plasma zinc disappearance and of serum ferritin with plasma zinc and plasma zinc disappearance. *J Lab Clin Med* 124:852–861.
- Yuzbasiyan-Gurkan V, Grider A, Nostrant T, Cousins RJ, Brewer GJ. 1992. Treatment of Wilson's disease with zinc: X. Intestinal metallothionein induction. *J Lab Clin Med* 120:380–386.
- Zalewski PD, Forbes IJ, Seamark RF, Borlinghaus R, Betts WH, Lincoln SF, Ward AD. 1994. Flux of intracellular labile zinc during apoptosis (gene-directed cell death) revealed by a specific chemical probe, Zinquin. *Chem Biol* 1:153–161.
- Ziegler EE, Edwards BB, Jensen RL, Filer LJ, Fomon SJ. 1978. Zinc balance studies in normal infants. In: Kirchgessner M, ed. *Trace Element Metabolism in Man and Animals—3*. Freising-Weihenstephan: Arbeitskreis fier Tierernahrungs-forschung. Pp. 292–295.
- Zlotkin SH, Cherian MG. 1988. Hepatic metallothionein as a source of zinc and cysteine during the first year of life. *Pediatr Res* 24:326–329.

**Ibid., Chapter 14, pp. 578–579.**

- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Examination Survey: Under-reporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Gibson RS, Ferguson EL. 1998. Assessment of dietary zinc in a population. *Am J Clin Nutr* 68:430S–434S.
- Hallberg L, Hulthen L. 2000. Prediction of dietary iron absorption: An algorithm for calculating absorption and bioavailability of dietary iron. *Am J Clin Nutr* 71:1147–1160.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1980. *Recommended Dietary Allowances*, 9th ed. Washington, DC: National Academy Press.
- NRC. 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC. 1989. *Recommended Dietary Allowances*, 10th ed. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Schoeller DA. 1999. Recent advances from application of doubly labeled water to measurement of human energy expenditure. *J Nutr* 129:1765–1768.
- USDA (U.S. Department of Agriculture). 1999. *USDA Nutrient Database for Standard Reference*, Release 13. [Online.] Available: <http://www.nal.usda.gov/fnic/foodcomp> [accessed February 2000].
- WHO (World Health Organization). 1996. Zinc. In: *Trace Elements in Human Nutrition and Health*. Geneva: WHO. Pp. 72–104.

## ARSENIC, BORON, NICKEL, SILICON, AND VANADIUM

*Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*  
 (ISBN 0-309-07290-5), Chapter 13, pp. 543–553.

- ABC (American Biogenics Corporation). 1988. *Ninety Day Gavage Study in Albino Rats Using Nickel*. Study 410-2520. Final report submitted to the U.S. Environmental Protection Agency, Office of Solid Waste, by Research Triangle Institute and American Biogenics Corporation under contract 68-01-7075.
- Adams MA, Bolger PM, Gunderson EL. 1994. Dietary intake and hazards of arsenic. In: Chappell WR, Abernathy CO, Cothern CR, eds. *Arsenic: Exposure and Health*. Northwood, UK: Science and Technology Letters. Pp. 41–49.
- Allen HE, Halley-Henderson MA, Hass CN. 1989. Chemical composition of bottled mineral water. *Arch Environ Health* 44:102–116.
- Ambrose AM, Larson PS, Borzelleca JF, Hennigar GR. 1976. Long term toxicologic assessment of nickel in rats and dogs. *J Food Sci Technol* 13:181–187.
- Anderson DL, Cunningham WC, Lindstrom TR. 1994. Concentrations and intakes of H, B, S, K, Na, Cl, and NaCl in foods. *J Food Comp Anal* 7:59–82.
- Anderson RR. 1992. Comparison of trace elements in milk of four species. *J Dairy Sci* 75:3050–3055.
- Andrews RK, Blakeley RL, Zerner B. 1988. Nickel in proteins and enzymes. In: Sigel H, Sigel A, eds. *Metal Ions in Biological Systems*, Vol. 23. New York: Marcel Dekker. Pp. 165–284.
- Anke M. 1986. Arsenic. In: Mertz W, ed. *Trace Elements in Human and Animal Nutrition*, Vol. 2, 5th ed. Orlando, FL: Academic Press. Pp. 347–372.
- Anke M, Groppel B, Gruhn K, Langer M, Arnhold W. 1989. The essentiality of vanadium for animals. In: Anke M, Bauman W, Braunlich H, eds. *6th International Trace Element Symposium*, Vol. 1. Jena, Germany: Friedrich-Schiller-Universitat. Pp. 17–27.
- Aposhian HV. 1997. Enzymatic methylation of arsenic species and other new approaches to arsenic toxicity. *Annu Rev Pharmacol Toxicol* 37:397–419.
- Armstrong CW, Stroube RB, Rubio T, Siudyla EA, Miller GB Jr. 1984. Outbreak of fatal arsenic poisoning caused by contaminated drinking water. *Arch Environ Health* 39:276–279.
- ATSDR (Agency for Toxic Substances and Disease Registry). 1992. *Toxicological Profile for Boron*. Atlanta: U.S. Public Health Service, ATSDR.
- ATSDR. 1998. *Toxicological Profile for Arsenic*. Atlanta: U.S. Public Health Service, ATSDR.
- Bakken N. 1995. *Dietary Boron Modifies the Effects of Vitamin D Nutriture on Energy Metabolism and Bone Morphology in the Chick*. Masters of Science thesis, University of North Dakota, Grand Forks.
- Barceloux DG. 1999. Vanadium. *J Toxicol Clin Toxicol* 37:265–278.
- Baxley MN, Hood RD, Vedel GC, Harrison WP, Szczech GM. 1981. Prenatal toxicity of orally administered sodium arsenite in mice. *Bull Environ Contam Toxicol* 26:749–756.
- Beaudoin AR. 1974. Teratogenicity of sodium arsenate in rats. *Teratology* 10:153–157.

- Becking GC, Chen BH. 1998. International Programme on Chemical Safety (IPCS) environmental health criteria on boron human health risk assessment. *Biol Trace Elem Res* 66:439–452.
- Boden G, Chen X, Ruiz J, van Rossum GD, Turco S. 1996. Effects of vanadyl sulfate on carbohydrate and lipid metabolism in patients with non-insulin-dependent diabetes mellitus. *Metabolism* 45:1130–1135.
- Boscolo P, Carmignani M, Volpe AR, Felaco M, Del Rosso G, Porcelli G, Giuliano G. 1994. Renal toxicity and arterial hypertension in rats chronically exposed to vanadate. *Occup Environ Med* 51:500–503.
- Byrne AR, Kosta L. 1978. Vanadium in foods and in human body fluids and tissues. *Sci Total Environ* 10:17–30.
- Byrne AR, Kosta L, Dermelj M, Tusek-Znidaric M. 1983. Aspects of some trace elements in human milk. In: Bratter P, Schramel P, eds. *Trace Element Analytical Chemistry in Medicine and Biology*, Vol. 2. Berlin: Walter de Gruyter. Pp. 21–35.
- Byron WR, Bierbower GW, Brouwer JB, Hansen WH. 1967. Pathologic changes in rats and dogs from two-year feeding of sodium arsenite or sodium arsenate. *Toxicol Appl Pharmacol* 10:132–147.
- Carlisle EM. 1980a. A silicon requirement for normal skull formation in chicks. *J Nutr* 110:352–359.
- Carlisle EM. 1980b. Biochemical and morphological changes associated with long bone abnormalities in silicon deficiency. *J Nutr* 110:1046–1055.
- Carlisle EM. 1981. Silicon: A requirement in bone formation independent of vitamin D1. *Calcif Tissue Int* 33:27–34.
- Carlisle EM. 1984. Silicon. In: Frieden E, ed, *Biochemistry of the Essential Ultratrace Elements*. New York: Plenum Press. Pp. 257–291.
- Carmignani M, Boscolo P, Volpe AR, Togna G, Masciocco L, Preziosi P. 1991. Cardiovascular system and kidney as specific targets of chronic exposure to vanadate in the rat: Functional and morphological findings. *Arch Toxicol Suppl* 14:124–127.
- Casey CE, Neville MC. 1987. Studies in human lactation 3: Molybdenum and nickel in human milk during the first month of lactation. *Am J Clin Nutr* 45:921–926.
- Chan PC, Huff J. 1997. Arsenic carcinogenesis in animals and in humans: Mechanistic, experimental, and epidemiological evidence. *J Environ Sci Health C15:83–122.*
- Chappell WR, Beck BD, Brown KG, Chaney R, Cothern CR, Irgolic KJ, North DW, Thornton I, Tsongas TA. 1997. Inorganic arsenic: A need and an opportunity to improve risk assessment. *Environ Health Perspect* 105:1060–1067.
- Chen CJ, Chen CW, Wu MM, Kuo TL. 1992. Cancer potential in liver, lung, bladder and kidney due to ingested inorganic arsenic in drinking water. *Br J Cancer* 66:888–892.
- Christensen OB, Moller H. 1978. Release of nickel from cooking utensils. *Contact Dermatitis* 4:343–346.
- Civantos DP, Lopez Rodriguez A, Aguado-Borruey JM, Narvaez JA. 1995. Fulminant malignant arrhythmia and multiorgan failure in acute arsenic poisoning. *Chest* 108:1774–1775.
- Cohen N, Halberstam M, Shlimovich P, Chang CJ, Shamoon H, Rossetti L. 1995. Oral vanadyl sulfate improves hepatic and peripheral insulin sensitivity in patients with non-insulin-dependent diabetes mellitus. *J Clin Invest* 95:2501–2509.
- Culver BD, Hubbard SA. 1996. Inorganic boron health effects in humans: An aid to risk assessment and clinical judgment. *J Trace Elem Exp Med* 9:175–184.

- Dabeka RW. 1989. Survey of lead, cadmium, cobalt and nickel in infant formulas and evaporated milks and estimation of dietary intakes of the elements by infants 0–12 months old. *Sci Total Environ* 89:279–289.
- Dabeka RW, McKenzie AD. 1995. Survey of lead, cadmium, fluoride, nickel, and cobalt in food composites and estimation of dietary intakes of these elements by Canadians in 1986–1988. *J AOAC Int* 78:897–909.
- Dabeka RW, McKenzie AD, Lacroix GM, Cleroux C, Bowe S, Graham RA, Conacher HB, Verdier P. 1993. Survey of arsenic in total diet food composites and estimation of the dietary intake of arsenic by Canadian adults and children. *J AOAC Int* 76:14–25.
- Dai S, McNeill JH. 1994. One-year treatment of non-diabetic and streptozotocin-diabetic rats with vanadyl sulphate did not alter blood pressure or haematological indices. *Pharmacol Toxicol* 74:110–115.
- Dai S, Vera E, McNeill JH. 1995. Lack of haematological effect of oral vanadium treatment in rats. *Pharmacol Toxicol* 76:263–268.
- Daniel EP, Lillie RD. 1938. Experimental vanadium poisoning in the white rat. *Public Health Rep* 53:765–777.
- Dang HS, Jaiswal DD, Somasundaram S. 1983. Distribution of arsenic in human tissues and milk. *Sci Total Environ* 29:171–175.
- da Silva FJ, Williams RJ. 1991. *The Biological Chemistry of the Elements: The Inorganic Chemistry of Life*. Oxford: Clarendon Press. Pp. 58–63.
- Desrosiers R, Tanguay RM. 1986. Further characterization of the posttranslational modifications of core histones in response to heat and arsenite stress in *Drosophila*. *Biochem Cell Biol* 64:750–757.
- Dieter MP. 1994. Toxicity and carcinogenicity studies of boric acid in male and female B6C3F<sub>1</sub> mice. *Environ Health Perspect Suppl* 102:93–97.
- Dimond EG, Caravaca J, Benchimol A. 1963. Vanadium: Excretion, toxicity, lipid effect in man. *Am J Clin Nutr* 12:49–53.
- Dobbie JW, Smith MB. 1986. Urinary and serum silicon in normal and uraemic individuals. *Ciba Found Symp* 121:194–213.
- Domingo JL, Llobet JM, Tomas JM, Corbella J. 1985. Short-term toxicity studies of vanadium in rats. *J Appl Toxicol* 5:418–421.
- Domingo JL, Paternain JL, Llobet JM, Corbella J. 1986. Effects of vanadium on reproduction, gestation, parturition and lactation in rats upon oral administration. *Life Sci* 39:819–824.
- Domingo JL, Gomez M, Llobet JM, Corbella J, Keen CL. 1991. Oral vanadium administration to streptozotocin-diabetic rats has marked negative side-effects which are independent of the form of vanadium used. *Toxicology* 66:279–287.
- Dourson M, Maier A, Meek B, Renwick A, Ohanian E, Poirier K. 1998. Boron tolerable intake: Re-evaluation of toxicokinetics for data-derived uncertainty factors. *Biol Trace Elem Res* 66:453–463.
- Eckhert CD. 1998. Boron stimulates embryonic trout growth. *J Nutr* 128:2488–2493.
- Engel RR, Receveur O. 1993. Re: “Arsenic ingestion and internal cancers: A review”. *Am J Epidemiol* 138:896–897.
- EPA (Environmental Protection Agency). 1975. Water programs: National interim primary drinking water regulations. *Fed Register* 40:59566.
- EPA. 1987. *Health Effects Assessment for Boron and Compounds*. EPA/600/8-88/021. Cincinnati, OH: EPA.
- EPA. 1988. *Special Report on Ingested Inorganic Arsenic: Skin Cancer; Nutritional Essentiality*. EPA 625/3-87/013. Washington, DC: EPA.

## ONLINE REFERENCES

## 1317

- EPA. 2000. *Integrated Risk Information System Database*. United States Environmental Protection Agency. [Online.] Available: <http://www.epa.gov/iris/subst/0271.htm> [accessed November 10, 2000].
- EPA. 2000. National primary drinking water regulations; Arsenic and clarifications to compliance and new source contaminants monitoring; Proposed rule. *Fed Register* 65:38887–38983.
- Fail PA, George JD, Grizzle TB, Heindel JJ, Chapin RE. 1990. *Final Report on the Reproductive Toxicity of Boric Acid (CAS No. 10043-35-3) in CD-1 Swiss Mice*. Research Triangle Park, NC: Department of Health and Human Services, National Toxicology Program.
- Fail PA, George JD, Seely JC, Grizzle TB, Heindel JJ. 1991. Reproductive toxicity of boric acid in Swiss (CD-1) mice: Assessment using the continuous breeding protocol. *Fundam Appl Toxicol* 17:225–239.
- Fawcett JP, Farquhar SJ, Thou T, Shand BI. 1997. Oral vanadyl sulphate does not affect blood cells, viscosity or biochemistry in humans. *Pharmacol Toxicol* 80:202–206.
- Fincher RM, Koerker RM. 1987. Long-term survival in acute arsenic encephalopathy. Follow-up using newer measures of electrophysiologic parameters. *Am J Med* 82:549–552.
- Fort DJ, Propst TL, Stover EL, Strong PL, Murray FJ. 1998. Adverse reproductive and developmental effects in Xenopus from insufficient boron. *Biol Trace Elem Res* 66:237–259.
- Fort DJ, Stover EL, Strong PL, Murray FJ, Keen CL. 1999. Chronic feeding of a low boron diet adversely affects reproduction and development in Xenopus laevis. *J Nutr* 129:2055–2060.
- Franke KW, Moxon AL. 1937. The toxicity of orally ingested arsenic, selenium, tellurium, vanadium and molybdenum. *J Pharmacol Exp Ther* 61:89–102.
- Franzblau A, Lilis R. 1989. Acute arsenic intoxication from environmental arsenic exposure. *Arch Environ Health* 44:385–390.
- Gartrell MJ, Craun JC, Podrebarac DS, Gunderson EL. 1985. Pesticides, selected elements, and other chemicals in adult total diet samples, October 1978–September 1979. *J Assoc Off Anal Chem* 68:862–875.
- Gawkrodger DJ, Cook SW, Fell GS, Hunter JAA. 1986. Nickel dermatitis: The reaction to oral nickel challenge. *Br J Dermatol* 115:33–38.
- Goering PL, Aposhian HV, Mass MJ, Cebran M, Beck BD, Waalkes MP. 1999. The enigma of arsenic carcinogenesis: Role of metabolism. *Toxicol Sci* 49:5–14.
- Goldfine AB, Simonson DC, Folli F, Patti ME, Kahn CR. 1995. In vivo and in vitro studies of vanadate in human and rodent diabetes mellitus. *Molec Cell Biochem* 153:217–231.
- Goldwater LJ. 1936. The urinary excretion of silica in non-silicotic humans. *J Ind Hyg Toxicol* 18:163–166.
- Gordon AS, Prichard JS, Freedman MH. 1973. Seizure disorders and anemia associated with chronic borax intoxication. *Can Med Assoc J* 108:719–721.
- Grantham DA, Jones JF. 1977. Arsenic contamination of water wells in Nova Scotia. *J Am Water Works Assoc* 69:653–657.
- Green GH, Lott MD, Weeth HJ. 1973. Effects of boron water on rats. *Proc West Sect Am Soc Anim Sci* 24:254–258.

- Grimanis AP, Vassilaki-Grimani M, Alexiou D, Papadatos C. 1979. Determination of seven trace elements in human milk, powdered cow's milk and infant foods by neutron activation analysis. In: Byrne AR, Kosta L, Ravnik V, Stupar J, Hudnik V, eds. *Nuclear Activation Techniques in the Life Sciences 1978*. Vienna: International Atomic Energy Agency. Pp. 241–253.
- Gunderson EL. 1995. FDA Total Diet Study, July 1986–April 1991, dietary intakes of pesticides, selected elements, and other chemicals. *J AOAC Int* 78:1353–1363.
- Haddad FS, Kouyoumdjian A. 1986. Silica stones in humans. *Urol Int* 41:70–76.
- Harris WR, Friedman SB, Silberman D. 1984. Behavior of vanadate and vanadyl ion in canine blood. *J Inorg Biochem* 20:157–169.
- Hei TK, Liu SX, Waldren C. 1998. Mutagenicity of arsenic in mammalian cells: Role of reactive oxygen species. *Proc Natl Acad Sci USA* 95:8103–8107.
- Heindel JJ, Price CJ, Field EA, Marr MC, Myers CB, Morrissey RE, Schwetz BA. 1992. Developmental toxicity of boric acid in mice and rats. *Fundam Appl Toxicol* 18:266–277.
- Heyliger CE, Tahiliani AG, McNeill JH. 1985. Effect of vanadate on elevated blood glucose and depressed cardiac performance of diabetic rats. *Science* 227:1474–1477.
- Hoey MJ. 1966. The effects of metallic salts on the histology and functioning of the rat testis. *J Reprod Fertil* 12:461–471.
- Hogan GR. 1990. Peripheral erythrocyte levels, hemolysis and three vanadium compounds. *Experientia* 46:444–446.
- Hood RD. 1972. Effects of sodium arsenite on fetal development. *Bull Environ Contam Toxicol* 7:216–222.
- Hood RD, Bishop SL. 1972. Teratogenic effects of sodium arsenate in mice. *Arch Environ Health* 24:62–65.
- Hood RD, Harrison WP. 1982. Effects of prenatal arsenite exposure in the hamster. *Bull Environ Contam Toxicol* 29:671–678.
- Hopenhayn-Rich C, Smith AH, Goeden HM. 1993. Human studies do not support the methylation threshold hypothesis for the toxicity of inorganic arsenic. *Environ Res* 60:161–177.
- Hopenhayn-Rich C, Biggs ML, Fuchs A, Bergoglio R, Tello EE, Nicolli H, Smith AH. 1996. Bladder cancer mortality associated with arsenic in drinking water in Argentina. *Epidemiology* 7:117–124.
- Huang YZ, Qian XC, Wang GQ, Xiao BY, Ren DD, Feng ZY, Wu JY, Xu RJ, Zhang FE. 1985. Endemic chronic arsenism in Xinjiang. *Chin Med J* 98:219–222.
- Hunt CD. 1996. Biochemical effects of physiological amounts of dietary boron. *J Trace Elem Exp Med* 9:185–213.
- Hunt CD. 1998. Regulation of enzymatic activity. One possible role of dietary boron in higher animals and humans. *Biol Trace Elem Res* 66:205–225.
- Hunt CD, Stoecker BJ. 1996. Deliberations and evaluations of the approaches, endpoints and paradigms for boron, chromium and fluoride dietary recommendations. *J Nutr* 126:2441S–2451S.
- Hunt CD, Shuler TR, Mullen LM. 1991. Concentration of boron and other elements in human foods and personal-care products. *J Am Diet Assoc* 91:558–568.
- IARC (International Agency for Research on Cancer). 1980. *Some Metals and Metallic Compounds*. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 23. Lyon, France: IARC.

- IARC. 1987. *Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42*. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Supplement 7. Lyon, France: IARC.
- IPCS (International Programme on Chemical Safety). 1998. *Environmental Health Criteria: 204: Boron*. Geneva: World Health Organization.
- Jansen JA, Andersen J, Schou JS. 1984a. Boric acid single dose pharmacokinetics after intravenous administration to man. *Arch Toxicol* 55:64–67.
- Jansen JA, Schou JS, Aggerbeck A. 1984b. Gastro-intestinal absorption and in vitro release of boric acid from water-emulsifying ointments. *Food Chem Toxicol* 22:49–53.
- Kanematsu N, Hara M, Kada T. 1980. Rec assay and mutagenicity studies on metal compounds. *Mutat Res* 77:109–116.
- Kelsay JL, Behall KM, Prather ES. 1979. Effect of fiber from fruits and vegetables on metabolic responses of human subjects. II. Calcium, magnesium, iron and silicon balances. *Am J Clin Nutr* 32:1876–1880.
- Kim H, Yu C, Maier RJ. 1991. Common cis-acting region responsible for transcriptional regulation of Bradyrhizobium japonicum hydrogenase by nickel, oxygen, and hydrogen. *J Bacteriol* 173:3993–3999.
- Konig A, Wrazel L, Warrell RP Jr, Rivi R, Pandolfi PP, Jakubowski A, Gabrilove JL. 1997. Comparative activity of melarsoprol and arsenic trioxide in chronic B-cell leukemia lines. *Blood* 90:562–570.
- Kreiss K, Zack MM, Landrigan PJ, Feldman RG, Niles CA, Chirico-Post J, Sax DS, Boyd MH, Cox DH. 1983. Neurologic evaluation of a population exposed to arsenic in Alaskan well water. *Arch Environ Health* 38:116–121.
- Ku WW, Chapin RE, Moseman RF, Brink RE, Pierce KD, Adams KY. 1991. Tissue disposition of boron in male Fischer rats. *Toxicol Appl Pharmacol* 111:145–151.
- Ku WW, Shih LM, Chapin RE. 1993. The effects of boric acid (BA) on testicular cells in culture. *Reprod Toxicol* 7:321–331.
- Lancaster JR. 1988. *The Bioinorganic Chemistry of Nickel*. New York: VCH Publishers.
- Lanoue L, Taubeneck MW, Muniz J, Hanna LA, Strong PL, Murray FJ, Nielsen FH, Hunt CD, Keen CL. 1998. Assessing the effects of low boron diets on embryonic and fetal development in rodents using in vitro and in vivo model systems. *Biol Trace Elem Res* 66:271–298.
- Lanoue L, Strong PL, Keen CL. 1999. Adverse effects of a low boron environment on the preimplantation development of mouse embryos in vitro. *J Trace Elem Exp Med* 12:235–250.
- Laskey JW, Phelps PV. 1991. Effect of cadmium and other metal cations on in vitro Leydig cell testosterone production. *Toxicol Appl Pharmacol* 108:296–306.
- Lee IP, Sherrins RJ, Dixon RL. 1978. Evidence for induction of germinal aplasia in male rats by environmental exposure to boron. *Toxicol Appl Pharmacol* 45:577–590.
- Levin-Scherz JK, Patrick JD, Weber FH, Garabedian C Jr. 1987. Acute arsenic ingestion. *Ann Emerg Med* 16:702–704.
- Litovitz TL, Klein-Schwartz W, Oderda GM, Schmitz BF. 1988. Clinical manifestations of toxicity in a series of 784 boric acid ingestions. *Am J Emerg Med* 6:209–213.
- Llobet JM, Colomina MT, Sirvent JJ, Domingo JL, Corbella J. 1993. Reproductive toxicity evaluation of vanadium in male mice. *Toxicology* 80:199–206.
- Look AT. 1998. Arsenic and apoptosis in the treatment of acute promyelocytic leukemia. *J Natl Cancer Inst* 90:86–88.

- Mahaffey KR, Corneliusen PE, Jelinek CF, Fiorino JA. 1975. Heavy metal exposure from foods. *Environ Health Perspect* 12:63–69.
- Maitani T, Saito N, Abe M, Uchiyama S, Saito Y. 1987. Chemical form-dependent induction of hepatic zinc-thionein by arsenic administration and effect of co-administered selenium in mice. *Toxicol Lett* 39:63–70.
- Mancinella A. 1991. Silicon, a trace element essential for living organisms. Recent knowledge on its preventive role in atherosclerotic process, aging and neoplasms. *Clin Ter* 137:343–350.
- Meacham SL, Hunt CD. 1998. Dietary boron intakes of selected populations in the United States. *Biol Trace Elem Res* 66:65–78.
- Meng Z, Meng N. 1994. Effects of inorganic arsenicals on DNA synthesis in unsensitized human blood lymphocytes in vitro. *Biol Trace Elem Res* 42:201–208.
- Moore JA. 1997. An assessment of boric acid and borax using the IEHR Evaluative Process for Assessing Human Developmental and Reproductive Toxicity of Agents. *Reprod Toxicol* 11:123–160.
- Morton W, Starr G, Pohl D, Stoner J, Wagner S, Weswig D. 1976. Skin cancer and water arsenic in Lane County, Oregon. *Cancer* 37:2523–2532.
- Murray FJ. 1998. A comparative review of the pharmacokinetics of boric acid in rodents and humans. *Biol Trace Elem Res* 66:331–341.
- Myron DR, Givand SH, Nielsen FH. 1977. Vanadium content of selected foods as determined by flameless atomic absorption spectroscopy. *J Agric Food Chem* 25:297–300.
- Nielsen FH. 1985. The importance of diet composition in ultratrace element research. *J Nutr* 115:1239–1247.
- Nielsen FH. 1996. How should dietary guidance be given for mineral elements with beneficial actions or suspected of being essential? *J Nutr* 126:2377S–2385S.
- Nielsen FH. 1997. Boron. In: O'Dell BL, Sunde RA, eds. *Handbook of Nutritionally Essential Mineral Elements*. New York: Marcel Dekker. Pp. 453–464.
- Nielsen FH. 1998. The justification for providing dietary guidance for the nutritional intake of boron. *Biol Trace Elem Res* 66:319–330.
- Nielsen FH, Flyvholm M. 1983. Risks of high nickel intake with diet. In: Sunderman FW Jr, ed. *Nickel in the Human Environment*. IARC Scientific Publications No. 53. Lyon, France: International Agency for Research on Cancer. Pp. 333–338.
- Nielsen FH, Penland JG. 1999. Boron supplementation of peri-menopausal women affects boron metabolism and indices associated with macromineral metabolism, hormonal status and immune function. *J Trace Elem Exp Med* 12:251–261.
- Nielsen FH, Uthus EO. 1990. The essentiality and metabolism of vanadium. In: Chasteen ND, ed. *Vanadium in Biological Systems*. Dordrecht, The Netherlands: Kluwer Academic. Pp. 51–62.
- Nishioka H. 1975. Mutagenic activities of metal compounds in bacteria. *Mutat Res* 31:185–189.
- NRC (National Research Council). 1999. *Arsenic in Drinking Water*. Washington, DC: National Academy Press.
- Oppenheim JJ, Fishbein WN. 1965. Induction of chromosome breaks in cultured normal human leukocytes by potassium arsenite, hydroxyurea and related compounds. *Cancer Res* 25:980–985.
- Oster MH, Llobet JM, Domingo JL, German JB, Keen CL. 1993. Vanadium treatment of diabetic Sprague-Dawley rats results in tissue vanadium accumulation and pro-oxidant effects. *Toxicology* 83:115–130.
- O'Sullivan K, Taylor M. 1983. Chronic boric acid poisoning in infants. *Arch Dis Child* 58:737–749.

- Paton GR, Allison AC. 1972. Chromosome damage in human cell cultures induced by metal salts. *Mutat Res* 16:332–336.
- Patriarca M, Lyon TD, Fell GS. 1997. Nickel metabolism in humans investigated with an oral stable isotope. *Am J Clin Nutr* 66:616–621.
- Patterson BW, Hansard SL, Ammerman CB, Henry PR, Zech LA, Fisher WR. 1986. Kinetic model of whole-body vanadium metabolism: Studies in sheep. *Am J Physiol* 251:R325–R332.
- Penland JG. 1998. The importance of boron nutrition for brain and psychological function. *Biol Trace Elem Res* 66:299–317.
- Pennington JA. 1991. Silicon in foods and diets. *Food Addit Contam* 8:97–118.
- Pennington JA, Jones JW. 1987. Molybdenum, nickel, cobalt, vanadium, and strontium in total diets. *J Am Diet Assoc* 87:1644–1650.
- Popplewell JF, King SJ, Day JP, Ackrill P, Fifield LK, Cresswell RG, di Tada ML, Liu K. 1998. Kinetics of uptake and elimination of silicic acid by a human subject: A novel application of  $^{32}\text{Si}$  and accelerator mass spectrometry. *J Inorg Biochem* 69:177–180.
- Price CJ, Marr MC, Myers CB, Seely JC, Heindel JJ, Schwetz BA. 1996a. The developmental toxicity of boric acid in rabbits. *Fundam Appl Toxicol* 34:176–187.
- Price CJ, Strong PL, Marr MC, Myers CB, Murray FJ. 1996b. Developmental toxicity NOAEL and postnatal recovery in rats fed boric acid during gestation. *Fundam Appl Toxicol* 32:179–193.
- Price CJ, Strong PL, Murray FJ, Goldberg MM. 1998. Developmental effects of boric acid in rats related to maternal blood boron concentrations. *Biol Trace Elem Res* 66:359–372.
- Przybyla AE, Robbins J, Menon N, Peck HD. 1992. Structure-function relationships among the nickel-containing hydrogenases. *FEMS Microbiol Rev* 8:109–135.
- Quatrehomme G, Ricq O, Lapalus P, Jacomet Y, Ollier A. 1992. Acute arsenic intoxication: Forensic and toxicologic aspects (an observation). *J Forensic Sci* 37:1163–1171.
- Rainey CJ, Nyquist LA, Christensen RE, Strong PL, Culver BD, Coughlin JR. 1999. Daily boron intake from the American diet. *J Am Diet Assoc* 99:335–340.
- Rehder D. 1991. The bioinorganic chemistry of vanadium. *Angew Chem Int Ed Engl* 30:148–167.
- Rezuke WN, Knight JA, Sunderman FW. 1987. Reference values for nickel concentrations in human tissues and bile. *Am J Ind Med* 11:419–426.
- Rowe RI, Eckhert CD. 1999. Boron is required for zebrafish embryogenesis. *J Exp Biol* 202:1649–1654.
- RTI (Research Triangle Institute). 1988. *Two Generation Reproduction and Fertility Study of Nickel Chloride Administered to CD Rats in the Drinking Water: Fertility and Reproductive Performance of the P<sub>0</sub> Generation. Final Study Report*. Report to Office of Solid Waste Management, US Environmental Protection Agency by Research Triangle Institute. RTI Project No. 472U-3228-07. Research Triangle Park, NC: RTI.
- Sabbioni E, Marafante E, Amantini L, Ubertalli L, Birattari C. 1978. Similarity in metabolic patterns of different chemical species of vanadium in the rat. *Bioinorg Chem* 8:503–515.
- Samman S, Naghii MR, Lyons Wall PM, Verus AP. 1998. The nutritional and metabolic effects of boron in humans and animals. *Biol Trace Elem Res* 66:227–235.
- Schnegg A, Kirchgessner M. 1975. Changes in hemoglobin content, erythrocyte count and hematocrit in nickel deficiency. *Nutr Metab* 19:268–278.

- Schoof RA, Yost LJ, Eickhoff J, Crecelius EA, Cragin DW, Meacher DM, Menzel DB. 1999. A market basket survey of inorganic arsenic in food. *Food Chem Toxicol* 37:839–846.
- Schroeder HA, Mitchener M. 1971. Toxic effects of trace elements on the reproduction of mice and rats. *Arch Environ Health* 23:102–106.
- Schwarz K, Milne DB. 1972. Growth-promoting effects of silicon in rats. *Nature* 239:333–334.
- Seaborn CD, Nielsen FH. 1993. Silicon: A nutritional beneficence for bones, brains and blood vessels? *Nutr Today* 28:13–18.
- Seaborn CD, Nielsen FH. 1994. Dietary silicon affects acid and alkaline phosphatase and <sup>45</sup>calcium uptake in bone of rats. *J Trace Elem Exp Med* 7:11–18.
- Shirasu Y, Moriya M, Kato K, Furuhashi A, Kada T. 1976. Mutagenicity screening of pesticides in the microbial system. *Mutat Res* 40:19–30.
- Simeonova PP, Wang S, Toriuma W, Kommineni V, Matheson J, Unimye N, Kayama F, Harki D, Ding M, Vallyathan V, Luster MI. 2000. Arsenic mediates cell proliferation and gene expression in the bladder epithelium: Association with activating protein-1 transactivation. *Cancer Res* 60:3445–3453.
- Smith AH, Goycolea M, Haque R, Biggs ML. 1998. Marked increase in bladder and lung cancer mortality in a region of Northern Chile due to arsenic in drinking water. *Am J Epidemiol* 147:660–669.
- Smith MK, George EL, Stober JA, Feng HA, Kimmel GL. 1993. Perinatal toxicity associated with nickel chloride exposure. *Environ Res* 61:200–211.
- Solomons NW, Viteri F, Shuler TR, Nielsen FH. 1982. Bioavailability of nickel in man: Effects of foods and chemically-defined dietary constituents on the absorption of inorganic nickel. *J Nutr* 112:39–50.
- Southwick JW, Western AE, Beck MM, Whitley T, Isaacs R. 1981. *Community Health Associated with Arsenic in Drinking Water in Millard County, Utah*. EPA-600/1-81-064. Cincinnati, OH: US Environmental Protection Agency, Health Effects Research Laboratory.
- Steffen RP, Pamnani MB, Clough DL, Huot SJ, Muldoon SM, Haddy FJ. 1981. Effect of prolonged dietary administration of vanadate on blood pressure in the rat. *Hypertension* 3:I173–I178.
- Stokinger HE. 1981. The halogens and nonmetals boron and silicon. In: Clayton GD, Clayton FE, eds. *Patty's Industrial Hygiene and Toxicology*, Vol. 2B. New York: John Wiley and Sons. Pp. 2978–3005.
- Sunderman FW Jr, Dingle B, Hopfer SM, Swift T. 1988. Acute nickel toxicity in electroplating workers who accidentally ingested a solution of nickel sulfate and nickel chloride. *Am J Ind Med* 14:257–266.
- Sunderman FW Jr, Hopfer SM, Sweeney KR, Marcus AH, Most BM, Creason J. 1989. Nickel absorption and kinetics in human volunteers. *Proc Soc Exp Biol Med* 191:5–11.
- Sutherland B, Strong P, King JC. 1998. Determining human dietary requirements for boron. *Biol Trace Elem Res* 66:193–204.
- Tabata M, Sarkar B. 1992. Specific nickel(II)-transfer process between the native sequence peptide representing the nickel(II)-transport site of human serum albumin and L-histidine. *J Inorg Biochem* 45:93–104.
- Takizawa Y, Hirasawa F, Noritomi E, Aida M, Tsunoda H, Uesugi S. 1988. Oral ingestion of SYLOID to mice and rats and its chronic toxicity and carcinogenicity. *Acta Med Biol* 36:27–56.
- Tao SS, Bolger PM. 1999. Dietary arsenic intakes in the United States: FDA Total Diet Study, September 1991–December 1996. *Food Addit Contam* 16:465–472.

- Tseng WP. 1977. Effects and dose-response relationships of skin cancer and black-foot disease with arsenic. *Environ Health Perspect* 19:109–119.
- Tseng WP, Chu HM, How SW, Fong JM, Lin CS, Yeh S. 1968. Prevalence of skin cancer in an endemic area of chronic arsenicism in Taiwan. *J Natl Cancer Inst* 40:453–463.
- Tsuda T, Babazono A, Yamanoto E, Kurumatani N, Mino Y, Ogawa T, Kishi Y, Aoyama H. 1995. Ingested arsenic and internal cancer: A historical cohort study followed for 33 years. *Am J Epidemiol* 141:198–209.
- Uthus EO. 1994. Diethyl maleate, an in vivo chemical depleter of glutathione, affects the response of male and female rats to arsenic deprivation. *Biol Trace Elem Res* 46:247–259.
- Uthus EO, Nielsen FH. 1990. Effect of vanadium, iodine and their interaction on growth, blood variables, liver trace elements and thyroid status indices in rats. *Magnes Trace Elem* 9:219–226.
- Uthus EO, Poellot R. 1992. Effect of dietary pyridoxine on arsenic deprivation in rats. *Magnes Trace Elem* 10:339–347.
- Uthus EO, Poellot RA. 1996. Dietary folate affects the response of rats to nickel deprivation. *Biol Trace Elem Res* 52:23–35.
- Uthus EO, Seaborn CD. 1996. Deliberations and evaluations of the approaches, endpoints and paradigms for dietary recommendations of the other trace elements. *J Nutr* 126:2452S–2459S.
- Vahter M. 1983. Metabolism of arsenic. In: Fowler BA, ed. *Biological and Environmental Effects of Arsenic*. Amsterdam: Elsevier. Pp. 171–198.
- Valentine JL, He SY, Reisbord LS, Lachenbruch PA. 1992. Health response by questionnaire in arsenic-exposed populations. *J Clin Epidemiol* 45:487–494.
- Wagner SL, Maliner JS, Morton WE, Braman RS. 1979. Skin cancer and arsenical intoxication from well water. *Arch Dermatol* 115:1205–1207.
- Waltschewa W, Slatewa M, Michailow I. 1972. Testicular changes due to long-term administration of nickel sulfate in rats. *Exp Pathol* 6:116–121.
- Wei CI, Al Bayati MA, Culbertson MR, Rosenblatt LS, Hansen LD. 1982. Acute toxicity of ammonium metavanadate in mice. *J Toxicol Environ Health* 10:673–687.
- Weir RJ, Fisher RS. 1972. Toxicologic studies on borax and boric acid. *Toxicol Appl Pharmacol* 23:351–364.
- Wester RC, Hui X, Maibach HI, Bell K, Schell MJ, Northington DJ, Strong P, Culver BD. 1998. In vivo percutaneous absorption of boron as boric acid, borax, and disodium octaborate tetrahydrate in humans: A summary. *Biol Trace Elem Res* 66:101–109.
- Yamamoto S, Konishi Y, Matsuda T, Murai T, Shibata MA, Matsui-Yuasa I, Otani S, Kuroda K, Endo G, Fukushima S. 1995. Cancer induction by an organic arsenic compound, dimethylarsinic acid (cacodylic acid), in F344/DuCrj rats after pretreatment with five carcinogens. *Cancer Res* 55:1271–1276.
- Yamato N. 1988. Concentrations and chemical species of arsenic in human urine and hair. *Bull Environ Contam Toxicol* 40:633–640.
- Yang TH, Blackwell RQ. 1961. Nutritional and environmental conditions in the endemic Blackfoot area. *Formosan Sci* 15:101–129.
- Zaporowska H, Wasilewski W. 1992. Haematological results of vanadium intoxication in Wistar rats. *Comp Biochem Physiol C* 101:57–61.
- Zaporowska H, Wasilewski W, Slotwinska M. 1993. Effect of chronic vanadium administration in drinking water to rats. *Biometals* 6:3–10.

Zielhuis RL, Wibomo AA. 1984. Standard setting and metal speciation: Arsenic. In: Nriagu JO, ed. *Changing Metal Cycles and Human Health*. New York: Springer-Verlag. Pp. 323–344.

Ibid., Chapter 14, pp. 578–579.

- Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W. 1987. Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. *J Nutr* 117:1638–1641.
- Briefel RR, Sempos CT, McDowell MA, Chien S, Alaimo K. 1997. Dietary methods research in the Third National Health and Examination Survey: Under-reporting of energy intake. *Am J Clin Nutr* 65:1203S–1209S.
- Gibson RS, Ferguson EL. 1998. Assessment of dietary zinc in a population. *Am J Clin Nutr* 68:430S–434S.
- Hallberg L, Hulthen L. 2000. Prediction of dietary iron absorption: An algorithm for calculating absorption and bioavailability of dietary iron. *Am J Clin Nutr* 71:1147–1160.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- IOM (Institute of Medicine). 1994. *How Should the Recommended Dietary Allowances be Revised?* Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- NRC (National Research Council). 1980. *Recommended Dietary Allowances*, 9th ed. Washington, DC: National Academy Press.
- NRC. 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
- NRC. 1989. *Recommended Dietary Allowances*, 10th ed. Washington, DC: National Academy Press.
- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Schoeller DA. 1999. Recent advances from application of doubly labeled water to measurement of human energy expenditure. *J Nutr* 129:1765–1768.
- USDA (U.S. Department of Agriculture). 1999. *USDA Nutrient Database for Standard Reference*, Release 13. [Online.] Available: <http://www.nal.usda.gov/fnic/foodcomp> [accessed February 2000].
- WHO (World Health Organization). 1996. Zinc. In: *Trace Elements in Human Nutrition and Health*. Geneva: WHO. Pp. 72–104.

## APPENDIX C

*Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate (ISBN 0-309-09158-6)*, Chapter 2, pp. 48–49.

- AAP (American Academy of Pediatrics). 1997. Breastfeeding and the use of human milk. *Pediatrics* 100:1035–1039.
- Butte NF, Garza C, Smith EO, Nichols BL. 1984. Human milk intake and growth in exclusively breast-fed infants. *J Pediatr* 104:187–195.
- Chandra RK. 1984. Physical growth of exclusively breast-fed infants. *Nutr Res* 2:275–276.
- Feinleib M, Rifkind B, Sempos C, Johnson C, Bachorik P, Lippel K, Carroll M, Ingster-Moore L, Murphy R. 1993. Methodological issues in the measurement of cardiovascular risk factors: Within-person variability in selected serum lipid measures—Results from the Third National Health and Nutrition Survey (NHANES III). *Can J Cardiol* 9:87D–88D.
- Health Canada. 1990. *Nutrition Recommendations. The Report of the Scientific Review Committee 1990*. Ottawa: Canadian Government Publishing Centre.
- Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. 1993. Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: The DARLING Study. *Am J Clin Nutr* 58:152–161.
- Heitmann BL, Lissner L. 1995. Dietary underreporting by obese individuals—Is it specific or non-specific? *Br Med J* 311:986–989.
- Hill AB. 1971. *Principles of Medical Statistics*, 9th ed. New York: Oxford University Press.
- Hovvander Y, Hagman U, Hillervik C, Sjolin S. 1982. The amount of milk consumed by 1–3 months old breast- or bottle-fed infants. *Acta Paediatr Scand* 71:953–958.
- Hytten FE, Leitch I. 1971. *The Physiology of Human Pregnancy*, 2nd ed. Oxford: Blackwell Scientific.
- IOM (Institute of Medicine). 1991. *Nutrition During Lactation*. Washington, DC: National Academy Press.
- IOM. 2000. *Dietary Reference Intakes: Applications in Dietary Assessment*. Washington, DC: National Academy Press.
- IOM. 2002/2005. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*. Washington, DC: The National Academies Press.
- Lichtman SW, Pisarska K, Berman ER, Pestone M, Dowling H, Offenbacher E, Weisel H, Heshka S, Matthews DE, Heymsfield SB. 1992. Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. *N Engl J Med* 327:1893–1898.
- Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER, Steele PD, Lashley E. 1991. What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 54:291–295.
- Neville MC, Keller R, Seacat J, Lutes V, Neifert M, Casey C, Allen J, Archer P. 1988. Studies in human lactation: Milk volumes in lactating women during the onset of lactation and full lactation. *Am J Clin Nutr* 48:1375–1386.
- NRC (National Research Council). 1986. *Nutrient Adequacy. Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.

- Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. 1996. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440–1449.
- Perloff BP, Rizek RL, Haytowitz DB, Reid PR. 1990. Dietary intake methodology. II. USDA's Nutrient Data Base for Nationwide Dietary Intake Surveys. *J Nutr* 120:1530–1534.
- WHO (World Health Organization). 2002. *The Optimal Duration of Exclusive Breastfeeding. Report of an Expert Consultation*. WHO/NHD/01.09. Geneva: WHO.
- Willett WC, Sampson L, Stampfer MJ, Rosner B, Bain C, Witschi J, Hennekens CH, Speizer FE. 1985. Reproducibility and validity of a semiquantitative food frequency questionnaire. *Am J Epidemiol* 122:51–65.

Ibid., Chapter 3, p. 72.

- Dourson ML, Stara JF. 1983. Regulatory history and experimental support of uncertainty (safety) factors. *Regul Toxicol Pharmacol* 3:224–238.
- FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization). 1982. *Evaluation of Certain Food Additives and Contaminants*. Twenty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series No. 683. Geneva: WHO.
- FAO/WHO. 1995. *The Application of Risk Analysis to Food Standard Issues*. Recommendations to the Codex Alimentarius Commission (ALINORM 95/9, Appendix 5). Geneva: WHO.
- Health Canada. 1993. *Health Risk Determination—The Challenge of Health Protection*. Ottawa: Health Canada, Health Protection Branch.
- Hill AB. 1971. *Principles of Medical Statistics*, 9th ed. New York: Oxford University Press.
- Klaassen CD, Amdur MO, Doull J. 1986. *Casarett and Doull's Toxicology: The Basic Science of Poisons*, 3rd ed. New York: Macmillan.
- Mertz W, Abernathy CO, Olin SS. 1994. *Risk Assessment of Essential Elements*. Washington, DC: ILSI Press.
- NRC (National Research Council). 1983. *Risk Assessment in the Federal Government: Managing the Process*. Washington, DC: National Academy Press.
- NRC. 1994. *Science and Judgment in Risk Assessment*. Washington, DC: National Academy Press.
- OTA (Office of Technology Assessment). 1993. *Researching Health Risks*. Washington, DC: Office of Technology Assessment.
- WHO (World Health Organization). 1987. *Principles for the Safety Assessment of Food Additives and Contaminants in Food*. Environmental Health Criteria 70. Geneva: WHO.
- WHO. 1996. *Trace Elements in Human Nutrition and Health*. Geneva: WHO.
- Zielhuis RL, van der Kreek FW. 1979. The use of a safety factor in setting health-based permissible levels for occupational exposure. *Int Arch Occup Environ Health* 42:191–201.

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- Dourson ML, Stara JF. 1983. Regulatory history and experimental support of uncertainty (safety) factors. *Regul Toxicol Pharmacol* 3:224–238.
- FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization). 1982. *Evaluation of Certain Food Additives and Contaminants*. Twenty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series No. 683. Geneva: WHO.
- FAO/WHO. 1995. *The Application of Risk Analysis to Food Standard Issues*. Recommendations to the Codex Alimentarius Commission (ALINORM 95/9, Appendix 5). Geneva: WHO.
- Health Canada. 1993. *Health Risk Determination—The Challenge of Health Protection*. Ottawa: Health Canada, Health Protection Branch.
- Hill AB. 1971. *Principles of Medical Statistics*, 9th ed. New York: Oxford University Press.
- Klaassen CD, Amdur MO, Doull J. 1986. *Casarett and Doull's Toxicology: The Basic Science of Poisons*, 3rd ed. New York: Macmillan.
- Mertz W, Abernathy CO, Olin SS. 1994. *Risk Assessment of Essential Elements*. Washington, DC: ILSI Press.
- NRC (National Research Council). 1983. *Risk Assessment in the Federal Government: Managing the Process*. Washington, DC: National Academy Press.
- NRC. 1994. *Science and Judgment in Risk Assessment*. Washington, DC: National Academy Press.
- OTA (Office of Technology Assessment). 1993. *Researching Health Risks*. Washington, DC: OTA.
- WHO (World Health Organization). 1987. *Principles for the Safety Assessment of Food Additives and Contaminants in Food*. Environmental Health Criteria 70. Geneva: WHO.
- WHO. 1996. *Trace Elements in Human Nutrition and Health*. Geneva: WHO.
- Zielhuis RL, van der Kreek FW. 1979. The use of a safety factor in setting health-based permissible levels for occupational exposure. *Int Arch Occup Environ Health* 42:191–201.

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