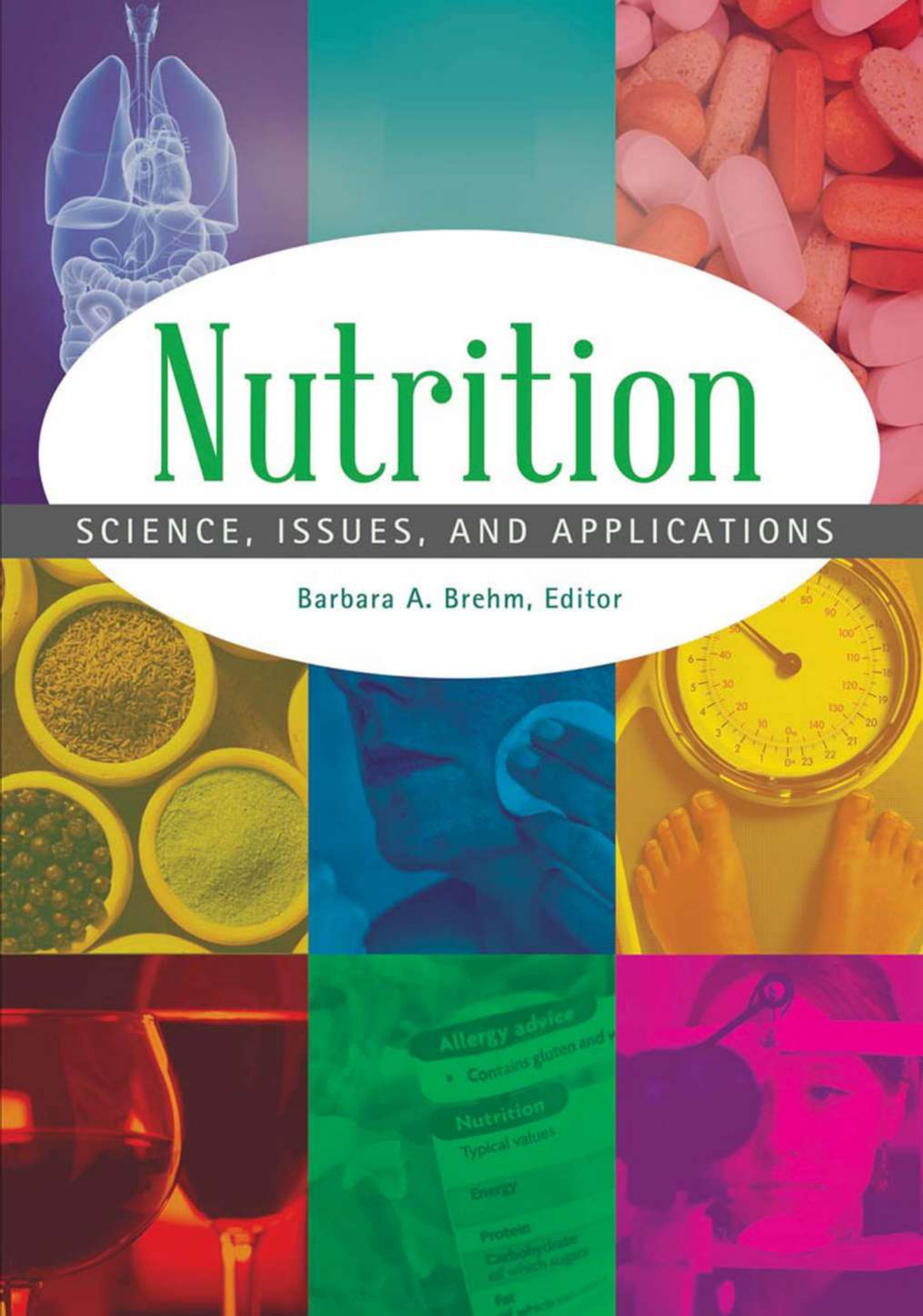

Nutrition
SCIENCE, ISSUES, AND APPLICATIONS
Barbara A. Brehm, Editor
Allergy advice
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Nutrition

Science, Issues, and Applications

Volume 1: A–H

Barbara A. Brehm, Editor

GREENWOOD™

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This book discusses treatments (including dietary therapies, dietary supplements, medications, and mental health therapies) for a variety of symptoms and disorders, and a variety of organizations. The authors have made every effort to present accurate and up-to-date information. However, the information in this book is not intended to recommend or endorse particular treatments or organizations, or substitute for the care or medical advice of a qualified health professional, or used to alter any medical therapy without a medical doctor's advice. Specific situations may require specific therapeutic approaches not included in this book. For those reasons, we recommend that readers follow the advice of qualified health care professionals directly involved in their care. Readers who suspect they may have specific medical problems should consult a physician about any suggestions made in this book.

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Fad Diets
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Women, Infants, and Children, Special Supplemental Nutrition Program for

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Cholesterol
Dental Caries (Cavities)
Detoxification
Diarrhea
Digestion and the Digestive System
Diverticular Disease
Enteral Nutrition
Enzymes, Digestive
Esophagus
Food Allergies and Intolerances
Gallbladder and Gallbladder Disease
Gastro-esophageal Reflux Disease
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Glycemic Index and Glycemic Load
Inflammatory Bowel Disease
Insulin

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Irritable Bowel Syndrome
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Arthritis and Nutrition
Attention-Deficit Hyperactivity Disorder and Nutrition
Autism and Nutrition
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Cancer and Nutrition
Cardiometabolic Syndrome
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Peptic Ulcers
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Premenstrual Syndrome
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Enrichment and Fortification
Female Athlete Triad
Fetal Alcohol Syndrome and Disorders
Infant Formula
Iron-Deficiency Anemia
Lactation
Older Adults, Nutrition Needs
Pregnancy and Nutrition
Premenstrual Syndrome

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Boron
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Choline
Chromium
Copper
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Enrichment and Fortification
Fatty Acids
Fluoride
Folate and Folic Acid
Functional Foods
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Iodine
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Linoleic Acid
Lipids
Magnesium
Manganese
Minerals
Molybdenum
Multivitamin and Mineral Supplements
Niacin
Nickel
Pantothenic Acid
Phosphorus
Potassium
Protein
Riboflavin
Selenium
Sodium and Salt
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Triglycerides
Vanadium
Vitamin A
Vitamin B6
Vitamin B12
Vitamin C
Vitamin D
Vitamin E
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Vitamins
Water Needs; Water Balance
Zinc

Obesity

Adipose Tissue
Appetite
The Atkins Diet
Bariatric Surgery
Body Composition
Body Mass Index
Brown Adipose Tissue
Calorie
Cardiometabolic Syndrome
Diabetes, Type 2
Energy Balance
Fad Diets
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The French Paradox
Hunger, Biology of
Ketosis and Ketogenic Diets
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National Weight Control Registry
Obesity, Causes
Obesity, Definition and Health Effects
Obesity, Treatment
Portion Size
The Poverty-Obesity Paradox
Public Policy on Nutrition
Sugar-Sweetened Beverages
Weight Watchers

Organizations and Programs

Academy of Nutrition and Dietetics
Health Canada
National Weight Control Registry
Nutritionists and Dietitians
School Lunch Program
Supplemental Nutrition Assistance Program
U.S. Department of Agriculture
U.S. Food and Drug Administration
U.S. Pharmacopeial Convention Verification Mark
Women, Infants, and Children, Special Supplemental Nutrition Program for

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Allyl Sulfides (Organosulfurs)
Alpha-Lipoic Acid
Anthocyanins
Antioxidants
Arginine
Astaxanthin
Berberine
Beta-Carotene
Black Cohosh
Caffeine
Capsaicin
Carnitine
Carotenoids
Catechins
Choline
Coenzyme Q10
Creatine
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Pyruvate and Pyruvic Acid
Quercetin
Resveratrol
S-Adenosylmethionine
Saponins
St. John's Wort
Zeaxanthin

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Appetite
Attention-Deficit Hyperactivity Disorder and Nutrition
Autism and Nutrition
"Brain Foods"
Cognitive Restructuring
Depression and Nutrition
Detoxification
Eating Disorders
Feeding Disorders
Female Athlete Triad
Food Addiction
Food Cravings
Hunger, Biology of
Mood and Food
Obesity, Causes
Obesity, Definition and Health Effects
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Orthorexia
Premenstrual Syndrome

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Creatine
Electrolytes
Female Athlete Triad
Glycemic Index and Glycemic Load
Iron-Deficiency Anemia
Sports Beverages
Sports Nutrition
Sports Supplements

Toxins

Alcohol
Arsenic
Copper
Detoxification
Fluoride
Foodborne Illness and Food Safety
Heterocyclic Amines and Polycyclic Aromatic Hydrocarbons
Hydrogenation
Lead
Mercury
Nickel
Raw Milk
Trans Fatty Acids

Preface

Nutrition news is everywhere. Opinions on the best way to eat often clash with one another, however, which bewilders and frustrates consumers. Nutrition-related health problems can prompt patients and family members to seek more information on healthful eating—but the search often leads to more questions than answers. The purpose of this encyclopedia is to provide the information needed for a deeper understanding of today's most thought-provoking topics in nutrition, and to help readers make more informed decisions about food choices and dietary patterns.

Human nutrition is a broad and multidisciplinary subject that combines physiology, biochemistry, psychology, and sociology. The entries in this encyclopedia give a basic overview of the most important and relevant nutrition topics for which readers are likely to seek information. This encyclopedia also provides a foundation for students taking introductory nutrition courses. It discusses the most common and interesting topics regarding human nutrition, provides solid background on the topics, and is a starting point for further research. The entries include relevant definitions, background, and a balanced perspective of current knowledge. The essays are written at a level accessible to upper-grade high school students, college students, as well as other readers. Each entry offers suggestions for further reading and research.

The material provided by this encyclopedia is helpful for students studying nutrition and other fields in which nutrition is important, such as medicine and health. Consumers will find the information helpful for making decisions about diet, and for understanding current controversies in nutrition and health.

Scope: Science, Issues, and Applications

People often seek information about nutrition because they wish to understand nutrition issues currently in the news, and want information to make decisions about what to eat to be healthy and to prevent or treat health problems. Nutrition issues are best understood in the context of relevant scientific information. Each entry presents a scientific background to illuminate some of the current issues related to the topic. Health applications are outlined conservatively so as to discourage readers from trying potentially useless, expensive, or harmful nutrition remedies that lack sufficient research support.

This encyclopedia contains 281 entries that encompass the most interesting and current topics in nutrition. Topic areas include the following:

- Nutrition-related health issues, including acne; Alzheimer's disease; arthritis; cancer; cardiovascular disease; food allergies and intolerances; inflammation; and osteoporosis.
- Obesity-related issues including approaches to weight control; body composition; body mass index (BMI); energy balance; and obesity-related health problems (e.g., type 2 diabetes).
- Psychological issues and the role played by nutrition in each area, including autism; attention deficit hyperactivity disorder; brain foods; depression; eating disorders; and food addiction.
- Basic human nutrition, including the digestive system and the major organs of digestion; and each nutrient and class of nutrients, including proteins, carbohydrates, fats, vitamins, minerals, and water.
- Phytochemicals in foods and dietary supplements, from alpha lipoic acid to zeaxanthin.
- Toxins that can contaminate food, including arsenic, lead, and mercury; and those caused by foodborne illnesses.
- Environmental issues and their interaction with nutrition and the food supply, including climate change; genetically modified foods; organic foods and farming; and sustainable agriculture.
- Ideas about eating, such as detoxification; the Locavore Movement; the Paleolithic diet; the Slow Food Movement; and public policy and nutrition.

Special Features

In addition to entries covering a wide range of nutrition topics, this encyclopedia includes special features to assist readers in the search for information and understanding. Students completing class assignments such as research papers also will find these features helpful.

- **Introduction to information literacy**. Nutrition topics often are fraught with controversy and one-sided, sensational media coverage that blows the results of a single study out of proportion. The introduction to this encyclopedia—"Fact or Fiction? Evaluating Nutrition Information"—provides a brief overview of the scientific methods used by researchers studying topics in nutrition. The overview can help readers evaluate research findings described in the popular media.
- **Further reading**. Each entry lists at least two easily accessible articles or authoritative websites for readers seeking more information.
- **Research issues**. Many entries include guidance on research areas for students seeking project topic ideas. These issues might stimulate further reading and research for school presentations or papers, or simply spur on the curious reader to find more information about a nutrition topic.

- **Sidebars**. Sidebars (boxed text) accompany some entries to provide noteworthy and relevant applications for entry information. A sidebar accompanying the topic "Eating Disorders," for example, provides suggestions for helping someone who might have an eating disorder.
- **Recommended resources**. At the end of volume 2 of the encyclopedia, a list of general resources provides a list of well-respected accessible sources of nutrition information for readers seeking more information. It also includes pertinent websites and a note about some websites to avoid.

Additionally, these features can help readers find information in *Nutrition: Science, Issues, and Applications*.

- Cross-references to other essays in the encyclopedia that can provide relevant information are included in each entry.
- A comprehensive index to the entire work is located at the end of volume 2.
- A "Guide to Related Topics" at the front of each volume lists all of the entries in the book categorized under broad topics.

Acknowledgments

I am deeply grateful to Smith College for funding several valuable research assistants, especially two of my graduate students, Patricia Cipicchio and Lisa P. Ritchie, who helped extensively with research, writing, and editing this encyclopedia. The students I have worked with over my 30-plus years of teaching nutrition have helped me understand the interests of young people and how to best guide them in productive research. Their interests helped inform the topic selection for the encyclopedia, and many of my advanced students also helped with research and writing. Smith College truly strives to remain true to its mission of educating women of promise for lives of distinction.

Special thanks to the many writers—including many former students—who contributed to this encyclopedia. Your extensive research, interdisciplinary perspectives, and willingness to write second and third drafts helped to shape the quality of this encyclopedia. Thank you.

I would also like to thank my developmental editor, Anne Thompson, for her advice and guidance throughout the planning and writing of this work. Her experience, knowledge, insight, and good humor have been invaluable.

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Introduction: Fact or Fiction? Evaluating Nutrition Information

Is milk bad for you? Are low-carb diets or low-fat diets better for losing weight? Should you eat more turmeric to prevent cancer? Does red wine reduce risk for heart disease? These deceptively simple questions are difficult to answer. Often, the answer begins with the phrase, "It depends . . . " followed by a mile-long list of issues to consider. Most people lose interest before hearing the full response.

Why can't scientists figure out the answers to these and other nutrition questions? Why do the experts seem to disagree on everything—from how much vitamin D people need each day to whether genetically modified foods are risky? Answers to these questions are elusive for several reasons. A brief overview of the research process helps to explain why.

The Goal of Science: Determining Relationships among Variables

Scientists use logic, observation, and reasoning to determine relationships among variables. A variable is something that can take on two or more values. Body weight, daily calorie intake, and blood cholesterol levels are examples of variables. Scientists conduct investigations to try to understand how the change in one variable—typically called an "independent variable" or "treatment variable"—is related to or causes change in another variable, the dependent variable. To untangle these relationships, scientists use established research practices to identify the underlying truth as effectively as possible. In the study of nutrition, the most common of these practices include experimental studies and correlational studies.

Experimental Studies

Experimental studies have the most control over the subjects and variables involved. Typically, an experimental situation is designed and administered, and the results are observed. Some of the ways that scientists conducting experimental studies strive to achieve accuracy in the results include the following.

Isolate the Effect of Independent Variables

To observe and understand the relationships between variables, researchers try to hold all nonexperimental variables as constant as possible. Thus, the

independent and dependent variables are the variables that change during the experiment. An example is researchers that are interested in the effect of omega-3 fatty acid intake on certain chemicals in the brain. They design an experiment that uses two groups of rats; one group is given a diet enriched with omega-3 fatty acids, and the other group receives a control diet. To make the differences in diet the only independent variable, researchers attempt to keep all other conditions the same. They use exactly the same strain, age, and sex of rat for both groups, and house, feed, handle, and care for all rats identically. At the end of the experiment, when the brain chemical levels are compared, the scientists are more certain that any changes in these chemicals were caused by differences in activity level.

Experiments with humans tend to present a different set of challenges. Sometimes researchers have little or no control over the variables in their studies. Therefore, instead of controlling outside variables, they simply try to keep the variance of values for the outside variables as similar as possible for all groups. For example, if researchers want to find out whether students who consume more servings of fruits and vegetables report less stress and greater levels of well-being than other students, they might solicit a large group of volunteers. Obviously, the students will not be littermates with identical genetic material. Participants will have many other differences as well. To try to make the groups as similar as possible, investigators use a process called random assignment. Random assignment to groups or treatments means that each subject has the same chance of getting into a given group. By assigning students randomly to groups (one group consumes more fruits and vegetables, another gets an alternative treatment as similar as possible to the other group, perhaps a diet focused on whole grains), researchers hope the groups vary in similar ways on factors such as health, sleep habits, exercise, or anything else that might affect feelings of stress and well-being. Some students in each group will not be getting enough sleep, some will be breaking up with their romantic partners, and some will have parents going through a divorce. The researchers, however, hope that the level of background emotional distress will be similar for each group.

Control for the Expectations of Subjects and Researchers

Expectations strongly influence the way humans experience life, therefore science tries to control these as much as possible. Subjects in the experiment should not know whether they are receiving a treatment that might cause a certain effect. The group receiving the actual experimental variable of interest is called the "treatment group." A "control group" does not receive or undergo the treatment or variable being tested. Ideally, the subjects in the control group receive a "placebo." A placebo closely matches the treatment condition but lacks the ingredient believed to be exerting an effect. This group "controls for" the placebo effect. The "placebo effect" refers to the fact that subjects in a study might demonstrate changes in the dependent variable simply because they are getting attention or expecting an effect, rather than because the independent variable itself is causing the change. In some nutrition studies, inert pills that look the same as the nutrient or supplement being tested are given. Both groups think they are getting "the real thing." Even in

animal studies the control group receives a placebo. If the treatment group receives injections of a nutrient, then the control group receives injections of an inert substance to control for the effect of the injection procedure.

The expectations of the researchers performing the experiment also can get in the way of accurate results. Even the most careful and well-meaning people tend to see what they expect or want to see. (This expectation can be strengthened when the researcher's income or grant money is dependent upon experimental results.) Experimenters might throw out data that do not conform, thinking that an error has occurred. They could miss certain observations that they were not expecting to see. In the best type of testing—a double-blind study—neither the researchers running the tests nor the subjects know who is in the experimental group or who is in the placebo treatment group. Of course, someone knows, but that person assigns numbers to subjects and is not directly involved in administering the study. In the health sciences, a double-blind experimental study usually is used to test medical treatments or drugs. Many of these are called double-blind randomized control trials, meaning that they use double-blind methods with subjects that are randomly assigned to groups. Such studies are considered the "gold standard" of experimental methods, as they have the most experimental control.

Use Statistical Methods to Evaluate the Probability That Results Were Due to Chance

Statistical methods are based on mathematical models of probability. Statisticians use these methods to examine experimental data. They compare groups and examine how the values of one variable change in relationship to other variables or treatments. Because most variables vary somewhat, there always is the possibility that the variance observed between groups is due to random chance, rather than being an effect of the independent variable. Scientists using statistical methods can calculate the likelihood that differences observed in experimental data are significant—which means that the results have a low likelihood of occurring purely by chance. Statistical methods also are used in correlational research.

Correlational Research

Experimental study designs often are not feasible. For example, it might be unethical to administer the treatment variable of interest to subjects—such as asking people to consume trans-fatty acids or increased levels of salt—because health risks are associated with these behaviors. Instead, scientists must just observe what naturally occurs in people who choose these behaviors. Sometimes it is not possible for subjects or experimenters to be blind to the treatment: Participants can determine whether they are consuming a low-calorie diet. The time course of the development of chronic disease often is an issue, as is the cost of following participants for several years.

Correlational research methods commonly are employed by scientists when a true experiment is not feasible or might not yield the best information. In

correlational research, values on variables of interest are observed and recorded, and statistical methods are used to evaluate the relationship—or correlations—among variables. Such research methods enable investigators to draw conclusions about how the behavior of one variable is related to another. When two variables are associated with each other (correlated), they vary together. When one variable increases, the other variable either increases or decreases. For example, because intake of red meat is correlated with heart disease, epidemiological data should show that as the amount of red meat consumed per day increases so does likelihood of heart disease occurring.

Epidemiological studies collect data on free-living populations and use statistical methods to observe associations and draw conclusions. Such studies can take several forms. Case-control studies are a type of correlational research commonly used by epidemiologists and medical researchers, in that naturally occurring disease patterns are observed. In case-control studies, researchers examine people who have the variable of interest; for example, colon cancer. Researchers then select a comparable group of people who do not have colon cancer as the "control" group. The researchers try to match the control group to the other group on as many variables as possible, including age, gender, and socioeconomic status. The groups then are compared on variables of interest to the researchers; for example, the intake of fruits, vegetables, and dietary fiber.

Most case-control studies are retrospective—they look back in time. Evidence and conclusions drawn from such studies are not considered to be as strong as that of prospective research, in which investigators gather data about the present, recording answers over time. This is because time—along with a disease diagnosis—can blur the memory. People trying to answer questions about what they ate many years ago can err. Prospective research measures variables as they occur. People usually are more accurate when reporting how much fish they ate this week, or how much alcohol they drank yesterday, than when recalling consumption patterns from many years ago.

Sometimes epidemiological studies simply collect a large amount of information on a great number of people and analyze the data without forming case-control comparisons. In 1948, for example, researchers performing a new study called the "Framingham Heart Study" began collecting data on a group of 5,209 men and women who were between the ages of 30 and 62 and from the town of Framingham, Massachusetts. The study's goal was to determine major risk factors for heart disease. This study was one of the first to find an association between lifestyle factors—including diet, smoking, physical activity—and heart disease. The original volunteers still are being followed, and new groups have been added to this exciting study. More information about the Framingham Heart Study can be found on its website (https://www.framinghamheartstudy.org/about-fhs/history.php).

When evaluating the results of epidemiological studies, or other studies that generate correlations, it is important to remember that correlations might not necessarily have a cause-and-effect relationship. Correlations only show that two (or more) variables vary together; they cannot demonstrate that one is causing the other to change. Sometimes there is a cause-and-effect relationship, but other times

another factor could be causing both of the other variables to change together. For example, it has been observed that countries with populations that have a greater daily average intake of fat tend to have increased rates of breast cancer. As further studies have been conducted, however, the total daily fat intake does not appear to cause most breast cancer. It is possible that a third factor, for example, increased intake of meat, reduced intake of fruits and vegetables, or living in a polluted, industrialized country, is linked to both fat intake and breast cancer rate.

Epidemiological studies, however, can suggest causative relationships which then are explored with other studies. Experimental studies in laboratory animals could demonstrate a biologically plausible mechanism for causation. When a large number of epidemiological studies all find a similar association between two variables, scientists take note, especially when studies find the same result for different groups of people. Case-control studies also can strengthen an observation. Often statistical techniques combine the data from several studies into one large analysis, called a meta-analysis, to get a clearer picture of a correlation. In the end, however, take care to never assume causation in correlational data.

Research Ethics

The ethical conduct of scientists and their institutions sometimes comes under intense scrutiny when reports of fraudulent data or inaccurate statistical calculations come to light. It usually is other scientists who uncover the unethical behavior of their peers. Such behavior fortunately is fairly rare. Although scientists are human and do make mistakes—and even lie from time to time—on the whole, the process of science is eventually self-correcting and leads to improvements in long-term understanding.

All research institutions have strict guidelines concerning research ethics, and researchers are punished when the rules are broken—often losing their research funding and even their jobs. Guidelines spell out every detail of the research process. Especially important are the rules concerning the use of human subjects. Every institution has an independent board that reviews research proposals to make sure that people are treated ethically, that experimental protocols are not harmful, and that subjects are given as much information as possible about the potential benefits and costs of their participation. Additionally, use of laboratory animals is strictly regulated. Ethical guidelines provide protocols and training for researchers to ensure that they treat their subjects appropriately.

Most journals and professional meetings ask researchers to give full disclosure of all special interests that might influence their work. For example, sources of funding from grants and the researcher's participation in other relevant organizations must be listed in the article.

Continued Questioning, Analysis, and Research

For scientists, the research process is never over because the results from one study always suggest more questions that lead to more thinking, hypotheses, testing, and

analysis. Scientists avoid the use of the words "prove" or "proof," which imply that conclusions are unquestionable and beyond the shadow of a doubt. Science is built upon doubt and critical analysis. When scientists evaluate the conclusions of their studies, they use a softer language. They say, "Our studies support the idea that . . ." or "Our data suggest that . . ." even when the results are very strong and meaningful.

Peer Review, Publication Bias, and Science Reporting

Results of a study are not accepted by the scientific community until the research reporting the findings has gone through the peer-review process (in which other scientists evaluate the study) and have been accepted for publication. Even after publication, other scientists question the experimental methods, the statistics, and the results.

Although the peer-review process is designed to ensure that scientific research is as accurate as possible, it has been shown that journals are more likely to publish "interesting" studies—in which an independent variable is shown to influence a dependent variable—rather than studies in which no effect is found. This means that important studies showing no relationship are less likely to be published, thus confounding understanding. A study finding that a higher vitamin D intake in laboratory rodents leads to lower cancer rates, for example, probably would be more likely to be published than a study that does not find an effect. Over time an accurate picture of relationships generally emerges as more studies are conducted, but this can take several years. Publication bias reminds readers that exciting results of a single study should be taken with a grain of salt (or something more healthful), until additional studies support that relationship.

People should be cautious when reading scientific reports about research in the popular media. Even though the research could be very interesting, science reporters might overstate a study's conclusions to attract readers. Years ago when researchers found a link between consumption of tomato products and reduced risk of prostate cancer, for example, headlines blared, "Pizza reduces cancer risk." Such news stories and headlines are misleading.

Food Consumption and Dietary Patterns

The human diet is a complicated variable. Identifying helpful and harmful foods, food components, and dietary patterns is difficult for a variety of reasons, including those listed below.

- People consume a wide variety of foods each day, and diets also can vary considerably from day to day; simply obtaining accurate food records from people is challenging.
- Individuals generally consume more than 25,000 bioactive food constituents—including nutrients and phytochemicals—in any given diet, therefore it is not easy to determine the influence of any given compound (WCRF/AICR, 2007).

- Results obtained in the laboratory with in vitro cell cultures could have little relevance to human beings. For example, although beta-carotene slows cancer cell growth in vitro, use of beta-carotene supplements by former smokers is associated with an increased risk of lung cancer.
- Dietary compounds interact with the digestive system and other constituents from food as food is broken down and absorbed. Therefore even though a dietary constituent attacks cancer cells in vitro, this effect might not occur in the body. Digestive enzymes can alter and inactivate the constituent's chemical structure. Active constituents could bind to dietary fiber and not be absorbed, or might not be absorbed from the diet in amounts sufficient to produce a significant effect. If they are absorbed, nutrients and phytochemicals then must travel in the bloodstream, where they can be influenced by various biochemical pathways in the liver, kidney, and other organs. The constituents might never even come into contact with cancerous cells; and if they do, they could behave differently in the body than in the lab.
- Animal studies can be helpful but they do not always apply to humans.
- Dietary components can influence different people in different ways depending upon their genetics, as demonstrated by the fields of nutrigenomics and nutrigenetics.
- Influence of a nutrient or other phytochemical often depends upon the dosage of the substance. Many compounds are ineffective at low doses, helpful at moderate doses, and harmful at high doses.
- Timing in a person's life cycle can shape the influence of particular dietary factors on cancer risk. For example, women who experience famine before age 10 have a reduced risk of developing precancerous breast tissue later in life, and women who experience famine after age 18 have an increased risk (WCRF/AICR, 2007).

Evaluating Nutrition Information

People should use a cautious, critical approach when evaluating nutrition information. The following strategies can help readers separate fact from fiction.

- Before adopting information gleaned from a book or article about nutrition, always consider the source. Television shows, websites, blogs, books targeting the general public, and articles published in the popular media often blow research results out of proportion. If the sources cite studies, then try to find and read the peer-reviewed studies to determine whether the media reports actually match the study findings.
- Is the information source selling products that are supported by the reported research results? For example, a website that sells dietary supplements might overstate the results of studies on a given supplement.
- Search well-respected journals, professional organizations, and websites (see the "Recommended Resources" included in this book). What do these sources say about the subject?

- Look for studies produced by experts in the area of interest. Especially helpful are review articles and meta-analyses that examine the big picture, and that discuss the evidence on both sides of the issues.
- Seek the advice of a nutrition professional or health care provider before taking dietary supplements, especially when being treated for a health problem.
- Healthy young people should strive for good intake of nutrients and phytochemicals through good food choices rather than from dietary supplements, unless otherwise directed by a health care provider. (For example, people with iron-deficiency anemia might be directed by a health professional to take iron supplements.)

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A

Academy of Nutrition and Dietetics

The Academy of Nutrition and Dietetics (AND) is the world's largest organization of certified nutrition specialists, and includes registered dietitians (RD) and registered dietetic technicians (DTR). This organization began life as the American Dietetics Association (ADA) but was renamed in 2012. Lenna F. Cooper founded the ADA in Ohio during World War I in 1917. The ADA's focus originally was on assisting the government's emergency food conservation initiative (Barber, 1959). Today, however, the Academy's objective is to improve national health through empowering dietetic professionals, providing education, and performing research and advocacy work. The AND manages *The Journal of the Academy of Nutrition and Dietetics*, a monthly peer-reviewed publication for members, educators, and scholars. The AND website (EatRight.org) is maintained by the AND to provide evidence-based scientific information on disease, exercise, and general health concerns; it also includes healthy recipes and daily tips for maintaining a healthy lifestyle.

The Academy maintains several offshoot organizations, including the AND Foundation, the Accreditation Council for Education in Nutrition and Dietetics (ACEND), and the Commission on Dietetic Registration (CDR). The AND Foundation is a charity organization that incorporates scholarships, awards, and the "Kids Eat Right" initiative. The Accreditation Council for Education in Nutrition and Dietetics oversees accreditation for educational programs completed prior to RD and DTR certification. The Commission on Dietetic Registration provides independent board certification for nutrition, dietetics, and specialties administering the RD and DTR legally protected titles. This protection is suggested to prevent the dissemination of inaccurate nutritional information by less qualified or less educated individuals in the field. Approximately 72% of the Academy's 75,000+ members are registered dieticians. The Academy of Nutrition and Dietetics has legal control over titles describing expert or professional nutritional practice, thus acquiring the title is an elaborate and highly regulated process. The general process is described below.

Registered Dietitian Certification Process

- Bachelor's degree in nutrition from ACEND-accredited university
  - Coordinated Program (CPD)
  - Dietetic Program (DPD)

- 1,200 hours of a ACEND-accredited internship
  - Offered through CPD program, and independently through health care facilities and the foodservice industry
  - Approximately 6 to 12 months needed to complete the program
- Pass national RD examination through CDR (additional specialization certifications in sports, pediatrics, and others is offered by CDR)
- Maintain professional certification through continuing education program

The Academy of Nutrition and Dietetics is not associated with the government; however, the AND maintains strong communication with the government through its Washington, DC, headquarters. The ADA's 2010 Kids Eat Right initiative works in conjunction with White House efforts to end childhood obesity by mobilizing members in community nutrition education and through policy-based advocacy (Academy of Nutrition and Dietetics, 2013; Academy of Nutrition and Dietetics, 2010).

The AND is not without criticism from members and the public. Many members are frustrated by the Academy's conflicting nutrition messages, and are concerned about possible influence of the AND's corporate sponsors, such as Coca-Cola and McDonald's. Critics have charged that the AND's core stance, "there is no 'good' or 'bad' food," could be tainted by monetary gain—thus risking the Academy's reputation as a science-based organization (Burros, 1995). The Academy also maintains strong, highly criticized financial affiliations with the pharmaceutical industry (Babjak, 2009). Despite criticism, however, the AND's membership continues to grow steadily and its publication remains the most often-read journal among Academy members (Lipscomb, 2011).

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See Also: Nutritionists and dietitians.

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Acne

Acne (*Acne vulgaris*) is the most prevalent chronic skin disorder. It occurs when hair follicles become blocked by dead skin cells and oils—leading to the development of blackheads, pimples, infection, and inflammation. The most severe form of acne—cystic acne—includes infection of the hair follicles and associated structures in the deeper skin layers, forming cysts and deep scarring. Acne occurs most commonly on the face, neck, shoulders, chest, and back, and is most likely to appear during periods of hormonal change, such as adolescence.

Throughout the years, the dermatological community has strongly disputed the relationship between acne and nutrition. Recent studies, however, indicate that certain dietary components—especially food with a high glycemic load, and possibly dairy products—can increase acne severity. Anti-inflammatory foods and supplements might reduce the inflammation associated with acne. Although not everyone with acne responds to dietary changes, some people with acne who adhere to the dietary changes do experience some improvement in the condition.

Skin is lubricated by oil called "sebum," which is produced by microscopic sebaceous glands. These glands open into the hair follicle. The concentration of sebaceous glands is greater on the face and scalp. Acne is associated with overproduction of sebum, which appears to interfere with the normal shedding of dead skin cells. An accelerated turnover of skin cells (more shedding of dead skin cells) also can exacerbate acne. Bacteria from the skin can thrive in the hair follicle, stimulating the body's inflammatory response as immune cells attempt to rid the body of infection.

Treatment for acne includes medications—some applied topically and others taken internally—which reduce bacteria concentrations, slow the production of sebum, and open pores. Some medications influence the levels of the sex hormones, which seem to exacerbate acne development. Nutrition is not considered a primary factor in acne causation or treatment, although dietary changes can be moderately helpful for some people.

Medical reports associating acne and nutrition persisted from the late 19th century until the late 1960s, and dietary restriction was part of standard acne therapy throughout those years. Foods high in sugars and fats, including chocolate, generally were believed to exacerbate acne symptoms. Studies conducted from the 1960s onward, however, failed to find associations between these foods and acne; and suggesting dietary alterations to improve acne in patients became controversial. Recently, interesting evidence linking acne symptoms to a variety of dietary components has revived the acne-nutrition discussion. Another

interesting nutrition-related component of acne treatment is the development of medications derived from vitamin A.

Diet and Acne

As a general rule regarding acne and nutrition, what is good for one's health is good for one's skin. Consuming a healthful diet provides skin with the nutrients needed for its good health. Adequate hydration also is important for healthy skin. Acne involves high levels of inflammation, therefore consuming foods high in antioxidants might be helpful in some cases. Important antioxidant nutrients include the vitamins C and E, the mineral selenium, and phytochemicals such as the carotenoids. Some researchers have explored potential diet-related mechanisms that might influence the acne-development process. Early evidence, for example, suggests that microorganisms inhabiting the gastrointestinal tract could influence levels of inflammatory activity throughout the body (Bowe & Logan, 2011).

Some researchers have argued that epidemiological evidence suggests that acne is a phenomenon of Western civilizations having populations that consume a high concentration of foods that have a high glycemic index (Melnik, 2012). Dairy and high-glycemic carbohydrates have been theorized to contribute to insulin resistance and to an increase in blood insulin levels (Liakou, Liakou, & Zouboulis, 2012). Chronically elevated blood insulin levels appear to influence cellular activity in a number of ways that could contribute to acne occurring in vulnerable individuals (Melnik, 2012). Prescribing a low-glycemic index diet to treat acne patients, however, has not yet been explored in a systematic fashion.

What is a person with acne to do? Dermatologists suggest that people with acne keep a food diary to use in developing a healthful, well-balanced diet that reduces or eliminates potential problematic foods—such as dairy and wheat—and increases servings of vegetables high in antioxidants and servings of fish containing healthy oils that can help combat inflammation. Meeting with a dietitian for meal-planning advice also is recommended, especially for growing adolescents. Eliminating foods must not lead to poor diets. It can take several weeks for dietary change to have an effect. Although dietary change alone does not appear to be a fully effective treatment for acne, it might be helpful when used in combination with prescribed skin care and medications.

Vitamin A Medications for Acne

Vitamin A, also called "retinol," is found naturally in fish oils such as cod liver oil. Precursors to vitamin A, carotenoids, are found in many fruits and vegetables. Prescription medications derived from vitamin A compounds reduce inflammation in mild to moderate acne. Tretinoin ("Retin-A"), adapalene ("Differin"), and other topical retinoid products work to prevent oil and skin-cell trapped pores. Severe acne—especially the type of acne that involves deep inflammation in the sebaceous glands that is not responsive to any other treatment—sometimes is treated with a vitamin A derivative, isotretinoin ("Accutane"), that is taken internally. Isotretinoin

can have serious side effects, therefore patients using the drug must be monitored closely. Serious birth defects can result when pregnant women take isotretinoin, however; therefore women of childbearing age must be especially careful to avoid conceiving while taking this drug.

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See Also: Antioxidants; Glycemic index and glycemic load.

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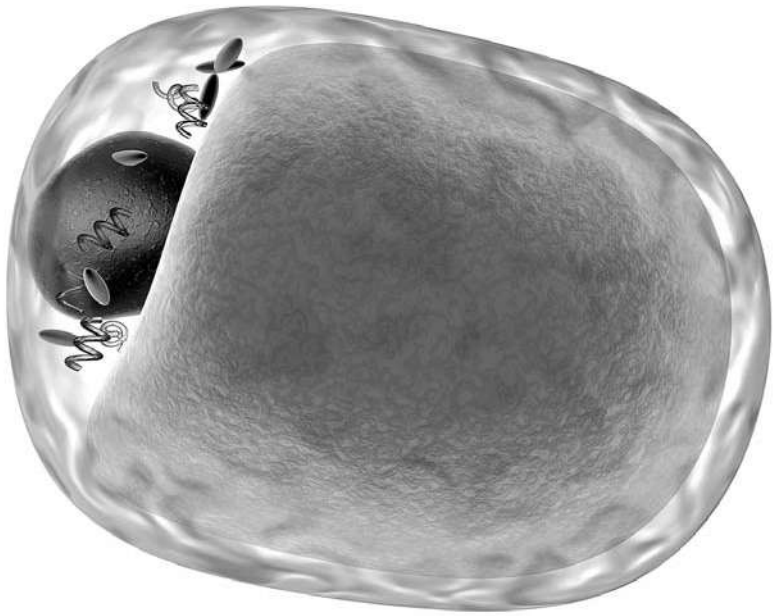
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Adipose Tissue

Adipose tissue refers to body tissues composed primarily of fat storage cells, called "adipocytes." Adipocytes are specialized for storing energy in the form of triglyceride molecules. Triglyceride is manufactured by the liver from excess fuel substrates, which are the nutrients that provide the body with energy: carbohydrates, proteins, and fats. (Alcohol also supplies calories, but it is not considered to be a nutrient.) After the liver manufactures triglycerides from excess energy the triglycerides are sent into the bloodstream, primarily in the form of chylomicrons and other lipoprotein compounds. From the bloodstream the triglyceride is picked up by adipocytes and shuttled into storage.

In addition to their energy storage functions, adipose tissue, adipocytes, and triglyceride molecules perform several other vital physiological and anatomical



Fat cells, or adipocytes, are specialized cells capable of synthesizing and storing fat, in the form of triglycerides. Up to 90% of an adipocyte's volume may be composed of triglycerides. (Spectral-design/Dreamstime.com)

functions in the body. Pads of adipose tissue help to cushion vital organs, such as those in the abdomen. Adipose tissue pads also serve as shock absorbers throughout the body, including in the synovial joints. Many important body structures are composed of fats, including the cell membranes, the sheath surrounding many nerve cells, and some components of bone marrow. Fat located in these places is referred to as "essential fat" because it is essential for health. Essential fat contributes about 3% to 5% of total body weight.

Sex-Specific Adipose Stores

Women have an additional category of essential fat called "sex-specific fat." It is found in the breasts, hips, and thighs. Sex-specific fat explains why the leanest of females has more body fat than the leanest of males. A great deal of energy is required to run the menstrual cycle and to grow and nurse a baby, hence the extra energy stores. Sex-specific fat stores contribute about 5% to 9% of body mass in women.

Intramuscular Triglycerides

Some fat is found in muscle tissue, in the form of intramuscular triglycerides (IMTG). This fat stores energy and can be used to support muscular contraction

during physical activity. In general, IMTG are most commonly used during submaximal exercise of medium intensity. IMTG also are used along with muscle glycogen (a form of starch storage) during resistance exercise. Research indicates that women use about twice as much IMTG as men do during exercise, and that exercise training improves skeletal muscle's ability to metabolize IMTG for fuel. The ability to use IMTG for fuel can vary with glucose tolerance—an indication of how well blood sugar is regulated by the body.

One study, for example, examined the use of IMTG in obese subjects having normal or impaired glucose tolerance, thus qualifying subjects for a diagnosis of prediabetes (Perreault, Bergman, Hunerdosse, Playdon, & Eckel, 2010). The average BMI of the men and women participating in the study was about 31.5, and the average body composition was about 36% fat. The subjects were 45 to 70 years old and fairly sedentary. The researchers found subjects with prediabetes had greater levels of IMTG and showed a lower rate of IMTG use at rest as compared with subjects who had normal glucose tolerance. This research supports the observation that prediabetes has a wide range of effects upon energy-production systems and not simply blood-sugar regulation.

So are IMTG a good thing? Young, lean endurance athletes seek to maximize their utilization of IMTG stores to supply fuel for activities such as endurance running, cycling, and swimming. Trained muscles effectively draw on these stores, and IMTG stores contribute to performance. These stores, however, are higher in older adults and not linked to improved performance. In fact, in older adults, the IMTG stores increase and the number of mitochondria decline. The triglycerides must get into mitochondria to be metabolized into energy. One study found that older men and women had more IMTG not in contact with mitochondria (Crane, Devries, Safdar, Hamadeh, & Tarnopolsky, 2010). Both old and young subjects had similar levels of daily physical activity, therefore the researchers concluded that, with age, muscle cells become less efficient at producing energy from IMTG. And, as noted, obese individuals also have higher IMTG stores. Therefore whether IMTG is good or bad depends upon the amount, a person's age, a person's training status, the BMI, and glucose tolerance.

Subcutaneous Fat

Approximately a third of a person's body fat is stored under the skin. These fat stores are called "subcutaneous fat." Some subcutaneous fat is helpful as insulation, keeping warmth within the body in cold weather. People who have observed (or remember being part of) a pool or lake full of children probably recall the thinner children having less tolerance for staying in cool water, and the heavier children were comfortable for longer periods. Conversely, people with extra subcutaneous fat lose heat less quickly in hot environments and have increased risk of heat illness, especially during high-intensity and prolonged physical activity. Subcutaneous fat improves the appearance of the face, helping to support the skin. The faces of very thin people usually look older in later life than those of their heavier peers.

Brown Adipose Tissue

Brown adipose tissue (BAT) is a special type of fat that contains a greater density of capillaries and mitochondria than that of white fat. Brown fat cells generate heat and in cool environments help mammals maintain body temperature without shivering. Researchers have speculated that the greater levels of BAT in lean people as compared with obese individuals might partly explain differences in body composition. Higher levels of BAT contribute to a higher resting metabolism and the ability to consume more calories without gaining weight. Once thought to be present in significant amounts only in infants, now—through nuclear imaging techniques—BAT has been shown to be present in adults.

Visceral Adipose Tissue

Visceral adipose tissue (VAT) consists of fat stored around the abdominal organs, including the liver, stomach, intestines, and kidneys. Excess VAT appears to be the link between obesity and negative health effects such as artery disease, type 2 diabetes, hypertension, and inflammatory disorders (Cornier et al., 2011). Although waist circumference gives some information about central obesity (excess fat storage in the torso), it does not reveal whether the excess fat is subcutaneous or VAT. Computerized tomography (CT) scans provide information on the volume of fat inside the abdomen, but such tools are not yet commonly used for diagnosis. Symptoms such as the metabolic syndrome, with disorders of blood sugar and blood pressure regulation, indicate the need for lifestyle change to reduce VAT and restore normal metabolic functions.

Adipose Tissue: More Than a Storage Depot

Adipose tissue participates actively in metabolic regulatory processes, communicating extensively with other cells, tissues, and organs in the body. For example, an interesting messenger affected by adipose stores is called "adiponectin"—a hormone-like molecule produced by adipose tissue as well by as other tissues. Higher levels of body fat have been associated with lower levels of adiponectin (Liu et al., 2012). Adiponectin helps insulin get sugar from the bloodstream into cells, where it can be stored or burned for energy. This observation might help explain the insulin resistance that often develops with obesity (Liu et al., 2012).

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Research Issues

Scientists have begun to explore what factors influence the location of adipose tissue stores. They are particularly interested in factors that lead to excess storage of visceral fat.

Researchers continue to uncover a variety of health risks associated with visceral adipose tissue (VAT). They are exploring what these health risks are, and the biochemical and physiological mechanisms responsible for these risks. Researchers also are trying to determine why some people with excess VAT develop health problems and others do not.

See Also: Body composition; Brown adipose tissue; Energy balance; Obesity, definition and health effects

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Adolescence and Nutrition

Adolescence refers to the transition from childhood to adulthood, which begins with puberty. On average, girls begin puberty when they are between 10 and 13 years old, and boys begin when they are between 12 and 15 years old. Adolescence frequently is divided into three stages: early adolescence (11 to 14 years of age), which is characterized by increased cognitive development and the physical changes that accompany puberty; middle adolescence (15 to 17 years of age), which is characterized by increased independence; and late adolescence (18 to 21 years of age), when teenagers transition into adulthood.

Puberty is a dynamic period of rapid growth and physical, cognitive, and social/emotional maturation; it is second only to infancy in the rate of change taking place in the body. All this development requires additional calories and nutrients, particularly protein, calcium, and iron. Proper nutrition during this critical time leads to improved mood, enhanced school performance, increased energy, and better health in adulthood. Consequences of inadequate nutrition during adolescence can influence the rest of a person's life and include osteoporosis, anemia, increased risk of heart disease, and type 2 diabetes.

Adolescence also is a period of change in lifestyle, as children transition into more independent teenagers and begin to make decisions—including food

decisions—for themselves. Because teenagers often are influenced by a need to fit in, the decisions they make are easily swayed by their peers and the media. Teens frequently succumb to advertisements for fad diets, acne solutions, and other claims to help them look and feel good. They live in a world of conflict, where they are expected to look slim or strong, but they are being encouraged to eat foods full of sugar, fat, and sodium that can contribute to overweight and obesity. This impossible mix encourages eating disorders and poor body image. Schools and caregivers play a critical role in educating and encouraging adolescents to make healthful food decisions, as well as providing healthy, realistic role models for adolescents.

Nutritional Needs

Adolescents' nutritional needs depend on age, sex, height, weight, and activity level. Females generally require between 1,600 and 2,400 calories a day, and males generally require 1,800 to 3,200 calories per day. These calories should come from nutrient-rich foods such as a variety of protein foods, whole grains, vegetables, fruits, and low-fat dairy products. The best meals include an assortment of foods from different food groups. Unfortunately, most adolescents do not eat the 2½ to 6½ cups of fruits and vegetables or the 2 to 3 ounces of whole grains recommended per day, and they eat twice the maximum recommended daily intake of sodium (2,300 mg each day) (CDC, 2013).

Calcium and iron are two nutrients critical for growth and development that adolescents frequently lack. Over the last 20 years, soft drinks have been replacing milk as the preferred beverage of adolescents. The Dietary Reference Intake for calcium is 1,300 mg per day, which corresponds to three servings of milk, yogurt, or cheese. Calcium also can be found in fortified beverages (such as orange juice), leafy greens like kale and broccoli, and almonds. Calcium is necessary for strong bone development, and inadequate intake during adolescence can lead to decreased bone mass, increased bone fractures, and osteoporosis later in life. Iron is another common deficiency, especially among girls. Iron deficiency can lead to fatigue and decreased concentration, both of which can impact school performance. All adolescents are at risk of developing iron deficiency anemia during growth spurts when their bodies need more of all nutrients; however, girls are particularly at risk because they lose iron during menstruation (in menstrual blood). Meat is a rich source of iron, therefore vegetarians can be at risk for iron deficiency if they do not eat enough iron-containing foods (such as leafy greens, fortified cereal, and beans) or take a vitamin supplement. Other nutrients commonly found in meat that vegetarians must be sure to consume include protein, zinc, and vitamin B12.

Healthy and Unhealthy Eating Habits

Adolescent lifestyles can cause irregular eating habits. Teens tend to stay up late, snack often, eat on the go, skip meals, and consume fast food or other highly processed foods. Although these habits are not necessarily unhealthy by themselves, food choices made because of such habits can be very unhealthy. According to the

American Academy of Pediatrics, for example, 20% to 30% of teenagers do not eat breakfast (American Academy of Pediatrics, 2013). Adolescents who eat breakfast regularly have a lower body mass index than teens who do not eat breakfast. Breakfast gives kids more energy and the ability to focus on school. Easy breakfast foods also can be nutritious—a bowl of fortified cereal with milk and a glass of juice provides fiber, calcium, vitamins, and iron. Skipping meals often leads to excess eating later in the day, and adolescents frequently consume foods such as chips and cookies, which are high in calories and low in nutrients.

Adolescents who perceive themselves as being overweight—regardless of whether they actually are overweight—are more likely to have irregular meals and to skip meals. Skipping meals can lead to inadequate nutrition intake, increased snacking on unhealthy foods, and overeating at the next meal. Poor body image also leads to a variety of other unhealthy eating habits and eating disorders. Many adolescents attempt fad diets that require cutting out entire nutrient groups such as fats or carbohydrates, both of which are essential (in healthy amounts) for the body to grow and develop properly. Eating disorders—including anorexia nervosa, bulimia nervosa, and binge eating disorder—are characterized by extreme attitudes and behaviors toward food. The attitudes toward food often coincide with other issues, such as stress, anxiety, depression, and substance use. Eating disorders are serious medical conditions that can lead to the development of life-threatening problems, such as heart conditions and kidney failure, as well as other complications of malnutrition.

One of the best ways to improve adolescent eating patterns is to eat regular meals as a family. Teens who eat with their families are more likely to consume healthier foods and get better grades, and they are less likely to engage in risky behaviors, such as smoking, drinking, and drug use (CDC, 2012).

Acne

Acne affects the majority of teenagers. Myths connecting diet to acne abound, but numerous scientific studies have failed to show a strong connection between the two. The best method for treating acne continues to be eating a balanced diet, exercising regularly, and practicing good hygiene. Although vitamin A and its analogs are ingredients in several acne medications, consuming extra vitamin A will not prevent acne and also can be toxic.

Sugar-Sweetened Beverages and Caffeine

Sugar-sweetened beverages (SSBs) are beverages that contain added caloric sweeteners such as high-fructose corn syrup or sucrose. The SSB category includes soft drinks, fruit drinks, sports drinks, energy drinks, and sweetened coffee and tea drinks. Importantly, SSBs tend to have few nutrients and are thought to be the greatest source of added sugar in North American diets. Adolescents who drink soft drinks regularly drink less juice and milk and consume approximately 200 calories more per day than those children who do not (Temple, 2009).

Caffeine is a stimulant that arouses the central nervous system. Although moderate caffeine consumption among adults (equivalent to 400 mg per day, or 2 to 4 cups of coffee) generally is considered safe, little research has been done on the effects of caffeine on children and adolescents. The American Academy of Pediatrics encourages little to no consumption of caffeine by children or adolescents (AAP, 2011), and Health Canada considers the maximum safe limit to be 2.5 mg per kilogram of body weight (Government of Canada, 2012). Following these guidelines, a 100-pound child (45 kg) should consume no more than 100 mg of caffeine per day, which is less than one cup of coffee.

Caffeine consumption by adolescents is on the rise and has increased by 70% since 1977 (Temple, 2009). In addition to soft drinks and coffee, adolescents are getting their caffeine from less traditional sources, such as energy drinks, gum, mints, and other products to which caffeine has been added. Energy drink advertisements often specifically target adolescents. Energy drinks are not the same as sports drinks. Sports drinks contain carbohydrates, minerals, electrolytes, and flavoring, and are intended to replace water and electrolytes lost through sweat during physical activity. By contrast, energy drinks contain stimulants, such as caffeine, guarana, and taurine, as well as sugar. Some energy drinks contain 500 mg of caffeine—as much as 14 cans of caffeinated soft drinks (AAP, 2011).

Much remains unknown about caffeine's effects on adolescents; however, several trends are apparent. Many adolescents are not getting enough sleep, and sleep disruption is a clear side effect of caffeine. Sleep deprivation can lead to lack of energy and focus, increased moodiness, depression, slower reaction time, and impaired judgment. Additionally, SSBs and energy drinks are high in sugar—contributing to obesity, tooth decay, and other physical problems.

The American Academy of Pediatrics states that energy drinks are never appropriate for children or adolescents. It encourages limited to no consumption of sports drinks, as well. Instead, the Academy recommends that adolescents consume water during exercise and juice and low-fat milk with meals.

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See Also: Acne; Caffeine; Eating disorders; Energy drinks; Iron-deficiency anemia; Obesity, causes; Sugar-sweetened beverages.

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Agave Syrup

Agave is a genus of plant found primarily in Mexico, where this edible plant has been used for centuries. In Mexico, Aztecs made pins, thread, rope, and even



Blue agave plant. Agave plants are characterized by succulent leaves and can tolerate hot, dry climates such as those found in the southern United States and in South America. Agave syrup is produced from the juice taken from the core of the plant once the leaves are removed. (Jorge M. Vargas Jr./Dreamstime.com)

medicine from agave stalks and leaves. The most well-known species is the blue agave, which contains aguamiel—"honey water"—sap that is fermented into tequila. Since the mid-1990s, aguamiel made from the leaves and stalks of blue agave and several other agave species has been processed into syrup and sold commercially as an all-natural sweetener and sugar alternative. Agave syrup is a common choice for vegans looking for a sugar substitute other than honey. Agave syrup labeling has been the subject of debate, as the agave must undergo heating, filtering, and often chemical treatment that can change its molecular structure and yield various amounts of refined fructose.

One tablespoon of agave contains about 60 calories, as compared to 40 calories in a tablespoon of white (table) sugar. Table sugar is composed of an equal ratio of fructose and glucose molecules, and agave syrup is 55% to 90% fructose, giving agave its much sweeter quality. Although glucose and fructose are both absorbed by the small intestine, fructose must be metabolized directly by the liver, but glucose can be carried in the blood stream and metabolized throughout the body. When too much fructose is ingested it cannot be converted for immediate use by the body, and instead is converted by the liver into triglycerides then enters the blood stream or is stored as body fat.

Agave syrup's health benefits are attributed to its low glycemic index (20–30), which means that it provides minimal elevation to blood sugar levels, although this property has not been conclusively determined through scientific research. The American Diabetes Association considers it to be in the same class as other sweeteners such as table sugar, molasses, and high-fructose corn syrup—which should be ingested in limited quantities. Similarly, the American Botanical Council considers agave to be safe in the amounts normally found in food and drink, but does not recommend it for use by pregnant women (Horton, n.d.).

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See Also: Fructose; Glycemic index and glycemic load.

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Alcohol

Alcoholic drinks contain ethanol, an organic molecule with the chemical formula C_2H_5OH that can cause alcohol intoxication upon consumption. Ethanol is produced by fermentation, a process by which yeast converts sugar (glucose) to

alcohol and carbon dioxide. There are three main groups of alcoholic beverages: beer, wine, and spirits. Beer is produced from barley, hops, water, and live yeast. Wine is produced by fermentation of grapes. Spirits are alcoholic beverages with the greatest percentage of ethanol; they require a distillation step following fermentation. The distillation step enables the ethanol content in an alcoholic beverage to be concentrated and greater than that in beer or wine.



Alcoholic beverages. The alcohol content of beverages varies considerably. In general, health educators consider "one drink" to be the equivalent of 5 fluid ounces of wine, 12 fluid ounces of beer, or 1.5 fluid ounces of liquor. (PhotoDisc, Inc.)

Alcohol use is embedded in many cultures and is perceived as socially acceptable by a majority of people in North American. About 70% of U.S. adults drink alcohol, at least occasionally, and most do so in a responsible fashion. However, 25% of U.S. adults report having alcohol-related problems or have behaviors that put them at risk for developing problems (National Institute on Alcohol Abuse and Alcoholism, 2005). This translates into a very ,large number of people for whom alcohol poses a problem. Human consumption of alcohol has been shown to have both deleterious and positive effects. The World Health Organization (WHO) estimates that harmful use and abuse of alcohol leads to roughly 2.5 million deaths per year (WHO, 2014).

Cultural History of Alcohol

Alcohol is present in all cultures in some manifestation. Evidence of the earliest preparations of alcoholic beverages can be traced back to 7000 BCE to 6600 BCE in ancient Chinese civilizations (Gately, 2008). Other evidence of the presence of alcohol in ancient cultures is found in the artifacts of people from the Fertile Crescent from around 5400 BCE to 5000 BCE. The artifacts portray people cultivating plants for alcohol production (Gately, 2008). Alcohol production spread from the Fertile Crescent to northern Europe, with evidence found in Scotland of crops grown to produce beer in 3800 BCE (Gately, 2008). Similar evidence of alcohol and its production has been found in Mayan, Indian, Asian, and African ancient cultures. All of

Strategies for Reducing Alcohol Intake

The National Institute on Alcohol and Alcohol Abuse (NIAAA) offers excellent information on its website, "Rethinking Drinking," for people who wish to assess their drinking behavior. Some excerpts are included below. The complete online information provides helpful links for measuring and keeping track of drinks, and a downloadable booklet. The NIAAA also suggests that, if people wish to reduce their drinking but have not been able to do so after two or three months, they should consider quitting drinking, getting professional help, or both. Suggested strategies include the following.

- Keep track—Start a list and note each drink before consuming it. This can help slow down a person's drinking, when needed.
- Count and measure—Know the standard drink sizes so that drinks can be counted accurately. Measure drinks when drinking at home.
- Set goals—Decide how many days a week to drink and how many drinks to have, and include some days of no alcohol consumption. Low-risk drinking for alcohol disorders can be as many as 14 drinks per week for men, and 7 drinks per week for women.
- Pace and space—When drinking, pace oneself; sip slowly. Have no more than one standard alcoholic beverage or cocktail per hour. Use "drink spacers"; alternate drinks, and between every alcoholic drink have a non-alcoholic beverage, such as water, soda, or juice.
- Include food—Don't drink on an empty stomach; food helps slow the alcohol absorption.
- Find alternatives—Fill free time by developing new, healthy activities, hobbies, and relationships, or renewing ones that have been missed. Find healthy ways to manage moods or to be comfortable in social situations without drinking alcohol.
- Avoid "triggers." Decide what triggers drinking and plan how to avoid the triggers.
- Plan to handle urges—Remember all the reasons for changing drinking behavior, and even plan to ride out the urges and let them pass.
- Know your "no." Have a polite and convincing "no thanks" ready. The more frequent the hesitation, the more often a person will succumb to drinking.

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these cultures seemed to recognize and use alcohol as a pleasurable or relaxing substance, but they used alcohol for religious reasons as well.

Modern-Day Social and Cultural Aspects of Alcohol

In most modern-day societies, alcohol is viewed as a pleasurable substance or drug rather than a nutrient or a necessary substance. Alcohol frequently is served in social situations of adults and teenagers. Most countries around the world have a legal drinking age of 18; however in the United States, the legal drinking age is 21.

Advocates of lowering the drinking age in the United States believe that lowering the drinking age would decrease harmful, secretive drinking behaviors in adolescents. It has been demonstrated, however, that teenagers across the world engage in harmful drinking patterns, regardless of whether the legal drinking age is 18 years of age or 21 years of age (Grube, 2005). Among teenagers, binge drinking is predominant, as opposed to moderate or safe drinking. Binge drinking is defined as consuming five or more alcoholic beverages in one sitting. It accounts for the three leading causes of death for adolescents aged 12–20, which include unintentional injury, homicide, and suicide (Miller, Naimi, Brewer, & Jones, 2007). Although binge drinking is common in adolescents and young adults, it also is prevalent in older adults. According to the CDC, 70% of all binge drinking episodes can be attributed to adults who are 26 years of age or older, and more than half of the alcohol consumed by adults is via binge drinking (CDC, 2012). Although most adults drink moderately, binge drinking tends to account for a large part of the drinking culture in most societies.

Effects on the Body

Blood Alcohol Concentration

When consumed, ethyl alcohol absorption starts in the stomach and continues in the small intestine. From the small intestine alcohol moves into the blood and travels directly to the liver where only 10% to 20%, of the alcohol in the blood can be broken down at one time. The remaining alcohol circulates in the blood stream until it eventually can be broken down by the liver. It can take roughly 2 hours for one drink to be fully metabolized. The measurement of intoxication therefore can be quantified by blood alcohol content or concentration, known as BAC, which is defined as the percentage of alcohol in one's blood. Research has shown that cognitive function becomes increasingly impaired as BAC rises. At a BAC of 0.05% (5% blood concentration of alcohol), the frontal lobe is defined as sedated and reasoning and judgment become impaired. At 0.10% BAC, the areas of the brain devoted to speech and vision become impaired, resulting in slurred speech and impaired coordination. At 0.30% the drinker experiences stupor and confusion. At a BAC ranging from 0.40% to 0.60% the drinker can suffer from unconsciousness and cardiac or respiratory failure (Insel, Ross, McMahon & Bernstein, 2014).

The speed of alcohol absorption into the body depends on a number of factors, such as the contents of the stomach before drinking an alcoholic beverage, the size of the person drinking, and the sex of the person drinking. On average, women appear to be more susceptible to the effects of alcohol. This partly is due to differences in size and body composition; women are generally smaller than men with a greater percentage of body fat for a given size. Alcohol diffuses primarily into lean tissue. This means that a given amount of alcohol tends to be more concentrated in the lean body mass of women.

The differences in the rate of alcohol metabolism also appear to differ between the sexes. Women's stomachs produce lesser amounts of a key enzyme responsible for breaking down alcohol—alcohol dehydrogenase. Thus, women's bodies generally

break down alcohol more slowly, so blood alcohol levels remain high for longer periods. These observations help explain why women develop alcohol-related disorders at lower alcohol intakes than those of men. Larger body sizes also are equipped with larger livers that can metabolize alcohol more effectively. Food also slows the absorption rate of alcohol by the stomach and the small intestine by minimizing contact between alcohol and the permeable lining of the stomach and small intestine. Other factors such as sugar content and aeration of alcohol in a carbonated beverage make alcohol more readily absorbable, thus increasing its effect on the consumer.

Alcohol Metabolization

After alcohol is ingested, enzymes begin metabolizing alcohol in the stomach and small intestine. Alcohol and its byproducts are absorbed in the small intestine and carried to the liver via the portal vein. In the liver, alcohol is converted to acetaldehyde by the enzyme alcohol dehydrogenase. The product of this reaction, acetaldehyde, then is metabolized to acetic acid radicals by acetaldehyde dehydrogenase. The acetic acid from this reaction binds with Coenzyme A to form acetyl-coA using the enzyme acetyl-coA synthetase (HAMS Harm Reduction Network, Inc., 2009). Acetyl-coA then can be used for the energetic needs of the cell. Cytochrome P450, which is highly activated in heavy drinkers, is another enzymatic pathway used to metabolize alcohol in the endoplasmic reticulum of cells (Zakhari, 2006). Catalase is another enzyme in the peroxisomes of cells that metabolizes alcohol and produces hydrogen peroxide in the process. Although there are various pathways to metabolize alcohol, most alcohol is metabolized using the alcohol dehydrogenase and acetaldehyde dehydrogenase mechanism that occurs in the liver.

Alcohol Addiction

Alcohol is considered a drug and can be addicting. Alcoholism is a biological and psychological disorder that is defined by problematic drinking behaviors that include uncontrollable craving and consumption of alcohol. Alcoholism can progress quickly and create severe damage to the health and social well-being of an alcoholic. Alcoholism develops through a myriad of factors including stress, social environment, genetic disposition, and predisposing mental health conditions. Long-term alcohol abuse is detrimental to the physical health of an individual. It causes a variety of disorders including brain damage, psychological disorders, liver disease, and cardiovascular disease, and can lead to systemic organ failure. Alcoholism can be deadly, but many treatment plans have been developed to combat it. Medical professionals can use psychotherapy and drug therapies to help people complete treatment for alcohol withdrawal.

Brain and Behavioral Changes

Alcohol use and abuse can lead to neurological deficits including behavioral changes. Alcohol is a central nervous system (CNS) depressant. Short-term,

small-to-moderate consumption of alcohol can cause irritability, aggression, and short-term memory loss. Because alcohol is a CNS depressant, consumption leads to an increase in risk-taking behavior and impaired judgment. Long-term alcohol consumption can lead to decreased concentration, decreased memory ability, and impaired brain development along with many other neurological deficits. Long-term alcohol consumption also can perpetuate many psychological disorders, including depression, anxiety, sleep disorders, bipolar disorder, and substance-abuse disorders. Alcohol particularly affects adolescents and other young people, as the brain is rapidly changing and developing. Studies also have shown that alcohol sensitizes the neurocircuitry of the addiction pathway in adolescents and young adults, making them more prone to alcohol addiction (Guerri & Pascual, 2010).

Alcohol abuse is strongly associated with a plethora of harmful behaviors, including accidental death and injury due to motor vehicle accidents, drowning, burns, and firearm accidents. Alcohol abuse is linked to domestic violence as well as to other forms of violence, including homicide and suicide. Poor decision making under the influence can result in unwanted, unplanned, and unprotected sexual activity and can cause other relationship problems.

Liver Disease

Regular consumption of alcohol is known to cause liver disease. Alcohol contributes to liver disease by infiltrating liver fat, and can cause hepatitis (inflammation of the liver) and cirrhosis (replacement of liver tissue with scar tissue). As alcohol is metabolized, acetaldehyde builds up in the body. Acetaldehyde is a toxin that is considered harmful and promotes liver disease. Liver disease as a result of high levels of alcohol ingestion affects women faster and with use of a smaller amount of alcohol. Roughly 10% to 15% of clinical alcoholics eventually develop liver disease. Alcohol-related fatty liver disease can be fully reversed; however alcohol-induced hepatitis and cirrhosis are not reversible. For alcoholic liver disease that can't be cured; liver transplants are the only treatment option.

In heavy drinkers, the enzymes cytochrome P450 and catalase are highly active. These enzymes contribute to tissue damage. When cytochrome P450 metabolizes ethanol, the following toxic byproducts are produced: Reactive oxygen species (ROS) (free radicals), hydroxyethyl, superoxide anion, and hydroxyl radicals (Zakhari, 2006). When catalase breaks down alcohol, increased levels of hydrogen peroxide occur. The build-up of these toxins leads to the oxidative stress that causes tissue damage associated with liver disease.

Cancers

Alcohol also can lead to liver cancer. The products of the various reactions carried out to metabolize ethanol contribute to the toxic and mutagenic effects of alcohol consumption on the body. The products of alcohol metabolism—acetaldehyde and aldehyde—can alter DNA structure to promote more hepatocyte (liver

cell) regeneration. Also, in livers with decreased function due to significant alcohol consumption, hepatocytes regenerate faster than in healthy livers. This could promote dysregulated hepatocyte replication and, therefore, cancer. Acetaldehyde and aldehydes also bind to lysine residues of various cellular proteins and cause them to change and promote tumorigenicity. The ROS produced from cytochrome P450 metabolizing alcohol interact with proteins and DNA, and affect their function and promote tumorigenicity (McKillop & Schrum, 2009).

Alcohol and its metabolites can initiate cancers in other areas of the body as well. Alcohol intake, even at relatively low levels, is associated with increased risk of cancers of the respiratory system; breast cancer; and cancers of the gastrointestinal (GI) tract, including the mouth, esophagus, stomach, colon, and rectum.

Inflammation of the Gastrointestinal Tract and Pancreas

Excessive alcohol intake is the primary cause of esophagitis (inflammation of the esophagus), gastritis (inflammation of the stomach), and pancreatitis (chronic inflammation of the pancreas).

Fetal Alcohol Spectrum Disorders

Scientists have long known that alcohol can be a teratogen, a substance that disrupts fetal development and can cause irreversible damage. Fetal alcohol spectrum disorders include a wide range of physical, behavioral, and cognitive abnormalities that are caused by exposure to alcohol during fetal development. Not all babies exposed in utero to alcohol develop alcohol-related disorders, and scientists continue to look for the biological mechanisms behind alcohol's effects on fetal development. Because researchers have not been able to define a "safe" level of alcohol intake that poses no risk to a developing fetus, pregnant women are strongly encouraged to avoid alcohol.

Positive Effects of Alcohol: Cardioprotective Effects

Many studies have shown that moderate alcohol consumption can be cardioprotective, as moderate alcohol consumption has been linked with a reduced risk for cardiovascular diseases. In particular, red wine consumption has been shown to have cardioprotective qualities. Red wine has antioxidants (flavonoids), which protect the cardiovascular system in many ways. These antioxidants are associated with a decreased concentration of LDL (low-density lipoprotein) cholesterol and an increased concentration of HDL (high-density lipoprotein). These antioxidants also reduce blood clotting and alter lipid profiles after meals. In one study, scientists used a hypercholesterolemic swine model to examine the effects of alcoholic beverages on the heart. Moderate consumption of red wine and vodka was shown to reduce cardiovascular risk by improving collateral-dependent perfusion through various mechanisms (Chu et al., 2012).

Type 2 Diabetes

Alcohol has been shown to decrease the risk of type 2 diabetes in moderate alcohol drinkers. Researchers have shown that some of the reasons alcohol is associated with lowered risk of diabetes is because moderate alcohol consumption increases insulin sensitivity and levels of HDL cholesterol. The anti-inflammatory properties of moderate alcohol consumption also can lead to the protective properties of alcohol against type 2 diabetes. Alcohol consumption at any level greater than moderate consumption, however, increases the risk of type 2 diabetes.

Stress Relief

Moderate amounts of alcohol might provide some relief from stress, because alcohol is a central nervous system (CNS) depressant. Such relief is temporary, however, as the effect of alcohol wears off with time. Although alcohol can be used to relieve stress, being dependent on alcohol for stress relief can lead to addiction. Researchers have found that the results of studies on the relationship between stress relief and alcohol are inconsistent. Experts have come to the consensus, however, that most anti-stress benefits of alcohol are associated with a myriad of other characteristics including family history of alcoholism, environment, types of stress, gender, and personality traits.

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Research Issues

According to the World Health Organization (WHO), harmful alcohol use is one of four common risk factors—along with tobacco use, poor diet, and physical inactivity—for the four main groups of noncommunicable diseases: cardiovascular diseases, cancer, chronic lung diseases, and diabetes. Many countries around the world are grappling with the health problems of alcoholism and alcohol abuse. WHO's *Global Status Report on Alcohol and Health* provides more information on this topic.

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See Also: Fetal alcohol syndrome and disorders; The French paradox; The liver; Resveratrol.

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Allyl Sulfides (Organosulfurs)

Allyl sulfides (organosulfurs) are organic sulfur-containing phytochemicals (compounds that occur naturally in plants). Allyl sulfides are found in plants belonging to vegetables in the onion and garlic families, including onions, leeks, chives, shallots, and all varieties of garlic. They are known for their pungent odor and possible antitumorigenic properties. Allyl sulfides occur in a variety of classes, the most common of which—allicin—is responsible for the flavor of garlic. The compound is synthesized by the enzyme alliinase which is activated when a garlic bulb is crushed. Garlic has been used over time in traditional Eastern medicine to treat ailments from fungal and bacterial infections to poor digestion and parasites.

The biochemical significance of allyl sulfides in the body is wide ranging. Studies show that the compound helps prevent cancer by blocking the initiation and promotion stages of tumor development. Allyl sulfides modify pathways in charge of cell proliferation, helping to reduce general tumor incidence and

suppress tumorigenesis (the creation of new tumors). The main methods by which allyl sulfides block cancerous growth are by inducing apoptosis, or cell death, and by stimulating genes that serve to suppress tumors.

Research shows that garlic preparations featuring allyl sulfides boost the immune system by increasing the presence of natural killer immune cells in the body. Garlic preparations also stimulate digestive enzymes that help remove toxins from the body, and even might be effective in repellents for mosquitoes and other insects. Although allyl sulfide and garlic supplements are widely available, their effectiveness could be tempered through interactions between allyl sulfides and different levels of selenium, vitamin A, and fatty acids. Eating vegetables from the onion and garlic families appears to be associated with more health benefits than consuming dried preparations or supplements.

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See Also: Garlic.

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Alpha-Linolenic Acid

Alpha-linolenic acid (ALA) is an essential omega-3 fatty acid, which means that for proper growth and development ALA must be obtained from the diet. This fatty acid contains 18 carbon atoms and 3 carbon-carbon double bonds, and is found in both plant and animal foods. Flaxseed, canola, soy, walnuts, chia seeds, and pumpkin seeds are good sources of alpha-linolenic acid, with flaxseed being the richest. ALA also is found in some dairy foods and red meat, and in cooking oils, medicinal oils, and dietary supplements. Most people consume most of their ALA from soybean oil, as it is found in many different foods such as salad dressings and mayonnaise. ALA deficiencies are rare because people require only a small amount of ALA per day (1.1 to 1.5 grams) (Schardt, 2005).

The two other main types of omega-3 fatty acids are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). These have longer chains and are found in seafood. Omega-3 fatty acids have been associated with a number of health benefits. The human body, however, can convert alpha-linolenic acid into only small amounts of EPA and DHA. The health benefits associated with ALA are not as strongly supported as those of EPA and DHA.

Some evidence suggests that diets with increased ALA help to reduce risk of heart disease and heart attacks. One study showed that over a six-year period, people who had high dietary intakes of ALA had a 59% lower risk of heart attacks, compared to people with the lowest ALA intakes (Therapeutic Research Faculty, 2009). The Nurses Health Study found that women who consumed more dietary ALA had half of the risk of heart disease as those who consumed the least amount (Schardt, 2005). Dietary ALA might slow the buildup of arterial plaque that causes heart disease and reduce the risk of high blood pressure.

Because alpha-linolenic acid can be changed into EPA and DHA, and both are anti-inflammatory, it is thought that ALA also can reduce inflammation. Some preliminary research suggests that diets high in ALA can decrease inflammation and improve lung function in asthma patients (Ehrlich, 2011).

A large epidemiological study found that men who consumed the most ALA in their diet had a greater risk of developing prostate cancer as compared to men consuming the lowest levels of ALA. Other studies, however, have found no risk. A meta-analysis of 16 studies did find a small association between ALA levels in diet, blood, and tissue samples with increased risk of prostate cancer, but attributed this association to publication bias rather than to a negative effect of ALA (Simon, Chen, & Bent, 2009). Nevertheless, such findings suggest that ALA supplements probably should be avoided until research has ruled out the possibility that ALA could increase cancer risk.

People taking anticoagulant medication should check with a health care provider before consuming high amounts of ALA, because ALA can increase the blood-thinning effects of these drugs and raise the risk of bleeding.

Catherine M. Lenz

See Also: Fatty acids.

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Alpha-Lipoic Acid

Alpha-lipoic acid—also known as lipoic acid and thioctic acid—is an antioxidant that is synthesized by the human body. It is found in every cell and helps the cells convert glucose into energy. It also counteracts the negative effects caused by free radicals in the body. Alpha-lipoic acid is both fat-soluble and water-soluble, which means it can work in all areas of the body. Some research suggests that alpha-lipoic acid might be useful in regenerating and reactivating other antioxidants, such as the vitamins C and E, and thus it could help strengthen the effects of other antioxidants in the body.

Alpha-lipoic acid is found in some foods, such as spinach, broccoli, potato, yam, carrot, beet, yeast, and red meat. After it was first discovered, alpha-lipoic acid was viewed as a vitamin that the body cannot produce, but it later was discovered that the body does synthesize alpha-lipoic acid. The signs of a deficiency for this antioxidant are hard to characterize, because it works with other nutrients in the body. Deficiency symptoms are similar to those of insufficiency of the other antioxidants, such as reduced muscle mass, memory problems, and weakened immune function. There currently is no dietary reference intake for alpha-lipoic acid, but it is a popular antioxidant supplement. Dosages of 20 mg to 50 mg per day are generally considered safe but—as with most supplements—long-term safety data are lacking. Some research suggests that high doses of alpha-lipoic acid can cause thiamine or biotin deficiency, and side effects can include headache, muscle cramps, skin rash, and allergic reactions.

Alpha-lipoic acid was discovered in 1937 as a compound in certain bacteria. Its antioxidant functions have been recognized and studied since 1939, and in the 1960s several groups of researchers began to investigate therapeutic applications. Alpha-lipoic acid was observed to work well as a remedy for intake of toxic substances, and physicians prescribed large doses of it to patients diagnosed with mushroom poisoning and heavy-metal poisoning. It was also given to patients with liver cirrhosis and diabetic neuropathy, because it was observed that many of these patients had lower than average levels of alpha-lipoic acid.

Alpha-lipoic acid continues to be prescribed as a treatment for diabetic neuropathy, a painful complication that often is found in people with type 1 diabetes. Diabetic neuropathy is thought to be at least partly a result of oxidative stress, and the ability of alpha-lipoic acid to perform in both water and fat tissue allows it to penetrate all the areas of nerve cells. These treatments use very high doses of alpha-lipoic acid which are administered intravenously with medical supervision. Treatments have proven to be helpful for some patients. Alpha-lipoic acid also has been observed to reduce the blood sugar levels in diabetics. Diabetic patients using

alpha-lipoic acid must be monitored to ensure that blood sugar levels do not fall too low.

Additional research investigating other potential therapeutic uses for high doses of alpha-lipoic acid is under way. Some research suggests that alpha-lipoic acid could be helpful in reducing blood sugar levels and improving insulin sensitivity of people who have type 2 diabetes. Other studies aim to establish alpha-lipoic acid's potential ability to treat radiation injury, Alzheimer's disease, cataract formation, and stroke. Studies on the capability of alpha-lipoic acid to lessen some negative side effects of chemotherapy have produced supportive results. Antioxidants, however, also have the potential to reduce the effectiveness of some chemotherapy agents, therefore cancer patients must work with their oncologists to determine whether alpha-lipoic acid supplementation might be useful.

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See Also: Antioxidants; Vitamins.

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Alternative Sweeteners (Sugar Substitutes)

The term "alternative sweetener" refers to a variety of substances that can be used instead of sugar (sucrose) in a range of foods and beverages. Manufacturers choose alternative sweeteners based on whether they are nutritive (have calories and supply energy) or nonnutritive (do not have calories or supply energy), their taste and texture, and their chemical properties. Sugar substitutes in baked goods, for example, must be able to withstand heat, and those used in gum should not promote tooth decay. The names of alternative sweeteners can be confusing, and sometimes even are misleading. Table 1 describes and compares the most common sugar substitutes.

Lisa P. Ritchie

See Also: Agave syrup; Artificial sweeteners; Honey; Stevia; Sugar alcohols.

Table 1. Alternative Sweeteners (Sugar Substitutes)

Name	Description	Examples
Artificial Sweeteners (also called "nonnutritive sweeteners," "high-intensity sweeteners")	Synthetic sugar substitutes are significantly sweeter than sugar. Artificial sweeteners are nonnutritive, and supply few to no calories or carbohydrates per serving.	• Acesulfame potassium (Sunett, Sweet One) • Aspartame (Equal, NutraSweet) • Neotame • Saccharin (SugarTwin, Sweet'n Low) • Sucralose (Splenda)
Sugar Alcohols (also called "artificial sweeteners," "polyols," "nutritive sweeteners")	Sugar alcohols are a group of sweeteners used in processed foods as a lower-calorie substitute for sugar that does not promote tooth decay. On average, they supply 2 calories per gram as compared to 4 calories per gram for sugar. Sugar alcohols can have a laxative effect when eaten in large quantities.	• Erythritol • Hydrogenated starch hydrolysate • Isomalt • Lactitol • Maltitol • Mannitol • Sorbitol • Xylitol
Natural Sweeteners (also called "sugar substitutes," "nutritive sweeteners")	"Natural sweetener" is a general term for sweeteners that contain no added colors, flavors, or other food additives. In the United States, the FDA does not have guidelines for "natural" products. In Canada, "natural" foods must meet standards specifying that they have been minimally processed. The sweeteners provide energy and are chemically similar to sugar, but they have different textures and flavors as compared to table sugar.	• Agave nectar • Barley malt • Date sugar • Fruit juice concentrate • Honey • Maple syrup • Rice syrup

(*continued*)

Table 1. Continued

Name	Description	Examples
Novel Sweeteners (sweeteners that fit into a variety of categories)	These sweeteners are "novel" because they are new to the market. They do not fit neatly into any of the other categories. Stevia, for example, comes from a plant and many consider it a natural, nonnutritive sweetener; however, only its highly refined form is approved as a food additive in Canada and in the United States. Tagatose also occurs naturally, but is manufactured from lactose. Although it is low in carbohydrates, it is not considered sugar free.	• Stevia extracts (Pure Via, Truvia), also called "Rebaudioside A," "Reb-A," and "rebiana" • Tagatose (Naturlose) • Trehalose



Alternative sweeteners. Consumers often choose alternative sweeteners, such as those pictured here, in order to reduce their intake of sugar and calories. (iStockphoto.com)

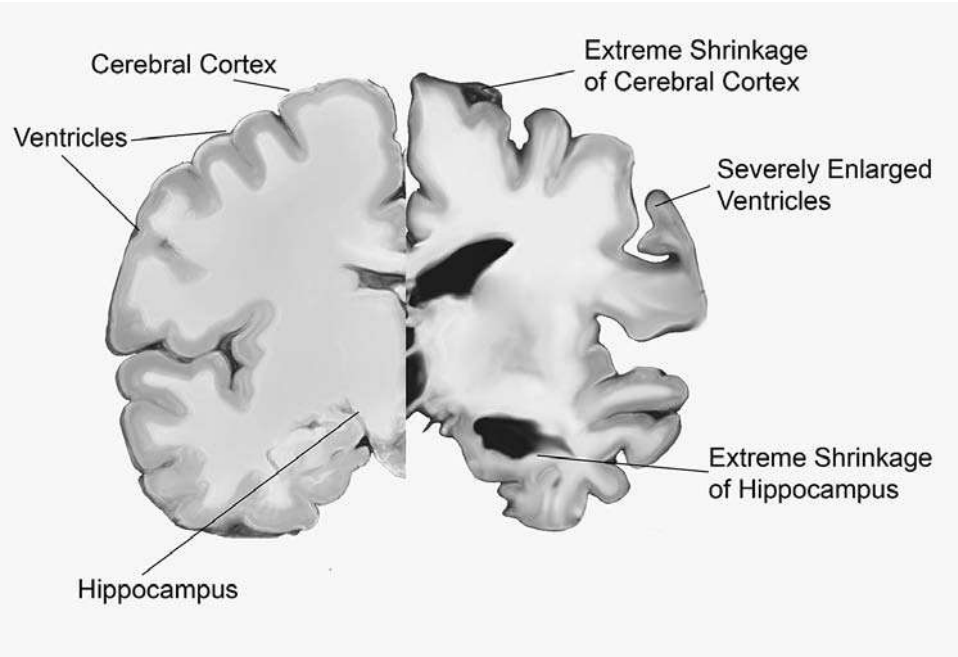
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Alzheimer's Disease and Nutrition

Alzheimer's disease (AD) is an irreversible, progressive brain disease that accounts for 50% to 60% of all cases of dementia and is estimated to affect 35.6 million people worldwide (WHO & Alzheimer's Disease International, 2012). Dementia is characterized by cognitive decline, reduced daily activities, and neurophysiological abnormalities. Patients with AD progressively worsen until recalling memories and responding to their environment become difficult to impossible tasks. The majority of people who suffer from the disease are 65 years of age and older; however, there are rare cases of early onset AD due to a genetic vulnerability that presents in patients who are between 30 and 50 years old.



Comparison of a brain before and after development of Alzheimer's disease. Loss of neuron number and function occurs in many areas. (National Institutes of Health/National Institute on Aging)

Although little is known about how the disease begins, it is likely that damage to the brain starts more than a decade before the symptoms appear. The brain is composed of a network of billions of neurons and neuronal connections. In Alzheimer's disease, abnormal protein deposits—specifically intercellular beta-amyloid plaques and intracellular tau tangles—cause neurons to communicate and transmit signals less efficiently. These abnormal protein deposits cause an immune response leading to brain inflammation when cells such as astroglia and microglia—neuronal homologs of pathogen-eating macrophages—gather to destroy the plaques as the tangles initiate cell death. Although at first this might seem beneficial to the brain, AD causes chronic inflammation that stresses and kills nearby healthy cells in addition to the diseased cells. These cells include the astroglia and microglia that die and aggregate at the beta-amyloid plaques due to beta-amyloid's adhesive qualities. Over time, the neurons fail to function properly and fail to communicate, ultimately causing cell death. The damage eventually spreads to an important brain structure—the hippocampus. The hippocampus is vital in memory consolidation, memory recall, and spatial recognition. As a result, the first symptoms to appear are problems in memory and recognition. By the final stages of Alzheimer's, neuronal apoptosis (cell death) is widespread, and the brain tissue has shrunk significantly. Thus, in end-stage AD, patients lose the ability to communicate, sense spatial orientation, and care for themselves.

Alternative and Complementary Health Therapies for Alzheimer's Disease

The following information on the use of complementary and alternative therapies—including nutrition therapy—for Alzheimer's disease and dementia is excerpted from the U.S. government National Center for Complementary and Alternative Medicine.

- There presently is no convincing evidence from a large body of research demonstrating that a dietary supplement can prevent worsening of cognitive impairment associated with dementia or Alzheimer's disease, including the use of ginkgo, omega-3 fatty acids/fish oil, vitamins B and E, Asian ginseng, grape seed extract, and curcumin. Additional research on some of these supplements is under way.
- Preliminary studies of some mind and body practices such as music therapy suggest that they might be helpful for some of the symptoms related to dementia, such as agitation and depression.
- Mindfulness-based stress-reduction programs might be helpful in reducing stress among caregivers of patients with dementia. Studies suggest that a mindfulness-based stress-reduction program is more helpful for improving mental health than is attending an education and support program or just taking time off from providing care.
- Complementary health approaches shouldn't be used as a reason to postpone seeing a health care provider about memory loss. There are treatable conditions, such as depression; adverse reactions to medications; and thyroid, liver, or kidney problems, which all can impair memory.
- Some complementary health approaches and supplements can interact with medications and also can have serious side effects. Talk to a health care provider before adding dietary supplements or other complementary health approaches.

National Center for Complementary and Alternative Medicine (NCCAM). (2014). *5 things to know about complementary health practices for cognitive function, dementia, and Alzheimer's disease*. Retrieved from http://nccam.nih.gov/health/tips/alzheimers

Interestingly, the disease is named after a German psychiatrist and neuropathologist, Dr. Alois Alzheimer, who in the early 1900s cared for a patient with rapidly declining and severe dementia. The patient's symptoms included memory loss, language problems, and erratic behavior (NIH, 2013). The autopsy of the diseased brain revealed cellular changes in the nervous tissue which caused a loss of neuronal connections. These cellular changes later were identified as neurofibrillary tangles and plaques, which are hallmark characteristics of Alzheimer's disease.

Disease Risk Factors

Scientists have not yet determined the causes of Alzheimer's disease; however it is likely that the causes include a mixture of genetic, environmental, and lifestyle factors. Those who have a first-degree relative with Alzheimer's are more likely to

develop the disease. The risk increases if more than one family member has been diagnosed. Research has found that there are several genes that increase the risk of having Alzheimer's. The gene that has the strongest link to late onset Alzheimer's is APOE-e4, one of the four common forms of the apolipoprotein E gene. Each individual inherits some form of the APOE gene, and those who have inherited one copy of APOE-e4 have increased risk of developing AD. Those who inherit two copies of the variant 4 gene have an even greater risk of developing the disease; however, the existence of the variant four genes does not guarantee that the person will develop AD. Scientists have estimated that APOE-e4 is implicated in 20% to 25% of Alzheimer's cases (Alzheimer's Association, 2013).

One of the greatest mysteries of Alzheimer's disease remains unsolved: Why does the risk increase with age? Although the disease is not a normal part of growing older, after age 65 the risk of developing Alzheimer's doubles every five years. After age 85, the risk of developing the disease is about 50% (Alzheimer's Association, 2013). Research on how brain function changes with age has begun to illuminate how age-related changes can harm neurons and contribute to the neurological damage observed in Alzheimer's. Normal age-related changes in the brain include neuroinflammation and production of free radicals—both of which contribute to cell death and brain atrophy.

Treatment and Prevention

Medication

Currently there is no cure for Alzheimer's disease. Those who develop Alzheimer's usually are prescribed FDA-approved medication. There are two ways in which AD medication functions. One way is to inhibit cholinesterase, an enzyme that breaks down the memory neurotransmitter acetylcholine. The medication works by inhibiting the activity of cholinesterase, thus slowing the disease progression, as the memory loss experienced is associated with deficiencies in acetylcholine. The second method is medication that regulates the activity of glutamate, which is involved in learning and memory, through an NMDA receptor antagonist. The NMDA, N-methyl-D-aspartate receptor is a glutamate receptor that predominantly is involved in sending excitatory signals in the brain to help form memories. Thus the agonist triggers the NMDA receptor and increases memory-forming activities. The antagonist drugs protect neurons against excess glutamate that is released by cells damaged by Alzheimer's causing excitotoxicity in the brain. Additionally, antagonist drugs target NMDA receptors, because they can become over-activated and trigger an excess of Ca^{2+} ions to enter neuronal cells, thus activating a series of intracellular processes that promote cell death (Alzheimer's Association, 2013).

Lifestyle and Cardiovascular Health

Lifestyle contributes to the development of AD. It has been observed that risk increases with conditions that damage the heart and blood vessels including

hypertension, heart disease, stroke, diabetes, and high cholesterol. Autopsy results show that 80% of individuals with Alzheimer's also had some type of cardiovascular disease. In fact, autopsy studies suggest that the hallmarks of Alzheimer's disease—the plaques and tangles—might be present in the brain without causing symptoms unless the brain also shows evidence of vascular disease (Alzheimer's Association, 2013). The brain is nourished by the heart; with each heartbeat, 20% to 25% of the body's blood is carried to the brain to receive oxygen and nutrients. Thus, conditions disrupting blood flow to the brain lead to nerve damage.

Experts believe that controlling cardiovascular risk factors might be the best approach to protect brain health. A heart-healthy lifestyle includes regular exercise. In fact, some research has suggested exercise might directly benefit brain cells as a result of increased blood and oxygen flow. Strong evidence suggests exercise actually protects the brain from AD, due to the proven benefits to the cardiovascular system. Conversely, cardiovascular risk factors also appear to increase AD risk. For example, a long-term study of 1,500 adults found that those who were obese in middle age were twice as likely to develop Alzheimer's, and those who also had high cholesterol and hypertension were six times as likely to develop the disease (Alzheimer's Association, 2013).

Nutrition: Heart-Healthy Diet

A heart-healthy diet is a balanced diet that includes a variety of foods such as vegetables, fruits, whole grains, low-fat dairy products, and lean protein. Nutritionists suggest eating dark-skinned fruits and vegetables, such as kale, eggplants, blueberries, and plums, because these foods have high levels of antioxidants and polyphenols to protect the brain from free radicals and oxidative damage. Metal ions are known to catalyze production of free radicals and induce dementia. Several studies have suggested that metals such as lead, iron, aluminum, copper, and zinc are involved in Alzheimer's pathogenesis. Although specific metal chelators—molecules that bind to metal ions—have been tested in Alzheimer's disease therapy, there has been little success. This is thought to be due to late administration of the chelators after extensive brain damage already has occurred. It therefore is thought that regular consumption of dietary polyphenols, which are known to chelate metals, could prove to be protective against AD (Ramesh, Rao, Prakasam, Sambamurti, & Rao, 2010).

Some studies have suggested associations between an atherogenic blood lipid profile and AD. Diets that are high in added sugars and processed fats are thought to be associated with a poor cholesterol profile. This consists of an increase in low-density lipoproteins (bad cholesterol) and a decrease in high-density lipoproteins (good cholesterol). Experts believe that cholesterol plays a role in AD because cholesterol acts in both the production and aggregation of amyloid beta in the brain. However, HDL (good cholesterol) also has been shown to protect brain cells. Thus, to promote brain health, experts suggest reducing the intake of sugar-sweetened food and beverages, and foods that have added fats and sugars.

Additionally, evidence suggests a relationship between type 2 diabetes and Alzheimer's disease. Type 2 diabetes is characterized by high blood glucose levels

and a blunted response of cell membrane receptors to insulin. Of those people with type 2 diabetes, 70% develop Alzheimer's disease (Weller, 2013). Research suggests that the underlying mechanism is the disruption of an essential enzyme that typically rids the brain of amyloid plaques—a hallmark of Alzheimer's pathology. In general, high sugar intake appears to be risk factor for AD, even for people who do not have diabetes.

Nutrition: Omega-3 Fatty Acids

Studies have noted that the consumption of fish is associated with a reduced risk of developing Alzheimer's (Morris, 2009). Long-chain omega-3 fatty acids are found almost exclusively in fish such as salmon, tuna, and mackerel. Docosahexaenoic acid (DHA), a type of omega-3 fatty acid, makes up key structures in the brain, including the neuronal membranes and the phospholipids contained in the cerebral cortex. Animal studies with DHA supplements showed enhanced control of neuronal membrane excitability, marked membrane transmission, and decreased oxidative stress in the brain. In the Framingham Study, those patients who were free of dementia and were being treated with high DHA levels (median age of 76 years) had a significant 47% reduction in the risk of developing dementia in the subsequent nine years (Schaefer et al., 2006). There is consistent evidence across all studies that omega-3 fatty acids and fish can help reduce the risk of Alzheimer's. More studies presently are examining the effect of fish oil supplements on progressive cognitive impairment and on the risk of Alzheimer's disease.

Nutrition: Micronutrients

Some studies suggest that high intake of specific vitamins is associated with a reduced risk of developing Alzheimer's; however reports are inconsistent. Limited evidence suggests that low folic acid concentrations in the blood can increase AD risk. Elevated levels of plasma homocysteine are associated with increased risk for the development of dementia and Alzheimer's disease (and cardiovascular disease); this risk factor is modifiable because plasma homocysteine levels can be reduced by folic acid consumption. Epidemiological studies suggest that vitamin E and vitamin C might help reduce inflammation and oxidative stress in the brain (Alzheimer's Research Center, 2013). Additionally, vitamin D deficiency is common among the elderly, but it has been found that increased serum concentrations of vitamin D are associated with reduced risk of AD.

Nutrition: Ketogenic Diet

A specialized diet that is thought to be beneficial to Alzheimer's patients and decrease the risk of developing the disease is the ketogenic diet. The diet consists of high fat intake, adequate protein intake, and low carbohydrate intake. The diet has been used successfully in epileptic patients in countries around the world. More recently the diet is being used for patients with other diseases, including Alzheimer's

disease. A high carbohydrate diet is very deleterious—individuals favoring such diets had an 89% greater risk for mild cognitive deficits, as compared to a 44% risk for individuals on a high-fat diet, according to one analysis (Roberts, 2012). It is not known how the ketogenic diet influences brain activity in epilepsy and AD. The low blood sugar levels achieved with a ketogenic diet are thought to be beneficial, but other explanations for altered brain function also are being explored.

Nutrition: Reducing Brain Inflammation

Oxidative stress and inflammation accompany AD pathogenesis. The process of glycation—or the addition of a sugar group to a lipid or protein—dramatically increases the production of free radicals and inflammation in the brain (Stetka & Perlmutter, 2014). Amyloid-beta—the protein that comprises amyloid beta plaques found in AD-affected brains—can be glycated and promote free radical production and inflammation. It is not well understood whether oxidative stress and inflammation are a cause or consequence of Alzheimer's disease, but it would seem logical to try to reduce its development. This can be accomplished through diet by avoiding obesity, and omitting the added sugars and fats that can spur inflammation. Consuming foods known to be anti-inflammatory also could be beneficial. For instance, omega-3 fatty acids have been known to help reduce inflammation. Thus, it seems to be helpful to eat foods such as salmon, tuna, and mackerel which are high in omega-3 fatty acids. It is most beneficial if fish are baked or broiled rather than fried or salted. Nuts such as almonds and walnuts also can help fight inflammation because they are rich in fiber, calcium, vitamin E, and omega-3 fatty acids. Nuts also have high levels of antioxidants that can defend against and repair damage caused by inflammation. Spices such as turmeric and ginger have been known to reduce inflammation.

Animal studies have shown that diets supplemented with antioxidants result in heightened learning acquisition and memory. Antioxidants can be found in a wide range of fruits and vegetables, such as beets, tomatoes, raspberries, and blueberries, as well as many other foods, including green tea and chocolate. Studies have shown that vitamin E might play a role in protecting the body from pro-inflammatory molecules known as "cytokines." Both the Chicago Health and Aging Project and the Rotterdam study concluded that a high dietary intake of vitamin E is associated with a lower risk of AD. Vitamin E can be found in dark green vegetables, such as spinach, kale, and broccoli.

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Research Issues

Some researchers have suggested that Alzheimer's disease (AD) is similar to type 2 diabetes, and some even are calling AD "type 3 diabetes." The brain manufactures insulin which signals neurons to take up the glucose they need for their work. If the cells in the brain are overwhelmed with too much insulin—produced in response to high blood sugar—then the insulin receptors in the cell membrane become less sensitive to insulin's presence. If poor insulin

sensitivity turns out to be a major mechanism in the development of AD, then a healthful diet and the prevention of obesity will become even more central in public health efforts to prevent or delay the onset of Alzheimer's.

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See Also: Antioxidants; Blood sugar regulation; Cardiovascular disease and nutrition; Diabetes, type 2; Insulin.

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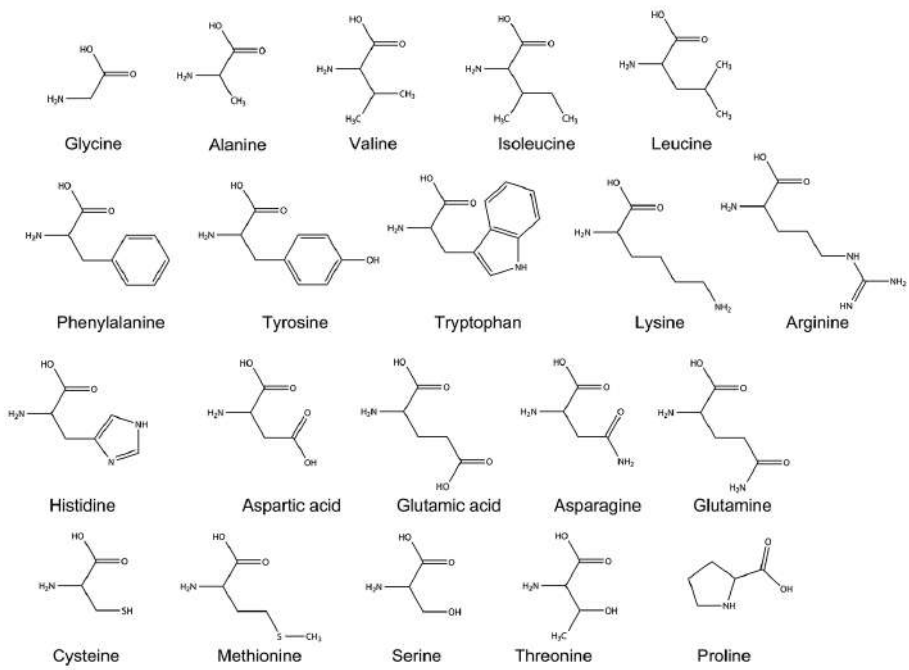
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Amino Acids

Amino acids are organic compounds that serve as the building blocks of proteins. Amino acids are essential to human life, and also are found in all plant and animal cells. Researchers have identified hundreds of amino acids in nature. Of these, there are about 20 amino acids that are proteinogenic, from which every living thing produces a large number of proteins. Proteins are responsible for countless functions and provide structure to numerous tissues.

In terms of human nutrition, amino acids can be divided into three categories: essential, nonessential, and conditionally essential. Essential amino acids are amino acids that the body cannot produce on its own, and must therefore be consumed. Nonessential amino acids are naturally produced by the body, and do not need to be supplied through diet as long as sufficient protein is present in the diet. Conditionally essential amino acids are amino acids that the body normally produces, but which become essential during certain circumstances, such as during illness or when the body does not have the proper enzymes to make them; at such time, these amino acids must be consumed through the diet. Amino acids are categorized in Table 1.



Chemical formulas for 20 amino acids. (Dreamstime.com)

Table 1. Classification of Amino Acids

Essential Amino Acids	Nonessential Amino Acids	Conditionally Essential
Histidine	Alanine	Arginine
Isoleucine	Arginine	Cysteine
Leucine	Asparagine	Glutamine
Lysine	Aspartic Acid	Glycine
Methionine	Cysteine	Proline
Phenylalanine	Glutamic Acid	Tyrosine
Threonine	Glutamine	
Tryptophan	Glycine	
Valine	Proline	
	Serine	
	Tyrosine	

Amino Acid Structure

The basic amino acid structure is composed of a central carbon atom (C) that is linked to a hydrogen atom (H), an amino group ($-NH_2$), a carboxylic acid group (-COOH), and a unique side group commonly designated by the letter "R." The R group is what distinguishes different amino acids, and each amino acid has a unique R group. When two amino acids join to form a protein, they form a peptide bond. A peptide bond occurs when the amino group of one amino acid joins with the carboxyl group of another amino acid and water (H_2O) is released. A dipeptide is two amino acids that are joined by a peptide bond. Tripeptides have three amino acids joined by peptide bonds, oligopeptides have 4 to 10 amino acids joined by peptide bonds, and a polypeptide has more than 10 amino acids joined by peptide bonds.

Amino acids often are likened to letters, and proteins are words spelled with those letters. Proteins can be quite large, containing thousands of amino acids. These chains of amino acids bend and coil, forming unique three-dimensional structures with shapes that depend upon the amino acid interactions with one another. The function of a protein molecule often depends upon this three-dimensional shape.

Amino Acid Function

Amino acids serve a considerable number of functions in the human body through the action of proteins. Functions include fluid balance, acid-base balance, structural and mechanical support (muscles, bone, skin, hair), immune response (antibodies), regulation of chemical processes (enzymes), chemical messengers (hormones), and transporters (cell membrane channels and pumps, carriers). Individual amino acids often are precursors to specific neurochemicals. For example, tryptophan is a precursor for the neurotransmitter serotonin.

Amino Acid Digestion and Absorption

Amino acids enter the body in the form of proteins. Once ingested, polypeptide bonds are broken down and the end result is single amino acids. Protein digestion begins in the stomach, where hydrochloric acid (HCl) unfolds the protein's unique structure, increasing surface area and thus making it easier for digestive enzymes to gain access to the amino acid chain. This process is known as protein denaturation. Following denaturation the proenzyme pepsinogen is released, and then is activated by the acidic environment of the stomach; the activated form of pepsinogen is pepsin. Next, pepsin breaks down 10% to 20% of ingested proteins into smaller polypeptide units or single amino acids.

After leaving the stomach, polypeptides and amino acids enter the small intestine, where most digestion takes place. The pancreas and intestinal lining then release proteases—enzymes that further break down peptide groups into ever smaller units—which then are absorbed as single amino acids into the bloodstream. Once absorbed, amino acids are available to the body for the synthesis of cellular proteins. Any proteins that are not digested are excreted in feces.

Amino Acid Pool and Protein Turnover

All cells need single amino acids to build proteins. Cells continually break down and build proteins. When proteins are broken down the amino acids are released into the bloodstream. Free amino acids are found throughout the body and collectively are referred to as the "amino acid pool." Amino acids from the amino acid pool are used whenever the body needs amino acids for synthesis of proteins.

The body is skilled at reusing amino acids. This recycling of amino acids is called "protein turnover." Protein turnover helps the body meet its amino acids needs. The body synthesizes about 300 grams of protein each day; about 200 grams of this protein comes from protein turnover (Insel, Ross, McMahon, & Bernstein, 2014). When dietary protein intake is too low to meet the body's needs for amino acids, protein breakdown increases to supply the amino acid pool. This can result in the breakdown of essential body tissues, such as muscles.

Protein Quality

Foods which contain all the essential amino acids are referred to as "complete" or "high-quality" proteins. Those foods that lack one or more essential amino acid are referred to as "incomplete" or "low-quality" proteins. Consuming a balanced and varied diet ensures that all the essential amino acids are present.

Amino Acids and Diet

Amino acids are found in every food group, and it is not difficult to achieve an adequate intake of amino acids with a varied diet. Foods highest in protein include most animal-derived products such as meats, fish, poultry, eggs, and dairy products.

Legumes, nuts, and grains also contain protein. Combining plant sources of protein enables people to ensure they have an adequate intake of all essential amino acids. Combining grains and legumes, for example, provides all essential amino acids. Many health authorities advise including a wide variety of protein foods in a diet, limiting the consumption of certain proteins such as red meat—which has been associated with health risks—and increasing intake of seafood and plant proteins.

Amino Acid Supplements

Many amino acid and protein supplements are marketed and sold to athletes with the promise of enhancing endurance and muscle strength. Amino acids can come from either food or supplements. Protein supplements marketed to athletes often feature whey protein, which is high in the branched-chain amino acids leucine, isoleucine, and valine. "Branched chain" refers to the R group structure. These amino acids might be helpful for recovery from strenuous exercise. Some studies suggest that muscle cell injury and recovery time can be lessened with consumption of these amino acids near the time of exercise.

Amino acids also are given as supplements to people with certain diseases and the elderly, when they either are unable to produce particular amino acids or simply lack adequate protein sources in their diet. Studies suggest that daily essential amino acid supplementation improves the quality of life, symptoms of depression, muscle function, and nutrition of institutionalized elderly patients (Rondanelli et al., 2011).

Paula Sophia Seixas Rocha

See Also: Digestion and the digestive system; Protein; Vegetarian and vegan diets; Whey protein.

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Anthocyanins

Anthocyanins are powerful antioxidants found in plants and provide pigmentation to flowers, fruits, and some leaves. Responsible for providing the vibrant reds, blues, and purples prominent in berry plants like bilberry, strawberry, blueberry, and black currant, these water-soluble substances are critical for attracting animals for pollination and seed dispersal. Anthocyanins also impart color to red onions, red cabbage, black beans, grapes, nectarines, and pomegranates. There are more than 500 different types of anthocyanins, differentiated by the nature and positioning of their attached sugar molecules.

The biological interactions that incorporate anthocyanins are complex, making their actions difficult to study in the human body. Not only is it difficult to track their metabolic breakdown after ingestion, but anthocyanins never act independently and are readily oxidized and degraded. They exist as isolated molecules as well as in highly concentrated groups called "anthocyanic vacuolar inclusions," that could intensify their antioxidant properties. Although the release of reactive oxygen species (ROS) is a normal byproduct of cellular metabolism, abnormally high amounts alter the structure of cell membranes and are indicative of disease. The ability of anthocyanins to scavenge ROS makes them effective in reducing the risk of cardiovascular disease by reducing oxidative stress that can lead to ischemia, high blood pressure, and inflammation (Wallace, 2011). Anthocyanins also serve to regulate various signaling pathways whose dysfunction can contribute to the development of cardiovascular disease (CVD).

Anthocyanins are thought to sharpen visual acuity by enhancing the regeneration of rhodopsin, a pigment found in photoreceptor cells of the eye that helps to detect light. Preliminary research with anthocyanin compounds in vitro suggest possible anti-cancer effects, although it is unclear whether this research will develop into therapeutic applications. Bilberry extract supplements have become popular for people experiencing eye strain and those concerned with eye health. These supplements seem to be safe at doses of 25 mg to 50 mg. No other evidence currently provides strong support for taking anthocyanin supplements. Consuming plenty of anthocyanin-rich fruits and vegetables appears to be the best option for maximizing the protective effects of these helpful phytochemicals.

Patricia M. Cipicchio

See Also: Antioxidants; Phytochemicals.

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Antioxidants

Antioxidants are compounds that neutralize chemicals known as "free radicals." Free radicals are molecules that have a single electron, making the molecules highly reactive as they "look" for another electron to complete the incomplete valence. In cells, free radicals can take electrons from other molecules, including those in important structures such as DNA and cell membranes. By donating electrons to stabilize free radicals, antioxidants in the human body help to prevent or delay some types of cell damage.

Some antioxidants are natural and others are man-made. Antioxidants are found in foods such as fruits, vegetables, and whole grains. Antioxidants such as carotenoids, lutein, lycopene, vitamin C, and vitamin E can help healthy cells from being damaged by free radicals (Academy of Nutrition and Dietetics [AND], 2014). Although there is extensive research supporting the idea that a diet with high intake of fruits and vegetables lowers the risk of many chronic diseases, it is difficult to pinpoint how certain antioxidants might be directly responsible for the lower risks of specific diseases. Furthermore, individuals who consume a large amount of fruits and vegetables often also engage in overall healthier lifestyles, which might account for the lower risks of diseases (NIH, 2014b).

Free Radicals and Antioxidants

Free radicals come from a variety of sources. Individuals can be exposed to free radicals via the environment from sources such as cigarette smoke, air pollution, and sunlight (NIH, 2014b). Free radicals also are produced in the body during normal oxidative metabolism, the process by which energy is produced in the mitochondria from oxygen and the fuel precursors carbohydrates, proteins, and fat. When the human body converts food into energy, unstable molecules are formed as part of the natural process of breaking down food. Free radicals trigger cell damage, which can lead to oxidative stress. Some research shows that oxidative stress is partly responsible for diseases such as cancer, cardiovascular diseases, diabetes, Alzheimer's disease, Parkinson's disease, cataracts, and age-related macular degeneration (NIH, 2014b). Antioxidants counter the damage by counteracting the oxidative stress.

Fruits and Vegetables Rich in Antioxidants

Carotenoids

There are approximately 600 carotenoids in foods, and beta-carotene, lycopene, and lutein are three types that are known to reduce damage from free radicals. Foods high in carotenoids decrease risk of prostate cancer; cancers of the mouth, pharynx, esophagus, stomach, colon, and rectum; and decrease risk of macular degeneration. Good food sources with high concentrations of carotenoids are tomatoes, carrots, spinach, brussels sprouts, sweet potatoes, winter squash, and broccoli.

Vitamin E

Vitamin E is associated with reduced risk of cancer, heart disease, and cataracts. Good food sources of vitamin E are vegetable oils, salad dressings, margarine, wheat germ, whole grain products, seeds, nuts, and peanut butter.

Vitamin C

Vitamin C helps protect against infection and damage to body cells and bruising. Additionally, Vitamin C is essential for collagen production, and for the absorption of iron and folate in the digestive tract. Good food sources of vitamin C are oranges, grapefruits, tangerines, strawberries, sweet peppers, tomatoes, broccoli, and potatoes.

Consuming Antioxidants in Foods

The best way to increase intake of dietary antioxidants is to consume a wide variety of fruits, vegetables, whole grains, nuts, seeds, and plant oils. Foods that are packed with antioxidants and can be consumed as a meal or snack include: peanut butter on whole wheat toast with a fruit salad; baked potato with olive oil topped with broccoli, tomatoes, and carrots; and a spinach salad with sweet peppers, carrots, tomatoes, nuts, seeds with extra virgin olive oil as dressing. One way to consume a nutrient-dense diet is to "eat a rainbow" as part of every meal, by filling half of a plate with a mixture of fruits and vegetables (Fruits and Veggies More Matters [FVMM], 2014). Eating a rainbow every day means consuming red, dark green, yellow, blue, purple, white, and orange fruits and vegetables.

Dietary Supplements

Antioxidants also are available in the form of dietary supplements. Consuming natural antioxidants in fruits and vegetables as part of a normal diet is healthful; taking high-dose supplements of antioxidants might not be safe. Antioxidant supplements can have negative interactions with some medications, so it is important to contact the prescribing health care provider when planning to add antioxidant supplements to a regimen. People taking anticoagulant (blood-thinning) drugs, for example, who also are taking high doses of vitamin E supplements could be at risk for bleeding (NIH, 2014b). Smokers who take high doses of beta-carotene could increase their risk of lung cancer. Taking high doses of vitamin E might increase the risk of prostate cancer and of hemorrhagic stroke.

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See Also: Dietary supplements; Phytochemicals.

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Appetite

Appetite refers to the psychological desire to eat. It is influenced by a variety of factors, including internal signals and cues from the environment. Sensory perceptions, as well as social and emotional triggers and expectations, all impact what and how people eat. Although there are physiological components to how appetite is experienced, there are a greater number of environmental and psychological influences.

It is important to note that appetite is not the same as hunger. Although hunger is the physiological *need* to eat, appetite describes the psychological *desire* for food. Appetite can cause a craving for a particular food even when hunger is absent. Conversely, appetite can be suppressed due to various emotional or medical reasons even though the body is hungry and in need of nutrients. This is an important topic for many reasons. Appetite—arguably even more than hunger—dictates what a person eats, how much a person eats, as well as when and why a person eats. Eating too little or too much, or eating foods that are not healthy simply because they taste or look good can affect a person's health. Psychological influences on appetite can negatively impact a normally healthy lifestyle.

Although occasionally straying from healthful foods and portion sizes is not harmful, in the long term such eating habits can contribute to many health problems, including obesity, type 2 diabetes, hypertension, and liver disease. Furthermore, discovering how to physiologically control or suppress appetite might be helpful in the prevention and treatment of obesity and obesity-related health problems.

Physiological Factors

A variety of neurochemicals work together to influence appetite. The influences of neuropeptide-Y (NPY) have been researched extensively, it appears to work by increasing feelings of hunger and as an appetite stimulator. Ghrelin, produced in the stomach, and leptin, produced in fat cells, are largely responsible for the rise and fall of NPY, and therefore the increase and decrease of appetite. Although

Prescription Medications for Appetite Suppression

Several prescription medications for the treatment of obesity work as appetite suppressants; they help people eat less, but they also can cause problems. The Weight-control Information Network's online information should be consulted for information on how these drugs work and their potential side effects. The medications discussed include the following:

- Lorcaserin (sold as "Belviq")
- Phentermine-topiramate (sold as "Qsymia"); phentermine (sold as "Adipex-P," "Oby-Cap," "Suprenza," "T-Diet," and "Zantryl")
- Benzphetamine (sold as "Didrex")
- Diethylpropion (sold as "Tenuate" and "Tenuate Dospan")
- Phendimetrazine (sold as "Adipost," "Bontril PDM," "Bontril Slow Release," and "Melfiat")

Among these types of drugs phentermine is the one used most often in the United States.

Weight-control Information Network (WIN). (2013). *Prescription medications for the treatment of obesity*. National Institute of Diabetes and Digestive and Kidney Diseases. Retrieved from http://win.niddk.nih.gov/publications/prescription.htm

ghrelin promotes hunger by stimulating NPY, rising before a meal and falling afterward, leptin quells hunger by inhibiting NPY, suppressing appetite after a meal.

A release of NPY has been shown to increase food intake in both animal and human studies. Neuropeptide-Y is released in states of starvation or food deprivation, as well as when confronted with psychologically desirable foods. The former is to be expected. When the body is in a state of hunger, it is not surprising that appetite would be signaled. The release of neuropeptide-Y when confronted with psychologically desirable foods affects food intake, and this has clear and dangerous implications for those who are overweight or obese—appetite can be stimulated even when the body is satiated and does not need food. This could lead individuals to develop a habit of overeating, because the eating environment or the person's emotional or social states encourage constant and generous consumption.

Leptin release has been correlated with weight loss as it suppresses appetite. Low leptin levels, whether resulting from decreasing fat stores or abnormal leptin function, are correlated with subjective perceptions of hunger and appetite. Individuals with persistently low leptin levels have been reported to experience incessant feelings of hunger. People who are obese appear to develop leptin resistance; the body does not respond appropriately to the presence of leptin. Leptin resistance is associated with increased appetite and hunger.

Sensory Perception

Sensory perceptions of food can influence mood and appetite before and after meals, and significantly impact an individual's weight. The presentation, taste, smell, and texture of food all influence food intake. These factors often can cause

individuals to consume far greater amounts of food than their hunger dictates, and also are likely to determine what types of food individuals choose.

Portion size has a very interesting effect on consumption. Multiple studies have shown that the amount of food people tend to eat increases with larger portion sizes. The bigger the portion or the size of a plate, the more food a person tends to consume. This has strong implications in today's world, where portion sizes now are larger than ever. The current eating environment in the United States promotes over consumption by producing inexpensive food in large quantities. Increasing portion sizes have been revealed to correspond with increasing rates of obesity.

Psychological Factors

Emotional states can work to increase or decrease appetite. Although some people are prone to having increased appetites when experiencing negative emotions, other people lose their appetites—particularly when prompted to feel sad. Many people use eating to cope with negative emotions. When food is utilized to deal with issues such as low self-esteem or depression, disordered eating habits commonly develop. An increased appetite in response to a negative mood appears to be a learned behavior, in which a person learns to associate improvements in mood with food consumption. This mood improvement could result from activation of the pleasure centers of the brain, as well as altered neurochemical levels in other areas of the central nervous system. Negative emotions eventually trigger an increase in appetite and then an increase in eating behavior, which reduces negative emotions.

Generally, eating habits established due to long-term exposure to stressors are not positive. They do not aid in the maintenance of a healthy lifestyle. In an interesting study of college women, researchers found that more than 80% of participants' appetites were noticeably different when stressed, and of the 80% of subjects who reported having healthy diets, 66% failed to make healthy choices when experiencing stress (Kandiah, Yake, Jones, & Meyer, 2006). Stress is likely to negatively impact health, as it encourages individuals to under- or overeat, and to eat unhealthy foods that lack a variety of nutrients.

Social and Environmental Factors

Social factors can influence appetite. When eating with friends or relatives, individuals might feel comfortable and eat only as much as they need. Other times, social environments provide a distraction from one's sense of satiety (the feeling of having had enough to eat), and people can continue to experience an appetite and the drive to continue eating, even though they are full. Social factors could create feelings of stress that influence appetite.

Cultural influences also shape a person's appetite. As children grow up they create associations with particular foods. The presence of comfort foods or foods associated with special occasions can stimulate appetite. Similarly, foods regarded as unpleasant can decrease appetite.

The eating environment could influence appetite. A calm and relaxing environment generally is conducive to a healthy appetite, allowing individuals to experience the drive to eat as pleasant, and eating as being pleasurable. Conversely, a noisy, stressful environment could interfere with appetite signals, decreasing or increasing appetite depending upon how an individual responds to stress. The presence of tasty food can increase appetite even though one has had enough to eat. Seeing the dessert menu, for example, can stimulate appetite even after having just finished a large meal. Obesity experts claim that most areas of North America are "obesogenic environments," in that the environments stimulate appetite and push individuals toward overeating, while limiting opportunities for physical activity.

Appetite Stimulants and Suppressants

Various illnesses and medical conditions can cause a decreased appetite even when the body is hungry and in need of food. A loss of appetite is called anorexia. Many cancer treatments interfere with appetite, for example, causing cancer anorexia. A decreased appetite often is seen with illness, and can result in unintentional weight loss. People experiencing unintentional weight loss and a decreased appetite should consult their health care providers to rule out an underlying illness. Older adults often experience a decreased appetite, especially if their senses of taste and smell become less sharp.

Medications that stimulate appetite are known as orexigenics. One example is a drug that is a synthetic version of marijuana. This drug can stimulate appetite and relieve pain.

Understanding how appetite works in the body and in the mind can be useful in offering treatment to obese individuals. Appetite suppressant medication, however, has not yet proved to be very helpful for the long-term treatment of obesity. These medications suppress appetite in the short term, but appetite eventually returns to normal. Medications also have several negative side effects. People should not take these medications for more than a few months, at which time eating returns to normal and weight lost weight often is regained.

Cassandra C. Greene

Research Issues

A variety of magazine and newspaper articles encourage individuals to exercise to suppress appetite and lose weight. Exercise has been shown to influence appetite short term, especially in overweight individuals. High-intensity workouts such as interval training appear to have a stronger appetite-reducing effect than that of more moderate activity levels. High-intensity exercise can result in longer elevations of blood glucose levels and lower blood concentrations of hunger hormones (Reynolds, 2013a). Theoretically, a regular exercise schedule could suppress appetite continuously and decrease the occurrence of overeating or eating between meals. Most studies on exercise and appetite have been short term, however. Little to no evidence suggests that the effect of exercise on appetite actually leads to significant weight loss.

See Also: Hunger, biology of; Mindful eating; Obesity, causes.

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Arginine

Arginine, also known as L-arginine, is a semi-essential amino acid involved in protein metabolism and the synthesis of urea and creatine within the body. The body also converts arginine into nitric oxide (NO), which acts as an important vasodilator that causes blood vessels to open wider to increase blood flow. Arginine is considered a semi-essential amino acid because the body normally is able to make it in sufficient amounts. This amino acid, however, could be required to be supplied by diet or supplementation in some physiological conditions, such as malnutrition, excessive ammonia production, burns, infections, peritoneal dialysis, urea synthesis disorders, and sepsis. Deficiencies can result in symptoms including constipation, alopecia, skin problems, slow-healing wounds, and fat buildup in the liver. This amino acid occurs naturally in meats, dairy products, many nuts, legumes, and whole grains such as buckwheat, barley, and brown rice.

Arginine was first isolated from a lupin seedling extract in 1886 by Ernst Schulze, a Swiss chemist. In 1998, the Nobel Prize in physiology was awarded to Robert Furchgott, Louis Ignarro, and Ferid Murad for their discoveries concerning NO as a signaling molecule. Because NO is created from arginine, the pharmaceutical and nutraceutical fields began marketing arginine as a dietary supplement. Because it stimulates the body to make proteins, arginine often is marketed to athletes. Additionally, many athletes look to vasodilation to increase blood flow and the delivery of nutrients and oxygen to exercising muscles, thus stimulating protein synthesis and decreasing recovery time. Current research, however, suggests that physiological concentrations of arginine in healthy individuals are enough to saturate the enzymes responsible for making NO, and concludes that

arginine supplementation does not cause an increase in enzymatic activity or NO production (Alvares, Conte-Junior, Silva, & Paschoalin, 2012).

Although arginine supplementation might not be beneficial for healthy individuals, several potentially helpful medical applications are under investigation. Arginine supplementation has been shown to aid patients with urea-synthesis deficiencies—which cause a buildup of dangerous nitrogen in the body—by helping to shift the way nitrogen is processed and aid in its elimination. Early evidence from several studies also suggests that arginine supplementation in patients with coronary artery disease and angina can help increase blood flow to the heart and arteries via the NO pathway. Arginine supplementation could aid other circulatory disorders, including erectile dysfunction and intermittent claudication (poor blood flow) in the legs. Studies also show that arginine can aid in wound healing, and when given with hydroxymethylbutyrate (HMB) and glutamine it can slow muscle wasting in certain disease states, such as AIDS.

The supplemental usage of arginine is limited by its absorption rates and bioavailablity within the body. When consumed, it is converted to L-citrulline or L-ornithine by the liver. After conversion, it can enter the bloodstream and be absorbed by peripheral tissue. Due to poor intestinal uptake of arginine during normal conditions, citrulline supplements might be prescribed instead. During disease conditions intestinal uptake of arginine can increase. There is no standard or well-established dosage recommended for arginine. Research studies commonly use two to three grams administered orally two to three times daily.

It is important to consult a health care provider before starting arginine supplementation due to its unwanted interactions with many medications, herbs, and other dietary supplements. Side effects of arginine supplementation include low blood pressure, stomach cramps, and nausea. Although often prescribed for people with congestive heart failure and chest pain, those who already have suffered a heart attack should not take arginine, as it can increase risk of death in some groups of heart patients. Arginine supplementation also can aggravate herpes symptoms in people with this virus. People with asthma should be wary of taking this supplement, as should people taking prescription medicine to control blood sugar levels.

Chelby J. Wakefield

See Also: Amino acids.

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Arsenic

Arsenic is a naturally occurring element that exists in the environment in both organic and inorganic forms. It is found in soil, rocks, water, and air, and can be released during erosion, forest fires, volcanic activity, and through human acts such as mining. Arsenic is considered an essential nutrient, with daily intake ranging from about 12 mcg to 40 mcg. The function of arsenic in human health is not clear, although animal evidence suggests it might be involved in the metabolic pathways of the amino acid methionine.

Arsenic is an odorless and tasteless class 1 carcinogen, or cancer-causing agent. In small amounts arsenic has been used to combat a variety of ailments as far back as Hippocrates (460 BCE–370 BCE), who employed arsenic sulfate to treat ulcers. In 1909, German scientist Paul Ehrlich discovered an arsenic-based cure for syphilis known as "Salvarsan," which in the 1940s was replaced by penicillin. The harmful health effects of arsenic have largely eliminated its application in contemporary medicine, aside from its use in isolated cancer treatments. It is commonly used in industry to strengthen alloys and is most often found in pesticides and treated wood products.

Because the element dissolves easily in groundwater, it also is found in food—especially fish, poultry, rice, and starchy vegetables. Food products usually contain organic arsenic, which currently is considered less harmful by the Food and Drug Administration, as opposed to inorganic arsenic which can be fatal (FDA, 2011). Total arsenic presence in bottled and public drinking water is restricted to 10 ppb by the Environmental Protection Agency, which also is considering standards for other beverages such as apple juice. In 2011, consumers in the United States became alarmed when arsenic levels greater than 10 ppb were found in samples of apple juice and grape juice, according to *Consumer Reports*, an expert, independent nonprofit organization whose goal is to educate consumers about products in the marketplace (Consumer Reports, 2012). The FDA countered stating that its own testing did not find high arsenic levels in juices, but consumers remain concerned. Especially worrisome is children's arsenic intake, because many children in the United States drink relatively large amounts of apple juice. In 2012, higher than expected levels of arsenic were found—this time by the FDA and several other groups—in many samples of rice from around the world (FDA, 2012). Arsenic levels in rice products, including rice milk, rice baby cereal, and rice cakes also were found to be greater than expected.

Arsenic toxicity is highly variable between individuals and is thought to be affected by nutrition. In rats, the element has been shown to interfere with absorption of copper in the body. Vitamins C and E might help relieve oxidative stress caused by arsenic. Prolonged exposure to arsenic can lead to many types of cancer, particularly of the lung, skin, and bladder. Exposure also can cause skin lesions, anemia, diabetes, and neurological problems (CDC, 2009). Acute effects include headaches, gastrointestinal distress, convulsions, and hair loss. Its lethal dose in adults is estimated to be 70 mg to 200 mg.

Patricia M. Cipicchio

Research Issues

The FDA, USDA, Consumer Reports, and other organizations are continuing to monitor arsenic levels in the food supply. Their websites contain interesting information about their monitoring processes and their findings, as well as advice for concerned consumers.

See Also: U.S. Food and Drug Administration.

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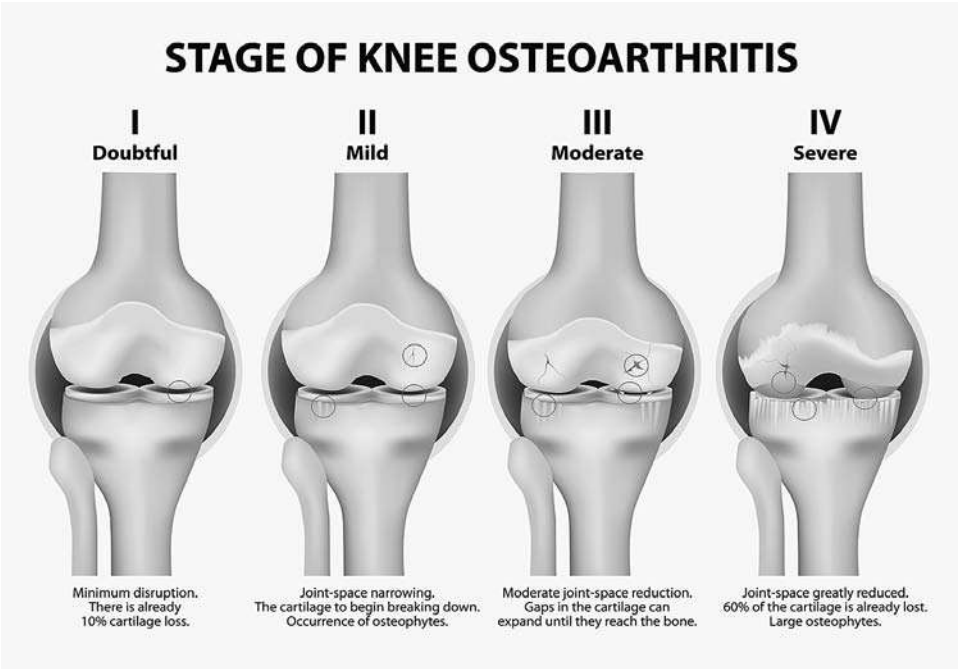
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Arthritis and Nutrition

Arthritis refers to a group of diseases that involve painful inflammation and stiffness of the musculoskeletal system, especially the joints. It is the leading cause of disability in adults in the United States (CDC, 2011). The word "arthritis" comes from the Greek word "arthron," meaning "joint," and the Latin term "itis," meaning "inflammation." There are more than 100 different types of arthritis, and they vary in prevalence from common to rare. In the United States, as many as 50 million adults (22%) have been doctor-diagnosed with arthritis, with



Stages of knee osteoarthritis. (iStockPhoto.com)

the condition being the second most frequent reason for consulting a doctor (CDC, 2011). The most common forms of arthritis are osteoarthritis (OA) and rheumatoid arthritis (RA). Nutrition does not seem to play a major role in the causation of arthritis. Nutrition is, however, an important component of arthritis management, along with other lifestyle-change recommendations and appropriate medications.

Osteoarthritis

Osteoarthritis or "degenerative arthritis" is characterized by the breakdown of cartilage in a joint, often caused by trauma or overuse. It eventually leads to abnormal bone changes and the failure of the joint's mobility. Cartilage is a flexible connective tissue that protects joints, helping to maintain stability and flexibility. Cartilage does not contain blood vessels, which helps to explain why the rate of cartilage growth and repair is relatively slow. Osteoarthritis also might affect the synovium—a fluid-filled sac that surrounds the joint and provides nutrients and oxygen to the joint components. The surrounding muscle and tendons also can be involved.

In the early stages of OA, the cartilage becomes swollen and loses elasticity, which results in the formation of tiny cracks within cartilage tissue that hinder joint

function and leave the cartilage vulnerable to further damage. The fragmentation of the cartilage surface can lead to remodeling of the bone and invasion by blood vessels. Inflammation also commonly occurs in the synovium, causing pain and swelling, and can exacerbate cartilage deterioration. Osteoarthritis is not a systemic disease, and only occurs in those joints with deterioration, most commonly affecting the joints of the spine, knee, hand, foot, and hip.

Rheumatoid Arthritis

Rheumatoid arthritis is a chronic, systemic, inflammatory autoimmune disorder affecting the synovium, and leading to joint damage and bone destruction. The disease begins in the small joints, such as the hands and feet, and extends to larger joints. In RA, the immune system attacks the tissues that line joints, including cartilage. The inflamed synovium proliferates across the joint and becomes heavily infiltrated with inflammatory cells. The invading synovium also produces enzymes that decrease cartilage integrity and stimulate bone erosion. Additionally, the surrounding soft tissue becomes inflamed, and new blood vessel growth occurs. Together with the invasion of cartilage and bone into the joint surface, this leads to deformity and progressive physical disability. Intestinal inflammation, abnormal gut microflora, and lipid abnormalities, including insulin resistance correlated to inflammation, also are associated with RA.

Epidemiology

Osteoarthritis is a much more common disease than is rheumatoid arthritis. The number of people affected by arthritis is large with a wide-ranging impact on society. Approximately 1 in 3 people with arthritis (31%) between the ages of 18 and 64 report work limitations due to arthritis, and arthritis is strongly associated with major depression (CDC, 2011). Worldwide, approximately 9.6% of men and 18.0% of women have OA, and about 0.3% to 1% of people have RA (WHO, 2013). Rheumatoid arthritis has a relatively lower prevalence in poorer countries (WHO, 2013). Both OA and RA are more prevalent in women; it has been noted that 24.3% of women and 18.3% of men in the United States have been diagnosed with arthritis; the prevalence increases with age and is higher among women than men in every age group (CDC, 2011).

Although premature mortality is quite low in people with arthritic diseases, the morbidity associated with the disease can be very high, varying greatly among individuals. Joint stiffness and pain are the most prominent symptoms, and arthritis often causes reduced mobility and a lower level of physical activity that result in some degree of physical disability (CDC, 2011). This morbidity related to arthritis also comes as an economic cost to both the individual and to society. Arthritis is among the most common reasons for working days lost, amounting to a huge economic impact worldwide. In 2003, the total cost attributed to arthritis and other rheumatic conditions in the United States was 128 billion dollars, up from 86.2 billion dollars in 1997 (CDC, 2011).

History

Arthritis was one of the first diseases to be clinically recognized, having been described by ancient Egyptian medical texts and Greek scholars. The symptoms of the disease were also referred to in an Ayurvedic medical text. Ayurvedic medicine is a form of Hindu traditional medicine that is native to the Indian subcontinent, 123 CE (Stetka & Wel, 2013). Early Greek scholars, including Hippocrates (~460–357 BCE), and later medieval Europeans ascribed joint maladies to the "flux" of congested humors, in which bad humors were thought to drip into affected joints. Archeological remains also give evidence of arthritis's long past, extending to dinosaurs, Neanderthals, and early humans (Stetka & Wel 2013).

Symptoms and Diagnosis

General signs and symptoms of arthritis include swelling in one or more joints, stiffness around joints that lasts for at least an hour in the morning, constant or recurring pain or tenderness in a joint, difficulty in moving joint, and warmth or redness around joint (CDC, 2011). A general physician or rheumatologist often will review a patient's medical history and order lab tests, including blood and urine tests and imaging tests such as x-rays or MRIs, to make a diagnosis (CDC, 2011). Both OA and RA can be classified according to severity using criteria set out by the American College of Rheumatology.

Osteoarthritis can manifest in different ways, but it is usually diagnosed when health care providers note a loss of cartilage within synovial joints, associated with loss of bone mass and the thickening of the joint capsule. (The joint capsule is the thin, fibrous sac that surrounds the joint and that contains lubricating fluid.) Rheumatoid arthritis usually is diagnosed when patients have arthritis of at least one joint area and achieve a certain "score" that is based on the American College of Rheumatology's criteria. These criteria include location and number of involved joints; symptom duration; severity of RA symptoms such as swelling or deformity; and positive blood results for serum rheumatoid factor.

Causes and Risk Factors

Osteoarthritis sometimes is brought about by another disease or condition. This includes trauma or repetitive use, infectious diseases, or other inflammatory diseases, such as gout. Gout is a complex form of arthritis that occurs when either the kidney does not excrete enough uric acid or the body produces too much, and, consequently, uric acid crystals can accumulate in joints. The accumulation of crystals results in inflammation, swelling, and severe attacks of pain. Obesity is another common contributor to OA, as excess adipose tissue increases systemic inflammation and can put added stress on damaged joints, particularly the knees and hips.

Rheumatoid arthritis appears to be caused by the interaction between many genetic and environmental factors. Genetic susceptibility can be seen in twin and

family studies that have shown an increase in the risk of developing RA among relatives. Certain shared alleles, called "rheumatoid epitopes," could help predict disease severity and outcome. Rheumatoid arthritis seems to peak in the fifth decade of life, and socioeconomic status seems to affect the outcome of—rather than cause of—the disease; lower socioeconomic status is linked with a worse prognosis. Smoking and dietary choices also are likely to affect the risk of developing RA and also the outcome of the disease. People in geographic zones that eat a Mediterranean diet, including a lifelong consumption of fish, olive oil, and cooked vegetables, have lower rates of RA occurrence and severity.

Treatment

Arthritis treatment recommendations vary greatly from lifestyle changes to prescription medicine therapies, and depend on type and severity of arthritis and the individual. Because arthritis has no cure, the goals of treatment are to reduce pain, limit joint damage, maximize function, and maintain or improve the quality of life. Treatment usually consists of a combination of medication and nonpharmacologic therapies, such as physical therapy, occupational therapy, patient education, and weight loss (for people who are overweight).

There are many medications on the market to help in the management of arthritis, including analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), disease-modifying antirheumatic drugs (DMARDs), biologic response modifiers, and corticosteroids (CDC, 2011). These medications aim to reduce pain and decrease inflammation, often by slowing or blocking the immune system—which can leave the patient susceptible to other health problems (CDC, 2011). Other suggested practices include exercise, proper diet, rest and relaxation, surgery (in some cases), and heat/cold therapies (CDC, 2011).

Nutrition

People with arthritis are at risk for nutritional deficiencies. One reason could be that inflammation is associated with the production of cytokines, the activators of immune cells that increase resting metabolic rate and protein breakdown. Medications also can cause conditions that are associated with decreased appetite, such as peptic ulcers or gastritis. People with arthritis who experience significant disability frequently have difficulty shopping for groceries and preparing nutritious meals.

For people with arthritis, a proper diet means eating a variety of foods that balance caloric intake and physical activity, choosing a diet with plenty of vegetables and fruits, and choosing foods low in synthetic trans fats, added sugars, and alcohol. Following a healthy diet nurtures a healthy weight and improves overall health, which might be important in managing arthritis and its symptoms. Additionally, foods with anti-inflammatory properties might help reduce the inflammation associated with both OA and RA. Some of the dietary components and eating patterns that have been investigated as possible factors in the management of OA and RA include the following.

Omega-3 Fatty Acids and Gamma Linolenic Acid

Omega-3 fatty acids play a role in modifying the inflammation process and the regulation of pain, decreasing cytokine activity and cartilage breakdown. It has also been suggested that omega-3 levels are inversely correlated with cardiovascular disease, which is seen in many patients with RA; are associated with lower risk of developing the disease; and can work alongside other medications, such as NSAIDs, to decrease inflammation (Stamp et al., 2005). Omega-3 fatty acids can be found in oily fish (e.g., salmon, tuna, mackerel), some vegetables (including soybeans, tofu, kale, collard greens, and winter squash), and walnuts, flaxseed, and pecans (Nelson & Zeratsky, 2013).

Gamma linolenic acid (GLA) is a fatty acid precursor to anti-inflammatory compounds made by the body. Gamma linolenic acid is found in evening primrose oil, borage oil, and black currant oil supplements. Preliminary research has shown that GLA supplements might help reduce arthritis symptoms.

Antioxidants and Vitamins

Eating foods rich in antioxidants could decrease the oxidation that leads to increased cell and tissue damage in inflammatory arthritis. Antioxidants such as vitamin C, vitamin E, selenium, carotene, lycopene, and flavonoids slow the process of oxidation and remove free radicals. Colorful vegetables and fruits are rich in antioxidants: leafy greens including spinach and kale, beets, blueberries, and cranberries. Beans, nuts, green tea, red wine, dark chocolate, and certain spices such as cinnamon, ginger, and turmeric also are rich in antioxidants. Vitamin D also could exert anti-inflammatory effects. Probiotic foods and supplements could help to address the intestinal inflammation present with RA.

Supplements and Herbs

Although it always is better to consume needed nutrients from whole foods, diet supplementation can be beneficial for arthritis treatment. Some recommended supplements include fish oil (which contains high levels of omega-3 fatty acids), antioxidant supplements, and some herbal supplements (NCCAM, 2013). Although the use of herbal supplements is quite controversial, some of the recommended types are thunder god vine (side effects could outweigh anti-inflammatory benefits), bosweillia, ginger, rosemary, and green tea (NCCAM, 2013; Weil, 2013). Glucosamine and glucosamine chondroitin supplements might help reduce pain in people with moderate to severe arthritis pain, but appear to be less effective for those with milder pain.

Specialty Diets

Some research suggests that vegetarian and vegan diets could improve clinical symptoms of arthritis, as could many low-fat diets that aim to reduce animal

product consumption. As noted, another beneficial eating plan suggested is the Mediterranean diet. Other research suggests that dietary lectins—found in carbohydrates such as rice, potato, and wheat products—increase permeability and bacterial overgrowth in the gut that could lead to increased production of immune cells. People with arthritis might find that replacing some dietary lectins with fruits and vegetables helps reduce arthritis symptoms.

Controversial Diets

Little research supports the notion that elimination diets, fasting, and "miracle" food diets are safe and effective ways to reduce inflammation. There is little scientific evidence to show that cutting out a specific food, or relying on one as a cure, are effective treatment options. Fasting, although associated with reduced inflammation in the short term, can lead to dehydration and serious nutritional deficiencies and is not recommended as a viable long-term treatment option.

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Research Issues

Research continues to investigate possible foods and supplements that may help to treat both osteoarthritis and rheumatoid arthritis. The website of the Arthritis Foundation (http://www.arthritistoday.org/arthritis-treatment/natural-and-alternative-treatments/supplements-and-herbs/supplement-guide/), lists additional foods and supplements that one day could become established as helpful arthritis remedies.

See Also: Antioxidants; Inflammation; Marine omega-3 fatty acids.

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Artificial Sweeteners

Artificial sweeteners are used in a variety of products in place of sucrose (sugar). They also are called "high-intensity sweeteners" and "nonnutritive sweeteners" (NNS) because they are many times sweeter than sucrose and can be used in miniscule amounts, providing few (if any) calories. Unlike sugar, they do not promote tooth decay. Artificial sweeteners can be found in diet soda, yogurt, chewing gum, and many other processed foods; they also commonly are tabletop sweeteners, and some can be used in home cooking.

Artificial sweeteners are regulated as food additives in the United States by the U.S. Federal Drug Administration (FDA) and in Canada by Health Canada. These regulatory agencies set acceptable daily intake (ADI) values that represent the maximum amount considered safe to consume daily over a lifetime. Acceptable daily intake values generally are calculated to be 100 times less than the smallest amount that might be harmful to health. For example, the ADI of aspartame is 50 milligrams per kilogram of body weight. For an average adult, this is roughly equivalent to consuming 16 12-ounce diet sodas daily (Insel, Ross, McMahon, & Bernstein, 2013). Despite these regulations, controversy over the safety of artificial sweeteners abounds. For each sweetener some studies confirm safe usage and other studies suggest alarming risks. (See "Research Issues" for more information on the debate.)

A similar debate ensues over the health benefits of artificial sweeteners. Many people use artificial, or nonnutritive, sweeteners and products containing them to help cut sugar and calories from their diet. Both the American Heart Association and the American Diabetes Association support the use of NNS as one way to combat obesity and its resulting complications (Strawbridge, 2012). Yet both institutions also caution that NNS should be consumed in moderation as part of a nutritious diet. This is particularly true for children and pregnant women—NNS, although considered safe, should not be consumed in place of the nutritious foods necessary for growth and development.

The debate centers on studies that have shown a connection between consumption of NNS and weight gain (Strawbridge, 2012). One explanation for this is that people who consume a diet product subsequently allow themselves to eat more food. The reasoning is, "I am drinking diet soda, so I can have the fries," or "These are reduced-calorie cookies, so I can eat the whole box." The result is more caloric intake rather than less. Another hypothesis is that NNS might change the way people experience food. The intensity of the artificial sweetness could cause naturally sweet foods to seem less sweet, and therefore less appealing. This could be compounded by a lack of satiety from foods and beverages containing NNS—although they taste sweet they do not satisfy, which can increase cravings for more sweets.

It could be decades before research confirms purported benefits or dangers of artificial sweeteners. Meanwhile, they are consumed around the world in a wide

variety of products, and research and development into new sweeteners is ongoing. Following are descriptions of the artificial sweeteners currently approved for use in the United States and Canada.

Saccharin

Saccharin is more commonly known by the brand name Sweet'N Low. It is 300 times sweeter than sucrose. Saccharin is the oldest of the artificial sweeteners, but its long life has not been without controversy. A white crystalline derivative of a coal-tar compound, it was discovered in 1879 when a chemist forgot to wash his hands before dinner, and his food then tasted remarkably sweet. By the early 1880s, saccharin was being marketed as a nonnutritive sweetener, and it was used not only to sweeten foods and drinks, but also as an all-purpose panacea (Hicks, 2010). The controversy surrounding saccharin began around the end of the 19th century, as Americans began demanding more government oversight of the food industry. Despite several attempts to ban the substance (on the grounds that it was a coal-tar derivative and therefore must not be safe for humans), its popularity persisted—helped in part by the strong backing of President Theodore Roosevelt, who took a saccharin pill daily (Hicks, 2010). During WWI and WWII, it received widespread use as an inexpensive sugar substitute.

In 1958, a mixture of saccharin and another artificial sweetener, cyclamate, was introduced as the pink-packeted sugar replacer, Sweet'N Low, which became a diner staple. The diet soft drink, "Tab"—introduced by Coca-Cola in 1963—propelled saccharin's popularity even further. In 1968, however, researchers found a connection between cyclamate and bladder cancer in rats. A study conducted in 1970 found the same connection between saccharin and bladder cancer in rats. As a result of these findings, cyclamate was banned, and saccharin was required to display the following warning label: "Use of this product may be hazardous to your health. This product contains saccharin, which has been determined to cause cancer in laboratory animals" (National Cancer Institute, 2009). Research continued, both on the effects of saccharin and in the development of artificial sweeteners that could replace it. (Aspartame hit the markets in the early 1980s, followed shortly thereafter by acesulfame potassium, both with research supporting their safety.) Ultimately, researchers concluded that the mechanism causing bladder cancer in rats did not exist in humans, and saccharin's reputation was largely exonerated. In 2000, the warning labels were removed from products in the United States, and saccharin was taken off the U.S. National Toxicology Program's list of substances reasonably anticipated to cause cancer in humans. Canada is considering relisting saccharin as a safe food additive (Health Canada, 2010). Neither country has reapproved cyclamate as a food additive, although it is available for direct purchase in Canada and has a warning label.

Aspartame

Aspartame is known more commonly by the names "Nutrasweet" and "Equal." It consists of a combination of two amino acids, phenylalanine and aspartic acid.

Because aspartame is a protein, the body can digest and absorb it, so it does provide calories. It is 200 times sweeter than sugar and is used in miniscule amounts to sweeten foods, however, so the calories contributed are few. It was approved by the FDA for use in some foods in 1981 and for use in beverages in 1983 (Insel et al., 2013). Products with aspartame must carry a warning label for people that have phenylketonuria, which is a rare genetic disorder that prevents the breakdown of the phenylalanine. Some people report adverse reactions to aspartame, including dizziness, headaches, nausea, and seizures, but research has not confirmed any connection.

Acesulfame K (Acesulfame Potassium)

Acesulfame K is commercially available under the name "Sunette" and is 200 times sweeter than sugar. It has been approved in the United States since 1988 and in Canada since 1994. The human body cannot digest it, therefore it provides no energy. It is heat stable and can be used in baked goods, but it has a strong aftertaste, so it is frequently used in combination with other artificial sweeteners.

Sucralose

Sucralose, also known by the brand name "Splenda," has been approved for use in Canada since 1992 and in the United States since 1998. Sucralose is manufactured by replacing three hydrogen-oxygen groups on the sugar molecule with three chlorine atoms; the process creates a nonnutritive compound that is 600 times sweeter than sugar. It is heat stable, so it creates products with long shelf lives, and it can be used in home cooking.

Neotame

Neotame is derived from the same amino acids used to make aspartame, but it is significantly sweeter—7,000 to 13,000 times sweeter than sugar. Neotame is safe for individuals who have phenylketonuria. Neotame is approved for use in the United States and Canada; but as one of the newer sweeteners, it is not yet associated with any brand names and is just beginning to be used in products, frequently in combination with other sweeteners.

Novel Sweeteners

The sweeteners tagatose, trehalose, and refined stevia (this excludes whole leaf and crude stevia) recently have been determined to be "generally recognized as safe" (GRAS) by the FDA. The GRAS status means that enough research on the additive has been completed for it to be used for its intended purposes without regulation. Of these three, only stevia is approved for use in Canada.

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Research Issues

If you type the sentence "Are artificial sweeteners safe?" into an online search engine, you will find thousands of websites, research studies, and opinion pieces arguing for or against the use of these synthetic sweeteners. Some claims are backed by scientific evidence, and others are backed by hearsay and misinformation. Clearly, the debate over the use and safety of artificial sweeteners is complex.

See Also: Alternative sweeteners (sugar substitutes); Food additives; Stevia; Sugar alcohols.

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Astaxanthin

Astaxanthin is a powerful antioxidant in the carotenoid family. Astaxanthin is a reddish pigment, and contributes to the coloration found in some plants, algae, and bacteria. In the presence of high levels of ultraviolet (UV) light, the algae *Haematococcus pluvialis* produces large amounts of astaxanthin, possibly for protection from UV damage. Astaxanthin also is incorporated into the flesh of animals that consume foods with this pigment, including salmon, trout, lobster, and krill. Astaxanthin is responsible for the pink feathers of flamingos. At birth, flamingoes are white; their feathers become pink as the flamingoes consume red algae and shrimp. Although research suggests that astaxanthin has the potential to confer several health benefits in humans, at present the research is preliminary.

Charles Weedon, an organic chemistry professor, discovered astaxanthin in 1970 when using magnetic resonance spectroscopy to study carotenoid pigments. In 1987, the U.S. Food and Drug Administration approved the use of astaxanthin as an additive in the agriculture and aquaculture industries to enhance the color of farmed meat and fish, and in 1999 it became an approved dietary

supplement. One serving of Atlantic salmon has approximately 1 mg of astaxanthin per serving, and Pacific salmon contains 4 mg to 5 mg.

Astaxanthin acts as an antioxidant, and appears to reduce the oxidation of fats in vivo. Oxidation of low-density lipoprotein cholesterol in the bloodstream appears to accelerate the process of artery disease, therefore researchers are investigating whether astaxanthin might slow this oxidative process. Researchers also hope that astaxanthin's antioxidant effects might reduce levels of inflammation. Preliminary investigations in vitro and in animal models suggest this might be the case. A few studies in humans have found that supplementation with astaxanthin did reduce markers of oxidative stress (Fassett & Coombs, 2012). Researchers also are studying astaxanthin's potentional to protect the eye from UV damage, possibly preventing the formation of cataracts and slowing macular degeneration. There currently is no evidence that these effects occur in humans, however. Astaxanthin has been found to reduce hypertension in rats genetically altered to develop hypertension, but not in normotensive rats.

Astaxanthin supplements appear to be relatively safe, although long-term data are not available. Astaxanthin is not recommended for women who are pregnant or nursing. Therapeutic dosages used in research generally have ranged between 4mg and 10 mg daily.

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See Also: Antioxidants.

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The Atkins Diet

The Atkins Diet, named after cardiologist Dr. Robert C. Atkins, is a nutrition-based weight-loss regime that focuses on carbohydrate restriction as a means to increase the use of fat for energy, and decrease stored body fat. The premise of the diet is that weight gain is produced by excess carbohydrate intake which causes a rise in insulin. The increase in insulin stimulates the uptake and storage of glucose and other nutrients—primarily as triglycerides—contributing to an increase in body fat levels. The Atkins Diet involves eliminating or drastically reducing carbohydrate consumption to reduce insulin levels and to drive the body to burn fat as fuel, producing substantial weight loss.

Many people who adhere to the diet lose weight and often experience associated health benefits, including improved blood sugar regulation and blood lipid levels, reduced blood pressure, and fewer markers of systemic inflammation. Critics argue that the diet is difficult to follow and is not associated with long-term weight-loss maintenance. Some people on the diet experience an increase in blood lipid levels. The diet's low fiber content increases risk for constipation. The high protein intake also might increase the risk of kidney stones and of bone mineral loss.



Dr. Robert C. Atkins was the creator of the Atkins diet and best-selling author of *Dr. Atkins' New Diet Revolution* (2002). Although nutritionists originally regarded the Atkins diet as too high in fat, newer research suggests the diet might not be as harmful as once believed, at least over a short period of time. (Time & Life Pictures/Getty Images)

The dietary regime is organized into four phases, Induction (Kick-Start), Ongoing Weight Loss (Balancing), Pre-Maintenance (Fine-Tuning), and Lifetime Maintenance. The dieter determines the start point and duration of the phases; however, the plan offers suggestions based on degree of obesity, target weight, and individual dietary restrictions. During the Induction phase carbohydrate intake is limited to 20 g per day, 12 g to 15 g of which are expected to come from non-starchy vegetables. This value is increased throughout the phases to an individualized amount that is as much as 90 g to 120 g per day. (As a point of reference, the U.S. Dietary Reference Intake is at least 130 g of carbohydrates per day.) The structured diet, listing only the allowed foods for each phase, is often referenced as the Atkins Nutritional Approach (ANA). Exercise is suggested but not required, increased water intake is encouraged to offset the diuretic effect of the diet, and vitamin supplementation is encouraged to replace lost nutrients.

Although Robert C. Atkins is credited with the popularity of carbohydrate-restrictive meal plans, he did not invent low-carbohydrate diets. This credit is attributed to Dr. Alfred W. Pennington, whose extensive research on the impact of animal protein consumption on weight loss was published in the early 1950s. After adopting Pennington's diet for himself, cardiologist Atkins became a medical consultant helping patients reach an ideal weight with his low-carbohydrate diet plan.

Gaining popularity, Atkins was featured on "The Tonight Show" and various magazines before publishing *Dr. Atkins' Diet Revolution* in 1972 (Martin, 2003). After its initial period of popularity, the cardiologist's diet plan became less popular during the 1990s, with the widespread promotion of the health benefits associated with low-fat diets. The diet regained popularity in the early 2000s along with similar low-carbohydrate and high-protein diets including The Zone and The South Beach Diet. In addition to several subsequent diet books, Atkins International markets frozen meals, prepackaged snacks, and shakes throughout the United States. Atkins International also maintains a mobile app, free progress trackers, and an online forum community.

People who adhere to the Atkins Diet generally lose weight, and the diet has been found to be at least as effective as other weight-loss diets in the short term (Shai et al., 2008). People who lose weight on the Atkins Diet often experience health benefits. Unanticipated due to the liberal consumption high-fat meats and dairy thus elevating dietary saturated fat, several studies of the diet have found some reduced cardiovascular risk factors including reduced serum triglycerides, improved HDL cholesterol, and reduced levels of systemic inflammation (Gogebaken et al., 2011). Similar improvements, however, are experienced by people who lose weight by following other types of diets.

During the first phase of the Atkins Diet, dieters achieve a state of ketosis. Ketosis refers to a metabolic state in which the body is producing higher than normal levels of compounds called ketones. The body increases its manufacture of ketones when its supply of carbohydrate is low. Many organs of the body can manufacture energy from ketones. Interestingly, a ketogenic diet has been shown to be very effective in reducing the frequency of seizures in people with epilepsy; and a modified Atkins Diet now is promoted as an accessible way to help people with epilepsy to achieve ketosis (Kossoff, Cervenka, Henry, Haney, & Turner, 2013). The Atkins Diet claims to promote weight loss without hunger. Followers of the diet usually do experience low levels of hunger because of their high protein intake and because they enter a state of ketosis.

Critics of the diet argue that the rapid weight loss often achieved during the induction phase is a result of water loss, or diuresis, and not an increase in adipose metabolism. Carbohydrate-restrictive diets trigger the mobilization of glycogen, depleting the body's storage along with the 2 g to 3 g of water bound to each gram of glycogen. Substantial weight loss in the subsequent phases has been attributed to decreased caloric intake due to limited food options, circulating ketones acting as an appetite suppressant, and a satiation effect of increased protein consumption.

On the grounds that most studies have evaluated the diet for a short period and have used a small sample size, medical professionals fairly conclusively agree that the long-term safety and efficacy of the Atkins Diet remain in question. Reducing dietary glycemic load through avoidance of processed carbohydrates has become an established recommendation for reducing risk for obesity, heart disease, type 2 diabetes, and hypertension; and the Atkins Diet does promote this practice. Some researchers question the wisdom of a high protein intake, however,

which increases stress on the kidneys and also might accelerate bone mineral loss (Huggett et al., 2012).

An interesting meta-analysis that examined data from a number of studies on low-carbohydrate diets found that low-carbohydrate diets actually were associated with increased rates of premature death from all causes except from cardiovascular disease (Noto, Goto, Tsujimoto, & Noda, 2013). The meta-analysis included only eight studies, therefore these results are considered preliminary. The researchers have speculated that the low intake of fruits, vegetables, and fiber could explain the greater mortality rates.

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Research Issues

A great deal of research supports the notion that a high intake of fruits and vegetables is associated with positive health outcomes. Using the Atkins diet website (http://www.atkins.com/Program/Overview.aspx), try to construct a list of five to nine fruit and vegetable servings. How many grams of carbohydrates are contained in the foods listed? Imagine trying to consume only 20 grams of carbohydrate per day. Can you find five servings of vegetables that would provide 20 or fewer grams of carbohydrate?

See Also: Ketosis and ketogenic diets; Obesity, treatment.

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Attention-Deficit Hyperactivity Disorder and Nutrition

Attention-Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder characterized by inattention, distractibility, hyperactivity, and impulsivity. The *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) is the handbook used to diagnose mental disorders, and it classifies ADHD with several diagnostic criteria. These criteria include at least six symptoms of inattention and/or hyperactivity and impulsivity, lasting for a period of at least six months; onset of the majority of symptoms before age 12; symptoms present themselves in at least two different settings (i.e., home, work, school, social situations); symptoms have a direct impact on social, academic, or occupational functioning or development; and symptoms cannot be better explained by another mental disorder. Individuals with ADHD can present as predominantly inattentive, predominantly hyperactive and impulsive, or a combination of both.

Attention-Deficit Hyperactivity Disorder often is treated with various forms of psychotherapy and psychiatric medications. Stimulants such as Ritalin, Concerta, Focalin, and Adderall regularly are prescribed to adults and children age six years and older. Although these drugs have proven to be effective in those with ADHD, they also can result in serious side effects such as heart palpitations, decreased appetite and weight loss, tics or disordered movements, anxiety, and insomnia. Due to the controversy concerning the over-prescription of stimulants, recent research has explored the relationship between nutrition and ADHD to determine whether dietary factors might help prevent or treat ADHD.

Symptoms of ADHD

Inattention

- Difficulty staying on task
- Easily distracted
- Frequent careless errors
- Difficulty paying attention
- Difficulty organizing activities (i.e., time management, meeting deadlines)
- Frequently loses or misplaces possessions
- Does not seem to listen during conversation
- Difficulty following instructions

Hyperactivity-Impulsivity

- Difficulty remaining seated
- Inability to sit still
- Difficulty waiting one's turn (in activities and/or conversations)

- Blurting out answers before questions have been completed
- Excessive talking
- Difficulty adapting to new situations

Prevalence

- Affects an estimated 11% of children ages 4 to 17 in the United States (CDC, 2013).
- Although most individuals are diagnosed during childhood, ADHD can be diagnosed at any age. Approximately 4.1% of adults ages 18 to 44 in the United States are diagnosed each year (ADHD, 2008).
- The rate of ADHD diagnoses in boys is double the rate for girls (CDC, 2013).
- Girls are more likely to be diagnosed with predominantly inattentive type, and boys are more likely to have a combined-type diagnosis.
- Diagnoses in the United States increased from 7.8% in 2003 to 11% in 2011 (CDC, 2013).

Nutrition and ADHD

Overall, there are mixed conclusions regarding nutrition and ADHD. Some experts claim that artificial food colorings and preservatives are to blame, others believe that symptoms could be due to nutritional deficiencies. Still other experts think that hyperactivity and attention issues can be avoided by eating a healthy, balanced diet. One recent study compared ADHD symptoms in individuals who followed a typical "Western diet" (i.e., processed meats, high-fat dairy products, soft drinks) versus those who adhered to a healthier dietary pattern (i.e., whole grains, fruit, vegetables, legumes, fish) (Howard et al., 2011). ADHD symptoms were markedly diminished in those people adhering to a healthy diet.

Many critics deem ADHD nutritional studies to be unreliable. Dr. Feingold's research (discussed below) has been widely criticized for its lack of double-blind studies and control groups, invalid diagnoses, subjective responses, and small sample sizes. Many studies rely on observational data from teachers and parents, which can drastically impact results. Further, most scientists looking at food colorings fail to study additives individually, making it difficult to identify the true cause of any correlational effect. Finally, ADHD diets could result in several nutritional deficiencies. This can be particularly dangerous for children and individuals with outstanding medical issues.

Nevertheless, many caregivers try dietary manipulations to determine whether such changes might be helpful for children with ADHD. There appear to be several dietary factors that could affect ADHD. Artificial food colorings as well as vitamin and mineral deficiencies might contribute to the duration and intensity of ADHD symptoms. Dietary regimens have been designed specifically for the treatment of ADHD. Many studies have shown a positive relationship between diet and ADHD.

Table 1. Artificial Food Colors

Artificial Food Color	Common Name	Foods
Blue No. 1	Brilliant blue	Baked goods, ice cream, cereals, candy, beverages
Blue No. 2	Indigotine	Candy, beverages
Green No. 3	Fast green	Candy, gelatin, beverages
Red No. 3	Erythrosine	Baked goods, candy, cereals, popsicles
Red No. 40	Allura red	Beverages, candy, pastries, sausages, cereals, gelatin
Yellow No. 5	Tartrazine	Candy, chips, ice cream, pickles, cereals, baked goods
Yellow No. 6	Sunset yellow	Jam, candy, sausages, baked goods, beverages, gelatin
Citrus Red No. 2	Citrus red	Added to skins of some Florida oranges
Orange B		Sausage casings

Source: Created from data in Stevens et al. (2011).

Artificial Food Colorings

There are nine synthetic food dyes currently approved by the U.S. Food and Drug Administration.

Food colorings are added to foods to reduce color loss due to changes in light, air, or temperature; to correct natural variations and changes in color; to make food more appealing; and to enhance natural colors. Many medications (both prescription and over-the-counter drugs) also contain artificial food colorings. Although both natural and artificial dyes can be used, the food industry usually relies on synthetic dyes because they are more efficient, stable, and cost effective. Some experts claim as much as 8% of children with ADHD could have symptoms attributed to artificial food colors, and that 30% might improve with dietary changes (Nigg, Lewis, Edinger, & Falk, 2012). Authors also paired food colorings with the preservative sodium benzoate, however, thus complicating their conclusions. Some research suggests correlation between tartrazine and behavioral problems in children, including increased irritability, restlessness, impulsivity, and sleep disturbances. The possible link between food colorings and ADHD has served as a reference for various ADHD diets.

Diets

In 1973, Dr. Benjamin Feingold suggested a link between hypersensitivity or intolerance to certain foods and hyperactivity in children. He proposed a diet free of natural salicylates and artificial flavors that he called the "Kaiser Permanente Diet," or "K-P Diet." By 1977, Dr. Feingold claimed that 60% to 70% of his pediatric patients had improved. Critics, however, argued that his work was premature and lacked structure. Nevertheless, scientists have used Feingold's work as a basis for their own research studies, as well as for diets that followed.

Table 2. Special Diets That Have Been Tried for ADHD

Diet	How It Works	Avoid
Feingold's Kaiser-Permanente or K-P Diet	Elimination of artificial food colorings, foods containing natural salicylates, and certain preservatives.	All artificial colors and flavors; preservatives BHA (butylated hydroxyanisole), BHT (butylated hydroxytoluene), TBHQ (tertiary butylhydroquinone), and sodium benzoate; and foods with natural salicylates (almonds, apples, apricots, berries, currants, grapes, nectarines, oranges, peaches, plums, tangerines, cucumbers, green peppers, tomatoes, cloves, chili powder, coffee, and tea).
Elimination diet	Elimination of foods for a maximum of 2 weeks, and gradually reintroducing them until the potential triggers are found.	All artificial colors, flavors, and preservatives; chocolate; wheat, rye, barley; eggs; processed meats; citrus fruits; legumes; peanuts
Ketogenic diet	High in fat, low in carbohydrates.	Grains, high-carbohydrate fruits and vegetables, processed foods.
Low-sugar diet	A decrease of glucose in the brain appears to slow EEG rhythms. Many parents believe this to have an effect on their child's hyperactive behavior. Further research is needed, however, to confirm the correlation between sugar and symptoms of ADHD.	Refined carbohydrates, such as sugar, honey, flour, maple syrup, corn syrup, and fruit juice.

Nutrients and Dietary Supplements

Several nutrients have been studied in relation to the prevention and treatment of ADHD. Those best studied include the following.

- Polyunsaturated Fatty Acids (PUFAs)—Omega-3 and omega-6 fatty acids are known to play an important role in cognitive and behavioral functioning. One study found a significant decrease in ADHD symptoms in children assigned to omega-3 and omega-6 supplementation versus placebo (Richardson & Montgomery, 2005). Further research has shown significant variability in results, however, depending on the type of fatty acid used, method of administration, dosage, duration of study, and response measures.
- Zinc—Low serum zinc has been reported in children with ADHD. Zinc promotes dopamine metabolism and functioning involved in ADHD. Serum supplementation has been correlated with increased levels of attention, as well as an increased response to d-amphetamine (Millichap & Yee, 2012).
- Iron—Iron deficiency has been associated with cognitive and learning disorders. Iron helps to regulate the dopaminergic system. Although research is

limited, lower levels of iron have been correlated with more severe ADHD symptoms and cognitive deficits. One study found supplementation to be effective in treating children with ADHD, especially those with the inattentive subtype (Soto-Insuga et al., 2013).

- Magnesium—Low levels of magnesium have been found in children with ADHD. Magnesium is important for several nerve and brain functions, and has been associated with nervous and muscular excitability. Deficiencies in magnesium might be correlated with increased hyperactivity, inattention, insomnia, and distractibility.

Although many studies suggest a nutritional correlation with ADHD, results remain inconclusive. Larger sample sizes, greater age ranges, and long-term follow-up studies are needed to test the validity of these claims.

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See Also: "Brain foods"; Depression and nutrition; Ketosis and ketogenic diets; Marine omega-3 fatty acids.

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Autism and Nutrition

Autism is a neurodevelopmental disorder affecting 1 in 110 children in the United States. This disorder is more common in males and is characterized by impaired social interactions, poor communication skills, gastrointestinal problems, and repetitive behaviors. Children having autism present symptoms by three years of age. Scientists do not yet know what causes autism, but they have proposed some potential risk factors, including genetic vulnerability, reduced gut microbiota, infection, altered immune response, and nutrition. Autistic children are known to have poor diet quality due to their unusual eating patterns and behaviors (Privett, 2013). Data from a comprehensive meta-analysis indicate that children with autism have significantly more feeding problems than do their peers (Sharp et al., 2013). Because many autistic children are found to have food aversions and sensitivities along with behavioral issues, parents and caregivers sometimes turn to dietary interventions hoping to reduce the children's symptoms.

Researchers at Marcus Autism Center at Emory University School of Medicine found that children with autism have inadequate nutrition more often than those unaffected (Autism Speaks, 2013). Those affected by autism might not obtain adequate intake of all nutrients, which theoretically could lead to neurochemical imbalances that in turn could influence behavior. Chronic eating problems have been associated with social difficulties and reduced academic performance. Nutrition is implicated as a potential area for the prevention and treatment of autism. Areas of study have included maternal nutrition during key developmental stages, the impact of dietary supplements on children with autism, and creating special diets for children with autism.

Maternal Nutrition

It is suspected that maternal nutrition might be involved in the onset of autism. Past studies have focused on prenatal vitamins high in folic acid and other B vitamins in relation to autism risk. One research group found that women who took prenatal vitamins three months before conception and in the first month of pregnancy had a 40% lower risk of their child developing autism (Schmidt et al., 2012). Additionally, the children of mothers who took folic acid supplements before or during their first trimester were found to have fewer behavioral problems at 18 months of age, and have social competence and reduced hyperactivity when older than 18 months. This could be because folic acid and other vitamins are crucial for neurodevelopment.

Polyunsaturated fatty acids (PUFAs) have been studied in relationship to autism because they play a critical role in normal brain development. Several studies have shown that arachidonic acid (AA), eicosapentaenoic acid (EPA), and docosahexanoic acid (DHA) are needed for brain growth and memory formation and consolidation. This implies that a maternal PUFA deficiency could contribute to the characteristic behavioral symptoms of children with autism. Polyunsaturated fatty acids are recognized to alter levels of brain-derived neurotropic factors

(BDNFs) that regulate neurogenesis and affect learning and memory. Polyunsaturated fatty acids are precursors to anti-inflammatory lipids that are required for protecting neurons from oxidative stress, which is why some researchers suggest that maternal supplements should include adequate levels of PUFAs. Studies have revealed that children of mothers who had a high intake of PUFAs—such as omega-3 fatty acids—before and during pregnancy had a lesser risk of developing autism as compared to children of mothers with the lowest PUFA intakes (Lyall, Schmidt, & Hertz-Picciotto, 2014).

Vitamin D deficiency has been proposed as a risk factor for autism because vitamin D is important in neurodevelopmental processes, such as neuronal differentiation and metabolism of neurotropic factors (Lyall, Schmidt, & Hertz-Picciotto, 2014). Maternal vitamin D deficiency has been associated with impaired language development in offspring between the ages of 5 years old and 10 years old. Autism has been linked with a mechanism involving both serotonin and vitamin D. Vitamin D regulates the production of the neurotransmitter serotonin in the brain. Maternal vitamin D deficiency results in the overproduction of serotonin. The overproduction of serotonin hinders the metabolic pathway in which vitamin D stimulates the production of a family of T cells that prevent maternal autoantibodies from attacking the fetal brain and causing severe damage (Patrick & Ames, 2014). Supplementation of vitamin D is affordable and could reduce a child's risk of developing autism.

Dietary Supplements

Vitamins (especially A, B6/B12, C, and D) and minerals (especially magnesium, calcium, and zinc) have been suggested to improve symptoms associated with autism. Several studies have found reduced intake of several vitamins and minerals in children with autism as compared to neurotypical children of similar age. In an Autism Research Institute (ARI) survey parents reported that putting their children on supplements improved their children's behaviors. Improvements were noted for vitamin B12 (72% better), vitamin B6 (51% better), and zinc (54% better) (Adams, 2013). Analyzing vitamin D serum levels showed significantly lower measurements for children with autism than for those unaffected (Meguid, Hashish, Anwar, & Sidhom, 2010).

In a large double-blind study, a balanced multivitamin/mineral supplement regimen led to significant improvements for children with autism in their expressive language, tantrumming, hyperactivity, and other behavioral symptoms (Adams et al., 2011). Additionally, there were marked improvements in the children's metabolic processes, which included methylation, sulfation, and oxidative stress. Researchers have hypothesized that a portion of autistic children have inefficient vitamin B metabolism and reduced methylation capacity (Schmidt et al., 2012). Therefore, micronutrient supplementation could help boost deficient metabolic processes in individuals with autism. Interestingly, pharmaceutical treatments were compared to micronutrient supplementation, and it was found that supplements were either comparable to or more effective than pharmaceutical treatments

in terms of children with autism positively increasing their scores on clinical scales, such as the Childhood Autism Rating Scale and Childhood Psychiatric Rating Scale (Mehl-Madrona, Leung, Kennedy, Paul, & Kaplan 2010).

In terms of fish and fish oil supplements, there are both studies supporting and negating that they reduce behavioral symptoms. An open-label study of 30 autistic children, for instance, noted that fish oil supplements resulted in improved levels of fatty acids and two-thirds of the cohort had improved behavioral symptoms (Meguid, Atta, Gouda, & Khalil, 2008). Other studies have found no statistical significance of fish oil supplements for reducing hyperactivity and other behavioral problems (Amminger, Berger, Schäfer, Klier, Friedrich, & Feucht, 2006).

Special Diets

The gluten-free, casein-free (GFCF) diet is widely implemented by parents of children with autism (Hurwitz, 2013). Despite its popularity, there is limited evidence supporting drastic change in autistic children on the GFCF diet. The GFCF diet is an elimination diet where the person does not eat anything containing gluten, such as wheat products, or casein, a protein found in dairy products such as milk and yogurt. The diet has the potential to improve an autistic child's functioning and gastrointestinal symptoms, which is why parents try this nutrition regimen. One study noted that 27% of parents have their affected child on a special diet—such as the GFCF diet—at a given time but, overall, half of the cohort had tried a special diet for their child at one time or another (Hurwitz, 2013). Studies claim that the GFCF diet is accessible and can be implemented alongside pharmacological treatment. This special diet is driven by the Opioid-Excess Theory of autism that describes how gluten and casein are not properly digested in the gastrointestinal tract by autistic children. One study found that, in their cohort, 37% of children with autism have abnormal intestinal permeability compared to controls (Kral, Eriksen, Souders, & Pinto-Martin, 2013). Once absorbed, it has been observed that gluten and casein proteins transform into opioid peptides that leak into the bloodstream and cross the brain's blood-brain barrier; this has become known as "the leaky gut hypothesis" (Hurwitz, 2013). In the brain, these opioid peptides behave as real opioids by attaching to the opioid neuroreceptors. The theory describes how opioid receptor binding negatively impacts neurotransmission causing maladaptive behaviors and increasing symptoms associated with autism.

The ideology of the GFCF diet is to remove all gluten and casein from the child's diet to stop the progression of excess opioids in the brain. Studies have reported mixed effectiveness of the GFCF diet in terms of behavioral and developmental effects. In three of the studies of a larger meta-analysis, researchers found no support for the diet as there were no significant improvements in the children's language, attention, and activity level (Hurwitz, 2013). An ARI survey, however, found that 69% of parents rated their children as having improved on the GFCF diet as compared to 28% reporting no change (Adams, 2013). Further research has been conducted, reporting 81% of children with autism improving significantly on the GFCF diet by the third month; large improvements were made in eye contact,

mutism or inability to speak, learning skills, hyperactivity, and panic attacks (Cade et al., 2000). Many health care providers recommend that parents try the GFCF diet because trying it is the only way to determine whether the diet will help the particular individual. Other special diets have been proposed for children with autism, but the GFCF diet has by far the most support of parents and the most studies conducted by researchers.

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See Also: Marine omega-3 fatty acids.

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Bariatric Surgery

Bariatric surgery refers to surgical procedures performed for the purpose of reducing body weight in people who are obese. Obesity is a costly health problem associated with several serious chronic health conditions. Many obesity experts think that bariatric surgery is one of the best methods to achieve significant and long-term weight loss and to reduce the negative impact of obesity-related health problems such as type 2 diabetes, hypertension, arthritis, and sleep apnea. Weight-loss surgeries alter the digestive system to facilitate weight loss by physically limiting how much a person can eat, reducing the absorption of calories, or both. Bariatric surgery is suggested for patients in urgent need of decreasing body fat levels and combating physiological problems associated with obesity. It is recommended for those who have exhausted other traditional avenues for weight loss, such as proper diet and exercise. All bariatric surgeries, however, require patients to make permanent changes in eating behaviors to reduce risk of complications, reduce the need for repeat surgeries, and to maintain weight loss.

The National Institutes of Health suggest a list of criteria to evaluate whether a person is a proper candidate for bariatric surgery (National Institutes of Health, 2014). In general, people most likely to benefit from these surgeries and for whom the benefits outweigh the risks include men who are more than 100 pounds overweight and women who are more than 80 pounds overweight, or people who have a BMI exceeding 40. The majority of bariatric surgery patients are severely obese, with average BMI levels exceeding 45 (Padwal et al., 2011). Bariatric surgery also sometimes is recommended for people whose BMI is 30 to 35 or greater and who have obesity-related health problems that will be alleviated by weight loss. It is important for all potential patients to be prepared to commit to positive lifestyle changes following surgery, as the procedure is only the initial step to achieving good health.

Types of Major Bariatric Surgeries

Over time, a variety of bariatric surgeries have been developed. In 1952, Dr. Victor Henrikson of Gothenburg, Sweden, was credited with performing an intestinal resection specifically for the management of obesity. In 1954, A. J. Kremen published the first case report of a jejunoileal bypass (JIB) procedure for



Lap-band placed on a replica stomach. People with the lap-band initially feel full with small volumes of food, and thus reduce their food intake. (iStockPhoto.com)

obesity. This procedure linked the upper and lower parts of the small intestine, thus bypassing the portion of the small intestine between these two points. Despite the effectiveness of JIB, it often was associated with gas-bloat syndrome, electrolyte imbalance, and liver damage. With the introduction of gastric bypass in 1967 as a safer more effective alternative, JIB fell out of favor by the early 1980s.

Current bariatric surgical procedures are classified as either restrictive, malabsorptive, or both. Restrictive procedures leave less room for food intake by physically restricting the stomach size to slow down digestion. The stomach normally holds three to four pints (about one liter), shrinking to just a few ounces post surgery. Food is digested and absorbed normally, however the change in stomach size makes the patient quickly feel full, so the hope is that less food is eaten. Malabsorptive procedures change the way food is digested by rerouting food through the digestive tract, making it harder for the body to absorb calories. Malabsorptive procedures are more invasive. Restrictive procedures generally have fewer complications and lower mortality rates, and the malabsorption procedures lead to greater weight loss. The physician's surgical preference, the patient's health, local hospital circumstances, and new technical developments all influence the choice of which bariatric procedure is best for each individual. The most common procedures are listed below.

- Adjustable gastric banding: Adjustable gastric banding (AGB) restricts food consumption by limiting how much food the stomach can hold. It is the second most common weight loss surgery, following gastric bypass. Adjustable gastric banding—sometimes referred to as the Lap-Band system—involves placing an inflatable silicone ring around the upper portion of the stomach to restrict the amount of food a person can consume. A tube leads from the band to a small port under the patient's skin near the stomach. The physician can manipulate the volume of water injected or withdrawn from the band, which is how the band can be expanded or emptied, similar to inflating or deflating a balloon. When the band is inflated it creates a small pouch where food collects after being swallowed. From within the pouch, food can drain slowly into the rest of the stomach. Gastric banding is considered by many to be the safest and least invasive bariatric surgery.
- Sleeve gastrectomy: Sleeve gastrectomy—also known as vertical sleeve gastrectomy (VSG) or stomach stapling—is another type of restrictive surgery. This type of surgery was introduced in the United States in 2007, and still is considered to be an experimental weight-loss surgery by most insurance companies, so it is much less common than AGB. The procedure surgically reshapes the stomach, leaving much less space for food. Sleeve gastrectomies remove the portion of the stomach responsible for manufacturing ghrelin, the hormone that stimulates hunger, although it is unclear how long this effect lasts. This could help eliminate the physical feeling of hunger in patients. The part of the digestive track where the stomach meets the intestines is left untouched, allowing the stomach to function and empty normally. This surgery sometimes is used in high-risk patients as the first stage of bypass surgery, especially biliopancreatic diversion surgery (described below) for high-risk patients. Many patients lose weight with this surgery alone, however, and avoid further procedures. In other cases, a second surgery occurs within 6 to 18 months after the initial surgery.
- Intragastric balloon surgery: This restrictive procedure inserts an intragastric balloon into the stomach. Once inside the stomach the balloon is inflated. It can remain in the stomach for up to six months. The intragastric balloon has not yet been approved by the U.S. FDA but has been approved in Canada and many other countries.
- Roux-en-Y gastric bypass (RYGB): This bypass surgery is the most common of all bariatric surgeries due to its effectiveness for long-term weight loss. The Roux-en-Y gastric bypass is both a restrictive and a malabsorptive procedure, in which a small stomach is formed, as is done in other restrictive procedures. Additionally, the stomach and small intestine are surgically reconfigured so that food literally bypasses the section of the small intestine that absorbs the majority of calories and nutrients, entering directly into the lower segment of the small intestine. Due to limited nutrient absorption, nutritional supplements are necessary. This procedure is not reversible.
- Biliopancreatic diversion: The biliopancreatic diversion (BPD) procedure also combines restrictive and malabsorptive techniques. Its effect is similar to

Roux-en-Y, but the surgery keeps some stomach function intact after the lower two-thirds of the stomach is removed and attached to the distal segment of the small intestine (the ilium). The BPD procedure generally only is performed on severely obese patients. The BPD usually includes a link from the detached upper portion of the duodenum into the ilium, called the duodenal switch.

When first developed, bariatric surgeries involved open surgical incisions for the surgeon to perform the operation. Currently, about 90% of procedures are performed laparoscopically, requiring several smaller incisions. A laparoscope is a small, tubular instrument with a camera attached; it is inserted through small incisions in the abdomen. Laparoscopy procedures limit the patient's risk for the development of incisional hernias, making it a safer alternative to large-incision surgeries. Surgeons also are developing endoscopic surgical techniques for bariatric surgeries, in which surgery is performed from within the digestive system using very small tools inserted through the patient's mouth.

Eating Post-Surgery

Eating is limited for the initial weeks following weight-loss surgery to allow the stomach and digestive tissues to heal. A liquid diet is mandated for approximately two to three weeks, followed by reintegration of soft foods. Upon the re-entry of solid foods into the diet, the patient will feel full very quickly. Eating must be completed slowly so that foods are thoroughly chewed, so they can pass smoothly through the new opening. Many patients report regurgitating foods during the initial months post-operation due to a lack of room in the stomach. Dry, fibrous foods such as rice, bread, popcorn, and nuts can cause discomfort if not completely chewed.

Effectiveness

Effectiveness rates of bariatric surgeries vary widely. Data on long-term weight-loss maintenance are scarce. Short-term results show weight loss that exceeds the degree of weight loss typically experienced using medications and lifestyle measures only. For the first year following surgery, weight loss is about 30 kg to 50 kg (66 to 110 lbs). Results are higher for RYGB (about 43 kg or 95 lb) than for AGB (about 30 kg or 66 lb) (Osterweil, 2013). Especially intriguing are studies showing that the weight loss experienced with bariatric surgeries has significant health benefits. Patients experiencing significant weight loss have about a 40% lower rate of premature mortality and a 92% lower rate of mortality associated with diabetes (Osterweil, 2013). Data such as these have led to increasing health insurance coverage for bariatric surgeries.

Results vary widely from patient to patient, however. Some people might not lose a significant amount of weight, or even might gain weight post-operation. Achieving maximum results and avoiding regaining weight require permanent lifestyle changes. Regular physical activity and proper nutrition can aid in a patient's weight loss and maintenance. Health indicators are best improved through

changing health behaviors, regardless of whether weight is lost. Studies show that many individuals are unable to maintain the weight lost following surgery, thus missing out on long-term benefits.

Risks and Adverse Effects

All surgeries have accompanying risks and weight-loss surgeries are no exception. In fact, surgery becomes riskier as BMI increases. Serious risks associated with the surgeries include excessive blood loss, blood clots, infection, adverse reactions to anesthesia, and leaking of the digestive contents from the digestive system. In rare cases—less than 1 in 1,000 procedures—death can result. Problems that can develop following surgery include a variety of gastrointestinal symptoms such as nausea and vomiting, stomach pain, and gastroesophageal reflex disease. Many patients experience stretching of the esophagus or stomach pouch over time. For AGB surgery, sometimes the gastric band moves or even injures the stomach, which requires an additional surgery. Some patients develop incisional hernias, and the intestines push through the incision site. Gallstones are common with rapid weight loss. Some people experience obstruction of the stomach, small intestine, or bowel; stomach perforation; or ulcers. Patients also can experience dumping syndrome, in which food passes too quickly from the stomach into the small intestine, causing diarrhea, nausea, and weakness. According to the medical literature, AGB procedures generally have the lowest risk of adverse events, approximately 7% (Osterweil, 2013). RYGB procedures have about a 17% risk. The more complicated BPD procedure has adverse complication rates of about 38%.

Malabsorption surgeries require lifelong adherence to dietary supplements, because the malabsorption extends to nutrients as well as calories. Especially problematic are poor absorption of iron, which can lead to iron-deficiency anemia; poor absorption of calcium, which can lead to low bone mineral content and osteoporosis; and low absorption of vitamin B12 with multiple deficiency symptoms.

Approximately one quarter of bariatric surgery patients undergo plastic surgical corrections after significant weight loss has occurred (Klassen et al., 2012). Massive amounts of excess skin and remaining fat tissue can cause hygiene issues and self-esteem problems, and are corrected by plastic-surgery body "lifts." The body's natural ability to retract skin depends on the patient's age and speed of weight loss, and often is exhausted within the first few months following weight loss.

Impact on Psychological Well-Being

Psychosocial benefits of bariatric surgery are related to freedom and lifestyle flexibility following weight loss, such as increased mobility, stamina, and improved self-esteem and body image. Bariatric surgery patients often feel good about taking control of their lives and value their weight loss success. Patients experiencing psychological problems before surgery, however, still might experience these problems following surgery.

A significant proportion of patients who undergo bariatric surgery have binge-eating disorder. Binge eaters are more likely to report psychological disorders, drop out of weight-loss treatment, and regain weight following surgery. Binge eating often is a coping mechanism for stress and can induce potentially dangerous effects post-surgery. In patients, binging on sugary foods or overeating can induce sweating and nausea, involuntary vomiting, or diarrhea. Weight-loss surgery, however, also is viewed as a therapeutic intervention for limiting food consumption and eliminating binge-eating symptoms, therefore promoting psychological improvement.

Allison M. Felix

Research Issues

Should bariatric surgeries be performed on adolescents? Adolescents appear to recover at least as well as adults from the surgeries and experience similar health benefits. Some experts argue that having surgery as early in life as possible will reduce the negative health effects of obesity. Others worry that adolescents might not be psychologically prepared to cope with the demands of surgery and will have more difficulty sticking to the lifestyle changes required by the surgical procedures.

See Also: Digestion and the digestive system; Energy balance; Obesity, causes; Obesity, definition and health effects; Obesity, treatment.

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Berberine

Berberine is a bright yellow alkaloid found in the roots, stems, and bark of plants of the *Berberis* species. Some of the common members of this group are goldenseal, Chinese goldthread, Oregon grape, tree turmeric, and barberry. Berberine, traditionally used in Chinese and Ayurvedic medicines, is most widely recognized for its antimicrobial properties. This alkaloid is used clinically to treat bacterial diarrhea, ocular trachoma, and intestinal infections caused by parasites. Preliminary research suggests that berberine also could have anti-inflammatory effects as well as qualities that combat cardiovascular conditions, high cholesterol, type 2 diabetes, and tumors.

Berberine appears to influence bacterial diarrhea caused by organisms such as *Escherichia coli* and *Vibrio cholerae* in a variety of ways. Studies in both animals and humans suggest that berberine acts to decrease the amount of water and electrolytes secreted by the intestines, as well as to slow contractions of intestinal smooth muscle—prolonging the time it takes for substances to pass through. In vitro studies suggest berberine also can act directly on microbes by blocking the ability of the bacteria to bind to the epithelial cells lining the intestinal lumen, which prevents the first step of infection.

Berberine traditionally has been used for its antifungal and antiprotozoal abilities and presently is used to treat intestinal parasites. Experiments have shown that berberine can cause morphological changes; inhibition of growth, multiplication, and respiration; can interfere with nuclear DNA; and can destroy many pathogenic organisms.

Two small clinical studies conducted on humans have suggested that berberine might be effective for the treatment of an eye infection known as ocular trachoma. When berberine chloride was used in eyedrops of patients with this infection—caused by the bacteria *Chlamydia trachomatis*—berberine seemed to enhance protective mechanisms in the host cells that then were able to eliminate the infection (Berberine, 2000).

Berberine appears to have beneficial effects on the cardiovascular system and reduces symptoms of the metabolic syndrome. Berberine sometimes is used in the treatment of heart failure. It seems to prevent harmful arrhythmias by encouraging cardiac contractions and reducing blood pressure. Studies also have shown that this alkaloid can act as a vasodilator. A recent meta-analysis of clinical trials in humans indicates that berberine lowers blood level of total cholesterol and LDL cholesterol and raises HDL cholesterol levels (Dong, Zhao, Zhao, & Lu, 2013). Berberine might help regulate glucose and lipid metabolism. A study in patients with type 2 diabetes mellitus comparing berberine to the diabetes drug metformin over a three-month period found that hemoglobin A_{1c}, fasting blood glucose levels, plasma triglycerides, and insulin resistance all were decreased in patients taking berberine. The results were comparable to the effects of the diabetes drug metformin (Yin, Huili, & Jianping, 2008).

Some research suggests berberine someday could be useful in the prevention or treatment of some cancers. In vitro experiments have demonstrated that

Berberine can inhibit the transcription factor activator protein 1 (AP-1), which normally functions to affect proliferation, differentiation, and programmed cell death. Berberine also might be involved in signal cascades that concern inflammation and the formation of cancer. The alkaloid has also been found to inhibit DNA synthesis in lymphocytes, leading to its anti-inflammatory effects. Berberine is part of a third anti-inflammatory mechanism that inhibits key molecules of the inflammatory process in response to an injury (Singh, Duggal, Kaur, & Singh, 2010). Berberine has been shown to inhibit cyclooxygenase-2 (COX-2) transcription and N-acetyltransferase (NAT) activity in colon and bladder cancers in vitro, giving it anti-tumor qualities. Preliminary studies also suggest that berberine could be helpful for preventing osteoporosis and dementia.

For most clinical uses, 200 mg is taken by mouth two to four times a day. Increased intake can cause GI-tract irritation, low blood pressure, heart damage, and other symptoms. It should not be taken by women who are pregnant because it can cause uterine contractions. Berberine also can cause brain damage in infants, and therefore should not be used by infants or women who are breast-feeding.

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See Also: Herbs and herbal medicine.

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Beta-Carotene

Beta-carotene is a member of the carotenoid family, which includes naturally occurring fat-soluble compounds responsible for the red, orange, and yellow pigments found in fruits, vegetables, and some whole grains. Beta-carotene can be found naturally or produced synthetically and is known for its antioxidant

properties. It is not itself an essential nutrient but is a source for the essential nutrient, vitamin A. There is some evidence that, taken long-term as a supplement, beta-carotene could have harmful effects, especially in smokers.

Scientist Heinrich Wachenroder coined the term "carotene" in the 19th century, after he crystallized the compound from the carrot root. Carrots now are well known as a major source for beta-carotene. Other foods rich in beta-carotene include pumpkins, mangos, apricots, cantaloupe, sweet potatoes, spinach, kale, and red peppers. (In dark green vegetables, the chlorophyll masks the beta-carotene pigment.) Beta-carotene and other carotenoids are responsible for about 50% of the recommended intake of vitamin A in the North American diet.

Beta-carotene is converted to the essential nutrient, vitamin A, in the small intestine. Vitamin A is an important nutrient in regulating a number of biological functions; and deficiencies of the vitamin can lead to abnormal bone development, problems in the reproductive system, drying of the cornea, and eventually death. To receive adequate vitamin A from beta-carotene, a daily intake of 1,800 mcg (1.8 mg) of beta-carotene is recommended. Daily consumption of five servings of fruits and vegetables generally yields about 6 mg to 8 mg of beta-carotene.

The history of research on beta-carotene supplements provides one of the best cautionary tales regarding the failed promises of dietary supplements. Epidemiological studies conducted in the early 1980s found associations between higher fruit and vegetable consumption and reduced risk of several types of cancer. A high intake of fruits and vegetables was similarly associated with a high intake of beta-carotene. Scientists reasoned that, in diets high in fruits and vegetables, beta-carotene might be the component responsible for reducing cancer risk.

Eager to reap the potential benefits of this association, a number of experimental trials were begun to test this hypothesis. One of the first trials was conducted in Finland, using male smokers as subjects. Researchers thought that the effects of beta-carotene on cancer risk would be especially apparent in this vulnerable population. The experiment, called the Alpha-Tocopherol, Beta-Carotene (ATBC) study followed 29,133 men for 5 to 8 years. When the results were analyzed in 1994, they revealed that subjects receiving the beta-carotene supplement showed a surprising 18% increase in risk of lung cancer (EBSCO, 2012).

In 1996, a similar trial was ended early when subjects receiving beta-carotene showed a 46% greater cancer risk. This study, known as the Beta-Carotene and Retinol Efficacy Trial (CARET) included male subjects who were either current or former smokers, or had been exposed to asbestos. Subsequent studies in women and men, including smokers and nonsmokers, have not found a significant benefit associated with beta-carotene supplements. A high intake of fruits and vegetables still is recommended, and associated with a decreased risk of many types of cancer. Nutrition experts believe that the antioxidant activity of beta-carotene is probably beneficial when beta-carotene is consumed in foods as part of a healthful diet.

Beta-carotene supplements are considered effective in reducing the risk of sunburn in people with the inherited disease erythropoietic protoporphyria (EPP) and might be effective for people who sunburn easily but do not have the disease. High-dose antioxidants might interfere with chemotherapy drugs or radiation

therapy. Thus, the decision to take beta-carotene supplements while undergoing cancer treatment should be carefully considered (Mayo Clinic, 2012). Low doses of beta-carotene often are found as a component of multivitamin supplements, to provide all or part of the recommended intake for vitamin A. Because beta-carotene is fat soluble, requiring dietary fat for absorption, beta-carotene in food and supplements is absorbed more effectively when taken with meals containing some fat.

Signs of a toxic level of beta-carotene include dizziness and a (reversible) yellowing of hands and feet. Although beta-carotene likely is safe when taken in limited quantities or for specific medical concerns, supplements are not recommended for general use due to increasing evidence of the dangers of beta-carotene supplementation. Many health authorities (American Heart Association, American Cancer Society, World Cancer Research Institute, and World Health Organization's International Agency for Research on Cancer) recommend getting beta-carotene from food sources until research concludes that supplements are equally as safe and effective.

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Research Issues

Researchers do not yet understand why beta-carotene supplements are associated with an increased risk of cancer in smokers and people exposed to asbestos. Some experts have suggested that high beta-carotene intake from supplements might inhibit the absorption and utilization of other carotenoids that could be important. Other researchers suggest that, at high doses, some antioxidants can become harmful.

See Also: Antioxidants; Carotenoids; Vitamin A.

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Biotin

Biotin is a B vitamin; it also is called vitamin B7, vitamin H, and coenzyme R. Biotin, like all vitamins, is an organic compound that is necessary for normal growth, development, and maintenance of basic functions in the body. Biotin is water soluble, which means that the body does not store it, so it must be consumed regularly. Biotin deficiency is rare because it exists in a variety of foods and only is needed by the body in small amounts (approximately 30 mcg for the average adult) (Ehrlich, 2011). Bacteria that reside in the small and large intestine also synthesize biotin, but it is unknown how much of this the body absorbs. All B vitamins act as coenzymes, or compounds that help enzymes function, and play a critical role in energy metabolism.

Background

A variety of researchers played a role in discovering biotin and its functions, which started with the investigation of a curious condition called, "egg white injury." In 1916, scientist W. G. Bateman discovered that rats consuming a surplus of raw egg whites with an otherwise healthy diet fared poorly, but consumption of cooked egg whites caused no problems. In 1933, another researcher, Margaret Averil Boas, found that rats consuming raw egg whites developed a skin rash. In 1936 German scientists Fritz Kogl and Benno Tonnis isolated a substance in egg that they called "biotin" because of its similarity to substances called "bios" that are needed for yeast growth. A number of other researchers isolated the same substance and gave it other names, including vitamin H and coenzyme R.

In 1942, biotin's structure was confirmed, although for many years its biological functions remained unclear (Ensminger, Ensminger, Konlande, & Robson, 1993). It now is known that biotin is required for many metabolic processes. The reason raw egg white consumption often led to skin rashes and other symptoms is because egg whites contain a substance called avidin. When raw, avidin binds to biotin and prevents its absorption. (Heat denatures avidin, therefore consuming cooked egg whites presents no risk for biotin deficiency.) "Egg white injury" is caused by biotin deficiency.

Role of Biotin in the Body

Biotin is absorbed in the upper part of the small intestine. Once inside a cell, biotin's coenzyme form is activated to assist with fat and carbohydrate metabolism. Biotin promotes the synthesis of fatty acids and glucose by helping to break down amino acids and transfer carbon dioxide to other compounds. Fatty acids and glucose then can be used by the body as fuel for energy.

Biotin Deficiency

Biotin deficiency is rare for people consuming a healthy diet. Instances of deficiency often are connected to conditions or circumstances that make it difficult for

individuals to absorb nutrients, such as Crohn's disease, diabetes, long-term intake of antibiotics or antiseizure medication, long-term tube feeding, or as a result of the surgical removal of the stomach. Biotinidase deficiency is a genetic disorder that occurs in approximately 1 in 60,000 newborns. It results in an inability to reuse or recycle biotin, but can be managed with lifelong biotin supplements (U.S. Library of Medicine, 2008). Individuals or animals that consume an excess of raw egg whites (a dozen or more daily over multiple months) also can develop a biotin deficiency (Insel, Ross, McMahon & Bernstein, 2013).

Symptoms of biotin deficiency can include the following.

- Thinning hair
- Glossitis (a bright red, swollen tongue)
- Red, scaly rash around the eyes, nose, and mouth
- Dry eyes
- Muscle pain
- Muscle weakness
- Tingling in the arms and legs
- Fatigue
- Depression

Daily Recommended Intakes

Because biotin deficiency is rare, there is little research on how much biotin individuals should consume. The average intake therefore is determined mathematically from the average intake of infants, which is based on biotin levels in human milk (Insel, Ross, McMahon, Bernstein, 2013). Recommendations are as follows (Ehrlich, 2011).

- Adolescents 14 to 18 years: 25 mcg
- 19 years and older: 30 mcg
- Pregnant women: 30 mcg
- Breast-feeding women: 35 mcg

Food Sources

The food sources containing biotin include liver, salmon, cauliflower, carrots, cereals, bananas, yeast, soy flour, cooked oats, egg yolks, rice bran, milk, soybeans, nuts, wheat, legumes, pork, cheese, avocado, raspberries, and oysters.

Health Benefits of Biotin

Biotin is necessary for proper growth and function of the body. Biotin supplements, however, only are necessary for individuals with proven biotin deficiency. Many biotin supplements are advertised as an effective treatment for a variety of issues, from hair loss and graying hair, to brittle nails and improved blood sugar regulation. None of these claims has been confirmed consistently by research. A

study in 2008 showed that a supplement containing both chromium and biotin helped regulate blood sugar levels in people with diabetes. Further research is needed, however, to understand how significant the benefits might be (University of Maryland Medical Center, 2013).

Upper Level Intake and Toxicity

There is no determined Tolerable Upper Intake Level (UL) for biotin. If biotin is overconsumed, then the body removes it through sweat, urine, and feces.

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See Also: Vitamins.

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Black Cohosh

Black cohosh is a dietary supplement made from the root of the black cohosh plant, which grows naturally in the eastern United States. The plant is a perennial woodland plant that grows 4 to 8 feet tall and has long white flowers. The scientific names for black cohosh are *Actaea racemosa* and *Cimicifuga racemosa*. It is also known as black snakeroot, bugbane, bugwort, rattleroot, and rattlewood. The herb is often recommended to relieve menopausal symptoms, such as hot flashes, irritability, mood swings, and sleep disturbances.

Nearly 200 years ago, Native Americans used black cohosh root to relieve menstrual cramps, symptoms of menopause, and a multitude of other ailments. In 19th-century America, black cohosh was popular among a group of alternative practitioners. They called it "macrotys" and prescribed it to treat rheumatism, lung conditions, neurological conditions, and conditions that affected

women's reproductive organs. In Europe, black cohosh has been used widely to treat premenstrual discomfort, painful menstruation, and menopausal symptoms for more than 40 years.

Black cohosh is most often taken to treat menopausal symptoms, premenstrual symptoms, and menstrual cramps. Germany's regulatory agency for herbal medicine, Commission E, has approved black cohosh for these purposes. Black cohosh is the main ingredient in an over-the-counter German menopausal remedy called Remifemin. Scientific studies regarding the efficacy of black cohosh for the treatment of menopausal symptoms, however, have produced mixed results. Several studies have found black cohosh to be as effective as hormonal treatments, but others have found black cohosh to be no more effective than placebo treatments.

Women with breast cancer often seek help for menopausal symptoms, which are frequent side effects of treatment. Black cohosh has been believed to contain phytoestrogens, including a compound called fukinolic acid, potentially exerting estrogen-like effects in the body. The exact action of the compounds in black cohosh is unclear, however, as studies on possible estrogen-like effects have been contradictory. Additionally, some in vitro studies on human breast cancer cell lines have found black cohosh to inhibit cancer development, and other studies have reported that black cohosh stimulates cancer development. This confusion has led to a general reluctance to recommend the use of black cohosh to women with breast cancer.

Black cohosh can be used in several different forms including capsules, solutions, tablets, tinctures, and powders. The typical suggested dose is 20 mg to 200 mg daily, 1 g to 2 g of dried root powder, or 10 to 60 drops of tincture a day. It also can be made into a tea; however, teas might not be as effective as the standardized extract of black cohosh in relieving menopausal symptoms. Black cohosh can be taken for up to six months and then it should be stopped, as studies demonstrating the safety of long-term use are lacking.

Black cohosh has been associated with some negative side effects, including stomach discomfort, headaches, and weight gain. Rash, nausea, and vomiting also have been reported. Slow heart rate, uterine cramps, dizziness, tremors, joint pain, and light-headedness have been observed with very high doses. In a few cases, liver damage associated with use of black cohosh has been reported. Black cohosh therefore is not recommended for people who consume alcohol regularly or who have liver disorders. It also should not be used by women who are pregnant or breast-feeding.

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See Also: Herbs and herbal medicine; Phytoestrogens.

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Blood Sugar Regulation

The term "blood sugar" refers to blood glucose levels. The body regulates blood glucose levels very carefully because blood glucose is an important source of energy, especially for the central nervous system (CNS). When blood glucose levels fall too low or rise too high, people experience symptoms of CNS dysfunction, including dizziness, disorientation, confusion, unconsciousness, and—in extreme cases—even death.

Blood glucose levels are controlled by two important hormones produced by the pancreas—insulin and glucagon. Specialized cells in the pancreas, called "beta cells," release insulin when blood glucose levels get too high. Insulin binds with receptors on cell membranes that enable cells to take up glucose from the blood, thus reducing blood glucose levels. The cells either use the glucose for energy, if energy is needed, or store it for future use. Liver and muscle cells can convert glucose to glycogen, a type of carbohydrate that quickly can be converted back into glucose as needed. If glycogen stores are full, then the glucose can be converted to triglycerides and stored as fat. Fat is stored in adipose tissue but can also be stored in muscles and in the liver. "Fatty liver" is a harmful condition that can result when energy intake exceeds energy needs over time. (Fatty liver also can develop due to excessive alcohol intake.)

If blood glucose levels fall too low, other specialized cells in the pancreas, called "alpha cells," release the hormone glucagon. Glucagon signals the liver to break down glycogen and release glucose into the bloodstream. As the liver releases glucose into the blood, the blood glucose levels rise to meet the body's immediate energy needs. The liver also can produce glucose from other precursors, such as amino acids; the process is known as "gluconeogenesis."

Another hormone, epinephrine, released by the adrenal glands as part of the stress response—the "fight-or-flight" response—also increases blood sugar level via the same mechanisms as glucagon. The stress hormone cortisol increases blood sugar level by stimulating gluconeogenesis. Adequate blood sugar is essential when responding physically to stress—to fuel muscle contraction, increased heart rate and breathing rate, and the other systems that contribute to

fighting or fleeing. Of course, modern-day humans do not always respond to sources of stress by fighting or running away, but blood sugar rises nonetheless as the body prepares to respond to a perceived danger. Drugs that mimic the effects of epinephrine—such as caffeine and nicotine—also raise blood sugar levels.

Blood sugar levels also vary in response to the foods a person consumes, and foods vary in their effect on blood sugar level. Foods with low carbohydrate content contribute little glucose as these foods are digested and absorbed. Foods with high carbohydrate content result in rising blood sugar levels because the glucose is released into the bloodstream. The rate at which a food raises blood sugar levels depends upon the chemical structure of that food. A measurement known as glycemic index represents the speed with which glucose appears in the bloodstream and how high blood sugar levels rise following consumption of a given food. A food with a high glycemic index raises blood sugar levels quickly and to relatively high levels. Foods with lower glycemic indices are digested more slowly, and glucose is released more gradually into the bloodstream. The higher the blood sugar level, the greater the amount of insulin released by the pancreas. High glycemic index foods include white bread, white potatoes, and sugar-sweetened beverages. Low glycemic index foods include those composed primarily of protein and fat, such as eggs, meat, and seafood, and low-starch vegetables such as lettuce, spinach, broccoli, and sweet peppers.

Knowledge of blood glucose regulation enhances understanding of the difficulties presented by conditions that disrupt this process. In people with type 1 diabetes mellitus, the pancreas loses the ability to produce insulin due to the destruction of insulin-producing beta cells. Without insulin, blood glucose levels rise after food consumption as carbohydrates are digested and absorbed, but the glucose is unable to enter the cells. People with type 1 diabetes are able to give themselves insulin. They must time its administration to achieve good control of blood sugar levels. People with type 1 diabetes develop a schedule of insulin administration, meals, and physical activity that tries to mimic nature's intended insulin response, making sure insulin is available when nutrients are being absorbed from meals and that blood sugar does not dip too low during physical activity.

People with type 2 diabetes mellitus usually produce adequate insulin (until later stages of the illness), but the insulin receptors on the cell membranes do not respond well to insulin. People with this condition are said to be insulin resistant, meaning that their insulin receptors "resist" the action of insulin. Although insulin is present in adequate concentrations in the blood, blood glucose remains high because the cell membrane receptors for insulin are not responding and allowing the cells to take up the glucose from the blood. Insulin resistance and type 2 diabetes are often components of the metabolic syndrome usually associated with obesity and low levels of physical activity.

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Research Issues

How does the body provide optimal glucose levels to muscles during exercise? Scientists do not yet have the full answer to this question. During exercise, great volumes of glucose must be able to enter the exercising muscle cells. Yet, during exercise, insulin levels decline as glucagon and other hormone levels rise to stimulate the liver to release glucose into the bloodstream. How does glucose get into the cells if insulin is not present to stimulate the glucose transporters? The same glucose transporters help cells take up glucose at rest and during exercise; however, signaling molecules other than glucose must be involved in facilitating this process. Interestingly, when muscle is stimulated by insulin, the glucose taken up primarily is stored, and muscle stimulated by exercise oxidizes the glucose to produce energy for muscular contraction, rather than storing it (Wasserman et al., 2011).

See Also: Carbohydrates; Cardiometabolic syndrome; Diabetes, type 1; Diabetes, type 2; Glucose; Glycemic index and glycemic load; Glycogen loading; Hyperglycemia; Hypoglycemia; Insulin.

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Body Composition

Body composition refers to an estimate of the proportions of a person's mass that are composed of fat, bone, muscle, and other tissues. Body composition tests used in a nutrition and health context typically divide body mass into fat mass (FM) and everything else, or fat-free mass (FFM). Body composition is interesting because two people who have the same height and weight can look very different and have very different body types. Data from body composition tests can help nutrition professionals make nutrition and weight control recommendations for clients.

How Is Body Composition Measured?

There are many ways to estimate body composition. All are based on the fact that muscle and fat differ in important ways. Each technique uses one of these differences to estimate how much of the body is FM. Some techniques are used primarily in research and medical settings, and others are likely to be available in exercise physiology laboratories and in health and fitness facilities. Techniques used in research and medical settings including the following.

- Hydrometry. Hydrometry methods give an estimate of total body water (TBW). Because fat tissue contains very little water, finding out how much water is in a given body allows researchers to estimate FM and FFM for a given body size. Subjects are given some form of tracer that diffuses into all water compartments. A sample of water, such as saliva, is taken, and TBW extrapolated from the tracer amount in the sample. Hydrometry procedures are expensive and are used primarily for research and medical purposes.
- Dual-energy x-ray absorptiometry. Dual-energy x-ray absorptiometry (DEXA) technology uses two x-ray energies to measure bone density and body composition. It is becoming common for older clients at risk for developing osteoporosis to receive DEXA scans to evaluate and monitor changes in bone density. Dual-energy x-ray absorptiometry technology produces a very accurate estimate of body composition. It currently is used to assess body composition primarily in research settings.
- Medical imaging techniques. Magnetic resonance imaging (MRI) and computed tomography (CT) both are used to assess body tissues and can be used to calculate body composition. MRIs and CT scans also can provide information on the location of adipose tissue stores. These techniques provide good information but are expensive and primarily are used for research on body composition.

Techniques more widely available, and more likely to be used in nutrition and health settings, include the following.

- Hydrostatic or underwater weighing. For this test, a subject sits on a seat underwater. The seat is attached to a scale which measures the person's weight. The heavier a person is in the water, the greater his or her density. Density refers to weight per volume. Two people with the same weight for a given height, or body mass index (BMI), can have different densities. A denser person has more FFM and less fat. By calculating density from water weight, a person's body fat percentage can be estimated. Error can occur with this measure because the density of non-fat tissues, such as bone, varies from person to person; the test calculations, however, rely on an average value. Similarly, percent fat prediction equations take into account the air remaining in the lungs after a complete exhalation. If this volume is estimated and not measured, or if the person has difficulty exhaling and holding the breath underwater, then

body-composition estimates will not be as accurate. Underwater weighing tanks most likely are found in research and academic settings, such as in kinesiology department facilities.

- Air displacement. Some instruments estimate body composition from air displacement. The heavier a person is for a given size, the denser the person is. As with underwater weighing, higher density means less fat tissue. Individual variations in tissue density reduce the accuracy of body composition predictions. Air-displacement equipment is most commonly found in research and academic settings.
- Bioelectrical impedance analysis (BIA). Bioelectrical impedance analysis tests are based on the fact that fat conducts electricity more slowly than nonfat tissue, which contains quite a bit of water. BIA equipment sends a weak electrical current through the body. The speed of the current reflects relative fat in the body. BIA measures assume a constant body water content for various tissues, so anything that alters hydration status or causes water retention affects BIA body-composition estimates. Dehydration, premenstrual water retention, elevated muscle glycogen levels, and food in the stomach also can interfere with the accuracy of BIA body composition estimates. BIA equipment is found in many health and fitness facilities. Because equipment is quite portable and easy to use, BIA often is the technology of choice at health fairs.
- Anthropometric measures. Anthropometry means "the measurement of humans," and refers to measures that describe physical characteristics. The anthropometric measures used for estimating body composition include circumferences and skinfolds. Circumference, in this context, refers to the distance around a particular body part, such as the waist, hips, or upper arm. Circumferences are usually taken with a tape measure, and then entered into an equation to predict body fat. Skinfold thickness is measured with calipers at several standard anatomic sites. These measurements then are entered into prediction equations to predict body composition. Circumference and skinfold measures are most accurate when taken by an experienced test administrator; however, body-fat predictions based on these measures often still are inaccurate because the equations that are used are based on population averages and might not apply to a given individual. Some health and nutrition professionals use circumferences and skinfolds as "stand alone" measures. When taken over time they can show changes in and of themselves, without predicting body composition from them. If a person is losing fat, for example, the waist circumference might decrease. Anthropometric measures are the least expensive—but also are the least accurate—means of estimating body composition.

Researchers have a fairly rough idea of the range of body fat percentiles that are normal and healthy for various population groups, although less information is available for ethnic minorities. The healthy range for adult males can be anywhere from 6% to 24%, and for adult women are anywhere from 14% to 34%, depending

upon the person's build and body type. Athletes tend to be leaner, although this varies by sport.

The most accurate measures of body composition are not readily available to most people. The most common measures have an error range of at least +/-4 percentage points. This means that if a body composition test—such as a hydrostatic weighing or skinfold test—estimates body composition at 20%, it actually can be somewhere between 16% and 24%. Because body composition changes very slowly, even with weight loss, the most readily available assessment methods lack the precision required to find meaningful change.

When Are Body Composition Tests Helpful?

Body composition tests can be helpful in several situations, including the following.

- A person who has begun exercising more—especially performing more strength training—and is gaining a little scale weight, but appears to be getting more muscular, not fatter. Body composition tests might verify that lean or muscular people are not fat. Their weight gain is healthy muscle gain (not fat gain).
- People who have a normal BMI or weight but lack muscle size and strength. These people could fall into the category of "normal weight obesity," which is associated with the same health risks as obesity. A body composition test might help motivate such people to improve eating and exercise behaviors.
- Athletes attempting to reach a specific weight category or weight minimum might find body composition tests helpful to see if their weight goal is realistic. Coaches and athletic trainers, for example, often monitor high school wrestlers' body composition scores to be sure athletes are not trying to lose too much weight to get into a lower weight category.
- People who have a high BMI (or weight) but appear fairly muscular. A body composition test can help reassure them that they are not overly fat, and that they should not focus on losing weight, unless other obesity-associated health risks indicate that some weight loss would be beneficial.

Body composition tests are most accurate when performed by experienced professionals. If body composition measures are taken over time, then the same test should be used repeatedly and, if possible, the same professional should perform the test each time.

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Research Issues

When do excess adipose tissue stores become a health risk? Exploring information from the entries in this encyclopedia on adipose tissue, body mass index, and obesity provides a good context for understanding how body composition assessment is useful in clinical settings.

See Also: Adipose tissue; Body mass index; Obesity, definition and health effects.

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Body Mass Index

Body mass index (BMI) is a measure commonly used to assess weight and obesity, and is calculated from a person's weight and height. Although BMI is not a measure of body composition, it can be a useful indicator of body fat of most people—especially when used in conjunction with other measures, such as waist circumference. Unlike most body composition assessment techniques, BMI is easy to obtain and can help guide individuals and clinicians in their assessment of a person's risk for the development of obesity-related health problems. Body mass index is even more useful as a public health indicator; epidemiologists use BMI to observe population obesity trends. For some individuals, BMI might not be a good indicator of body composition. Body size alone might not reflect body composition, especially for people with an exceptionally great amount of muscle mass, or people with sarcopenic obesity, for whom BMI appears normal but the person has such low muscle mass that "normal" weight is composed of too much body fat.

Body mass index has been used as an assessment tool since the middle of the 19th century. Originally created by Belgian mathematician Adolphe Quetelet, it was called the Quetelet index. It is calculated by dividing a person's weight by the square of his or her height. The formulas provided below are used (CDC, Body Mass Index, 2014).

For metric units of measure:

- BMI = weight (kg) / [height (m)]^2
- Example: Weight = 68 kg, height = 165 cm (1.65 m)
- Calculation: 68 ÷ $(1.65)^2$ = 24.98

For English units of measure:

- BMI = weight (lb) / [height (in)]^2 × 703
- Example: Weight = 150 lbs, height = 5'5" (65")
- Calculation: [150 ÷ $(65)^2$] × 703 = 24.96

Online tools are widely used to calculate BMI (CDC, Body Mass Index, 2014). Body mass index charts also are available (*see* table 1).

- To use the table, find the appropriate height in the left-hand column labeled height.
- Move across to a given weight (in pounds).
- The number at the top of the column is the BMI at that height and weight.
- Pounds have been rounded off.

BMI is interpreted for adults 20 years of age and older using the following categories.

- Underweight: BMI below 18.5
- Normal: BMI = 18.5–24.9
- Overweight: BMI = 25–29.9
- Obese: BMI 30.0 and greater

Table 1. Body Mass Index (BMI) Calculation

BMI	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**35**
Height (inches)	**Body Weight (pounds)**																
58	91	96	100	105	110	115	119	124	129	134	138	143	148	153	158	162	167
59	94	99	104	109	114	119	124	128	133	138	143	148	153	158	163	168	173
60	97	102	107	112	118	123	128	133	138	143	148	153	158	163	168	174	179
61	100	106	111	116	122	127	132	137	143	148	153	158	164	169	174	180	185
62	104	109	115	120	126	131	136	142	147	153	158	164	169	175	180	186	191
63	107	113	118	124	130	135	141	146	152	158	163	169	175	180	186	191	197
64	110	116	122	128	134	140	145	151	157	163	169	174	180	186	192	197	204
65	114	120	126	132	138	144	150	156	162	168	174	180	186	192	198	204	210
66	118	124	130	136	142	148	155	161	167	173	179	186	192	198	204	210	216
67	121	127	134	140	146	153	159	166	172	178	185	191	198	204	211	217	223
68	125	131	138	144	151	158	164	171	177	184	190	197	203	210	216	223	230
69	128	135	142	149	155	162	169	176	182	189	196	203	209	216	223	230	236
70	132	139	146	153	160	167	174	181	188	195	202	209	216	222	229	236	243
71	136	143	150	157	165	172	179	186	193	200	208	215	222	229	236	243	250
72	140	147	154	162	169	177	184	191	199	206	213	221	228	235	242	250	258
73	144	151	159	166	174	182	189	197	204	212	219	227	235	242	250	257	265
74	148	155	163	171	179	186	194	202	210	218	225	233	241	249	256	264	272
75	152	160	168	176	184	192	200	208	216	224	232	240	248	256	264	272	279
76	156	164	172	180	189	197	205	213	221	230	238	246	254	263	271	279	287

For BMI greater than 35, see http://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmi_tbl2.htm

Source: National Heart, Lung, and Blood Institute. (n.d.) Body Mass Index Table 1. Retrieved from http://www.nhlbi.nih.gov/guidelines/obesity/bmi_tbl.htm

Body mass index is calculated the same way for children and adults, but the BMI of children and adolescents is evaluated in terms of how their BMIs compare to others of their age and gender. Tools for calculating and evaluating the BMI for children and teens can be found on the Centers for Disease Control and Prevention website (CDC, About BMI for children and teens, 2014).

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See Also: Body composition; Obesity, causes; Obesity, definition and health effects; Obesity, treatment.

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Boron

Boron is an essential trace mineral vital to plant health and occurs naturally in compounds called borates, which are a variety of salts and minerals found in the earth's crust. In humans, boron appears to participate in a number of important roles. Preliminary research suggests that boron is involved with bone growth as well as regulation of inflammatory and immune-system responses, and probably brain health (Samman, Foster, & Hunter, 2012). Healthy amounts could be involved in steroid-hormone metabolism, might participate in the actions of vitamin D and estrogen, and could assist with the proper absorption of magnesium and calcium (EBSCO, 2012). Boron supplements increasingly are being used by postmenopausal women to promote bone health and mass, although evidence for benefits is preliminary.

In the 1870s, boron became the main ingredient in substances used for preserving meat and dairy foods (Nielsen, 2008). These preservatives proved critical in avoiding food crises during both World War I and II, but fell out of favor by 1950, due to increasing evidence for boron's toxicity in high doses. Boron still is mined for its use in glass and ceramics, as well as is flame retardants, detergents, and soaps.

A key component for cell walls in plants, the element is found in most fruits and vegetables, especially dried fruits such as prunes and raisins. It also is found in other plant foods including nuts and legumes. The boron content of all foods varies with geographical location and soil content. Lack of boron has been found to disrupt the life cycle of frogs, causing atrophy of reproductive organs and death of more than 80% of embryos within the first 96 hours (Nielsen, 2008). Boron

deficiency interferes with proper brain function in humans, with subjects exhibiting poor performance on psychomotor tasks involving manual dexterity and eye-hand coordination, as well as on cognitive tests of attention, spatial perception, and short- and long-term memory (Penland, 1998). A few correlational studies suggest that greater intakes of boron could be associated with reduced risk of hormonally sensitive cancers, such as breast and prostate cancers (Samman, Foster, & Hunter, 2012). These studies suggest that further research in this area is warranted. Although no daily recommended intake (DRI) has been set for boron, its intake is considered to be insufficient below 0.4 mg per day, with optimal health effects gained from ingesting about 1 mg per day (Nielsen, 2008). Usual dietary intake is between 0.87 and 1.35 mg per day for adults (Neilsen, 2008). Exposure to excess boron is rare. Symptoms include nausea, poor appetite, weight loss, and decreased sexual activity. The Tolerable Upper Intake Level for boron is 20 mg per day for adults.

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See Also: Minerals.

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Bottled Water

"Bottled water" refers to drinking water that is sold in a variety of containers, including individual serving bottles, quarts, liters, and "carboys" (a large glass or plastic bottle) for water coolers. Bottled water can come from any of several water sources, including springs, aquifers, and even municipal water supplies. The production and marketing of bottled water became popular in North America in the 1980s, and the market has continued to expand as consumers worry about pollution

of their local water supplies. As health authorities urge people to consume fewer sugar-sweetened beverages, many individuals are turning to bottled water as a convenient and healthful beverage alternative. Environmental groups have recently become alarmed, however, at the environmental costs of the bottled water industry. Discussions concerning the purchasing of water supplies by private organizations to sell as bottled water have brought questions of water-supply ownership and management into the public eye.

Several types of bottled water are available (FDA, 2010). Mineral water comes from a protected underground source and must contain at least 250 parts per million (ppm) of dissolved minerals, such as calcium and magnesium. Spring water is taken from an underground supply that flows naturally to the surface. Artesian water comes from a confined underground aquifer located below the natural water table. Purified water is tap water or groundwater that has been treated by distillation, deionization, or reverse osmosis.

The debate about whether bottled water is healthier than tap water has been of great significance in recent years, especially as bottled water becomes more pervasive. Bottled water often is thought to be cleaner and taste better than public tap water, but this difference varies depending upon the source and processing of the bottled water, as well as the specific municipal water supply. Bottled water often is claimed to originate from springs, lakes, or mountain streams, and tap water is assumed to come from more local supplies. In reality, some tap water comes from the same places as bottled water, including springs and lakes. Additionally, many types of bottled water actually are forms of filtered tap water. Investigations in 2006–2008 revealed that some bottled waters contained more contaminants than are found in most municipal water supplies. This news prompted many consumers to become more aware of the quality of their tap water and that of their bottled water.

Standards for municipal water are set and enforced in the United States by the Environmental Protection Agency (EPA) and in Canada by Health Canada. Municipal water suppliers must release reports at regular intervals listing contaminants found. Bottled-water products are not required to do this. The production and labeling of bottled water is regulated by the Food and Drug Administration in the United States. In Canada, Health Canada is responsible for the health and safety standards for bottled water, and also helps to regulate labeling policies. The Canadian Food Inspection agency is responsible for setting and enforcing standards for the packaging, labeling, advertising, and production of bottled water. Bottled water and tap water generally have the same safety and the same problems. Consumers therefore should make decisions about what type of water to drink by considering the safety of their home water supply; the cost, taste, and fluoride content of water; and the environmental concerns about the costs of bottled water.

Many consumers have expressed fear about contamination of bottled water by the bottle itself. Evidence suggests that chemicals from the plastic bottle can leak into the water. This is especially likely to occur as the bottles age or are exposed to heat, such as being left in a hot car.

Environmental groups have attempted to educate consumers about the hidden costs of bottled water, including the generation of solid waste, as a majority of bottles end up in landfills rather than recycling facilities. The production of bottled water requires petroleum and water to produce the plastic bottles and transport the product, often for long distances. Additionally, some groups are concerned that the privatization of global water supplies and the diversion of water to produce bottled water for resource-rich countries could leave some communities in resource-poor areas with inadequate water supplies.

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Research Issues

Some schools and workplaces have attempted to reduce use of bottled water by supplying people with reusable containers and urging them to fill containers at home or from drinking fountains. In schools, these efforts often are promoted by student clubs and organizations that focus on environmental awareness and sustainability.

See Also: Water needs, water balance.

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"Brain Foods"

The term "brain foods" refers to food that is thought to have a positive influence on brain structure and function. Research suggests that food-derived signaling molecules influence metabolism and synaptic plasticity which reflects positively

on cognitive function. Cognition is defined as the mental processes used to gain knowledge and process information through responses such as learning, attention, and memory. Foods that contain omega-3 fatty acids, flavonols and antioxidants, folic acid, and vitamin E show some evidence of contributing to brain health.

Evidence indicates that omega-3 fatty acids, including α-linolenic acid, eicosapentaenoic acid (EPA), and docosahexanoic acid (DHA), have a significant role in cognition and mental health. Studies have found an increased risk of schizophrenia, depression, and dementia in subjects that have deficiencies in omega-3 fatty acids (Dauncey, 2008). Specifically, high levels of DHA have been found to increase protein-lipid interactions. This results in enhanced cell membrane flexibility because DHA is a key component of neuronal membranes—which translates to increased neuronal activity and better cognitive functioning.

Some studies suggest that, in rodent models, supplementation with DHA could promote greater concentrations of hippocampal brain-derived neurotropic factor (BDNF) and enhanced cognitive function. Brain-derived neurotropic factors alter specific cell signaling pathways in the brain which results in an increase in neurogenesis, learning, and memory. The known pathway where the conversion of α-linolenic acid to EPA to DHA occurs is not efficient. Thus, the required EPA and DHA levels for brain functioning are dependent on dietary intake (i.e., oily fish). Dietary intake, however, is more complicated than just eating foods high in omega-3 fatty acids to enhance cognition; there must be a balance between the intake of foods that are high in both omega-3 and omega-6 fatty acids. Fatty acids in general can affect multiple pathways molecularly in the brain, based upon their binding to receptors in the cell nucleus. In this way, fatty acids can regulate the transcription of various genes important for brain structure and function.

Flavonols are a member of the flavonoid family, a group of compounds found in various fruits, tea, and cocoa (Vauzour, 2012). Studies suggest that flavonol-rich foods improve blood flow in the brain. Optimal blood flow to the brain enhances adult neurogenesis (the creation of new nerve cells) and positively affects cognitive performance. Additionally, flavonols could help to reduce the oxidative damage that the brain experiences due to its high metabolic rate and the vulnerable polyunsaturated fatty acids that comprise neural membranes. The antioxidant lycopene—found in tomatoes and other fruits and vegetables—might help protect the brain against free-radical damage to cells (Lewin, 2014). Several flavonol and flavonoid-based diets have become highly publicized due to the link found between foods high in antioxidants and benefits to neural functioning (Gómez-Pinilla, 2008). For instance, studies examining blueberry supplementation in aged animals showed improved memory and learning (Vauzour, 2012). These results seem to occur in humans, as well. One study found that blueberry juice supplementation for 12 weeks had beneficial effects in humans in terms of improving learning and memory (Joseph, Shukitt-Hale, & Willis, 2009).

Folic acid found in foods such as spinach and orange juice has been shown to be vital to brain structure and function, especially during development (Gómez-Pinilla, 2008). Folate deficiency can result in neurological disorders, such as depression and cognitive deficits. Preliminary studies have indicated that long-term folic acid supplementation can minimize age-related cognitive decline in older adults. Folic acid also is thought to lower homocysteine levels in the blood. Elevated levels of homocysteine could increase the risk of stroke and cognitive impairment (Lewin, 2014).

The micronutrient vitamin E has been shown to correspond to better cognitive functioning (Sorgen, 2014). Foods high in vitamin E include nuts, seeds, and green leafy vegetables. It has been suggested that dietary intake of vitamin E can act as a protective factor against cognitive decline, particularly in the elderly. Vitamin E has been associated with improved mitochondrial activity, which translates to better cognitive function (Gómez-Pinilla, 2008). The mechanisms behind vitamin E are not well understood, but likely relate to antioxidants' effects on ridding the brain of free radicals to protect synaptic membranes from oxidation. Research on use of vitamin E supplements indicates that they sometimes are linked with negative health effects, therefore nutritionists usually advise consumers to obtain adequate vitamin E from food.

Nutritionists also advise that, although research on single nutrients and brain function might seem intriguing, it is unlikely that a single nutrient will be found to exert a strong effect on the brain, given the many nutrients, foods, and lifestyle factors that influence brain development and health. Rather, individuals should strive to consume a healthful diet, including brain foods such as nuts, seeds, oily fish, blueberries and other berries, a variety of vegetables, moderate amounts of tea, and even a little dark chocolate.

Victoria E. von Saucken

See Also: Alzheimer's disease and nutrition; Antioxidants; Attention-Deficit Hyperactivity Disorder and nutrition; Autism and nutrition; Depression and nutrition; Fatty acids; Phytochemicals; Polyphenols.

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Breast-Feeding

The term "breast-feeding" refers to the practice of nourishing an infant with human milk, generally by allowing the infant to suck on the mother's breast. Breast-feeding practices, however, also can include feeding breast milk to the infant using a bottle. Health organizations, including the World Health Organization, the U.S. Centers for Disease Control and Prevention, and Health Canada, unanimously agree that—with very few exceptions—breast milk is the best source of nutrition for infants. Breast milk provides infants practically all of the nutrients required until they reach six months of age. Although infant-formula producers have tried to replicate the composition of breast milk, they have not yet been able to create the many growth factors, enzymes, antibodies, and other immune-system compounds found in human milk. In addition to its superior nutritional benefits, the act of breast-feeding offers benefits for mothers and contributes to strong emotional bonds between mother and child. Breast-feeding at birth is associated with a number of health benefits for babies, both while children are young and also later in life. Although breast milk is the preferred choice for infants, it is not always an acceptable option for mothers. Many mothers struggle with the physical challenges presented by breast-feeding and find it difficult to balance the demands of lactation and work.

Breast-Milk Nutrition

Breast milk provides almost all of the nutrients that are essential to an infant's growth and development. A combination of fats, cholesterol, proteins, carbohydrates, vitamins, minerals, and other components present in breast milk create the ideal recipe for the health and vitality of infants.

Fats are the primary source of calories in an infant's diet. Infants grow at a rapid rate and therefore require much sustained energy. A diet rich in fat helps promote growth and weight gain. Infants are able to ingest only a certain amount of fluid each day, therefore that fluid must provide an adequate amount of fat. In addition to providing caloric energy, fat plays a role in infant brain development and neural networks. Recent research has focused on the presence of long-chain polyunsaturated acids in human milk, specifically arachidonic acid (AA), and docosahexenoic acid (DHA). These acids are found in the structural lipids of cell membranes and are especially important in the structure of the neurons in the central nervous system, including the brain. The fat content of breast milk

varies widely, depending upon the mother's diet. Women who consume strictly vegetarian diets and few marine products can produce lesser amounts of the fatty acids AA and DHA. Breast milk contains enzymes that speed the infants' digestion of fats, thus the fat in breast milk is digested more easily than that in formula.

Breast milk also contains an abundance of cholesterol, which is important in infant brain development. Cholesterol is a primary component in the myelin sheaths located on the axons of the neurons. Myelin sheaths allow for neural impulses to be conducted efficiently.

Human breast milk contains two types of proteins—whey and casein—in a 60:40 ratio. This protein ratio contributes to the digestibility of breast milk and supports the growth of helpful bacteria, such as lactobacillus, in the infant's digestive tract. Lactose (milk sugar) is the primary carbohydrate found in breast milk.

Breast milk contains adequate amounts of all vitamins except for vitamin D. In recent years, pediatricians in North America have recorded several cases of vitamin D deficiency in breast-fed babies. Deficiency is especially likely to develop in babies born in winter months, and in those always protected from the sun by clothing and sunscreen products. For this reason, mothers are advised to give babies a vitamin D supplement and allow babies to be exposed to sunshine, when possible, to stimulate vitamin D production.

Breast milk appears to contain an adequate amount of iron for the first six months of an infant's development. Although the iron content in breast milk is relatively low as compared to formula, the iron in breast milk is absorbed more easily. Iron-containing foods, including iron-fortified foods, should be introduced into a baby's diet by six months of age.

Health Benefits

The first three to five days of an infant's life are the most crucial for breast-feeding. This is because breast milk is at first a sweet, yellow substance known as colostrum, which contains a high concentration of immune cells. The presence of colostrum has been correlated with positive development of an infant's immune system. The protective benefits of breast milk, however, continue throughout the breast-feeding period.

Several substances in breast milk enhance immunity in the baby's gastrointestinal (GI) tract, including the secretory immunoglobulin A (IgA) antibodies. When a mother encounters pathogens, her body manufactures antibodies specific to each one. The antibodies pass into the mother's breast milk and escape breakdown in the baby's GI tract because they are protected by the so-called "secretory" component. Once in the baby's GI tract, the antibodies bind with the targeted infectious agents and prevent them from passing through the lining of the GI tract. This protection is especially important in the earliest days of life, because the infant does not begin to make his or her own secretory IgA until several weeks or months after birth. The secretory IgA antibodies disable pathogens without harming helpful GI tract flora or causing inflammation. This is important because, although inflammation helps

fight infection, sometimes the process overwhelms the GI tract. An infant could suffer more from the inflammatory process than from the infection itself when inflammation destroys healthy tissue.

The large quantities of the immune system molecule interleukin-10 found in breast milk also help inhibit inflammation. A substance called "fibronectin" enhances the phagocytic activity of immune cells (called "macrophages"), inhibits inflammation, and helps repair tissues damaged by inflammation. Several other breast-milk molecules help disable harmful microbes. Mucins, certain oligosaccharides (sugar chains), and glycoproteins (carbohydrate–protein compounds) bind to microbes and prevent them from gaining a foothold in the lining of the GI tract. Many of breast milk's immune cells, including T lymphocytes and macrophages, attack invading microbes directly.

Breast-milk compounds also help in other ways. Some decrease the supply of nutrients such as iron and vitamin B12 that harmful bacteria need to survive. A substance called "bifidus factor" promotes the growth of helpful gut flora which crowd out pathogens. Retinoic acids—a group of vitamin A precursors—reduce the ability of viruses to replicate. Some of the hormones and growth factors present in breast milk stimulate the baby's GI tract to mature more quickly, thus making it less vulnerable to dangerous invaders. These immune benefits of breast milk result in fewer GI tract infections, ear infections, and respiratory tract infections for breast-fed babies.

Studies have found that breast-fed babies have reduced rates of childhood asthma and other allergies, lower rates of sudden infant death syndrome (SIDS), and reduced risk for developing type 1 diabetes. Breast-feeding advocates often cite reduced rates of childhood obesity as a positive impact of breast-feeding, which could help to explain why breast-fed babies have lower rates of type 2 diabetes and cardiovascular disease later in life.

Benefits to Mothers

The practice of breast-feeding offers several benefits to mothers. The hormone oxytocin that is released during breast-feeding stimulates the uterus to contract more quickly to its pre-pregnancy size. Oxytocin often is called the "bonding hormone," because it is associated with feelings of pleasure, love, and relaxation, which might help to explain why women who breast-feed have reduced rates of post-partum depression. Women who breast-feed appear to have a lesser risk for breast and ovarian cancers later in life. Because the production of milk in the mammary glands requires a large supply of calcium, research indicates that nursing mothers could lose bone mineral during lactation, although bone density appears to recover once lactation ends.

Breast-Feeding Recommendations

Public health experts and pediatricians in North American universally recommend breast-feeding exclusively for a baby's first six months of life, and continued

breast-feeding (in addition to appropriate solid food) for at least the first year. The World Health Organization recommends exclusively breast-feeding for the first six months, with continued breast-feeding for at least the first two years of a child's life. Longer breast-feeding practices are associated with improved infant survival and child health, better maternal health, and reduced health care costs for families and communities.

Contraindications to Breast-Feeding

Mothers infected with HIV or who have untreated tuberculosis are discouraged from breast-feeding in countries where safe infant formula can be obtained. Women taking any medications should check with their health care providers to be sure that breast-feeding is recommended. Many drugs make their way into breast milk and could have harmful effects on an infant.

Prevalence of Breast-Feeding

Until relatively recently in human history, breast-feeding has been the norm for infant nutrition. Mothers carried their infants throughout the day and fed them as needed. Royalty and upper-class women in some cultures hired other lactating mothers, often known as "wet-nurses," to provide their infants with breast milk. The practice of breast-feeding began to decline dramatically in the United States and Canada in the early 1900s, as infant formula and bottles became available. The popularity of breast-feeding began to increase in the 1960s, however, as research establishing the benefits of human milk and breast-feeding developed.

Government surveys estimate that, in the United States, presently about 75% of mothers begin breast-feeding their babies at birth, but less than 50% of mothers are still breast-feeding after 6 months. Many women introduce other sources of nutrition, including formula, and only about 16% of mothers feed their babies only breast milk for 6 months (CDC, 2011). Breast-feeding rates in Canada are higher, with more than 85% of mothers initiating breast-feeding at birth, and about 26% exclusively breast-feeding for at least 6 months (Health Canada, 2012). Factors associated with greater rates of breast-feeding include a higher level of education attained by the mother, greater household income, and a mother who is married rather than unmarried.

Challenges to Breast-Feeding

Despite the evident superiority of breast milk to infant formula, many women still choose not to breast-feed. Some mothers experience physical difficulties with breast-feeding. It can take several days to establish a breast-feeding routine that works for both mothers and babies. Babies initially might have difficulty latching on and drinking enough to support adequate growth and development. Some mothers experience a great deal of physical discomfort when breast-feeding.

Lactation consultants—professionals who specialize in breast-feeding—often can help resolve such issues.

Several social factors can interfere with breast-feeding. Partners and other family members might discourage the practice. Some cultural groups regard breast-feeding as unnecessary or a nuisance. A majority of women in North America today work for pay, and most work environments are not conducive to breast-feeding. Lactating employees must take several breaks during the day to either feed their babies or to pump and refrigerate their milk.

Environmental Impact of Infant-Feeding Practices

Breast-feeding is associated with a lesser environmental impact than that of formula feeding. Lactating mothers must consume more calories to produce milk, therefore their food consumption increases by about 600 calories per day. The environmental impact of this increased food consumption varies with the mother's food choices. The manufacture of formula has a greater impact, as it requires factories, supplies, and fuel. Formula must be placed in containers and shipped, often long distances, requiring more fuel. Plastic bottles, nipples, and other feeding paraphernalia also have environmental costs associated with their production, disposal, and recycling.

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Research Issues

The U.S. Centers for Disease Control and Prevention think that hospitals could do much more to promote breast-feeding practices, especially by providing support to new mothers and their families. Some of their suggestions can be found on the CDC website, listed in the Further Reading section.

See Also: Colostrum; Infant formula; Lactation.

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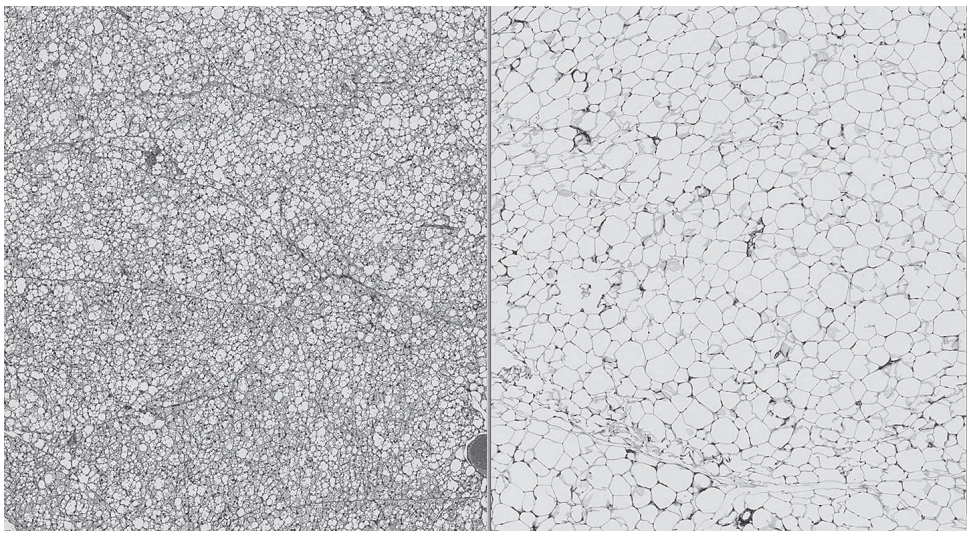
Brown Adipose Tissue

Brown adipose tissue (BAT), unlike white adipose tissue, is a special type of fat that is associated with positive health benefits. Greater levels of BAT are associated with lower measures of body mass index (BMI), a weight-for-height measure used to estimate obesity. In other words, people with more BAT are less likely to be obese. Once thought to play a negligible role in human physiology, researchers now believe that humans have significant amounts of BAT, and that this fat tissue acts as an endocrine organ, producing neurochemicals that influence processes such as blood glucose regulation and resting metabolic rate.

Brown adipose tissue seems to have been described as early as 1551, but it wasn't until the 1900s that it was recognized as being present in all mammals. Scientists initially were interested in the role BAT plays in generating heat, especially for mammals during their arousal following hibernation. This ability to produce heat plays an essential role in the survival of these mammals, which must function in a cold environment. The heat production by BAT also was recognized as providing a survival advantage for human infants—about 5% of an infant's body mass is BAT. Brown adipose tissue enables infants to generate heat without shivering, a process known as "non-shivering thermogenesis." Once thought to be present in significant amounts only in infants, nuclear imaging techniques have shown that BAT also is present in human adults (Ravussin & Kozak, 2009).

Brown adipose tissue contains a greater density of capillaries and mitochondria (the cellular organelles responsible for energy production) than that of white fat. Although most mitochondria produce adenosine triphosphate (ATP) to fuel metabolic processes, the mitochondria in BAT are "energy inefficient" for ATP production and produce heat from fuel precursors, such as glucose and fats, instead of producing ATP. In addition to keeping people warm, BAT appears to help them get rid of extra calories by "burning them up"—turning them into heat, rather than storing them (Ravussin & Galgani, 2011). Researchers have speculated that the higher levels of BAT in lean individuals as compared with obese individuals could partly explain differences in body composition. Greater levels of BAT might contribute to an increased resting metabolism and the ability to consume a more than average amount of calories without gaining weight.

Research suggests that regular exercise stimulates white adipocytes to become brown adipocytes (Bostrum et al., 2012). During exercise, a cellular messenger made in muscles and dubbed "irisin" (named after the Greek messenger goddess



Brown fat's color comes from its greater density of blood vessels. Brown fat is metabolically more active than white fat, expending more calories, and thus, helping to prevent excess body fat. (Vetpathologist/Dreamstime.com)

Iris) is produced. Irisin moves from the muscle to the bloodstream and appears to communicate with white adipose tissue, "telling" it to develop into BAT, especially in the visceral area. Increasing irisin levels in the blood of mice results in an increase in energy expenditure, with no changes in physical activity level or food intake (Bostrum et al., 2012).

Research suggests that BAT might play an important role in blood glucose regulation and energy balance. One interesting study transplanted BAT from healthy mice into mice that had developed pre-diabetes as a result of a high-fat diet (Stanford et al., 2013). After 8 to 12 weeks, the mice receiving the BAT transplant had decreased body weight and fat mass, and improved blood sugar regulation, increasing their insulin response to blood glucose. Brown adipose tissue appears to achieve these results in part because it increases levels of important signaling molecules that improve blood glucose regulation. This effect of BAT could help to explain why regular exercise, by increasing BAT, improves blood glucose regulation.

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Research Issues

Researchers hope that by understanding the signaling messengers—such as irisin, which is generated by brown adipose tissue—new drugs to treat obesity can be developed. Although availability of these drugs still is a long way off, pharmaceutical treatment of obesity generally has been disappointing, and new strategies are needed.

See Also: Adipose tissue; Energy balance; Obesity, definition and health effects.

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C

Caffeine

Caffeine is a bitter substance found in the seeds, leaves, and fruits of certain plants. Beverages made from these plant components also contain caffeine. The most commonly consumed caffeinated beverages are coffee and tea. Caffeine also occurs naturally in chocolate. Caffeine is added to many foods, beverages, dietary supplements, and over-the-counter drugs. It is somewhat addictive, and withdrawal symptoms include headache, fatigue, drowsiness, and irritability.

One of the most-studied drugs in the world, it has been consumed in some form for centuries by people in just about every culture. Research examining the effect of the consumption of caffeine and caffeine-containing beverages on health suggests that, in general, small doses do not appear to do too much harm to most people. Small-to-moderate amounts even can provide beneficial effects for some people. Caffeine does become harmful at higher doses, however, and some people are better off avoiding caffeine altogether.

Caffeine is similar in structure to the neurochemical adenosine, which slows brain activity. By blocking adenosine receptors caffeine blocks adenosine's effects. This explains caffeine's positive psychological effects, such as reducing feelings of fatigue, improving concentration, and enhancing mood. Caffeine's negative psychological effects, including increased anxiety, irritability, nervousness, and insomnia, also are a result of blocking the action of adenosine in the brain.

Considered a sympathomimetic drug, caffeine's effects mimic those of the sympathetic nervous system—the branch of the nervous system that produces the fight-or-flight stress response. This response causes heart rate, blood pressure, and muscle tension to temporarily increase as the body prepares to fight or flee in response to danger. Metabolic rate increases somewhat and appetite can be reduced, which is why many weight-loss products contain caffeine.

Sensitivity to the effects of caffeine varies considerably from person to person. Smokers remove caffeine from their bodies twice as fast as nonsmokers and thus could be less sensitive to caffeine's effects. People who rarely consume caffeine generally are much more sensitive to caffeine's many effects, but people accustomed to caffeine experience less-pronounced reactions.

Most adults appear to self-regulate caffeine consumption fairly well. They learn—perhaps through trial and error—what amount of caffeine helps them feel alert and productive and at what point to stop consuming it before any

negative effects develop. Negative side effects, such as stomachache, nausea, nervousness, insomnia, and anxiety, encourage most people to limit caffeine consumption.

Some people, however, develop negative symptoms from very small doses of caffeine and therefore should avoid it entirely. Experiencing any of the effects listed below suggests that one should limit or eliminate caffeine intake.

- Irregular heartbeat: Some people experience an irregular heartbeat when they consume caffeine. Their hearts feel like they are beating much too fast or are "skipping beats."
- Feelings of stress and anxiety: Many people experience feelings of stress and anxiety when they consume caffeine. Adding insult to injury, people also are more likely to overindulge in caffeine when they feel stressed. Yet, because caffeine's effects mimic the stress response, it can leave people feeling even more stressed.
- Insomnia: People who suffer from difficulty sleeping should try reducing or giving up caffeine to see if this solves the problem. Some people find that even when they consume caffeine only in the morning it aggravates sleep problems that night.
- High blood pressure: Blood pressure rises for a fairly short time following caffeine ingestion. Although this rise does not appear to be harmful for most people, those with hypertension might benefit by reducing caffeine intake.
- High intake: High intake of coffee and other caffeinated products has been associated with some health problems, such as increased risk for ovarian and pancreatic cancers. Risks usually are associated with consuming more than five cups of coffee per day (Lueth, Anderson, Harnack, Fulkerson, & Robien, 2008).
- Bone density and osteoporosis: Some studies have suggested a link between caffeine consumption and the risk of osteoporosis in elderly women. This has not been found, however, for younger women who drink just a cup or two of a caffeinated beverage a day (Cooper et al., 2009).
- Reproductive concerns: A high caffeine intake might interfere with fertility, therefore couples having difficulty conceiving should try reducing caffeine. High caffeine consumption during pregnancy is associated with birth defects in laboratory animals, and with miscarriage and low birth weight in humans, therefore only small amounts of caffeine (or none) should be consumed during pregnancy (Patel & Rizzolo, 2012). Caffeine makes its way into breast milk, and nursing mothers who consume caffeine could end up with irritable, fussy babies who have trouble sleeping.
- Ulcers and heartburn: Coffee, not caffeine, increases the production of stomach acids, therefore decaffeinated coffee is not a solution for related problems. People having digestive problems should reduce coffee intake or switch to tea.

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Research Issues

Many people have suggested that the caffeine content of food, beverages, supplements, and over-the-counter drugs should appear on the label. It is easy to consume caffeine without realizing how much one is ingesting. Caffeine is added to many body-building and sports supplements, for example because it has a slightly ergogenic effect, allowing people to work harder than they work without caffeine. Caffeine also can give users a more positive feeling, and thus make users more likely to consume the supplement again. Caffeine also works to reduce perception of pain, so it is added to many pain-reliever formulations. Tables of caffeine content in familiar foods are available from the Center for Science in the Public Interest (CSPI) (http://www.cspinet.org/new/cafchart.htm), but labeling would further reduce guesswork.

See Also: Chocolate; Coffee; Energy drinks; Tea.

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Calcium

Calcium is the most abundant mineral found in the human body and plays a key role in a variety of functions. Not only is calcium essential to maintain the structural integrity of bones and teeth, it also is necessary for signaling and enzymatic processes in blood vessels, neurons, and the endocrine system, and plays an important role in muscular contraction. Calcium is found in a variety of foods and dietary supplements and has many health-related effects.

Calcium is an essential nutrient that must be consumed for a person to maintain health. It is absorbed in the body by two different mechanisms. When calcium is consumed, either from a food or supplemental source, it moves through the esophagus and stomach until it reaches the small intestine. In the small intestine,

calcium passes into the endothelial lining of the duodenum via active transport. Once inside the cell, the calcium molecule binds to the carrier protein, "calbindin," whose formation is dependent upon vitamin D. Calbindin transports calcium to the basal membrane (where the absorptive cell of the digestive tract communicates with the bloodstream), where calcium is actively pumped out of the cell and into the bloodstream. After entering the bloodstream, calcium is transported throughout the body to perform its many functions. If calcium intake is high, then the mineral also is absorbed in the jejunum and ileum via passive diffusion then passes through the tight junctions and into the bloodstream.

The amount of calcium that is absorbed depends on the calcium source, the amount taken at one time, the person's age, vitamin D availability, and other food components. On average, people absorb about 30% of the calcium they consume. Increased levels of vitamin D allow for more calcium to be absorbed from the gastrointestinal tract. Absorption rate is highest during peak growth times of life, including infancy, puberty, and pregnancy. As people age, their ability to absorb calcium declines. Oxalic acid, which is found in many vegetables, and phytic acid, found in greens, also can reduce the amount of calcium that is absorbed. Two major forms of calcium, citrate and carbonate, are found in most calcium supplements. Calcium carbonate is best absorbed when it is taken with food and calcium citrate can be absorbed with or without food.

Calcium is found in many foods, but is highest in concentration in dairy products such as milk, yogurt, and cheese. It also is found in many vegetables including Chinese cabbage, kale, and broccoli as well as in fish with edible bones. Grains, such as bread, pasta, and cereals naturally have very little calcium in single servings, but because they often are eaten in large quantities they can be a source of calcium. Grains and other foods also commonly are fortified with calcium and therefore can be good sources of the mineral. Many people take calcium citrate or calcium carbonate in the form of dietary supplements.

Excess calcium is stored in bones and teeth, and 99% of the body's calcium can be found in these structures. Blood calcium levels are highly regulated and when calcium levels become too low more is released from the bones into the blood. Throughout life, bones are continuously being remodeled. During times of growth, however, more bone is being built than broken down, therefore it is important to have a sufficient calcium intake. Thus, recommended calcium intake differs with age, sex, and stage of life.

Infants, growing children, and adolescents require significant amounts of calcium to grow strong bones. In the United States and Canada, the Recommended Dietary Allowance (RDA) for calcium suggests that both males and females ages 9 to 18 years old consume 1,300 mg per day, because bone is being formed. During early and middle adulthood bones reach peak bone mass (at ~30 years old), and at this point the rates of building and breakdown are the same. For people ages 19 to 50 years old, the RDA is 1,000 mg per day of calcium. In aging adults and postmenopausal women, more bone is being broken down than is being built. Women older than age 50 and men older than age 70 should consume 1,200 mg of calcium per day. Pregnant and lactating women should try to consume 1,300 mg per day.

Young women with amenorrhea, due either to low caloric intake or too much exercise, have lower calcium absorption (because of reduced estrogen levels), which puts them at risk for inadequate calcium levels. Lactose intolerance and vegan diets, due to a lack of dairy products, also are often found to cause low calcium levels. Not only can calcium deficiency be caused by malabsorption or low intake, it can be due to increased excretion from the body. Calcium excretion in the urine increases when there is high protein and high sodium intake. Excretion also can be affected by some medicines (Office of Dietary Supplements, 2013).

Calcium performs important roles in bone as well as in other tissues. In bones, calcium becomes part of a crystalline structure called hydroxyapatite, which surrounds collagen. Osteoblasts and osteoclasts work to form and dismantle bone, respectively. Calcium is important for bone strength, but can be released into the bloodstream when it is needed in other body tissues and to maintain a constant blood calcium concentration. The process of turning bone into calcium is regulated by vitamin D, parathyroid hormone, and the hormone calcitonin.

When calcium is not being stored in the bones it is aiding in many other functions. In neurons, action potentials travel down axons and trigger a calcium release. This calcium release causes vesicles within the neuron to release neurotransmitter into the synapse, to propagate the nerve signal throughout the body. In muscles, the neurotransmitter acetylcholine is released onto the muscle cells, which leads to downstream calcium release within the muscle fibers. The calcium molecules bind to proteins that are part of the contractile machinery, controlling muscle contraction. Calcium also can bind to the protein calmodulin. The calcium-calmodulin complex plays a part in regulating secretion, cell division, and the movement of cilia. Calcium also is important for blood clotting.

Too much or too little calcium can influence a wide range of health issues. Adequate levels of calcium must be consumed to reach peak bone density by age 30. If not enough calcium is absorbed to replace bone calcium loss, low bone mineral levels and, eventually, osteoporosis can develop. Osteoporosis is a disease of porous and fragile bones that affects more than 10 million adults in the United States, 80% of whom are women (Office of Dietary Supplements, 2013). Studies show that getting adequate calcium might reduce risk of hypertension. Some studies have found that high calcium consumption lowers the risk of colon and renal cancers as well as reducing the risk of nonmalignant colon tumors. Conversely, other research, such as the results of the Women's Health Study, does not show a correlation between calcium levels and colon or rectal cancer. Some studies even suggest that high calcium intake increases the risk of prostate cancer.

Many studies have attempted to elucidate the effect of calcium on cardiovascular disease (CVD). It is thought that by decreasing the intestinal absorption of lipids, relatively high levels of calcium could decrease the risk of CVD. Recent studies found that men who ingested more than 1,000 mg per day of supplemental calcium, however, had a 20% increase in their risk of CVD. Results from the Women's Health Initiative suggest that taking calcium supplements increased the risk of CVD in women, but results from the Women's Health Study found that calcium decreased the risk. Experts agree that, at some level, high intakes of

calcium can lead to hypercalcemia, which is high blood calcium. Hypercalcemia can lead to increased blood clotting, calcification of the blood vessels, and stiffening of the arteries, all of which contribute to cardiovascular disease (Xiao et al., 2013). Experts recommend that calcium be obtained from food rather than supplements when possible, as risks appear to be higher with supplements. Additionally, upper limits for calcium have been set at fairly low levels to discourage high consumption of calcium. The U.S. and Canadian recommendations for upper limits of calcium intake are 2,000 mg per day for people older than age 51, 2,500 mg per day for people ages 19 to 50, and 3,000 mg per day for people ages 9 to 18.

Calcium might interact with certain medications. It can reduce the absorption of bisphosphates, fluoroqinolones and tetracycline antibiotics, levothyroxine, phenytoin, and tiludronate disodium. Diuretics also have been found to decrease calcium excretion in the kidneys which increases blood calcium concentration. Glucocorticoids, mineral oil, laxatives, and antacids with magnesium or aluminum can lead to reduced blood calcium levels.

Renée J. Robilliard

Research Issues

Not everyone agrees with the high calcium Daily Recommended Intakes of the United States and Canada. In many countries calcium intake is about 300 mg to 600 mg per day, compared with the recommended 1,000 mg to 1,200 mg per day for Americans, depending on age. Osteoporosis rates are very low in many of these countries, perhaps because citizens get more exercise or sun exposure (Harvard School of Public Health, 2013).

See Also: Cardiovascular disease and nutrition; Female athlete triad; Osteoporosis.

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Calorie

A calorie is a unit of heat energy, and the term comes from the Latin root for heat, "calor." A calorie is the amount of energy needed to raise the temperature of one gram of water by one degree centigrade under standard conditions. Because the heat absorption capacity of water changes with water temperature, water temperature should be defined for calorie definitions. Standard initial water temperature is usually defined as 14.5 degrees C, at 1 atmosphere pressure. In common usage, the term calorie also refers to energy, both the energy contained in food and the energy expended by animals, including humans. On food labels, the term calorie generally refers to a kilocalorie (kcal) (1,000 calories) and is the amount of energy needed to raise the temperature of one kilogram of water by one degree centigrade. Sometimes the term "Calorie" (rendered with an initial capital letter) is used to represent kilocalorie. A calorie is equal to approximately 4.184 joules.

The calorie first came into use as a unit of heat energy in early 19th-century France, when Nicholas Clément introduced the term in a series of lectures on the fuel efficiency of steam engines. Several decades after its first use, the term was translated into English and came to represent the energy needed to raise the temperature of water. The use of calories in relation to human dietary needs was popularized in the United States by W. O. Atwater in 1887, after he used calories in his articles on food and in his tables of food composition (Hargrove, 2007). At the start of the 20th century, the word became further entrenched in common usage in the United States, due in great part to the USDA Farmers' Bulletins food databases. From there, as Americans became increasingly interested in weight management, the word began appearing in articles and books, garnering the interest of nonscientists across the country. The calorie was adopted for use in the nutritional facts panels on U.S. food labels, in contrast to the many other countries that use kilojoules rather than kilocalories in describing food energy content.

Continued use of the calorie in a nutrition context is a practice mostly isolated to the United States and the United Kingdom. Although the calorie predates the joule as a unit of food energy by nearly 60 years, many nations officially transitioned from the use of the calorie to use of the joule in 1954, when the International System of Units (SI) was adopted (Hargrove, 2007). Within the SI system, the unit for energy in any form is the joule (J), which—in direct contrast to the comparatively ambiguous nature of the calorie—corresponds with energy measurements and conversion factors in all other SI-based branches of science (Food and Agriculture Organization of the United Nations, 1971). Regardless of its context within the realm of international scientific standards, however, the calorie remains the primary unit of food energy for hundreds of millions of consumers around the world.

As units of food energy, calories convey how much energy is stored in a food's chemical bonds waiting to be released when the body breaks down those bonds for its own energy. Chemical bond energy is measurable in the form of heat given off during the oxidation of a given substance. The chemical bond energy in a particular food can be determined using a calorimeter. This device functions by completely

burning a given food sample in a chamber that is surrounded by a fluid, such as water. The temperature change of the fluid reflects the energy value of the food. Temperature change then can be directly converted into calories. In a similar fashion, calorimetry can measure energy expenditure in people and animals. For example, a person could be placed in a chamber surrounded by water. The heat given off by the person causes an increase in the water temperature, which is measured and converted to calories.

The calorie content of food as measured by calorimetry probably does not exactly match the calories actually captured by people with the processes of digestion, absorption, and metabolism of food (Nelson & Zeratsky, 2013). Nevertheless, calorie counts on food labels still provide a helpful guide for evaluating the relative energy content of foods. In general, carbohydrates and proteins provide 4 kcals per gram; fat provides 9 kcal per gram; and alcohol contains 7 kcal per gram.

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See Also: Energy balance; Metabolic rate; Metabolism.

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Cancer and Nutrition

Cancer is a class of more than 100 diseases that is characterized by unregulated cell growth. Cancer begins with changes to a cell's genetic material, its DNA, which alter the cell's normal behavior. Rather than growing, dividing, and dying in a typical way, cancer cells do not stop dividing—producing abnormal cells that continue to reproduce. In most types of cancer (the exception is cancers of the blood cells), the abnormal cells accumulate and cause the formation of masses of tissue called "tumors." Malignant (cancerous) tumors eventually can crowd and replace healthy

tissue, interfering with organ function. Malignant tumors also can release cells that travel to other parts of the body, via the lymphatic system or bloodstream, in a process called "metastasis," in which the cells invade other organs and cause new tumors. The transformation that produces cancer cells from normal cells involves multiple steps. Only about 5% to 10% of cancers seem to be caused primarily from inherited genetic factors. The rest are believed to be caused by repeated damage to DNA and the cells over time by environmental factors, such as radiation, viruses, and chemicals. Lifestyle behaviors, including smoking, unprotected sexual activity, sun exposure, physical activity, and diet contribute to cancer risk by causing genetic changes or by influencing other factors that help or hinder cancer cell growth and development. In the United States, researchers suggest that about one-third of cancer deaths can be attributed to tobacco use, and another third is linked to poor diet and inadequate physical activity, including obesity and being overweight (Kushi et al., 2012). The causes and risk factors for many cancers, however, are unknown.

The word "cancer" has been traced to Greek physician Hippocrates, who lived around 460 BCE to 370 BCE. In his writings, Hippocrates described several kinds of cancer tumors with the Greek words "carcinos" and "carcinoma," from the Greek word for crab, presumably from the projections reaching out from the tumor body that produced a crab-like shape (ACS, 2014). Another Greek physician, Galen, who lived and worked in the second century CE, used the word "oncos," which means "swelling," to describe the tumors he observed (ACS, 2014). Today, the word "oncologist" refers to a cancer specialist.

Approximately half of all men and one-third of all women in the United States will face a cancer diagnosis at some point during their lives (ACS, What is cancer? 2012). Many cancers are curable, especially if caught early; there are millions of cancer survivors in the United States and around the world. Nevertheless, cancer is a leading cause of death, with 8.2 million deaths worldwide being attributed to cancer in 2012 (WHO, 2014). For men in the United States, the most common cancers that cause death are cancers of the lung and bronchus, prostate, colon and rectum, pancreas, and liver. For women, the leading causes of cancer deaths are cancers of the lung and bronchus, breast, colon and rectum, pancreas, and ovary (ACS, Cancer Facts & Figures 2012, 2012). The many types of cancer differ significantly from one another in terms of causation, risk factors, diagnosis, and treatment. Dietary recommendations for cancer prevention, however, are similar for the types of cancer that appear to be influenced by diet.

Research on cancer and lifestyle behaviors can identify "in the long run, on the average" cancer risks; it cannot explain why any given individual develops cancer. Many people with healthful lifestyles still develop cancer, but others with multiple cancer risk factors never do.

The Processes of Cancer

The development of cancer is a complex, multistep process. It involves changes in a cell's DNA as well as the metabolic pathways in which proteins that influence

cellular function are created from the DNA template. It also is influenced by the processes involved with cell division and differentiation. These changes generally occur over a long period, often decades. Food components can influence these processes—both positively and negatively—at every step.

Cancer begins with changes in a cell's genetic material, the DNA that resides in the chromosomes found in the nucleus of the cell. These initial changes are caused by carcinogens, typically chemicals (e.g., asbestos and formaldehyde), microbes (e.g., hepatitis C virus, some strains of human papilloma virus), or radiation (ultraviolet light; x-rays) that alter the DNA. Researchers estimate that cells and their DNA experience hundreds of injuries each day that have the potential to cause the DNA changes that lead to cancer (WCRF/AICR, 2007). Fortunately, very few of these cause harm. Some damage does not influence the genes that lead to cancer. Often, DNA repair mechanisms fix or eliminate damaged sections, including those that might cause cancer; and cells could die before the damage becomes permanently captured in daughter cells. Over time, however, DNA damage can accumulate. Carcinogens and other compounds also can cause cell damage by altering how DNA is translated (or not) into proteins; influencing DNA repair mechanisms; and affecting communication among cells within a tissue.

Cells respond to a wide variety of messenger molecules known as "cytokines," which help to stimulate or suppress cell division and differentiation, and cell death ("apoptosis"). Some compounds (dietary and other) favor the proliferation of potentially cancerous cells over normal cells through a variety of pathways, a process known as "promotion." Estrogens are believed to be promoters for certain types of cancer, for example, because they increase the proliferation of cells in the breast, and over time, increase the risk of some types of breast cancer. Some systemic factors—such as high levels of oxidation and inflammation—favor the development of cancer by setting the stage for more DNA damage and increased levels of growth factors that signal cells to replicate (WCRF/AICR, 2007).

Bioactive substances in the diet—including nutrients and phytochemicals—can enhance or inhibit cancer development via these pathways and processes. Dietary factors also can influence the strength of the immune system, which in some cases attacks cancer cells in the body. Dietary factors can inhibit the process of angiogenesis (the formation of new blood vessels) that, in the context of cancer, provide oxygen and nutrients and remove wastes from growing cancerous tumors.

Cancer and Nutrition

Research suggests that some foods and beverages and their components, as well as overall dietary patterns, are associated with cancer risk. In addition to the foods themselves, agricultural and food-processing practices, along with methods of food preservation and preparation also influence cancer risk (WCRF/AICR, 2007). It has become apparent that excess body fat, which itself is influenced by dietary pattern as well as physical activity, increases cancer risk.

Identifying helpful and harmful foods, food components, and dietary patterns is difficult for a number of reasons. People consume a wide variety of foods each day, and a person's diet also can vary considerably from day to day; thus, simply obtaining accurate food records from people is challenging. Individuals generally consume more than 25,000 bioactive food constituents—including nutrients and phytochemicals—in any given diet, so it is not easy to tease out the influence of a specific compound (WCRF/AICR, 2007). Results obtained in the laboratory with in vitro cell cultures could have little relevance for humans. For example, although beta-carotene slows cancer cell growth in vitro, use of beta-carotene supplements by former smokers is associated with an increased, rather than decreased, risk of lung cancer.

Dietary compounds interact with the digestive system and other constituents from food as food is broken down and absorbed. Too much supplementary vitamin E (which usually is available as d-alpha tocopherol), for example, can block the uptake of the other seven types of vitamin E that occur in the diet, or of other important compounds. After digestion and absorption, potentially helpful nutrients and phytochemicals travel in the bloodstream and are metabolized and stored via various biochemical pathways in the liver, kidney, and other organs—they might never even come into contact with cancerous cells. If they do, they could behave differently in the body than they do in the lab. Animal studies can be helpful, but might not always apply to people. Dietary components probably influence different people in different ways, depending upon their genetics, as demonstrated in the fields of nutrigenomics and nutrigenetics.

To further complicate research on nutrition and cancer, the influence of a given factor upon cancer risk depends upon dose of the nutrient or other phytochemical. Many compounds are ineffective at low doses, helpful at moderate doses, and harmful at high doses. Timing in the life cycle also can shape the influence of particular dietary factors on cancer risk. For example, as compared to adequately fed females, women who experience famine before the age of 10 have a reduced risk of precancerous breast tissue later in life, and women who experience famine after the age of 18 have greater risk (WCRF/AICR, 2007).

The World Cancer Research Fund and the American Institute for Cancer Research administer ongoing reviews of cancer-related research (WCRF/AICR, 2014). In addition to periodic reports, the agencies also strive to keep their database of research current through the Continuous Update Project (WCRF/AICR, 2014). Expert panels release dietary guidelines that reflect their analysis of the research conducted to date. Their recommendations include the following.

- Be as lean as possible within the normal range of body weight. The panel advises that people should avoid excess weight gain at all ages, and especially avoid becoming overweight or obese. Evidence linking cancer risk, including cancer mortality, to excess body fat has grown significantly in recent years. Extra body fat increases level of inflammation throughout the body, and promotes the growth of many types of cancer.

- Be physically active as part of everyday life. Physical activity levels should be appropriate for the individual's health and fitness. Research suggests that public health guidelines for physical activity are a good start, but that more is generally better in terms of reducing cancer risk. Physical activity reduces inflammation and contributes to healthful body fat levels.
- Limit consumption of energy-dense foods and sugary drinks that promote weight gain. To reduce cancer risk, the panel advises replacing foods with little nutrition value with healthful foods, especially vegetables.
- Eat mostly plant foods. Consume at least five servings of non-starchy vegetables and fruits each day. Consuming additional servings—especially of vegetables—is even more beneficial. Relatively unprocessed grains and legumes are preferred over refined products, as consumption of refined starchy foods should be limited. A diet based mostly on plant foods has high levels of many nutrients, phytochemicals, and dietary fiber, which all are linked with reduced cancer risk. Plant-based diets also tend to be low in red and processed meat, and foods made with refined grains and added sugars.
- Limit intake of red meat and avoid processed meat. Red meat refers to beef, pork, lamb, and goat. Processed meats include meats that are salted, smoked, cured, or have preservatives added, and include hot dogs, sausages, salami, pepperoni, ham, and many deli meats. These meats have been linked with increased cancer risk, partly due to the dietary patterns in which they are found, but also because of the cancer-causing chemicals such as nitrosamines that form from red meat components such as carnitine. Polycyclic aromatic hydrocarbons, which are produced in meats cooked at high temperatures, have been shown in human epidemiological studies to increase the risk of cancer. According to a report from the National Cancer Institute (2010) researchers found that "high consumption of well-done, fried, or barbecued meats was associated with increased risks of colorectal, pancreatic, and prostate cancer."
- Avoid or limit alcohol. Alcoholic drinks all increase cancer risk in a dose-related fashion, with no health benefits associated with light or moderate drinking (unlike the relationship between alcohol intake and cardiovascular disease). Even consuming just 1 or 2 drinks per week increases risk of breast cancer, for example. Scientists do not understand exactly how alcohol increases risk, although they know that one of the products of alcohol metabolism—acetaldehyde—is a carcinogen. Alcohol also might increase cancer risk because it can increase a woman's blood estrogen level.
- Avoid salted-preserved, salted, and salty foods. These have been associated with an increased risk of stomach cancers.
- Limit exposure to aflatoxins by avoiding moldy grains and legumes. Aflatoxins are carcinogenic compounds produced by certain species of mold, most common in corn and peanuts.
- Aim to meet nutritional needs through diet alone. Research on dietary supplements is not very supportive using supplements to prevent cancer. Although

evidence for some supplements occasionally suggests beneficial effects, there usually is equal evidence for a given supplement as showing no effect and, in a few cases, as causing harm. The WCRF/ACRI experts acknowledge that dietary supplements can be helpful for some people in certain situations, such as vitamin B12 for vegans. Dietary supplements even might be advised for the prevention of a few cancers. The panel recommends that a person meet with a qualified nutrition expert to determine which supplements might be individually recommended. The panel, however, discourages supplement use on a general basis. Even though supplements might provide a few dietary components, they do not provide the thousands of components that occur naturally in a plant-based whole-foods diet.

Barbara A. Brehm

Research Issues

Why does obesity increase cancer risk? Obesity might contribute to cancer risk in several ways. Scientists are examining certain biochemical pathways that could help to explain this risk. Obesity is associated with insulin and leptin resistance, for example. Chronically elevated blood insulin and leptin levels increase the production of certain growth factors that stimulate cell proliferation, potentially increasing the growth and reproduction of potentially cancerous cells. Enzymes in adipose tissue convert sex hormone precursors to active hormones—including estrogens—in women. Increased estrogen levels are associated with cancers of the breast and uterus. The World Cancer Research Fund/American Institute for Cancer Research report in the Further Reading section provides more information on the biochemical mechanisms associated with a variety of cancer risk factors, including obesity.

See Also: Alcohol; Antioxidants; Beta-carotene; Carnitine; Dietary supplements; Fiber; Food additives; Heterocyclic amines and polycyclic aromatic hydrocarbons; Inflammation; Nutritional genomics; Obesity, definition and health effects; Phytochemicals; Phytoestrogens; Sodium and salt; Vegetarian and vegan diets; Vitamin E.

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Capsaicin

Capsaicin is a chemical compound found in many types of hot peppers and often is isolated for medicinal purposes. Jalapeno, habanero, chili, and cayenne peppers all owe their spicy flavor to the capsaicin found in the placenta tissue surrounding their seeds. According to the Scoville Heat Index, a measure of capsaicin content, habaneros contain the highest concentration of capsaicin, with a variety in the Yucatan containing more than 300,000 Scoville units. Pure capsaicin reaches up to 16,000,000 Scoville units. The compound is an irritant to mucous membranes, and produces a painful burning sensation by binding to receptors in the cell membrane of sensory receptors. This action releases a chemical called "substance P," which sends the brain the same pain signal as an abrasion or burn might.

Despite its ability to invoke the sensation of pain, capsaicin is the critical ingredient in topical analgesics for chronic pain relief, used often for arthritis, peripheral neuropathy, fibromyalgia, and back pain. It causes an initial spike in the release of substance P which results in a brief burning sensation, but which also depletes neurons of this pain-signaling chemical so that the brain can no longer perceive messages of pain from affected neurons (De Silva., El-Metwally, Ernst, Lewith, & Macfarlane, 2011). Capsaicin creams also are recommended for some skin conditions that are accompanied by itchiness, such as psoriasis. Although these creams offer temporary relief from pain or itchiness, their effects are fairly mild and are not long lasting.

Research in laboratory animals suggests that capsaicin might contribute to heart health in several ways (American Chemical Society, 2012). It appears to help lower serum levels of LDL cholesterol, and even contribute to the regression of atherosclerotic plaques. Capsaicin also seems to block the activity of a gene that causes the small muscles around arteries to contract, which increases blood pressure because of increased resistance to blood flow. By blocking this action, capsaicin allows blood vessels to open and accommodate more blood flow at a lower pressure, thus lowering arterial blood pressure. Capsaicin also shows antioxidant activity.

Interesting research on capsaicin and cancer suggests that pure capsaicin inhibits its activation of carcinogens and induces cancer cell apoptosis (cell death) in human cancers in vitro and in human cancers transplanted onto laboratory rodents (Bley, Boorman, Mohammad, McKenzie, & Babbar, 2012). These results counter epidemiological research that had suggested that capsaicin actually might act as a carcinogen in humans. The carcinogenic culprits appear not to be capsaicin per se, but rather the pesticides, insecticides, herbicides, fertilizers, molds, and other contaminants that can enter the body with hot peppers. In one analysis, 55% of hot peppers in the United States was found to be contaminated with a variety of 51 different pesticides (Environmental Working Group, 2010). In any case, research on capsaicin and cancer is too preliminary to recommend specific cancer prevention intakes of either capsaicin or hot peppers. Indeed, the U.S. FDA issued a warning against this action to a dietary supplement manufacturer in 2011 (US FDA, 2011). Consumers who enjoy spicy foods should use organic sources of hot peppers.

Capsaicin is available as a supplement that sometimes is referred to as cayenne pepper in its over-the-counter form. It stimulates digestion by increasing the production of gastric juices. Although evidence is not conclusive, capsaicin also might help increase the body's metabolic rate and therefore contribute to weight-loss efforts.

Patricia M. Cipicchio and Barbara A. Brehm

See Also: Cancer and nutrition; Dietary supplements.

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Carbohydrate Loading

Carbohydrate loading refers to the practice of manipulating diet and physical activity to maximize the storage of glycogen in the liver and skeletal muscles. Glycogen is a type of starch consisting of many glucose units, and is the body's primary form of carbohydrate storage. The body manufactures glycogen from dietary carbohydrates. Carbohydrate loading is practiced primarily by endurance athletes before important contests, with the goal of beginning the contest with optimal glycogen stores. Carbohydrate loading sometimes is recommended to patients prior to surgery, so that they begin the recovery period with a good energy supply. Carbohydrate-loading practices can stimulate muscle and the liver to store greater than normal amounts of

Maintaining Optimal Energy Stores

Athletes vary in their response to carbohydrate-loading protocols. Many athletes are disappointed with carbohydrate-loading results, or think that the minimal results are not worth the time and effort required by the protocols. Success in endurance athletic events is more related to months of well-planned training and nutrition support rather than carbohydrate loading for a short period before a contest.

Suggestions for maintaining optimal glycogen stores throughout the training process include the following (ADA, 2009).

- Train regularly for the sport. Training increases the ability of muscles to store and use glycogen, thus the muscles required for the sport become very good at storing and using energy. Muscles also get better at using fat for energy, which results in a "glycogen-sparing" effect; the glycogen stores last longer.
- Consume food or drink with plenty of carbohydrate and some protein within an hour following each practice or competition. The muscles' glycogen storage chemistry is in high gear following exercise, so give them the carbohydrate they need to pack in energy for the next workout or competition. It can take 24 to 48 hours to replenish glycogen stores, so start right away.
- Be sure to include carbohydrate foods in meals or snacks that follow vigorous exercise. Include carbohydrate foods in other meals as well.
- Alternate difficult and easy training days, and give the body at least one day of rest each week. Taper off before important contests. Rest allows glycogen stores to build to optimal levels, in addition to allowing the body adequate time for recovery.

glycogen. People vary in their responses to carbohydrate-loading regimens, but the bulk of the evidence suggests that the practice generally improves both glycogen stores and athletic performance (ADA, 2009).

Importance of Glycogen for Endurance Activity

The body's primary sources of energy for physical activity are glycogen and fat. Muscle glycogen provides fuel for muscle contraction, and liver glycogen provides a steady supply of glucose to maintain optimal blood glucose (blood sugar) levels. The brain relies primarily on glucose delivered by the blood for fuel, therefore when blood glucose levels fall hypoglycemia results, presenting symptoms such as nausea, disorientation, fatigue, and confusion. These symptoms interfere with performance.

The body relies heavily on glycogen for moderate- to high-intensity exercise. Low-intensity activities such as walking primarily rely on stored fat for energy, and low to moderately intense activities such as jogging use both fat and glycogen for fuel. About 50% to 60% of energy used during one to four hours of continuous, moderately vigorous activity comes from carbohydrates (ADA, 2009). The rest is supplied by fat and some protein.

On average, people can store roughly 2,000 kilocalories of energy as glycogen, although this varies considerably with a person's size, training status, and diet. Liver and muscle glycogen stores can run low after about 90 minutes of endurance activity. It is important to note that glycogen stored in non-exercising muscles is not readily available to the exercising muscles. This means that the body can't really access all of the stored muscle glycogen.

Endurance athletes are particularly concerned about maximizing glycogen stores for training and performance. Optimal glycogen stores depend on an adequate intake of dietary carbohydrates. Research suggests that many athletes could improve their performance by consuming greater amounts of carbohydrate (ADA, 2009). Glycogen stores need not be depleted to be suboptimal. Some athletes consistently might consume somewhat less than optimal carbohydrate intakes for the energy demands of their sport.

Carbohydrate Loading and Pre-Surgery Nutrition

For surgical patients, glycogen loading appears to reduce risk of surgical complications, speed recovery, and reduce the length of a hospital stay. Carbohydrate loading usually is employed as a component of optimal preoperative nutrition that also includes immune-enhancing foods and supplements. Researchers have found that entering surgery in a fed rather than a fasted state (patients usually are told to fast at least eight hours prior to surgery), by using special carbohydrate drinks, does not interfere with anesthesia procedures. It also helps keep the body in an anabolic state (building tissue up rather than breaking it down), which enhances healing and reduces the lean body mass loss associated with bed rest (Kratzing, 2011).

Carbohydrate Loading and Athletic Performance

Many endurance and ultra-endurance athletes engage in carbohydrate loading in hopes of boosting their glycogen stores to even greater levels than normal. Another word for carbohydrate loading is "glycogen supercompensation." The idea is to stimulate production of the enzymes responsible for storing glycogen by sending the message that energy demands are high and that current glycogen stores are inadequate. Early experiments in glycogen loading had athletes "strip" glycogen supplies by exercising to exhaustion a week before a major competition, and then follow with three days of a low-carbohydrate diet with moderate training, leaving the muscles and liver glycogen depleted. Three days of high-carbohydrate intake followed, with little exercise performed. This resulted in increased glycogen stores (Ahlborg, Bergström, Ekelund, et al., 1967).

Most people find this procedure difficult and fatiguing. Many athletes report feeling lethargic and depressed if they train when carbohydrate intake is low. Researchers also have expressed concern that such extreme dietary manipulation could lead to the loss of muscle tissue and to other negative health effects, including increased risk for upper-respiratory infections because of immune-system suppression.

Fortunately, the low-carbohydrate diet phase does not appear to be essential for stimulating extra glycogen storage. A gradual combination of tapering exercise volume and increasing carbohydrate intake seems to be just as effective for improving athletic performance. Most endurance athletes who use carbohydrate loading simply incrementally reduce exercise, and maintain a high intake of carbohydrates (approximately 10 g/kg body weight/day) for three or four days before competition.

Some researchers have experimented with other loading methods. One interesting study had seven male cyclists perform three minutes of very hard cycling, and then consume a very high carbohydrate diet (about 10 g carbohydrate per kg body weight) during the following 24 hours (Fairchild et al., 2002). The researchers found that glycogen stores doubled from the previous day's pre-exercise levels.

Individual responses to carbohydrate loading and, indeed, to any type of dietary manipulation vary tremendously. Several studies have questioned whether any kind of carbohydrate loading—aside from providing adequate carbohydrate in the diet—improves performance. Results regarding the effectiveness of carbohydrate loading for female athletes have been somewhat mixed, but experts suggest that women generally do improve performance when extra calories along with extra carbohydrates are added to the diet for several days before competition (ADA, 2009).

Carbohydrate loading can have several potentially negative effects. Athletes must practice any type of dietary change during training, not during competition. Athletes who add new foods or change the volume or timing of food intake can experience abdominal cramps or diarrhea. Successful carbohydrate loading adds two to four pounds (one to two kg) of body weight. This is mostly water weight, because each gram of carbohydrate is stored with three grams of water, but the extra weight bothers some athletes.

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Research Issues

Most carbohydrate-loading studies have used male subjects, partly because female subjects can vary somewhat in their glycogen-storing capacities depending upon the phase of their menstrual cycle, and researchers don't want this variable to interfere with the results (ADA, 2009). Data on female subjects also have been more variable, as some study subjects restrict calorie intake and thus could fail to achieve adequate carbohydrate intake.

See Also: Blood sugar regulation; Carbohydrates; Glycemic index and glycemic load; Hypoglycemia; Sports nutrition.

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Carbohydrates

Carbohydrates are a large group of organic molecules that include sugars, starches, and some types of dietary fiber. The word "carbohydrate" comes from the raw materials from which carbohydrates are made. Plants make carbohydrates from carbon dioxide (source of the term "carbo") and water (hydrate), using energy from the sun. All carbohydrates contain only carbon, hydrogen, and oxygen.

The simplest carbohydrate structures are called "monosaccharides." Monosaccharides provide the basic units for other carbohydrate molecules. Monosaccharides also serve as components in genetic material and important

compounds, such as adenosine triphosphate (ATP) involved in the metabolic pathways responsible for the production of energy in animals. Typical dietary sugars are composed of two monosaccharides, and are called "disaccharides." Larger structures composed of many monosaccharide units are called "oligosaccharides" (3 to 10 units) and "polysaccharides" (more than 10 units). Plant carbohydrates provide energy and dietary fiber to the animals that eat them. Animals also produce carbohydrates from the food they eat, primarily for the purpose of storing energy. Informally, the term "carbohydrate" (or "carbs") is used to refer to foods that contain relatively high concentrations of carbohydrate molecules. Most cultures of the world rely on carbohydrate foods for a majority of daily calories.

Simple Carbohydrates

Sugars, also known as "simple carbohydrates," are relatively small molecules of carbohydrate found naturally in fruits and vegetables, as well as milk. They are especially concentrated in sweeteners such as table sugar (usually made from sugar beets or sugar cane), honey, molasses, and maple syrup. Corn syrup is a sweetener made from the sugar in corn. Many food products contain added sweeteners.

The term sugars refer to monosaccharides and disaccharides. Monosaccharides are the simplest carbohydrate structures, containing three to seven carbon atoms. Monosaccharides generally contain carbon, hydrogen, and oxygen in a ratio of two hydrogen atoms and one oxygen atom to each carbon atom, for a molecular formula of $C_nH_{2n}O_n$. The most common monosaccharides in the human diet contain six carbons, and include glucose, fructose, and galactose.

Glucose is the most common monosaccharide found in nature. Glucose provides the types of chemical bonds from which people can capture energy. Glucose is carried in the bloodstream to all cells of the body to be used as an energy-production substrate. The term "blood sugar" refers to blood glucose level. Glucose rarely is found as a single unit in foods, but instead forms part of disaccharide structures. Fructose is the sweetest of the monosaccharides, and binds with glucose to form the disaccharide sucrose, found in many sweet foods. Galactose is the monosaccharide that is bound to glucose to form lactose, the disaccharide known as milk sugar.

The "pentoses" are five-carbon monosaccharide molecules. Best known of the pentoses are "ribose," a component of ribonucleic acid (RNA) and "deoxyribose," a component of deoxyribonucleic acid (DNA). The body synthesizes pentoses, therefore these monosaccharides need not be included in the diet.

The three most common disaccharides in the human diet are sucrose (composed of glucose plus fructose), galactose (glucose plus lactose), and maltose (two glucose units). Maltose is found in germinating grains and is a product of the breakdown of starch.

During digestion, simple sugars are broken down into monosaccharides that are transported into the bloodstream. The liver converts fructose and other

monosaccharides into glucose or other molecules, including large chains of glucose called glycogen. Monosaccharides can also be converted into fats.

Complex Carbohydrates

Complex carbohydrates are larger molecules of carbohydrate and include starches and some types of dietary fibers. Oligosaccharides consist of 3 to 10 glucose units, and are found in a variety of foods. Common oligosaccharides include "raffinose" (3 glucose units) and "stachyose" (4 glucose units), found in legumes. Human digestive enzymes are unable to break the molecular bonds that hold the glucose units together, but intestinal bacteria can break these bonds, producing intestinal gas in the process. Human milk contains more than 100 different oligosaccharides that help babies in a number of ways, including binding with pathogens, serving as food sources for helpful bacteria, and promoting normal infant brain development. Oligosaccharides can serve as starches or dietary fibers, depending upon whether they can be broken down in the digestive tract.

Polysaccharides contain more than 10 glucose units and often are composed of hundreds of glucose units strung together in various formations. These formations determine the properties of the starch, including the speed at which it is digested and absorbed (a quality known as "glycemic index") and its behavior in recipes. The two primary starch formations in plants are "amylose" and "amylopectin." Amylose is composed of long straight chains of glucose units. Amylopectin contains long branching chains of glucose units. Starch polysaccharides are found in plant foods and products made from plants. Grains and grain products; root vegetables, such as potatoes, carrots, beets, and cassava; and vegetables that are the seeds of plants, such as corn, peas, and beans are high in starch. During digestion, starches are broken down into glucose units.

Glycogen is a form of starch manufactured by animals. Humans manufacture and store glycogen primarily in the liver and in skeletal muscles. Glycogen serves as a source of glucose when the body needs fuel. Liver glycogen is converted to glucose and released into the bloodstream when blood glucose levels fall too low. Skeletal muscles use glucose liberated from glycogen to fuel muscle contraction. Many athletes are careful to consume adequate amounts of carbohydrate to maximize glycogen stores so that they have adequate energy for training and performance. Athletes preparing for important endurance events even might consume significant amounts of carbohydrate for a few days prior to an event to maximize their glycogen stores.

Dietary fiber refers to structures that are not broken down by the digestive system. Dietary fiber comes primarily from plants. Some types of dietary fiber—such as cellulose—are composed of carbohydrates. Humans lack the necessary digestive enzymes to break down these structures, and fiber instead passes through the digestive system, adding bulk to the stools. Adequate intake of dietary fiber contributes to good health. Most dietary guidelines encourage people to consume adequate amounts of vegetables, fruits, legumes, and whole grains to promote a healthy intake of dietary fiber.

All types of fiber increase food volume without adding a significant number of calories. High-fiber meals generally provide feelings of satiety with fewer calories than low-fiber meals. A high-fiber diet could promote colon health by providing an environment inside the GI tract that favors the growth of beneficial bacteria—the probiotics.

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Research Issues

Many people regard carbohydrate foods as "bad." Yet carbohydrates are contained within a wide range of foods. Some of these foods, such as most vegetables, generally are regarded as very nutritious. Other foods high in carbohydrates, such as cakes, cookies, and soft drinks, obtain a majority of their calories from processed grains and sugars, and typically are higher in empty calories (calories that deliver little nutritive value). The dietary reference intake for carbohydrates is at least 130 g per day for children and adults. Most North Americans consume at least 50% of their calories as carbohydrates, which amounts to more than 250 g per day. What do public health experts say about making good choices for foods that provide carbohydrates? What are the characteristics of "good carbs"? What are the characteristics of "bad carbs"?

See Also: Blood sugar regulation; Fiber; Fructose; Glucose; Glycemic index and glycemic load; High-fructose corn syrup.

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Cardiometabolic Syndrome

Cardiometabolic syndrome (CMS) is an umbrella term for a combination of medical disorders. In the United States, it affects approximately 25% of adults age 20 and older, and up to 45% of adults age 50 and older (Kumar, Vishal, & Nema, 2013). Cardiometabolic syndrome is widely referred to as "metabolic syndrome X," "syndrome X," "metabolic syndrome," and "Reaven's syndrome." According to the scientific statement of the American Heart Association and the National Heart, Lung, and Blood Institute, CMS is diagnosed in men and women

who possess three or more of the following risk factors: central adiposity, elevated fasting glucose levels, elevated resting blood pressure, high triglyceride levels, and low HDL cholesterol levels. The more risk factors individuals possess, the greater their risk for the development of serious medical conditions such as Type 2 diabetes, heart disease, and stroke.

History

Although cardiometabolic syndrome is a relatively new concept, researchers have noted the clustering of cardiovascular risk factors associated with the syndrome since the 1920s. In 1988, Dr. Gerald Reaven noted several risk factors that commonly cluster together and increase the risk for cardiovascular disease, which he called "syndrome X" (Grundy et al., 2005). Reaven noted that insulin resistance is the underlying factor of CMS.

Central Adiposity

Central adiposity, or central obesity, is the accumulation of excess body fat in the torso, especially around the internal organs. This is identified as having an "apple" shape. Central adiposity is a key causal factor in the development of insulin resistance, the main feature in the development of cardiometabolic syndrome. For diagnostic purposes, waist circumferences of 40 inches (102 cm) or more in men, and of 35 inches (89 cm) or more for a woman are considered risky. The body mass index (BMI) system of measurement, which uses weight and height, is the typical diagnostic tool for obesity. Although the presence of central adiposity is more highly correlated with cardiometabolic risk factors than with elevated BMI numbers, the prevalence of CMS has been shown to increase across BMI categories with approximately a much higher prevalence for severe obesity compared with non-obese.

Blood Sugar Levels

High blood sugar levels are a major component of cardiometabolic syndrome. Fasting blood glucose tests measure the blood glucose level after eight hours of fasting. High blood sugar levels are defined by a fasting blood glucose test result of greater than or equal to 100 milligrams per deciliter (mg/dL). Fasting blood glucose levels of 100 to 125 mg/dL are considered "prediabetes," or a condition likely to lead to type 2 diabetes. A fasting glucose of 126 mg/dL or greater suggests the person has diabetes mellitus.

Glucose is the energy source for cells. It is derived from food broken down during digestion. Blood glucose levels increase when the digestive system absorbs glucose, activating the hormone insulin to help control blood glucose levels. Impaired fasting glucose levels indicate that the cells are responding to insulin inadequately, a condition known as insulin resistance. This condition often develops into type 2 diabetes, which is the most common form of diabetes. In later stages of

type 2 diabetes, insulin resistance is coupled with inadequate insulin production by the pancreas.

High blood glucose levels can contribute to the formation of atherosclerotic plaques, the hallmark of artery disease. Atherosclerotic plaques build up in the arteries, restricting oxygenated blood flow to major organs. Obesity and high blood sugar levels are associated with inflammation in the arteries. Inflammation can cause plaques to rupture, and plaque material to break off and interrupt blood flow. Artery disease is the leading cause of heart attack and stroke.

Hypertension

Hypertension, commonly referred to as "high blood pressure," affects approximately one-third of the total U.S. population (AHA, 2013). High blood pressure is strongly associated with obesity and commonly occurs in insulin-resistant persons, linking it to CMS. It contributes significantly to cardiovascular disease and is the leading global risk factor for premature mortality. Hypertension is diagnosed when resting blood pressure is ≥130/85 mmHg. (One or both of these numbers can be high for a diagnosis of hypertension.)

Atherogenic Dyslipidemia

Atherogenic dyslipidemia refers to blood lipid levels that are associated with an increased risk of artery disease. Atherogenic dyslipidemia frequently is characterized by the combination of three lipid abnormalities: elevated triglycerides, low levels of high-density lipoprotein (HDL) cholesterol, and high levels of low-density lipoprotein (LDL) cholesterol.

Triglycerides are the most common form of fat found in the diet and in the blood. The body manufactures triglycerides from excess calories, and stores the excess triglycerides to be used for energy. A serum triglyceride level of 150 mg/dL or greater contributes to a diagnosis of CMS. High-density lipoprotein cholesterol is inversely related to artery disease risk; that is, higher levels of HDL cholesterol are associated with lower risk. Low levels of HDL cholesterol contribute to a diagnosis of CMS—less than 40 mg/dL for men and less than 50 mg/dL for women. Although not a component of a CMS diagnosis, higher LDL levels put an individual at risk for CMS. Low-density lipoprotein is the major cholesterol carrier in human blood. High LDL cholesterol in the blood is a strong CVD risk factor because oxidized LDL compounds can enter the arterial wall and contribute to the formation of atherosclerotic plaque. LDL cholesterol levels of 130 to 159 mg/dL are considered borderline high, and levels of more than 160 mg/dL are considered high by the National Cholesterol Education Program (DHHS, 2005).

Causes and Risk Factors

Experts are unsure exactly why cardiometabolic syndrome develops. It is understood, however, that various risk factors contribute to the different causes. CMS is closely

linked to the body's metabolism and insulin resistance. Insulin resistance is present in the majority of people diagnosed with cardiometabolic syndrome, and believed by researchers to be the underlying cause. Insulin resistance generally increases with the severity of obesity, although this resistance can exist at any given level of body fat. Given that obesity commonly is associated with insulin resistance, the two risk factors both influence the development of other cardiometabolic risk factors.

Additional factors contribute to the development of CMS, such as advancing age. Advancing age commonly affects all levels of pathogenesis, thus increasing the likelihood for the development of CMS as a person ages and among an older cohort. A pro-inflammatory state, reflected in an elevation of C-reactive protein, also is associated with insulin resistance and atherogenesis. Excess adipose tissue releases inflammatory cytokines that increase one's pro-inflammatory state. Sedentary lifestyle and family history—especially having a sibling or parent with diabetes—increase risk of CMS. A personal history of diabetes, including gestational diabetes, also increases risk.

Polycystic ovarian syndrome (PCOS) is an endocrine disorder characterized by hormone imbalance and affecting a woman's fertility. A woman is diagnosed with PCOS if she reports at least two of the following symptoms: an excess of androgen production, menstrual abnormalities, and polycystic ovaries. Obesity is associated with an increase in hyperandrogenism and menstrual irregularity in women, both of which are symptoms of PCOS. ("Hyperandrogenism" refers to greater than normal levels of male sex hormones, often accompanied by symptoms such as acne and excess facial hair). There is a discrepancy between whether PCOS or obesity comes first, but women with either risk factor are more likely to develop cardiometabolic syndrome. A study on cardiometabolic risk confirmed that the prevalence of CMS is approximately four times higher in women with PCOS compared to the general population (Cussons, 2008).

Women of African-American and Mexican-American ethnicity are more likely to develop CMS than are men from those groups. This could be because women generally have a greater number of risk factors, including central adiposity, PCOS, and obesity, and thus are more susceptible to the development of cardiometabolic syndrome. In combination with genetic and behavioral factors, hormonal changes at menopause contribute to the prevalence of CMS in women (Yu et al., 2013).

Treatment

There is no single treatment to cure cardiometabolic syndrome, however risk factors can be reduced though pharmacological therapies and therapeutic lifestyle changes. To best treat the totality of CMS, it is important to focus on the suggested treatments for each risk factor. The primary treatment of CMS is lifestyle therapy, including increased physical activity and an anti-atherogenic diet. Lifestyle intervention can reduce the risk of heart disease, diabetes, and stroke (Kumar, Vishal, & Nema, 2013). Pharmacological therapies frequently are used to improve lipid profile, blood pressure, and blood glucose regulation. Gastrointestinal surgeries for weight loss also are recommended in some cases.

Diet

Obesity is a central feature of the syndrome that is linked to the majority of risk factors attributing to CMS, therefore weight loss can greatly assist in the management of the syndrome. Diet intervention can drastically alter one's fasting glucose levels and, in turn, can decrease a person's risk for or severity of type 2 diabetes. When combined, diet and exercise are among the most effective treatments for obesity.

The Mediterranean Diet, based on the typical diet of Mediterranean cultures, is rich in omega-3 fatty acids, vegetables, whole grains, and nuts. Research suggests that the antioxidant rich and highly anti-inflammatory diet provides specific benefit for individuals affected by cardiometabolic syndrome (Blaha & Tota-Maharaj, 2012).

The "DASH-style" diet plan, or "Dietary Approaches to Stop Hypertension," was developed to reduce blood pressure without medication for patients with hypertension (Salehi-Abargouei et al., 2013). The diet is rich in fruits, vegetables, and low-fat dairy. It includes grains, especially whole grains; lean meats, fish, and poultry; nuts and beans. It is high fiber and low to moderate in fat. The DASH diet lowers blood pressure through a rich source of nutrients associated with reduced blood pressure levels, such as potassium, calcium, and magnesium (Salehi-Abargouei et al., 2013).

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Research Issues

As obesity rates in childhood and adolescence increase worldwide, so does the prevalence of cardiometabolic syndrome (CMS). How should CMS be diagnosed and treated in children and adolescents? The International Diabetes Federation has good information on this emerging topic.

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See Also: Bariatric surgery; Blood sugar regulation; Cardiovascular disease and nutrition; Cholesterol; Diabetes, type 2; Hypertension and nutrition; Inflammation; Insulin; Lipoproteins; Obesity, definition and health effects; Triglycerides.

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Cardiovascular Disease and Nutrition

Cardiovascular disease (CVD) refers to diseases of the heart and the blood vessels. It includes all types of heart disease, stroke, and artery disease. In the United States, cardiovascular disease is the leading cause of death among both women and men, causing one in three deaths per year (Go et al., 2013). The most common form of heart disease is coronary artery disease (CAD), also called "coronary heart disease," in which the arteries supplying the heart muscle with blood become thickened with plaque deposits. Coronary artery disease is the cause of death for about 380,000 people per year in the United States (CDC, 2014).

Another form of CVD is a stroke, which occurs when there is an interruption of blood flow to the brain, because of either a blockage or a break in an artery supplying the brain. In the United States, stroke causes about 1 in 19 deaths per year, with approximately 795,000 strokes occurring each year (Go et al., 2013). Artery disease is the most common cause of stroke. Of all types of cardiovascular disease, artery disease is most influenced by nutrition as well as by other lifestyle factors. People can slow and even reverse the progression of artery disease and reduce their risk of heart attack and stroke by consuming a healthful diet and making other

lifestyle changes. A healthy diet also can help control several risk factors for CVD, including diabetes, hypertension, blood lipid profile, and obesity.

The Process of Atherosclerosis

Artery disease, or atherosclerosis, is a condition that develops when fatty deposits build up gradually within the inner walls of arteries. These fatty deposits are called plaques and are composed of cholesterol, cellular waste, calcium, immune cells, blood platelets, and other substances. Plaque buildup narrows the arteries, inhibiting blood flow; it also damages the arterial lining, so the arteries are unable to respond appropriately to signaling molecules that help to regulate blood flow and blood pressure. Over time plaques can become inflamed and unstable. If plaques rupture, then blood clots can form as the body attempts to repair artery damage. When blood clots block blood vessels they can cause a heart attack or stroke.

To understand the relationship between diet and artery disease, it is helpful to understand the process of atherosclerosis. Atherosclerosis begins with the oxidation of the compounds that carry fat and cholesterol in the blood stream, the lipoproteins. In particular, oxidation of low-density lipoproteins (LDLs) causes the LDLs to bind to the artery lining. The cells lining the arteries respond to this binding as an injury, signaling immune cells to come in and repair the damage. As immune cells called "macrophages" (a type of white blood cell) try to ingest the LDLs, the process of inflammation accelerates. The cells lining the artery proliferate in an attempt to heal the damaged area. Over a period of years, this process of plaque deposition leads to artery disease. The processes of oxidation and inflammation contribute to the development of atherosclerosis. Factors—including dietary nutrients and phytochemicals—that reduce LDL levels in the bloodstream, reduce the oxidation of LDLs, and limit the body's inflammatory response can help to slow the process of atherosclerosis.

Risk Factors

Artery disease does not appear to have one simple cause. Instead, the process is influenced by a number of variables, known as "risk factors." Dozens of risk factors have been identified. Some risk factors are outside of a person's control, including age (risk increases with age); genetics (having close relatives who experienced a heart attack before the age of 55 for males; 65 for females); and gender (women develop artery disease later in life than men).

Some risk factors are somewhat modifiable, including metabolic disorders that accelerate the progression of artery disease. Such disorders include diabetes (high blood sugar levels increase arterial inflammation and injure the artery lining); hypertension (high blood pressure injures the artery lining); and harmful blood lipid levels (higher levels of LDLs and lower levels of high-density lipoproteins [HDLs] are associated with artery disease). Obesity, especially excess fat in the abdominal region, increases risk of the cardiometabolic syndrome and the previously listed

disorders. Obesity also is associated with increased levels of inflammation. These disorders are somewhat modifiable in the sense that they can be at least partially controlled by medications and lifestyle change, including dietary change.

Other modifiable risk factors include tobacco use (smoking increases oxidation of LDLs, increases blood pressure, and damages the artery lining); sedentary lifestyle (regular physical activity helps to normalize blood sugar regulation and blood pressure, raise HDL levels, and improve emotional health); chronic stress; and poor emotional health (chronic stress, anger, anxiety, and depression increase artery disease risk through a variety of mechanisms).

Diet and Cardiovascular Disease

Researchers have been interested in a possible relationship between lifestyle (including diet) and cardiovascular disease since the 1950s, when cardiovascular disease began to emerge as a leading cause of death in many countries. Early epidemiological studies suggested that countries with a Western diet suffered from higher rates of CVD than other countries. A Western diet is characterized by a higher intake of animal products and processed foods, with a lower intake of plant foods. This observation led to decades of research and speculation regarding which specific elements of the Western diet might be responsible for the development of artery disease. Researchers, the food industry, and consumers have hoped that by eliminating the causal elements from the Western diet, eating could go on with relatively minor changes in food choices. For example, in the 1980s, cholesterol and fat consumption were believed to be the primary drivers of the development of atherosclerosis, so people were urged to choose low-fat and low-cholesterol versions of familiar foods, for example, low-fat dairy rather than high-fat dairy products, low-fat meats, and even low-fat cookies. Ongoing epidemiological research using advanced statistical analyses revealed associations between trans fatty acids and glycemic load with increased risk of CVD (Jakobsen et al., 2009). Recent research continues to debate whether specific dietary components—such as carbohydrates or saturated fats—contribute to the development of artery disease (Chowdhury et al., 2014; Jakobsen et al., 2009). Such research is the basis for the dietary recommendations created by the U.S. Department of Agriculture (the U.S. Dietary Guidelines) and the American Heart Association (see sidebar).

Many experts have argued that it might be unrealistic to blame one or two dietary components for the progression of artery disease, and that it is likely that dietary pattern is more important. In epidemiological studies, for example, diets high in saturated fat have been associated with higher rates of artery disease. A statistical association, however, does not prove causation. This association might also be explained by other factors associated with a diet high in saturated fat, such as a high intake of animal protein or a low intake of plant foods, along with a low intake of dietary fiber, phytochemicals, and certain vitamins and minerals. Some researchers have argued that examining overall dietary pattern would be more applicable in terms of generating dietary recommendations.

A Healthy Diet to Help Prevent Heart Disease

A good, healthy diet can help to prevent heart (cardiovascular) disease. As the National Library of Medicine's Medline *Heart Disease and Diet* (2013) website suggests, making these types of changes in what adults eat can make a real difference.

- Add Fruits and Vegetables. They provide fiber, vitamins, and minerals. Eat five or more servings a day.
- Choose Good Grains. Low-fat breads, cereals, crackers, rice, pasta, and starchy vegetables (e.g., peas, potatoes, corn, winter squash, lima beans) are high in B vitamins, iron, and fiber and low in fat and cholesterol. Whole-grain foods should include at least half of daily grain intake. Grain products provide fiber, vitamins, minerals, and complex carbohydrates. Avoid refined grains, such as that found in white bread, pasta, and baked goods.
- Eat Healthy Protein. Meat, poultry, seafood, dried peas, lentils, nuts, and eggs are good sources of protein, B vitamins, iron, and other vitamins and minerals.
- Avoid High-Fat Meats. These include prime cuts of steak, duck, goose, kidneys, and liver, and processed meats such as sausage, hot dogs, and high-fat lunch meats.
    - Eat no more than 5 to 6 cooked ounces of lean meat, poultry, and fish daily.
    - Eat two servings of fish per week.
    - Consume lower-fat versions of milk and other dairy products; they have protein, calcium, the B vitamins niacin and riboflavin, and vitamins A and D.
- Beware of Trans Fatty Acids. These are found in fried foods, commercial baked foods (donuts, cookies, and crackers), processed foods, and hard margarines.
- Consume Sugar and Alcohol Sparingly. Women should have no more than one alcoholic drink daily; men should not have more than two alcoholic drinks daily.

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Relatively few well-controlled experimental studies have been conducted to examine the effect of diet and lifestyle change on the progression of artery disease. The best of these studies have been led by cardiologist Dean Ornish. Dr. Ornish was the first to demonstrate that a program of lifestyle change—as compared with standard treatment—actually could lead to regression of atherosclerotic plaques in the coronary arteries in subjects with CAD, something thought to be impossible until the results of these studies were published (Ornish et al.,1990). Subsequent studies by Ornish and his colleagues have continued to support these initial observations (Silberman et al., 2010). Ornish's dietary guidelines for reversing atherosclerosis emphasize a whole food, plant-based diet. The diet is low in fat, cholesterol, animal products, sugar, caffeine, sodium, and alcohol, and is high in fiber, phytochemicals, vitamins, and minerals. Specific guidelines for reversal of heart disease include the following.

- Low fat—Less than 10% of calories in this diet come from fats. This goal is achieved by severely restricting all added fats in the diet, even "healthful" fats such as oils, nuts, and avocadoes.

- Cholesterol—The 10-mg limit is achieved by eliminating all meats and egg yolks.
- Animal products—Only 0 to 2 servings per day of nonfat dairy and egg whites are included.
- Sugar—Permitted in moderation; two or fewer servings per day of non-fat sweets.
- Caffeine—The only caffeine source included in this diet is green tea, because its antioxidant benefits outweigh its risk for most people, although Ornish cautions that people with cardiac arrhythmias and elevated stress levels should avoid all caffeine.
- Sodium—Moderate levels permitted unless other medical reasons, such as hypertension, suggest that the level should be very low.
- Alcohol—One drink per day is allowed but is "not encouraged."
- Soy—One serving of soy per day is encouraged.
- Supplements—A low-dose multivitamin and mineral supplement and a marine omega-3 fatty acid supplement are recommended. Depending on one's health risks, calcium also could be recommended.

Ornish advises that following the low-fat diet is only one part of the heart-disease reversal treatment protocol used in his studies. Participants also increase physical activity and stress-reduction practices, and engage in group counseling to improve emotional health and social support. Because of the strength of the evidence Ornish and his colleagues have collected to support the efficacy of the program, the Ornish program now is reimbursed by some insurance companies for people with demonstrated CAD who want to avoid surgical procedures, if possible.

Some experts argue that because a very low-fat diet is difficult to follow, a Mediterranean-type diet also could help to reduce risk of CVD (Estruch et al., 2013). Epidemiological and some experimental evidence suggests that people who consume a Mediterranean diet could have lower rates of heart disease than people who consume a Western diet, but experiments have not yet demonstrated reversal of heart disease with regression of plaque when following such a diet. It should also be noted that the Ornish diet offers less-stringent recommendations for apparently healthy people who simply want to prevent heart disease (as opposed to people who have documented artery blockage or who already have had a cardiovascular event, such as a heart attack or stroke) (Ornish Spectrum, 2014).

Dietary recommendations for the prevention of stroke echo those for artery disease, because artery disease causes about 2 in 3 strokes. Hypertension increases risk for the other type of stroke that is caused by an aneurism, a tear or break in the artery. Dietary recommendations for reducing hypertension are similar to those for the prevention of artery disease. Additionally, a very low sodium (salt) intake is recommended (1,500 mg or less), along with a high intake of potassium, magnesium, and calcium through consumption of vegetables, fruits, and low-fat dairy products. The Dietary Approaches to Stop Hypertension (DASH) diet has been

shown to help control hypertension (National Heart, Lung, and Blood Institute, 2014).

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Research Issues

Recent research on the association of a compound called tri-methylamine-N-oxide (TMAO) with increased risk of heart disease suggests that a high intake of animal products might accelerate the progression of atherosclerosis. Tri-methylamine-N-oxide is synthesized by the liver from trimethylamine (TMA). Trimethylamine is made by bacteria residing in the colon from the precursors choline and carnitine. Choline is a nutrient plentiful in egg yolks. Carnitine is an amino acid plentiful in meat, especially red meat. It is not known whether TMAO contributes to cardiovascular disease, but the higher levels of TMAO observed in meat eaters compared with vegetarians has been suggested as a possible explanation for the link between a Western diet and cardiovascular disease (Koeth et al., 2013). Some researchers suggest that a high intake of animal protein, more than the saturated fat and cholesterol found in animal products, could be one of major causes of atherosclerosis (Campbell, 2014).

See Also: Antioxidants; Cardiometabolic syndrome; Carnitine; Cholesterol; Choline; Diabetes, type 2; *Dietary Guidelines for Americans*; The French paradox; Glycemic index and glycemic load; Hypertension and nutrition; Lipoproteins; Mediterranean diet; Obesity, definition and health effects; Phytochemicals; Trans fatty acids; Vegetarian and vegan diets.

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Carnitine

Carnitine is a compound that can be found in most cells in the human body. It is synthesized—mainly in the liver, but also in the kidneys—from the amino acids lysine and methionine. Carnitine is a generic term that includes L-carnitine, propionyl-L-carnitine, and acetyl-L-carnitine. Carnitine is significant for the body's energy production because it helps transport long-chain fatty acids into the mitochondria where they can be metabolized for energy. Carnitine also carries toxic metabolic byproducts out of the mitochondria, and thus helps keep this important organelle functioning at an optimal level. Carnitine is most concentrated in tissues of the body where fatty acids are the major source of energy, such as skeletal and cardiac muscle.

Generally, the human body synthesizes sufficient carnitine to satisfy its daily need; however some people do not make sufficient carnitine, and others are unable to transport carnitine into the tissues that need it. Dietary sources highest in carnitine include red meats such as steak and ground beef. Much lower amounts are found in dairy products, fish, and poultry. Dietary carnitine is absorbed by the small intestine then enters the bloodstream. The kidneys can conserve carnitine efficiently, as they are estimated to reabsorb 95% of serum carnitine (Hidgon & Drake, 2012). As a result, the excretion of carnitine generally is minimal.

Several conditions can cause a deficiency of carnitine in the body. One such condition is primary systemic carnitine deficiency, which is a rare autosomal recessive disorder that results from genetic mutations. The genetic mutations cause a carnitine-transporter protein to lose its ability to transport carnitine through the plasma membrane. People who have this disorder have a high urinary loss of carnitine and low intestinal absorption of dietary carnitine. Primary systemic carnitine deficiency causes serious symptoms, such as skeletal myopathy, hypoglycemia,

and progressive cardiomyopathy. Primary systemic carnitine deficiency is fatal if it is not treated; treatment for this disorder requires a high supplemental intake of carnitine. Unlike primary systemic carnitine deficiency, secondary carnitine deficiency can be caused by either acquired or genetic conditions. Dietary management is the main treatment for secondary carnitine deficiency. People who have secondary carnitine deficiency are advised to follow a high-carbohydrate and low-fat diet, which decreases the need for the oxidation of fat, thereby decreasing the need for carnitine.

Potential Benefits

Carnitine has been studied extensively by scientists and researchers, as it has shown potential for the prevention and treatment of various diseases and conditions. Evidence is strongest for carnitine's role in helping to treat cardiovascular disease. A meta-analysis of 13 studies examining the effect of L-carnitine treatment versus placebo or control treatments on the outcome of 3,629 participants who had experienced a heart attack found that those receiving carnitine showed a 27% reduction in all-cause mortality, a 40% reduction in chest pain symptoms, and a 65% lower rate of heart rate arrhythmias (DiNicolantonio, Lavie, Fares, Menezes, & O'Keefe, 2013). Some studies have found that carnitine treatments can be helpful for reducing symptoms of heart failure and peripheral vascular disease (Ehrlich, 2011). Studies examining the effect of acetyl-L-carnitine in treating diabetic neuropathy suggest that acetyl-L-carnitine might be effective in improving neurophysiological parameters and in reducing pain over a one-year period (Ehrlich, 2011).

Carnitine is a popular supplement among athletes because it is thought to be able to improve performance by making fat more available for energy production. Research, however, generally has not found a performance benefit associated with carnitine supplementation.

Evidence suggests that the concentration of carnitine in body tissues decreases as people age (NIH, 2013). Researchers have suggested that the decline in the concentration of carnitine might lower the integrity of the mitochondrial membrane; mitochondrial decay is believed to be a factor in the aging process. Experiments with aged rats have shown that the supplementation of carnitine reduces mitochondrial decay and improves performance on memory-demanding work (NIH, 2013). Further studies in humans are needed to determine whether the same effect would be observed in people.

Risks

Recent research on the association of a compound called tri-methylamine-N-oxide (TMAO) with increased risk of heart disease suggests that further research is needed to clarify possible risks associated with carnitine supplementation. TMAO is synthesized by the liver from trimethylamine (TMA). Trimethylamine is made by bacteria residing in the colon from the precursors choline and carnitine. It is not known whether TMAO contributes to cardiovascular disease, but the higher levels

of TMAO observed in meat eaters compared to vegetarians has been suggested as a possible explanation for the link between higher intakes of red meat and cardiovascular disease (Koeth, Wang, Levison et al., 2013).

Fei Peng

See Also: Choline.

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Carotenoids

Carotenoids are a class of phytochemicals that includes more than 600 natural pigments. These compounds give fruits and vegetables their vibrant yellow, orange, and red colors, such as those seen in sweet potatoes, melons, tomatoes, papayas, and pumpkins. In the human diet, carotenoids are associated with a number of health benefits. All of the carotenoids have antioxidant activity. Less than 10% of the carotenoids can be converted by the body into vitamin A. Many studies have found associations between the increased consumption of foods high in carotenoids and a reduced risk of heart disease and some types of cancer. Because carotenoids are fat soluble, consumption along with dietary fats such as olive oil is recommended.

Carotenoids are categorized into two major groups, carotenes and xanthophylls. Carotenes are hydrocarbons. The most common carotenes in the human diet are alpha-carotene, beta-carotene, and lycopene. Alpha-carotene and beta-carotene can be transformed into vitamin A, and the human body produces the most vitamin A from beta-carotene. Many studies have found strong associations between a high beta-carotene intake from food and several health benefits. Studies using beta-carotene supplements, however, generally have failed to find health benefits. Several well-designed experiments have even found an increased risk of lung cancer in smokers who consume beta-carotene supplements. Lycopene is a

red-orange pigment plentiful in tomatoes and watermelon. Lycopene appears to be more bioavailable in cooked rather than raw foods. Diets high in foods containing lycopene have been associated with a reduced risk of prostate cancer in men; it is unknown whether supplements containing lycopene have the same association.

Xanthophylls are composed of oxygen, carbon, and hydrogen. They have antioxidant properties that limit photo-oxidative damage in plants and protect humans from free radical damage. The most common xanthophylls in the human diet are beta-cryptoxanthin, lutein, and zeaxanthin. Beta-cryptoxanthin can be converted to vitamin A. Lutein and zeaxanthin are stored in the retina and lens of the eye. Consumption of foods with high concentrations of these xanthophylls appears to exert protective effects on the eye, slowing the progression of macular degeneration and the formation of cataracts. Food high in lutein and zeaxanthin include dark leafy greens such as spinach and kale.

In various studies, foods high in carotenoids—including many fruits and vegetables—have been associated with a reduced risk of cancer and heart disease. The antioxidant activity of the carotenoids might protect the lining of arteries and fat in blood from free radicals and oxidative stress. In vitro studies have shown that carotenoids appear to influence intercellular signaling. Carotenoids also might improve immune function, although this could be an effect of vitamin A activity. Because carotenoids play a substantial role in the production of vitamin A, ingestion of foods with these pigments is necessary to maintain proper levels of vitamin A.

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See Also: Antioxidants; Beta-carotene; Eye health, and nutrition; Lutein; Lycopene; Phytochemicals; Vitamin A; Zeaxanthin.

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Carrageenan

Carrageenan is a substance extracted from the red seaweed commonly found off the coast of North America, Great Britain, and Continental Europe. Although carrageen has no nutritional value, it is added to food products to thicken, emulsify, stabilize, and improve the overall texture of the food. It often is used in dairy products and dairy substitutes, such as ice cream, yogurt, cottage cheese, soy milk, rice

milk, and almond milk. It also is found in other foods and products, such as toothpaste, cosmetics, and processed meats. Carrageenan currently is labeled by the FDA as being "Generally Recognized as Safe." Even though it is permitted in many products, however, some scientific studies have led researchers to question the overall safety of this additive and its effect on the digestive system. In response to these studies, some physicians advise individuals with gastrointestinal symptoms and conditions to eliminate carrageenan from their diets.

Since the 1930s, carrageenan has been used in many food products. In France, acid is added to carrageenan at high temperatures to create a product that is sold as a treatment for peptic ulcers and as a bulk laxative (Therapeutic Research Faculty, 2009). Products containing carrageenan have been used in North American to treat cough, bronchitis, peptic ulcers, and constipation, although the evidence to support such uses is fairly weak. Carrageenan does appear to pull water into the intestine, contributing to its laxative effect (Therapeutic Research Faculty, 2009).

Although presently there are few studies to support the claims of carrageenan's health benefits, multiple studies—primarily led by Joanne Tobacman, MD, a physician-scientist at the University of Illinois College of Medicine—suggest that carageenan could have harmful physiological effects. Studies from Dr. Tobacman's lab have found that carrageenan and its breakdown in the body can lead to intestinal inflammation that can contribute to many chronic illnesses, such as irritable bowel syndrome, ulcerative colitis and other inflammatory bowel disorders, and colon cancer (Bhattacharyya et al., 2012). Tobacman and colleagues argue that it is the foreign chemical structure in carrageenan that stimulates an innate immune response that can lead to these symptoms, as well as to chronic inflammation. There are two forms of this additive, undegraded and degraded. Undegraded carrageenan is used in food products (Weil, 2012). Degraded, low molecular weight carrageenan is recognized as a "possible human carcinogen" by the International Agency for Research on Cancer, and has been used in the medical research community for decades to induce acute inflammation in lab animals to test anti-inflammatory drugs. Although undegraded carrageenan is listed as safe, studies have shown that carrageenan in food has contained trace amounts of degraded carrageenan, and that the acidic environment of the stomach could convert undegraded carrageenan to the degraded form. Research groups such as the Cornucopia Institute, a non-profit food- and farm-policy research organization, have advised consumers—especially those with gastrointestinal conditions—to completely avoid products containing carrageenan.

Elizabeth Kleisner

See Also: Food additives.

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Catechins

Catechins are a type of polyphenols, organic compounds composed of phenol groups, known for their distinct aroma. Sometimes referred to as tannins, catechins are well-known components of green and white teas and also are found in many fruits, potatoes, garlic, and some nuts. These polyphenols are secondary metabolites, or flavonoids, which are molecules that do not contribute directly to the body's life-sustaining processes, but the absence of which could cause a variety of long-term impairments. Catechins are found in their highest natural concentrations in green tea leaves with epigallocatechin gallate (EGCG) being the most abundant, making up 65% of the total catechin concentration (Holloway & Oshimi, 2006).

The potential health benefits of catechins are numerous. Research shows strong evidence for their support in the immune system where they prevent the adherence of bacteria and viruses to cell membranes (Murase et al., 2002). In vitro experiments suggest that some catechins could stimulate apoptosis of human cancer cells, and a number of trials of catechin treatment for cancer patients are under way (National Cancer Institute, 2014). Catechins are especially active in the vascular system where they help reduce blood pressure and cholesterol levels, as well as prevent the growth of new blood vessels that help feed tumorous growth (Zaveri, 2005). As powerful antioxidants, catechins scavenge reactive oxygen species, helping to reduce inflammation and oxidative damage that interferes with proper cell functioning. In laboratory rats, catechins have been shown to reduce the liver damage associated with alcohol intake (Bharrhan et al., 2011).

Tea catechin supplements have been shown to reduce the weight gain that occurs in rats with high fat diets (Lu, Zhu, Shen, & Gao, 2012). Although it is too soon to recommend catechin supplements, drinking several cups of green tea a day appears to be safe for most people, although people sensitive to caffeine might need to modulate their intake. A number of human cancer trials are under way,

using EGCG and other catechins. Descriptions of these trials can be accessed at the National Cancer Institute's website (http://www.cancer.gov/drugdictionary?cdrid=506041).

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See Also: Antioxidants; Cancer and nutrition; Tea.

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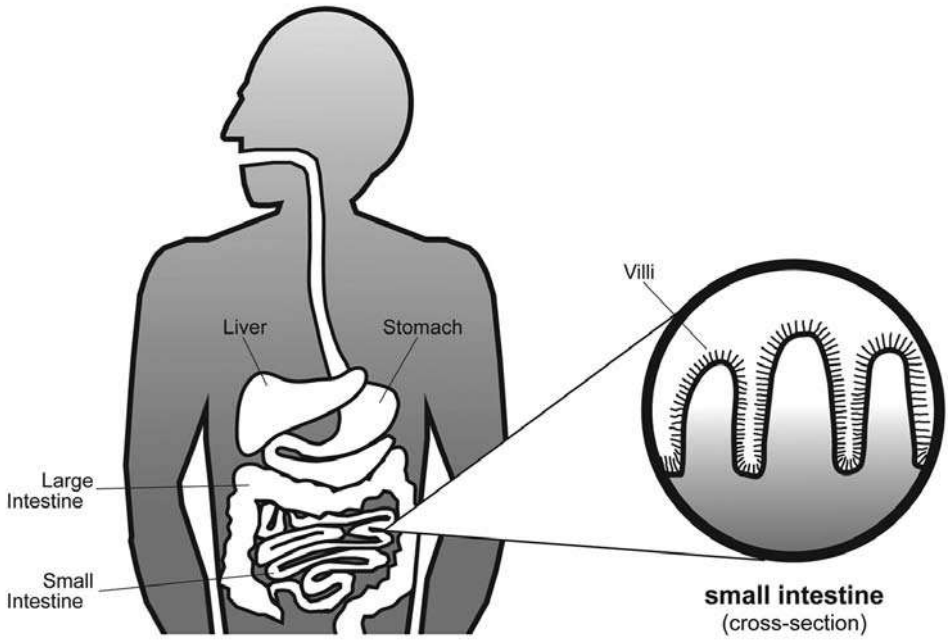
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Celiac Disease

Celiac disease is an autoimmune condition that can affect both children and adults. It is also referred to as "celiac sprue" and "gluten sensitive enteropathy" (GSE). If a person with this disorder consumes gluten—a mix of proteins that are stored in the seeds of wheat, barley, and rye—then the individual's immune system reacts by attacking the lining of the small intestine and, consequently, the body is unable to obtain the nutrients that it needs. It is a lifelong condition that affects approximately 1 in 133 people in the United States. Research continues in an effort to better understand the condition and to find possible treatments for the disease. This is extremely important because the condition can be both physically and emotionally taxing. Celiac disease is a condition that greatly affects the individual's daily life but can be managed with some increased effort.

History

Celiac disease is thought to have first developed when people changed their diets from those of simple hunter/gatherer cultures to those of agrarian societies



Villi are part of the lining on the intestine wall that aids in digestion. (ABC-CLIO)

when new crops were added to the food supply, including grains. Most people were able to adapt to the new food antigens, but food intolerances appeared in those who could not. Celiac disease was not identified or named, however, until about 8,000 years after people began eating wheat. In the first century CE, Aretaeus of Cappadocia, a Greek physician, wrote about "The Coeliac Affection." He named it after the Greek word, "koelia," meaning "abdomen" (Guandalini, 2007). In the early 19th century, Dr. Mathew Baillie wrote about a chronic diarrheal disorder causing malnutrition. It was not until about 75 years later that an English physician, Samuel Gee, described the "celiac affection" and presented the modern definition of the disease. After much research and many years, celiac disease was accepted as an autoimmune condition with a known trigger and autoantigen around the year 1990 (Guandalini, 2007).

Autoimmune diseases in general affect 3.5% of the U.S. population. In the United States, the prevalence of celiac disease is 1 in 133, or almost 1%. The prevalence for African Americans, Asian Americans, and Hispanic Americans is estimated to be 1 in 236. Researchers think that celiac disease affects at least 3 million Americans, but about 95% of these people are undiagnosed (University of Chicago Celiac Disease Center, 2012). It often takes several years for people with celiac disease to be diagnosed.

Physiology

The cause of celiac disease is still unknown. Researchers have discovered that it is partly hereditary. The prevalence of celiac disease in people with first-degree relatives who also have the disease is 1 in 22. Certain genes also seem to play a role in this disease. Two specific genes, HLA-DQ2 and HLA-DQ8, correlate with a person's risk of having the condition; and HLA-DQ2 is found in about 95% of individuals with celiac disease (Schoenstadt, 2013). About 30% of people without the disease have one of the two genes. This means that other factors must be involved. For example, situations such as surgery, pregnancy, childbirth, viral infection, or severe emotional stress might trigger the disease. Researchers believe that the cause of celiac disease most likely is a combination of genetic and environmental factors.

Although the symptoms of celiac disease vary among individuals, they often occur in the digestive system as well as in many other parts of the body. Young children and infants commonly suffer from digestive symptoms caused by the disease. Symptoms include abdominal bloating and pain; chronic diarrhea; vomiting; constipation; pale, foul-smelling, or fatty stool; and weight loss. Along with these, children also could suffer from irritability, delayed growth, delayed puberty, or dental enamel defects due to malabsorption of nutrients.

Adults often have symptoms unrelated to the digestive system. These symptoms include unexplained iron-deficiency anemia, fatigue, bone or joint pain, arthritis, bone loss or osteoporosis, depression or anxiety, tingling numbness in hands and feet, seizures, missed menstrual periods, infertility or recurrent miscarriage, canker sores inside the mouth, and a skin rash. Symptoms can vary in severity. Some people might show no symptoms but could develop complications over time, including malnutrition, liver diseases, and cancers of the intestine.

Researchers are studying the reasons for such variation of symptoms and severity. Symptom severity could be related to the age that the individual started eating foods containing gluten and the amount of these foods eaten. Studies show that symptoms appear later in individuals who were breast-fed longer. Symptoms also depend on a person's age and the amount of damage done to the small intestine. Individuals have a greater chance of developing long-term complications if they go for a long period without diagnosis.

Celiac disease is difficult to diagnose because it is characterized by symptoms that are similar to those of other diseases. It is sometimes confused with irritable bowel syndrome, iron-deficiency anemia, inflammatory bowel disease, diverticulitis, intestinal infections, or chronic fatigue syndrome. Because of this, celiac disease often is underdiagnosed and misdiagnosed. Doctors now are more aware of the symptoms, however, and there now are more reliable tests—this causes diagnosis rates to increase. The first tests performed to diagnose the disease often are blood tests. These measure the levels of two antibodies whose levels increase with celiac disease: anti-tissue transglutaminase antibodies and anti-endomysium antibodies. Additional blood tests are performed if the results come back negative and the disease still is suspected. For these tests to be accurate, it is important that the

person being tested continues to eat a diet containing gluten. Otherwise, they might test negative for celiac disease even if it is present. To confirm the diagnosis an intestinal biopsy is performed. The doctor uses an endoscope to remove small pieces of tissue from the small intestine to check for damage to the villi. Screening for celiac disease is sometimes recommended to family members of a person with the disease as a precautionary measure.

Treatment

Although there is no known cure for the disease, treatment options do exist. Currently the only treatment is a gluten-free diet. Many individuals work with a dietician to create a gluten-free diet plan. People with the disease must learn to read the ingredients on the labels of all foods and identify those that contain gluten. Most people see improvement just days after starting the diet. In almost all cases, the symptoms disappear, intestinal damage heals, and further damage is prevented. In children, the small intestine takes about three to six months to heal, but it could take a couple years for adults. To stay healthy, individuals with celiac disease must stick to a gluten-free diet for the rest of their lives. In rare cases intestinal injury continues even when on a strict gluten-free diet; this is called refractory celiac disease, and it occurs when the intestines have been severely damage. In such cases, the patient might need to receive nutrients intravenously.

A gluten-free diet means eliminating foods that contain wheat, rye, and barley. "Plain" meat, fish, rice, fruits, and vegetables do not contain gluten. To maintain a healthy gluten-free diet, a person must use non-gluten containing ingredients when cooking and baking. Potato, rice, soy, buckwheat, or bean flour, for example, can be used instead of wheat flour. Gluten-free products also are available from many organic and mainstream food stores. It is important, though, that individuals with the disease verify that their foods were not contaminated with gluten during processing or preparation. For example, a person with celiac disease should not use a toaster that has been used to toast regular wheat bread. Individuals should be extremely cautious when eating out, and should ask a waiter or chef when uncertain about the ingredients used in a meal. Gluten also is used in some medications and other products, such as lipstick and play dough. Reading product labels therefore is crucial. This diet might seem difficult at first, but people are able to adjust and get used to the new lifestyle.

Emotional Adjustments

Many people with celiac disease suffer emotionally because diagnosis often is prolonged. When first diagnosed, the individual might experience anxiety, insecurity, isolation, fear of the unknown, and lack of information. There are celiac support groups that help people adjust to this way of life and to address such problems. As individuals struggle to become accustomed to a new way of eating, they experience emotions such as relief at finally finding out what was wrong, grief over the loss of their former lifestyle, and difficulty in finding appropriate food. These

feelings don't last forever, but one must continually explain the disease to those around them. Staying healthy takes personal determination, family support, and a doctor who knows how to treat celiac disease.

Rebecca E. Ryder

Research Issues

Currently, a diagnosis of celiac disease is only considered confirmed following a biopsy of the small intestine. These biopsies usually are accomplished with an endoscopy procedure, in which a tube is snaked down the esophagus, through the stomach, and into the small intestine, where a tissue sample is taken. Although it is not extremely painful, most patients find the procedure uncomfortable. New diagnostic techniques are being studied including capsule endoscopy, in which the patient swallows a capsule containing a small video camera that records the small intestine. Additionally, researchers are experimenting with the idea of breeding new grains that lack key gluten proteins. New celiac disease treatments on the horizon include devising ways to retrain the immune system to no longer respond to gluten. A number of new drug treatments also are being evaluated.

See Also: Food allergies and intolerances; Small intestine.

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Chamomile

Chamomile is an herb. The term "chamomile" refers to two species of plant that have daisy-like flowers, German Chamomile (*Matricaria recutita*) and Roman Chamomile (*Chamaemelum nobile*). Both species of plants originate from the Mediterranean region and were widely used in antiquity in Egypt, Greece, and Rome. Today chamomile also is grown in North America and is recognized as a popular ingredient in herbal tea. Chamomile is believed to work as a mild sedative as well as a digestive aid.

The origins of chamomile date back to 1550 BCE where it can be found on the Eber's medical papyrus. It was celebrated by the ancient Egyptians as a gift from the sun god, Ra, and was an ingredient in embalming oil. It was the Greeks who gave this herb the name "chamomile" and it was used medicinally to treat headaches, female disorders, and digestion problems. By the 17th century, the English herbalist Nicholas Culpeper put forth the idea that it could be used to remedy digestive problems. Chamomile is believed to have arrived in North America in the 16th century with European immigrants. Since that time it has gained popularity for its medicinal, therapeutic, and cosmetic benefits (Gahagan, 2013).

The German Chamomile plant can be found in areas that provide full sun and well-drained soil. It is the variety that is most widely used in North American. The flowering tops of chamomile plants are used in various forms, including tea bags, tinctures (alcoholic extract), and aromatic oils. The use of the tea is believed to help with minor cases of digestion problems such as nausea, abdominal pain, bloating, and irritable bowel syndrome (National Center for Complementary and Alternative Medicine, 2013). Chamomile also is used to help with sleeping problems, muscle tension, and anxiety. Laboratory studies suggest that chamomile extracts provide a helpful effect in both mild to moderate anxiety and mild to moderate depressive disorders (Amsterdam et al., 2012). For cosmetic use, chamomile is used to soothe the skin from burns, acne, puffiness, mouth sores, and eczema. It is found in lotions, sprays, and facial cleansers.

Chamomile appears to be safe for most people. Because chamomile has anticoagulant properties, however, people taking an anticoagulant drug are advised not to drink or use chamomile. People who have experienced prior allergic reactions to plants in the daisy family—which includes ragweed—also could experience allergic reactions to chamomile.

Angelica O. Patlan

See Also: Herbs and herbal medicine.

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Childhood Nutrition

A healthy, balanced diet is essential during childhood for proper growth and development, including organ formation and function, cognitive and neurological development, and a strong immune system. Ensuring that a child receives adequate nutrition, however, is not always easy. Children can be picky eaters and caregivers are not always sure how much food children need as compared to adults. Both undernutrition and obesity continue to be critical issues affecting children worldwide. Conflicting information regarding food allergies, as well as the effects of additives in food also cause concern and confusion.

Nutritional Requirements

Infants have unique nutritional needs, but by the time babies are a year old, a wide variety of foods can be incorporated into their diets, as long as the foods do not pose a choking risk. The average one-year-old child requires between 850 and 1,000 kilocalories per day. This amount increases gradually until it doubles by age 10. The USDA recommends 6 ounces of grains, 2½ cups of veggies, 1½ cups of fruit, 2 to 3 cups of milk, and 5 ounces of protein foods per day for kids aged 6 to 11 years. Children have small stomachs, therefore 6 small meals a day often is a more appropriate meal plan than 3 big meals.

A balanced diet generally meets all of a child's nutritional requirements, and both the American Medical Association and the Academy of Nutrition and Dietetics recommend that children get nutrition from healthy foods rather than from vitamin supplements. Deficiencies in calcium, iron, and certain vitamins, however, are a concern for children who do not eat a balanced diet. Multivitamin supplements might be recommended for children who are failing to thrive, have severe food allergies or a chronic disease, or follow a restrictive diet, such as a vegan diet. The most common nutrient deficiency around the world is iron. Iron deficiency can affect a child's mood, energy level, attention span, and ability to learn. A healthy diet is the best way to prevent and treat iron deficiency. Good sources of iron include leafy green vegetables, oatmeal, meats, eggs, legumes, peanut butter, liver, baby formula with iron, breast milk, and iron-fortified cereal.

Picky Eaters

Children can be picky eaters and often dislike certain textures, colors, or flavors, such as particularly rich or spicy foods. Young children's taste buds are more sensitive than adults', which is one reason that mild flavors appeal to young children. Sometimes "picky eating" is simply less appetite resulting from a slowing growth rate. This is particularly common for children at around ages 3 and 4 years; other times it is an expression of independence for children who want to exert some control over their environment. Nutritionists recommend that caregivers be patient with picky eaters, set a healthy example, and continue to expose them to a wide variety of nutrient-rich foods. It could take eight to ten food exposures before the child accepts the new food. When given some autonomy in choosing foods and amounts, however, children usually outgrow these eating habits. Caregivers who are concerned about a picky eater becoming malnourished should talk to the child's health care provider.

Malnutrition

Malnutrition is caused by inadequate food intake or a diet lacking one or more nutrients; it can also be caused by problems with absorption and digestion that are linked to certain medical conditions. Hunger and malnutrition are responsible for 60% of child deaths worldwide (Insel, Ross, McMahon, & Bernstein, 2013). The signs and symptoms of malnutrition can vary, but they can include low energy, poor immune function, poor growth, muscle weakness, learning difficulties, and osteoporosis. Poverty, political crises, natural disasters, and epidemics all are common causes of malnutrition.

Vegetarian and Vegan Children

With careful planning, alternative diets such as vegetarianism or veganism can be healthy and safe for children. Vegetarian and vegan diets often are low in vitamins D and B12, calcium, zinc, and iron, but these nutrients can be absorbed through fortified products. Animal proteins can be replaced with wheat and rice products, as well as legumes and nuts. Vegan children also should consume dairy-free beverages that are fortified with calcium and B12.

Obesity

The number of obese children in the United States has more than doubled in the past 30 years, and was up to 18% in 2010 (CDC, 2013). Obese children are more likely to become obese adults, and have a higher risk of developing health problems later in life, such as heart disease, metabolic syndrome, and hormone-related cancers.

Diets that are high in sugar and fats, reliance on fast food, excessive snacking, limited physical activity, and environmental factors (such as no safe place to play)

all have an impact on whether children become overweight or obese. Treatment should begin with assessing the child's physical activity and diet. The American Academy of Pediatrics recommends that children watch no more than 1 or 2 hours of entertainment media per day, and no television or other entertainment media is recommended for children younger than 2 years of age (American Academy of Pediatrics, 2014).

Many children spend significant time at childcare centers, therefore care providers have just as great an influence on children's diets as home care providers do. For this reason, childcare providers should go through nutrition and physical activity trainings to help prevent unhealthy eating habits that could lead to diet-related illnesses and obesity. Children should be taught how to make healthy choices regarding food and physical activity.

Allergies

From 1997 to 2011, the number of food allergies increased in children younger than age 18; they are now thought to occur in 6% to 8% of children (Branum & Lukacs, 2008). Six foods (milk, egg, peanuts, tree nuts, fish, and shellfish) cause 90% of all allergic reactions to foods. Considerable research is examining the increase. A common hypothesis, referred to as the "hygiene hypothesis," is that living in more-sterile environments interrupts the immune system function and development, leading to an increase in allergic reactions and autoimmune diseases.

Another hypothesis is that delaying giving children foods that commonly cause allergic reactions might increase the risk of developing an allergy. The American Academy of Pediatrics formerly recommended that pregnant women and young children avoid eating common-allergy foods. The Academy, however, changed this recommendation because of lack of evidence (Greer, Sicherer, & Burks, 2008). Studies of countries where pregnant women and young children eat common-allergy foods have much lower rates of food allergies than countries where these foods are delayed (like the United States and the United Kingdom). Many scientists now believe repeated exposure to a common-allergy food at a young age teaches the body to tolerate the allergens, thus decreasing the likelihood of an allergic reaction. The LEAP Study (Learning Early about Peanut Allergy) is an international clinical research study based in London that is currently investigating the best way to prevent peanut allergy in young children. Researchers are testing both the avoidance of peanut in infancy and the measured, repeated consumption of peanut-containing foods in infancy (Immune Tolerance Network, 2013).

Hyperactivity

According to a comprehensive review of research connecting diet to attention-deficit disorder (ADD) and attention-deficit hyperactivity disorder (ADHD) in children, researchers Millichap and Yee (2012) conclude that diet can decrease

ADHD symptoms, particularly when complemented with medication. There is no single dietary trigger, however—diet is but one factor of many affecting children's behavior and cognitive function. Dietary changes supported by research include lessening consumption of refined sugar, sodium, and total fat; increasing long-chain polyunsaturated fatty acid consumption (omega-3 and omega-6 fatty acids); and limiting artificial colors.

Lisa P. Ritchie and Ava B. Castro

Research Issues

In both the United States and Canada, steroid-based growth hormones can be given to meat cattle to increase their size. In the United States—but not Canada or the European Union—protein-based hormones can be given to cattle to increase milk production. These practices have sparked considerable debate regarding their consequences to human health and for children in particular. The considerable research findings have been inconclusive, however, and the FDA continues to promote the safety of these practices. One concern is that the increasing number of girls reaching puberty before age 12 could be connected to meat and dairy consumption. How can this be determined? Is earlier puberty linked to an increase in meat and dairy consumption, or is earlier puberty linked to an increase in the consumption of meat and dairy that have been treated with growth hormones? The use of hormones is not the only change in the meat and dairy industry over the past 50 years. Cows are milked far more frequently than in the past, for example, including during late stages of pregnancy, when the levels of naturally occurring hormones are 33% higher than normal. Is this affecting not only early puberty, but other increased cancer rates as well? Is earlier puberty not a result of meat and dairy consumption, but of increasing rates of obesity and inactivity?

See Also: Breast-feeding; Food allergies and intolerances; Infant formula; Iron-deficiency anemia; Obesity, causes; Obesity, definition and health effects; Phenylketonuria (PKU).

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Chlorella

Chlorella is a unicellular, freshwater green alga that has been hailed as a superfood with numerous benefits to the immune system. The species most commonly consumed by humans is *Chlorella pyrenoidosa*, which also is called "sun chlorella." Chlorella grows best on the surfaces of shallow ponds in warm air. When swallowed whole, chlorella is indigestible due to its tough cell wall. Most chlorella tablets contain chlorella growth factor (CGF), which comprises about 5% of a single chlorella specimen. Chlorella growth factor is water soluble and full of vitamins and amino acids. It is extracted from the microbe and then can be taken orally or through an injection. Chlorella is very popular in Japan, where it is sold as a medicinal supplement and often is recommended by doctors.

In the decade following World War II, a hunger crisis seemed imminent as the world's population boomed and farmers struggled to keep up with the demand for crops. While looking for a cheap and easily produced alternative to traditional foods, scientists turned to potential non-agricultural sources of nutrition, such as chlorella. A single chlorella microbe contains an impressive amount of fats and calories, as well as fiber, vitamins, minerals, and all of the essential amino acids. In fact, more than half of the dried product is composed of protein.

The world population did indeed double between 1950 and 1990, but the predictions that agriculture would be overwhelmed by the population were proven wrong. The farming of chlorella also turned out to be much more involved and inefficient than previously thought. In 1950, pharmaceutical company Pfizer estimated that a pound of chlorella would cost one dollar to produce, as opposed to the

six cents required to produce a pound of soy (Belasco, 1997). The idea of chlorella as a mass-produced food source was abandoned. In the 1970s and 1980s, however, health food enthusiasts in Japan claimed that chlorella was a miracle supplement. Chlorella sold for up to $50 per pound in health food stores, and it was shipped to the Western world and marketed as an oriental herb (Belasco, 1997). The claims for chlorella's powers ranged from controlling weight and boosting the immune system to curing or preventing cancer.

The alleged health benefits of chlorella have been praised widely, but little scientific evidence exists to support the claims. A handful of small, preliminary studies suggest that additional research might find support for potential health benefits. In a 1990 study, for example, cancer patients with brain tumors were given chlorella tablets as supplements to their regular medications for two years. The chlorella did not have a significant effect on the patients' survival, but it did have a notable impact on their immune systems. Patients' lymphocyte and neutrophil counts were almost completely normal, which is unusual considering they were undergoing chemotherapy and taking immunosuppressant drugs (Merchant & Andre, 2001). Merchant and Andre conducted another study in 2001 in which they focused on chronic diseases. They found that a supplement of 10 g of chlorella tablets and 100 mL of chlorella extract daily for two months helped to ease the symptoms of fibromyalgia in some of the study participants (Merchant & Andre, 2001). In a separate clinical trial, participants showed a decrease in serum cholesterol level when taking chlorella supplements (Merchant & Andre, 2001). More evidence is needed, however, before chlorella supplements can be recommended for these effects.

Some people report that, for the first week after beginning to take chlorella tablets, they experience some gastrointestinal cramping and general discomfort, as well as diarrhea and mild nausea. Because chlorella could help stimulate the immune system, it should be avoided by people who have autoimmune diseases.

Siobhan M. Prout

See Also: Spirulina.

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Chloride

Chloride is an essential mineral that helps maintain the balance of fluids within the body, and is an important ingredient in gastric juices secreted by glands in the stomach—especially hydrochloric acid. Chloride comprises 70% of the body's negatively charged particles, thus chloride plays a pivotal role in the conduction of electrical impulses that enable the nervous system to function. As a negative ion it often binds with cations such as sodium, which forms table salt (NaCl) and is the primary source of chloride for humans. Chloride also is found in many foods, especially seaweed, tomatoes, lettuce, celery, and olives.

Chloride deficiency is rarely observed. It is most likely to occur in conditions marked by frequent vomiting, which causes the loss of hydrochloric acid from the stomach contents. Frequent vomiting can occur with the eating disorder bulimia. When frequent self-induced vomiting occurs over a long period (several weeks or months), low blood chloride levels can occur, a condition known as "hypochloremia." Hypochloremia also can occur with other situations that involve extreme loss of bodily fluids through sweating, vomiting, or diarrhea. When the body is chloride deficient the pH of the blood increases. This condition is known as "alkalosis." Alkalosis is a life-threatening state that is accompanied by lethargy, irritability, muscle weakness, and dehydration. Occasionally, ingesting too much water also can result in hypochloremia, causing similar symptoms. Because healthy individuals with adequate water intake are able to excrete excess chloride in urine and sweat, the toxic effects of sodium and potassium typically are felt before those of chloride. High blood chloride levels are uncommon, except with severe dehydration or as a side effect of some medications.

The adequate intake of chloride for adults is 2.3 g per day, and ensures normal ion concentration. The adult upper limit for chloride intake is set at 3.6 g per day. The average daily intake of chloride from salt for people in North American, however, is about 4.5 g per day. Limiting the daily intake of salt—both as table salt and from prepared foods—can help people achieve a more desirable chloride intake.

Patricia M. Cipicchio

See Also: Electrolytes; Stomach.

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Chocolate

Chocolate is a food or flavoring produced from the seeds of the cacao tree. Chocolate often is made into powdered, paste, or solid forms, usually with sweeteners and other ingredients added. Chocolate is especially popular in candy form, but is also added to other foods, such as milk. Chocolate's roots reach back to ancient Mesoamerica (a region that includes what is today parts of Mexico and Central America), where it was first used as a medicinal treatment. The cocoa produced then would be unrecognizable to modern-day connoisseurs. The cacao seed now undergoes a complex process of roasting, grinding, pressing, and mixing into a refined cocoa product.

The merits of chocolate long have been the subject of debate. For many years, chocolate was considered a junk food having no nutritive value. Cocoa, the main ingredient of chocolate derived from cacao seeds, however, has been shown to



Cocoa or cacao beans in a cacao pod. The pod has a thick, rough rind. The white seeds inside turn brown as they dry. (U.S. Department of Agriculture)

contain compounds that could be beneficial to health. Chocolate contains flavonoids and other phytochemicals, which have recently sparked research interest. Some studies suggest chocolate may improve insulin resistance and cardiovascular health. However, the health effects of chocolate depend upon how it is prepared. A majority of commercial chocolate products, including most chocolate candy, has a low content of flavonoids and antioxidants in addition to high concentrations of sugar.

History of Chocolate

Mesoamerican civilizations are believed to have used cacao seeds and have produced cocoa as early as 600 BCE (Lippi, 2013). A cocoa beverage was used by these civilizations for medicinal purposes. Hernán Cortés was the first conquistador to document the existence of chocolate in 1528 and brought cocoa to Spain for sampling by King Charles. Much later, in 1753, Carl Linnaeus dubbed the *Theobroma* cocoa plant, from which cocoa is developed, the "Chocolate Tree."

Chocolate's euphoric, romantic effects were immediately observed upon its introduction to Europe (Lippi, 2013). The Catholic Church disapproved of chocolate due to these effects (Lippi, 2013). European doctors were quick to incorporate chocolate into medical treatments, citing observations of cocoa uses from Mesoamerica. The *Badianus Manuscript*, written in 1552 by M. De La Cruz, a Mexican teacher, describes the therapeutic uses of cocoa to treat a variety of indigenous disorders and diseases, especially angina, various digestive symptoms, and dental issues. These medical uses in the Americas inspired the European use of chocolate as a treatment for such things as weight loss, weight gain, and digestive issues. Additionally, cocoa was thought to be a nervous-system stimulant (Lippi, 2013).

Chocolate Production

Chocolate is typically divided into three varieties: dark, milk, and white. These chocolates are distinguished by their different ratios of cocoa liquor and cocoa butter. Chocolate production begins with the harvesting of cacao seeds (also referred to as "cocoa beans") from cacao trees. To produce cocoa liquor, the seeds are fermented, dried, cleaned, and roasted. The seeds then are cracked open to harvest the cocoa nibs, which are ground to produce the cocoa mass. Cocoa liquor is the paste made from the nibs of cocoa beans, and contains most of the nutritional components of interest. Cocoa butter is the fatty portion of chocolate refined from the cocoa liquor. The non-fatty portion of cocoa liquor, resulting from the ground and roasted nibs, often is called "nonfat cocoa solids." The nonfat cocoa solids have relatively high concentrations of polyphenols, vitamins, and fiber. Dark chocolate is distinguished by a greater percentage of cocoa liquor. Milk chocolate contains added dairy product (usually powdered milk or sweetened condensed milk) and a lesser percentage of cocoa liquor. White chocolate has no cocoa liquor; it simply is produced from cocoa butter and other additives.

The amount of cocoa liquor in the chocolate determines the percent cocoa, and ultimately what type of chocolate is produced. A minimum of 35% cocoa liquor is needed for the production of dark chocolate. In the United States, generally 10% to 12% cocoa liquor by weight is used for the production of milk chocolate (Katz, Doughty, & Ali, 2011).

Nutrition Content of Chocolate

The fatty acids of the cocoa butter are a combination of saturated and unsaturated fatty acids. There is an unusually high concentration of stearic acid, which has a neutral effect on the cholesterol profile, appearing to neither increase nor decrease serum cholesterol levels.

The nonfat cocoa solids (which make up the majority of chocolate liquor) include the bran of the cocoa seed, which contains fiber. Most fiber is lost in the processing of the cocoa seed; however about 1.7 to 0.6 grams of fiber are found in a 100 kcal portion of dark or milk chocolate (Katz, Doughty, & Ali, 2011). Cocoa contains mostly insoluble fibers. There are very low amounts of other vitamins and minerals in the nonfat cocoa solids. These micronutrients include copper, magnesium, potassium, and iron. A number of phytochemicals are found in the nonfat cocoa solids and are of particular interest in recent research.

Chocolate and Health

Modern studies of the possible health benefits of chocolate were inspired by studies of the Kuna Island natives. Kuna Island is located off the coast of Panama. Kuna Indians have an unusually low risk for heart disease and lower blood pressure than other groups having comparable salt intake and weight (NIH, 2011). It was noted that the Kuna consume more than ten times the amount of cocoa as compared to the average American. Additionally the Kuna people consume a much less processed form of cocoa, thought to be higher in flavonoids. Upon moving away from the island, Kuna natives experience an increased risk in heart disease, an increase in blood pressure, and a decrease in cocoa intake. It is unclear how much of the explanation for these observations can be attributed to chocolate. Nevertheless, the research generated by these studies has led to some interesting findings.

Antioxidants and Chocolate

Cocoa is a very flavonoid-rich food. Flavonoids are credited for the main antioxidant properties of chocolate, and flavonoid antioxidants are associated with the plasma's ability to better protect itself from oxidative damage. Plasma is the fluid component of human blood, and contains many molecular elements that are essential to nutrition, immune function, and clotting. Flavonoids also are being investigated for antibacterial, antiviral, anti-inflammatory, and anticancer roles, although these functions have not yet been linked specifically to chocolate's flavonoids.

Most flavonoids are found in the cocoa liquor and derive from the nonfat chocolate solids. Higher concentrations of cocoa liquor are correlated with higher amounts of flavonoids and more antioxidant properties. Flavonoid concentrations often vary greatly between different chocolates; this probably is due to variance in cocoa-seed processing.

Health Benefits of Chocolate

A recent meta-analysis supports the idea that cocoa flavonoids help reduce insulin resistance and improve blood glucose regulation (Hooper et al. 2012). These observations in part could be due to chocolate's effects on endothelial function. Endothelial function refers to the normal dilation and constriction of the arteries due to adequate responses to signaling molecules such as nitrous oxide. Improvements in endothelial function also could explain the association of chocolate consumption with reductions in resting diastolic blood pressure and with heart health. Researchers have proposed that the improved blood flow seen in chocolate studies might explain preliminary results observing better cognitive function with chocolate consumption. Consumption of chocolate has been shown to improve mood in many people, and chocolate appears to have an effect on the central nervous system, possibly through the release of neurotransmitters associated with positive affect in the reward system of the brain.

Recommendations for Chocolate Intake

People who enjoy chocolate and hope for health benefits from its consumption are advised to consume up to 3 oz (85 g) of dark chocolate daily. Chocolate should be labeled as containing at least 65% cocoa. This amount of chocolate can contain hundreds of calories, so people adding chocolate to their diets must subtract calories in other areas to avoid weight gain.

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See Also: Antioxidants; Phytochemicals.

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Cholesterol

Cholesterol belongs to a group of chemical compounds called sterols and is found both in foods and in the human body. Cholesterol is made from four linked hydrocarbon rings with a hydrocarbon group at one end and a hydroxyl group at the other end. It is an important lipid involved in membrane permeability and fluidity, and is found in varying degrees in practically all animal membranes. Cholesterol is the precursor of steroid hormones such as progesterone, testosterone, estrogens, and cortisol. It also is the precursor of vitamin D. Cholesterol can be obtained from both animal products in a diet and be synthesized de novo by the body from its precursor acetyl CoA, an activated carrier molecule of great importance in cellular metabolism. The liver manufactures bile from cholesterol. Bile is important for the digestion and absorption of fats and fat-soluble vitamins. The liver is the major site of cholesterol synthesis in mammals. The small intestine also produces significant amounts of cholesterol. The rate of synthesis of cholesterol by the body can vary greatly, based on how much cholesterol is consumed in the diet. Blood levels of cholesterol and cholesterol-transport compounds are somewhat predictive of a person's risk for the development of artery disease and its complications, including heart attack and stroke. Overall diet patterns, as well as several dietary components, appear to influence blood cholesterol levels.

Cholesterol in both the diet and as a component of artery disease came under scrutiny in the 1950s as researchers began to investigate artery disease etiology. Observing that arterial plaque contains high concentrations of cholesterol and other lipids, researchers began to explore the association between dietary cholesterol and fats, serum cholesterol levels, artery disease development and progression, and end points such as heart attack and stroke. Researchers now believe that intake of dietary fat and cholesterol does influence artery disease development, but in complex ways, primarily through the behavior of cholesterol-carrying compounds known as lipoproteins.

Cholesterol is transported from its sites of synthesis or absorption to the sites of use, and finally to the liver for excretion by transport molecules called lipoproteins. Lipoproteins are composed of cholesterol, triglycerides, phospholipids, and proteins. They have nonpolar, hydrophobic regions in the center, with polar regions on the exterior, allowing the compounds to travel in the aqueous environment of

the body. Lipoproteins exist in several forms; they are classified based on their increasing density in plasma. Higher levels of low-density lipoprotein (LDL) cholesterol are associated with increased risk of artery disease. Low-density lipoproteins appear to promote arterial damage when they become oxidized and bind with the artery lining. Higher levels of high-density lipoprotein (HDL) cholesterol, however, are associated with lower risk of artery disease; thus LDLs are known as the "bad" cholesterol, and HDLs are known as the "good cholesterol." The HDLs transport cholesterol from plasma and deliver it to the liver where cholesterol is converted to bile and excreted. Additionally, HDLs shuttle cholesterol throughout the body to the tissues where cholesterol is used to synthesize the steroid hormones.

Cholesterol and Artery Disease

High serum cholesterol levels increase artery disease risk. This risk was first observed in people with abnormally high serum cholesterol levels because of an inherited condition known as familial hypercholesterolemia. This condition is characterized by deposition of cholesterol in various tissues. Familial hypercholesterolemia is not due to diet failure, but rather to the inability the LDL receptors located throughout the body to take up triglycerides because of a defect in the LDL receptors.

As research continued to accumulate evidence that blood levels of total cholesterol, LDL cholesterol, and HDL cholesterol are related to artery disease risk, in 1985 the U.S. National Heart, Lung, and Blood Institute (NHLBI) launched the National Cholesterol Education Program (NCEP). The program has promoted public education regarding the importance of diagnosing and treating high cholesterol levels. High LDL cholesterol levels can be reduced by both lifestyle measures and medications. Lifestyle measures that promote healthful blood cholesterol levels include regular physical activity, weight control to achieve healthful body fat levels, and a heart-healthy diet.

Diet and Cholesterol

Studies on serum cholesterol, foods, and diet pattern have found that dietary change and cholesterol-lowering functional foods and dietary supplements are possible alternative therapies for lowering plasma total cholesterol and LDL cholesterol, especially for people whose blood cholesterol level is slightly high but not high enough to necessitate the prescription of cholesterol-lowering medication. Dietary patterns associated with improved blood cholesterol levels include almost any weight-loss diet, including low-carbohydrate diets (such as the Atkins diet), low-fat diets, and Mediterranean-type diets. Weight-loss diets are effective for short-term cholesterol reduction. For long-term weight-loss maintenance and blood cholesterol control, both low-fat and Mediterranean-type diets have strong support. Nutrition professionals recommend diets high in plant foods, including fruits, vegetables, and legumes. Consumption of foods high in saturated fats, such as high-fat

What Do Your Cholesterol Numbers Mean?

Lipoprotein cholesterol levels are predictive of heart disease risk, therefore adults are urged to monitor these levels. The National Heart, Lung, and Blood Institute (NHLBI) launched the National Cholesterol Education Program (NCEP) in November 1985. The following advice comes from NCEP's Web site. More-detailed information is available there.

Everyone age 20 years and older should have their cholesterol measured at least once every 5 years. It is best to have a blood test called a "lipoprotein profile" to determine cholesterol numbers. Cholesterol levels are measured in milligrams (mg) of cholesterol per deciliter (dL) of blood. This blood test is done after a 9- to 12-hour fast and gives information about the following.

- Total cholesterol
- LDL (bad) cholesterol—The main source of cholesterol buildup and blockage in the arteries
- HDL (good) cholesterol—Helps keep cholesterol from building up in the arteries
- Triglycerides—another form of fat in the blood

If it is not possible to get a lipoprotein profile done, knowing the total cholesterol and HDL cholesterol can provide a general idea about cholesterol levels. If total cholesterol is 200 mg/dL or more, or if HDL is less than 40 mg/dL, then a lipoprotein profile should be performed. For comparison, cholesterol numbers are provided in the tables below.

Table 1. Cholesterol Level Categories

Total Cholesterol Level	Category
Less than 200 mg/dL	Desirable
200–239 mg/dL	Borderline High
240 mg/dL and greater	High

* Cholesterol levels are measured in milligrams (mg) of cholesterol per deciliter (dL) of blood.

Source: U.S. Department of Health and Human Services. (2005). *High blood cholesterol: what you need to know*. Retrieved from http://www.nhlbi.nih.gov/health/public/heart/chol/wyntk.htm

Table 2. LDL Cholesterol Level Categories

LDL Cholesterol Level	LDL-Cholesterol Category
Less than 100 mg/dL	Optimal
100–129 mg/dL	Near optimal/above optimal
130–159 mg/dL	Borderline high
160–189 mg/dL	High
190 mg/dL and greater	Very high

Source: U.S. Department of Health and Human Services. (2005). *High blood cholesterol: what you need to know*. Retrieved from http://www.nhlbi.nih.gov/health/public/heart/chol/wyntk.htm

HDL (good) cholesterol protects against heart disease, thus, for HDL, higher numbers are better. A level less than 40 mg/dL is low and is considered a major risk factor because it increases the risk for developing heart disease. HDL levels of 60 mg/dL or more help to reduce the risk of heart disease.

Triglycerides also can increase heart disease risk. Levels that are borderline high (150–199 mg/dL) or high (200 mg/dL or more) could require treatment for some people.

U.S. Department of Health and Human Services. (2005). *High blood cholesterol: what you need to know*. Retrieved from http://www.nhlbi.nih.gov/health/public/heart/chol/wyntk.htm

meats and processed meats, should be reduced. Although intake of dietary cholesterol does not appear to have a strong effect on serum cholesterol levels in healthy people, some public health organizations continue to recommend keeping daily cholesterol intake below 300 mg. People with type 2 diabetes, obesity, or heart disease appear to be most sensitive to cholesterol intake and should try to limit foods such as eggs that are high in cholesterol.

Several specific foods and food components exert modest cholesterol-lowering effects. They appear to work through a variety of mechanisms; for example, many act as bile acid sequestrants. Excessive cholesterol can be eliminated from the body via formation of bile acids, and secretion of bile into the small intestine. Bile acid sequestrants bind bile acids in the intestine, and inhibit their reabsorption by producing an insoluble complex. Inhibition of bile acid reabsorption decreases hepatic cholesterol concentration, increases synthesis of bile acids from cholesterol, and causes an entry of plasma cholesterol into the liver, because the lowered level of hepatic cholesterol increases the expression of LDL receptors. Phytochemicals in a variety of foods also appear to interact at other steps in cholesterol pathways. Foods and food components that might influence serum cholesterol levels include the following.

- Foods with water-soluble dietary fibers—Non-digestible polysaccharides and fermentation-produced short chain fatty acids are the active ingredients in water-soluble fibers. They work by inhibiting bile acid reabsorption and cholesterol absorption. Oatmeal, oat bran, and other high-fiber foods contain water-soluble fiber.
- Fish and omega-3 fatty acids—These foods alter blood lipid profile. Walnuts, almonds, and other nuts also have beneficial fatty acids and fiber.
- Plant sterols and stanols—These phytochemicals often are added to margarines and other foods designed to help control blood cholesterol levels. They block the reabsorption of cholesterol.
- Olive oil—Using olive oil for cooking and for salad dressing is associated with reductions in blood cholesterol.
- Other phytochemicals: Garlic, soy foods, and green tea contain an abundance of phytochemicals that have shown cholesterol-lowering effects in some studies.

Many dietary supplements and herbal remedies claim to help reduce high blood cholesterol levels. One of the most effective is red yeast rice, a therapeutic agent from traditional Chinese medicine. Red yeast rice is prepared by fermenting a type of yeast over rice. This herbal medicine contains statins similar in nature to those in cholesterol-lowering medication. High-dose niacin supplements can also be helpful for reducing LDL cholesterol and raising HDL cholesterol. Some studies, however, have found increased stroke risk in patients already taking statins who were given high-dose niacin supplements. Because both red yeast rice and high-dose niacin supplements behave as drugs, use should be carefully monitored.

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See Also: Cardiovascular disease and nutrition; Gallbladder and gallbladder disease; Lipids; Lipoproteins; The liver; Niacin.

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Choline

Choline is a substance that is similar in structure and function to vitamins, so it is commonly referred to as a "vitamin-like compound." It plays several significant roles in the human body. In healthy people the liver is able to synthesize most of the choline required for good health from the amino acid precursors methionine and serine. Because deficiency symptoms develop in some people (especially men) on a choline-free diet over time, however, choline is classified as an essential nutrient, meaning it must be obtained from the diet. A relative latecomer to the Dietary Reference Intakes table, choline was first recognized as an essential nutrient by the Institute of Medicine in 1998. The adequate intake for choline is 550 mg per day for adult men and 425 mg per day for adult women. Choline is plentiful in a mixed diet, as it is found in many foods, including meats, liver, eggs, nuts, beans, cauliflower, and spinach.

Functions

Choline forms part of the important neurotransmitter acetylcholine. It is also a component of bile, which aids in the digestion of lipids. Choline is a component of—and is required for—the synthesis of several phospholipids which serve as structural components of cell membranes, including a form of lecithin called phosphatidylcholine. Some of these phospholipids also are precursors for the intracellular messenger molecules diacylglycerol and ceramide. These messengers are important for healthy cellular function. Choline also serves as a donor of methyl groups (CH_3), a step in many important metabolic pathways. Researchers have explored possible health benefits related to choline intake.

Cognitive Function

Choline's role in the formation of the neurotransmitter acetylcholine has prompted research into the relationship between choline intake and cognitive function. Preliminary research with small groups of Alzheimer's disease patients found that those receiving supplemental choline showed a slight improvement in symptoms as compared to a control group (EBSCO, 2009). Similarly, research with a small group of stroke patients found slightly better chance of full recovery in the patients receiving choline as compared to those in the control group (EBSCO, 2009).

Liver Disease

When choline deficient, some people develop a condition called "fatty liver" and show signs of liver damage. Choline is required to form part of very low-density lipoprotein (VLDL) molecules which transport fat from the liver to tissues. Without choline, VLDL particles cannot be synthesized and fat accumulates in the liver, eventually leading to liver damage (Ziesel, 2009). In rats, a deficiency in choline also is associated with increased liver cancer and increased sensitivity to carcinogenic chemicals, although the implication of these observations for humans presently is unknown.

Neural Tube Defects

A few preliminary studies suggest that higher than recommended choline intakes might be beneficial for preventing birth defects known as "neural tube defects." Such neural tube defects include spina bifida, in which the developing spinal column fails to close properly, and anencephaly, in which the brain fails to develop properly. In a recent case-controlled study of pregnant women, higher dietary choline levels were associated with fewer neural tube defects in the children (Zeisel, 2009). The B vitamin folate is well known as a methyl donor, important for the high levels of cellular division that occur during fetal development. It is possible that future research will show that adequate choline levels also are important in this context.

Cardiovascular Disease

As a methyl group donor, choline might assist in the conversion of homocysteine to methionine. Higher serum homocysteine levels are associated with greater levels of systemic inflammation and an increased risk of artery disease. Researchers do not know whether elevated levels of homocysteine actually cause heart disease, and research linking serum choline levels to cardiovascular disease is weak.

Toxicity

High doses of choline result in a fishy body odor, vomiting, low blood pressure, and increased sweating. The fishy odor is due to excessive production and excretion of thimethylamine (TMA), a product of choline. The tolerable upper intake level of choline was set by the Food and Nutrition Board in 1998 at 3.5 g per day for adults.

Recent research on the association of a compound called tri-methylamine-N-oxide (TMAO) with increased risk of heart disease suggests that choline supplementation should be avoided unless medically necessary. TMAO is synthesized by the liver from TMA. Thimethylamine is made by bacteria residing in the colon from the precursors choline and carnitine. (Carnitine is an amino acid that is plentiful in meat.) It is not known whether TMAO contributes to cardiovascular disease, but the higher levels of TMAO observed in meat eaters as compared to vegetarians has been suggested as a possible explanation for the link between higher intakes of red meat and cardiovascular disease (Koeth, Wang, Levison et al., 2013).

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See Also: Carnitine; Lecithin; Lipids; Phospholipids.

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Chromium

Chromium is a trace mineral that is essential for various biological processes. It is relatively abundant in the earth's crust and is a transition element, which means it can exist in many ionic forms (Chromium I-VI). It primarily is found in two forms, however, trivalent chromium (Cr III) and hexavalent chromium (Cr VI). The dietary form is trivalent chromium and essential to the human body. The hexavalent form generally is a by-product of industrial pollution and can be very hazardous to human health. This entry focuses on trivalent chromium. Chromium has been found to play an important role in insulin metabolism, and also in metabolizing carbohydrates, fats, and proteins.

Chromium was first discovered by French chemist Louis Nicolas Vauquelin in 1797; however, its nutritional value was not discovered until 1957, by NIH scientists Walter Mertz and Klaus Schwarz (Pazirandeh, Bums, & Griffin, 2014). Mertz and Schwarz discovered that a compound extracted from the kidneys of pigs was able to reverse hyperglycemia in rats and was termed "glucose tolerance factor" (Pazirandeh, Bums, & Griffin, 2014). This later was found to be chromium. Interestingly, one hospital found that several of their patients on parenteral nutrition feeds (a method of delivering nutrition intravenously with special formulas) developed signs of diabetes, including weight loss, neuropathy, and impaired glucose tolerance. This was reversed when 150 to 250 mcg per day of chromium was added to the feeding solution. Thus, chromium now is a standard component of intravenous nutrition for critically ill patients.

Chromium is required in very small amounts. True chromium deficiency is rare in the nonhospitalized patient population, and there are no well-documented diseases associated with chromium deficiency in the general population. Chromium is absorbed via the small intestine and transported in the circulation bound to albumin and transferrin. Intestinal absorption has been estimated to be less than 0.4% to 2.5% of the amount ingested; the rest is excreted in the feces (Pazirandeh, Bums, & Griffin, 2014). There is enhanced absorption of chromium in the setting of iron and zinc deficiency, likely because chromium competes with iron and zinc for intestinal absorption. Certain medications can interfere with chromium absorption, including nonsteroidal anti-inflammatory medications and antacids (Kroner, 2011). Vitamin C coadministration enhances the absorption of chromium. Chromium can be lost from the body in the urine if the diet contains an excessive amount of simple sugars (more than 35%), or in times of physical stress, such as during rigorous exercise, pregnancy, or illness (Kroner, 2011).

Chromium's role in the body is not entirely clear, but it does appear to play a role in glucose tolerance and it enhances the action of insulin. Chromium is taken up by insulin-dependent cells and goes through a series of steps that leads to activation of tyrosine kinase, an enzyme that propagates insulin activity (Kroner, 2011). Insulin, in turn, allows for entry of glucose into most cells; glucose then can be used to fuel various processes within the body.

The relationship between chromium and diabetes has been studied, and several studies have shown improvement in glucose tolerance with chromium

supplementation both in vitro and in vivo. Two double-blind, placebo-controlled studies examining the effects of chromium on factors such as weight loss, metabolic syndrome, and glucose tolerance did not find a significant benefit for those participants taking chromium versus those who took a placebo (NIH, 2013; Igbal, Cardillo, & Volger, 2009). Another large analysis, however, suggested that supplementation with chromium picolinate could have a beneficial effect for patients with diabetes (Kroner, 2011). Patients had improvement in glucose levels, decreased LDL cholesterol and triglycerides, with improvement in HDL levels (Kroner, 2011). Because not all studies have found beneficial results, however, the American Diabetes Association cautions that chromium supplements probably only are helpful for people with a chromium deficiency.

The Institute of Medicine currently recommends a dietary intake of 30 mcg to 35 mcg of chromium per day for adult men, and 20 mcg to 25 mcg daily for adult women, with slightly higher doses for lactating and pregnant women (up to 45 mcg per day) (NIH, 2013). Dietary sources of chromium include some meats, vegetables including green peppers and black pepper, broccoli, and whole-grain products (*see* Table 1) (NIH, 2013). Likewise, toxicity from chromium intake has not been well documented, and at this time the Food and Nutrition Board has not defined a recommended upper limit. Some possible side effects of excessive chromium

Table 1. Selected Food Sources of Chromium

Food	Chromium (mcg)
Broccoli, ½ cup	11
Grape juice, 1 cup	8
English muffin, whole wheat, 1	4
Potatoes, mashed, 1 cup	3
Garlic, dried, 1 teaspoon	3
Basil, dried, 1 tablespoon	2
Beef cubes, 3 ounces	2
Orange juice, 1 cup	2
Turkey breast, 3 ounces	2
Whole wheat bread, 2 slices	2
Red wine, 5 ounces	1–13
Apple, unpeeled, 1 medium	1
Banana, 1 medium	1
Green beans, ½ cup	1

Source: National Institutes of Health. Office of Dietary Supplements. (2013). *Chromium. Dietary Supplements Fact Sheet.* http://ods.od.nih.gov/factsheets/Chromium-HealthProfessional/

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intake include decreased iron absorption, and there have been some case reports of renal failure, stomach irritation, liver problems, and stomach ulcers associated with high intake of chromium supplements, but these cases are rare and are potentially due to other coexisting variables.

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See Also: Minerals.

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Climate Change and Global Food Supply

The term "climate" refers to patterns of temperature, precipitation, humidity, wind, and seasons; the term "climate change" refers to changes in these patterns. The impacts of climate change can be seen not only on the weather system but in ecosystems as well. Both are linked to effects on the global food supply. Environmental changes have been on the forefront of political and scientific debate in how to handle policy and technology in preparation for the future. The world population has continued to increase, and because environmental changes suggest changes in food security, the relationship between climate change and food supply is especially relevant.

The earth has gone through—and continues to experience—climatic changes, and has been subject to many cycles of warm and cool periods. The earth currently is leaving a cool period and entering a warm period. The speed of the current warming trend is attributed to a variety of factors, including changes in solar activity and increased production of greenhouse gases that capture and accumulate heat from the sun. The present increase in average global temperature is predicted to continue, and will influence local climates, weather patterns, and ecosystems in many ways.

Climate Change and Agriculture

The interconnectedness between climate change and food supply is quite clear. Agricultural crops need a healthy and stable environment to provide for the human population. Because plants require specific water availability, temperatures, healthy soil, and insects for growth and reproduction, climate change has put many agricultural systems at risk. Natural ecosystems, as well as human economies and cultures, have emerged and have been sustained by stable climate patterns. Because so many systems are tied to climate, a change in climate therefore means a change in the ecosystems of people, plants, and animals.

To see the interconnection between climate change and ecosystems, imagine, for example, a change in the usual timing of rains or a change in seasonal temperatures. The blooming of plants and the production of fruits or the hatching of insects would be in disarray. This, in turn, would affect the synergy between pollination of crops, food for migrating birds, spawning of fish, water supplies for drinking and irrigation, forest health, and more. Climate change can increase diseases in crops and other plants, as well as in farm animals. Weeds and pests also are influenced by the weather and climate change.

Current climate-change patterns have been associated with an increase in extreme weather events, such as tornadoes, hurricanes, and other storms, usually accompanied by heavy precipitation, floods, and coastline storm surges. Heat waves and droughts also are becoming more common in various parts of the world. Weather extremes always have been a part of agriculture, but these extremes are predicted to become more common and thus more disruptive to food production. The effect of severe weather on agricultural production is familiar to most people. Increased temperatures can reduce crop yields. Droughts or heavy rains can destroy crops completely.

Climate Change and Freshwater Supplies

Climate change is likely to affect an already precarious freshwater supply in many world regions. Droughts influence not only agricultural crops, but also farm animals and people. Flooding can cause contamination of water supplies, as sewage and unsanitary groundwater infiltrate stores of drinking water. Increased temperatures have caused the melting of snow and ice in many regions, causing sea levels to rise. Rising sea levels threaten vulnerable coastline communities around the world. Coastline storm surges bring flooding and disruption of drinking-water supplies, along with damage to farms and other food production, storage, and transportation systems in a region.

Climate Change and Food Security

According to the World Health Organization, food security occurs "when all people at all times have access to sufficient, safe, and nutritious food to maintain a healthy and active life" (WHO, 2013). Food security relies not only on food production, but also on adequate storage and transportation systems—all of which can be disrupted by extreme

weather, such as severe storms and flooding. Climate change not only affects food production directly through changes in ecological conditions, but also indirectly by affecting growth and distribution of incomes and thus demands for agricultural produce.

When food production or food availability declines, food prices increase. Individuals in richer countries enjoy a diverse food supply and are better able to handle an increase in food prices. People in poor countries, however, already have limited access to sufficient high-quality and nutritious foods. They might subsist on staple grains, consuming a single food such as rice or wheat as part of each meal and obtaining a majority of daily calories from that one food. A change in price or availability of that food staple is extremely disruptive to food security for such individuals. Families in some countries normally spend 75% of their income on food and cannot adapt to further increases in food prices (Carty, 2012). Increased food prices also often lead to civil unrest. In 2008, for example, food riots erupted in more than 20 countries, with unrest toppling the Haitian government (Gillis, 2012). Poorer countries are less able to cope with extreme weather or political events that disrupt the production, storage, and transportation of food to its citizens than are resource-rich countries. Therefore the increasing prices are not the only problem; sometimes food simply is not available in certain areas.

Future Directions

Scientists and environmental organizations are attempting to predict patterns of climate change using various models. Although no one can say exactly how climate change will proceed over the coming decades, change itself appears to be a certainty. Local, national, and world organizations must work together to diversify food production, storage, and transportation systems. Communities must invest in sustainable and resilient agriculture to increase local access to food and to increase food reserves that could become available to regions suffering from food insecurity. Communities at all levels must increase disaster preparedness so that they can respond as effectively as possible when severe weather strikes, and ensure that residents have access to clean water and food. Countries and nongovernmental funding agencies must support research on the effects of climate change and the managing of ecosystems under the influence of climate change and severe weather. Comprehensive study of specific regional and local effects of climate change must be performed to help understand and manage the state of the future food supply.

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Research Issues

In the United States, Hurricane Katrina in 2005 and Hurricane Sandy in 2012 caused disruption of freshwater supplies and food availability. Use the Internet to access local news reports written during one of these disasters and find descriptions of how these storms influenced water and food availability for local residents. Examine the local and national response to these disasters. What actions appeared to be most effective? What should local and national governments do to reduce the negative impact of future storms?

See Also: Global hunger and malnutrition; Sustainable agriculture.

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Coenzyme Q10

Coenzyme Q10 (CoQ10) is a naturally occurring compound found in the mitochondria of cells. It participates in pathways of cellular respiration and energy production, and is a member of the ubiquinone group of compounds. Forms of CoQ10 can function as both lipid-soluble antioxidants and as electron carriers in ATP production. As an antioxidant, CoQ10 reduces free radicals by giving up its outer shell electrons as well as accepting electrons from other atoms, thus preventing the production of lipid peroxyl radicals which can damage cellular components. In the electron transport chain, CoQ10 co-performs the role of an electron carrier with vitamin K2 in several enzyme complexes.

The term "ubiquinone" is derived from the words "ubiquitous"—chosen because early chemists observed these compounds in all animal cells—and "benzoquinone," which is a chemical group found in ubiquinone structures. Ubiquinones contain 1 to 12 5-carbon isoprene units. CoQ10 has 10 isoprene units, hence its name. CoQ10 was first isolated in 1957 by Frederick Crane (Crane, 2007). The name "ubiquinone" was coined in England by Professor R. A. Morton, who identified CoQ10 in rat liver. In 1958, scientist Karl Folkers discovered the exact chemical structure of CoQ10 and developed processes to synthesize it (Discovery, 2014). In 1978, Peter Mitchell received the Nobel Prize in Chemistry for his research on CoQ10 in mitochondrial energy transduction and his chemiosmotic hypothesis.

Mitchell's hypothesis suggested that most ATP synthesis in cells comes from the electron transport chain—the electrochemical gradient across the inner membranes of mitochondria—by using the energy from specialized electron carriers that are formed by breaking down energy-rich molecules (Press Release, 1978).

Because CoQ10 is produced by the body it is not considered an essential nutrient. The human body, however, also obtains CoQ10 from foods. The foods highest in CoQ10 include meat and fish, but CoQ10 also is found in oils, nuts, seeds, and some fruits and vegetables. Physiological CoQ10 levels decline with age and certain disease states. This has prompted researchers to investigate possible therapeutic benefits of supplementing with this compound. Research suggests that CoQ10 supplements could be effective for reducing high blood pressure and the symptoms of congestive heart failure (Mayo Clinic Staff, 2013). Preliminary evidence suggests that CoQ10 supplementation might be helpful for a number of other health problems, although more research is required to confirm these potential benefits. Researchers presently are exploring the use of CoQ10 supplements for many conditions, including the following (Mayo Clinic Staff, 2013).

- Age-related eye disease—CoQ10 might slow the development of age-related macular degeneration and cataracts, probably because of its antioxidant activity.
- Coronary artery disease—CoQ10 appears to reduce levels of inflammation in the arteries.
- Muscle weakness accompanying statin therapy—Statins reduce production of CoQ10, therefore supplementation might offset this effect.
- Parkinson's disease and other neurological disorders—CoQ10 appears to have neuroprotective effects.
- Male infertility—CoQ10 contributes to the production of healthy sperm.
- Asthma—CoQ10 might help counteract the inflammatory processes associated with an inappropriate immune response.
- Cancer—CoQ10 might reduce the risk of breast cancer. The role of CoQ10 in breast cancer carcinogenesis is unclear, but it might reduce the growth of cancer cells by reducing inflammation and oxidative stress. CoQ10 also has been used to reduce the side effects of chemotherapy, especially in children.
- Chronic fatigue syndrome—CoQ10 could enhance energy production for people with chronic fatigue syndrome.

Because of its important roles in energy production, CoQ10 supplements often are used by athletes, although research supporting this use is sparse. Supplements seem to be fairly safe up to doses of about 1,200 mg per day in healthy adults (Higdon, Drake, & Stocker, 2014). Typical doses are closer to 30 mg to 100 mg per day. Coenzyme Q10 has been known to negatively interfere with anticoagulant therapies. People taking CoQ10 for health problems should work with their health care providers to be sure the supplement is recommended for their situations.

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See Also: Dietary supplements.

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Coffee

Coffee, as it is commercially sold and used, refers to the roasted seeds of the berries (also called "cherries") of the coffee tree. Coffee also refers to the beverages produced from the infusion of ground roasted coffee seeds with boiling water. The word "coffee" can also refer to the flavor of these beverages (as in "coffee ice cream"). Coffee is a popular beverage around the world and accounts for about 71% of adult caffeine intake in the United States (O'Keefe et al., 2013). Coffee often is imbibed for its beneficial effects on mental state, increasing alertness and productivity. Long-term coffee consumption is associated with a number of significant health benefits, and daily consumption of 2 to 3 cups appears to be safe for most adults. Coffee's negative short- and long-term effects, however, might outweigh its benefits for some groups.

Contrary to popular belief, coffee beans are not true beans. This common misconception comes from the seed's bean-like shape. Most coffee cherries contain two green seeds having flat sides that face each other. Within the Coffea genus, there are more than 6,000 species of shrubs and trees. Because of the wide range of characteristics expressed in coffee plants, botanists disagree on which plants can be accurately classified as coffee trees. There are 25 to 100 plants that are true coffee plants (NCA, 2014).

It is estimated that coffee was first brewed and drunk in the 13th century, but the first credible accounts come from the 15th century. Coffee was probably first brewed by Sufi monks in Yemen. The legend of Kaldi is widely recounted as the genesis of coffee. It is a story of a shepherd who noticed that when his goats ate a particular type of berry, they became exceptionally high-spirited. It is said that Kaldi then harvested the berries, roasted them, boiled them, and drank the resulting liquid (NCA, 2014).

Types of Coffee

Coffee beans sold for commercial use are one of two species, Coffea canephora, (more commonly called "robusta"), and Coffea arabica. Arabica beans account for approximately 70% of coffee beans sold globally. These plants are more disease-prone than the robusta species. The caffeine in arabica beans accounts for about 1% of the mass. Robusta beans produce coffee that has a distinctive taste and has 50% to 60% more caffeine than coffee made from arabica beans. Robusta coffee accounts for the other 30% of commercially grown and sold coffee.



Cup of hot coffee. Black coffee has no calories. Some of the potential health benefits of coffee drinks may be blunted if large amounts of cream and/or sugary syrups are added. Some 16 oz. specialty coffee drinks have over 600 calories. (Johannes Gerhardus Swanepoel/Dreamstime.com)

Cultivation and Processing

Coffee plants require rich soil and they thrive in climates with frequent rain, mild temperatures, (between 59 and 75 degrees F), and shaded sun. The best regions for growing coffee are those that are subtropical. Arabica thrives at high altitudes between 1,800 and 3,600 feet, and robusta grows best at altitudes between sea level and 3,000 feet. Frequent rainfall causes the coffee plants to flower continuously, and allows for two harvesting seasons (NCA, 2014).

Although some coffee trees can grow to be 20 to 30 feet tall, during cultivation they are commonly pruned to be short. It takes approximately 3 to 4 years for coffee trees to bear fruit. Once trees have started to bear fruit, the cherries are picked using one of two methods. In one method, the trees are strip-picked, and all cherries are harvested at one time. In an alternative, more labor-intensive method, cherries are selectively picked one at a time at peak ripeness. Selectively picked cherries are processed into beans that are usually more expensive than strip-picked varieties (ICO, n.d.).

Once picked, the coffee cherries are processed using one of two methods. The dry method of processing coffee, more frequently utilized in regions where water is scarcer, involves drying the cherries in the sun. While the cherries dry out, they are raked several times a day to prevent spoiling. When the cherries reach 11%

moisture content, usually after several weeks, they are gathered and stored (NCA, 2104).

An alternative to the dry method of processing coffee is the wet method. This process requires that the freshly harvested cherries be passed through a pulping machine, in which the skin and pulp are separated from the seed and washed away with water. The beans then are separated by weight using water; the heavy beans sink to the bottom of channels, and the lighter beans float to the top. Once separated by size, the beans are immersed in water-filled tanks to ferment for 12 to 48 hours. The fermentation process eliminates the slimy mucilage that remains attached to the beans after the skin and pulp are separated from the seed. After fermentation, the seeds are rinsed again and then sent to dry. The wet-processed beans can be machine dried in large tumblers, or be sun dried. Once dried the beans are ready for export (NCA, 2014).

Roasting

Roasting is the process by which green coffee seeds are turned into the brown coffee beans that are used in brewing and cooking. Before roasting the coffee seeds are green, grassy smelling, and spongy. Roasting brings out the oils and aromas that give coffee beans their unique qualities. There are very few industry-wide standards of roasting, therefore names and qualities of roasts often differ from roaster to roaster (NCA, 2014).

In general, coffee is categorized by the color of the beans as light, medium, medium-dark, or dark roasts. Light roasts are light brown in color. Because they are roasted for a shorter time and the oils inside of the beans do not break through to the surface, light-roast beans are not as shiny as are those which undergo other types of roasts. Medium roasts have a medium-brown color, a stronger taste, and are non-oily. In the United States, medium roasts are highly favored. Medium-dark roasts are characterized by a slightly oily outside, and a bittersweet aftertaste. Dark roast beans have a shiny oily surface and a pronounced bitter taste.

Decaffeination

There is significant demand for caffeine-free coffee by people who wish to enjoy the flavor, aroma, and health benefits, but do not wish to experience coffee's stimulant effects. Several techniques can be used to decaffeinate coffee. Some of these processes use chemicals to absorb or dissolve caffeine and others, such as Swiss water processing, use a series of water baths. Decaffeination processes remove about 97% of the caffeine naturally present in coffee.

Health Issues: Benefits and Risks

Coffee contains more than 1,000 components. Caffeine—the addictive component of coffee—is by far the most comprehensively researched of coffee's constituents and is associated with a myriad of symptoms, as well as both positive and negative

health effects. Chlorogenic acid is one of coffee's polyphenolic compounds, and is associated with helpful antioxidant activity. Lignans in coffee are phytoestrogens, and could have beneficial health effects in this capacity. The most interesting studies of coffee's health effects, however, come not from examination of a single compound, but from large epidemiological studies. These studies have found several interesting associations.

- Cardiovascular disease—Epidemiological studies suggest that coffee intake is associated with slightly reduced risks of heart disease and stroke. These findings were somewhat surprising, as earlier studies suggested that coffee might increase harmful blood lipids and increase blood pressure. Subsequent research found that the diterpenes cafestrol and kahweol do increase serum low-density lipoprotein cholesterol levels, but are effectively removed by paper coffee filters. Research also has shown that caffeine does cause a transient increase in resting blood pressure, but that this increase is small in regular coffee drinkers. Coffee might improve arterial health because of its antioxidants or its positive effects on blood glucose regulation.
- Diabetes mellitus type 2 and cardiometabolic syndrome—Both decaffeinated and regular coffee consumption are associated with improved insulin sensitivity and glucose regulation. Coffee consumption is associated with lower risk of type 2 diabetes mellitus.
- Parkinson's disease—Consumption of both coffee and tea are associated with reduced risk of Parkinson's disease, at least in men, suggesting that caffeine might be the active agent. The effect in women is less robust. Some research suggests that coffee reduces risk for older women who are not taking estrogen medications, but not for older women taking estrogen medications.
- Alzheimer's disease—Epidemiological studies have shown that coffee intake over the course of decades can decrease risk of Alzheimer's. Researchers are unsure of the exact mechanisms through which coffee exerts this effect. Studies suggest that trigonelline, a constituent of coffee, has been shown to regenerate axons and dendrite of neurons in vitro (Butt & Sultan, 2011). Antioxidant activity of phytochemicals also could play a role in the prevention of Alzheimer's disease.
- Liver disease—Coffee drinkers have a lower risk of cirrhosis and liver cancer.

Although coffee consumption is associated with many health benefits, research also shows that coffee can increase risk for some conditions. Many individuals are sensitive to caffeine and experience a variety of negative effects, including anxiety, heart palpitations, irritability, nervousness, tremor, and insomnia. Other negative effects include the following.

- Elevated serum LDL cholesterol levels—elevation in atherogenic blood lipids primarily is observed in people who drink large amounts of unfiltered coffee.
- Heartburn—Overconsumption of coffee can cause heartburn from gastroesophageal reflux in vulnerable individuals.

- Reduced iron absorption—People with iron-deficiency anemia should avoid consuming coffee with their supplements or with meals.
- Increased risk of miscarriage during pregnancy—High levels of coffee consumption (more than 1 to 2 cups per day) have been associated with a slightly increased risk of miscarriage.
- Osteoporosis—Coffee consumption is associated with a slightly increased risk of osteoporosis and hip fracture in older adults. Consuming adequate calcium and vitamin D could reduce this risk.

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Research Issues

The worldwide coffee trade exerts an enormous impact on many countries, especially resource-poor countries. Because coffee growing and production is such a large industry, it also has large environmental impacts. Issues of environmental sustainability associated with coffee farming can be explored on the International Coffee Association's website, as well as by doing other research.

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See Also: Caffeine; Polyphenols.

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Cognitive Restructuring

Cognitive restructuring is a step-by-step technique used to recognize, challenge, and eventually change distorted thoughts, assumptions, and predictions. It can be utilized

to avoid automatic maladaptive thinking patterns that negatively affect a person's behavior. By avoiding distorted ways of thinking, individuals learn to approach situations in a less rigid and more productive way. Cognitive restructuring can be especially helpful in regard to nutrition. By changing maladaptive thought patterns, individuals can master the skills needed to practice healthy eating and exercise habits.

History

Albert Ellis and Aaron T. Beck are two major figures accredited with cognitive restructuring techniques. In 1957, Albert Ellis devised the beginnings of Rational Emotive Behavioral Therapy (REBT), an approach that targeted irrational beliefs to change negative psychological outcomes. Ellis relied on what he called the "ABC Model." The ABC model contains three elements: A (activating event), B (beliefs), and C (consequences). "A" represents an activating event; "B" represents the underlying beliefs regarding the activating event; and "C" represents the emotional and behavioral consequences of one's interpretations. Ellis demonstrated that psychological distress often results from negative interpretations of an event, rather than the event itself.

Ellis's work became a foundation for Aaron T. Beck's cognitive therapy (CT), which is at the core of what is known today as cognitive behavioral therapy (CBT). Beck was particularly interested in studying ways in which negative thinking contributed to depression. Beck observed that his patients possessed a negative bias toward reality, something he referred to as the "cognitive triad": distorted negative views of the self, life experience, and future. Testing the reliability of these "automatic thoughts" through cognitive restructuring, he thought, could help his patients overcome depression.

Procedure

There are several approaches to cognitive restructuring. Below is a simplified version that illustrates the procedure step by step.

1. Identify the situation.
2. Identify negative emotions associated with the event.
3. Identify thoughts, beliefs, or assumptions associated with these emotions.
4. Evaluate the evidence for and against those beliefs.
5. Challenge these automatic thoughts with rational responses.

The first step in cognitive restructuring is to pinpoint the triggering event for one's negative or uncomfortable emotions. Being as specific as possible when identifying these emotions can assist in recognizing distorted thinking. Evaluating the evidence encourages individuals to observe their thoughts from an objective standpoint. For example, "Would these rules apply to my friends and family?" "What is the worst thing that could happen?" Using constructive doubt about negative thinking can serve as a helpful reality check.

The goal of the last step—challenging the automatic thoughts with rational responses—is to determine a more realistic way of thinking that, while helpful, validates the emotions associated with the original maladaptive thought. Even if the individual understands the rationale of the new thought, it might not feel true right away. Negative thinking patterns often result from years of reinforcement, and therefore can take time to reverse. It is important to practice this new way of thinking to make these new thoughts feel more believable. This will allow for the development of new coping strategies and, it is hoped, a change in behavior. Table 1 gives an example of cognitive restructuring.

Cognitive Distortions

Cognitive distortions are distorted or irrational thinking patterns about the self, world, or future. They often stem from a fear of failure. Clinging to these beliefs allows for very little flexibility and can have a significant effect on one's motivation, self-esteem, and ultimately, behavior. Below are some examples of cognitive distortions.

- All-or-nothing thinking / black-and-white thinking. People or situations are perceived as either "good" or "bad," and anything falling short of perfect feels like failure. Example: If I don't follow my meal plan perfectly this week, I can officially say I'm a hopeless case.
- Overgeneralization: Perceiving an isolated negative event as a never-ending pattern of defeat. Example: I was too tired to run for more than 20 minutes today . . . I'll never be a good athlete!
- Mental filter: Dwelling on a single negative detail exclusively until the perception of the entire event is darkened. Example: My doctor complimented my efforts because my glucose levels have been better with my dietary changes, but said I should consume more leafy greens. I'm clearly not trying hard enough.
- Disqualifying the positive: Disregarding positive experiences by insisting that they "don't count." It doesn't matter that I made healthy food choices today, because yesterday's meals were a disaster.
- Jumping to conclusions: Negatively interpreting any event without substantial evidence to support it.
- Mind reading: Irrationally concluding that someone is reacting negatively without substantial evidence. Example: Everyone in this restaurant thinks I have no self-control over what I'm eating.
- Fortune-teller error: Predicting a negative event and insisting that it will come true. Example: I will never develop healthy eating patterns.
- Magnification (catastrophizing) or minimization: Exaggerating the significance a negative event or minimizing the significance of a positive one. Example of magnification: I miscalculated the amount of carbohydrates I consumed today! My day is ruined. Example of minimization: Why would I thank her for baking me a birthday cake? I have a gluten intolerance.

Table 1. Cognitive Restructuring

Situation	Emotions	Automatic Thought	Supporting and Refuting Evidence	Rational Response
I ate a donut at today's meeting even though I have been trying to eat less junk food.	Frustration Shame Disappointment Anger Hopelessness	*I already strayed from my meal plan so I might as well forget about following it for the rest of the day.*	Support: *Given that I ate the donut, I will not have followed 100% of my meal plan by the end of the day.* Refute: *Eating more junk food won't bring me any closer to my goal, and it certainly won't undo my actions.*	*Today's eating will not be perfect, but just because things didn't go according to plan doesn't mean I have to throw myself completely off track. I can start over at any point and still make my day's efforts count.*

- Emotional reasoning: Forming beliefs based on emotional, rather than logical, aspects or events. Example: I feel like I've gained five pounds, so it must be true.
- "Should" statements: Holding rigid beliefs that things ought, or ought not, be a certain way. Example: I should have gone to the gym today despite feeling ill.
- Labeling and mislabeling: Replacing an error or negative event with oneself or someone else by affixing a label to the individual. Example: I didn't achieve my weight goal. I'm such a failure.
- Personalization: Blaming oneself for the negative outcome of an event for which the individual is not responsible. Example: If I had encouraged healthier eating habits, my child wouldn't have developed an eating disorder.

When Can People Use It?

Cognitive restructuring can be used to live a healthier, more productive life. It often is used to treat mental illness, and also can help manage eating and exercise behaviors related to acute or chronic illnesses. Examples include the following.

- Diabetes
- Obesity
- Eating disorders
- Heart disease

- Digestive diseases such as celiac disease, irritable bowel syndrome, ulcers, and gastric reflux
- Allergies and sensitivities (e.g., soy, gluten, lactose)
- Stroke
- Cancer
- High blood pressure
- Autoimmune disorders
- Osteoporosis

Efficacy

Studies have shown cognitive restructuring to be a reliable and effective method for minimizing levels of distress. It has been proven to be highly effective for individuals of different age groups, backgrounds, and medical histories. Cognitive restructuring is used widely in CBT for treatment of depression, anxiety disorders, post-traumatic stress disorders, eating disorders, and autism. Recent studies also have shown benefits of cognitive restructuring in adults with ADHD. Frequent use of strategies for coping, homework compliance, and willingness resulted in reduced rates of symptoms. People with certain skills and personality traits, however, might be more apt to practice the technique successfully. It has been questioned whether cognitive restructuring is as effective in older adults, whose executive functioning skills often decline with age, as it is in the younger population. Executive functioning includes cognitive processes such as working memory, verbal reasoning, planning, problem solving, inhibitory control, and self-monitoring. Impairment or deficits in any one of these areas can drastically affect an individual's aptitude for cognitive restructuring.

Criticisms

- It's not enough. Although many individuals find cognitive restructuring helpful in their day-to-day lives, some find it difficult to do alone. In some cases, these maladaptive thought patterns can be indicative of a more serious condition for which it is imperative that one seek help from a health care provider.
- It's an escape tactic. Some critics argue that cognitive restructuring teaches individuals to suppress, rather than confront, their thoughts. This allows them to avoid pain and anguish associated with the uncomfortable event, and to distance themselves from their experiences.
- The chicken or the egg? The sequence of steps in cognitive restructuring has been questioned. Do emotions stem from beliefs or are beliefs a response to emotions?

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See Also: Eating disorders; Obesity, treatment.

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Colostrum

Colostrum, also known as "first milk," is a nutrient-rich mammary secretion, produced by female mammals in late pregnancy and the few days after giving birth. It is a great source of nutrients such as protein, fat, carbohydrates, vitamins, and minerals. Additionally, it is full of immune, growth, and tissue-repair factors, which are all beneficial to the development of the newborn. Colostrum has numerous antimicrobial agents, such as lactoferrin, lysozyme, and lactoperoxidase, which are responsible for helping the newborn's immune system to mature. Colostrum is particularly rich in antibodies that are able to provide a passive immunity for newborns. The health benefits of colostrum are one reason that health organizations around the world encourage mothers to breast-feed their infants. Two major growth factors—insulin-like growth factors 1 and 2, and transforming growth factors alpha and beta—are found in colostrum. These growth factors have regenerative effects on many structural body cells, and they stimulate wound healing and muscle and cartilage repair in vitro.

In 1912, L.W. Famulener showed that immunized goats were able to pass on their immunity to their offspring through colostrum (Wheeler, Hodgkinson, Prosser, & Davis, 2007). In 1922, colostrum was found to have a greater concentration of antibodies than found in mature milk. In the same year, Theobald Smith and Ralph B. Little performed an experiment on calves that demonstrated the importance of colostrum in providing protection against bacterial infections (Smith &

Little, 1922). In the experiment, 22 calves were separated into two groups. One group of 10 calves received colostrum after birth, and they all survived. Another group of 12 calves did not receive colostrum and 8 of the 12 died, mostly due to bacterial infections. It was discovered that calves that did not receive colostrum lacked specific agglutinins in the blood, which made them vulnerable to infectious bacteria. By 1930, it was confirmed that mammary glands accumulate and secrete agglutinating antibodies that are directed against pathogens, to give the newborns protection.

Because of the large amount of nutrients and antibodies in colostrum, it often is used by people both as medicine and supplement. Bovine colostrum has been used as a raw material for immunonoglubulin-rich commercial products and supplements. Some animal studies have shown that growth factors in bovine colostrum can promote cell growth in the intestine. These immunonoglubulin products therefore sometimes are used as treatments for patients who have gastrointestinal tract infections, and are used as supplements by those who want to prevent gastrointestinal infections.

Northfield Laboratories, for example, produces a product called "Gastrogard" that is designed to prevent diarrhea caused by rotavirus in young children. This product is a special type of colostrum known as hyperimmune bovine colostrum, in which cows are exposed to a particular microbe so that they will manufacture antibodies for the microbe, which then make their way into the colostrum. This type of colostrum can be effective for the treatment of several types of infectious diarrhea. Colostrum supplements have demonstrated some positive effects on athletic performance, especially for sprint-event athletes. Bovine colostrum products appear to be safe, although long-term comprehensive studies have not been conducted.

Fei Peng

See Also: Breast-feeding.

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Copper

Copper (Cu) is an essential trace mineral. It is an important component of the enzymes involved with iron metabolism. Copper helps with collagen formation (a component of many organs in the body, such as bone and muscle), myelination of nerve cells, immune function, and cardiovascular function. Copper converts ferrous iron to ferric iron to be transported into the blood by transferrin, thus helping to prevent anemia. Copper is a component of the antioxidant enzymes, the superoxide dismutases. The human body, however, does not require large amounts of copper, and most cases of deficiency result from too much supplementation with other minerals, such as zinc.

Researchers identified the essential need for copper with experimental animals in 1928. Evidence regarding copper deficiency, however, in humans did not emerge until the 1960s. Research on two genetic disorders involving copper metabolism, including Wilson's disease (a very rare condition which causes copper toxicity) and Menke's syndrome (causes copper deficiency) inspired interest in copper and led to new discoveries about its metabolism and physiological functions.

The small intestine absorbs approximately 50% of dietary copper, but this depends on the amount of copper found in the food and additional dietary factors. Albumin helps transport copper from the intestinal cells to the liver where approximately two-thirds is involved with ceruloplasmin, the enzyme that catalyzes the oxidation of iron. Research indicates healthy adult bodies have 100 mg of copper with distribution to the liver, brain, blood, and bone marrow. The body stores limited amounts of copper and excretes the excess amounts.

Food Sources and Dietary Recommendations

The recommended dietary allowance (RDA) for both adult men and women is 900 micrograms per day. Copper is found in a limited variety of foods; the richest sources include organ meats such as liver, shellfish, nuts, seeds, legumes, peanut butter, and chocolate. Soymilk, black beans, pistachios, spinach, blackberries, baked potatoes with skins, and lean slices of ham also are good sources. Dietary surveys in the United States suggest adults consume about 1.2 milligrams of copper each day.

Copper Deficiency and Menke's Syndrome

Humans rarely experience high levels of copper deficiency, but this commonly occurs among premature infants due to their limited copper stores at birth and their rapid growth rate. Excessive supplementation with additional minerals (zinc and iron) can cause a secondary copper deficiency, leading to iron-deficiency anemia. Young children with a copper deficiency can suffer from bone abnormalities, likely caused by poor synthesis of connective tissue. Additionally, copper-deficient individuals experience elevated blood cholesterol, impaired glucose tolerance, and

heart-related issues. During pregnancy, fetal growth and development is negatively impacted if the woman is copper-deficient.

Menke's syndrome is rare (1 in 50,000 live births) (Insel, Ross, McMahon, & Bernstein, 2014), but can be fatal and irreversible if copper-histidine treatment (increases copper absorption) is not administered within the first days of life. This genetic disorder occurs when copper is not absorbed in the bloodstream, creating a lack of functional copper-containing proteins. Copper accumulates in the intestinal wall, causing buildup that could lead to neurological degeneration; brittle, depigmented, kinky hair; abnormal connective-tissue development; low bone density; osteoporosis; and poor growth.

Copper Toxicity and Wilson's Disease

Copper toxicity is uncommon. The Tolerable Upper Intake Level (UL) is 10,000 micrograms per day. Copper poisoning can develop if people consume beverages that have absorbed copper from containers. The U.S. Environmental Protection agency limits copper levels in drinking water to 1.3 mg per liter (Higdon, Delage, & Prohaska, 2014). Copper often is found in well water, which should be tested for mineral content. Individuals can consume copper unknowingly from using copper cookware (copper pots and pans lined with other metals such as stainless steel, however, are safe) or consuming water that has traveled through copper pipes, especially untreated hot water.

Wilson's disease is rare genetic disorder, occurring among 1 in 200,000 individuals (Insel, Ross, McMahon, & Bernstein, 2014). This disorder limits copper excretion in bile, causing toxic buildup in the liver, brain, kidneys, and eyes. Accumulation of copper in the red blood cells triggers the onset of anemia. The symptoms of Wilson's disease are often undetected until adolescence or early adulthood. Without treatment, individuals develop liver and neurological complications. Chelation therapy helps reduce copper toxicity by binding and eliminating copper and supplementing the diet with zinc, which decreases the absorption of copper.

Carolyn Gross

See Also: Minerals; Zinc.

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Cordyceps Sinensis

Cordyceps are a group of parasitic fungi that parasitize, kill, and then grow on a variety of insects. There are many species of cordyceps, and each grows on a single insect host species. The most common types of cordyceps for consumption is cordyceps sinensis, a type of cordyceps that has been part of traditional Chinese medicine for more than 700 years. Cordyceps sinensis officially was classified as a drug in the Chinese Pharmocopoeia in 1964. Cordyceps supplements also have become popular around the world, although scientific research documenting health benefits is preliminary. In this entry the word "cordyceps" refers to cordyceps sinensis, the type of cordyceps used in Chinese medicine and in dietary supplements.

Cordyceps sinensis is produced in nature when a host caterpillar ingests fungal spores which grow inside the caterpillar, eventually causing the host organism to die. After the host's death, the fungus continues to grow and eventually emerges from the corpse. Cordyceps are harvested mainly in the high-altitude regions of the Tibetan plateau. The time frame for harvesting is very short, as the cordyceps needs to be harvested right after the fungus emerges from the corpse of the host and before the fungus releases spores, which causes the cordyceps to shrivel up and become useless. Wild cordyceps are very expensive in the market. In international trade, (wild) cordyceps were priced at anywhere between US$20,000 and US$40,000 per kg in 2013, with typical consumption in the scale of grams. Cordyceps can also be grown in the laboratory on cultures in a controlled environment replicating the temperatures and high-altitude conditions of Tibet.

Although popular in traditional Chinese medicine for many years, the potential health effects of cordyceps only have recently garnered interest in the West, where it is viewed as a type of alternative medicine and herbal supplement. The interest was sparked when, in 1993, three female runners set world records in the 1,500-, 3,000-, and 10,000-meter races at the National Games in Beijing, China. The runners tested negative for typical performance-enhancing drugs, however cordyceps sinesis extracts were revealed to be part of the runners' diets. Traditional Chinese medicine typically prescribes cordyceps as a general strengthening tonic, especially for use after a serious illness, and to improve the health of the lungs and kidneys. It also has been used to treat ailments ranging from bronchitis to diabetes to eyesight problems. In North America, cordyceps supplements are marketed with properties such as antiaging, "pro-sexual," anti-cancer, and immune boosting. Preliminary studies suggest that cordyceps might deserve further investigation for possible effectiveness in controlling high blood pressure, high blood cholesterol levels, and high blood glucose levels, and for reducing cancer risk.

Studies on cordyceps are a relatively new endeavor, therefore the potential side effects of taking cordyceps are not well known. There have been rare cases of dry mouth, nausea, diarrhea, and systemic drug allergy. Clinical trials on rabbits for a period of 3 months used 10 g per kilogram of weight ingested daily and resulted in no significant side effects on the liver, kidney, and blood (Chen, Wang, Nie, & Marcone, 2013). That dosage (10g/kg) is much more than typically is consumed by

humans. Anecdotal information on the use of cordyceps for cancer patients was based upon a dosage of 3 g to 5 g daily. Consuming too much cordyceps is not necessarily better, as studies have shown that the effectiveness of cordyceps in rats peaked at 8 mg per kilogram of weight per day and decreased at 10 mg per kilogram of weight per day (Chen, Wang, Nie, & Marcone, 2013). There is a concern regarding heavy-metal contamination, however, if wild cordyceps are not sourced from the right place. Due to the significant cost of cordyceps, unscrupulous sellers might insert heavy metal into the fungi to increase its weight and its selling price.

Yuxin Li

See Also: Dietary supplements.

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Creatine

Creatine is an amino acid made naturally by the body that helps to supply energy to all cells, especially muscle cells. It also is available as a dietary supplement and generally is used as an ergogenic aid. A nutritional ergogenic aid is any supplement, food product, chemical, or dietary manipulation that enhances a person's physical performance ability. The body uses creatine to produce the molecule phosphocreatine, which helps to replenish adenosine triphosphate (ATP), the body's primary energy molecule. Phosphocreatine is especially important for energy production during the first few seconds of exercise. Ninety-five percent of the body's creatine is stored in skeletal muscles. The body's remaining creatine reserves are found in the brain and other tissues with heavy energy demands.

In 1847, German scientist Justus von Liebig discovered more intramuscular creatine in wild foxes than in captive foxes, providing evidence for its role in energy production in skeletal muscles. Later, a nutritional supplement, called "Fleisch

Extrakt," was made from beef and created as a cheap substitute for people who were unable to get enough meat in their diet. The extract essentially became the first creatine supplement. Today, a variety of creatine supplements claim to promote the body's muscle-building processes and contribute to greater muscle strength, volume, and power.

A 150-pound male adult requires approximately 2 g of creatine daily for normal functioning. The greater a person's muscle mass, the greater the daily need. Because the body can make creatine from amino acid precursors, there is no recommended dietary allowance for creatine. Creatine can be obtained from meat, such as beef, pork, chicken, and fish; relatively small amounts of creatine also are available from milk and cranberries. Heat contributes to creatine degradation, therefore overcooked meat tends to have reduced creatine content. Creatine also is synthesized by the liver, pancreas, and kidneys from the amino acids L-arginine, glycine, and L-methionine and then is transported throughout the body in the blood. Omnivores generally obtain about 1 g of creatine from their diets and make another gram from other amino acid precursors. Strict vegetarians and vegans ingest almost no creatine, as the exclusion of meat in one's diet eliminates the primary source of creatine. Vegetarians and vegans do make creatine, given adequate protein intake, although the extent of creatine production depends on the person's diet.

In tissues, creatine serves as a critical energy storage component of the phosphagen—or creatine-phosphate—energy system, which is utilized for brief, high-intensity activity. In its active form, creatine combines with a phosphate group to form a molecule called "phosphocreatine." For instantaneous energy, such as a powerful muscle contraction, phosphocreatine readily gives up its phosphate group to adenosine-diphosphate (ADP) to form ATP, a process facilitated by the enzyme creatine kinase. A high-energy bond between two phosphate groups in this molecule provides a burst of energy when broken. The reserves of phosphocreatine in muscles typically last for up to 15 seconds of intense activity, and then take 5 minutes of rest to be fully restored. Fast twitch, type-II muscle fibers use creatine most, as they split ATP at a high rate. These muscle fibers are recruited for fast, high-intensity exercise. Slow twitch, type-I fibers use creatine sparingly, as they are utilized more frequently for endurance exercises.

Creatine supplementation for muscle-building purposes has increased in popularity in recent years. Numerous studies have shown that creatine supplementation combined with appropriate exercise training can improve anaerobic capacity and increase lean muscle mass. The method by which creatine promotes synthesis of new muscle, known as "myogenesis," is not fully understood. One theory is that creatine's volumizing properties might allow muscles to retain more fluid. In the first few weeks of a supplementation regimen, 2 lbs to 5 lbs of increased body mass are gained strictly due to fluid retention. This increased fluid could make more of the molecular building blocks of muscles, especially amino acids, accessible for immediate use (Francaux & Poortsmas, 2006). A second theory suggests that creatine simply might help generate the capacity for more exercise by making more phosphocreatine available to muscles and helping muscles recover more quickly

from exertion. This would allow for more muscle growth due to an increased ability to train. A third theory suggests that creatine might contribute to hyperplasia, the creation of entirely new muscle cells from progenitor cells. Lastly, increased creatine levels could influence other anabolic hormone concentrations in the body that encourage muscle cell growth.

The effectiveness of creatine supplementation for females is not well established, as most recommendations and research focus on its use in adult males. Further, 20% to 30% of users do not significantly respond to creatine supplementation in any way. Individuals who respond best to creatine have low initial levels of creatine and phosphocreatine and a greater quantity and cross-sectional area of type II muscle fibers. Vegetarians and vegans usually benefit from creatine supplementation. The elderly population has shown marked improvement in strength and fat-free mass when using creatine along with resistance training.

The American Academy of Pediatrics (AAP) strongly discourages use of creatine supplements in children and adolescents (Metzl, Small, Levine, & Gershel, 2001). Although creatine supplements appear to be relatively safe for healthy, young adults, no long-term safety data are available. Additionally, the AAP is concerned that using ergogenic aids such as creatine often leads to the use of more dangerous supplements and drugs by children and teens (Eisenberg, Wall, & Neumark-Sztainer, 2012).

Too much creatine can have negative health effects and puts undue stress on the kidneys. Short-term effects of creatine can include diarrhea, muscle cramping, dehydration, and asthmatic symptoms. Some researchers have expressed concern about altered kidney and liver function. Consequently, creatine supplementation requires careful calculation and development of a well-planned regimen. Creatine interferes with several prescription drugs, therefore people using prescriptions drugs—and, indeed, anyone with medical issues—should consult their physicians before beginning a creatine-supplementation program.

Although evidence is not strong, creatine supplementation shows some promise for aiding in disorders characterized by cachexia ("wasting syndrome"), including muscle atrophy. Creatine use by people with muscular dystrophy has revealed increased lean body mass and improved voluntary muscle contraction. Results of creatine use have been disappointing for patients with human immunodeficiency syndrome. Limited success has been observed in some studies of patients with chronic obstructive pulmonary disease and congestive heart failure.

Additional applications for creatine in relation to its role in the brain also have been explored. High-dose creatine has been shown to have some neuroprotective effects in neurodegenerative disorders such as Huntington's Disease and Parkinson's Disease (Gualano, Artioli, Poortmans, & Lancha, 2010). Supplementation might help to stabilize creatine kinase levels, or decrease the need for it if the enzyme is not functioning properly. Creatine also has been shown to block the formation of aggregates within cells that are thought to trigger apoptosis, or cell death. More evidence is needed to confirm or refute the benefits of creatine supplementation in these disease states.

Patricia M. Cipicchio

Research Issues

Some of the problems reported with creatine supplementation could be related to other ingredients—such as caffeine and ephedra—found in supplement preparations. Researchers are exploring the interactions between creatine and other supplement ingredients. Research continues to explore creatine's therapeutic uses in disease states.

See Also: Dietary supplements; Energy balance.

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Curcumin

Curcumin is the principal component of turmeric, giving turmeric its yellow color and contributing to its characteristic flavor. Turmeric is derived from the rhizomes of *Curcuma longa,* a member of the ginger family. A rhizome is a modified stem of a plant that spreads underground and is capable of allowing the growth of new shoots and roots. Turmeric is a common component of curry and mustard preparations. It is used widely in the cuisine of South Asian cultures and the yellow mustard commonly used in North America. The bright yellow color of turmeric comes from phytochemical pigments known as "curcuminoids," several of which are thought to be therapeutic; the most studied curcuminoid is curcumin. Curcumin comprises approximately 75% of turmeric's curcuminoid content (Higdon, Drake, & Yang, 2009).

Curcumin supplements commonly contain a substance called piperine, which comes from black pepper and enhances the absorption of curcumin from the small intestine. In the laboratory, in vitro, and in animal studies, curcumin exhibits antioxidant and anti-inflammatory effects. Curcumin also has been shown to inhibit several carcinogenic processes in vitro. Researchers therefore are studying its

usefulness in treating a variety of chronic illnesses, including Alzheimer's disease, rheumatoid and osteoarthritis, and cancer.

The progression of Alzheimer's disease is associated with inflammation and oxidative damage. Alzheimer's disease is characterized by the formation of clumps of proteins in the brain that appear to inhibit normal nerve activity. These clumps, also called "plaques," are composed of proteins called amyloid beta. Studies show that curcumin inhibits amyloid beta formation in vitro. When injected into mice, curcumin crosses the blood-brain barrier (BBB) and significantly decreases biomarkers for inflammation and oxidative damage, amyloid plaque, and amyloid beta-induced memory deficits. Clinical trials currently are underway to determine whether curcumin crosses the human BBB and whether it is as efficacious in humans.

Curcumin treatment has shown some effectiveness for the treatment of joint pain associated with both rheumatoid and osteoarthritis. In one study, curcumin supplements were found to be about as effective as ibuprofen in the treatment of knee pain caused by osteoarthritis, reducing pain and increasing mobility (Kuptniratsaikul et al., 2009). Researchers hypothesize that these results come from curcumin's anti-inflammatory activity.

In vitro, curcumin appears to induce apoptosis (cell death) in a wide range of cancer cells. Human trials using curcumin for cancer treatment are under way. Thus far, curcumin has been most promising for cancers of the gastrointestinal tract, including colorectal cancers. Once curcumin is absorbed from the small intestinal, its bioavailability is quite low. Researchers are exploring ways to deliver curcumin intravenously as an anticancer drug.

Some researchers have suggested that it is premature for consumers to take curcumin supplements in hopes of preventing health problems (Burgos-Moron et al., 2010). Curcumin is metabolized by the liver and intestine and has low bioavailability. This means that high doses of curcumin are required if administered orally to achieve adequate tissue levels of the substance for a therapeutic effect. No research has evaluated the long-term safety of such high intakes, however. Like many phytochemicals, curcumin could behave as an antioxidant at low doses, but be a pro-oxidant at high doses and contribute to cellular activity that potentially could encourage—rather than discourage—processes that increase cancer risk.

Curcumin can act as a blood thinner and slows the formation of clots; it is should not be taken with anticoagulants or by those who have pre-existing bleeding disorders. Because it also can cause increased bleeding during surgery, curcumin supplementation must be discontinued two weeks prior to surgery. Curcumin eases the flow of bile from the liver to the gallbladder, thus preventing the formation of gallstones. If gallstones already exist, however, then curcumin can exacerbate the problem by flushing them into the bile duct, thereby causing additional blockage (Higdon, Drake, & Yang, 2009). The safety of curcumin supplements has not been established for pregnant women. South Asian cultures consume about 0.15 g of curcumin per day as part of a normal diet, year after year. This level is associated with beneficial health effects and appears to be safe for most people (Burgos-Moron et al., 2010).

Sonya Bhatia and Barbara A. Brehm

See Also: Alzheimer's disease and nutrition; Arthritis and nutrition; Cancer and nutrition; Inflammation; Phytochemicals.

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D

Daily Values

The following information is adapted from the U.S. Food and Drug Administration *Guidance for Industry: A Food Labeling Guide* (2013). "Daily values" are a set of dietary standards used on food labels to help consumers understand the nutrient content of food products. The daily values were established in 1993 and do not always match current "Daily Recommended Intake" (DRI) values. The Food and Nutrition Board of the National Academy of Sciences, along with Health Canada, establishes recommended intake level for a variety of nutrients for 22 different population groups, based on age, gender, and, for women, conditions of pregnancy and lactation. The daily values are a single set of values drawn from this information that is useful for food labeling. Food labeling in the United States is overseen by the Food and Drug Administration.

According to the FDA (2014), there are two sets of reference values for reporting nutrients in nutrition labeling: daily reference values (DRVs), and reference daily intakes (RDIs). These values assist consumers in interpreting information about the amount of a nutrient that is present in a food, and comparing nutritional values of food products. The DRVs are established for adults and children four years of age or older, as are RDIs, except for protein. The DRVs are provided for total fat, saturated fat, cholesterol, total carbohydrate, dietary fiber, sodium, potassium, and protein. The RDIs are provided for vitamins, minerals, and for protein for children younger than four years of age and for pregnant and lactating women.

To limit consumer confusion, however, labels include a single term (i.e., daily value [DV]) to designate both the DRVs and the RDIs. Specifically, the label includes the percent DV except for protein. Protein information is not required unless a protein claim is made for the product or if the product is to be used by infants or children younger than four years of age. The following table lists the DVs based on a caloric intake of 2,000 calories, for adults and children four years of age and older.

To calculate the percent DV, determine the ratio between the amount of the nutrient in a serving of food and the DV for the nutrient.

Barbara A. Brehm

See Also: Dietary Reference Intakes.

Table 1. Daily Values

Food Component	Daily Value
Total Fat	65 grams (g)
Saturated Fat	20 g
Cholesterol	300 milligrams (mg)
Sodium	2,400 mg
Potassium	3,500 mg
Total Carbohydrate	300 g
Dietary Fiber	25 g
Protein	50 g
Vitamin A	5,000 International Units (IU)
Vitamin C	60 mg
Calcium	1,000 mg
Iron	18 mg
Vitamin D	400 IU
Vitamin E	30 IU
Vitamin K	80 micrograms (µg)
Thiamin	1.5 mg
Riboflavin	1.7 mg
Niacin	20 mg
Vitamin B6	2 mg
Folate	400 µg
Vitamin B12	6 µg
Biotin	300 µg
Pantothenic acid	10 mg
Phosphorus	1,000 mg
Iodine	150 µg
Magnesium	400 mg
Zinc	15 mg
Selenium	70 µg
Copper	2 mg
Manganese	2 mg
Chromium	120 µg
Molybdenum	75 µg
Chloride	3,400 mg

Source: U.S. Food and Drug Administration. (2013). *Guidance for Industry: A Food Labeling Guide.* Retrieved from http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/LabelingNutrition/ucm064928.htm

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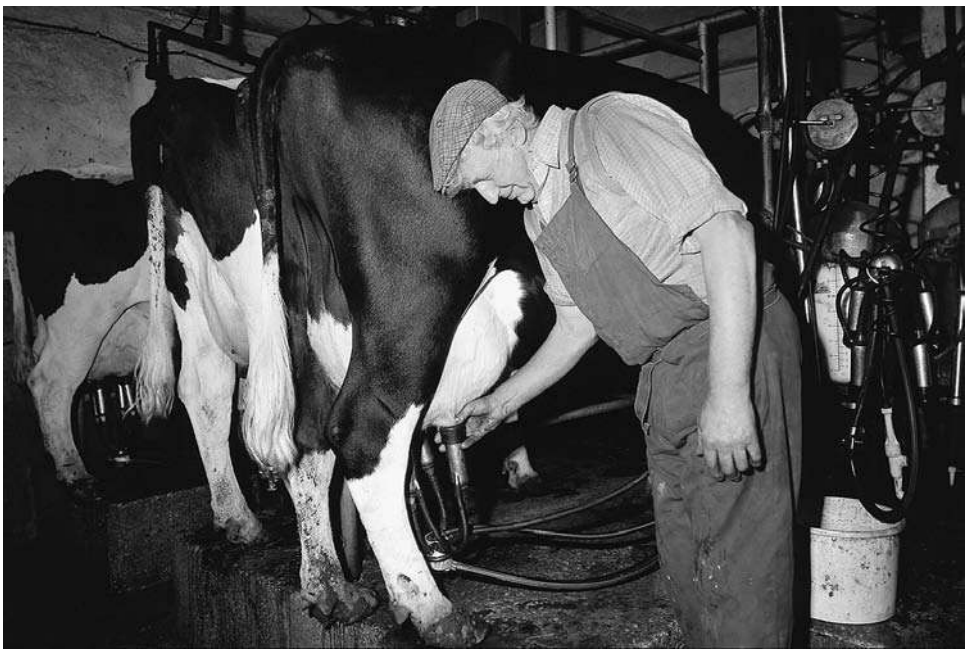
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Dairy Foods

Dairy products refer to food items that contain milk. Female mammals produce milk for the nourishment of their offspring. Throughout their lives, some people continue to drink milk and consume products made from the milk of animals, including cows, sheep, goats, horses, camels, yaks, and buffalo. Numerous essential nutrients are found in milk, including vitamins, minerals, and protein. Dairy products include yogurt, kefir, and cheese, produced by the fermentation of milk; frozen dairy desserts, such as ice cream, ice milk, and frozen custard; and butter and whipped cream, produced from churning milk or cream. Some people experience bloating, cramping, and other forms of digestive discomfort when they consume dairy products because they have an enzyme deficiency that results in lactose intolerance—difficulty digesting the sugar contained in milk. Many questions regarding the health benefits of dairy products have arisen over the past several decades, as consumers strive to make sense of public health dietary advice.

Nutritional Components of Milk

Cow's milk is approximately 87% water by weight. About 4.9% of milk is carbohydrate, primarily in the form of lactose, a disaccharide (sugar). About 3.4%



This dairy farmer is attaching a milking machine to one of his cows. Dairy cows are milked on a consistent schedule, usually twice daily, to maintain optimal milk production. (Corel)

of milk is composed of fats, and of this fat 65% is saturated, 29% is monounsaturated, and 6% is polyunsaturated fatty acids (Cornell, Nutritional components, 2014b). About 3.3% of milk is protein. Milk has all nine of the essential amino acids, as do other animal products (Cornell, Nutritional components, 2014b). Milk contains a number of vitamins, most notably vitamin A (an 8 oz serving of 2% milk provides about 15% of the DRI); riboflavin (35% of the DRI); and vitamin B12 (47% of the DRI) (Cornell, Nutritional components, 2014b). One cup of fortified milk contains about 20% of the DRI for vitamin D. For many people, milk is an important source of many minerals. One cup of 2% milk provides 30% of the DRI for calcium; 7% of the DRI for magnesium; 30% of the DRI for phosphorus; 8% of the DRI for potassium; 11% of the DRI for selenium; 7% of the DRI for sodium; and 10% of the DRI for zinc (Cornell, Nutritional components, 2014b).

Pasteurized versus Unpasteurized

When milk is pasteurized it goes through a heating process that kills microorganisms—many of which can cause serious and even potentially lethal foodborne illnesses. Unpasteurized milk is the same thing as "raw milk," and it has not gone through pasteurization. Although raw milk is preferred by some people for its flavor and potentially helpful microbes and other components, the U.S. Food and Drug Administration cautions that the benefits of consuming raw milk do not outweigh the risks of foodborne illness. It is highly recommended that women who are pregnant, children, and older adults avoid raw milk (FDA, 2013).

Lactose Intolerance and Dairy Allergies

Lactose is a monosaccharide carbohydrate found in milk. For the body to be able to digest lactose it uses lactase (an enzyme found in the small intestine) to break lactose down into simpler molecules that then are absorbed into the blood. People who produce little or no lactase are not able to digest lactose and are considered lactose intolerant. A majority of people from many ethnic groups, including people of African American, Asian American, and Native American descent are lactose intolerant. Although some lactose-intolerant individuals can ingest small portions of dairy products or consume dairy if they take lactase medication, high rates of lactose intolerance around the world have led many public health experts to question the validity of recommending daily dairy intake in dietary guidelines, such as the U.S. Dietary Guidelines.

People with dairy allergies develop allergic symptoms when they consume dairy products or the exacerbating proteins, such as whey and casein, from dairy products. Allergic symptoms include hives, difficulty breathing, nausea, and vomiting. People with milk allergies even can experience anaphylactic shock, a medical emergency marked by swelling of the airways and difficulty breathing.

Other symptoms of dairy allergies include diarrhea, abdominal cramps, and runny nose.

Dairy and Health

The health impacts of dairy consumption vary with the type of dairy product consumed. Products high in fat and added sugar (e.g., ice cream) can contribute many calories with little nutritive value; intake of these products should be limited. Research has explored the association and impact of milk and dairy-product consumption on a number of health issues, including those listed below.

Cardiovascular Disease

When scientists found an association between saturated fat intake and risky blood lipid levels (which are associated with artery disease, the most common form of cardiovascular disease), public-policy groups advised consumers to switch from whole milk, which is almost 3.5% fat (by weight) to milk with less fat (2%, 1%, or skim milk). Over time, researchers discovered that not all saturated fatty acids have the same effects in the body. For example, fatty acids with shorter chain lengths (10 or fewer carbons) are absorbed from the digestive tract and transported in the bloodstream differently from longer chain saturated fatty acids, and do not seem to cause harmful changes in blood lipid levels. Stearic acid, a saturated fatty acid with 18 carbons, also does not appear to negatively influence blood lipid levels. Therefore, although milk fat is composed of about 65% saturated fats, 10% of these are the shorter chain-length variety and 14% is stearic acid (Cornell, Human health, 2014a). Therefore, the impact of whole-milk consumption on artery disease might not be as harmful as was once believed (German et al., 2009). Nevertheless, public-health groups, including the U.S. Department of Agriculture (USDA), still urge consumers to choose lower fat milk varieties to limit saturated fats and calories. Dairy producers are experimenting with the types of food dairy cows consume, to determine whether the fatty acid profiles can become more healthful if cows consume organic or grass-based diets (Benbrook, Butler, Latif, Leifert, & Davis, 2013).

Hypertension

Increased intakes of low-fat dairy products are associated with small but significant decreases in blood pressure, especially in people with borderline hypertension and in African-Americans. The most effective version of the well-studied Dietary Approaches to Stop Hypertension (DASH) diet recommends 2 to 4 servings of low-fat or nonfat dairy products per day. Researchers believe that it could be the calcium found in dairy products that helps to normalize blood pressure, but the magnesium and potassium also are thought to be helpful. Bioactive proteins found in milk also could influence the activity of arteries, and thus contribute to a better blood pressure response (German et al., 2009).

Osteoporosis

Osteoporosis is characterized by low bone-mineral density and fragile bones prone to fracture. Early studies suggested that, because milk contains large amounts of calcium, dairy products should be helpful for the prevention of osteoporosis; research has generally found this to be the case (Cornell, Human health, 2014a). Especially important is calcium intake during childhood and adolescence, because peak bone mass is attained in young adulthood.

Theoretical concerns regarding the impact of a high protein intake on net endogenous acid production led to the questioning of whether milk's high protein content might mean that the risks of milk consumption outweigh its benefits. "Net endogenous acid production" refers to the metabolic effect of foods on physiological acid levels, normally well regulated by the kidneys in young people, but less well controlled in older adults—those most prone to osteoporosis. When the pH of the blood becomes too acidic, it is believed that calcium is drawn from the bones to neutralize pH. Well-controlled studies, however, support the positive effect of dairy consumption on bone density. Although calcium excretion does increase with a high protein intake, the calcium in milk contributes to a net calcium gain (Cornell, Human health, 2014a; Schardt, 2011). The protein in milk also can be helpful to frail older adults—the group most prone to debilitating fractures. Protein intake in this group is often too low. Bones are about 50% protein, and without adequate protein intake bone structure can be compromised (Cornell, Human health, 2014a). Vitamin D is another nutrient critical to bone health, and dairy products fortified with vitamin D can help people achieve better dietary intakes of this nutrient.

Cancer

Good evidence suggests that milk protects against colorectal cancer (Schardt, 2011). One meta-analysis found that people who drank at least one cup of milk a day had a 15% lower risk of being diagnosed with colorectal cancer than those who drank fewer than two glasses per week (Schardt, 2011). Both calcium and vitamin D are thought to contribute to the effect of dairy on colorectal cancer risk. Dairy consumption also might help reduce risk for bladder cancer. Conversely, high calcium intakes—especially intakes of more than 1,200 mg per day—have been associated with increased risk for prostate cancer. Greater dairy consumption is associated with increased levels of certain growth factors that have been linked to better bone density, but also are linked to an increased risk of certain cancers, including prostate cancer. Dairy consumption does not appear to be associated with breast cancer risk, however.

Weight Loss

Although early studies suggested that dairy products might be helpful for weight loss, other studies have been less supportive. Dairy products can be part of

a healthful, low-calorie diet, but the key to losing weight is the reduction of calorie intake and the development of lifelong healthful eating behaviors.

Dairy Politics

Whether dairy foods should be part of a healthful diet often inspires passionate debate. Why? Many political and environmental issues are linked to dairy consumption. Some nutrition researchers bristle at the inclusion of daily dairy consumption in national dietary guidelines, because many people are lactose intolerant. Some people charge the USDA—which regulates the dairy industry—with catering to the dairy lobby rather than putting the public's health first. Groups concerned with sustainable agriculture and animal cruelty object to the treatment of dairy animals, especially the use of growth hormones to increase milk production, antibiotics to increase growth and prevent disease, and confinement feeding procedures. Even grass-fed dairy operations draw criticism from environmentalists, as the methane naturally excreted by cows and other dairy animals contributes to greenhouse gases thought to influence climate change. Water pollution and land conversion (from forest to pasture) also can exert negative environmental impacts.

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Research Issues

Critics have charged that the U.S. Department of Agriculture, whose mission includes the promotion of agricultural products, could be influenced by special interests as it designs dietary guidelines. Some critics have suggested moving the design of dietary guidelines to a science-based department, such as the Centers for Disease Control and Prevention or the Institute of Medicine (Willett & Ludwig, 2011).

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See Also: Climate change and global food supply; Food allergies and intolerances; Hypertension and nutrition; Lactose intolerance; Microbiota and microbiome; Organic food and farming; Osteoporosis; Raw milk; Sustainable agriculture; Whey protein.

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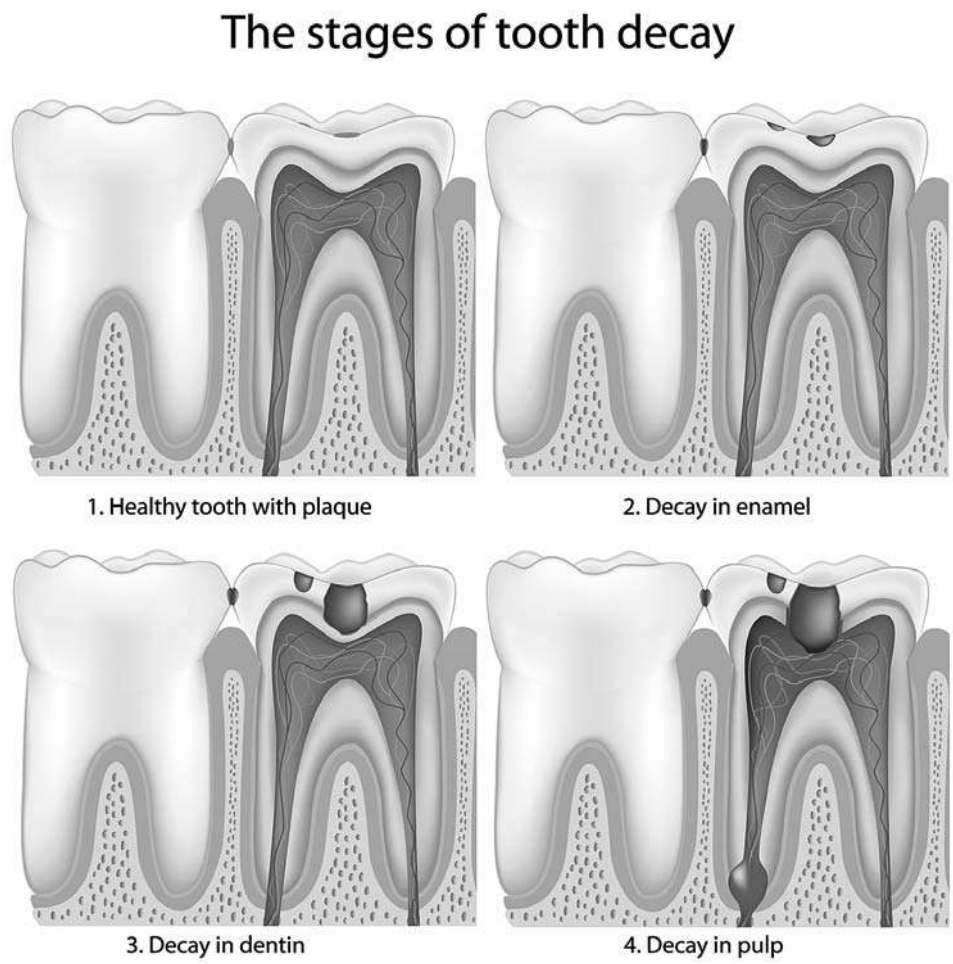
Dental Caries (Cavities)

Dental caries commonly are known as cavities and are a symptom of tooth decay. Tooth decay occurs when acid produced by bacteria living in the mouth erode a tooth's protective enamel. Proper dental care and good oral hygiene are both important to one's oral health. Additionally, good oral health is also an important part of one's overall health. Routine dental care can prevent cavities from forming and enables dentists to treat cavities in their early stages. According to the American Dental Association ([ADA], 2013b) as many as 100 million Americans forego their routine dental care each year.

Cavities

Both helpful and harmful bacteria reside in the mouth. These bacteria live on teeth, gums, tongues, and other areas in the mouth. Most foods and drinks, such as cookies, soda, juice, and even milk, contain both natural and added sugars. The sugars provide a food source for these bacteria. The bacteria and sugars are part of a biofilm that forms around the teeth, better known as plaque. Acid is produced when the bacteria metabolize sugars. It is this acid that causes cavities.

A cavity destroys a tooth's enamel, which is the outer layer of the teeth. The destruction of the tooth's enamel causes it to lose minerals. A white spot forms on areas where minerals have been lost (NIH, 2014). If this process continues and the enamel is weakened and destroyed then a cavity forms; cavities can continue to grow and must be repaired with a filling by a dentist. This process,



Tooth decay begins when bacteria living in the plaque on the teeth metabolize sugars, producing acid as a byproduct. Fluoride applications can reverse very early stages of tooth decay, but if left untreated, decay can spread to the interior of the tooth and cause pain and inflammation. (Shutterstock.com)

however, can be stopped or even reversed in its early stages by repairing the enamel with minerals from salvia, toothpaste with fluoride, and other fluoride treatments (NIH, 2014).

Dental Health Basics

To avoid cavities, it is important to follow the tips listed below as recommended by the ADA (2013d).

Dental Care Costs

It is important to take advantage of good dental care. Regular teeth cleaning performed by a dental professional can reduce the plaque and tartar (hardened plaque) that houses harmful bacteria. The expense of dental care, however, deters people from visiting a dentist regularly. The Affordable Care Act (ACA) (also commonly referred to as "Obamacare") offers dental coverage for adults via most of the state marketplaces (ADA, 2013a). The ACA Web site (www.healthcare.gov) can help people locate a plan that fits their budget.

Aside from the state marketplaces, dental-school clinics provide lower-cost dental care; some collect only partial payment to cover the cost of materials and equipment. Dentists and hygienists also might donate their services at no cost to those who cannot afford to pay. Overall, good oral care can prevent greater expense in the future. Dental caries can progress to a point where required treatments are much more costly. Regular dental care also is an important investment in overall health, as, in addition to dental caries, gum disease can result from poor oral hygiene.

- Brush for two minutes with a fluoride toothpaste at least twice a day
- Floss between teeth daily
- Consume a healthful diet
- Limit snacking, especially avoiding sticky, sugary foods.

In addition to a good home dental care routine, regular dental visits for professional cleaning and oral examination can prevent and catch small cavities when they are easier to treat.

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See Also: Fluoride; The mouth.

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Depression and Nutrition

Depression is a broad term used to describe persistent feelings of sadness, hopelessness, and emptiness. The *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) is the handbook used to classify or diagnose mental disorders. It provides diagnostic criteria for the seven clinical depressive disorders, including major depressive disorder (MDD), dysthymia, premenstrual dysphoric disorder, substance/medication-induced depressive disorder, depressive disorder due to another medical condition, other specified depressive disorder, and unspecified depressive disorder. Depression affects about 7% of the U.S. population (American Psychiatric Association, 2013). Women are diagnosed with depression about twice as often as men. There is some evidence that nutrition plays a part in depression.

Major depressive disorder is the most representative of these types of depression. Its diagnostic criteria include constant depressed mood or loss of interest in the same two-week period; significant distress or impairment; mood is not due to effects of a substance or other medical or psychiatric condition; manic and hypomanic episodes have never occurred. Other symptoms include the following.

- Anhedonia (loss of ability to find pleasure in activities)
- Poor concentration and difficulty making decisions
- Insomnia
- Weakness or fatigue
- Aches and pains
- Significant weight loss (not attributable to dieting) or weight gain
- Irritability
- Anxiety
- Suicidal ideation or attempt
- Feelings of worthlessness

It is important to not underestimate the potential seriousness of depression. In extreme cases, people experiencing depression might commit suicide to end their suffering. Suicide is the third leading cause of death for individuals between 10 and 24 years old.

Depression often is treated with various forms of psychotherapy, medication, and electroconvulsive therapy (ECT). Hospitalization could be warranted, especially if people are at risk of harming themselves or others. Mild to moderate depression might respond to lifestyle measures, such as regular exercise, adequate sleep, and a healthful diet.

Depression and Overall Diet Quality

Some studies suggest that overall diet quality could be related to depression risk. One group of researchers conducted a five-year longitudinal study consisting of more than 3,000 middle-aged male and female participants (Akbaraly, Brunner, Ferrie, Marmot, Kivimaki, & Singh-Manoux, 2009). It was found that individuals whose diets consisted mainly of whole foods (that is, foods that are as close to their natural form as possible, including generous intakes of vegetables, fruits, and fish) had a lower rate of depression, as opposed to those who consumed more processed foods.

A study from the Harvard School of Public Health examining the link between diet and depression in 43,685 participants in the Nurses' Health Study found that those consuming a more inflammatory diet showed higher risk for depression (Lucas et al., 2014). Participants were free of depression at the beginning of the study. An inflammatory diet pattern refers to a diet that is associated with greater levels of blood markers of inflammation, including C-reactive protein, interleukin-6, and tumor necrosis factor alpha receptor 2 (Lucas et al., 2014). According to analyses by the research group, an inflammatory dietary pattern is relatively high in sugar-sweetened beverages, refined grains, red meat, diet soft drinks, and margarine, but low in olive oil, green leafy and yellow vegetables, wine, and coffee. The researchers hypothesized that inflammation could increase risk for depression through several mechanisms. Proinflammatory cytokines (immune cell messengers) might have a negative effect on neurotransmitters. The decline in endothelial function (which influences arterial health) associated with inflammatory markers also could influence brain health (Lucas et al., 2014).

Two other epidemiological studies in women have shown associations between a Mediterranean diet and depression, with higher intakes of fruits, vegetables, legumes, fish, poultry, wine, and olive oil predicting lower risk of depression (Rienks, Dobson, & Mishra, 2013; Sanchez-Villegas et al., 2009). A study of 9,272 men and 3,132 women in France found that greater risk for depression was associated with low-fat and high-snack diets in women (Le Port et al., 2013). In men, greater risk for depression was predicted by low-fat, Western, high-snack, and high fat–sweet diets. (A more Western dietary pattern typically is characterized as having relatively greater consumption of red and processed meats, sweets and desserts, french fries, and refined grains.)

Although there probably is not one perfect diet that guarantees no risk of depression, the studies discussed above seem to indicate that greater intakes of plant foods (fruits, vegetables, legumes) and healthful fats along with reduced intakes of refined grains, added sugars, artificial fats, and dessert-type foods are more likely to reduce depression risk.

Depression and Nutrients

Recent studies have shown several links between nutritional deficiencies and risk of depression. Some studies have found a positive relationship between

neurotransmitters (such as dopamine, norepinephrine, and serotonin) and amino acids in natural supplements.

A number of nutrients play important roles in the metabolism of neurotransmitters and brain health (*see* Table 1). Research on these individual nutrients is intriguing. Megadosing on individual nutrients, however, is not generally associated with significant improvement for most people with depression. Rather, people should strive to achieve recommended intakes for all vitamins and minerals.

Table 1. Nutrients Linked to Depression

Nutrient	Health Benefits	Effects on Depression	Food Sources	Daily Value
B6	• Essential for the communication of neurotransmitters • Vital for the synthesis of hemoglobin needed to carry oxygen throughout the body • Low hemoglobin levels are associated with depression	Given its role in the tryptophan-serotonin pathway, it has been suggested that a B6 deficiency might contribute to symptoms of depression	Salmon, bananas, avocado, potato	2.0 mg
Folate	• Important for cell growth and the production of DNA	Increasing folate intake has been associated with a decrease in depressive symptoms; deficiencies in people with depression have also been reported	Asparagus, spinach, legumes, broccoli	400 mcg
B12	• Essential for metabolism • Forms new red blood cells and nerve cells • Involved in DNA synthesis	Studies have shown that individuals with a high intake of B12 are less likely to experience depression	Seafood, meat, poultry, dairy, eggs	6 mcg
Magnesium	• Important for nerve and heart function • Reduces blood pressure	Some research has shown magnesium supplements to be beneficial to people with depression; however, excessive calcium intake might alter the bioavailability of magnesium after absorption	Whole grains, broccoli, potato, nuts, legumes	310–400 mg

(*continued*)

Table 1. Continued

Nutrient	Health Benefits	Effects on Depression	Food Sources	Daily Value
Omega-3	• Important for brain function and cardiovascular health. Research has shown that countries that consume high amounts of fish per capita have lower rates of depression	Although studies remain inconclusive, research shows that omega-3 fatty acids promote cognitive and behavioral function, and ease symptoms of mood swings and depression	Fish, walnuts, flaxseeds	(No daily value set) Nutritionists generally recommend 1.1-1.6 g
Zinc	• Essential for cell growth • Important for the regulation of endocrine, immune, and neuronal systems • Facilitates the development of bones and sexual organs	Individuals with depression have been found to have low concentrations of zinc in the blood	Meat, dairy, whole grains, nuts, legumes	15 mg
Vitamin D	• Important for absorption of calcium from the intestines • Involved in storage of calcium in the bones • Facilitates cell development	Rates of depression have been linked to deficiencies in vitamin D	Milk, salmon, sardines, tuna	400 I.U.

Research generally supports an increased consumption of omega-3 fatty acids from foods and supplements as a possibly helpful dietary change for mild to moderate depression.

Herbs and Natural Supplements

Several herbs and dietary supplements have preliminary support for their beneficial effects in reducing symptoms of depression. Some of the most studied of these include the following.

Inositol

Although not an essential nutrient, inositol is important for muscle and nerve function, as well as for the transmission of serotonin. Inositol can be found in

legumes, whole grains, citrus fruits, and cantaloupe. Side effects from supplements can include nausea, fatigue, dizziness, and headache.

Tryptophan

Tryptophan is an amino acid that assists in the production of serotonin. There still are safety concerns regarding contaminants detected in samples of tryptophan. In 1990, after 1,500 individuals developed eosinophilia myalgia syndrome, the FDA temporary recalled L-tryptophan products.

Saffron

Saffron supplements are composed of extracts found in various parts of the saffron plant. Research has shown that saffron and antidepressants are similarly effective in improving symptoms of depression. Although its specific medical properties are unknown, saffron's antioxidant and radical scavenger properties could contribute to its antidepressant effects. Side effects can include headache, nausea, anxiety, and decreased appetite.

Sam-E (an abbreviation for the chemical S-adenosyl methionine, or S-adenosylmethionine)

A natural compound that assists in the transmission of serotonin and dopamine in the brain. Although not a stimulant, Sam-E claims to boost mood and attention levels and is used for the treatment of attention-deficit disorder (ADHD). Side effects can include anxiety and skin rashes.

St. John's Wort

The St. John's Wort supplement is derived from a yellow flower, the Hypericum perforatum. The exact mechanisms of its antidepressant effect remain unclear. It has been suggested that the hypericin and hyperforin extracts found in St. John's Wort interact with the nerve receptors involved in depression. Side effects can include gastrointestinal issues, itching, fatigue, increased sensitivity to sunlight, and headache.

Eating a balanced diet has been shown to be beneficial in decreasing depressive symptoms and promoting overall health and well-being. Some studies have shown that supplements are beneficial to some individuals experiencing mild depression. Severe depression should be treated by a professional health caregiver, such as a psychiatrist, however, and usually requires antidepressants or other psychiatric treatment. People experiencing symptoms of depression should seek help from a professional.

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See Also: "Brain foods"; Inflammation; Mood and food; S-adenosylmethionine; St. John's wort.

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Detoxification

Detoxification refers to the processes by which toxins are removed from the body. The term "detoxification" is used in several different contexts. The human body employs a wide variety of physiological processes to eliminate waste products and potentially toxic substances. Detoxification in this context refers to these physiological processes. The term detoxification also refers to medical treatments designed to remove environmental toxins—particularly heavy metals such as lead or mercury—from the body. The term also is used to describe numerous products and practices thought to promote good health by accelerating or furthering the body's natural detoxification processes. The popularity of "detox" diets, therapies, and products has risen dramatically in recent years, yet there is little empirical evidence substantiating the extensive health claims made by supporters.

Physiological Detoxification Processes

The lungs, colon, kidneys, lymphatic system, and liver all play integral roles in detoxifying the body. Carbon dioxide—a byproduct of respiration—is excreted by the lungs. Without this function, excess carbon dioxide would build up in the bloodstream and eventually result in death. The colon forms feces, allowing undigested materials to be eliminated from the gastrointestinal tract. Microorganisms throughout the body, and especially in the gastrointestinal tract, help to break down some potentially carcinogenic substances. Hydration status and electrolyte balance are maintained by the kidneys, which excrete water, salts, and nitrogen-containing waste. The lymphatic system transports proteins and particulate matter too large to be absorbed into the blood away for removal, preventing these substances from accumulating in the interstitial fluid (the solution surrounding cells). Perhaps the most vital organ in physiological detoxification, the liver, often is referred to as the body's primary filter. It removes toxic chemicals from the blood and neutralizes or breaks them down. The byproducts of these metabolic processes are released either into the bile the liver produces or back into the bloodstream. Thus, the byproducts ultimately leave the body as components of feces or urine. Sweat glands also help reduce the burden of heavy metals in the body by moving toxic elements into the sweat (Sears, Kerr, & Bray, 2012). These physiological detoxification processes continuously remove waste products and help to maintain health.

Medicinal Detoxification for Toxic Metals

Some types of medicinal detoxification treatments have widely recognized therapeutic value for individuals with certain conditions. One such example is chelation therapy for the treatment of heavy metal poisoning, such as lead or mercury poisoning. Heavy metal poisoning occurs when metals are not metabolized by the body and instead accumulate in the soft tissues. Heavy metal poisoning can occur from environmental pollution and from jobs that involve working with metals such as lead, mercury, cadmium, and arsenic. Chelation comes from the Greek word "chele," meaning "claw," and refers to the mechanism by which the chelating chemical binds to the metals. In chelation therapy, a substance such as the synthetic amino acid EDTA (ethylene diamine tetraacetic acid) is intravenously injected. The EDTA and other chelation agents bind to heavy metals, enabling them to be released from the soft tissues and excreted in urine. Chelation has numerous side effects; chelating agents also bind to minerals such as calcium, so chelation therapy can cause bone damage. Chelation therapies also carry a small risk of kidney damage and heart failure.

Chelation Therapy for Chronic Health Problems

Chelation therapy has been promoted as an alternative treatment for many chronic illnesses, including artery disease, cancer, multiple sclerosis, and Alzheimer's disease. Given that the effectiveness of alternative applications of chelation therapy

for most of these conditions has not been established through scientific study, it could be associated with more risks than benefits for most patients.

The one possible exception is chelation therapy for artery disease, specifically to prevent subsequent cardiovascular events in people who have already suffered a heart attack. A small study followed about 1,700 such adults in the United States and Canada (Lamas et al., 2013). Subjects were randomly assigned to treatment groups. After one to five years, the group receiving the chelation treatment had somewhat lower rates of cardiovascular events such as heart attacks or strokes than the group receiving a placebo treatment. People with diabetes had even more clinically significant benefits. Researchers caution that larger studies should continue to explore the efficacy of chelation therapy before clinical recommendations can be made.

Detox Products

A multitude of supplements and other items are advertised as at-home methods of medicinal detoxification—ways to remove or enhance the body's ability to remove toxins. Manufacturers often include a feature meant to confirm that their product works as advertised; detox patches and ionic saltwater foot spas, for example, change color after use, which is said to be visual evidence that toxins have been drawn out of the body. In fact, the patches contain water-soluble herbal extracts and simply change color in response to moisture. The footbaths' color change results from iron oxides in the electrodes.

Detox supplements contain a wide range of ingredients. Though their efficacy has not been established, most herbal formulas carry little risk unless the individual using them is allergic to a certain ingredient or is taking a drug that produces a harmful interaction. Some detox teas and tablets contain stimulant laxatives such as senna, however, which can be dangerous in large doses or if used for a prolonged period, and can result in dehydration, electrolyte imbalance, and reduced bowel function.

Intestinal Cleansing

An extension of the idea that laxatives assist the body in eliminating toxins, colonic irrigation is a common detox therapy. In colonic irrigation, low-pressure water pumps and small tubes are used to flush waste from the colon. The underlying belief is that fecal matter lingering in the colon results in a buildup of toxins that are absorbed into the bloodstream, causing fatigue and general poor health. Gastroenterologists, however, argue that the concept of fecal matter adhering to the intestinal walls as "sludge" is inaccurate—bowel transit time varies, but waste does not remain in the body indeterminately (Harvard Medical School, 2008). Colonic irrigation carries risks similar to those of heavy laxative use—dehydration, electrolyte imbalances, and impaired bowel function. Increased fiber and water intake are recommended as safer alternatives for people considering colonics due to constipation.

Detox Diets

Fasting, juicing, and certain eating regimens also are said to detoxify the body and promote weight loss. Some suggestions are far from controversial, including drink more water, eat more leafy green vegetables, and avoid processed foods. It is unclear, however, whether these diets carry any health benefits independent of such suggestions. Weight loss associated with the regimes is unsurprising given that most—if not all—include caloric restriction. Doctors and nutritionists worry that the "detox mentality" will lead individuals to fluctuate between periods of unhealthy eating and fasting or restrictive eating rather than making long-term lifestyle changes (Crowe, 2010).

Psychological Aspects

Enthusiasm for detox diets, therapies, and products could stem from sources other than actual health benefits achieved through enhanced removal of toxins from the body. The placebo effect appears to have a powerful influence: An individual who believes that he or she is engaging in a health-promoting behavior typically feels good about it. In the case of very low-calorie detox diets, restriction can trigger a "starvation high" marked by increased release of endorphins, which further enhances the individual's sense of well-being. Doctors and dietitians warn that associating restriction with positive feelings can contribute to the development of an eating disorder (Iliades, 2011).

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See Also: Lead; The liver; Mercury.

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Diabetes, Type 1

Diabetes mellitus, commonly known as diabetes, occurs when a person has high blood glucose (blood sugar) due to inadequate insulin production, or because the body's cells do not respond properly to insulin, or both. There are three main types of diabetes: type 1 diabetes, type 2 diabetes, and gestational diabetes. Type 1 diabetes is less common than type 2 diabetes, representing approximately 5% of all diabetes cases (CDC, 2011). Type 1 diabetes is an autoimmune disease that usually begins in childhood or adolescence but can develop at any age. Type 1 diabetes occurs when a person's immune system mistakenly destroys the insulin-producing beta cells in the pancreas. Insulin is required for normal blood glucose regulation; it signals cell membrane receptors to take up glucose from the blood, allowing glucose to enter cells. Without the release of insulin, glucose stays in the blood, creating a condition known as hyperglycemia, or high blood glucose. Scientists do not yet know what causes the body's immune system to attack insulin-producing cells or why the onset of the disease begins so early in life. People with type 1 diabetes must learn to manage their blood sugar levels with insulin medication and by regulating the factors that can influence blood sugar, such as diet, physical activity, and stress.

Type 1 diabetes was recognized by ancient civilizations around the world. The first use of the word diabetes has been traced to 230 BCE and Greek physician Appollonius of Memphis. Diabetes comes from the Greek word for "to flow through," or "siphon," based on the observation that type 1 diabetes is characterized by excessive urination. Second century Greek physician Aretaeus of Cappadocia was one of the first to write a thorough clinical description of the disease. Seventeenth-century London physician Thomas Willis diagnosed diabetes in his patients by tasting their urine. Sweet urine indicated a positive diagnosis. He called his diagnosis "diabetes mellitus"; the word "mellitus" was derived from "mel," the Latin word for "honey" (Sattley, 2008).

Before the discovery of insulin and the development of medical insulin in the early decades of the 1900s, treatment for type 1 diabetes consisted of various ineffective strategies and restrictive diets that did little to halt the course of the disease, which always ended within a few years of diagnosis with the patient's death. Insulin, isolated from the pancreases of animals, was first used on humans in 1922. Commercial insulin initially was produced from the pancreases of cows or pigs, as this insulin is most similar to human insulin. Since 1983, biotechnology has harnessed bacteria to produce insulin. In this process, the human gene for insulin production is inserted into bacteria, stimulating the organisms to produce human insulin.

Until recently, type 1 diabetes was referred to as juvenile diabetes because it typically strikes during childhood. Because adults also can suffer from the disease, it was later renamed insulin-dependent diabetes mellitus. People with type 2 diabetes, however, also can become insulin dependent. Therefore, several years later, the disease was renamed "type 1 diabetes," to better distinguish between the various types of diabetes.

Although the cause of type 1 diabetes is unknown, researchers suspect genetic factors could be involved, as people with a parent or sibling with type 1 diabetes are at greater risk for developing the disease. Caucasians have a higher risk than other groups, and certain countries—such as Finland and Sweden—have higher rates. Several dietary factors have been associated with increased risk of developing type 1 diabetes, including consumption of cow's milk and cow's milk formula in infancy, and low vitamin D levels.

Symptoms and Diagnosis

Symptoms of type 1 diabetes usually develop over a short period. Some symptoms include excessive thirst, frequent urination, blurred vision, weight loss, constant hunger, and extreme fatigue. If hyperglycemia is not controlled, people with diabetes can develop ketoacidosis and even suffer a life-threatening diabetic coma.

Type 1 diabetes is diagnosed using a variety of blood glucose tests (ADA, 2014a). These tests typically are administered twice to obtain an accurate diagnosis.

- A1C: The glycated hemoglobin (A1C) test measures the percentage of hemoglobin that is bound to glucose. Hemoglobin is the compound that carries oxygen in red blood cells. Higher A1C measures reflect greater exposures of hemoglobin to blood glucose. The A1C measure reflects average blood glucose levels over the previous three months, because that is the average lifespan of red blood cells. Patients are diagnosed with diabetes if their A1C level is 6.5% or more. An advantage of the A1C test is that patients do not need to fast before the blood tests are administered.
- Fasting plasma glucose test: This test checks the blood glucose levels after a person has not eaten for at least eight hours. Diabetes is diagnosed if blood glucose is 126 mg/dl or greater.
- Oral glucose tolerance test: This test measures how the body responds to glucose. At the beginning of the test, the patient gives a blood sample to determine the fasting blood glucose level. Then the patient consumes a sweet drink containing 75 to 100 grams of glucose. After two hours, another sample of blood is collected from the patient to measure the glucose level. Diabetes is diagnosed if the blood glucose level is equal to or greater than 200 mg/dl.
- Casual (or random) or plasma glucose test: A blood sample can be taken at any time that the patient experiences diabetic symptoms. People are diagnosed if their blood glucose reaches 200 mg/dl or more.

Medical and Lifestyle Treatments

Diabetes increases a person's risk for several health problems. Some of the more severe long-term consequences of type 1 diabetes include hypertension, artery disease, kidney disease, blindness, and damage to the nervous system. In some cases, circulatory problems can lead to heart attack, stroke, and lower-limb amputations. Risk of long-term complications decreases with good blood glucose control.

Medication

People diagnosed with type-1 diabetes must take insulin every day. Several different types of insulin are available; these vary by concentration, duration, and speed of action. Insulin is either injected or infused. Common forms of insulin delivery are via syringe (shots), insulin pen (an instrument that is filled with insulin and looks like a pen), and insulin pump. An insulin pump is a small device that releases insulin via a catheter under the skin of the abdomen. Insulin infusions also can be administered under medical supervision through intravenous fluids.

Physical Activity Recommendations

Regular physical activity can help to prevent the long-term complications associated with diabetes. People with type 1 diabetes, however, often fear engaging in physical activities because exercise influences blood sugar regulation. Fortunately, scientists have found that people with type 1 diabetes can exercise safely and effectively. It is critical to develop an understanding of how one's body responds to exercise, and learn to balance insulin, food intake, and physical activity. When planning to exercise, diabetics might have to reduce insulin dosage. For unplanned exercise, people might need to ingest extra carbohydrates. The American Diabetes Association recommends five days of moderate to intense aerobic exercise for 30 minutes per session, and two to three days of strength training per week (ADA, Exercise, 2014b).

Nutrition

A heart-healthy diet is recommended for people with diabetes. A well-planned diet that includes plenty of vegetables, fruits, and whole grains, and limited intake of added fats and sugars helps reduce risk of the chronic health problems associated with diabetes. Additionally, people with type 1 diabetes must follow a regular meal plan that has been developed with a dietitian to ensure that carbohydrate intake and timing accommodates physical activity level and insulin dosage.

People with type 1 diabetes must monitor intake of carbohydrates because carbohydrates increase blood glucose levels. Type 1 diabetics should select foods with low glycemic index. A food's glycemic index indicates how much and

how quickly the carbohydrate food elevates blood glucose. Foods high in added sugars—such as soft drinks—generally should be avoided. Consuming meals that include healthful fats and fiber can slow the absorption of carbohydrates from the digestive system, and thus slow the rise in blood glucose following a meal.

Limiting unhealthy fats is part of a healthful diet, especially for diabetics who have an increased risk for cardiovascular diseases. Unhealthy fats consist of saturated and trans fats. These fats can increase blood cholesterol levels, which increases the risk of heart disease. Foods high in saturated fats include butter, cream sauces, high-fat dairy and meats, lard, poultry skin, and salt pork. Foods high in trans fats include processed snacks and baked goods that contain hydrogenated oil, shortening, stick margarines, and various fast-food items. Healthy fats are found in foods high in monounsaturated fats and omega-3 fatty acids. Monounsaturated fats can help lower "bad" LDL cholesterol levels, and are found in avocado, olive oil and olives, sesame seeds, canola oil, and peanut butter. Omega-3 fatty acids reduce inflammation in the arteries and reduce risk of blood clots. Foods containing high amounts of omega-3 fatty acids are salmon, herring, rainbow trout, sardines, walnuts, and ground flaxseed.

Fruits and vegetables are high in antioxidants and other phytochemicals that help to protect the arteries and organs vulnerable to the oxidation caused by high blood glucose levels. People with type 1 diabetes should consume low levels of sodium to avoid hypertension, and use alcohol in moderation, because alcohol exerts a strong influence on blood glucose levels.

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Research Issues

Researchers are working to develop a cure for type 1 diabetes. A cure for this disease only can be achieved by stopping the autoimmune destruction of pancreatic beta cells, and restoring insulin production (JDRF 2014). Promising areas include the transplantation of pancreatic beta cells to the pancreas or liver of people with type 1 diabetes. Scientists also are trying to develop methods of generating pancreatic beta cells from stem cell precursors.

See Also: Blood sugar regulation; Cardiovascular disease and nutrition; Diabetes, type 2; Hyperglycemia; Hypoglycemia; Insulin.

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Diabetes, Type 2

Diabetes mellitus is a group of disorders characterized by abnormal blood sugar regulation. Blood sugar level is influenced by a number of factors, several of which contribute to the development of type 2 diabetes mellitus (T2D) when disrupted. Problems occur at the cell membrane-receptor level, causing the body's cells to become less responsive to the hormone insulin and sluggish in their uptake of glucose from the blood. Additionally, over time insulin production can decline, further compromising blood-sugar regulation processes. Type 2 diabetes is the most common kind of diabetes; approximately 80% of people with diabetes have type 2. The onset of T2D is gradual and most commonly affects adults and the elderly. In the past 20 years, however, the incidence of children and adolescents diagnosed with type 2 diabetes has increased. People with type 2 diabetes often are overweight or obese and do not exercise regularly. Decreasing caloric intake with or without weight loss surgery; weight loss; and increasing levels of physical activity can restore normal blood glucose regulation for many people with T2D, at least for a number of years.

Type 2 diabetes occurs when the cell membrane receptors do not respond appropriately to insulin, a hormone that is produced by the pancreas beta cells. This condition is called insulin resistance, meaning the receptors "resist" responding to insulin. Insulin resistance requires an increased output of insulin to regulate blood glucose levels. In the early stages of this condition (before an actual diagnosis of T2D), blood glucose levels are normal, but insulin levels are higher than normal. Over time, the severity of insulin resistance can increase to the point where even higher insulin levels cannot achieve adequate glycemic (blood glucose) control; this results in hyperglycemia (high blood glucose). If blood glucose is only slightly elevated (a fasting blood glucose of 100 to 125 mg/dl), the condition is called prediabetes. After some time, unless intervention occurs, insulin resistance typically worsens and blood glucose levels become high enough for a diagnosis of type 2 diabetes (a fasting blood glucose level of 126 mg/dl or higher). People with type 2 diabetes often experience problems with insulin production over time, as the number of

pancreatic beta cells appear to decline. Therefore, during the early stages of T2D, insulin levels are normal or even high, but eventually they can decrease, making blood glucose levels even more difficult to control.



People with diabetes can monitor their blood glucose levels to obtain feedback on the efficacy of their treatment efforts. With one of the most common monitoring methods, people place a drop of blood onto a test strip of paper that is then analyzed by a glucose meter. (National Institutes of Health)

Symptoms and Diagnosis

Symptoms of type-2 diabetes might not be detected for several years in the beginning stages of this disease. Regular symptoms that occur in T2D include increased thirst and urination, fatigue, higher incidence of infections and slow healing of sores, increased hunger, weight loss, patches of darkened skin, and blurred vision. Fluids in the body tissues are depleted in response to the increased amounts of glucose in the bloodstream. In T2D, the kidneys excrete the excess glucose in the bloodstream, along with the fluid required to make extra urine. This causes dehydration, so people become thirstier and start a more frequent cycle of drinking and urination. People sometimes experience fatigue and some irritability because their cells are not getting enough glucose.

All forms of diabetes can lead to several long-term complications, especially if blood glucose levels remain high over a long period. Complications can include poor wound healing that can lead to amputation; heart and blood vessel diseases; Alzheimer's disease; kidney disease resulting in reduced kidney function that can lead to kidney failure and treatment with dialysis; and eye problems, including blindness. People with T2D experience a slower healing process for several reasons, which include poor circulation, nerve damage, and weaker immune system. People with diabetes have a higher risk of artery disease—marked by plaque deposition in the arteries—which causes a decrease in blood circulation and limits the amount of nutrients and oxygen available to heal a wound. Diabetes increases risk for the development of neuropathy (nerve damage). The most common form is peripheral neuropathy, which starts at the foot and can eventually affect the whole leg. As a result, type-2 diabetics with neuropathy might be unaware of an injury, which could lead to an open sore that is vulnerable to infection. In severe cases, when the wound is not treated properly and in time, an infection that won't heal can lead to amputation. Artery damage can affect the arteries supplying the heart with blood, a condition known as coronary artery disease—the leading cause of heart disease. The artery disease and inflammation associated with diabetes

Diabetes in Children and Adolescents

"SEARCH for Diabetes in Youth Study" is a multicenter study funded by the CDC and NIH to examine diabetes (type 1 and type 2) among children and adolescents in the United States. SEARCH findings for the communities studied include the following.

- During 2002–2005, 15,600 youth were newly diagnosed with type 1 diabetes annually, and 3,600 youth were newly diagnosed with type 2 diabetes annually.
- Among youth younger than 10 years of age, the rate of new cases was 19.7 per 100,000 each year for type 1 diabetes, and 0.4 per 100,000 for type 2 diabetes. Among youth 10 years of age and older, the rate of new cases was 18.6 per 100,000 each year for type 1 diabetes, and 8.5 per 100,000 for type 2 diabetes.
- Non-Hispanic White youth had the greatest rate of new cases of type 1 diabetes (24.8 per 100,000 per year among those younger than 10 years of age and 22.6 per 100,000 per year among those ages 10–19 years).
- Type 2 diabetes was extremely rare among youth aged 10 years of age and younger. Although still infrequent, rates were greater among youth aged 10–19 years than in younger children, with higher rates among U.S. minority populations than in non-Hispanic Whites.
- Among non-Hispanic White youth 10–19 years of age, the rate of new cases was greater for type 1 than for type 2 diabetes. For Asian/Pacific Islander and American Indian youth 10–19 years old, the opposite was true—the rate of new cases was greater for type 2 than for type 1 diabetes. Among non-Hispanic Black and Hispanic youth aged 10–19 years, the rates of new cases of type 1 and type 2 diabetes were similar.

A table showing the rates of new cases of diagnosed diabetes among people younger than 20 years of age in the United States is provided in the CDC *National Diabetes Fact Sheet.*

Centers for Disease Control and Prevention (CDC). (2011). *National Diabetes Fact Sheet: National Estimates and General Information on Diabetes and Prediabetes in the United States, 2011.* U.S. Department of Health and Human Services. Retrieved from http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf

increases risk of Alzheimer's disease, a type of dementia. Prolonged exposure to high blood glucose levels damage the kidney, causing a gradual decline in kidney function. Diabetes increases risk for several eye diseases, including diabetic retinopathy, cataracts, and glaucoma. Diabetic retinopathy is caused by damage to the blood vessels of the retina, interfering with vision. Cataracts involve a clouding of the eye lens, and glaucoma is characterized by an increase in fluid pressure in the eye that damages the optic nerve.

Some tests used to determine whether a person has type 2 diabetes include measuring fasting blood glucose levels, the glycated hemoglobin (A1C) test, the oral glucose tolerance test (OGTT), and the random/casual plasma glucose test. Doctors usually administer tests twice to ensure an accurate diagnosis. The first test uses a fasting blood sample and measures blood sugar. Diagnosis is made if the results show blood sugar level at 126 mg/dL or greater. The A1C test calculates

the percentage of hemoglobin attached to glucose; it reflects average blood sugar levels over previous two to three months. Diagnosis is made if the percentage of hemoglobin attached to sugar is 6.5% or greater. The OGTT measures blood glucose level two hours after a person consumes a sugary drink. Diagnosis is made if blood sugar levels exceed 200 mg/dL. The casual or plasma glucose test is a blood test taken whenever the patient starts to experience any diabetic symptoms. Diagnosis is made if blood sugar levels are 200 mg/dL or more.

Treatment

Treatment for T2D usually begins with monitoring blood sugar levels, and changing eating behaviors and physical activity levels to improve blood glucose regulation. Doctors recommend that patients with type 2 diabetes check their blood sugar levels at least once a day, depending on type of treatment administered. Blood sugar levels vary throughout the day in response to different factors such as eating, alcohol intake, stress level, medication, type and duration of physical activity, and (for women) hormone fluctuations. Testing blood sugar regularly can help people understand the links between blood sugar and these factors, and can indicate whether more aggressive treatment is indicated. In people with excess fat, weight loss (fat loss) usually improves blood glucose regulation.

Weight loss can be achieved through lifestyle change programs or weight-loss surgery. It is important to note that surgery is effective only if it leads to reduced food intake and weight loss, and if these changes are maintained. The benefits of surgery are lost if harmful eating habits are resumed and weight is regained. Many medications can help people with type 2 diabetes achieve better blood sugar control. None reverse the disease, but they can slow the development of long-term complications.

Diet

Healthy eating is a critical component in the treatment of T2D, both for improving glucose levels and for weight control in people who have excess fat. A healthful diet for type 2 diabetics emphasizes a reduced calorie intake, if the person is overweight; a relatively low intake of carbohydrates, focusing primarily on vegetables; increasing intake of dietary fiber; reducing intake of foods with added fats and sugars; and maintaining or increasing intake of healthy fats. People diagnosed with T2D should meet with a dietitian who can help them plan delicious and nutritious meals that follow these recommendations.

Reducing intake of carbohydrates is critical, because these are the source of blood glucose. High-sugar foods such as non-diet sodas and fruit juice should be avoided. The healthiest carbohydrates are found in foods such as fruits, vegetables, low-fat dairy products, legumes, and whole grains. Intake of most starchy foods must still be limited, however. Many people with diabetes learn how to keep track of carbohydrates' glycemic load to reduce the impact of carbohydrates on blood glucose levels. Dietary fiber reduces the rise in blood sugar level following a meal,

therefore a diet high in fiber is encouraged for people with T2D. Healthy fats commonly are found in almonds, walnuts, peanut butter, avocados, olives, and canola. Fish with good levels of omega-3 fatty acids, including salmon, bluefish, halibut, and sardines also are recommended.

Because T2D increases a person's risk of cardiovascular disease, people with diabetes usually are advised to follow dietary recommendations for the prevention of artery disease. Type 2 diabetics should avoid foods high in saturated fats, trans fats, and sodium. Saturated fats are found in many meats and high-fat dairy products. Foods rich in these fats include beef, hot dogs, bacon, and sausage. Trans fats should be avoided completely and are found in baked goods, processed snacks, and margarine. Clinicians recommend that people with type 2 diabetes limit sodium intake to less than 2,300 mg per day, because people with T2D often develop hypertension.

Physical Activity

Regular, almost daily, physical activity is recommended to improve glycemic control, reduce cardiovascular diseases, and help maintain a healthy weight for people with diabetes. Several studies have shown that exercise improves insulin sensitivity and blood sugar regulation, even without weight loss. Additionally, exercise stimulates blood glucose uptake by muscle tissue in an insulin-independent molecular pathway (Colberg et al., 2010). This means that glucose uptake by muscle during exercise is normal even in people with diabetes. These effects of physical activity are short lived. The insulin-independent pathway remains active for only a few hours after exercise, but insulin sensitivity remains elevated for up to 72 hours (Colberg et al., 2010). Researchers are exploring the molecular mechanisms through which these effects occur. With exercise, muscles release peptide (protein) molecules. These molecules help the muscles communicate with the nervous, endocrine, and immune systems. They generally have an anti-inflammatory effect on the body and appear to contribute to many exercise benefits, such as better blood sugar regulation and reduced artery disease (Pedersen, 2011). In addition to its effects on insulin sensitivity and blood glucose uptake by skeletal muscle, physical activity can contribute to a negative energy balance, fatty acid oxidation, and weight loss. Physical activity can help normalize high blood pressure and improve blood lipid profile and arterial function.

Recent research suggests that exercise decreases the likelihood that prediabetes will develop into type2 diabetes by 58% when subjects engage in exercise for at least 150 minutes per week (Colberg et al., 2010). The American College of Sports Medicine and the American Diabetes Association recommend at least 150 minutes per week of moderate aerobic exercise, with some amount of physical activity at least five days a week. Some studies suggest that longer periods of exercise are even more effective. A combination of resistance training (at least three times a week) and aerobic activity is even more beneficial for improving blood glucose regulation than aerobic exercise alone (Colberg et al., 2010).

Medical Treatment

A significant number of medications are available to help improve blood glucose control. Drugs often are prescribed in a variety of combinations, depending upon a person's diagnosis. Some drugs enhance the sensitivity of cells to insulin; others increase insulin production and release in the pancreas. Some drugs decrease the amount of glucose the body absorbs from food by inhibiting the breakdown of carbohydrates in the digestive system. Other drugs inhibit the liver's production and release of glucose. Glucose monitoring and diet and exercise records can help patients and health care providers work together to find the medications that work best.

Active Lifestyle Treatment Can Reverse or Delay Type 2 Diabetes for Some People

Type 2 diabetes often can be reversed—or at least postponed—with appropriate lifestyle changes, primarily changes in diet and physical activity. A recent study demonstrated total reversal of type 2 diabetes in 7 of 10 subjects undergoing 8 weeks of intensive dietary intervention. The 10 participants consumed a very low-calorie diet of 600 calories per day for eight weeks. The results showed that 70% of the participants (seven) no longer had symptoms of T2D by the end of the study. This outcome is similar to that seen with bariatric (weight-loss) surgeries, following which most people only can eat small portions of food and thus experience dramatic weight loss. Dramatic lifestyle change is difficult for most people, however. Less-stringent lifestyle changes also have been shown to reverse or postpone type 2 diabetes. Research by Wing and colleagues (Wing et al., 2011) found significant improvement in cardiovascular disease risk factors after one year when overweight and obese people with T2D lost 5% to 10% of their body weight through prescribed diet and exercise. This is important because type 2 diabetics who are overweight are more at risk for developing cardiovascular diseases. People diagnosed with diabetes or prediabetes should work with their health care providers to achieve optimal glucose control using a combination of diet, physical activity, weight loss, and, if necessary, medication.

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Research Issues

Researchers still are exploring the relationship between type 2 diabetes and obesity. Obesity might contribute to the T2D disease state in several ways, many of which presently are under investigation. Insulin resistance could result from defects in signaling molecule production or function, either inside or outside the cells. The process might be influenced by lipotoxicity, in which fatty acids or their products interfere with cellular response to insulin. Obesity also could interfere with optimal pancreatic beta cell function via the deposition of amyloid in the islet cells, excess fat deposits in the pancreas, oxidative stress, and inflammation, or interfere with signaling molecules that modulate insulin release (Taylor, 2013). An increase in the concentration of fatty acid metabolites is associated with an increased rate of beta cell death via apoptosis.

See Also: Blood sugar regulation; Cardiometabolic syndrome; Diabetes, type 1; Glycemic index and glycemic load; Hyperglycemia; Hypoglycemia; Insulin; Obesity, definition and health effects.

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Diarrhea

Diarrhea is a health problem characterized by loose, frequent, watery stools. For most adults in North America, diarrhea usually is nothing more than an annoyance that quickly passes even with no treatment. Chronic diarrhea can be indicative a serious underlying medical condition, however. If diarrhea is severe and prolonged, it can lead to dehydration—which can be particularly dangerous in infants and children, and in people with health problems. In resource-poor countries, dehydration from diarrhea is a leading cause of death, especially in infants and young children. Globally, diarrheal illnesses are responsible for 1 in 9 child deaths (CDC, 2014). Diarrhea has many causes. Treatment consists of addressing the causes of the illness and giving rehydration medications.

In some cases, diarrhea is a useful physical response. The body develops diarrhea to assist in the elimination of harmful agents from the digestive tract. The rate of peristalsis, the muscular contractions that move food and waste

through the digestive system, increases. Additionally, inflammation and some infectious agents sometimes draw more water into the large intestine. (During normal digestive processes, water is absorbed from the material in the large intestine back into the body.) The increased movement of watery stools through the large intestine enhances removal of potentially dangerous microorganisms and chemicals.

Diarrhea can be caused by many factors, including infectious agents such as certain bacteria, viruses, and parasites. Such agents often enter the digestive system from contaminated water and food, or from hands that have come into contact with infectious agents. Diarrhea also can result from food allergies and intolerances, including celiac disease and lactose intolerance. Chronic diarrhea can be a symptom of inflammatory bowel diseases, such as Crohn's disease and ulcerative colitis, and functional bowel disorders, such as irritable bowel syndrome. Some medications, including antibiotics and antacids containing magnesium, can cause diarrhea. Even feelings of stress can lead to bouts of diarrhea.

People experiencing acute episodes of diarrhea should drink plenty of water. Sports beverages that replace electrolytes also can be helpful. Foods high in fiber and fat should be avoided. Bland foods such as bananas, white rice, applesauce, toast, and crackers often are recommended. Adults who have diarrhea should seek medical care when diarrhea does not resolve after several days, or if diarrhea is accompanied by any of the following (Donowitz & Fordtran, 2013).

- Severe abdominal or rectal pain
- Fever of 102 degrees F or higher
- Blood or pus in the stools
- Black or tarry stools

Children should receive medical care for the same symptoms, but earlier in the course of diarrhea, for example, if severe diarrhea persists for longer than 24 hours (Donowitz & Fordtran, 2013). Infants and young children should receive medical care very early as well, especially if they are not taking fluids. Infants and children can die from even just one day of severe dehydration (Donowitz & Fordtran, 2013).

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See Also: Digestion and the digestive system; Diverticular disease; Foodborne illness and food safety; Inflammatory bowel diseases; Irritable bowel disease; Large intestine.

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Dietary Guidelines for Americans

The *Dietary Guidelines for Americans* (DGA) is a document that provides the foundation for all federal nutrition programs. The *Dietary Guidelines* are created by the United States Departments of Agriculture (USDA) and Health and Human Services (HHS) to guide nutrition policy in the United States and are revised every five years. The guidelines will be revised again in the fall of 2105, and they should be reviewed at the USDA's website; currenty there are available at http://www.cnpp.usda.gov/dietaryguidelines.htm.

The DGA are designed to provide a consistent, evidence-based summary of recommendations regarding nutrition advice for generally healthy people older than two years of age. The goals of the advice offered by the DGA are not only to help people to avoid deficiency diseases caused by poor nutrition, but to encourage people to make food choices that will reduce their risk for chronic diseases such as obesity, type 2 diabetes, hypertension, heart disease, and cancer. By law, all federal dietary recommendations, such as the MyPlate nutrition advice, must be consistent with the DGA.

History and Development

The DGA grew out of work that began in 1970s by the U.S. Senate Select Committee on Nutrition and Human Needs, chaired by Senator George McGovern. During this time, epidemiologists were trying to determine the factors that increased a person's risk for heart disease, the leading cause of death in the United States. Reviewing the existing research—much of it focused on the link between high blood lipid levels and heart disease risk—the Committee issued a report, *Dietary Goals for the United States,* in 1977. This landmark document marked the beginning of a shift in federal nutrition policy away from the prevention of nutrient-deficiency diseases, which were becoming increasingly rare in the U.S. population, and toward the prevention of heart disease and other chronic illnesses. The report advised people to reduce the consumption of refined and processed sugars, total fat, saturated fat, cholesterol, and sodium, and to increase the consumption of complex carbohydrates and naturally occurring sugars. At the time, it was believed that higher amounts of fat in the diet translated into higher blood lipid levels, and a low-fat diet was thought to lower blood fat levels. Polyunsaturated fats were believed to be less harmful than saturated fats. These basic recommendations were translated into the following dietary advice that was issued in the 2010 Dietary Guidelines.

- Increase consumption of fruits, vegetables, and whole grains
- Decrease consumption of:
  - refined and processed sugars and foods high in such sugars
  - foods high in total fat and animal fat, and partially replace saturated fats with polyunsaturated fats
  - eggs, butterfat, and other high-cholesterol foods
  - salt and foods with high salt content
- Choose low-fat and non-fat dairy products instead of high-fat dairy products

Although some groups applauded the government's efforts to improve the eating habits of U.S. citizens and stem the rising tide of heart disease, many people questioned the scientific validity of the committee's report. Industry groups, such as those that produced meat and dairy products, challenged the guidelines that could impact their members' interests. In an effort to improve the scientific foundation of government dietary advice, the U.S. Department of Agriculture and the U.S. Department of Health and Human Services formed a group of scientists charged with evaluating and revising the goals into an evidence-based set of dietary guidelines. The committee wrote the first version of the DGA, titled *Nutrition and Your Health: Dietary Guidelines for Americans,* which was released in 1980. Not surprisingly, this report also was met with criticism from both scientists and industry groups. This response prompted Congress to direct the USDA and HHS to establish another committee to gather and review the criticism, and advise on future revisions of the DGA, which were issued in 1985 and 1990. In 1990, the National Nutrition Monitoring and Related Research Act mandated the USDA and HHS to update the DGA every five years, directed by a Dietary Guidelines Advisory Committee. This procedure continues to operate, with the secretaries of the USDA and HHS appointing new advisory committees every revision cycle, and releasing new versions of the DGA every five years.

Over time, the Dietary Guidelines Advisory Committees have tried to make the revision procedures more research based. In 2009, the USDA created a Nutrition Evidence Library (NEL), compiling the scientific research articles related to diet and health. The USDA and HHS also established a public comments database for feedback from the scientific and lay communities as the guidelines were being revised. In these ways, the Advisory Committee has attempted to expand the input that shapes the DGA.

Dietary Guidelines

The DGA consist of 23 key recommendations that are spelled out in a 100-plus-page document available on the Internet (*Dietary Guidelines for Americans,* 2011). Recommendations from the Dietary Guidelines include the following.

Balance Calories to Manage Weight

This guideline encourages people to balance calorie intake with expenditure throughout all the life stages. It encourages people to increase physical activity and reduce sedentary behaviors. Emphasis in this section is on achieving and sustaining a healthy weight.

Consume Nutrient-Dense Foods and Beverages

Nutrient density refers to the nutritive value per calorie of a given food. If one food has a higher nutrient density than another, it means it has more nutrition per calorie. For example, milk has a higher nutrient density than soda, because

milk contains more protein, vitamins, and minerals than soda. The dietary guidelines emphasize the observation that people get too many of their calories from solid fats (trans fatty acids and saturated fatty acids), added sugars, and refined grains. These ingredients add calories but have little helpful nutrition. Foods and beverages high in these ingredients often are said to be "empty-calorie" foods, meaning that the calories contribute little toward a person's nutritional needs. The guidelines urge readers to avoid empty-calorie foods and make good food and beverage choices by looking for foods that contribute positively to one's nutritional needs.

Foods and Food Components to Reduce

This section of the *Dietary Guidelines* goes into some depth on several issues. Much of this advice is difficult to translate into food intake and thus is confusing for consumers. The issues addressed include the following.

- Sodium: The guidelines recommend that sodium intake be reduced to less than 2,300 mg per day for healthy young people. The guidelines suggest an even lower limit, 1,500 mg, for about half of the population, including people older than 50, all African-Americans (who have a higher risk of hypertension), and anyone with hypertension, diabetes, or kidney disease.
- Saturated fatty acids: The guidelines recommend reducing these to less than 10% of total daily calories, and replacing them with unsaturated fats.
- Cholesterol: The guidelines recommend less than 300 mg per day.
- Trans fatty acids: The guidelines recommend keeping these as low as possible by limiting consumption of products with hydrogenated oils.
- Refined grains: The guidelines suggest limiting food with refined grains, especially those with added sugars, sodium, and solid fats.
- Alcohol: The guidelines suggest limiting alcoholic beverages to one per day for women and two per day for men, if alcohol is consumed at all.

Foods and Nutrients to Increase

Individuals are cautioned to stay within their calorie needs as they increase the foods listed below.

- Increase vegetable and fruit intake: Health and nutrition professionals have been universally pleased to see this advice take center stage in the *U.S. Dietary Guidelines*.
- Eat a variety of vegetables: This guideline encourages consumers to expand their vegetable choices and to include dark-green, red, and orange vegetables in their diet, as well as beans and peas.
- Consume at least half of all grains as whole grains: This guideline encourages people to replace refined grains with whole grains. For example, the guidelines advise people to replace white rice with brown rice and use whole-wheat products in place of those made with white flour.

- Increase intake of fat-free or low-fat milk and milk products: Consumers are encouraged to look for non-fat or low-fat dairy products such as milk, yogurt, and cheese.
- Choose a variety of protein foods: The protein food group is no longer called the "meat" group. Better sources of protein include seafood, lean meat and poultry, eggs, beans and peas, soy products, and unsalted nuts and seeds.
- Increase the amount and variety of seafood: Consumers are encouraged to consume seafood in place of some other meats, but to consume a variety to avoid high intakes of heavy metals such as mercury.
- Replace protein foods that are higher in solid fats with choices that are lower in solid fats: This guideline encourages people to reduce intake of saturated fat.
- Use oils to replace solid fats: This guideline's goal is similar to the one above.
- Choose foods that provide more potassium, dietary fiber, calcium, and vitamin D: These nutrients are likely to be low in the average diet. The guideline urges consumers to increase consumption of vegetables, fruits, whole grains, milk, and milk products.

Criticisms of the *Dietary Guidelines for Americans*

Many scientists and consumer groups have criticized the DGA. One of the most common points of contention concerns the continuing recommendations for the restriction of saturated fats and promotion of a relatively high intake of grain products. Many experts believe the evidence for a harmful effect of saturated fats on artery disease is not well supported by the research (Malhotra, 2013). Additionally, many researchers now believe that a high intake of carbohydrates, especially added sugars and refined grain products, contributes to obesity, type 2 diabetes, and heart disease (Willett & Ludwig, 2011).

One of the most well-respected critic groups of the DGA is led by Walter Willett and colleagues from the Harvard School of Public Health. In a letter to the Advisory Committee for the 2010 DGA, Willett and colleagues outlined several criticisms of the DGA.

- Evidence to support recommending three servings of milk per day is lacking and could cause harm to some people. Additionally, if everyone consumed this much milk per day, milk production in the United States would need to double, which would exert a serious negative impact on the environment.
- Recommendations for a high intake of lean meat could be problematic, as research has found a link between intake of red meat and risk for colorectal cancers.
- Recommendations for a high intake of folic acid for women of child-bearing age should be stronger.
- Recommendations that half of grain products consumed can be refined grains is not scientifically based, as these foods can contribute to obesity and associated health risks.

Willett and colleagues also have charged that members of the USDA have ties to industries, such as the dairy and cattle industries, that present a conflict of interest with their ability to appoint members to the advisory committee who can provide objective advice. Willett and colleagues have suggested that responsibility for the DGA be shifted to a more science-based organization, such as the Centers for Disease Control and Prevention.

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Research Issues

Some critics of the *Dietary Guidelines for Americans* (DGA) have charged that the guidelines are too vague and that they should more clearly name the foods to be avoided, such as empty-calorie foods. Read the DGA, and then make a list of foods whose consumption probably should be limited. Soft drinks, for example, generally are considered empty-calorie foods. What other foods and food categories contain food components that should be reduced?

See Also: Public policy on nutrition.

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Dietary Reference Intakes

Dietary Standards

Dietary standards are important for the planning and evaluating of individual diets; the planning and evaluating of diets for different groups of individuals; and making nutrition policy decisions. An example of a nutrition policy decision is the amount of foods or vouchers for foods that are to be provided for individuals who are a part of the Special Supplemental Nutrition Program for Women, Infant, and Children (WIC). The WIC program provides supplemental foods, health care referrals, and nutrition education to low-income pregnant, breast-feeding, and non-breast-feeding postpartum women; infants; and nutritional-risk children up to age five. Dietary standards also are useful to nutritionists who plan meals for institutions such as schools and hospitals.

History

In 1938, Health Canada published the Recommended Nutrient Intakes (RNIs) as a dietary standard. Three years later, in 1941, the United States published the Recommended Dietary Allowances (RDAs). In 1989, the tenth and final version of the RDAs was published (Insel et al., 2013). In the mid-1990s, a new framework for dietary standards—the Dietary Reference Intakes (DRIs)—was published as a joint effort between Health Canada and the United States Food and Nutrition Board of the National Academy of Sciences to set dietary standards to replace the RNIs and RDAs. In 1997, the first set of DRIs was published for calcium, phosphorus, magnesium, vitamin D, and fluoride (Insel et al., 2013).

Definitions

The DRIs include: estimated average requirement (EAR); recommended dietary allowance (RDA); adequate intake (AI); and tolerable upper intake levels (UL). The U.S. Department of Agriculture (USDA, 2014b) defines estimated average requirement (EAR) as "the average daily nutrient intake level estimated to meet the requirement of half the healthy individuals in a particular life stage and gender group."

Recommended Dietary Allowance (RDA) is defined as "the average daily dietary nutrient intake level sufficient to meet the nutrient requirement of nearly all (97% to 98%) healthy individuals in a particular life stage and gender group" (USDA, 2014b). The DRI values are derived from the EAR values. There are RDA values for calcium, carbohydrate, copper, folate, iodine, iron, magnesium, molybdenum, niacin, phosphorus, protein, riboflavin, selenium, thiamin, vitamin A, vitamin B6, vitamin B12, vitamin C, vitamin D, vitamin E, and zinc (USDA, 2014d).

Adequate intake (AI) is defined as "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" (USDA, 2014b). Adequate intake information is available for alpha-linolenic acid, biotin, chloride, choline, chromium, fat (for infants 0 to 12 months old), fluoride, linoleic acid, manganese, pantothenic acid, potassium, sodium, total fiber, vitamin K, and water (USDA, 2014d).

Tolerable upper intake level (UL) is defined as "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" (USDA, 2014b). For individuals who are one year old or older there are UL values for boron, calcium, chloride, choline, copper, folate, fluoride, iodine, iron, magnesium, manganese, molybdenum, niacin, nickel, phosphorus, selenium, sodium, vitamin A, vitamin B6, vitamin C, vitamin D, vitamin E, vanadium, and zinc. For infants 0 to 12 months old there is UL information for calcium, fluoride, iron, selenium, vitamin A, vitamin D, and zinc.

Tables

The USDA (2014c) has a website with much useful information (http://fnic.nal.usda.gov/dietary-guidance/dietary-reference-intakes/dri-tables). Information is provided for the different life-stage groups, such as infants, children, male adults, female adults, pregnant women, and lactating women.

- Dietary Reference Intakes: Recommended Intakes for Individuals—Comprehensive DRI tables for vitamins, minerals, and macronutrients such as calcium, carbohydrates, copper, folate, iodine, iron, magnesium, molybdenum, niacin, phosphorus, protein, riboflavin, selenium, thiamin, vitamin A, vitamin B6, vitamin B12, vitamin C, vitamin D, vitamin E, and zinc.
- Dietary Reference Intakes: Recommended Dietary Allowance and Adequate Intake for Vitamins and Elements—Similar to Recommended Intakes for Individuals.
- Dietary Reference Intakes: Upper Intake Levels for Vitamins and Elements—Carbohydrates, cholesterol, polyunsaturated fatty acids, saturated and trans fatty acids, total fat, and total fiber.
- Dietary Reference Intakes: Macronutrients—Carbohydrates, fat, fatty acids, fiber, and protein.
- Dietary Reference Intakes: Estimates Average Requirements—Calcium, carbohydrates, copper, folate, iodine, iron, magnesium, molybdenum, niacin, phosphorus, protein, riboflavin, selenium, vitamin A, vitamin C, vitamin D, vitamin E, thiamin, vitamin B6, vitamin B12, and zinc.
- Dietary Reference Intakes: Electrolytes and Water—Chloride, inorganic sulfate, potassium, sodium, and water.

Online DRI Calculator

The USDA (2014c) has an online calculator called Interactive DRI for Health Care Professionals (http://fnic.nal.usda.gov/fnic/interactiveDRI/). The calculator

enables individuals to determine their DRI values for nutrients after entering their sex, age, height, weight, physical activity level. After the user enters the required information, the online calculator is able to determine the individual's body mass index (BMI) and daily calorie needs.

The calculator provides information on:

- Macronutrients in terms of a-linolenic acid, carbohydrates, dietary cholesterol, fat, linoleic acid, protein, saturated fatty acids, total fiber, total water, and trans fatty acids;
- Vitamins in terms of biotin, carotenoids, choline, folate, niacin, pantothenic acid, riboflavin, thiamin, vitamin A, vitamin B6, vitamin B12, vitamin C, vitamin D, vitamin E, and vitamin, K; and
- Minerals (elements) in terms of arsenic, boron, calcium, chromium, copper, chloride, fluoride, iodine, iron, magnesium, manganese, molybdenum, nickel, phosphorus, potassium, selenium, silicon, sodium, sulfate, vanadium, and zinc.

Health care practitioners can help individuals understand the information provided by the online DRI calculator.

Susana Leong

See Also: Daily values; Health Canada; U.S. Department of Agriculture.

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Dietary Supplements

A dietary supplement is a product manufactured from ingredients that could be found in the diet—components of plants and animals. The ingredients can be concentrated or changed in other ways, however, so that in the end they bear little resemblance to food. Dietary supplements are a multibillion-dollar-a-year industry in the

United States, Canada, and other countries around the world, with new formulations appearing on the market daily. The advertisements and product labels for dietary supplements often are very sophisticated, and the products mimic pharmaceutical preparations. The regulation of dietary supplements, however, is very different from the regulation of drugs. Consumers therefore must be wary when using supplements.

In the United States, the regulation of dietary supplements is described in the Dietary Supplement Health and Education Act (DSHEA), which was enacted by Congress in 1994. This Act allows manufacturers to market many products as "dietary supplements" rather than as drugs. To qualify as a "dietary supplement," the product must contain one or more of the following substances: "a vitamin; a mineral; an herb or other botanical; an amino acid; a dietary substance for use by man to supplement the diet by increasing the total dietary intake (e.g., enzymes or tissues from organs or glands); or a concentrate, metabolite, constituent, or extract" of the above (U.S. Food and Drug Administration, 2009). In the United States, the sale of dietary supplements is regulated by the U.S. Food and Drug Administration (FDA), a division of the Department of Health and Human Services.

The DSHEA mandates that manufacturers of dietary supplements ensure that their products are safe before selling them. Supplements do not require approval before being sold, however, nor must manufacturers submit any studies to the FDA before marketing a new product. Products sometimes contain substances that are not listed, such as caffeine. The FDA is not required to evaluate a product unless it receives enough complaints about the product. When the FDA becomes aware of a questionable dietary supplement, it must show that product is unsafe before it can be removed from the marketplace. An example of such action occurred in 2004, when the FDA declared that ephedrine could no longer be used in dietary supplements. The FDA ruling followed the heat stroke death of Baltimore Orioles pitcher Steve Bechler, a death attributed to ephedrine. (Ephedrine still can be a component of over-the-counter medicines, which are regulated more strictly).

The DSHEA does not mandate that dietary supplements be effective. If a product is shown to be ineffective, then the FDA does not require that the product be removed from shelves. If many complaints are received, however, then the Federal Trade Commission (FTC) can take action by investigating fraudulent advertising.

Some sports-nutrition and weight-loss products—such as sports drinks and energy bars—fall into the category of food, and not supplements. Both foods and supplements are subject to labeling requirements of the Nutrition Labeling Education Act of 1990 (NLEA). A supplement will have a "Supplement Facts" panel on the label. The NLEA prohibits labels from claiming that a product or its ingredients help to treat or prevent disease, except for certain health claims allowed by the FDA. Because sports performance is not a disease, statements claiming to improve performance are allowable without manufacturers providing proof that the claim is true. Many experts have urged reform to require better regulation of dietary supplements (Denham, 2011).

About half of the U.S. population, and approximately 70% of adults age 71 and older, take dietary supplements regularly (Bailey et al., 2011). About one-third of U.S. adults take a multivitamin mineral supplement (Bailey et al., 2011). Health

Canada reports similar use among Canadians. Many people take supplements on the advice of their health care providers. For example, people at risk of osteoporosis might be taking vitamin D and calcium. Supplements to slow the progress of macular degeneration appear to be supported by good research. People with heart disease often are told to take fish oil supplements. The *Dietary Guidelines for Americans* recommends including foods fortified with folate for women during their childbearing years, and vitamin B12 supplementation for people age 50 and older. People with iron-deficiency anemia usually are prescribed iron supplements.

Canadian Regulations

In Canada, dietary supplements are more tightly regulated. A product must be authorized for sale by the Natural Health Products Directorate. The manufacturer must show evidence of safety and efficacy of the product. The Directorate also imposes regulations on good manufacturing practices, labeling and packaging requirements, and the reporting of adverse reactions.

Is Natural Always Safe?

One of the biggest problems with supplement use is that consumers often assume that because the product is "natural," it is harmless. This belief can lead to consuming high levels of compounds that have negative side effects. Even vitamins and minerals can be harmful if people consume too much of them. Most vitamin and mineral supplements contain safe levels, but some consumers could get the same vitamin in different preparations. For example, a consumer might take a multivitamin supplement, an additional supplement for eye health, and a preparation for the immune system. Each of these is likely to contain zinc and vitamin A, both of which can be toxic at high doses. People who take several different preparations should read the labels, and add up the dosage they are getting for each vitamin and mineral. Consumers can check the safe upper limits against the charts for Tolerable Upper Intake Levels produced by the Food and Nutrition Board (Food and Nutrition Board 2005). Consumers also must remember that many foods contain added nutrients, such as calcium. People might consume orange juice, waffles, cereal, and antacids with calcium added, for example. It is easy to exceed the safe upper limit for calcium (2,500 mg) if taking calcium supplements and consuming calcium in the diet.

Supplement-Drug Interactions

People who take supplements should inform their health care providers about their intake. Many supplements interact with drugs, or could have effects on particular health conditions. Vitamin E, fish oil supplements, gingko biloba, and other herbal preparations can act as "blood thinners," for example, reducing the speed at which blood clots. This is beneficial for many people, but patients facing surgery are reminded to stop taking these drugs for several days before surgery to avoid excess blood loss.

Buyers Beware

Many supplement manufacturers are honest and provide helpful products and good information on use of their products. Unfortunately, others stretch the truth, and some are frauds. The Federal Trade Commission can prosecute companies whose advertising is false or misleading, but it could take the FTC years to get a product off the market. In the meantime, consumers must investigate products for themselves.

Consumers should remember that testimonials from users and endorsements by doctors or scientists do not prove that a product is safe or effective. Some people see results simply because they believe that they will—this is called the "placebo effect." Doctors and scientists promoting products might have mail-order degrees, or believe in the product because they are well paid to promote it.

Aside from a basic multivitamin and mineral supplement, children and teens should avoid using supplements unless prescribed by their health care providers, for two reasons. One reason is that little information is available about the long-term safety of these chemicals. The second reason is that most supplements have not been tested in children or adolescents. The effects of supplements could be very different in young people, and the potential for harm rarely is worth the potential health benefits. Similarly, pregnant women and nursing mothers should avoid using most supplements, except for those prescribed by their health care providers.

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Research Issues

In many countries, herbal medicines and other dietary supplements are widely prescribed by health care providers. Researchers in Germany have produced many good reports on a wide variety of supplements. There are called the Commission E Reports and can be accessed through the American Botanical Council website (http://cms.herbalgram.org/commissione/index.html).

In the United States, not all supplements contain the ingredients in the quantities stated on the label. Some are contaminated with unhealthy ingredients such as lead or mercury. Some do not dissolve quickly enough in the human digestive tract to be absorbed effectively. An independent testing agency, ConsumerLabs, tests products and publishes results. These reports are available online to subscribers (www.consumerlab.com).

See Also: Herbs and herbal medicine; Multivitamin and mineral supplements; U.S. Pharmacopeial Convention and USP-verified mark. Supplement use also is discussed in the entries for many of the individual nutrients (e.g., calcium, iron).

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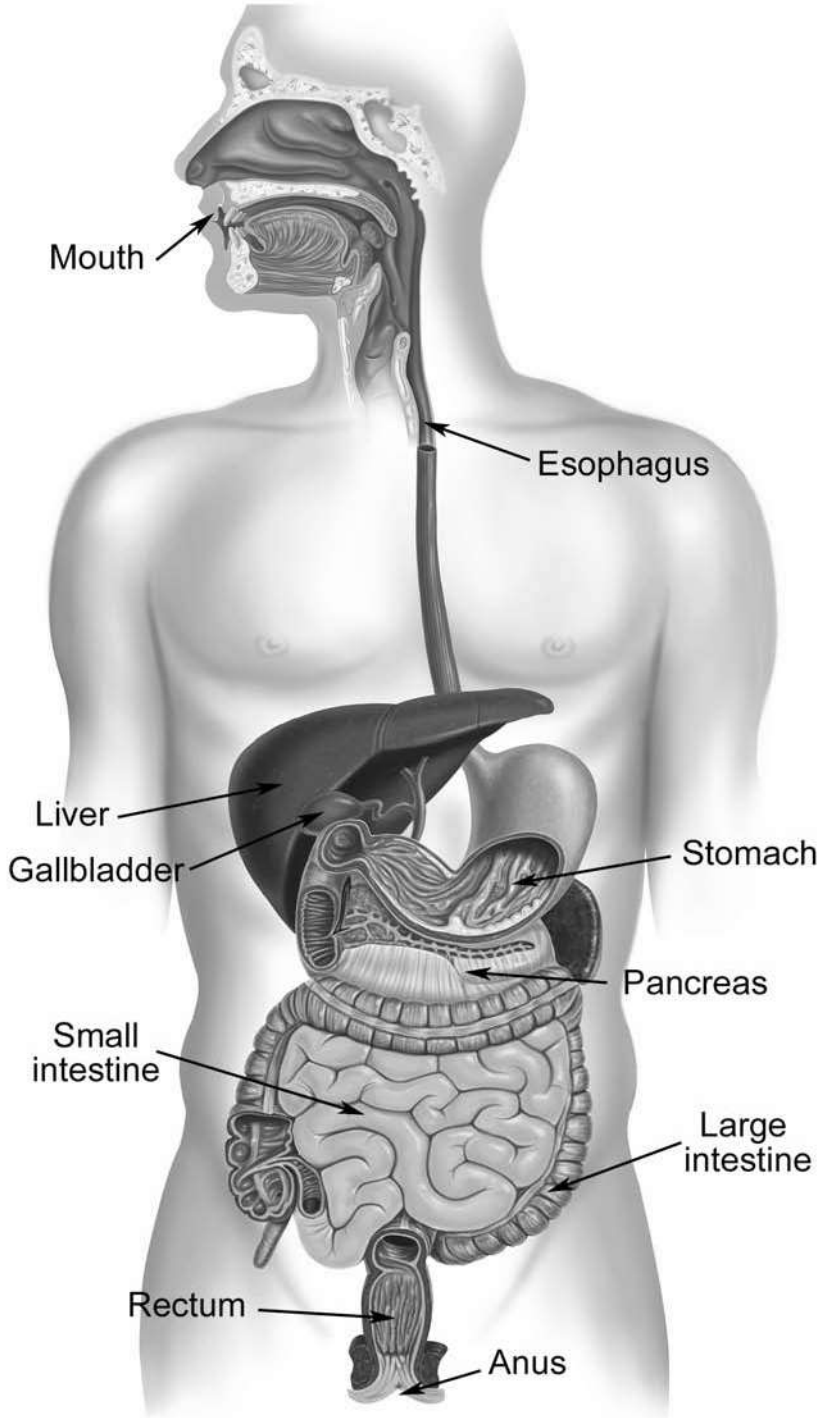
Digestion and the Digestive System

Digestion is the process of breaking down food into its constituent nutrients and into other chemicals to make these molecules available for absorption and utilization in the body. Food is broken into smaller pieces by mechanical processes (e.g., chewing in the mouth, churning in the stomach) and chemical processes. Digestion and nutrient absorption occur in the digestive system. The core of the digestive system is the gastrointestinal (GI) tract, a long hollow tube that begins at the mouth, where food is ingested, and ends at the anus, where the unabsorbed matter is excreted as "stool."

The GI tract includes the mouth, esophagus, stomach, small intestine, large intestine (which includes the colon and the rectum), and the anus. The digestive system also includes a number of accessory organs that contribute digestive fluids that assist with the chemical breakdown of food, including the salivary glands, liver, gallbladder, and pancreas. Digestion is regulated by the nervous and endocrine systems, through the action of nerves and their neurochemicals, and hormones, respectively. Chemical messengers released by the digestive organs themselves, along with the microbiota in the large intestine, contribute to the regulation of digestion.

The Gastrointestinal Tract

The organs of the GI tract share several similarities in their structure. Each organ, from the esophagus to the anus, is composed of several specialized tissue layers. The innermost layer that lines the organ, and through which the digestive matter passes, secretes mucus that protects the organ and eases the passage of contents. The lining of the stomach contains specialized cells that produce hydrochloric acid, which aids the chemical digestion of food; digestive enzymes; and hormones that regulate digestive processes. The cells lining the small intestine are



The human digestive system. (Shutterstock.com)

responsible for the absorption of most nutrients from the digestive mass; some chemical digestion also occurs in these cells.

The organs of the GI tract contain two or more layers of smooth muscle that work in a coordinated fashion to produce waves of movement that propel food down the GI tract and contribute to the mechanical breakdown of food. This movement is known as "peristalsis." Ring-like bands of muscle, known as "sphincters," prevent the backflow of GI contents. A sphincter located where the esophagus empties into the stomach, for example, prevents stomach contents from flowing back into the esophagus. (When this sphincter does not function properly, heartburn, also known as "gastroesophageal reflux," occurs.)

Steps in the Process of Digestion

Digestion can be broken down into a series of steps by following the path of ingested food.

Mouth

Digestion begins when food is taken into the mouth. The teeth crush the food as is chewed and the salivary glands secrete saliva to moisten the food. Saliva also contains some enzymes that begin the chemical breakdown of food, particularly starch. The tongue moves the food around in the mouth so that it can be thoroughly chewed. Once the food is chewed, it is swallowed into the esophagus.

Esophagus

The esophagus moves the food to the stomach via the smooth muscle contractions of peristalsis. The mucus produced by the lining of the esophagus helps the food to slide easily.

Stomach

The lower esophageal sphincter, located where the esophagus meets the stomach, opens to allow the chewed food to pass into the stomach, then closes to keep the food in the stomach. As food accumulates in the stomach, the stomach secretes hydrochloric acid to create an environment conducive for the chemical breakdown of molecular bonds. This acid environment also kills many microorganisms, which helps prevent the development of foodborne illnesses. The stomach also releases special enzymes to speed the digestion of protein, and releases a substance necessary for the absorption of vitamin B12. The food mass in the stomach is called "chyme." When chyme leaves the stomach, about 10% of fat, 10% to 20% of protein, and 30% to 40% of carbohydrate bonds have been completely broken down (Insel et al., 2014). The chyme gradually leaves the stomach over the course of 1 to 4 hours. The pyloric sphincter, located where the stomach empties into the

small intestine, allows small amounts of chyme—about 2 ml per minute—to pass into the small intestine.

Small Intestine

The majority of digestion and absorption occurs in the small intestine. As the chyme enters the small intestine, the pancreas releases a basic fluid containing bicarbonate to neutralize the acidic chyme. The pancreas also releases digestive enzymes into the small intestine to further the chemical breakdown of the molecules in the chyme. The small intestine adds more digestive enzymes to the mix. The presence of fat in the chyme signals the gall bladder to release bile, which is produced by the liver but stored in the gall bladder. Bile helps break large groups of fat molecules into smaller groups, allowing greater exposure of the molecules to digestive enzymes. The absorptive cells lining the small intestine take up small molecules from the chyme. These molecules are further broken down and sent into the circulatory and lymphatic systems to be carried to all parts of the body. The chyme typically moves through the small intestine in about 3 to 10 hours, and then enters the large intestine through a sphincter called the "ileocecal valve."

Large Intestine

The large intestine is comprised of the colon and the rectum. The peristaltic movement of the colon is much slower than that of the small intestine. The chyme passes slowly through the colon, taking about 18 to 24 hours to reach the rectum (Insel, Ross, McMahon, & Bernstein, 2014). The large colonies of bacteria residing in the colon further digest some of the remaining matter, providing the host with a small number of additional calories and vitamin K. The colon absorbs water, sodium, chloride, potassium, some polysaccharides, and vitamin K from the chyme. The remaining mass is composed of dietary fiber, bacteria, and water, and is stored in the rectum until defecation. When a person responds to the urge to pass the stool, the rectal muscles relax and the anus opens, expelling the stool.

Barbara A. Brehm

See Also: Esophagus; Gallbladder and gallbladder disease; Gastroesophageal reflux disease; Large intestine; The liver; Microbiota and microbiome; The mouth; Pancreas; Small intestine; Stomach.

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Diverticular Disease

Diverticular disease refers to disorders associated with the development of diverticula in the colon and the rectum. Diverticula (diverticulum is the singular form) are marble-sized, bulging sacs that form in the inner layers of the colon and rectum, and then push out through weak areas in the wall of the colon. Diverticulosis is a disorder marked by the presence diverticula. Diverticulosis often has no symptoms and is common in countries where people consume diets high in processed foods and low in fiber. Diverticular bleeding can result when one of the small blood vessels in a diverticulum breaks. This condition can require surgery if bleeding continues. Diverticulitis is diagnosed when the diverticula become inflamed and infected. Diverticular disease affects about 40% of people 65 years and older, and 60% of people 80 years and older (McNevin, 2013). Almost everyone older than age 80 have diverticula, although not all go on to develop diverticular disease (McNevin, 2013). Diverticular disease usually can be treated with antibiotics, rest, and a change in diet. Serious cases can require surgery.

Diverticular disease was described as early as the 17th century. Medical research on these disorders, however, did not begin in earnest until the 20th century. Rates of diverticular disease began to increase in North America, England, and Australia at about the same time that the use of refined grains became popular, in the early 1900s. This association has led researchers to suggest that a low-fiber diet increases risk of diverticular disease, but the exact mechanism for the causation of diverticula remains unclear. It is possible that low-fiber diets contribute to constipation, and to increased pressure in the colon during elimination. Stool particles can become trapped inside the diverticula and increase the risk of infection. Low-fiber diets could alter the composition of the bacterial colonies residing in the colon, contributing to the proliferation of harmful bacteria that increase risk of infection in the diverticula.

Most people with diverticulosis do not experience any discomfort or symptoms, although on occasion, they might experience cramping or feel slight abdominal discomfort. Symptoms that arise with diverticulitis include severe abdominal pain, fever, nausea, and a significant change in bowel habits. Abdominal pain often is sharp and sudden, and felt in the lower left side of the abdomen. Diverticular bleeding causes blood to appear in the stool. Bleeding can be severe; therefore if rectal bleeding occurs people should seek medical assistance immediately. Diverticular disease symptoms mimic those of many other digestive system disorders. To diagnose diverticular disease, patients usually undergo medical tests such as a CT scan or a colonoscopy.

Mild cases of diverticular disease are commonly treated with antibiotics, a liquid diet, and rest. In most cases these steps will assist the body in fighting the infection. More serious cases can require the administration of intravenous antibiotics. In a minority of cases surgery is required. In severe cases, infection can create long-term complications. Peritonitis can result if infection spreads from the colon to the lining of the abdominal cavity (the peritoneum). Scar tissue that develops from infection can form blockages in the colon. Sometimes infected

diverticula develop abscesses, with the accumulation of pus, which can be drained via medical procedures. In extreme cases, fistulas can form. Fistulas are openings that develop between the colon and other organs, such as the bladder or vagina, or from the colon into the abdominal cavity. Fistulas usually are repaired with surgery.

Epidemiologists have attempted to determine the factors that help to prevent diverticular disease. They are trying to answer the question: Why do diverticula form? And why do some people with diverticulosis never develop diverticulitis, and others progress to serious complications? Answers to these questions are still unclear. Some evidence suggests that lifestyle factors predict risk of diverticular disease. Most—although not all—studies indicate that risk increases with smoking, sedentary lifestyle, obesity, and low fiber intake (Maconi, Barbara, Bosetti, Cuomo, & Annibale, 2011). Risk increases with age, which has led researchers to propose that diverticula might increase with age-related declines in the strength and elasticity of the colon wall.

Debate continues regarding the role of diet in preventing the progression of diverticulosis to diverticulitis. In general, a high-fiber diet is recommended, although some experts advise people with diverticulosis to avoid fibrous foods that can become caught in the diverticula, such as seeds, nuts, and popcorn kernels. People with diverticulosis should prevent constipation by exercising regularly; consuming plenty of fruits, vegetables, legumes, and whole grains; and developing regular bowel habits. Medications such as fiber supplements and stool softeners also might be helpful. Probiotic foods (e.g., yogurt) and supplements could be useful for developing a healthful bacteria balance in the colon.

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See Also: Fiber; Large intestine.

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E

Eating Disorders

Eating disorders are psychiatric illnesses characterized by extreme disturbances in eating behavior and severe distress concerning body weight or shape. Eating disorders can be chronic, with symptoms lasting years or even decades. The *Diagnostic and Statistical Manual of Mental Disorders* (DSM-V) is the handbook used to classify or diagnose mental disorders. It lists four categories of eating disorders, listed below.

Anorexia Nervosa

The three diagnostic criteria for Anorexia Nervosa (AN) are (1) Restriction of food intake resulting in significant weight loss (or for children and adolescents, resulting in the failure to gain or maintain weight relative to appropriate growth); (2) Intense fear of weight gain or being overweight, regardless of low weight; and (3) Extreme distress concerning body weight or shape, or lack of acknowledgment of the seriousness of the disorder. Individuals with AN usually fall below the normal range in terms of body mass index (BMI less than or equal to 18.5).

Other Symptoms

- Restrictive eating patterns or excessive dieting
- Food preoccupations, such as obsessions with calories and fat contents
- Eliminating entire categories of food (such as fats or carbohydrates) or specific foods from diet
- Food rituals, such as cutting food into small pieces or chewing and spitting
- Excessive exercise, despite injury
- Fear of (or avoiding) eating in public
- Misusing medication to achieve weight loss or prevent weight gain. This is especially true for diabetics, who might restrict insulin doses.

Subtypes

- Restricting type—Achieves significantly low weight by means of starvation and, in some cases, excessive exercise. The individual presents no signs of binge eating or purging.



Binge eating is a characteristic of both binge eating disorder and bulimia nervosa. During a food binge, people consume an unusually large amount of food, often "forbidden" foods high in fat, sugar, and/or salt. (PhotoDisc, Inc.)

How to Help a Friend Who Has an Eating Disorder

To get well, people with eating disorders require professional help. If you think that a friend could have an eating disorder, encourage him or her to talk to a trusted adult. Don't make the mistake of thinking that you simply can "talk your friend out of" this serious illness. Following are a few ideas on how you can help your friend get the help he or she needs.

- Reach out. Express your concern about your friend's eating disordered behaviors. Refer to specific instances (i.e., meals, social events, athletic activities) when you felt he or she engaged in disordered eating behaviors.
- Educate yourself. Read books, newspaper articles, and research written by trusted organizations to find helpful information about eating disorders. The list below can get you started.
  - National Eating Disorders Association. Check out their free and confidential online screening for eating disorders at https://www.mentalhealthscreening.org/screening/NEDA
  - National Institute of Mental Health
  - Active Minds, Inc.
  - Eating Disorder Hope
- Be mindful of your language. Refrain from making comments about people's bodies, including your own.
- Encourage your friend to seek help. Remind your friend that this is a serious, life-threatening condition that requires treatment.
- Seek medical attention. If your friend refuses to seek help, then tell an adult that you trust or someone else in authority, such as a school counselor, a medical professional, a parent, or a coach.

- Binge-eating/purging type—In addition to meeting the criteria for AN, the individual presents symptoms of binge eating or purging (i.e., self-induced vomiting or abuse of laxatives, diuretics, or enemas).

Statistics

- Highest mortality rate of any mental illness
- An estimated 10-to-1 female-to-male ratio
- Twelve times the mortality rate of all other causes of death in women 15 to 24 years of age
- Less than half fully recover
- An estimated 4% of affected individuals die

Medical Complications

- Low blood pressure and heart rate
- Dehydration

- Electrolyte disturbances
- Muscle loss and weakness
- Heart failure
- Kidney failure
- Anemia
- Osteopenia or osteoporosis
- Amenorrhea and infertility
- Lanugo (growth of fine hair on the body)
- Edema
- Growth problems
- Gastrointestinal issues

Bulimia Nervosa

There are five diagnostic criteria for Bulimia Nervosa (BN): (1) Regular episodes of binge eating (consuming an unusually large amount of food within a two-hour period accompanied by a sense of lack of control while eating); (2) Engaging in regular inappropriate compensatory behaviors, such as self-induced vomiting, abuse of laxatives or diuretics, restricting, or excessive exercise; (3) Episodes are present at least once a week for three months; (4) Severe distress concerning body weight or shape; and (5) Symptoms are not solely present during episodes of AN. Individuals with BN usually fall between the normal and overweight range in terms of BMI.

Other Symptoms

- Frequent trips to the bathroom after meals
- Restrictive eating patterns between binges
- Eliminating entire categories of food (such as fats or carbohydrates) or specific foods from diet that might trigger a binge
- Swelling of the glands in the neck and jaw
- Weight fluctuations
- Excessive exercise
- Calluses on the knuckles or hands as a result of purging
- Sore throat

Statistics

- Affects one to 1.5% of young women
- An estimated 10-to-1 female-to-male ratio
- An estimated 3.9% of affected individuals will die

Health Risks

- Electrolyte imbalances

- Cardiac arrhythmia (irregular heart beat)
- Gastric rupture
- Inflammation/rupture of the esophagus
- Tooth decay, enamel loss, and tooth staining
- Edema
- Peptic ulcers and pancreatitis
- Acid reflux disorder and other gastrointestinal issues
- Amenorrhea
- Infertility

Binge Eating Disorder

There are five diagnostic criteria for Binge Eating Disorder (BED): (1) Regular episodes of binge eating (consuming an unusually large amount of food within a two-hour period accompanied by a sense of lack of control while eating); (2) Episodes are accompanied by rapid eating, eating until uncomfortably full, eating when not hungry, eating alone because of feeling embarrassed by the behavior, or feelings of disgust or guilt after bingeing; (3) Severe distress associated with binge eating; (4) Episodes are present at least once a week for three months; and (5) Symptoms are not accompanied by compensatory behaviors, nor are they solely present during episodes of AN or BN. Individuals with BED usually fall in the ranges of normal, overweight, and obese in accordance with BMI.

Statistics

- Affects an estimated 1 to 5% of the general population
- An estimated 40% of affected individuals are male

Health Risks

- High blood pressure (hypertension)
- High cholesterol
- Cardiovascular disease
- Heart disease
- Type 2 diabetes
- Gallbladder disease
- Gastrointestinal issues

Eating Disorder Not Otherwise Specified

An Eating Disorder Not Otherwise Specified (EDNOS) is diagnosed when symptoms of eating disorders are present but do not meet the full diagnostic criteria of any specific category. Some examples of EDNOS include the following.

- Atypical anorexia nervosa: All symptoms of AN are present except that the individual's weight does not fall below the normal range.
- Bulimia nervosa (of low frequency/limited duration): The individual does not engage in compensatory behaviors at the minimum frequency or duration listed in the diagnostic criteria.
- Binge-eating disorder (of low frequency/limited duration): The individual does not engage in compensatory behaviors at the minimum frequency or duration listed in the diagnostic criteria.
- Purging disorder: The individual engages in purging behaviors but not binge eating.
- Night eating syndrome: The individual awakens during the night to engage in excessive eating, is aware of such behaviors, and experiences significant distress associated with night eating.

Statistics

- EDNOS is the most commonly diagnosed eating disorder
- An estimated 5.2% of affected individuals die

History

The most credited early physician with regard to eating disorders was Richard Morton, who described the first medical condition in history that is most akin to today's "anorexia nervosa." It wasn't recognized as a true medical condition, however, until 1873, when Sir William Gull devised the name "anorexia nervosa." Ernest-Charles Lasègue, a French physician, also published similar case studies that same year.

In 1952, anorexia nervosa was the first eating disorder to be recognized as a psychiatric illness in the first edition of the *Diagnostic and Statistical Manual* (DSM-I). With the publication of the DSM-III 28 years later, bulimia was added as a separate category.

Although exploration continued in the field of medicine, the majority of cases and discoveries remained hidden from the public eye until the 1970s. Psychoanalyst Hilde Bruch became widely known in the medical field of eating disorders after her publication of *Eating Disorders: Obesity, Anorexia Nervosa, and the Person Within*. Dr. Bruch went on to publish a book aimed at a more secular audience, *The Golden Cage: The Enigma of Anorexia Nervosa*, which is credited today as one of the first publications to spread eating disorders awareness among the general public.

One of the most recent contributions to the field of eating disorders was the publication of the fifth edition of the DSM. Using the criteria listed in the previous edition, DSM-IV-TR, it was found that two-thirds of individuals with eating disorders were diagnosed with EDNOS. Diagnosing patients with such an ambiguous diagnosis as EDNOS often results in providing treatment targeting other types of

eating disorders. Additionally, insurance companies are significantly less likely to reimburse patients for medical expenses due to "not otherwise specified" disorders. Physicians and families alike hoped that improving the diagnostic criteria for each category would reduce the high prevalence of diagnoses of unspecified eating disorders. Since the new edition's changes were proposed, evidence has pointed to a significant decrease in the diagnosis of EDNOS. It is anticipated that the new criteria outlined in the DSM-V will promote better treatment and reimbursement, and ultimately better prognoses.

Contributing Factors

Biological Factors

- Family history, having first-degree relatives with an eating disorder, especially with AN or BN
- Obesity, especially for individuals with BN
- Abnormalities in the brain in individuals with AN
- Possible genetic transmission

Environmental Factors

- Pressure to obtain the "perfect body"
- Cultural values of thinness
- Hobbies and careers that encourage thinness, such as athletics, dance, modeling, and acting
- History of childhood abuse, trauma
- Experiences of being teased about size, shape, or weight

Psychological Factors

- High levels of anxiety and/or obsessive traits
- Symptoms of depression
- Low self-esteem
- Feelings of lack of control

Comorbidity

Eating disorders have been found to exist alongside several psychiatric illnesses, including depressive, bipolar, anxiety, and substance-abuse disorders. Furthermore, comorbidity also has been found to exist with eating disorders and physical health conditions. Eating Disorder–Diabetes Mellitus Type 1 (ED-DMT1), a condition commonly known as "diabulimia," represents a dual diagnosis of an eating disorder and type 1 diabetes. Individuals with ED-DMT1 misuse insulin in an attempt to manipulate or lose weight.

Treatment and Outcomes

Eating disorders are multifaceted illnesses and should be treated by a team of professionals. There are three crucial aspects of treatment, medical, nutritional, and therapeutic. A specialist or primary care physician evaluates the individual's physical state of health. Regular weight-checks, vital signs checks, and blood tests usually are administered depending on the patient's status and the severity of symptoms. A nutritionist or dietician works with the individual to provide a meal plan to meet the individual's nutritional needs. There are several successful therapeutic approaches to eating disorders. These include, but are not limited to, those listed below.

Cognitive Behavioral Therapy

In Cognitive Behavioral Therapy (CBT), a therapist works with an individual to identify negative thought patterns and replace them with positive and effective ones. The notion of CBT is that changing a person's thoughts ultimately can change the person's behavior.

Dialectical Behavioral Therapy

In Dialectical Behavioral Therapy (DBT), an individual learns to identify and cope with uncomfortable or distressing thoughts that might be contributing to urges and behaviors. Gradually, the individual learns to tolerate his or her emotions without acting on them. Mindfulness techniques—such as muscle relaxation and deep breathing—are implemented as a way of accepting, rather than resisting, negative emotions.

Maudsley Approach

A relatively new model, the Maudsley Approach is family-based treatment specifically designed for children and adolescents with Anorexia Nervosa. Unlike other models, this treatment takes place at the patient's home. The primary goals are weight restoration, encouraging the children or adolescents to take control over their eating patterns, and providing the patient with familial support.

Medication

Some individuals also respond well to psychiatric medications, but it is important that this be used as a supplement to other means of treatment. Inpatient care is recommended when the individual has regressed or has failed to make any significant progress. Hospitalization also might be necessary if the eating disorder has become dangerous or life-threatening in a physical or psychological way.

Research has shown that earlier medical intervention results in a better prognosis. Many individuals continue to experience symptoms after treatment, however,

and require multiple bouts of treatment. Others have symptoms that last a lifetime. The duration and outcome of treatment ultimately depend on the individual's willingness to participate in treatment, the duration of the illness, the existence of comorbid disorders, and insurance coverage or reimbursement for treatment.

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See also: Feeding disorders; Food addiction.

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Echinacea

Echinacea is a genus of flower that is native to the North American Midwest and most often is used to treat the common cold and the flu. Three species of the plant, *Echinacea angustifolia*, *Echinacea pallida*, and *Echinacea purpurea*, commonly are used to create echinacea tablets, capsules, tinctures, ointments, and teas. The roots, leaves, and flower parts of the plant are used in herbal preparations. Due to the variety of methods employed to prepare echinacea supplements, and the multiple varieties of plant that are available for harvest, echinacea products vary widely. The mechanism through which echinacea is thought to impact health is uncertain, but it generally is thought to influence the normal immune response and reduce inflammation.

The word "echinacea" is derived from the Greek word "echinos," meaning "hedgehog"—a name attributed to the plant's large, spiky seed head. Echinacea

has been used for centuries to treat diseases such as malaria, syphilis, diphtheria, and scarlet fever. Archaeological evidence indicates that echinacea commonly was used by Native Americans for more than 400 years to treat infections, wounds, and many other ailments, and that settlers adopted the practice. Indeed, echinacea was listed on the U.S. National Formulary—an official list of medications approved for prescription in the United States—from 1916 to 1950. With the increasing development of antibiotics throughout the 1900s, however, therapeutic echinacea use in North America declined. Echinacea has become popular again in the United States, but as an alternative herbal remedy. Echinacea still is the primary treatment for minor respiratory-tract infections in Germany, where 1.3 million prescriptions for echinacea are written each year (EBSCO, 2012). Preparations from the leaves and flowers of *E. purpurea* are thought to be most effective.

Myriad variations in the production process result in different concentrations of echinacea's various chemical compounds in different commercially available products. Therefore, each particular product has different dosing instructions, indicating that vastly different amounts, concentrations, and varieties of the supplement are curative. For these reasons, studies of the restorative effects of echinacea have been difficult to compare to one another. Nevertheless, well-designed human studies suggest that echinacea is possibly effective for reducing the length and severity of respiratory-tract infection symptoms.

General guidelines for using echinacea recommend taking the supplement as soon as respiratory symptoms become apparent, and discontinuing use once symptoms are gone, which usually occurs within one to two weeks. Echinacea seems to be safe for most people. Occasionally, people allergic to plants in the ragweed, marigold, mum, and daisy families develop allergic reactions to echinacea products, including skin rashes, and rarely, anaphylaxis. Additionally, although short-term use of echinacea seems to be harmless, it is important to note that long-term effects of echinacea use have not yet been widely studied.

Elizabeth J. Thompson

See Also: Dietary supplements; Herbs and herbal medicine.

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Electrolytes

Electrolytes are positively or negatively charged ions that form when salts, acids, or bases dissolve in water. Ions are molecules that carry different amounts of electrons and protons, giving the molecule a net electric charge. This charge can be negative or positive—an ion with a negative charge is called an "anion," and an ion with a positive charge is called a "cation." Electrolytes are essential for water balance, blood pH (acidity), nerve and muscle function, and many other processes. Electrolytes commonly found in the human body include sodium, potassium, chloride, calcium, magnesium, and phosphate.

To maintain electrolyte balance, electrolytes are moved in or out of the cell through specialized ion pumps that are embedded in the cell membrane. These pumps are used by the cell to maintain specific electrochemical gradients and to regulate fluid volumes. The movement of electrolytes influences the movement of water into and out of cells; this is called "osmosis." When electrolytes are more concentrated on one side of the cellular membrane, osmosis moves water to the side with the greater electrolyte concentration so that the same concentration of ions is present both inside and outside of the cell.

Sodium is the primary cation in extracellular fluids, including the blood, and potassium is more highly concentrated inside the cells. Sodium-potassium pumps maintain these concentrations. The kidneys help to maintain correct levels of electrolytes in the body. During electrolyte imbalance—such as when a person is dehydrated—osmosis is disrupted, causing water to move out of the cell to equalize the ionic concentration gradient. When water moves out of the cell, the cell can shrink and eventually could die. Common causes of dehydration include illnesses accompanied by symptoms such as vomiting and diarrhea that lead to excess loss of body water; conditions that cause excessive sweating, such as exercising or working in the heat; and failure to drink enough water. Dehydration commonly is treated by oral ingestion of electrolyte solutions, such as with sports drinks or medicines such as Pedialyte, or by intravenous delivery. Electrolyte imbalances can accompany a number of health problems, such as heart failure and kidney disease.

Paula Sophia Seixas Rocha and Alexandra A. Naranjo

See Also: Calcium; Chloride; Minerals; Phosphorus; Potassium; Sodium and salt; Sports beverages; Water needs, water balance.

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Ellagic Acid

Ellagic acid is an antioxidant found in many fruits and vegetables that recently has shown promise for medicinal applications in humans. In the mid-1800s, the chemists Henri Braconnot and Michel Eugène Chevreul were the first to isolate ellagic acid from an oak gall-nut, an abnormal growth on plants stimulated by parasitic invasion (Hemingway, 1992). Ellagic acid serves a protective purpose in plants by blocking microbial infections, and also might prevent heavy-metal poisoning and predation by insects. Its highest concentrations are found in red raspberry plants, as well as in strawberries, blackberries, cranberries, pomegranates, walnuts, and pecans. Although ellagic acid is located primarily in leaves, fruits also contain the substance. Humans typically ingest the natural phenol as ellagitannin, or ellagic acid with glucose, a form that is water soluble and easy to digest.

Preliminary research thus far only has shown promise in human cell lines in vitro, and in animal models. For example, research has shown that extracts containing ellagic acid drawn from a selection of these plants alleviate some types of inflammation and serve as antioxidants. Although the mechanism is unknown, fruit extracts containing ellagic acid have reduced colon inflammation in rats (Rosillo, 2012). In an in vitro study of cultured human cells treated with walnut extract, inflammation of aortic lining cells was reduced, and the activity of osteoblasts increased (Papoutsi, 2008) (osteoblasts stimulate the formation of new bone tissue in vivo).

Laboratory research has produced some encouraging studies that illustrate ellagic acid's ability to bind with some carcinogenic—cancer-causing—molecules. Ellagic acid preparations have been shown to inhibit chemical-induced esophageal cancers, as well as skin and lung tumors in laboratory rodents. Preliminary research in this area, however, currently is insufficient to label any product as a viable treatment for cancer or other illnesses. New supplements and other products featuring ellagic acid have been frequent targets of the Food and Drug Administration as being in violation of the Federal Food, Drug and Cosmetics Act. False claims warrant increased awareness from consumers, who should seek professional advice when considering supplementing their diet with ellagic acid. Consuming more foods such as berries, pomegranates, walnuts, and pecans as part of a balanced diet is considered prudent advice.

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See Also: Antioxidants; Cancer and nutrition; Dietary supplements.

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Energy Balance

Energy balance refers to the relationship between energy taken in, or eaten, and energy expended, or "burned." A negative energy balance means that more energy is expended than is consumed. Over time, a negative energy balance causes the body to use stored energy for fuel. A positive energy balance means that more energy is consumed, or eaten, than expended. A positive energy balance encourages the body to store energy. The body can store a little energy as carbohydrate—in the form of glycogen—primarily in the liver and skeletal muscles. The majority of excess energy from a positive energy balance, however, is stored as adipose tissue. People whose energy intake is similar to their energy expenditure are said to be in energy balance, or energy equilibrium. Researchers and people trying to gain or lose weight are interested in the factors that contribute to energy balance because they influence the status of energy stores, especially adipose tissue. A positive energy balance over time results in excess adipose stores and obesity. A negative energy balance over time results in weight loss. In people who are overweight or obese, about 60% to 80% of this weight loss is composed of fat; lean tissue comprises some of the weight that is lost over a period of negative energy balance (Hill, Wyatt, & Peters, 2012). A negative energy balance also can result in muscle wasting and the use of important body tissues for fuel, as is the case in starvation.

Energy Intake

Energy intake can be measured in terms of kilocalories (kcals). People obtain energy from carbohydrates, fats, and proteins in the foods that they eat. The body is able to extract energy from the chemical bonds found in these molecules. Carbohydrates and proteins deliver 4 kcals per gram, and fats contribute 9 kcals per

gram. Alcohol also contains chemical bonds that can be used by people to make energy; alcohol has 7 kcals per gram.

Physiologists used to believe that all kilocalories were equal in terms of influencing body energy stores. Recently, an increased understanding of the way foods and their nutrients behave in the body and the complex biochemical processes in which they participate has overturned the mechanistic view of calories from food all having similar effects on adipose tissue storage. Some studies suggest that foods differ in their metabolic impact in ways that lead to variable effects on energy stores.

One study, for example, compared groups that were limiting calorie intake. One group included only whole-grain foods when consuming grains or grain products, and the other group was asked to avoid whole-grain foods (Katcher et al., 2008). Both groups consumed the same amount of calories and lost the same amount of weight during the 12-week study. The whole-grain group, however, lost more body fat from the abdominal region. Extra fat stores in the abdominal region are associated with negative health effects, including hypertension, type 2 diabetes, and heart disease. At the end of the study, subjects in the whole-grains group also had greater decreases in C-reactive protein (CRP) level, a marker of inflammation, than did the subjects in the other group (Katcher et al., 2008). Lower CRP levels and reduced levels of inflammation are associated with better health.

Some studies have suggested that beverages sweetened with fructose could be more likely to contribute to obesity and obesity-related health disorders than beverages sweetened with glucose. One such study found that fructose-sweetened beverages increased abdominal fat and blood lipids and decreased insulin sensitivity (a marker of good blood sugar regulation) in overweight and obese people more than the same amount of beverages sweetened with glucose (Stanhope et al., 2009).

The types of food kcals consumed throughout the day also have an effect on people's level of hunger and their appetite. Feelings of hunger can increase even though people have consumed "enough" calories if those calories have been stored and blood sugar drops. People seeking to reduce food intake must devise eating strategies that minimize feelings of hunger and do not trigger the body's fat-storage pathways.

Energy Expenditure

Daily energy expenditure refers to the total amount of energy used in a 24-hour period and commonly is measured in kcals. The body expends energy in many different ways. Metabolism refers to the entire collection of biochemical processes that occur in the body, many of which require energy. Most bodily functions—from digesting food to contracting muscles—require energy. Metabolic rate is the energy expenditure required to sustain metabolism in a given period, usually expressed per minute or per hour. Metabolic rate at any given moment depends upon activity level and the biochemical processes occurring in the body. Daily energy

expenditure often is divided into several components, including those listed below.

Basal Metabolic Rate or Resting Metabolic Rate

Basal and resting metabolic rate both are terms that refer to the energy required just to stay alive in a resting state. Basal metabolic rate (BMR) is measured while a person is awake but is resting and lying down. Resting metabolic rate (RMR) is measured when a person is in a seated position. For most people, RMR consumes more than half of the calories required in a 24-hour period.

The Thermic Effect of Food

The thermic effect of food (TEF) refers to the energy required for the processes of digestion and absorption. The term "thermic" refers to energy expenditure. This word is used because all of the body's metabolic processes generate heat; by measuring heat (calories), scientists can calculate energy use.

Why does eating take energy? Energy is required to chew food, contract the muscles of the gastrointestinal (GI) system, produce digestive enzymes and fluids, and absorb nutrients from the digestive system into the lymphatic system or bloodstream. The thermic effect of food is proportional to the amount of food consumed, and is about 8% to 10% of the kcals consumed (Hill, Wyatt, & Peters, 2012).

The Thermic Effect of Exercise

By far, the most-significant effect on metabolic rate is achieved with exercise. The thermic effect of exercise (TEE) refers to the calories used during exercise. During moderately vigorous physical activity, metabolic rate increases by a factor of 10 or more, burning hundreds of extra calories. The more vigorous the exercise, the more calories expended. After vigorous activity, metabolic rate remains elevated for a while, as the body returns to its resting level.

Nonexercise Activity Thermogenesis

The term nonexercise activity thermogenesis (NEAT) was coined by James Levine to describe activities that do not fall into the categories of sleeping, eating, or exercise (Levine, 2004). In this context, Levine uses the word exercise to refer to activity performed specifically for the purpose of playing a sport or for physical conditioning. Nonexercise activity thermogenesis includes all other activities, such as climbing stairs, chewing gum, and jiggling around when seated, as well as the activities of daily living, such as grocery shopping, cooking, and cleaning. NEAT can expend hundreds of calories per day and exert a significant effect on energy balance. High levels of NEAT appear to have significant health benefits. Conversely, research has found that long periods of sitting, even for people who exercise regularly, are associated with increased risk of obesity and metabolic syndrome.

Applications

Any condition that influences metabolic rate also influences energy balance. Pregnancy for example, raises metabolic rate as many systems gear up to support the growth of the baby. Many hormones influence metabolic rate, and can send a person into either negative or positive energy balance. Illness that decreases appetite or food intake can lead to a negative energy balance and catabolic state in which body tissues are broken down for energy. Growing children are in positive energy balance, as extra energy is consumed to supply the raw materials and support for growth and development.

Barbara A. Brehm

Research Issues

People trying to lose weight often wonder what types of exercise are best for increasing energy expenditure, not only during the exercise session itself, but during the period of recovery from exercise. High-intensity exercise burns more calories per minute, and can have a somewhat greater recovery energy cost. Calories still count, of course, so one hour of moderately vigorous walking might burn more calories than 20 minutes of interval training, depending upon the nature of the two workouts.

See Also: Calorie; Metabolic rate; Metabolism.

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Energy Drinks

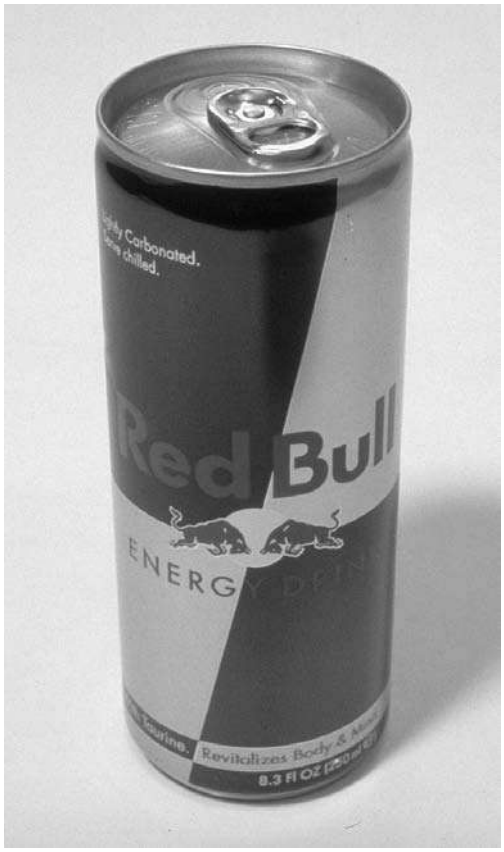
Energy drinks are beverages that contain caffeine, often in combination with other ingredients, such as vitamins, sugars, herbal supplements, amino acids, or guarana (a plant product high in caffeine). Energy drinks claim to provide a burst of extra energy to their consumers. The term "energy drink" was created by beverage companies and is not recognized by the U.S. Food and Drug Administration (FDA) or the U.S. Department of Agriculture (USDA). Energy drinks are regulated as dietary supplements.

The most common ingredients in energy drinks are caffeine, taurine, guarana, ginseng, and B vitamins. The primary ingredient is caffeine because of its taste and its potential to improve mental and physical performance. The amount of caffeine in energy drinks can range anywhere from 75 mg to more than 200 mg per serving, and some products contain more than one serving per container. The average moderate consumption of caffeine for most individuals is about 300 mg per day, whether from energy drinks or other sources.

Many people find caffeinated beverages such as energy drinks helpful in moderate amounts in situations requiring increased alertness, such as when driving, studying, or working. It is not known whether improvements experienced are due to the effects of caffeine alone, the herbal ingredients, or a combination of the two. Some people consume energy drinks to improve athletic performance. Caffeine does enhance athletic performance, perhaps by raising blood fat levels and enhancing reaction time. It is probable that improvements in athletic performance experienced with energy drinks primarily are due to the caffeine content. People seeking weight loss also turn to energy drinks in hopes of burning extra calories by increasing metabolic rate, a known effect of caffeine. A small increase in resting metabolic rate, however, is easily offset by the consumption of a few extra calories in the diet, and these drinks have not been shown to be effective for weight loss.

Taurine is an amino acid that the body is able to make from other amino acids. Taurine is plentiful in animal tissues, and in the diet comes from foods such as beef, pork, fish, and other meats. Some evidence has suggested that caffeine and taurine combined might improve mental performance. Other amino acids, such as carnitine, sometimes are added to energy drinks. Carnitine is involved in the metabolism of fat, although adding extra carnitine to the diet does not appear to aid weight-loss efforts.

Guarana is a compound that comes from the seeds of a Brazilian shrub. Guarana often is found in beverages from Brazil. The plant is added to energy drinks because it contains a large amount of caffeine, which increases energy and



Can of Red Bull, a highly caffeinated carbonated energy drink from Austria. In the United States, energy drinks are regulated as dietary supplements by the U.S. Food and Drug Administration. This means that products are not reviewed or approved by the FDA. Label claims are often exaggerated and misleading. (Photo by Anthony Verde/Time Life Pictures/Getty Images)

improves mental and physical performance, but it is not the main source of caffeine in energy drinks. Despite guarana's high concentration of caffeine (more than that in a coffee bean), in the United States it generally is recognized as safe as a natural flavoring substance. Ginseng is an herb that supposedly increases sense of well-being and stamina and reduces feelings of stress. Its effectiveness as a component of energy drinks has not been established. The B vitamins play many important roles in the production of energy from carbohydrates, fats, and proteins in the diet. Unless a person has a deficiency of a particular B vitamin, however, consuming extra B vitamins does not appear to increase alertness or improve athletic performance.

Energy drinks can be consumed in moderation safely. A moderate consumption of 300 mg caffeine per day is safe for most adults. Children, however, should limit their caffeine intake to less than 100 mg per day because caffeine has been associated with many negative effects in this age group, including behavioral problems and sleep disorders. Some people react negatively to caffeine and experience disturbing symptoms such as irritability, anxiety, irregular heart rhythms, insomnia, and stomach pain. Most energy drinks also contain added sugars, which can increase risk for obesity.

Recently, controversy has arisen over the sale and regulation of energy drinks because many believe they are dangerous to children and teenagers. Some people believe that the intake of excessive amounts of caffeine and the ability for young people to easily access it is a major problem. A common energy drink, 5-Hour Energy, for example, is ingested like a "shot" and claims that users will feel its effect within minutes. Many think that this type marketing toward youth is

Emergency Department Visits Involving Energy Drinks

- The number of emergency department (ED) visits involving energy drinks doubled from 10,068 visits in 2007, to 20,783 visits in 2011.
- Among energy drink–related ED visits, there were more male patients than female patients; visits doubled from 2007 to 2011 for both male and female patients.
- In each year from 2007 to 2011, there were more energy drink–related ED visits by patients who were 18 to 39 years of age than there were for all other age groups. The greatest increase, however, was patients 40 years of age or older, for whom visits increased 279%—from 1,382 visits in 2007, to 5,233 visits in 2011.
- In 2011, more than half of the energy drink–related ED visits involved energy drinks only (58%), and the remaining 42% also involved other drugs.

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inappropriate, and encourages a reliance on substances for psychological effects. Additionally, health professionals recommend that parents and other caregivers encourage children to develop healthful lifestyles that lay the groundwork for bountiful daily energy. Children and adolescents should achieve feelings of energy by developing regular sleeping habits, consuming a healthful diet, and getting plenty of vigorous exercise (American Academy of Pediatrics, 2011).

The combination of energy drinks and alcohol can be very dangerous because feelings of alertness can mask intoxication and give the impression of being sober, leading users to drive drunk and engage in other risky behaviors (Brache & Stockwell, 2011). One study found that bar patrons who drank energy drinks and alcohol were three times more likely to become highly intoxicated than were other patrons (Thombs, O'Mara, Tsukamoto, Rossheim, Weiler et al., 2010). Energy drink–consuming bar patrons also were also four times more likely to report intending to drive than other drinkers. Because of this, several states and colleges have banned alcoholic energy drinks.

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See Also: Alcohol; Caffeine; Dietary supplements.

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Enrichment and Fortification

Enrichment and fortification both refer to the adding of nutrients to food. Enrichment refers to the adding of nutrients normally present in a given food but which have been lost during processing. Fortification is defined as the addition of nutrients beyond those that are naturally present in a given food. Fortification and enrichment are terms often used interchangeably, and fortification is typically used as a general term for the addition of nutrients to foods. Enrichment and fortification began as efforts to prevent malnutrition but have expanded to include the creation of functional foods.

The implementation of food fortification in North America began in response to the prevalence of widespread health conditions that were shown to be directly related to nutrient deficiencies. Increased diagnoses of goiter, pellagra, rickets, beriberi, and scurvy created a public health need for better nutrition. Initially, many food manufacturers believed that nutrient deficiencies were the responsibility of the pharmaceutical companies. Public health agencies began to develop educational programs that were aimed at simultaneously creating a demand for fortified products while also encouraging the food industry to see the benefit of developing such products. Schoolteachers were provided with educational programs for their classrooms. Routine visits to the doctor began to include basic education about drinking milk fortified with vitamin D for the prevention of rickets, particularly in small children. Consumer demand soon was followed by industry competition to produce new and improved products that could make health claims. For instance, dairy manufacturers began adding vitamin D to milk and sought the American

Medical Association seal of approval to draw attention of both health-conscious mothers as well as medical providers.

In 1924, iodized salt became the first fortified food in the United States. In Michigan, iodine was added to salt to help prevent a disease of the thyroid gland called goiter. Soon after the introduction of iodized salt into the food supply, Michigan saw the prevalence of goiter drop from 38.6% to 9% (Backstrand, 2002). Iodized salt soon began to be produced throughout the United States. Iodized salt began a trend that later would be followed by other fortified staple foods, such as milk, flour, and various grain products. That same decade, an estimated 75% of infants in New York City suffered from rickets due to low vitamin D intake (Backstrand, 2002). A pellagra epidemic emerged from niacin deficiency. Health practitioners also were seeing beriberi and night-blindness at an increasing rate due to deficiencies in thiamin and vitamin A, respectively.

By 1941, with the impending possibility of U.S involvement World War II, malnutrition was perceived to be a matter of national security. Accordingly, the first Recommended Dietary Allowances (RDAs) were presented at the National Nutrition Conference for Defense. In addition to energy and protein recommendations, the new RDAs covered eight micronutrients—iron, calcium, thiamin, riboflavin, niacin, ascorbic acid, vitamin A, and vitamin D. The RDAs then were used to guide the fortification of foods that suffered nutrient losses due to refining processes. Corn for instance—which was a major dietary staple for low-income households—lost much of its niacin due to processing in motorized corn mills. Enrichment of corn and grain products with niacin soon eradicated the niacin-deficiency disease pellagra within these lower socioeconomic populations. New guidelines also allowed nutrients to be added above "natural levels" if other ways to correct nutritional deficiencies are not available. By 1958, the FDA established enrichment standards for refined grains products such as white bread, pasta, cornmeal, grits, and white rice.

The Food and Drug Administration (FDA) currently has general guidelines for the addition of nutrients to food. Once a documented need for adding a nutrient is established, the food to be fortified must be confirmed as a suitable vehicle to correct specific dietary insufficiency. Additionally, it's required that the nutrient have sufficient bioavailability and not be present at an excessive level. The nutrient also must be stable in customary storage conditions. In 1992, for example, the Centers for Disease Control and Prevention recommended that women of childbearing age achieve higher intakes of folic acid to prevent infant birth defects known as neural tube defects. Soon after, the FDA permitted the addition of folic acid to grain products.

Another approach to food fortification involves modifying food plants themselves. Biofortification currently allows for selective breeding or genetic modification of organisms to produce nutrient-dense foods. Compared to commercial fortification, biofortification generally requires a one-time investment mostly for research and design; for example, biological engineering has created self-fortifying seeds. Biofortification of staple foods can provide a direct method of ensuring daily consumption of nutrient dense foods. Golden Rice is genetically

engineered to synthesize its own beta-carotene, the precursor to vitamin A. Vitamin A deficiency is the leading cause of blindness in many countries around the world.

Biofortification faces numerous technological complications. Developing biofortified varieties leaves farmers concerned about sensory changes to current crops. For instance, increasing provitamin A concentration causes color changes. In addition to breeding plants for selective traits, other agricultural practices such as the use of specific soil fertilizers can aid in increasing nutrient concentration. Although debate about genetically modified foods continues, some scientists maintain that with good seed systems breeding for nutrient density can help to address public health demands related to nutrient insufficiencies.

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Research Issues

The FDA currently has little authority to regulate food-fortification efforts on the part of the food industry. An enormous variety of fortified foods can be found on supermarket shelves. Fortified beverages, breakfast cereals, meal-replacement bars, and many other products offer 100% of the Recommended Dietary Allowance for many nutrients. Many nutritionists are concerned that consumption of fortified food products could contribute to nutrient toxicity, in which consumer intake of certain nutrients can surpass the toxic upper limit for that nutrient. For example, the recommended upper limit for the daily intake of calcium for adults is 2,500 mg. If a person consumes three servings of dairy products, as recommended by nutrition guidelines, but also consumes calcium-fortified waffles and orange juice, and then takes a calcium-based antacid, this limit can be easily exceeded.

See Also: Dietary Reference Intakes; Genetically modified organisms; Iodine; Niacin; U.S. Food and Drug Administration.

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Enteral Nutrition

Enteral feeding provides nourishment to a person through a surgically placed tube in the gastrointestinal (GI) tract, either through the nose, throat, or abdominal wall. It is designed for individuals with functional digestive systems who are unable or unwilling to receive adequate nutrition by mouth. Enteral nutrition has been shown to decrease postsurgical complications, such as malnutrition, delayed wound healing, and infection, and to reduce the amount of time spent in hospital-care settings. Enteral nutrition can last for a short time or can continue throughout a person's life, depending upon medical conditions. Enteral nutrition can improve the quality of life for people who require nourishment in this manner.

History

Enteral feeding dates back to ancient Greece and Egypt, where solutions were inserted into the rectum to treat bowel disorders. Such solutions consisted of milk, wine, wheat, barley, eggs, and brandy. Gastrostomies were introduced in 1845 and had numerous complications, leading many physicians to use nasogastric tubes instead. The first percutaneous endoscopic gastrostomy was performed on an infant in 1979 by Dr. Michael Gauderer, who later published his method; it became a widely used technique in 1980s.

Feeding Tubes

Enteral nutrition can be administered by cervical pharyngostomy or esophagostomy, gastronomy, jejunostomy, or nasoenteral feedings (*see* Table 1). Several clinical factors exist in the decision-making process regarding the route of administration, such as the individual's medical, nutritional, and behavioral status.

G-tubes and J-tubes can be inserted through the skin with a surgical procedure known as percutaneous endoscopic gastrostomy (PEG). Radiological images can help guide surgery, and laparoscopic and open surgical procedures also can be used. The tube is held in place by a water-inflated balloon against the abdominal wall, as well as an external fixation device. A flat open and closeable "button" lies against the skin to enable easy feedings and prevent tube dislodgment.

Methods of Delivery

- Gravity tube feeding—liquid feeds are poured into a feeding bag and pulled by gravity into a drip chamber and through the tube.
- Bolus—liquid feeds are manually administered by syringe in 5- to 10-minute intervals.
- Continuous–liquid feeds are delivered by a feeding pump at a constant rate throughout the day and are often used overnight.

Table 1. Enteral Nutrition

Type	Route of Administration	Indications for Use	Short-term	Long-term
Cervical Pharyngostomy or Esophagostomy	Inserted through the throat and into the esophagus	Following head and neck surgery; rarely used due to hazardous and inconvenient placement.	✓	
Gastrostomy (G-tube)	Administers feeds directly into the stomach.	Avoids issues with speech and swallowing, as well as nasal and esophageal irritation		✓
Jejunostomy (J-tube)	Inserted through the small intestine, into the lumen of the jejunum.	Tracheal aspiration, reflux esophagitis, gastroparesis, gastric or pancreatic cancer. Decreased risk of reflux and aspiration, since this method bypasses stomach.		✓
Nasoenteral (Nasogastric, nasoduodenal, nasojejunal)	Inserted transnasally	Short-term solution; allows for easy removal	✓	

Potential Reasons for Enteral Feeding

- Anorexia nervosa
- Burns
- Cachexia
- Chemotherapy
- Chronic pancreatitis
- Dysphagia
- Esophageal obstruction
- Gastroparesis
- Head and neck cancer
- Hepatic failure
- Impaired consciousness
- Inadequate oral intake
- Inflammatory bowel diseases
- Intestinal failure
- Parkinson's disease
- Postoperative
- Psychological
- Renal failure
- Respiratory failure
- Sepsis
- Trauma

Enteral Feedings

Liquid feeds can consist of commercially prepared feeds or blenderized food, which is rarely used. Although blenderized feeds are less expensive, formulas are more common and have less potential for blockage. The two most common types of enteral feeds are polymeric and monomeric formulas. Polymeric formulas, which consist of macronutrients in isolate form, contain protein, triglycerides, and carbohydrate polymers, and are the most commonly used formulas in enteral feeding. Monomeric formulas consist of proteins in the form of peptides or amino acids, fat as long-chain triglycerides (LCTs) or a combination of medium-chain triglycerides (MCTs) and LCTs, and carbohydrates in the form as partially hydrolyzed starch maltodextrins and glucose. These formulas most often are suggested for individuals with digestive or absorption issues. Other specially designed formulas are administered to patients with renal failure, pulmonary insufficiency, cirrhosis, or diabetes.

During the first 24 to 48 hours, enteral feeding is monitored closely, especially for ill or injured patients. Meal plans are introduced gradually, beginning at 50% of the patient's total caloric intake and gradually increasing to 100%.

Complications of Enteral Feeding

- Acid reflux
- Aspiration
- Clogged tubes, which require regular cleaning
- Constipation
- Diarrhea
- Dumping syndrome (in cases of jejunostomy) in which hypertonic liquid enters the small intestine, causing severe abdominal pain, weakness, diaphoresis, tachycardia, and electrocardiographic changes.
- Impaired speech and swallowing, in cases of nasoenteric feeding
- Nasal and esophageal irritation, in cases of nasoenteric feeding
- Nausea
- Skin irritation at the gastrostomy or jejunostomy site
- Tube dislodgement

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See Also: Parenteral nutrition.

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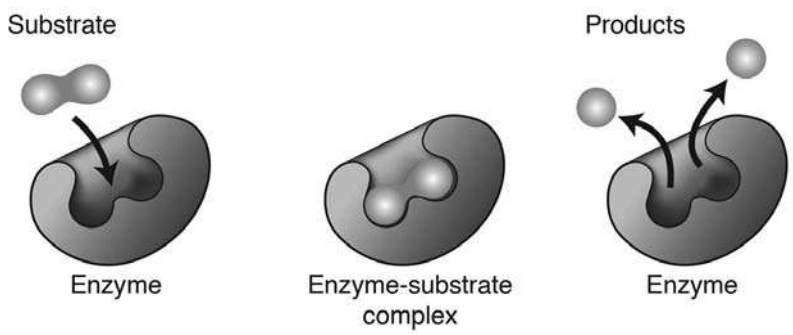
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Enzymes, Digestive

Enzymes are protein catalysts that serve to speed up biochemical reactions. Digestive enzymes are protein molecules that enable the breakdown of large food particles into fatty acids, peptides, amino acids, simple sugars, and other nutrients that can be absorbed by the body. Digestive enzymes play a major role in the chemical digestion of food. The three basic categories of digestive enzymes include (1) amylases, which assist in the break down of starches, also called "complex carbohydrates"; (2) lipases, which assist in the breakdown of fats; and



An enzyme is a biological catalyst and is almost always a protein. It speeds up the rate of a specific chemical reaction in the cell. The enzyme is not destroyed during the reaction and is used over and over. A cell contains thousands of different types of enzyme molecules, each specific to a particular chemical reaction. (Darryl Leja/National Human Genome Research Institute)

(3) proteases (also called "proteolytic enzymes"), which assist in the digestion of proteins.

Chemical digestion starts in the mouth where salivary glands secrete the enzyme amylase to break down starch into smaller carbohydrates. In addition to its role as an antibacterial aid in the mouth, lipase also is secreted to initiate the breakdown of fat molecules. Chief cells line the stomach and secrete pepsinogen, which becomes the proteolytic enzyme pepsin when activated by hydrochloric acid. Pepsin speeds the degradation of protein into smaller peptides for further digestion in the small intestine. A majority of the body's digestive enzymes are found in the small intestine, which receives secretions of pancreatic juice. Pancreatic juice contains the enzyme precursors trypsinogen and chymotripsinogen, which are converted into the active digestive enzymes trypsin and chymotrypsin in the small intestine. These proteases assist the breakdown of peptides into amino acids in the small intestine. Pancreatic juice also contains pancreatic amylase and pancreatic lipase. Additional digestive enzymes are present in the absorptive cells that line the villi of the small intestine. Here, disaccharides (small carbohydrate units) are broken down into monosaccharides by the enzymes sucrase, lactase, and maltase. These cells also contain peptidases for digesting peptides into amino acids. Cellulase is a digestive enzyme generated by bacteria in the gut to digest plant materials, such as the cell walls in cellulose.

Supplementing a diet with digestive enzymes typically is beneficial only for those with digestive deficiencies. Many supplements claiming to provide digestive enzymes simply are digested themselves once they reach the acidic environment of the stomach, because enzymes are proteins. There are a few digestive enzyme supplements, however, that have shown some therapeutic benefits. Taking the enzyme lactase enables the digestion of the milk sugar lactose, and enables people with lactose intolerance to consume some dairy products. (People with lactose intolerance do not manufacture enough lactase.) Lactase can be found in over-the-counter preparations, including tablets and drops. Lactase also is added commercially to dairy foods to produce products digestible for those with lactose intolerance.

Some common plant-derived proteolytic supplements include bromelain and papain, which contain enzymes made from pineapples and papaya plants, respectively. Bromelain is the primary ingredient in meat tenderizer, as it speeds the breakdown of the protein components in meat. Both papain and bromelain are thought to contribute to protein digestion in the human digestive tract, and could be helpful for relieving occasional indigestion. Bromelain appears to resist digestion, and can be absorbed into the bloodstream. Small studies have found some therapeutic benefit for bromelain in reducing sinus infections (EBSCO, 2012a). Although other claims have been made for the proteolytic enzyme supplements, significant evidence to support these claims generally is lacking, other than a few small studies.

Digestive enzyme supplements appear to be nontoxic and safe, although high doses might cause mild gastrointestinal discomfort and, occasionally,

allergic reactions. Because papain and especially bromelain appear to act as blood thinners, these should not be taken as supplements by people taking warfarin or other anticoagulants, without medical supervision. Bromelain also increases the blood concentration of certain antibiotics and should be avoided by people on antibiotic therapies.

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See Also: Digestion and the digestive system.

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Esophagus

The esophagus is an organ in the digestive system that creates a tube-like passage from the pharynx (area behind the mouth) to the stomach. There are two sphincters in the esophagus—one at its top and one at its bottom—that regulate the passage of food. The sphincter at the top of the esophagus is called the upper esophageal sphincter. When a person swallows, the upper esophageal sphincter opens to allow the passage of the "bolus"—a chewed ball of food—into the esophagus. Peristalsis, the contraction of muscles, moves the bolus down the esophagus toward the stomach. The lower esophageal sphincter opens to allow the food to move into the stomach. The lower esophageal sphincter prevents stomach contents from moving backward up into the esophagus.

The esophagus lies behind the trachea and the right side of the aorta. The esophagus is approximately 25 cm long and can be visualized as three parts, cervical, thoracic, and abdominal sections. The first section, the cervical esophagus, starts at the pharynx, at the C6 cervical vertebra and continues down to about the T5 thoracic vertebra. The middle section of the esophagus is known as the thoracic section, and starts at the T5 vertebra and extends to the diaphragm. The third part of the esophagus, the abdominal section, runs from the diaphragm to the stomach.

Like the other organs that comprise the gastrointestinal tract, the esophagus is composed of several tissue layers, the mucosa, submucosa, muscularis, and tunica adventitia. The innermost layer of the esophagus is the mucosa. It is named for the mucous glands that secrete mucus to the esophageal lining, helping to promote easy movement of food down the esophagus. The submucosa connects the mucosa to the muscularis. The submucosa is loose connective tissue that contains blood vessels, nerves, and esophageal glands. The muscularis layer is comprised of both circular and longitudinal muscle fibers. These muscles make up the majority of the width of the esophagus. The tunica adventitia is the outermost layer of the esophagus and is composed of dense connective tissue.

The muscles of the esophagus contract and relax in wave-like motions known as peristalsis, and push food down to the stomach. These muscular waves are so powerful that people can swallow, moving food down the esophagus, even when upside down. Other than during swallowing, the esophagus is empty.

Julia Leitermann

See Also: Digestion and the digestive system; Gastroesophageal reflux disease.

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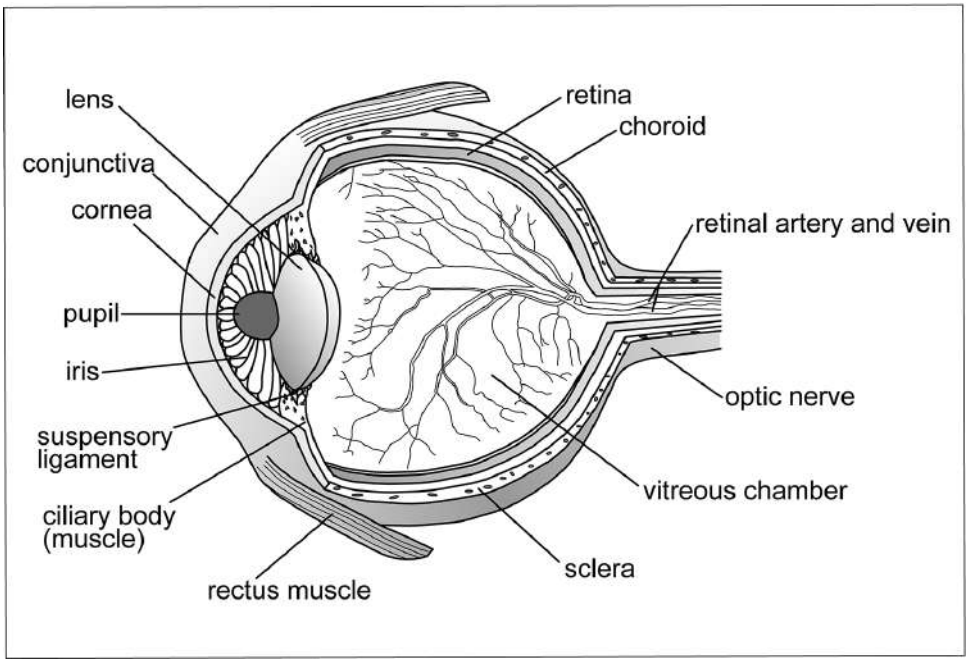
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Eye Health

Eye health appears to be strongly influenced by nutrition. Certain nutrient deficiencies can cause damage to eye structure and function, and consuming supplemental doses of other nutrients could slow the progress of two chronic eye problems associated with aging. Good nutrition also can reduce the risk of a vision problem associated with diabetes—diabetic retinopathy. Vitamin A and zinc are essential to healthy eye development and function; vitamin A deficiency is the leading cause of preventable blindness in children around the world. Vitamin A and zinc deficiencies also are associated with reduced visual acuity for both night vision and color vision. Certain antioxidants, including several vitamins, minerals, and phytochemicals, appear to prevent or at least slow the development of degenerative eye diseases, specifically macular degeneration and cataract formation. Long-chain fatty acids could help to prevent diabetic retinopathy. Research suggests that many people fail to obtain the recommended intake levels of these important nutrients (Rasmussen & Johnson, 2013).



Anatomy of the eye. The health of the eye is influenced by a person's diet. The eye functions by receiving light waves, yet it is also sensitive to damage from these light waves. (Sandy Windelspecht)

Vision and Xerophthalmia

Vitamin A is critical to eye health. It contributes to the reproduction of cells in the cornea and supports the function of the conjunctival membranes, which provide lubrication to the eye's surface. Additionally, a derivative of vitamin A—retinal—is essential for vision. It combines with the protein opsin to form rhodopsin on rod cells in the retina (Insel et al., 2014). When light enters the eye, it splits rhodopsin. This, in turn, sends electric impulses to the brain, which the brain interprets as black-and-white visual images. Rhodopsin then is regenerated, allowing for more light to be registered. If vitamin A levels are low, rhodopsin cannot be re-formed, leading to night blindness, which is the inability of the eyes to adjust to dim light or to regain vision quickly after bright light exposure. Similarly, vitamin A is found in iodopsin, a color-sensitive pigment on cone cells in the retina. Thus, low levels of vitamin A also can impair color vision. Vitamin A deficiency affects rod cells before cone cells, and therefore night blindness occurs before color vision is impaired (Insel et al., 2014).

Vitamin A is only found as retinol in foods of animal origin, with liver being the richest source. Vitamin A can be obtained indirectly from plant foods, however. The cartotenoids found in plants act as precursors to vitamin A. Of the carotenoids,

beta-carotene supplies the most vitamin A. The richest plant sources of provitamin A cartotenoids include orange and deep-yellow vegetables and dark-green leafy vegetables.

Vitamin A deficiency can lead to numerous health conditions. One of the first signs of vitamin A deficiency is night blindness. This can be corrected with early treatment, the administration of vitamin A. Failure to treat vitamin A deficiency, however, can lead to total blindness. Without an adequate supply of vitamin A, the cells in the cornea stop reproducing, as do the cells responsible for mucus production and secretion. The conjunctival membranes gradually lose the ability to lubricate the eye's surface. As the eye dries out and the cornea deteriorates, the eye becomes unable to wash away dirt and microbes, and becomes vulnerable to infection. White spots (Bitot's spots) can appear on the eye's surface, and in more severe cases the cornea can harden and scar. This condition is called "Xerophthalmia" and results in permanent blindness.

Although vitamin A deficiency is uncommon in North America and Western Europe, it is the leading cause of preventable blindness in malnourished children in more than half of all countries, especially countries in Africa and Southeast Asia (WHO, 2014). It is estimated that 250,000 to 500,000 vitamin A–deficient children become blind every year, and half of them die within 12 months of losing their sight (WHO, 2014). These statistics illustrate how vital vitamin A is to both eye health and to the human body in general.

The mineral zinc also plays an important role in eye health. Zinc is required for the optimal function of melanin-producing cells. Melanin is a pigment found in the iris and choroid of the eye that provides protection from ultraviolet and high-frequency visible light. (The choroid is the vascular layer of the eye, containing blood vessels and connective tissue.) Zinc also is a component of retinol-binding protein, a protein necessary for transporting vitamin A from the liver to the retina (Higdon et al., 2013). Additionally, it is required for the operation of the enzyme that converts retinol to retinal, the vitamin A form needed for rhodopsin. Zinc deficiency is associated with a decreased discharge of vitamin A from the liver to the eyes and therefore can lead to health issues similar to those which arise from vitamin A deficiency. Thus, people experiencing eye problems, such as night blindness, often are given zinc supplements along with vitamin A supplements. In the diet, zinc is found in shellfish, especially oysters, meats, and wheat bran.

Cataracts and Macular Degeneration

The two most common eye diseases in North America that have been linked with nutrition are cataracts and macular degeneration. Cataract formations are one of the leading causes of visual impairment around the world. Cataracts occur when proteins in the eye are damaged, often from oxidation processes (NEI, 2009). These proteins clump together, causing clouding in the lens. Most cataracts are related to aging, though other forms also can occur.

Macular degeneration, a chronic eye disease that typically occurs in older adults, causes vision loss due to the deterioration of the macula, a part of the retina

responsible for clear sharp vision (AOA, 2014b). Age-related macular degeneration (AMD) is the leading cause of blindness in people age 60 and older.

In addition to vitamin A and zinc, several other nutrients and antioxidant phytochemicals have been linked to eye health over the life span, including prevention of cataracts and macular degeneration. These include vitamin C, vitamin E, and the carotenoid antioxidants lutein and zeaxanthin. Vitamin C supports the health of the eyes' connective tissues, including the ocular blood vessels. High concentrations of vitamin C are present in the aqueous humor (the fluid found in the eye ball), the cornea, and the focusing lens of the eye. These high concentrations are believed to be an indication of the importance of vitamin C to eyesight. Vitamin C and vitamin E both exhibit antioxidant activity throughout the body, neutralizing harmful chemicals called free radicals. Free radicals can damage proteins and other cellular structures. Lutein and zeaxanthin are carotenoids found in high concentrations in the eye (AOA, 2014a). They are most concentrated in the macula, which is the central part of the retina. Lutein and zeaxanthin help to filter harmful light wavelengths to prevent eye damage. They also appear to behave as antioxidants in the eye, preventing oxidative damage. Dark leafy vegetables, such as spinach, collard greens, and kale, are good sources of lutein and zeaxanthin.

Multiple studies have shown that higher intakes of vitamin C and E are associated with a reduced risk for cataracts. The Nutrition and Vision Project, for instance, found that higher intakes of vitamin C and vitamin E lowered the risk for cortical and nuclear cataracts, and the Nurses' Health Study found that the need for cataract surgery was lower among women who used vitamin C supplements for 10 years or longer (AOA, 2014c). Similar results were found with lutein and zeaxanthin. The Health Professional's Follow-Up Study and the Nurses' Health Study both found that higher intakes of lutein and zeaxanthin were associated with a reduced need for cataract surgery (AOA, 2014c).

The Age-Related Eye Disease Study (AREDS) was one of the first studies to examine the relationship between nutrition and eye health. Beginning in 1997, the innovative longitudinal study sponsored by the National Institutes of Health lasted for approximately seven years. The focus of the clinical trial was to analyze the effects of antioxidant and zinc supplementation on the progression of macular degeneration and cataract formation in people at high risk for these diseases. The research found that the risk of progressing to advanced macular degeneration for people in earlier stages of AMD decreased by approximately 25% after taking high levels of vitamins C and E, beta-carotene, and zinc. A second trial, the Age-Related Eye Disease Study 2, replaced beta-carotene in the supplement formulation with two other carotenoids, lutein and zeaxanthin, and found this formulation to be equally effective (National Eye Institute, 2013). The replacement was recommended because beta-carotene supplementation has been associated with increased risk of lung cancer in smokers.

Treatment with the supplements used in the AREDS 2 has become the standard of care for people diagnosed with early-stage AMD or found to be at high risk for the disease. The supplements might not be helpful for others, however, and it should be noted that risks could be associated with use of dietary supplements.

Dietary supplements for eye health generally contain vitamin C, vitamin E, lutein, zeaxanthin, zinc, and copper. Copper is added because high doses of zinc prevent the absorption of copper, which can cause negative health effects.

Diabetic Retinopathy and Retinitis Pigmentosa

The most common types of diabetic retinopathy are marked by abnormal blood vessel growth in the retina. These blood vessels leak blood and can produce swelling in the retina, blurry vision, and blindness. Diabetic retinopathy is one of the negative long-term consequences of diabetes, and a leading cause of blindness. More than 4 million adults in the United States have some degree of diabetic retinopathy (Thomas & Chander, 2011). Optimal treatment for diabetes that helps maintain healthful glucose levels can help prevent or delay the development of diabetic retinopathy. Additionally, animal research suggests that the omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) might help to prevent retinopathies. This evidence underscores the importance of including food sources of these fatty acids in the diet. Good sources include cold-water fish such as salmon, sardines, and mackerel. Omega-3 fatty acids supplements also could be recommended for individuals at high risk for diabetic retinopathy.

Retinitis pigmentosa (RP) is a group of eye diseases characterized by damage to the light-sensitive cones and rods in the retina. Retinitis pigmentosa generally progresses slowly over time. Research suggests that high intakes of vitamin A, lutein, and DHA might help to slow vision loss somewhat (Berson et al., 2012).

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See Also: Antioxidants; Beta-carotene; Carotenoids; Diabetes, type 1; Diabetes, type 2; Dietary supplements; Lutein; Marine omega-3 fatty acids; Phytochemicals; Vitamin A; Vitamin C; Zeaxanthin; Zinc.

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F

Fad Diets

The term "fad diet" refers to a temporary eating plan employed to reduce body weight. The word "fad" implies something that is very popular for a short period, often without good reason for its popularity. Fad diets usually promise unrealistic weight loss results in a short time. They generally require followers to only eat certain foods or drink liquid concoctions and, in the process, severely limit calorie intake. Although people generally lose weight on fad diets, the weight usually is regained soon after the diet ends. Fad diets are thought to fail because they do not address the reasons a person is overweight; they do not teach lifelong healthful eating behaviors required to maintain a reduced body weight; and, in some cases, they even can lead to weight gain when frustrated dieters develop uncontrollable food cravings and overeat in response to food restriction. Characteristics of fad diets include the following.

Limited Food Choices

Fad diets often encourage individuals to consume a diet that might completely eliminate a major food group, such as carbohydrates. Some fad diets only permit a few specific foods to be consumed. A diet might only include eating fruit, for example, or even only a few specific fruits. The limited food choices result in a very low calorie intake, and thus, weight loss.

Incomplete or False Explanations for Weight Loss

Many fad diets offer unsupported explanations for why the diet causes weight loss. These diets often suggest that some sort of special component or ingredient in a particular food item contributes to increased weight loss. Some say that the food takes more calories to digest than are in the actual food itself. (No known food has this property.) Others claim that some combination of foods leads to extra "fat burning." Some foods are said to "rev up" the body's metabolic rate. Although some foods (such as spicy foods) can slightly elevate metabolic rate for a brief period, such elevations alone have not been shown to produce weight loss.

Proponents of detox diets have advised dieters to fast and rely on a liquid concoction to rid their body of harmful toxins. It often is promised that once the body

Very Low-Calorie Diets

The following information—taken from the Weight Control Information Network, an information service of the federal government's National Institute of Diabetes and Gastrointestinal and Kidney Diseases—defines a very low-calorie diet (VLCD) as a special type of diet that replaces all of your meals with prepared formulas, often in the form of liquid shakes. A VLCD can be used for a short time to promote quick weight loss among some people who are considered to be obese. People should not undertake a VLCD on their own. People who need to lose weight should talk to a health care provider about the approaches that might work best.

What Is a Very Low-Calorie Diet?

A VLCD is a special diet that provides up to 800 calories per day. Very low-calorie diets use commercial formulas, typically liquid shakes, soups, or bars, which replace all of the dieter's regular meals. These formulas are not the same as the meal replacements sold at grocery stores or pharmacies, which are meant to replace one or two meals a day.

- Depending on a number of factors, healthy adults require different amounts of calories to meet daily energy needs. A standard amount is about 2,000 calories.
- A VLCD only should be used for a short time—usually about 12 weeks.
- In general, VLCDs are not appropriate for children. In a few cases, they could be used with some adolescents who are being treated for obesity.
- Some people 50 years of age and older could have medical issues that might not make them good candidates for this type of diet.

What Are the Health Risks of a Very Low-Calorie Diet?

Doctors must monitor all VLCD patients regularly—ideally every 2 weeks in the initial period of rapid weight loss—to be sure patients are not experiencing serious side effects. Many patients on a VLCD for 4 to 16 weeks report minor side effects, such as fatigue, constipation, nausea, and diarrhea. These conditions usually improve within a few weeks and rarely prevent patients from completing the program.

National Institutes of Health. National Institute of Diabetes and Digestive and Kidney Diseases. *Very low-calorie diets*. (2012). Weight-Control Information Network. Retrieved from http://win.niddk.nih.gov/publications/low_calorie.htm

has cleansed itself of toxins, metabolic processes will be more efficient and result in weight loss. This statement has no scientific foundation. Weight lost on detox programs is likely attributable to the fact that few calories are consumed over the course of the program.

Celebrity and Success Story Advertisements

Advertisements for fad diets often feature a (paid) celebrity who has lost weight on the diet, or stories of individuals who have achieved success with the diet. As stated

above, it is not uncommon for weight loss to occur when people consume very few calories, so most fad diets can achieve results for a limited period.

Exaggerated Claims

Fad diets often promise unrealistic weight-loss results. Although initial weight loss on very restrictive diets can be quite significant (several pounds in the first week or two), most of this weight loss is water loss. Water loss occurs as the body uses stored glycogen. Glycogen is a starch that the body uses for energy and stores in the liver and muscles. Water is stored with glycogen therefore, as glycogen is used, water is lost. Fad diets also might promise other results, such as improved sexual function, athletic performance, and mood.

Special Products Could Be Required

Fad diets sometimes require individuals to purchase specific products to reach their weight-loss goals. Many detox diets, for example, rely on a certain drink regimen that is sold to consumers. Most fad diets that feature meal-replacement plans include specific liquid or powdered products that must be consumed daily.

Health Risks Associated with Fad Diets and Rapid Weight-Loss Plans

Fad diets occasionally do jump-start successful weight loss. Sometimes eating programs that initially might have been considered to be fad diets—such as the Pritikin Program—develop into successful behavior change programs with scientific support. The majority of people, however, regain any weight they lost.

Fad diets, and rapid weight loss in general, should occur with medical monitoring if diets are followed for more than a few days. Such diets can result in electrolyte imbalances and dehydration. Side effects also can include fatigue, dizziness, nausea, lightheadedness, and muscle aches.

Many overweight clients have a long history of dieting. In fact, many blame their dieting history for their problems with weight and food. Very restrictive eating can interfere with metabolism, hunger, appetite, and psychological relationships with food. Unsuccessful weight-loss attempts can lead to feelings of guilt and failure, food cravings, and—ironically—obesity, as food becomes too much of a focus in a person's life. Instead of following short-term, restrictive diets, it is more effective to develop healthful eating behaviors that an individual can follow for a lifetime.

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See Also: The Atkins Diet; Body composition; National Weight Control Registry; Obesity, treatment.

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Fast Food

"Fast food" refers to inexpensive food that is prepared and served quickly and easily and is sold in restaurants and at snack bars. The food often contains precooked or preheated ingredients that then are assembled into a meal by employees. There currently are 160,000 fast-food restaurants in the United States, and—according to a July 2013 Gallup poll—47% of people in the United States consume fast food at least once a week (Dugan, 2013). Fast food consumption is associated with higher energy, fat, and sodium intake, and lower intake of dietary fiber and some vitamins. Health problems associated with frequently eating fast food include obesity, type 2 diabetes, cardiovascular disease, asthma, rhinoconjunctivitis, eczema, and metabolic syndrome. In response to criticism, some fast-food companies have worked to create healthier meal options, but progress has been slow. Another controversial aspect of the fast-food industry is the aggressive marketing of its products to children.

A Brief History of Fast Food

White Castle, founded in 1921, generally is recognized as the first fast-food establishment. It initially sold mainly hamburgers, which many people in the United States were suspicious of due to concerns about sanitation and contamination of the meat (Smith, 2006). White Castle convinced its customers of the purity of its products and enjoyed great success, however, encouraging the creation of many other hamburger chains.

During the Great Depression, fast-food outlets flourished, providing motorists with cheap meals that were conveniently located in proximity to major highways. Most of the fast-food outlets were franchises, for which a businessperson looking to establish a new restaurant would pay a fee and purchase goods from the franchisor and then benefit from the recognizable name and marketing power of franchises.

In the 1940s and 1950s, fast-food restaurants that sold food other than the standard hamburgers, hot dogs, and french fries were created. Dunkin Donuts (1948), Dairy Queen ice cream (1940), and Baskin Robbins ice cream (1948)



McDonald's Happy Meal. Fast-food meals for children often feature collectable toys, as well as foods that appeal to children, such as french fries, fried chicken, and soft drinks. However, many fast food chains, including McDonalds, also serve salads, fruit snacks, yogurt, and other healthful options. (AP/Wide World Photos)

became popular and rapidly expanded, and restaurants that served chicken—such as Kentucky Fried Chicken (now KFC) and Church's Chicken—became popular in the early 1950s. Hamburger chains, however, still were the most popular franchises, and McDonald's, originally established in 1940 as a barbeque restaurant,

would go on the become the most popular fast-food restaurant of all, eventually opening more than 34,000 locations worldwide by 2013 (McDonald's, 2013; Smith, 2006). "Ethnic" fast food such as pizza and Mexican-style food started being served by restaurants like Pizza Hut (1958) and Taco Bell (1962).

Over time, fast-food outlets added more space for seating inside restaurants, as the number of families who preferred to eat in their cars decreased, and added a wider variety of menu options. McDonald's, for example, started serving chicken sandwiches as well as hamburgers, and pizza places started selling pasta dishes and sandwiches. Today, many fast-food chains have locations all over the globe, and their menus vary based on local tastes.

Nutrition and Health Effects

In general, most fast food is high in calories, fat, saturated fat, and sodium, and low in fiber, beta-carotene, and vitamins A and C (Paeratakul et al., 2003). The best-selling fast-food meals are high in red meat, fried potatoes, and refined grains, and low in milk, nuts, seeds, fruits, and vegetables (Paeratakul et al., 2003). For example, there are almost 600 calories and 35 grams of fat in a large hamburger, and there are 650 calories, 96 grams of sugar, and 14 grams of fat in a small Wendy's Caramel Frosty shake (Wendy's International, Inc., 2013).

One cause of the high caloric content of fast food meals is their increasingly larger portion sizes. In 1955, the largest amount of hamburger meat that McDonald's served weighed 1.6 ounces, and now the largest option contains 8 ounces of hamburger meat (Young & Nestle, 2007). By comparison, the 2010 *Dietary Guidelines for Americans* recommends that 5.5 ounces of protein foods be consumed per day by those on a 2,000 calorie food pattern (U.S. Department of Agriculture & U.S. Department of Health and Human Services, 2011). Soda (pop) serving sizes have dramatically increased as well. McDonald's originally served 7-ounce portions of soda, but now the largest serving size offered is 30 ounces (Young & Nestle, 2007).

Some common negative health effects associated with the consumption of fast food are listed below.

Weight Gain and Obesity

Weight gain is caused by consuming more calories than a body uses, and fast food promotes this positive energy balance for several reasons. Fast food often is served in extremely large portions, encouraging consumers to overeat. One meal can contain as many calories and grams of fat as an average person should consume in an entire day (U.S. Department of Agriculture & U.S. Department of Health and Human Services, 2011). The most popular fast-food options also contain large amounts of sugar, salt, and fat, which are the taste preferences that humans evolved thousands of years ago when nourishment was difficult to find; this can cause people to desire to consume large quantities of fast food. When

someone has a positive energy balance, extra calories are converted to triglycerides that are stored in fat cells called adipocytes. Excessive weight gain and fat storage can lead to obesity. The Coronary Artery Risk Development in Young Adults (CARDIA) study found that, over 15 years, frequent (greater than twice per week) fast-food consumption was associated with weight gain of 4.5 kg (9.9 lbs) more than infrequent (less than once per week) fast-food consumption (Pereira et al., 2005).

Insulin Resistance and Type 2 Diabetes

Type 2 diabetes occurs when the body becomes resistant to insulin. Insulin is a hormone that is released when blood glucose levels become too high (hyperglycemia). Risk of developing insulin resistance and type 2 diabetes increases with obesity, low levels of physical activity, and poor diet quality. The CARDIA study found that the frequency of fast-food consumption was directly correlated with insulin resistance, and that participants who consumed fast food more than twice a week had an increase in insulin resistance twice the rate of those who consumed fast food less than once a week (Pereira et al., 2005).

Metabolic Syndrome

Metabolic syndrome is defined as having three or more of the following conditions: excess abdominal fat, high blood glucose, high serum triglycerides, low HDL cholesterol, and high blood pressure. Many fast foods have a high glycemic load, which means that they cause blood glucose to quickly rise to very high levels. High triglycerides in the blood also are associated with frequent fast-food consumption because of the tendency for those who frequently consume fast food to eat more calories than they use, which results in higher levels of triglyceride production. Low HDL cholesterol is also connected to increased fast-food consumption, because elevated blood triglyceride levels are associated with low HDL cholesterol. High blood pressure can be caused by high blood glucose levels, which stimulate the release of the neurotransmitter epinephrine and hormone insulin into the bloodstream and an increase in blood pressure as part of the fight-or-flight response. The high sodium levels in the most popular fast-food meals also could contribute to high blood pressure.

Cardiovascular Disease

High LDL cholesterol levels, especially high levels of lipoprotein a—a substance containing LDL and the protein apoprotein a—can contribute to atherosclerosis. High levels of triglycerides also appear to contribute to greater amounts of plaque buildup. Atherosclerosis occurs when arteries progressively become hardened and narrowed due to a buildup of plaque formed from fatty material. It can cause heart attacks and strokes.

Asthma, Rhinoconjunctivitis, and Eczema

The International Study of Asthma and Allergies in Childhood (ISAAC) found that eating fast food more than three times per week was associated with an increased risk of severe asthma, severe rhinoconjunctivitis, and severe eczema (Ellwood et al., 2013). These disorders are associated with inflammation.

Fast-Food Restaurants' Healthier Options

In response to widespread criticism of their products' nutritional values, some fast-food chains have introduced new, healthier menu options and attempted to improve upon old products. McDonald's, Wendy's, and Burger King now offer apple slices and side salads as a substitute for french fries and fruit juices, and these chains offer low-fat and fat-free milk as substitutes for soft drinks. Subway offers 17 different sandwiches and 7 different salads containing less than six grams of fat (Subway, 2013). According to a study analyzing trends in nutritional quality of fast-food meals over a period of 14 years, meals at eight of the most popular fast-food chains have experienced a slight increase in nutrition quality. The chains were rated on a scale of 1 to 100 according to the amount of fruits, vegetables, grains, milk, meat and beans, oils, saturated fat, sodium, and calories from solid fat and added sugars their meals contained, with a score of 100 being the healthiest. The average score increased by three points (45 to 48 points) between 1997/1998 and 2009/2010, and the scores for meat, saturated fat, and calories from solid fats and added sugars improved over this period. In contrast, the scores for sodium levels and milk/dairy decreased, and none of the restaurants had scores near 100 (Hearst et al., 2013).

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See Also: Adolescence and nutrition; Childhood nutrition; Obesity, causes; Portion size.

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Fasting

Fasting is a broad term that can refer to complete abstinence from all foods and beverages, drinking only water, drinking only fresh fruit and vegetable juices, or severely limiting the foods one consumes. The purpose of fasting varies as widely as the definition. Common goals are losing weight, increasing lifespan, enhancing general health, and complying with religious traditions. Safety and recommended duration depend on the form of fasting performed and the condition of the person undertaking the fast.

Total Fasting

Dry fasting, or abstaining from all foods and beverages, and water fasting, or consuming only noncaloric drinks, both represent forms of total fasting. Dry fasting rarely appears outside of religious contexts. Conversely, inpatient water fasting—termed "therapeutic starvation"—was a prevalent treatment for morbid obesity throughout the 1950s and 1960s. Significant weight loss occurred under medical supervision, but follow-up studies showed that the majority of patients regained weight. The risk of micronutrient deficiencies and refeeding syndrome—potentially lethal abnormalities in electrolyte and fluid balance—can be reduced by the intravenous or oral administration of electrolytes, vitamins, and minerals during a fast and the gradual reintroduction to an unrestricted diet following the termination of a prolonged fast.

Nonetheless, numerous other health concerns exist. Weight loss resulting from prolonged fasting tends to lead to a greater loss of lean body mass as compared to more moderate diets. The physiology of fasting accounts for this phenomenon. After 12 to 24 hours of water fasting, circulating amino acids and the liver's glycogen stores become depleted, forcing the body to switch to breaking down fat and using ketone bodies, rather than glucose, as the primary energy source. Red blood cells lack mitochondria, however, which contain enzymes necessary for ketone utilization. Furthermore, ketones can provide up to 70% of the brain's energy requirements, but some level of glucose utilization is obligatory, triggering protein catabolism for glucose production. In the absence of dietary protein intake, the body resorts to breaking down muscle tissue to obtain amino acids for gluconeogenesis. Studies on calorie restriction as well as fasting have identified additional complications that can arise due to prolonged water fasting, including fatigue, irritability, apathy, depression, obsessive thoughts about food, and decreased physical activity and sex drive. Individuals on a long-term fast also can experience headaches, dizziness, low blood pressure, and cardiac arrhythmias. These adverse side effects suggest that total fasting could be difficult to maintain when unsupervised and can reduce overall quality of life.

Intermittent Fasting

Much of the current research on fasting focuses on intermittent fasting (IF): cycling between periods of unrestricted feeding and periods of fasting. Alternate-day fasting (ADF)—fasting every other day—is a popular iteration of IF. It garnered interest as another possible way to achieve the health benefits of daily calorie restriction (CR) in rodent models, which include increased longevity, reduced inflammation, increased insulin sensitivity, improved cognitive function, and decreased risk of cardiovascular disease, neurodegenerative disease, and cancer (Young, 2012). Whether these findings can be applied to humans is a topic of controversy.

Studies of IF of humans are far less numerous than those of mice and rats, but several show a significant effect on biomarkers of cardiovascular disease and diabetes, lowering LDL cholesterol, triglycerides, and levels of insulin and glucose in the blood (Collier, 2013). In contrast, evidence of increased longevity or reduced inflammation has not been established. Even in rodents, it is unclear whether decreased levels of circulating tumor necrosis factor-alpha (TNF-α) and C-reactive protein (CRP)—markers of inflammation—result from IF itself or merely the reduced body weight it causes (Rothschild, Hoddy, Jambazian, & Varady, 2014).

Intermittent fasting is thought to exert its anticancer effects by decreasing levels of insulin-like growth factor 1 (IGF-1) and to defend against Alzheimer's disease and Parkinson's disease by increasing the release of brain-derived neurotrophic factor (BDNF), a protein that heightens neurons' resistance to excitotoxic stress, thereby reducing neuronal cell death (Stipp, 2012). Intermittent fasting–induced increases in neurogenesis and autophagy, a process that involves the breakdown of damaged organelles and other intracellular waste products, might play a role as well. These mechanisms have not been verified in humans, however.

Similarly, a review of the existing literature exploring the impact of IF on cognitive function found that results were mixed, but impairment was more common than improvement (Benau, Orloff, Janke, Serpell, & Timko, 2014).

Intermittent fasting also has been investigated as a potential weight-loss strategy for humans. A 22-day trial of ADF in non-obese subjects recorded weight loss, but reports of irritability and persistently elevated hunger led the researchers to doubt that long-term compliance was likely (Heilbronn, Smith, Martin, Anton, & Ravussin, 2005). Growing attention has been directed at a variant of ADF—sometimes referred to as alternate-day modified fasting (ADMF)—that allows dieters to consume about 25% of their baseline energy needs, usually 500 calories for women and 600 calories for men, rather than eating nothing on fast days. In one study, obese subjects maintained their normal eating habits for two weeks to establish a baseline, and then practiced ADMF for four weeks with fast-day meals provided to them, and finally followed the diet for four weeks and made their own food choices on fast days. Weight loss and adherence to the diet remained consistent throughout the second and third phases, and cardioprotective effects—decreased total cholesterol, LDL cholesterol, and triglycerides—were found (Varady, Bhutani, Church, & Klempel, 2009).

A subsequent study showed habituation to ADMF by the second week of the diet, with obese subjects reporting reduced feelings of hunger and increased satisfaction with the diet. The lack of a hyperphagic response (abnormally increased appetite) on feed days appeared to contradict predictions that ADMF would trigger binge eating (Klempel, Bhutani, Fitzgibbon, Freels, & Varady, 2010). Each of these studies, however, was small and provided no long-term follow-up, indicating the need for large clinical trials to better establish the safety and effectiveness of ADMF.

Juice Fasting

Abstaining from solid food and consuming only fresh fruit and vegetable juices for anywhere from one day to one month, a practice known as "juice fasting," has grown in popularity as a "detox diet." Notwithstanding, the claim that it enhances the body's ability to remove toxins remains scientifically unsupported. Anecdotal reports of an improved sense of well-being could be attributable to the "starvation high"—caloric restriction increases the release of endorphins—and to the psychological appeal of purification. Although juices can serve as a helpful way to incorporate more servings of fruits and vegetables into one's diet, the juicing process removes the fiber and increases the glycemic index. Short-term juice fasts might not be harmful for healthy adults, but the high sugar and mineral content make them inadvisable for diabetics and people with hyperkalemia caused by kidney disease.

Religious Fasting

Most major religions share periods of fasting as a common feature, although the rules differ. Rather than losing weight or achieving other physical effects, religious

fasting often is intended to cultivate self-discipline, direct focus toward the spiritual, demonstrate devotion to a deity, purify the soul, or recognize sacred events. Fasting in Hinduism frequently coincides with religious festivals, and fasting in Buddhism is more prevalent among ascetics than laypeople. Prominent religious occasions accompanied by fasting include Ramadan in Islam, Yom Kippur in Judaism, and Lent in both Catholicism and Eastern Orthodox Christianity.

Ramadan fasting—which takes place from sunrise to sunset for one month—could be classified as intermittent fasting. Ramadan fasting also excludes beverages of any kind, however, whereas most IF protocols allow water and sometimes tea. Observing Yom Kippur, or The Day of Atonement, also involves forgoing eating and drinking of any kind, but lasts 25 hours (BBC, 2011). In the Catholic tradition, Lenten fasting means restricting oneself to a single meal per day on Ash Wednesday and Good Friday, as well as avoiding meat on all Fridays during the 40 days preceding Easter Sunday (United States Conference of Catholic Bishops, 2014). Eastern Orthodox guidelines are more stringent, requiring water fasting for short periods and excluding meat, eggs, and dairy products for the full duration. Consumption of oil and wine also might be limited (Public Broadcasting Service, 2010).

Ramadan and Eastern Orthodox Lenten fasting have been studied empirically in terms of their effects on nutrient intake, body mass index, and blood lipid profile. Results largely have been conflicting for Ramadan fasting. Lenten fasting and other Eastern Orthodox fasts were associated with increased fiber and carbohydrate intake, decreased fat, riboflavin, and calcium intake, reduced BMI, and lower levels of total and LDL cholesterol (Trepanowski & Bloomer, 2010). Excessive weight loss and vitamin and mineral deficiencies were not observed, indicating that these fasts are relatively safe for most people.

Notably, potentially at-risk groups such as children, pregnant or nursing women, and the ill are exempt from both Ramadan and Lenten fasting. Most Ramadan observers also can tolerate the negative water balance that results from daytime dry fasting without adverse health effects, but those who are especially vulnerable to extreme dehydration and heat stroke—such as industrial laborers—would need to take special precautions, request a reduced workload, or seek exemption from the fast.

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See Also: Inflammation; Ketosis and ketogenic diets; Obesity, treatment.

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Fatty Acids

Fatty acids are organic compounds composed of hydrocarbon chains with an organic acid (carboxyl) group at one end and a methyl (CH_3) group at the other end. In the context of human nutrition, fatty acids are found in foods and in the body. Fatty acids often are found as components of triglycerides and other larger structures, but they also can occur unbound, in which case they are often referred to as "free fatty acids." There are many types of fatty acids, and their function in the body varies with their structure. Many fatty acids, such as the long-chain polyunsaturated fatty acids (PUFAs) are beneficial to health. Ingestion of large amounts of saturated fatty acids from animal products is thought to increase risk of artery

disease. Some types of fatty acids must come from the diet. These are called essential fatty acids, and they include alpha-linolenic acid (ALA) and linoleic acid.

Fatty acids vary in the length of their hydrocarbon chains and in the types of bonds between the carbon atoms in these chains. Fatty acids found in foods usually have an even number of carbons, with a chain length of 4 to 24 carbons. Fatty acids with a chain length of fewer than 6 carbons are called "short-chain fatty acids"; medium-chain and long-chain fatty acids have 6 to 10, and 12 or more carbons, respectively. Some nutritionists use the term "very long-chain fatty acids" to refer to fatty acids with 20 or more carbons.

The carbon atoms in the fatty acid hydrocarbon chain can form single or double bonds with each other. Saturated fatty acids refer to fatty acids in which the bonds between carbon atoms all are single. Single carbon-carbon bonds are more stable than double bonds and affect the behavior of these fatty acids. Saturated fats tend to be more stable at higher temperatures, for example. This explains why butter (higher in saturated fatty acids) is a solid at room temperature, and plant oils (lower in saturated fatty acids) are not.

Unsaturated fatty acids have at least one carbon-carbon double bond. Monounsaturated fatty acids have one carbon-carbon double bond, and polyunsaturated fatty acids have more than one. The location of this carbon-carbon double bond helps to name the fatty acid, and affects the fatty acid's structure and behavior in the body. Omega-3 fatty acids have the carbon-carbon double bond at the third carbon from the methyl end of the fatty acid. Dietary sources of omega-3s include fish oils and some plant and nut oils. Fish oils contain special long-chain omega-3 fatty acids, including docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), which have been associated with beneficial health effects, including reduced levels of inflammation and slower rates of blood clotting. This is why many public-health recommendations suggest that people increase their consumption of fish. Oily fish such as salmon, tuna, sardines, mackerel, and herring have the highest concentrations of these fatty acids. Alpha-linolenic acid is another type of omega-3, although its effects on the health variables mentioned above do not appear to be as strong as those of DHA and EPA. Conversely, omega-6 fatty acids—found primarily in plant oils—have been associated with higher levels of inflammation and increased rates of blood clotting.

Trans fatty acids, (trans fats, or TFAs) usually are created by hydrogenation, a process used by food-product manufacturers to make fatty acids in foods more saturated, thus more stable and with a longer shelf life. Although TFAs technically have a carbon-carbon double bond, the arrangement of other atoms around the bond lead to a shape of the fatty acid that is more similar to saturated fatty acids. Greater intake of trans fats in the diet has been linked to higher rates of artery disease. Trans fats could increase this risk through effects on blood lipid levels (raising LDL cholesterol levels and lowering HDL cholesterol levels), effects on the function of the artery lining, and by making the blood more likely to form blood clots.

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See Also: Alpha-linolenic acid, Cardiovascular disease and nutrition; Cholesterol; Hydrogenation; Linoleic acid; Lipids; Marine omega-3 fatty acids; The Paleolithic diet; Trans fatty acids; Triglycerides.

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Feeding Disorders

Feeding disorders are characterized by patterns of severe disturbances in eating behavior. Individuals with feeding disorders have a high risk for poor social or physical development, as well as for learning disabilities. Some people experience social withdrawal and avoid eating in public. The *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) is the handbook used to classify or diagnose mental disorders. It lists feeding and eating disorders in the same chapter due to their shared disturbances in eating behavior. Unlike eating disorders, individuals with feeding disorders do not experience severe distress concerning body weight or shape. The DSM-5 lists three categories of feeding disorders.

Pica

The diagnostic criteria for pica include recurrent eating of nonfood items for at least one month; the eating behavior is abnormal for the individual's stage of development; the eating behavior is not accepted as a component of the individual's cultural practices; and the eating behavior is not a direct result of a mental disorder or medical condition. There are three main categories of substances: earth (geophagy), starch (amylophagy), and ice (pagophagy). Other common items include chalk, plaster, paper, charcoal, and baby powder.

Prevalence

- Between 1999 and 2009, the number of inpatient hospital stays for reasons related to pica nearly doubled (Zhao & Encinosa, 2011).
- Pregnant women have the highest rate of pica worldwide.
- Those who develop pica in childhood are more likely to outgrow their behaviors than those who develop it as adults.
- In 2009, 31% of children with pica who underwent inpatient treatment had autism spectrum disorders (Zhao & Encinosa, 2011).

History

Hippocrates documented the first case of pica-related behaviors in 400 BCE (Young, Wilson, Miller, & Hillier, 2008). It was not termed "pica," however, until 1542. As cases continued to surface in the 17th century, it became apparent that the disorder was most prevalent in pregnant women and children. In the 19th century, slaves in the United States were brutally punished if they engaged in pica-related behaviors. In contrast, other cultures condoned and even fostered these habits, making it difficult to identify pica as a true medical condition. Clay eating in particular currently is practiced in more than 200 cultures, and often is used to treat maladies such as diarrhea or morning sickness in pregnant women. Today, the condition is not classified as pica in the DSM-5 if the associated behaviors are a part of one's cultural habits or traditions.

Causes

There are several hypotheses about the etiology of pica and cravings associated with pica.

- Hunger—Food shortages and famine can trigger cravings of nonfood substances.
- Micronutrient deficiencies—Micronutrient deficiencies can disrupt enzymes in the brain associated with taste and appetite and result in pica-related behaviors, especially during pregnancy. Furthermore, pica substances inhibit absorption or bind micronutrients, leading to other health conditions (i.e., anemia).
- Protection against toxins and pathogens—Typical pica substances might absorb harmful chemicals in the gut, which protects the body from toxins and pathogens.
- Psychological stress—Eating behavior might serve as a self-soothing response to external stressors.
- Dyspepsia—Some individuals report a reduction in the discomfort associated with dyspepsia. This might be attributed to the alkalinity in typical pica substances, which can help with gastric acidity.

Comorbidity

- Mental retardation
- Developmental disabilities
- Autism spectrum disorders
- Schizophrenia
- Obsessive-compulsive disorder
- Medical complications
- Intestinal blockage
- Airway obstruction

- Anemia
- Lead or mercury poisoning, which can lead to kidney failure, cognitive deficits, seizures, coma, and death
- Absorption impairment, which can lead to nutritional deficiencies
- Acute weight loss
- Parasites due to the consumption of dirt or feces
- Birth complications in pregnant women
- High blood pressure
- Obesity, due to the consumption of highly caloric substances (e.g., laundry starch)

Treatment

Behavior modification has been shown to be effective in treating individuals with pica—especially children on the autism spectrum (Ferreri, Tamm, & Wier, 2006). This is especially relevant in food-aversion therapy, in which clinicians pair patients' aversive foods with an undesirable behavior or punishment for them to associate less pleasure upon consuming pica substances. The individual then is given positive reinforcement when choosing normative behaviors instead of pica-related behaviors.

Rumination Disorder

Rumination disorder is marked by the following symptoms: for at least one month, regurgitating food and then re-chewing, re-swallowing, or spitting out the food; the behavior is not a direct result of a gastrointestinal condition; the behavior is not a direct result of anorexia nervosa, bulimia nervosa, binge-eating disorder, or avoidant/restrictive food-intake disorder, or another mental disorder. It can develop during infancy, childhood, adolescence, or adulthood. Regurgitation behaviors can be especially self-soothing and self-stimulating for infants and those with neurodevelopmental disorders.

Prevalence

Little is known about the prevalence of rumination disorder. It is seen, however, in up to 10% of institutionalized patients with severe mental retardation (Fredricks, Carr & Williams, 1998).

History

The first case was documented in 1618 (Fredericks, Carr, & Williams, 1998). During the 18th century and 19th century, rumination disorder gained popularity in the entertainment and circus industry. People flocked to freak shows to watch individuals "perform" acts of rumination. Possible treatments did not surface

until the 1950s, in which clinicians took a psychodynamic approach. They thought ruminating behaviors to be a result of insufficient progress during the oral and ego phases of development. Behavioral treatments emerged 10 years later, and have been the source of extensive research ever since.

Causes

- Lack of stimulation
- Neglect
- History of abuse
- Stressful life events

Comorbidity

- Mental retardation
- Intellectual disability
- Generalized anxiety disorder

Medical Complications

- Malnutrition
- Weight loss (or failure to gain weight, as seen in infants, children, and adolescents)
- Gastrointestinal issues
- Upper-respiratory distress
- Dental problems
- Aspiration
- Pneumonia
- Primary cause of death in 5% to 10% of individuals who ruminate

Treatment

Both aversive and nonaversive behavioral treatments have been used to target rumination disorder.

- Aversive—Electric shock, withdrawal of positive reinforcement, and noxious tastes. For example, a clinician might decide to spray a patient's mouth with a bitter formula when she gags. These treatments were common until the late 1980s, when they became criticized for their poor ethical standards.
- Nonaversive—Satiation, in which large amounts of food are given to the individual in hopes of increasing oral stimulation and decreasing the desire to consume regurgitated materials; and differential reinforcement, in which positive reinforcement is given for desired behaviors and interfering behaviors are ignored.

Avoidant/Restrictive Food Intake Disorder

Avoidant/Restrictive Food Intake Disorder (ARFID) is characterized by severe disturbances in eating or feeding resulting in at least one of the following: weight loss (or failure to gain weight, as seen in infants, children, and adolescents), nutritional deficiency, poor psychosocial functioning, and relying on tube feeding or oral supplements in an attempt to meet nutritional needs. Examples of eating disturbances might be the avoidance of or disinterest in food, or distress about the consequences of eating. Some individuals might avoid a specific food because of its smell, color, or texture. Infants can exhibit irritability or apathy, especially during feeding. Diagnostic criteria for ARFID also include that the eating behavior is not accepted as a component of the individual's cultural practices; and it is not a direct result of anorexia nervosa, bulimia nervosa, binge-eating disorder, other mental disorder or medical condition.

Prevalence

Avoidant/Restrictive Food Intake Disorder most commonly is seen in infants and children. Those who develop food avoidance or restriction in infancy or childhood could present similar or identical eating disturbances in adulthood.

History

Before the DSM-5, ARFID was previously referred to Feeding Disorder of Infancy and Early Childhood. This new category was devised in part to reduce the number of diagnoses of Eating Disorder Not Otherwise Specified (EDNOS), ultimately improving the prognosis of affected individuals.

Causes

- Developmental impairments
- History of abuse or neglect
- Family history of eating disorders
- History of gastrointestinal issues

Comorbidity

- Anxiety disorders
- Obsessive-compulsive disorders
- Attention deficit hyperactivity disorder
- Autism spectrum disorders

Medical Complications

- Malnutrition

- Growth problems
- Weight loss (or failure to gain weight, as seen in infants, children, and adolescents)

Treatment

Possible treatment for ARFID remains inconclusive, but exposure therapy and cognitive-behavioral therapy have been suggested as a means of targeting avoidance behaviors.

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Research Issues

The Avoidant/Restrictive Food Intake Disorder (ARFID) classification grew out of a diagnosis known as "Feeding Disorder of Infancy and Early Childhood." Many infants, children, and adolescents have odd eating behaviors, and parents often have difficulty distinguishing between normal picky-eating and ARFID. To help understand how ARFID develops, reading case histories of people with this disorder can be helpful. An example is cited below, but you also might be able to find other descriptions by entering the term "Avoidant/Restrictive Food Intake Disorder" into a search engine.

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See Also: Eating disorders.

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Female Athlete Triad

The female athlete triad (the triad) refers to a syndrome composed of three components: low energy availability (not consuming enough calories), disruption of the menstrual cycle, and low bone density. The triad typically begins when an athlete embarks on a weight-loss program to improve her sport performance, limiting calorie intake and increasing exercise volume. For athletes who develop the triad, these measures lead to disruption of the menstrual cycle, and in some cases to amenorrhea, or absence of the menstrual cycle. This disruption in turn causes very low levels of estrogen, the primary female sex hormone. Over time, low estrogen levels accompanied by an inadequate diet result in negative effects on bone growth and maintenance, and bone disorders such as stress fractures, low bone density, and osteoporosis. Girls and women who develop osteoporosis as part of the triad rarely achieve normal bone density, even with a good diet and medical treatment.

The term "female athlete triad" was first coined in 1992 by sports medicine researcher Barbara Drinkwater. She and her colleagues had observed symptoms of osteoporosis in several young female runners. Especially alarming were the presence of vertebral compression fractures, fractures of the spinal vertebral bones, which result in spinal curvature and pain and are difficult to treat. Upon examining these young runners, the researchers found an association between menstrual irregularity and bone density: fewer menstrual cycles per year was associated with reduced bone density. It should be noted, however, that the triad can develop in girls and women who do not consider themselves athletes, but instead exercise recreationally. The triad also can develop in females with eating disorders who might or might not exercise excessively.

Statistics on the prevalence of the triad do not exist, although a number of studies have estimated how frequently the individual components of the triad occur (Gottschlich, 2012). Testing of various groups of female athletes have found rates of osteoporosis to be anywhere from 0% to 13%, compared to about 2% for the general population of young women. Somewhere between 22% and 50% of athletes show lower bone-density scores, versus about 12% of nonathletes. Menstrual dysfunction shows up in anywhere from 6% to 79% of female athletes, depending upon the group studied. Disordered eating patterns have been demonstrated in large numbers of women, including athletes, with rates of up to 62%.

Insufficient calorie intake or calorie restriction, sometimes accompanied by extreme dieting behaviors, appear to be the precipitating factors for the triad. A mismatch between calorie intake and energy expenditure creates an energy deficit: athletes are burning more calories than they are eating. This mismatch is not always intentional. In some cases, athletes might simply fail to ingest a sufficient

number of calories to meet the needs of their energy expenditure, even if their caloric intake is normal for a nonathlete of the same age. For example, a distance runner training at a high weekly mileage can burn hundreds of extra calories a day, and can fail to increase her intake to keep up with this level of energy expenditure. Other athletes practice some form of food restriction, intentionally eating less than they need to burn extra body fat. Some athletes might begin trying to burn extra fat with high levels of exercise training and food restriction, and go on to develop disordered eating and excessive exercise behaviors. Athletes participating in sports that emphasize or require a thin physique are most likely to develop the triad.

The body responds to energy deficits by suppressing the bodily functions necessary for growth and development, such as the menstrual cycle. Loss of the menstrual cycle and the resulting low estrogen levels lead to the skeletal problems observed with the female athlete triad. The most common problem observed in these athletes is a stress fracture—a small fracture that is caused by repetitive use. Low bone density, as measured by tests of bone mineral content, is seen in girls and women who have developed the triad. Maximum growth of bone mass occurs during puberty, especially between the ages of 11 and 14 in girls (Nazem, 2012). If an adolescent athlete develops the triad, she might never reach her potential optimal level of bone mass formation, and will begin adulthood with low bone density. (Although exercise is known to improve bone density in general, this is not the case for girls with amenorrhea, and the lack of estrogen interferes with the otherwise positive effects of exercise on bone development.)

Early identification of triad symptoms in young athletes is important so that long-term damage can be prevented. Education programs for coaches, parents, and athletes have been developed by sports medicine organizations to encourage awareness and early intervention when the triad symptoms of inadequate energy intake and menstrual disruption are suspected. Athletes experiencing repeated stress fractures should be assessed for osteoporosis and other triad symptoms. Treatment for athletes who have developed the triad consists of increasing calorie intake, decreasing exercise volume, and, in some cases, hormone therapy to treat low bone density. Many athletes, however, have difficulty reducing training schedules or altering their diets. In these cases, the triad is best managed with a team of experts that includes a mental health practitioner along with a physician and a dietician.

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Research Issues

Is sport participation generally helpful or harmful to health? What factors influence the answer to this question? Low calorie intakes and energy deficits are more common in some sports than others. Research indicates that sports favoring low body weight (distance running, cheerleading, some forms of dance) or a thin appearance for aesthetic reasons (ballet, figure skating, diving, gymnastics) can create a drive for thinness. Other sports, including team sports such as soccer, ice hockey, and basketball, actually might be protective—if they favor strength and larger size. It is interesting to look at the female athlete triad in the context of the entire sports experience for young women.

See Also: Eating disorders; Osteoporosis.

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Fermentation and Fermented Foods

Fermentation is a metabolic process through which certain organisms, including yeast and some types of mold and bacteria, obtain energy. During fermentation, organisms break down a compound such as sugar into simpler molecules, capturing energy from the substance's chemical bonds in the process. Fermentation reactions are anaerobic, which means they do not require oxygen. People have used fermentation to produce foods and beverages since prehistoric times. Fermentation also is used to produce biofuels, medicines, and other substances, and used in sewage treatment. Foods produced with fermentation reactions include beer, wine, bread, yogurt, cheese, sauerkraut, and pepperoni. The food product produced by fermentation depends upon the initial food undergoing fermentation and the organism used to produce the fermentation process. Some fermented foods, such as fermented vegetables and dairy products, contain significant numbers of probiotics—microorganisms that live in the human gastrointestinal tract and contribute to good health.

Although people have used fermentation to produce food and beverages for thousands of years, scientific study of fermentation biochemistry developed in the



Wine is made from crushed fruit and other tasty ingredients. Yeast is added to the fruit mixture and is responsible for the fermentation process. The fermentation process may occur in stainless steel tanks, as pictured here, or in other containers such as wine barrels and bottles. (Dreamstime.com)

early 20th century. Eduard Buchner, a German biochemist, received the Nobel Prize for Chemistry in 1907 in recognition of his work demonstrating that fermentation results from the action of enzymes produced by yeast. French scientist Louis Pasteur also studied the action of yeast in the fermentation process. Sir Arthur Harden, a biochemist from Great Britain, further clarified the enzymes and chemical processes of fermentation, receiving the 1929 Nobel Prize in Chemistry for this work.

The two main types of fermentation processes used to produce food are ethanol fermentation and lactic acid fermentation. In ethanol fermentation, sugars are broken down for energy, creating ethanol and carbon dioxide in the process. Ethanol fermentation occurs in bacteria and fungi, especially yeast. Ethanol fermentation is used to produce wine, beer, and bread. The carbon dioxide released in ethanol fermentation is what makes bread rise. (The ethanol evaporates when the bread is baked.) In lactic acid fermentation, sugar breakdown by bacteria produces lactic acid. (Human muscle cells use the same process for generating energy at high levels of exercise intensity, a process known as anaerobic energy production.) Foods produced using lactic acid fermentation include cheese, yogurt, vinegar, and soy sauce.

What Is Miso?

"Miso" is a seasoning made from fermented grains and legumes. It most commonly is used to flavor soups, salad dressings, and sauces. Like other fermented food products, miso contains helpful microorganisms that are thought to aid digestion and contribute to other health benefits. In modern-day Japan, most of the population still continues the very old custom of beginning their day with a warm bowl of miso soup. Miso soup is believed to stimulate digestion and energize the body.

Although rice and barley are the primary grains used in making miso, other grains such as millet can be used. Yellow soybeans are the primary beans used, although black soybeans, azuki beans, and chickpeas often also are part of a batch of miso. Generally, a type of bean, a grain, salt, and a culture are the only ingredients needed to make miso. Some people include a small amount of sea vegetables in their recipe to aid in the digestibility of the finished product.

Miso making is a double-fermentation process. The first fermentation is growing a culture using grain. The grain is inoculated with the spores of the *aspergillus* mold. In this fermentation, the inoculated grain is transformed into "koji" as the culture transforms the starches of the grain into simple sugars and creates an abundance of digestive enzymes. The second fermentation begins when the beans, koji, and salt are mixed and placed in large vats for a period that can range from three weeks to three years or more. The result is a salty paste that essentially is darker and more savory the longer it ages.

Robin Cole

Fermentation is used around the world to produce alcoholic beverages and to preserve food. In eastern and southeastern Asian countries, cabbage, vegetables, and sometimes seafood are fermented to make products such as pickles and kimchi. Pork and beef are fermented in southern and central Europe to produce cured sausages, such as prosciutto and chorizo. In West Africa, cassava root is fermented to make gari, a type of flour. Wheat flour is fermented to produce naan and other types of bread in south Asian countries. People around the world enjoy yogurt beverages such as kefir and lassi.

Fermentation is used with many different types of plant and animal products. Dairy products are made into yogurt, cheese, kefir, and other cultured-milk products. Honey can be fermented into the beverage called "mead." Fermented tea produces a drink called "kombucha." Fermented fish produces fish sauce; meat is made into sausages; fruit and vegetables are made into pickled products; and grains are used to produce alcoholic beverages and breads. Grains and legumes, such as soybeans, can be fermented to produce miso, a flavoring paste used in soups and many other dishes. Fermented soybeans are made into natto and tempeh.

Fermented food can offer many benefits. Fermentation can help to preserve foods, increasing food availability and dietary variety for consumers. Because fermentation organisms help to break down starches and fibers, they improve a food's

digestibility and reduce cooking time and cooking fuel use. Sometimes fermentation organisms increase nutrient content of a food. For example, the fermentation of some grains increases a food's content of amino acids and certain B vitamins. Fermentation can reduce the concentration of substances such as phytate that interfere with people's absorption of certain minerals, such as iron and calcium, in the digestive tract. In some cases fermentation can reduce the concentration of certain toxins in food. For example, cassava root, a basic food in the West African diet, exhibits lower total cyanide levels after fermentation.

Fermented foods contain a high concentration of probiotics and other microbiological content, for as fermentation organisms metabolize fuel substrates, they reproduce and thrive. Helpful intestinal bacteria and other microorganisms appear to improve the health of the gastrointestinal tract. They might have other health-promoting benefits as well, although research in this area still is preliminary.

Fermented foods tend to have high level of antioxidant activity. For example, a comparative study on garlic found that both fresh and aged garlic displayed strong antioxidant concentrations. Fermented black garlic, however, was discovered to have significantly higher phenolic content and antioxidant activity than fresh garlic (Kim, Nam, Rico, & Kang, 2012). In another study, kimchi demonstrated notably higher antioxidant activity compared to the same vegetables that did not undergo fermentation. The study concluded that fermentation helped to bring out antioxidant compounds in kimchi (Lee, Kim, Kang, Lim, Kim et al., 2010). Red wines fermented in oak barrels showed stronger concentrations of phenolic compounds after the 14 months of fermentation than before fermentation (Hernández, Estrella, Carlavilla, Martín-Álvarez, Moreno-Arribas, 2006).

Unfortunately, certain fermented foods have been associated with increased risk of esophageal and stomach cancers, particularly in countries where large amounts of pickled foods are consumed (WHO, 2013). It is possible that certain organisms used for fermentation, especially fungi, could be carcinogenic, although more research is needed to explain this association. Botulism is a toxic bacterium that thrives in an anaerobic environment, and has been found to occasionally contaminate fermented products, most notably fermented seafood products. Sanitary food production methods usually prevent contamination and food-borne illness from fermented foods.

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See Also: Microbiota and microbiome; Prebiotics; Probiotics.

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Fetal Alcohol Syndrome and Disorders

Fetal Alcohol Syndrome (FAS) is an irreversible condition caused by heavy consumption of alcohol during pregnancy. This syndrome is marked by pre- and postnatal growth retardation, certain characteristic facial abnormalities, and central nervous system deficits, including problems with memory and impulse control. Fetal Alcohol Syndrome falls under a grouping of disorders known as "Fetal Alcohol Spectrum Disorders" (FASD). This term refers to a wide range of conditions that can develop in people exposed to alcohol during prenatal development, with FAS representing the most severe extreme of the spectrum. These conditions include both physical and psychological problems. Although there are certain trademark characteristics that can be seen in many children who exhibit FASD, symptoms range from mild to severe. Presently, there is no known cure, although treatments for physical, cognitive, and behavioral problems can be helpful. Controversy exists regarding how much alcohol consumption leads to FAS and FASD, and public health recommendations regarding alcohol consumption during pregnancy vary among organizations and from country to country.

The connection between maternal alcohol consumption and the occurrence of mental, behavioral, and learning disabilities in children has been noted by various physicians throughout history. In 1973, the term "Fetal Alcohol Syndrome" was coined by physicians Kenneth L. Jones and David W. Smith who described the "tell-tale" signs of alcohol exposure in infants at birth and in young children. Children of mothers who drank daily and heavily appeared to be at greatest risk. Further research over the years confirmed the notion that alcohol acts as a teratogen, causing birth defects in the fetuses of laboratory animals.

Symptoms

Symptoms of FASD include growth retardation, facial malformation, and central nervous system disorders. Growth retardation is characterized by a child or infant whose weight/length/height is less than the tenth percentile. Common facial malformations include a very thin upper lip, small eyes, a short upturned nose, and a smooth skin surface between the nose and upper lip. Central nervous system (primarily brain) abnormalities include attention deficits, increased activity, intelligence and learning deficits, sleep disturbances, and poor motor skills. Although it is possible for a child to meet many of these criteria at once, a child does not need to exhibit all of these abnormalities to be classified as affected with FASD. There also are less common, but significant symptoms of FAS such as heart defects, eye and ear problems, and deformities of limbs, joints, and fingers.

Some children show some symptoms of milder FAS-type symptoms. These cases previously were categorized as fetal alcohol effects (FAE). In 1996, the U.S. Institute of Medicine (IOM) replaced the ambiguous FAE diagnosis with new terms. Alcohol-related neurodevelopmental disorder (ARND) refers to people with problems of behavior and learning, and alcohol-related birth defects (ARBD) refer to physical abnormalities (CDC, 2013). It often is difficult to diagnose ARND, ARBD, and FASD, because symptoms can be common to many other disorders.

Because Fetal Alcohol Spectrum Disorders are irreversible, affected infants will grow to become affected adolescents and adults. As children, those with FASD could face poor impulse control, poor attention span, and irritability, among other symptoms. This can make school and other daily tasks more difficult for them than for a child without FASD. During adolescence, symptoms can escalate into anxiety, depression, and difficulty controlling emotions. Adults who suffer from many of the symptoms of FASD often face hardships due to poor judgment and poor social skills as a result of the condition. Even everyday tasks such as grocery shopping, keeping clean, using public transportation, and cooking meals can present huge challenges for adults with FASD. They often have difficulty finding and keeping jobs, thus requiring lifelong community support (NOFAS, n.d.).

Causation

When alcohol is consumed during pregnancy, it enters the mother's bloodstream and then reaches the bloodstream of the developing fetus by crossing the placenta. A fetus metabolizes alcohol much more slowly than an adult, and therefore the fetus will have a higher blood alcohol concentration than the mother. Researchers do not know exactly how alcohol exerts its teratogenic effects. It might interfere with the delivery of oxygen and nutrients to developing tissues and organs. The variation in symptoms of FASD could be explained at least partially by the timing of alcohol exposure, as the influence of alcohol on the many processes of fetal development could vary. The effect of heavy alcohol exposure could be especially strong during the first trimester of pregnancy, when cells are differentiating and

forming the fetus's organs. This is unfortunate, because at this stage, many women do not yet know that they are pregnant.

What Level of Alcohol Intake Is Harmful?

Experts cannot say with certainty what level of alcohol intake during pregnancy is harmful. Researchers studying babies diagnosed with FAS often have been unable to ascertain degree of alcohol exposure in utero. Women might not accurately recall or report alcohol consumption during pregnancy, and heavy alcohol intake often occurs together with the use of other drugs, poor nutrition, and other factors that influence fetal development. Making the matter more complex is the fact that many babies born to mothers who drank heavily throughout pregnancy show no symptoms of FASD.

Because FAS is a serious and irreversible disorder, public health recommendations have generally erred on the side of caution, advising women to abstain from alcohol during pregnancy. In the United States, alcoholic beverages must carry a warning label stating, "According to the Surgeon General, women should not drink alcoholic beverages during pregnancy because of the risk of birth defects." Warning labels are also mandated in the United Kingdom, France, and Japan. In Canada, labeling regulations vary from province to province.

Evidence supporting such extreme caution is lacking. Recent well-designed epidemiological studies that have recorded how much alcohol women drink while pregnant (rather than asking women to remember what they drank months or years earlier) suggest that one or two drinks a day might not be harmful. Studies have examined not only alcohol consumption and FAS, but also alcohol consumption and milder symptoms such as behavioral problems and cognitive deficits of children at 3 years of age (Kelly, Sacker, Gray, Kelly, Wolke, & Quigley, 2008) and selective and sustained attention in 5-year-old children (Underbjerg et al., 2012). Nevertheless, most professional organizations continue to urge women to abstain or limit alcohol consumption during pregnancy.

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Research Issues

Public health authorities do not agree on how much alcohol is safe to consume during pregnancy. How can a woman decide what to do during her pregnancy? Although light drinking (a few drinks a week) appears to be relatively safe, might future research uncover as yet unidentified problems associated with even light alcohol consumption (Hanson, 2013)? How much risk is acceptable?

What should alcohol educators and medical professionals say to their pregnant patients? If public-health statements and health care providers contend that light drinking is probably safe, might some women take this to mean that any level of alcohol consumption is safe? Could these statements serve as a license to drink heavily? How would you counsel a friend who is wondering if she should drink during her pregnancy?

See Also: Alcohol.

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Fiber

Fiber refers to the components of food that cannot be digested. Fiber can be found in whole grains, legumes, fruits and vegetables, and foods made from these ingredients. Dietary fiber is the fiber the body gets from the diet. Functional fiber refers to the fiber that is added to foods, as is done in many breakfast cereals, or fiber that is made into a dietary supplement. In the gastrointestinal (GI) tract, fiber increases feelings of fullness during meal consumption, delays gastric emptying, slows blood glucose absorption, and binds bile acids, which could help remove cholesterol (a major component of bile) from the body. Many types of fiber serve as prebiotics, providing food and a healthful environment for helpful microorganisms in the GI tract. An adequate fiber intake has been associated with many positive health effects, including the prevention of constipation, diverticulosis, and cardiovascular disease. A high fiber intake can result in bloating, however, from the fermentation of fiber in the large intestine, and also can cause constipation if an inadequate amount of water is consumed.

Cultures around the world and throughout time have noted the beneficial effects of high-fiber foods on GI function. In 430 BCE, for example, Hippocrates noted that coarse wheat produced bulkier stools than refined wheat (Slavin, 2013). In the United States in the 1920s, physician J. H. Kellogg and other entrepreneurs promoted the use of wheat fiber as a cure to multiple health—and even social—problems. Scientific interest in the health benefits of dietary fiber grew in the 1950s as Irish missionary surgeon Denis Burkitt published his observations that GI dis-

eases common in Western countries were rare in most African groups. He attributed these differences to diet fiber content (Slavin, 2013). Although not all of Burkitt's ideas have withstood the test of time, his work stimulated increased research into the health effects of dietary fiber.

Types of Fiber

Dietary fiber comes primarily from plants. Most types of dietary fiber, such as cellulose, are composed of carbohydrates. Humans lack the necessary digestive enzymes for breaking down these structures, so they pass through the digestive system, adding bulk to the stools. There are many kinds of dietary fiber. Dietary fibers are classified as water soluble and water insoluble, and both groups have beneficial effects on health.

In general, water-soluble fiber attracts water and forms a gel-like mix in the digestive system. This mixture slows stomach emptying, helping a person to feel full longer. Delayed stomach emptying also means that glucose is absorbed from the digestive mass more slowly, thus preventing a rapid rise in blood glucose. A rapid rise in blood glucose can lead to high blood insulin levels. Water-soluble fiber tends to bind bile acids found in the small intestine. Bile acids are high in cholesterol. When the bile acids are bound to the fibrous mixture, their cholesterol is not available for reabsorption; thus, soluble fiber appears to be beneficial for people trying to reduce blood cholesterol levels. Water-insoluble fiber provides bulk to the feces and speeds its passage through the GI tract. Water-insoluble fiber reduces risk of constipation. It should be noted that the functions of water-soluble and water-insoluble fibers as described above often overlap. Psyllium fiber, for example, is primarily water soluble, yet still increases stool bulk. Some of the most common types of fiber in the diet include the following (Insel et al., 2014).

- Cellulose—Cellulose is composed of long, straight chains of glucose molecules. It is a component of the fibrous structures of plants and is found in fruits, vegetables, grains, and nuts.
- Hemicelluloses—Hemicelluloses generally are mixed with celluloses in plant structures and consist of monosaccharides with branching side chains. They are found in wheat bran, legumes, nuts, and vegetables.
- Lignins—Lignins contribute to the tough, fibrous portions of vegetables such as carrots. Unlike other dietary fibers, lignans are not carbohydrates.
- Pectins—Pectins are water-soluble, gel-forming carbohydrates found in all plants, especially fruits. Pectin is used to give texture to jellies and other food products.
- Gums and mucilages—These water-soluble fibers are found in most plants and are used in food products to improve texture and to thicken. The husk of the psyllium seed, known as "psyllium," is a mucilage and the primary component of many laxative products.

- Beta-glucans—This carbohydrate, water-soluble fiber is found in oats and barley and has been found to help lower blood cholesterol levels in some studies.
- Chitan and chitosan—These fibers are extracted from the shells of crabs and lobsters and sold as dietary supplements. They are marketed as being effective for weight loss, but evidence to support this claim is lacking.
- Inulin, oligofructose, and other oligosaccharides—These carbohydrates are found in many plants and resist digestion in the human GI tract, but serve as prebiotics for helpful microorganisms. They are smaller structures than the polysaccharide structures such as cellulose.

Adequate Intake of Fiber

Currently, adults in the United States consume only half of the recommended amount of fiber. The recommended adequate intake (AI) value for fiber is 14 g dietary fiber per 1,000 kcals, or for men ages 19 to 50, 38 grams per day; the value for men age 50 and older is 30 grams per day (Slavin, 2008). For women

Table 1. Examples of Foods That Have Fiber

Food	Amount of Fiber
½ cup of beans (navy, pinto, kidney), cooked	6.2–9.6 grams
½ cup of shredded wheat, ready-to-eat cereal	2.7–3.8 grams
⅓ cup of 100% bran, ready-to-eat cereal	9.1 grams
1 small oat bran muffin	3.0 grams
1 whole-wheat English muffin	4.4 grams
1 small apple, with skin	3.6 grams
1 medium pear, with skin	5.5 grams
½ cup of raspberries	4.0 grams
½ cup of stewed prunes	3.8 grams
½ cup of winter squash, cooked	2.9 grams
1 medium sweet potato, baked in skin	3.8 grams
½ cup of green peas, cooked	3.5–4.4 grams
1 small potato, baked, with skin	3.0 grams
½ cup of mixed vegetables, cooked	4.0 grams
½ cup of broccoli, cooked	2.6–2.8 grams
½ cup of greens (spinach, collards, turnip greens), cooked	2.5–3.5 grams

The recommended adequate intake value for fiber is 14 grams of dietary fiber per 1,000 kcals, or for men ages 19 to 50, 38 grams per day; the value for men age 50 and older is 30 grams per day. For women ages 19 to 50, the AI value is 25 grams per day, and for women age 50 and older it is 21 grams per day.

Source: U.S. Department of Agriculture and U.S. Department of Health and Human Services, *Dietary Guidelines for Americans,* 2010.

ages 19 to 50, the AI value is 25 grams per day, and for women age 50 and older it is 21 grams per day. (Older adults continue to need adequate fiber, but recommendations are lower because older adults need fewer calories to maintain their current weight.) Most dietary guidelines encourage people to consume adequate amounts of vegetables, fruits, legumes, and whole grains to promote a healthy intake of dietary fiber. See the table for a representative group of high-fiber foods.

As is the case for most dietary components, too much fiber, especially in the form of fiber supplements or concentrated sources of fiber such as wheat bran, can be problematic, causing diarrhea and intestinal discomfort. People trying to increase their fiber intake are advised to do so gradually so that their bodies have time to adjust to the new levels.

Health Benefits of Adequate Fiber Intake

Constipation refers to the production of hard, dry, and infrequent stool that is difficult to eliminate from the body. Fiber helps to prevent and treat constipation because it increases fecal bulk and helps waste pass more quickly through the gastrointestinal tract. Water-soluble fiber draws water into the fecal mass; thus, an adequate fluid intake is also important for the prevention and treatment of constipation.

Diverticulosis is a condition that occurs when pouches form along the walls of the colon. Low-fiber diets are associated with diverticulosis. Constipation is thought to contribute to diverticulosis as the muscles along the gastrointestinal tract become strained from pushing the hard stools, which increases the pressure on the colon and causes pouches to form. Conversely, diets rich in fiber allow for the easy passage and removal of the stools, which puts less pressure on the walls of the colon. Similarly, constipation increases risk for the development of hemorrhoids, a condition in which swollen and inflamed veins bulge into the rectum and anus. Straining during elimination is thought to worsen this condition.

Obesity is the condition of having excess body fat that often is a precursor to several negative health effects. The relationship between fiber intake and obesity is complex. Although dietary fiber intake is associated with lower risk of obesity, people with high-fiber diets often have diets that are more healthful in other ways. They also might exercise more. Nevertheless, high-fiber diets are thought to help reduce the chances of becoming overweight and to promote weight loss. Foods rich in soluble fiber make the body feel full because they take longer than other food sources to move from the stomach to the small intestine. Soluble fiber also attracts water molecules, which adds to the feeling of being sated. Along with giving the body a feeling of fullness, these fiber-rich foods often are low in calories and fats, making the body feel full and at the same time, allowing for a lower-calorie diet.

Type 2 diabetes occurs when the cells in the body become resistant to insulin, causing high blood glucose levels. Diets high in fiber are recommended for people with type 2 diabetes for two reasons. Fiber does not increase blood glucose levels

because most of it cannot be digested. The second reason is that research has shown that certain fibers slow the release of glucose from the digestive mass into the bloodstream.

The leading cause of cardiovascular disease is artery disease, in which the lining of the arteries becomes thickened by the presence of plaque. High levels of LDL-cholesterol increase the risk of artery disease. Experiments have shown that increasing fiber intake reduces blood LDL-cholesterol; and people who have high-fiber diets are less likely to develop artery disease than people with low-fiber diets. The body uses cholesterol to make bile, and because high intakes of fiber can bind with bile, removing it from the body in the feces, the body can take excess cholesterol from the blood to make more bile, reducing the overall amount of cholesterol in the bloodstream.

Healthful populations of microbiota in the gastrointestinal tract are associated with better health, including the reduced risk of infectious diarrhea, inflammatory bowel conditions, and even certain types of cancer. The relationship between dietary fiber and colorectal cancer is currently unclear, as short-term studies have failed to find a relationship.

Fiber Supplements

Most fiber supplements contain only soluble fiber because they can be dissolved in water, although some supplements contain a mixture of both soluble and insoluble fiber. Although fiber supplements should not be used to replace dietary fiber, they could be effective in lowering low-density lipoprotein (LDL) levels and blood glucose levels. Psyllium is one of the most popular fiber supplements. Because soluble fiber slows down digestion, fiber supplements can increase the amount of time it takes the body to absorb certain medications. It is recommended that medications and fiber supplements be taken at least one hour apart.

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See Also: Cardiovascular disease and nutrition; Cholesterol; Diverticular disease; Glycemic index and glycemic load; Grains; Large intestine; Lipoproteins; The liver; Microbiota and microbiome; Prebiotics; Probiotics.

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Fluoride

Fluoride is a naturally occurring mineral made from the element fluorine, which is the seventeenth most abundant element in the earth's crust. Fluorine is never naturally found in a free state. It only is encountered in combinations with other elements as a fluoride compound. The fluoride ion is found in all water sources including the oceans. Since its discovery, elemental fluorine has been used in a multitude of ways, primarily in the form of fluoride compounds which are used in the dental industry and for the purpose of public health. Although fluoride is not an essential nutrient and is not necessary for biological functioning, its effect in the body can have both positive and negative impacts on the health of an individual.

Discovery and Use of Fluoride

Karl W. Scheele was the first to identify the element fluorine in 1771. More than a century later, fluorine was first isolated by the French chemist F. Henri Moissan, who subsequently was awarded the Nobel Prize for Chemistry in 1906



Fluorite is the mineral form of calcium fluoride. It is used to make the forms of fluoride found in toothpaste and other dental care products. (Catalina Zaharescu Tiensuu/Dreamstime.com)

Dental Fluorosis in Children

The U.S. Centers for Disease Control and Prevention offer the following advice on preventing dental fluorosis in babies and young children.

What Is Dental Fluorosis?

Dental fluorosis is a change in the appearance of the tooth's enamel. These changes can vary from barely noticeable white spots in mild forms to staining and pitting in the more severe forms. Dental fluorosis only occurs when younger children consume too much fluoride—from any source—over long periods when teeth are developing under the gums.

Who Develops Dental Fluorosis?

Only children ages 8 years old and younger can develop dental fluorosis, because this is when permanent teeth are developing under the gums. The teeth of children older than 8 years, adolescents, and adults cannot develop dental fluorosis.

What Does Dental Fluorosis Look Like?

- Very mild and mild forms of dental fluorosis—Teeth have scattered white flecks, some white spots; "frosty" edges; or fine, lacy chalk-like lines. These changes are barely noticeable and are difficult to see except by a dental health care professional.
- Moderate and severe forms of dental fluorosis—Teeth have larger white spots and—in the rare severe form—rough, pitted surfaces.

Common sources of fluoride include the following.

- Toothpaste (if swallowed by young children)
- Drinking water in communities which fluoridate municipal sources
- Beverages and food processed with fluoridated water
- Dietary prescription supplements that include fluoride (e.g., tablets, drops)
- Other professional dental products (e.g., mouth rinses, gels, foams)

In the United States, water and processed beverages (e.g., soft drinks, fruit juices) can provide approximately 75% of a person's fluoride intake. Inadvertent swallowing of toothpaste and the inappropriate use of other dental products containing fluoride can result in greater intake than desired. For this reason the CDC recommends that parents supervise the use of fluoride toothpaste by children younger than 6 years of age to encourage them to spit out excess toothpaste. Children younger than 6 years old should not use fluoride mouth rinses because the mouth rinse could be repeatedly swallowed.

Centers for Disease Control and Prevention (CDC). (2013). *Dental fluorosis*. Retrieved from http://www.cdc.gov/fluoridation/faqs/dental_fluorosis/index.htm

(Dicciani, 2003). Varying forms of fluorochemicals have been used widely throughout history, most notably in health care. Fluorocarbons were used heavily in the refrigeration and air conditioning industries, as well as in fire extinguishers. Fluoropolymers and fluoroelastomers are used in the construction of homes,

buildings, motor vehicles, and in aerospace for the purpose of thermal, flame, chemical, and solvent resistance. One out of every five active pharmaceutical products is fluorinated, and fluorocarbons are used in synthetic blood substitutes and inhalation drug-delivery systems. The use of fluoride compounds for the prevention of tooth decay first was recognized by dental scientists in the 1930s and continues to this day (Centers for Disease Control, 2013). In the past, fluorine was used in the clinical setting to treat patients with hyperthyroidism (Galletti & Joyet, 1958).

Physiological Effect of Fluoride

Fluoride is absorbed systemically by the stomach and small intestine. In the bloodstream, fluoride enters mineralized tissues such as bones and developing teeth. It reacts with hydroxyapatite crystals in mineralized tissue, forming fluoroapatite, which hardens tooth enamel and bone mineral.

Although most food sources contain low levels of fluoride, there are several foods that are fluoride rich. These include marine fish that are consumed along with their bones and foods made with mechanically separated chicken. Elevated concentrations of fluoride are found in tea leaves, fruit juice, bottled water, and packaged food products made using fluoridated water.

An inadequate intake of fluoride can potentially lead to an increase in dental caries (cavities). Although there currently is little data to suggest the need for a Recommended Dietary Allowance (RDA), the Food and Nutrition Board (FNB) of the U.S. Institute of Medicine has established an Adequate Intake (AI) level based upon the desire to reduce dental caries effectively without creating the unwanted side effects associated with fluoride overexposure. The daily AI is 4.0 mg/day for adult men and 3.0 mg/day for adult women.

The effort to decrease dental caries has led to an increase in the use of fluoride in many consumable products. The use of fluoride to prevent tooth decay exists in topical and systemic forms. Topical fluorides strengthen existing teeth and prevent acid-producing bacteria from causing caries. Topical fluorides include toothpaste, mouthwash, and professional fluoride treatments performed in a dentist's office.

Systemic fluorides are ingested and absorbed by the body to become incorporated into developing tooth structures. Systemic fluorides give topical protection through their presence in saliva, which continually bathes the teeth and gives protection. Systemic fluorides are delivered through water fluoridation or dietary fluoride supplements such as tablets, drops, or lozenges. Through its interactions with calcium and phosphate, fluoride enhances the remineralization of tooth enamel that can be demineralized by acid-producing bacteria. Remineralized enamel is more resistant to bacterial acid and prevents further demineralization that might otherwise lead to dental caries.

The effects of fluoride absorption, however, can be harmful as well as helpful. Consuming fluoride in excessive amounts leads to acute fluoride poisoning, which is particularly dangerous for children. Signs of fluoride toxicity include abdominal pain, nausea, and vomiting. Over long periods, overexposure to fluoride can lead

to changes in bone structure known as skeletal fluorosis. The most severe form, "crippling skeletal fluorosis," also negatively affects ligaments and leads to muscle wasting, immobility, and neurological problems. A related problem of excessive fluoride use, though less severe, is dental fluorosis. The presentation of dental fluorosis can range anywhere from white spots on the enamel of teeth to marked staining and pitting, which causes serious cosmetic concerns. The increase in the use of fluoride in consumer products has led to an increased incidence of dental fluorosis over the past decades. According to a 1999–2004 U.S. national survey, 23% of people ages 6 to 49 years had some degree of dental fluorosis (Higdon & Delage, 2013).

Water Fluoridation

Although the use of fluoride spans many facets of life, significant controversy exists over the addition of fluoride to the public water supply. According to the Centers for Disease Control and Prevention, community water fluoridation is a safe, effective, and inexpensive way of delivering the benefits of fluoride to residents of a community. Fluoridating the public water supply allows all members of a community to benefit from the treatment, regardless of age, income, education, or socioeconomic status. The reduction in social barriers affords those with limited access to dental care the opportunity to reduce their risk of dental carries at no cost. Water fluoridation has been subject to public opposition and, in some instances, has been discontinued. In addition to concerns about the harmful effects of fluoride toxicity, many individuals and organizations oppose water fluoridation on the premise that the public is being medicated without consent (Fluoride Action Network, 2012). Nevertheless, studies have shown that over the course of a person's lifetime water fluoridation reduces tooth decay by about 25% (Centers for Disease Control, 2013).

Fluoride Supplements for Children

If children are living in an area without community water fluoridation, or they are at increased risk of developing tooth decay, then daily fluoride supplementation is recommended. The benefit of fluoride supplementation for at-risk children is to give them the protection against dental caries that they might not otherwise have due to location or socioeconomic status. Dentists and physicians, however, must use caution when prescribing fluoride supplements to children to avoid the negative effects of overexposure. Careful attention is required to ensure that a child is not consuming fluoride from other sources, such as bottled water or foods that are rich in fluoride. Misjudging a child's consumption of fluoride when prescribing supplementation could lead to dental fluorosis and other negative side effects. Due to the need for a child to take these supplements for an extended period, fluoride supplementation is less cost effective than community water fluoridation (American Dental Association, 2014).

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Research Issues

Infants and young children are at the highest risk for consuming too much fluoride. During the first 4 to 6 months of life, infants consume breast milk and infant formula almost exclusively. Infant formula contains fluoride, to ensure that infants meet their adequate intake levels for this nutrient. Formula comes in three forms—ready-to-serve liquid, powder, and concentrated liquids. The powder and concentrated liquid forms must be mixed with water. If the water used in mixing the formula is high in fluoride, then over time an infant's fluoride intake can be too high. People using infant formula should check with their pediatricians to be sure that infant fluoride intake is optimal.

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See Also: Dental caries (cavities).

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Folate and Folic Acid

Folate is a B vitamin. It is one of several compounds that the body converts to a family of coenzymes called "tetrahydrofolic acid." Folic acid is a similar compound. Folate and folic acid are also known as vitamin B9. Like all vitamins, folate is an organic compound that is necessary for normal growth, development, and maintenance of basic functions in the body. Folate is water soluble, which means that the body does not store it, so it must be consumed regularly. The terms folate and folic acid are often used interchangeably, but folate specifically refers to the form of the vitamin found naturally in food, whereas folic acid is its synthetic form. Folic acid is absorbed by the body more readily than folate because its structure is simpler.

Folate plays an important role in DNA and RNA production and maintenance in cells; it is particularly important for the synthesis of red blood cells. Consuming folate is essential for the human body to maintain proper cell development, but it is especially important for women of child-bearing age. Adequate folate intake significantly reduces the risk of neural tube birth defects (e.g., spina bifida, anencephaly). An embryo's neural tube closes within the first 28 days of pregnancy, which is before a woman might know she is pregnant; therefore, women should have adequate folate in their diets not only while pregnant, but also before they become pregnant. Folate could play a role in preventing other diseases, such as certain forms of cancer and cardiovascular disease, but further research is necessary to make any significant claims about these effects.

History

In the early 1930s, folate was identified as a substance found in green, leafy vegetables that helped prevent anemia during pregnancy. It is named after the Latin word for leaf, "folium," which is the same root for the English word "foliage." The connection between inadequate folate intake and neural tube birth defects was hypothesized in the 1960s and confirmed by the early 1990s through several randomized research studies. By 1992, the U.S. Public Health Service recommended that all women of child-bearing age consume 400 micrograms (mcg) of folic acid per day (U.S. Department of Agriculture and U.S. Department of Health and Human Services, 2014). By 1998, both the United States and Canada mandated that grain products, such as breads, pastas, and cereals, be fortified with folic acid. Since 1998, the average daily intake folic acid has increased by about 200 mcg per day, and neural tube defects in infants have decreased substantially, by about 36% in the United States and 46% in Canada (CDC, 2013).

Physiological Functions and Deficiency Symptoms

Folate, like all B vitamins, is a coenzyme (coenzymes help enzymes function). As a coenzyme, folate supplies and accepts single carbon compounds. This enables DNA to form. Folate also helps metabolize amino acids into derivative forms. Folate is critical for proper cell division throughout the body; without folate, new cells cannot divide because they cannot form new DNA. Red blood cells are particularly affected. If someone is deficient in folate, then red blood cells have enough protein to synthesize new cell parts, but they do not have enough DNA to form a second nucleus. The result is called a megaloblast, which is a large, immature cell. These cells cannot carry oxygen like mature red blood cells, and this results in anemia.

Anemia is the primary indicator of folate deficiency, but other symptoms include fatigue, depression, tongue inflammation, hair loss, diarrhea, mental confusion, nerve dysfunction, and cognitive problems. Individuals who are more prone to folate deficiency include those who consume large amounts of alcohol, as alcohol inhibits the absorption of folate. People with celiac disease, irritable bowel syndrome, or

other disorders that limit the body's ability to absorb nutrients also have an increased risk of folate deficiency.

Folate deficiency in pregnant women can lead to neural tube defects in the developing brain and spinal cord of the embryo, such as spina bifida (when the vertebrae do not form properly around the spinal cord) and anencephaly (when part or all of the brain is missing). Babies born with spina bifida can exhibit paralysis, learning disabilities, and other complications. Those born with anencephaly die shortly after birth. Researchers recommend that women of child-bearing age consume 400 mcg of folic acid per day.

Some studies have found a link between reduced intake of folic acid and increased rates of some kinds of cancers. Other studies have found that people who had higher folic acid intake have a reduced risk for cancers of the colon, breast, ovaries, pancreas, stomach, and esophagus. Other studies suggest that the effect of folic acid on cancer growth depends on when the folic acid is ingested. For example, because folic acid promotes cell division, taking folic acid could be harmful if cancerous or precancerous cells already are present (American Cancer Society, 2011). Some chemotherapy agents block the action of folic acid to limit cell replication in rapidly dividing cells, such as cancer cells. Until clearer evidence becomes available, the American Cancer Society recommends eating a varied diet, limiting alcohol consumption, and only taking a folic acid supplement when it is recommended by a doctor.

Food Sources and Supplements

Food sources of folate include dark, leafy greens such as spinach, lettuce, and broccoli; orange juice, melons, and bananas; legumes, mushrooms, and asparagus; and organ meats such as liver and kidney (*see* Table 1). Cooking and processing can destroy 50% to 90% of folate in food, thus the highest levels of folate are found in raw or lightly cooked (in minimal water) vegetables and fruits. Folic acid is more durable than folate and is used to fortify many grain-based foods, including cereals, breads, and pastas. Folic acid also can be consumed in the form of a supplement; it often is included in multivitamins. The Dietary Reference Intake (DRI) for folate for both male and female adults is 400 mcg per day; for pregnant women, the DRI is 600 mcg per day; and for lactating women is 500 mcg per day.

Tolerable Upper Intake Level

Folate from food sources can be absorbed by the body only in limited amounts, therefore there is no Tolerable Upper Intake Level (UL) for folate. Folic acid (from supplements or fortified foods), however, should not be consumed above the UL unless under the supervision of a doctor. The UL for folic acid is 1,000 mcg per day for adult males and females, as well as for pregnant and lactating women.

Excess folic acid can interact with some drugs, such as those used to treat some cancers (including methotrexate), epilepsy, and ulcerative colitis (National Institutes of Health, Office of Dietary Supplements, 2012). Additionally, folic acid

Table 1. Selected Food Sources of Folate and Folic Acid

Food	mcg DFE per serving	Percent DV*
Beef liver, braised, 3 ounces	215	54
Spinach, boiled, ½ cup	131	33
Black-eyed peas (cowpeas), boiled, ½ cup	105	26
Breakfast cereals, fortified with 25% of the DV†	100	25
Rice, white, medium-grain, cooked, ½ cup†	90	23
Asparagus, boiled, 4 spears	89	22
Spaghetti, cooked, enriched, ½ cup†	83	21
Brussels sprouts, frozen, boiled, ½ cup	78	20
Lettuce, romaine, shredded, 1 cup	64	16
Avocado, raw, sliced, ½ cup	59	15
Spinach, raw, 1 cup	58	15
Broccoli, chopped, frozen, cooked, ½ cup	52	13
Mustard greens, chopped, frozen, boiled, ½ cup	52	13
Green peas, frozen, boiled, ½ cup	47	12
Kidney beans, canned, ½ cup	46	12
Bread, white, 1 slice†	43	11
Peanuts, dry roasted, 1 ounce	41	10
Wheat germ, 2 tablespoons	40	10
Tomato juice, canned, ¾ cup	36	9
Crab, Dungeness, 3 ounces	36	9
Orange juice, ¾ cup	35	9
Turnip greens, frozen, boiled, ½ cup	32	8
Orange, fresh, 1 small	29	7
Papaya, raw, cubed, ½ cup	27	7
Banana, 1 medium	24	6
Yeast, baker's, ¼ teaspoon	23	6
Egg, whole, hard-boiled, 1 large	22	6
Vegetarian baked beans, canned, ½ cup	15	4
Cantaloupe, raw, 1 wedge	14	4
Fish, halibut, cooked, 3 ounces	12	3
Milk, 1% fat, 1 cup	12	3
Ground beef, 85% lean, cooked, 3 ounces	7	2
Chicken breast, roasted, ½ breast	3	1

Notes: * DV = Daily Value. The FDA developed DVs to help consumers compare the nutrient contents of products within the context of a total diet. The DV for folate is 400 mcg for adults and children aged 4 and older. The FDA, however, does not require food labels to list folate content unless a food has been fortified with this nutrient. Foods providing 20% or more of the DV are considered to be high sources of a nutrient.

† Fortified with folic acid as part of the folate fortification program.

The U.S. Department of Agriculture's Nutrient Database website lists the nutrient content of many foods and provides a comprehensive list of foods containing folate arranged by nutrient content and by food name. U.S. Department of Agriculture Agricultural Research Service. (2012). USDA National Nutrient Database for Standard Reference, Release 25.

Source: National Institutes of Health Office of Dietary Supplements. (2012). *Dietary Supplement Fact Sheet*. Table 2. Selected Food Sources of Folate and Folic Acid. Retrieved from http://ods.od.nih.gov/factsheets/Folate-HealthProfessional/

can mask the symptoms of other vitamin B deficiencies such as a deficiency in vitamin B12. Vitamin B12 deficiencies can be harmful to the central nervous system and also can cause megaloblastic anemia, especially in older individuals.

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See Also: Megaloblastic anemia; Pregnancy and nutrition; Vitamins.

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Food Addiction

Food addiction refers to compulsive overeating and an obsessive relationship with food. Researchers who have studied food addiction think that people who say they are addicted to food might respond to certain foods in a fashion that physiologically and psychologically is similar to the response of people to addictive drugs, such as heroin and cocaine. Indeed, research suggests that people addicted to food meet the diagnostic criteria for substance dependence. Additionally, the behaviors associated with food addiction fit the criteria for other behavioral addictions, such as gambling. Although not yet recognized as a psychological disorder with an official diagnostic criteria, food addiction could contribute to binge-eating disorder, a recognized clinical diagnosis, although not everyone addicted to overeating develops binge-eating disorder (American Psychological Association, 2013).

Addiction refers to the compulsive use of a substance or performance of an activity even though the person experiencing the addiction knows it is causing or is likely to cause harm. Addiction also is characterized by a loss of control over the substance use or behavior. Addiction to both substances and behaviors involves activation of the brain's reward pathways. With addiction, the use of the substance

or performance of the problem behavior also can change these reward pathways over time in ways that lead to tolerance (needing more of the substance/behavior to achieve a pleasurable feeling), craving (strong desires to use the substance/perform the behavior), and withdrawal symptoms (symptoms such as pain, irritability, restlessness, and difficulty sleeping) which develop when a person does not access the addictive substance or behavior.

People who describe themselves as addicted to food often experience significant distress regarding their lack of control over their food intake. This lack of control manifests in behaviors such as continuing to eat even though full and even though one wishes to not overeat. People addicted to food report emotional health problems such as anxiety, depression, and low self-esteem. They might feel sad or ashamed about eating or about their body weight, and report high levels of emotional overeating (overeating in response to negative emotions such as sadness, anger, or boredom). People with food addiction often say that they prefer to eat in private, avoiding social interactions because of eating behaviors and weight. People experiencing food addiction are more likely than others to develop obesity and obesity-related health disorders.

The Neurochemistry of Food Addiction

Scientists studying the brain's chemical response to foods have found a parallel between its response to food and to drugs. One of the most studied neurological pathways in research on food addiction is that of dopamine. Dopamine is a neurotransmitter—a chemical that sends messages from one nerve cell to another. Dopamine and its effects motivate people to eat as well as to engage in other "rewarding" behaviors, such as sex. Dopamine is known as the chemical that creates "wanting" and is essential for survival. Animals that lack dopamine, for example, starve to death because they have no motivation to eat.

Scientists have found that very obese people have lower levels of dopamine in the reward center of the brain as compared to people of normal weight. This is the same thing that occurs in cocaine addicts, alcoholics, and other addicts. This observation has led to the question, "Do people overeat because they are born with a dopamine system that doesn't respond, or do obese people have a low dopamine response because this area has been overstimulated by overeating?" To explore this question, a group of researchers fed rats calorie-dense foods that were high in sugar and fat, such as cookies and chocolate chips (Avena, Rada, & Hoebel, 2009). After a few months, the rats became obese and their reward center dopamine levels were less than those of rats fed a restricted diet. To see whether this change was the result of weight gain per se or the rats' diets, the researchers next fed the rats a restricted diet (of rat chow, not calorie-dense foods) having as many calories as that of the rats fed calorie-dense foods. This group also gained weight, but did not show a change in dopamine levels. In other words, the researchers found that the rats fed calorie-dense foods had a decrease in reward-center dopamine and the other rat group did not. This showed that weight gain alone did not cause a change in dopamine levels but the process of eating calorie-dense foods did (Avena, Rada, & Hoebel, 2009).

To test dopamine levels after weight gain in humans, one study examined 26 overweight and obese women (Stice, Yokum, Blum, & Bohon, 2010). The women who gained weight over a six-month period showed a lower dopamine response when they drank a milkshake than they had when the study began, six months earlier. The researchers suggested that a lower dopamine response might make one more likely to overeat in an attempt to restore normal dopamine levels, and yet, that same overeating can dampen the dopamine response further (Stice et al., 2011).

In a similar study, 30 teens who were at high risk for obesity (had two overweight or obese parents) were compared to 30 teens at low risk. All teens had a normal weight. The researchers found that the teens at high-risk for obesity had a greater dopamine response after drinking milkshakes than those that were at a low risk (Stice, Yokum, Blum, & Bohon, 2010). This study demonstrated that obese people could start out with an oversensitive dopamine system. This initial oversensitization could cause people to overeat, because eating is experienced as very leasurable. Over time, however, overeating could lead to a dampened response, which in turn leads to more overeating.

This research is important because it helps to establish the fact that food addiction has a physiological as well as a psychological basis, and that people who develop food addictions face strong cravings that drive them to overeat. This research helps both clinicians and those who feel addicted to food to better understand the problem of food addiction. It is hoped that this understanding also will lead to better strategies for prevention and treatment.

What Foods Are Most Addictive?

Many foods can activate reward pathways. The ingestion of chocolate, for example, causes one of the largest food-related rises in dopamine. In general, people with food addictions report being drawn to foods that are high in sugar and fat. Most of the foods people with food addiction crave are not found in nature, but instead are created in the kitchen or the laboratory. Most commonly craved are dessert foods such as cookies, cakes, donuts, and ice cream. These foods are calorie-dense, and it is easy to consume a lot of calories in a short span of time. The research described above suggests that, in vulnerable people, frequent consumption of these foods could alter reward pathways over time in ways that prompt further overeating.

Interesting research in rodents has found that addictive eating behavior, such as consuming a greater than normal amount of a given food, is more likely to occur when access to such foods is limited. Science writers have likened this observation to the experience of human beings "going on a diet," in other words, restricting access to certain foods (Liebman, 2012).

Treatment

After self-diagnosing or under clinical recommendation, some food addicts look for help in 12-step groups such as Food Addicts Anonymous, which have meetings

in many regions or are available online. Others consult nutritionists, doctors, psychologists, counselors, or eating-disorder specialists. These professionals often help clients to better understand which situations trigger cravings and overeating, and to learn how to avoid them or respond to them with behaviors other than overeating. People addicted to food often need professional help to improve their ability to cope with unpleasant emotions and to develop better ways of managing stress.

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See Also: Eating disorders; Food cravings.

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Food Additives

"Food additive" is a general term for substances added to food during the manufacturing process. There are three main types of additives: direct, indirect, and color. Direct additives are put in food products intentionally to keep them fresh and give them specific qualities, such as certain tastes or textures. Indirect food additives result from substances unintentionally entering food products during processing, packaging, and transport. Color additives are used to enhance natural color, maintain color despite storage conditions, or give foods a different color.

For centuries, humans have been adding salt, vinegar, and spices to food to reduce spoiling and enhance flavor. Today there are more than 3,000 substances included in the U.S. Food and Drug Administration's database of "Everything Added to Food in the United States" (U.S. Food and Drug Administration, 2013a), which can be accessed through the website (www.FDA.gov). Additives can be

Table 1. Types of Food Ingredients

Purpose	**Additives**	**Examples of products that might contain these additives**
Antioxidants: Preservatives used to prevent food discoloration and spoilage from the breakdown of fats from oxygen exposure.	Ascorbic acid, citric acid, calcium sorbate, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), vitamin E, propyl gallate	Cereal, chewing gum, snack foods, dried fruit
Antimicrobial agents: Preservatives used to prevent mold and fungus growth.	Sorbic acid, sodium benzoate, calcium propionate, salt	Cottage cheese, fruit juice, salad dressing
Artificial and alternative sweeteners: Used to sweeten foods with minimal calories.	Acesulfame K, aspartame, saccharin, sorbitol, stevia, sucralose, tagatose, xylitol	Diet soft drinks, reduced-sugar and sugar-free products
Bleaching agents: Used to whiten foods.	Ammonium chloride, bromates, peroxides	Flour, dairy products
Color: Used to make food look appealing or fun; used to associate a flavor with a specific color.	FD&C Blue Nos. 1 & 2; FD&C Yellow Nos. 5 & 6; annatto extract, beta carotene, grape skin extract, caramel color, saffron	Candy, cheese, vitamins, pickles, yogurt
Emulsifiers: Used to blend substances that frequently do not combine, such as oil and water.	Soy lecithin, monoglycerides and diglycerides, egg yolks, polysorbates	Baked goods, ice cream, mayonnaise, peanut butter
Flavoring and flavor enhancers: Used to give food specific tastes or to enhance flavors already present.	MSH, hydrolyzed soy protein, autolyzed yeast extract, salt, sugar, vanilla, monosodium glutamate (MSG)	Snack foods, soups, sauces, processed meats
Humectants: Used to retain moisture.	Glycerol, propylene glycol, sorbitol	Candy, dried coconut, marshmallows, rice cakes
Leavening agents: Used to make products rise and to achieve specific textures.	Baking soda, monocalcium phosphate, calcium carbonate	Bread, cake, cookies, crackers
Nutrient supplements: Used to enhance the nutrient content of foods. When nutrients are added to make up for those lost in processing, the product has been "enriched." When nutrients are added that were not there initially, the product is called "fortified."	Vitamins and minerals	Bread, cereal, milk, sports bars

Source: Types of Food Ingredients. In *Overview of Food Ingredients, Additives & Colors*, International Food Information Council (IFIC) and U.S. Food and Drug Administration, November 2004; revised April 2010. Retrieved from http://www.fda.gov/food/ingredientspackaginglabeling/foodadditivesingredients/ucm094211.htm

from natural or synthetic sources. Ascorbic acid (vitamin C), for example, can be extracted from citrus fruit, but it is more economical to make it in a laboratory. The table shows some of the more common food additives, why they are used, and examples of products in which they can be found.

Regulation

Food additive regulation varies greatly from one country to another. In the United States, the U.S. Food and Drug Administration (FDA) regulates food additives. When evaluating whether a substance should be approved for use as an additive, the FDA considers the chemical properties of the substance, the typical consumption amount, and the immediate and long-term health effects from consumption. If approved for use, the FDA creates standards for how much can be used and in what foods, and how it should be labeled. In general, the amount of additive allowed in a food product is 100 times less than the amount research animals have consumed with no observable effect. If evidence emerges that an additive in use might not be safe, then the FDA is responsible for conducting studies and, if necessary, preventing further use. On the production end, manufacturers must use additives only for their approved use, and must follow regulations known as Good Manufacturing Practices (GMP) that call for ingredients to be used only in the quantities necessary to achieve the desired effect.

The FDA does not regulate all substances added to food. If a substance is "generally recognized as safe" (GRAS), then it can be used by a manufacturer for its intended purpose without FDA regulation. To be considered GRAS, the substance must have a long history of safe usage in food, or have a body of scientific evidence confirming its safety (U.S. Food and Drug Administration, 2013b).

The safety of some food additives has caused some debate, including those additives regulated by the FDA as well as those considered GRAS. In 1958, the Delaney Clause of the Federal Food, Drug, and Cosmetic Act (named after New York congressman Jim Delaney) stated that no additive could be used that had been shown to cause cancer in humans or animals, even at doses much lower than typical human consumption levels. After numerous amendments, the Delaney Clause was repealed in 1996, and today the FDA considers an ingredient safe for consumption if there is "reasonable certainty in the minds of competent scientists that the substance is not harmful under its intended conditions of use" (U.S. Food and Drug Administration, 2013b).

Health Canada is the federal organization responsible for establishing safety, nutrition, packaging, advertising, and labeling standards for all foods sold in Canada. The Canadian Food Inspection Agency is responsible for enforcing these standards. Food additive approval includes a pre-market evaluation of the product's safety. Food additives must be effective for their intended purpose, and must not cause harm when used as intended. Proposals for new additives are reviewed by scientists from Health Canada. Canada does not have a list of GRAS substances, although the following substances are allowed to be added to foods without

specific regulation: Salt, sugar, starch, vitamins, minerals, amino acids, spices, seasonings, agricultural chemicals, and food-packaging materials.

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Research Issues

- What is the role of the government in regulating what people can and cannot eat?
  - If people want to eat it and businesses want to make it—despite possible risks—should the government allow it?
- How do regulatory agencies decide what is safe for consumption and what is not?
  - How are acceptable daily intake (ADI) amounts determined?
  - In the United States, what is required for a substance to be "generally recognized as safe" (GRAS)? Salt, sugar, and caffeine are GRAS—should they be? Why is refined stevia GRAS, but whole-leaf stevia is not?
  - Why do some countries approve ingredients that other countries do not?
- In 1958, the Delaney Clause was added to the Food, Drug, and Cosmetic Act. It stated that if any food additive was found to cause cancer in humans or animals, its use should not be allowed. In 1996, it was repealed as an archaic law incompatible with modern-day science. What do you think?
- How much and what type of research is needed to determine whether a food or food additive is safe?
  - Is a decade of research enough for a product that might be consumed daily for a lifetime?
  - Who is conducting the research? Some of the scientific studies proving the safety of artificial sweeteners were funded by the very companies who manufacture the sweeteners. Should this be allowed?
  - If a study determines a substance to be carcinogenic in animals, does that mean it will cause cancer in humans?

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See Also: Artificial sweeteners; Dietary supplements; U.S. Food and Drug Administration.

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Food Allergies and Intolerances

Food allergies involve activation of a type of immune response that, in some cases, can lead to life-threatening symptoms, a condition known as "anaphylaxis." People with severe food allergies, for example, can experience swelling of the throat and airways when they consume the offending food, making it difficult to breathe. Food intolerances are different from food allergies in that they do not involve the type of immune response that can lead to life-threatening symptoms. A food intolerance refers to a situation in which the ingestion of a certain food or food ingredient creates uncomfortable symptoms, often in the digestive tract, such as bloating or diarrhea. The most effective strategy for treating food allergies and intolerances is to identify and avoid the problematic foods. Digestive enzymes and other medical treatments might be available for some food intolerances. People who experience severe food allergies must carry medication, usually epinephrine, which is quickly injectable and can help counter the life-threatening symptoms of food allergies.

Food allergies affect about 4% of adults and about 5% of children in the United States; this number has increased significantly over the last decade (NIAID, 2012). Peanut allergies, for example, have tripled in the past 15 years (Slomski, 2012). It is unclear whether more diagnoses are being made as a result of increased knowledge or as a result of an actual increase in allergy frequency; it is also possible that some diagnoses are incorrect. Food intolerances affect a much greater number of people. Prevalence is difficult to estimate, because many people are never tested and instead simply avoid certain foods.

Food Allergies: Causes and Symptoms

A food allergy involves an adverse immune-system reaction to a food or component of food, usually a protein. There are several different ways in which the immune system can create an allergic response to food molecules. The most dangerous type of food allergy involves the production of an antibody known as

Food Allergy: Pregnancy, Breast-Feeding, and Introducing Your Baby to Solid Foods

Health care experts do yet not have enough conclusive evidence to tell pregnant women, nursing mothers, and mothers of infants how to prevent food allergies from developing in their children. It's essential to talk with a health care professional before changing your diet or your baby's diet. Health care experts, however, do know the following.

Pregnancy

- Pregnant women should eat a balanced diet.
- If allergic to a food, a pregnant woman should avoid consuming it.
- Pregnant women who have no food allergies—such as egg, tree nuts, peanut, fish, or cow's milk (all highly allergenic)—should not avoid them. There is no conclusive evidence that avoiding these foods will prevent food allergy from developing in an infant in the future.

Breast-Feeding

- Health care experts recommend that mothers feed their babies only breast milk for the first 4 months of life because of the health benefits of breast-feeding.
- Mothers who breast-feed do not need to avoid foods that are considered to be highly allergenic because there is no conclusive evidence that avoiding these foods will prevent food allergy from developing in their infants.

Introducing Solid Foods

- Health care experts in the United States currently suggest that you do not introduce solid food into your baby's diet until the baby is 4 to 6 months old.
- There is no conclusive evidence, however, to suggest delaying the introduction of solid foods after the baby 4 to 6 months old.
- There is no conclusive evidence to suggest delaying the introduction of the most common potentially allergenic foods (milk, egg, peanut) after the baby is 4 to 6 months old. Such delays will not prevent a child from developing an allergy in the future.

National Institute of Allergy and Infectious Diseases (NIAID). (2012, July 1). *Food allergy: An overview.* Retrieved from http://www.niaid.nih.gov/topics/foodallergy/documents/foodallergy.pdf

immunoglobulin (IgE). For reasons not yet understood, initial ingestion of the food allergen causes the body to mistakenly produce immunoglobulin antibodies to that particular food component. These antibodies then circulate in the bloodstream and attach to mast cells and basophils. Mast cells are located in all areas of the body, especially the respiratory system, the skin, and the gastrointestinal track. Basophils are found in the blood and in areas inflamed by an allergic reaction. When the food allergen is subsequently ingested, it binds to the immunoglobulin antibodies which

then trigger the mast cells and basophils to release large amounts of chemicals called "histamine." Histamine triggers the inflammation and swelling associated with an allergic response.

In most cases, an immunoglobulin-mediated food allergy develops within an hour after eating the food. The consumer often notices common symptoms, such as hives, itching, skin rashes, swelling of the face or throat, wheezing, congestion, trouble breathing, abdominal pain, diarrhea, nausea, vomiting, dizziness, lightheadedness, and fainting (Food and Drug Administration, 2013). A severe allergic reaction is called "anaphylaxis" and it produces life-threatening signs and symptoms such as swelling of the throat, shock, a drop in blood pressure, irregular or rapid pulse, and loss of consciousness. Anaphylaxis is potentially fatal.

Less-severe food allergies can be mediated by other types of immune responses. For example, immunoglobulin-mediated food allergies tend to develop more slowly with milder symptoms. Immunoglobulin-mediated responses might not be detected with standard diagnostic testing.

Food Allergies: Diagnosis and Treatment

To diagnose food allergies, health care providers might use a detailed history, an oral food challenge, an elimination diet, or skin or blood tests. The most reliable test for the diagnosis of a food allergy is to observe the symptoms that develop after a person has consumed a given food. This test is called an oral food challenge. Patients consume the potentially problematic food in increasing amounts, and alternating with placebo components, so that patients do not know when they are consuming the problem food. (It is possible to experience allergic reactions simply because one believes one has ingested a certain food, even when the food has not actually been ingested.) Because patients might develop a severe allergic response, many providers will not administer this test. In some cases, however, it is administered by experienced professionals in an environment that can provide immediate treatment should a severe reaction develop.

Elimination diets can take a variety of forms. The basic goal is to observe a person's response to a diet lacking—then later including—the potential food allergen. If allergic symptoms go away or do not appear when the food is absent, but appear when the food is added back into the diet, providers and patients can discover which foods are problematic. Elimination diets are not recommended for severe allergies, but can be helpful for milder food allergy symptoms.

Skin and blood tests measure levels of immunoglobulin antibodies, but can over-diagnose true allergies. This is because immunoglobulin antibodies could be present, but this does not indicate that a patient will develop a full-blown allergic response. Skin tests are rapid and usually are less expensive than a blood test. Two types of skin test commonly are used, the skin prick test and the intradermal test. The skin prick test is done by adding a drop of the alleged allergen onto the skin's surface which is either scratched or has a series of needle-pricks in it for the solution to enter. If the skin welts then the patient has a positive reaction and is allergic to the allergen. The intradermal test is done when the allergen did not test positive

during the skin prick test, but is still thought to be the suspect. The intradermal test is a much more sensitive test. The allergen is injected right into the skin which is then observed for signs of irritation. The blood tests look for antibodies and generally are performed on patients who can't have skin tests.

The most reliable treatment for suspected food allergies is to avoid problematic foods. Some research has focused on training a person's immune system to tolerate an allergenic food by introducing very small amounts of allergens in a controlled environment over time (Slomski, 2012). Oral immunotherapy has the person eat a small portion of the food, and sublinguinal immunotherapy introduces microscopic amounts of the food (for example 1/100th of a peanut) under a person's tongue. Such therapies still are in the experimental phase, and must be administered in a controlled environment where medical treatment is available in case of a severe allergic reaction.

Anaphylaxis: A Medical Emergency

It is important for people with allergies to be prepared for unexpected exposure. They should wear a medical alert bracelet stating the possibility that they might have a severe allergic reaction; carry an auto-injector device that contains epinephrine; and seek medical help immediately if they experience allergic reactions.

Food allergies are particularly prevalent in children; therefore, food allergies are of particular concern in the school environment. Almost 20% of children with food allergies have had allergic reactions after accidentally ingesting food allergens at school. Up to 25% of anaphylaxis reactions in school occur in children who were not previously diagnosed with a food allergy (Centers for Disease Control and Prevention, 2013). It is vital that school personnel are ready to manage students with known food allergies and those who have not been diagnosed with any food allergy.

Common Allergens and Food Labeling

Eight foods account for 90% of all allergens in the United States: milk, eggs, peanuts, tree nuts (almonds, walnuts, pecans), soybeans, wheat, fish, and shellfish (crab, lobster, shrimp) (U.S. Food and Drug Administration, 2013). A major food allergen is defined as any one of the eight foods listed above or an ingredient that contains protein derived from the allergen food groups.

In 2004, the U.S. Congress passed the Food Allergen Labeling Consumer Protection Act (FALCPA), which went into effect in 2006 to protect those with food allergies. Under the FALCPA, food labels are required to clearly name the allergens in the list of ingredients, and state in a list beneath the ingredients whether a food contains one of the major eight food allergen (Food and Drug Administration, 2013).

Soon after the implementation of FALCPA, food labeling was revised to take into account possible allergen contamination of products because of cross-contact, when an allergen not normally present in a food product can accidentally be

included in the product. Cross-contact can occur during harvesting, transportation, manufacturing, processing, or storage (Food and Drug Administration, 2013). To account for cross-contamination, labels now include statements such as "produced in a plant that processes wheat" or "may have come in contact with nut products." These advisory statements do not substitute for adhering to current and good manufacturing practices, and are required to be truthful and not misleading (Food and Drug Administration, 2013).

Food Intolerances

Food intolerance symptoms include intestinal gas, abdominal discomfort, diarrhea, hives, headaches, and irritability and usually come on gradually. These symptoms can result from an absence of an enzyme needed to fully digest a food, irritable bowel syndrome, food poisoning, sensitivity to food additives, reoccurring stress, and psychological factors (Li, 2013). Food intolerances include reactions to certain products that are added to foods to enhance the taste, add color, or protect against the growth of microbes. Food intolerances can be very uncomfortable but they are not immediately life threatening. Because symptoms of food intolerances often overlap with those of food allergies, people who experience such symptoms could benefit from allergy testing to rule out the possibility of a severe reaction. Two of the most common food intolerances include lactose intolerance and celiac disease.

Lactose is a sugar found in milk. Lactase is an enzyme in the lining of the gut that breaks down or digests lactose; when this enzyme is absent a person has lactose intolerance. The lactose stays in the digestive tract, producing a variety of digestive symptoms. Once it passes into the colon, it is broken down by bacteria, producing intestinal gas in this fermentation process.

Celiac disease is a food intolerance that elicits a unique physical response. Celiac disease, or gluten sensitive enteropathy, is an inherited condition that is triggered by foods containing gluten, and is present in about 1% of the population. People with celiac disease have an immune system that reacts negatively to the presence of gluten in the diet, but this response is not of the same nature as a typical allergic reaction, in that the immune system attacks the cells lining the small intestine, rather than stimulating anaphylaxis. Symptoms of celiac disease include abdominal pain, gas, bloating, diarrhea, constipation, malnutrition, fatigue, and weight loss. The damage to the inner lining of the small intestine reduces the ability of a person to absorb nutrients. If the symptoms are caught early enough and the person starts consuming a gluten-free diet, then the damaged tissues can heal. Diagnosis can include blood tests and a biopsy of the small intestine. Though food intolerances can provoke uncomfortable symptoms and bodily responses, they can usually be managed.

Mild forms of food intolerance often are referred to as "food sensitivities." People with food sensitivities find that certain foods "disagree" with them. They might feel that they have difficulty digesting the food, and they get a stomachache after eating it. People who have been on low-fat diets, for example, might find that

eating a high-fat food such as quiche, french fries, or a fatty burger disagrees with them and feels heavy and uncomfortable in the stomach. Although food sensitivities are milder than food intolerances, food sensitivities can be problematic for some people.

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Research Issues

Researchers and clinicians are trying to understand why the prevalence of allergies is increasing so rapidly. Several theories have been proposed. It might be that people are more aware of the potential danger of severe allergic reactions, and are more likely to seek medical advice when they experience minor food-allergy symptoms; thus, more people are diagnosed. Similarly, clinicians might over-diagnose food allergies, thinking that it is better to avoid a severe allergic response even if this results in several incorrect diagnoses (telling people that they might have a food allergy, when they actually do not). Diagnostic skin and blood tests also can be somewhat unreliable.

The hygiene hypothesis speculates that the rise in the prevalence of allergies could be the result of an environment that contributes to a "confused" immune system. The hygiene hypothesis is based on the observation that allergies are more common in resource-rich countries and urban environments, and that people in poorer countries and rural environments have fewer allergies. The hypothesis suggests that the immune system functions best in an environment with a certain environmental bacterial mix, such as that found on a farm. Because people use antibacterial products, frequently take antibiotics for illness, and avoid contact with microbes, this "hygiene" might deprive the immune system of the stimulation it requires to correctly discriminate between dangerous and harmless proteins and other substances.

Some studies suggest that changes in infant feeding practices might increase allergy risk. The introduction of formula-feeding and the delayed introduction of potentially allergenic foods into an infant's diet both have been explored as possible explanations for the increase in allergy diagnoses.

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See Also: Celiac disease; Digestion and the digestive system; Lactose intolerance; Microbiota and microbiome.

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Food Cravings

Food cravings can be defined as the overwhelming desire to consume a particular kind of food. People report that food cravings feel uncomfortable, in that the craving dominates a person's awareness until it either is satisfied or it passes. Research suggests that the brain reward circuitry response involved in food cravings is similar to that involved in drug cravings and addiction. Food cravings can range from mild to severe. Food cravings are not necessarily a problem if the craved food is obtainable and if eating it has no negative repercussions. If a person really wants a little cheese, for example, then he or she can eat a few small pieces of cheese and the craving is satisfied. Food cravings become problematic, however, for people who are trying to avoid overeating or who are restricting their food intake to lose weight. Many people report that food cravings can interfere with concentration and distract them from other activities. For some people, especially those with eating disorders, food craving can stimulate binge-eating behaviors that are experienced as distressing and uncontrollable. People tend to crave "forbidden" foods that are high in fat, sugar, and salt.

What Causes Food Cravings?

Researchers who have asked volunteers to record and analyze their food cravings think that a craving typically begins with thoughts about a particular food, often triggered by seeing the food or remembering something about eating the food. A person then might begin to focus on how good that food tastes or other positive associations about that food. Thinking about the food leads to an emotional "need" for it which then develops into an urge to obtain and eat that food. This explains why some people eat in response to viewing advertisements for food.

What determines which food is the object of a craving? There is little evidence to support the notion that people crave foods that supply a nutrient in which they have a deficiency. More likely, the food is associated with positive feelings in some way. Chocolate, for example, has chemicals that make some people feel good.

Similarly, carbohydrates help some people feel more relaxed. Cravings probably evolve from past experiences—both psychological and physiological—with the consumption of specific foods. For some people food cravings can trigger episodes of emotional overeating—a leading cause of obesity. Emotional overeating occurs when people eat to reduce emotional pain and relieve negative feelings.

Restrictive dieting can cause food cravings for several reasons. People are more likely to be drawn to foods categorized as "forbidden," because it seems to be human nature to want what one cannot have. Additionally, after following a bland diet for several days, people often begin to crave more flavorful foods, such as pizza. This is why nutrition professionals encourage people to see that all types of food can be included in a diet—if the food is consumed in reasonable portions and in the context of an otherwise well-balanced diet.

People also are more likely to experience food cravings when they are hungry. The hunger signal can evolve into a focus on a particular food. Restrictive diets also can make people feel stressed, grumpy, anxious, and depressed. These are the very emotions that can trigger the need for comfort foods—a need that can turn into cravings that increase the risk of emotional overeating.

Gender and Cultural Influences

Which foods are craved varies from culture to culture. Women in North America most commonly report craving chocolate, for example, and the most frequently craved food for women in Japan is sushi. In general, in North America women report experiencing more food cravings than men do. The causes for this difference can be complex. Women report experiencing more food cravings when they are premenstrual (a few days before the beginning of the menstrual cycle) and during the first few days of their periods than they experience at other times during the month. Researchers do not know whether hormonal changes cause different levels of hunger, or whether mood changes accompanying the menstrual cycle could be the motivating factor. In addition to the monthly hormone cycles, women are more likely than men to be restricting food intake and to feel hungry, factors that appear to stimulate food cravings. Food cravings also can increase during pregnancy. Although energy requirements do increase during pregnancy, scientists cannot explain why particular foods are craved.

Coping with Cravings

When eating a small portion of the craved food is not an option—because it tends to lead to overeating—exercise and mindfulness could be helpful. One interesting study suggests that exercise might help reduce cravings and consumption of craved foods, at least for chocolate (Oh & Taylor, 2011). Subjects were regular chocolate eaters who walked for 15 minutes or rested and were then given either a stressful task or an easier one. Throughout the tasks, chocolate was freely available. All volunteers had been deprived of chocolate for two days prior to the experiment, so cravings presumably were aroused. The subjects who exercised ate about half as much chocolate during the tasks as the subjects who did not.

Observations from alcohol addiction research might be applicable to food cravings. Researchers Ostafin and Marlatt encourage people in recovery and abstaining from alcohol to "surf the urge" (Ostafin & Marlatt, 2008). Many people fear that their feelings of craving will continue to increase—getting worse and more uncomfortable. According to Ostafin's and Marlatt's research, experiences of cravings actually rise and fall. The feeling of craving grows, then diminishes. When people become anxious about the craving, they feel much worse. The researchers advise people to allow themselves to mindfully observe and experience the craving, noticing the events, feelings, and thoughts that occur with the craving. Being "present" in the experience can make it less anxiety provoking. People who "surf the urge" usually observe that the craving gradually becomes less intense. Over time, the intensity of cravings tends to diminish as well (Ostafin & Marlatt, 2008).

One research study found that this theory did apply to a group of self-defined chocolate cravers (Moffitt, Brinkworth, Noakes, & Mohr, 2012). Ninety-four women and 16 men were randomly assigned to one of three groups: Wait-list control (for comparison purposes), cognitive restructuring, or cognitive defusion. The cognitive restructuring group was trained to become aware of unhelpful thoughts associated with food craving and change them to more helpful thoughts. If they found themselves thinking, "I want some chocolate," for example, they might reply to themselves, "I do not need chocolate. I can choose something more nutritious to eat." The cognitive defusion group similarly observed thoughts that were associated with food cravings, but instead of trying to change them, they simply acknowledged them and observed their thoughts and feelings. In response to the "I want some chocolate" thought, for example, they would think, "I notice I am having the thought that I would like to eat some chocolate."

All subjects carried bags of chocolate with them. At the end of the study the researchers compared how much chocolate was eaten by each group. The cognitive defusion group was more than three times as likely to abstain from eating chocolate as the cognitive restructuring group. Subjects reporting the most distress about cravings showed the most differences between groups (favoring the cognitive defusion training). In addition to eating less chocolate, the subjects in the cognitive defusion training group reported greater improvements in other eating behaviors and less distress regarding chocolate cravings.

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Research Issues

Very restrictive dieting in which certain foods or food groups—such as carbohydrates—are severely limited or prohibited is associated with a number of problems. One problem is the development of, or increase in the frequency and strength of, food cravings. Other problems include difficulty following the diet; rapid weight regain when the diet is stopped; and a decrease in resting metabolic rate if calorie intake is very low. Yet restrictive diets remain very popular. It is interesting to evaluate fad diets in the media, and to examine how restrictive they are, and whether they might lead to uncomfortable food cravings.

See Also: Chocolate; Cognitive restructuring; Food addiction.

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Food Gardens

A food garden is an area where a variety of fruits, vegetables, and herbs are planted, cultivated, and harvested for the purpose of relatively small-scale consumption. A food garden often is planted on a section of land, but it can also consist of raised beds, where food is grown in soil placed in boxes or other containers. Food gardens should be distinguished from more expansive fields or farms, the purpose of which nearly always is to feed larger masses of people a somewhat more limited variety of crops. Involvement with farm-based food growth has declined in the United States and Canada over time. The number of citizens farming in these two countries has dropped from more than 30% of the workforce a century ago to less than 2% today (National Institute of Food and Agriculture, 2011; Statistics Canada, 2009). The popularity of small-scale, home-based food growth has been on the rise in recent years, however, with many people beginning a garden for the first time (Butterfield, 2009). At present, the practice is fairly common; an average of approximately 36 million households in the United States maintain gardens each year (Butterfield, 2009).

Victory Gardens

Over the past century, food gardens have been especially popular during periods of national turmoil, partly because of the food shortages sometimes affiliated with such tumultuous times. During World War II, for example, the United States faced a possible national food shortage, and many people began growing so-called victory gardens. These were vegetable gardens planted to assure adequate food



First Lady Michelle Obama, with Assistant White House Chef Sam Kass and students from Bancroft and Tubman Elementary Schools, works in the White House's organic kitchen garden on October 20, 2010. The first lady uses the garden to teach children the importance of nutrition and the value of eating locally grown food. (The White House)

availability for both civilians and the troops. In 1943, when the United States entered WWII, the U.S. president and first lady actively encouraged the installation of victory gardens across the United States. In addition to First Lady Eleanor Roosevelt's decision to install a victory garden at the White House, President Roosevelt himself issued a mid-war statement emphasizing the necessity of such gardens.

> I hope every American who possibly can will grow a victory garden this year. We found out last year that even the small gardens helped. The total harvest from victory gardens was tremendous. It made the difference between scarcity and abundance. The Department of Agriculture surveys show that 42 percent of the fresh vegetables consumed in 1943 came from victory gardens. . . . Because of the greatly increased demands in 1944, we will need all the food we can grow. Food still remains a first essential to winning the war (Roosevelt, 1944).

Throughout the war, millions of various-sized victory gardens sprouted up in every corner of the nation, providing food for those who might have gone hungry and giving a sense of community to those who otherwise would have been left to cope with the coast-to-coast crisis alone.

Michelle Obama: Gardening and Health

After the war, White House food gardens of any substantial size were discontinued until 2008, when then-new First Lady Michelle Obama expanded Roosevelt's original blueprint and installed the first food garden at the White House in more than a half century (Burros, 2009). Mrs. Obama's garden was built for an entirely different reason than Mrs. Roosevelt's, however. Mrs. Obama's goal was to encourage healthy eating habits across a country in which growing rates of obesity were harming citizens' health. Coupling the revamped White House gardens with her overall campaign to help reverse the nation's growing obesity epidemic, Mrs. Obama particularly focused her outreach on a number of populations in which weight-related problems are especially high, including low-income and African-American communities. Her message: Homegrown foods are a relatively simple and cost-effective option, given the proper tools and education, for individuals seeking to revolutionize their family's—or their nation's—consumption patterns. In 2012, Mrs. Obama published a book, *American Grown: The Story of the White House Kitchen Garden and Gardens Across America,* discussing the White House gardens and promoting the idea that attaining healthier eating styles through home food gardening is an attainable and sustainable goal to pursue nationwide.

Motivations for Raising Food

Mrs. Obama's publicly touted experience with food gardening is both a hopeful gesture toward improving the health of vulnerable groups and a testament to the already changing landscape of food growth and consumption in North America. Of course, people have had food gardens for centuries, and those living in areas where farming is important and the soil is good have long planted and nurtured these gardens, whether living on a farm or in town. During the past several decades, however, food gardens have played new roles in the lives of many Americans. Although some gardeners still are concerned about food scarcity, most North American gardeners grow food to improve their health and quality of life. According to a Harris Poll conducted by the National Gardening Association, top reasons for gardening include to have better tasting food, to save money on food bills, to have better-quality food, and to grow food known to be safe (Butterfield, 2009). For some people gardening has become a much needed way to achieve the daily exercise necessary for long-term health; for others, gardening has come to provide a vital new means to control their food intake in ways that depart from the growing norm of mass-produced processed foods. Many people garden to obtain healthy organic foods without paying the high prices for comparable foods at grocery stores.

Community Gardens

Particularly in urban and suburban areas, aptly named "community gardens" have become increasingly popular and more widely supported in recent years. Such

gardens involve large, staked-out areas of crop-hospitable land in which those who wish to grow food away from their own properties can buy or rent a plot of community land for the duration of a growing season. Community gardeners often begin gardening to gain access to fresh food and enjoy being outdoors. The promise of community, however, is what many later assert as their main reason for deciding to sustain the practice over the course of several growing seasons or years. The prospect of connection-by-garden is the prime motivator for many in the quickly expanding ranks of newly arrived immigrants to the United States, who frequently use community gardens to forge new connections while working to maintain cultural traditions (Twiss et al., 2003). Some schools also have begun to plant gardens not only to show students—whether from inner cities or the suburbs—how certain fruits and vegetables originate and grow, but also to encourage better, more tasty and nutritious eating habits.

Social Movements and Food Gardens

Common motivations often bind food gardeners together. The promotion of food gardens is a central focus of many social movements. Movements promoting sustainable agricultural practices value food gardens as a way of producing food that consumes fewer natural resources than traditional farming practices. Similarly, the locavore food movement, which encourages people to consume as much food as possible from locations relatively close to their homes, values home food gardens for similar reasons. The Slow Food movement was formed in opposition to the spread of fast food, and the eating style and agricultural practices associated with the production of fast food. The Slow Food movement believes food gardens further its mission, promoting the pleasure of good food and encouraging people to enjoy local food in season.

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Research Issues

Many schools have begun food-garden programs aimed at teaching youths to recognize, value, and eventually grow a wide variety of fruits and vegetables. Initial studies indicate that such focused instruction tends to increase students' knowledge of the foods on their dining tables and subsequently enhances their desire to consume healthier foods (Somerset, 2008). The eventual goal of these school-based campaigns is to transform the North American diet starting from the ground up—literally and figuratively—by giving young people the very basic tools they need to create, and sustain, more healthful eating patterns. Many people enjoy investigating gardening efforts in their local communities, interviewing gardeners and those involved in community gardening projects. In many schools, students have been the organizing force behind school gardens, initiating garden projects that serve as a laboratory for science and nutrition classes as well as a source of fresh produce.

See Also: The locavore movement; Organic food and farming; Slow Food movement; Sustainable agriculture.

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Food Security and Food Insecurity

"Food security" is the extent to which all individuals have access to adequate safe and nutritious food to maintain a healthful lifestyle. The Rome World Food Summit of 1996 defined the term as a right of all people in its Declaration on World Food Security. Attended by representatives from 185 countries, the summit's resulting Declaration and Plan of Action were adopted with aims to meet global nutritional needs. Specific dietary needs and food preferences, including culturally appropriate foods, must be available as part of a food secure environment. Food security also considers the appropriate use of food including level of basic nutrition knowledge and sufficient water and sanitation.

The primary obstacles to sustaining a food secure environment are poverty and the inability to maintain lasting peace. Strategies for fostering food security include implementation of policies that improve physical and economic access to food, as well as policies that support sustainable agriculture, fishery, and forestry practices. Further, preparation for natural disasters and other states of emergency ensure that resources are allocated and preserved in a manner that facilitates food security.

In the United States, different levels of food security have been described in detail by the U.S. Department of Agriculture (USDA), from very low to marginal to high food security. Characteristics of a household with very low food security include adults who have lost weight, are hungry but do not eat, or have not eaten for an entire day. These homes are marked by reduced and disrupted eating habits due to lack of resources. In 2011, the Economic Research Service determined that 85.1% of households in the United States were food secure, and 5.7% experienced very low food security at some point in the year (Coleman-Jensen, Nord, Andrews, & Carlson, 2012).

In Canada, Health Canada measures food security. Not all provinces administer the questionnaires each year. The most recent data for the country as a whole come from 2008. At that time, 92.3% of Canadians were food secure, and 2.7% were severely food insecure (Health Canada, n.d.). (It should be noted that the United States and Canada use different questionnaires, thus the data are not directly comparable.)

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Research Issues

Every country in the world has concerns about food security for at least part of its population. The World Health Organization (WHO) studies food security in all nations and examines the many variables associated with food security. The WHO urges countries to consider its citizens' food security in decision making on major policy issues. Trade regulations, for example, can affect how much local agricultural produce is available to a country's citizens versus how much is exported. Similarly, trade agreements might or might not ultimately provide better access to food for the country's population, for example, by influencing standard of living.

See Also: The poverty-obesity paradox; Supplemental Nutrition Assistance Program; Women, Infants, and Children, Special Supplemental Nutrition Program for.

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Foodborne Illness and Food Safety

Foodborne illness, or "food poisoning," generally refers to sickness caused by consuming food that is contaminated by microorganisms, chemicals, and other substances hazardous to human health. People with foodborne illness often experience nausea, vomiting, diarrhea, and fever and the illness can take from minutes to weeks to develop. Because of its common symptoms and sometimes slow onset, many people do not recognize the actual cause of their sickness. Most cases of foodborne illnesses are mild and resolve without treatment, but some severe cases require hospitalization and sometimes cause deaths. According to the U.S. Department of Agriculture, preventable foodborne illnesses cause an estimated 48 million cases of sickness (one in six Americans) and 3,000 deaths each year in the United States, posing a serious challenge for public health (CDC, 2012).

Everyone is at risk of getting foodborne diseases. Many people, such as infants, young children, pregnant women, older adults and people with compromised immune systems, however, are at greater risk of experiencing more serious symptoms—and even death—once they become sick. According to USDA, foodborne sickness affects people so differently that some people can become seriously ill after ingesting only a few bacteria and others remain symptom-free even if they ingest thousands. Today, foodborne diseases can develop anywhere from the factory where the food is being produced and manufactured to the home kitchen where food is prepared and consumed. Some of the most common foodborne pathogens include the following.



Listeria bacterium. Listeria monocytogenes is the microorganism responsible for listeriosis. The bacteria is found in soil, water, and animal feces. In the food supply, it is most commonly acquired from raw milk and soft cheeses. (Centers for Disease Control and Prevention)

Norovirus

Noroviruses are the most common cause of foodborne illness in the United States (CDC, 2013d). Noroviruses cause inflammation of the stomach and intestines, a condition known as gastroenteritis. Symptoms include diarrhea, vomiting, nausea, stomach pains and sometimes headaches. These symptoms usually go away within several days without treatment, but they easily can cause severe dehydration and infected people could require medical attention—especially infants, older adults, and people with other

illnesses. Noroviruses are highly contagious through food and feces, and cause illness more rapidly in closed and crowded environments such as hospitals, schools, nursing homes, and cruise ships. Norovirus illnesses can be acquired through eating food contaminated with norovirus, contact with the feces of infected persons, and or even touching the surface of a contaminated object.

Each year norovirus causes between 19 and 21 million cases of acute gastroenteritis and contributes to from 570 to 800 deaths (CDC, 2013d). Norovirus illness can happen any time of the year, but especially in winter. Any food that is served raw or handled after being cooked can contain norovirus, particularly leafy greens, fresh fruits, and shellfish. There is no specific treatment for people infected with norovirus, but drinking water and sports beverages (without alcohol or caffeine) can alleviate the dehydration. People can acquire norovirus repeatedly because there are many different types of viruses.

Salmonella

Salmonellosis is a common intestinal infection caused by the bacteria salmonella, and affects all age groups. It is estimated to cause approximately 1 million cases of foodborne illness and almost 400 deaths annually (CDC, 2012a). Symptoms include fever, vomiting, abdominal pain, and diarrhea, and generally resolve in around five to seven days. Long-term effects of salmonellosis include abnormal bowel movement for months and reactive arthritis, or joint pains, eye irritation, and painful urination. In severe cases—primarily in infants, older adults, and people with compromised immune systems—the infection can move from the gastrointestinal (GI) tract into the blood stream and to other organs of the body, and even cause death if not treated promptly with antibiotics.

Salmonella lives in the intestinal tract of humans, animals, and birds. Infection usually is caused by eating raw or undercooked meat, poultry, or eggs contaminated with the feces of animals harboring these bacteria. Antibiotics generally are not prescribed unless the infection has spread from the GI tract. Industrial use of antibiotics to promote weight gain in livestock has resulted in antibiotic resistance of some salmonella strains. The risk of contracting salmonellosis can increase when travelling abroad to countries with poor sanitation, when living in group housing, and even when owning a pet.

Escherichia Coli (E. Coli)

Escherichia coli (E. coli) is a group of usually harmless bacteria that live in human and animal intestines. A group of Shiga toxin-producing E. coli (STEC), however, can produce severe illness marked by bloody diarrhea, kidney failure, and sometimes even death. The most common E. coli bacteria in North America is STEC O157:H7. Symptoms of E. coli infection include stomach cramps, often bloody diarrhea, vomiting, and low fever, and usually go away within five to seven days. Severe cases can be life threatening. Approximately 5% to 10% of people infected with STEC develop hemolytic uremic syndrome (HUS), a potentially

life-threatening form of kidney failure that develops about a week after infection (CDC, 2012b). The symptoms of HUS include less frequent urination, dark urine, and facial pallor. E. coli–infected persons usually get better in six to eight days.

Escherichia coli is spread via fecal matter and most commonly is caused by contaminated food, such as ground beef, unpasteurized milk, restaurant meals, contaminated water, and personal contact with animals and the feces of infected persons. In the case of E. coli O157:H7, no current treatment can cure the infection and relieve complications. Most people are advised to rest and increase hydration; antibiotics and anti-diarrheal agents should be avoided as they might increase the development of HUS (CDC, 2012b). People with severe cases should seek medical attention.

Clostridium Perfringens (C. Perfingens)

One of the most common causes of foodborne illness is *C. perfringens*, a bacterium found in the intestine of humans and animals. It is estimated to affect nearly one million Americans annually (CDC, 2014a). It causes food poisoning by producing spores that can survive in high temperatures and germinate—producing bacteria—during the cooling process. The most common food sources include beef, poultry gravies, and dried and precooked food, especially food that is cooked and kept warm for a long time before serving. As a result, outbreaks usually happen in large institutions like schools, cafeterias, and hospitals, and from catered food.

The bacteria produced by the spores produce a toxin that causes illness. Symptoms include diarrhea and abdominal pains, but no fever or vomiting, and usually last less than 24 hours; but severe cases can last up to two weeks. The infection is not contagious but older adults and infants are especially at risk. Infected persons should keep hydrated and seek medical assistance if dehydration occurs. Food associated with *C. perfingens* should be cooked thoroughly to recommended temperatures and be kept at a temperature that is either warmer than 140°F or cooler than 41°F (CDC, 2014a). Food should be served hot and perishable food should be refrigerated within two hours and heated before consumption.

Campylobacter

Campylobacteriosis, one of the most common causes of diarrheal illness in the United States, is caused by the bacterium campylobacter. It most commonly is acquired from raw and undercooked poultry, unpasteurized milk, and contaminated water. It is spread through fecal matter, but also can be acquired from the milk of infected cows. It is estimated to affect more than 1.3 million people in the United States each year, and approximately 76 people die annually from this illness (CDC, 2013b). Symptoms of campylobacteriosis include bloody diarrhea, cramping, abdominal pains, and fever. It usually resolves in one week without treatments, although some infected people might not experience any symptoms at

all. Campylobacter can spread to the bloodstream and cause life-threatening symptoms for people with compromised immune systems. Preventive measures include cooking poultry meats to safe minimum temperature, separating raw meat, and avoiding unpasteurized milk.

Clostridium Botulinum (C. botulinum)

Foodborne botulism is a rare but serious disease caused by the ingestion of the neurotoxin C. botulinum, often found in improperly processed canned foods. Clostridium botulinum is one of the most toxic substances known, causing around 145 cases of botulism annually in the United States, of which 15% are foodborne (CDC, 2014d). Symptoms of botulism include double vision, drooping eyelids, slurred speech, difficulty swallowing, and muscle weakness. In rare cases, death can result from failure of the respiratory muscles, but people usually are treated in time with an antitoxin now medically available, and with respiratory support.

Clostridium botulinum neurotoxin is prevalent in soil and marine sediments, and its spores can be found on the surface of fruits, vegetables, and seafood. This neurotoxin can be killed in boiling water, but its spores continue to thrive under low-oxygen conditions, such as during the canning process. Clostridium botulinum cannot grow below the pH of 4.5, therefore most acidic food, such as most fruits, tomatoes, and pickles can be processed at home safely. Food with higher pH values, however, should be processed using a pressure cooker. Preventative measures include using approved processes for home canning, discarding spoiled canned food, and boiling home-processed canned food for more than 10 minutes before serving (USDA, 2011).

Listeria Monocytogenes

Listeriosis is a serious infection that results from ingesting food that contains the bacterium listeria monocytogenes, most often present in raw food, soft cheeses, processed meat, unpasteurized milk, and smoked seafood. Each year, listeriosis affects approximately 1,600 people in the United States—primarily older adults, pregnant women, newborns, and people with weakened immune systems—causing about 260 deaths per year (CDC, 2014b). Infection during pregnancy will result in fever, fatigue, and aches, and possibly lead to miscarriage, stillbirth, or life-threatening infections in newborns. Other people might experience fever, headache, loss of balance, and convulsions.

Shigella

Shigellosis, also known as "bacillary dysentery," is an infectious disease caused by acquiring the bacterium shigella, found in the stools of an infected person. It can be acquired by eating vegetables grown in infected sewage or soils, contact with infected persons, and consuming contaminated food. Shigella also can be

found in water contaminated by sewage. Symptoms of shigellosis include diarrhea, fever, and stomach cramps and usually resolve in five or seven days. In healthy people, symptoms often are relatively mild, so the number of people who become infected each year is unknown; about about 14,000 cases are reported each year in the United States (CDC, 2013c).Young children might develop seizure and high fever in severe cases. Shigellosis can be prevented by good hygiene, especially after using the bathroom and changing soiled diapers. Shigellosis often occurs in high numbers in communities with poor sanitary conditions.

Staphylococcus Aureus

Staphylococcus aureus is a common bacterium found in the nose and on the skin of up to 25% of healthy people; its toxins are salt resistant and cannot be destroyed by heat (USDA, 2011). Staphylococcal food poisoning is a gastrointestinal disease that is acquired through contact with food workers with the bacterium and by eating contaminated food. Common sources of contamination are milk, cheese, sliced meat, puddings, some pastries, and sandwiches. Symptoms such as nausea, vomiting, stomach cramps, and diarrhea develop within one to six hours of consuming the contaminated food. Mild cases usually resolve in one to three days. Preventative measures include good hygiene; avoiding cooking when eye or nose infections are present; and refrigerating food properly.

Vibrio Vulnificus (V. Vulnificus)

Vibrio vulnificus is a bacterium that lives in warm seawater. Seafood contaminated with V. vulnificus can cause vomiting, diarrhea, and abdominal pains. For persons with chronic liver illness, it can infect bloodstream and cause fever and chills, blistering skin lesions, and septic shock (USDA, 2011). To prevent V. vulnificus infection, avoid eating raw oysters and other shellfish, cook shellfish thoroughly, avoid cross-contamination with raw seafood, and store leftovers properly in a refrigerator.

Hepatitis A

Hepatitis A is a highly contagious liver infection caused by the Hepatitis A virus. Symptoms might not occur until one month after exposure, and include jaundice, dark urine, fatigue, low-grade fever, and pale or clay-colored stools (CDC, 2014c). This infection most commonly is acquired through contaminated food or water, and through close contact with an infected person's blood, stool, or body fluids. Most mild cases can recover without treatment, and people with more severe cases are advised to rest and avoid alcohol or any substance that is toxic to the liver. Hepatitis A virus is found in infected people, fruits, vegetables, shellfish, and water. Preventative measures include vaccination, good hygiene, and avoidance of unclean water and food.

Bovine Spongiform Encephalopathy

Bovine Spongiform Encephalopathy (BSE), commonly known as "mad cow disease," is a progressive neurological disorder found in the nervous system of animals that are infected with prions, a modified form of normal protein. When animals eat tissues that are contaminated with abnormal prions, they can develop BSE. Abnormal prions are most likely to be found in the skull, brain, eyes, vertebral column, and spinal cord of cows at least 30 months of age; however, these body parts are not allowed in the human food supply (CDC, 2013a). Bovine Spongiform Encephalopathy has a very long incubation period—it can take months to years to develop symptoms after infection. Currently, BSE is fatal and incurable. There are some preventative measures that consumers can take, such as avoiding eating the body parts of cattle that are most likely to contain abnormal prions, and avoiding eating processed meat, especially meat from unknown sources.

Recommendations for Safe Food Practice

Consumers can take many measures to avoid contracting foodborne illnesses. First and foremost, personal hygiene is extremely important. It also is important for people handling food to clean their hands and the surfaces of work stations regularly. Secondly, food should be cooked or held at the correct temperature. Consumers should avoid leaving food in the "Danger Zone"—40° F to 140° F—in which foodborne bacteria grow very rapidly; food should be served hot and be refrigerated within two hours of serving (one hour during summer months) (USDA, 2011). Lastly, consumers should prevent cross-contamination by separating raw meat, poultry, and seafood during the purchasing, storage, preparation, and refrigerating processes.

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See Also: Arsenic; Lead; Mercury.

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The French Paradox

"The French Paradox" refers to the observation that the French people have a lower incidence of heart disease than that of people in many other countries, despite their seemingly high-fat diets. This phenomenon challenges the widely accepted notion that high-fat diets increase the risk of heart disease. As researchers have tried to find explanations for this paradox, the concept has gained a substantial amount of media and scientific attention. The main explanation for this paradox is that one or many aspects of the French diet and lifestyle might help reduce the risk of heart disease. Several studies suggest that the lower incidence in heart disease can be at least partly attributed to a higher per capita consumption of red wine. Other dietary factors and eating behaviors also could help explain the French Paradox.

Serge Renaud, a French scientist, first coined the term "French Paradox" in the early 1990s. In 1991, Maury Safer featured this new term in the CBS television show "60 Minutes." Safer presented the idea that despite a diet that is high in saturated fat, the French have one-quarter the rate of coronary heart disease as compared to the rate in the United States. The show credited this concept to the French people's high consumption of red wine (Safer, 1991). This resulted in a significant increase in wine sales in the United States and epidemiological studies examining the association of wine and heart disease.

Hundreds of studies were published as scientists attempted to find explanations for the paradox. Some blamed the positive associations between wine consumption and a reduced risk of heart disease on a statistical error, and other researchers suggested that different dietary factors—such as a high fruit and vegetable intake—are the true explanation. Still, for many years, the hypothesis that moderate drinking of red wine is associated with a reduced rate of heart disease remained the most supported (Ellison, 2011). Since then, evidence has emerged that suggests red wine alone does not provide the significant health effects as was once thought. The high consumption of fruits and vegetables, in addition to fresh, local, quality ingredients and mindful eating is thought to be a more plausible explanation (Vendrame, 2013; Weil, 2013).

The French and Saturated Fat

When researchers first began to discuss the French paradox, saturated fats were thought to raise total and low-density lipoprotein (LDL) blood cholesterol levels. In a groundbreaking study examining 40 dietary factors spanning 40 countries, a significant positive correlation was identified between intake of saturated fat and cholesterol and death by cardiovascular disease (Ferrieres, 2004). In this same study, it was found that French citizens represented an outlier in the study, as they consumed far more high-fat foods but maintained low incidences of coronary heart disease.

The French diet is higher in saturated fats (such as butter and cheese) than that of people in nearly every other nation, including the United States. Each French citizen consumes an average of forty pounds of cheese per year (Safer, 1991). Due to the conventional knowledge of saturated fat intake and heart disease, researchers in the 1990s predicted that the French would have an exceptionally high rate of heart disease. Instead, the rate was found to be exceptionally low. At the time, this finding surprised researchers. More recent studies suggest that saturated fat per se is not as risky as was once thought (Malhotra, 2013).

The French and Red Wine

Many studies suggested that alcohol, itself, might be the component providing the protection against heart disease. In fact, one research group estimated that consumption of red wine reduces risk of cardiovascular disease mortality by about 30% to 50% (Vidavalur et al., 2006). Alcohol intake has been found to raise

high-density lipoprotein (HDL) levels. Higher HDL levels are associated with reduced rates of blood clotting and reduced risk of heart disease.

Although light to moderate consumption of alcohol might reduce the risk of heart disease and other diseases, red wine consumption, as observed in the French, was thought to have a unique and stronger protective effect (Vidavalur et al., 2006). In fact, studies found that moderate wine consumption was associated with a decrease of 24% to 31% of all-cause mortality as compared with consumption of equivalent amounts (in terms of alcohol content) of beer or spirits (Ferrieres, 2004). This evidence suggested there is another component (or components) in red wine that makes moderate consumption that much more beneficial.

The hypothesized key ingredients in red wine linked to cardiovascular protection are polyphenols, particularly a polyphenol called "resveratrol." Resveratrol and other polyphenols are found in high concentrations in the skin and seeds of grapes and act to protect grapes from bacteria and fungi. Red wine is one of the largest sources of natural polyphenols in the diet. In red wine, polyphenols contribute to color, mouth feel, and, perhaps, the reduction of the risk of heart disease (Mochly-Rosen & Zalchari, 2010). Polyphenols might exert their effects through their antioxidant behavior. This behavior was thought to protect the heart in the following ways.

- Polyphenols might prevent blood clots—Polyphenols are known to decrease inflammation and increase the relaxation of blood vessels, which reduces obstruction to blood flow. A decrease in inflammation and an increase in artery relaxation reduce blood clot risk. Additionally, antioxidant polyphenols from red wine have been found to decrease the buildup of platelets, the blood compounds responsible for forming blood clots (Mochly-Rosen & Zalchari, 2010).
- Polyphenols might reduce oxidation of LDL cholesterol—Oxidized LDL initiates and encourages plaque accumulation in the artery lining. As LDL accumulates, the arteries begin to harden and narrow, a process called atherosclerosis. With this, the risk of heart disease increases. Thus, as resveratrol and other polyphenols reduce the oxidation, they also reduce risk of heart disease.

Over the years, there has been a strong and consistent amount of scientific data that indicates moderate alcohol consumption—especially of wine—has a beneficial impact on the heart. The U.S. Federal Dietary Guidelines indicate moderate consumption of red wine can be beneficial to health. In the United States, the Bureau of Alcohol, Tobacco, and Firearms and Explosives permits wine labels to include a statement regarding wine's health benefits (Insel, Ross, McMahon, & Bernstein, 2013). Unfortunately, there are both medical and societal risks of excessive or inappropriate use of alcohol. This makes the extensive use of wine for beneficial purposes—such as medical recommendations and treatments—difficult.

Although there is a strong association between moderate wine consumption and heart health, it is difficult to conclude that wine is the key factor reducing heart disease rates in France. Researchers have concluded that the amount of

polyphenols in red wine probably is not enough to produce significant positive effects (Vendrame, 2013). In epidemiological studies, it is a well-known fact that association does not always indicate causation. In other words, although the increased intake of red wine by French people goes along with reduced risk of heart disease, this observation does not prove that red wine is the cause. Today, most researchers believe that although red wine might play a role in explaining the French Paradox, the paradox can be attributed to other factors of the French diet and lifestyle, as well.

The French Diet and Lifestyle

Current research suggests that the low heart-disease rates despite the high-fat diet among the French can be associated with moderate wine consumption in combination with mindful eating and more fruit and vegetable intake. The lesser rates of heart disease in the French population could derive from a thoughtful and wholesome approach to preparing and eating food (Pollan, 2004). Eating is considered a pleasurable experience enjoyed with family and friends. This allows the French to consume smaller portions as well as snack and skip meals less frequently. Also, due to France's higher value of and mindful approach to cooking and eating food, there is an emphasis on fresh, local, and high-quality ingredients (Weil, 2013).

As a whole, the French population consumes less sugar, processed flour, and trans fats (Weil, 2013). These processed foods have extremely damaging effects on the heart and increase the risk of heart disease. In fact, researchers are now finding these foods are the major drivers of heart disease. Instead of sugary and processed foods, the French consume a rich amount of unprocessed foods, particularly fruits and vegetables (Vendrame, 2013). Fruits and vegetables contain dietary fiber and many phytochemicals, which act in ways similar to the polyphenols found in wine to decrease risk and occurrence of heart disease.

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See Also: Alcohol; Cardiovascular disease and nutrition; Fatty acids; Polyphenols; Resveratrol.

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Fructose

Fructose is a monosaccharide found in fruits and vegetables and is the sweetest of all natural sugars. Fructose commonly binds to glucose, forming the disaccharide sucrose. It is also found as a component of synthetic sweeteners such as high-fructose corn syrup, which is composed of water along with varying concentrations of fructose and glucose. Fructose also is called "levulose" and "fruit sugar." Fructose is absorbed by the small intestine and has mild effects on blood sugar levels as compared to other sweeteners. Unlike glucose—which can immediately enter the bloodstream from the small intestine and be metabolized throughout the body—fructose must be metabolized and converted to glucose by the liver before it can be used by the body. After fructose is processed by the liver the end product usually is glycogen, the body's form of long-term energy storage. When glycogen stores are full, fructose metabolism typically shifts toward generation of triglycerides and fatty acids. In high amounts, serum triglycerides are associated with heart disease. In individuals with fructose malabsorption, the small intestine does not absorb the sugar properly, leading to stomach pain and bloating, a condition that affects up to 40% of individuals in the Western Hemisphere (Hereditary Fructose Intolerance, 2011).

The average daily intake of fructose has increased during the past several decades with the introduction of high-fructose corn syrup into the food supply. This increase in consumption raises concerns about the long-term health effects of the sugar and its contribution to obesity. Conflicting reports on the topic, however, have made dietary recommendations regarding fructose tenuous. In animal models, fructose has been shown to contribute to insulin resistance, hypertension and other vascular issues, fatty liver, metabolic abnormalities, and hyperuricemia, which precedes gout (Lee, Bruce, & Dong, 2009). Fructose also might contribute to certain cancers, particularly pancreatic and intestinal cancers (Port, Ruth, & Istfan, 2012). In normal human subjects, fructose has been shown to increase

triglyceride levels after ingestion, but not after three hours, and it does not directly cause changes in body weight for people in energy balance (Dolan, Potter, & Burdock, 2010). In overweight and obese subjects, fructose could be linked to increased visceral fat and decreased insulin sensitivity. Although a definitive link between fructose and various dysfunctions has not yet been established in humans, the USDA considers consuming excess fructose—especially as a component of added sweeteners—to be undesirable.

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See Also: High-fructose corn syrup.

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Functional Foods

Although no single, universally accepted definition exists, the term "functional foods" generally refers to foods containing one or more ingredients thought to provide physiological benefits beyond basic nutrition. Popular sources have used the terms "functional foods" and "nutraceuticals" interchangeably; however, functional foods are distinct from nutraceuticals—which are products isolated from foods and typically sold in liquid or capsule form.

Both whole and processed foods can be considered functional foods—the key ingredient can be naturally occurring or added during the manufacturing process. For example, both salmon and fortified eggs—when serving as sources of omega-3 fatty acids—would be categorized as functional foods, given the claim that adequate consumption of omega-3 fatty acids could reduce the risk of coronary heart disease. Functional food products are a multibillion-dollar industry, and food

researchers and manufacturers are eager to develop food products that meet consumer demand.

History

The concept of functional foods originated in Japan in the 1980s, when the Ministry of Health and Welfare created the regulatory system known as Foods for Specified Health Use (FOSHU), in an effort to reduce rising health care costs (Hasler, 2002). Applicants seeking to have a product approved under FOSHU must demonstrate its safety and efficacy, presenting documentation of the basis for the health claim and the basis of the recommended intake of the functional ingredient. Functional foods gained popularity in the United States in the 1990s, but no comparable regulatory body has been established.

Health Claims and Marketing

Although functional foods are not legally defined in the United States, the Food and Drug Administration (FDA) does control the types of claims that can be made about functional foods. Manufacturers of these foods may include approved health claims in the advertising or packaging of their products, but cannot assert that the food treats disease or has an immediate effect—these claims are restricted to drugs. An oatmeal manufacturing company can claim that the fiber in its product "promotes heart health" or "reduces the risk of heart disease," but not that it treats existing cardiovascular issues. The FDA regulations also require that health claims for which there is limited or mixed scientific support include qualifying language to avoid misleading consumers.

Bioavailability and Physiological Relevance

A persistent concern with regard to functional foods is the bioavailability and concentration of the active ingredient. If the functional component is not readily available for absorption and utilization or if it is present in the food in very small amounts, then the product might not offer the desired health benefit (Academy of Nutrition and Dietetics, 2013). The example of omega-3 fatty acids provided above serves to illustrate this problem: Eggs produced by chickens fed flax seed contain mostly short-chain ALA, and salmon contains higher levels of the more bioavailable, long-chain fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

Some nutritionists are enthusiastic about the potential of functional foods in their modified form to improve the health of the general population without demanding drastic changes in diet, but others caution that products relying on added ingredients also tend to contain less of the compound of interest per serving, which can necessitate the consumption of unrealistic quantities of the food to obtain a sufficient amount of the functional component (Denny, 2013).

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See Also: Dietary supplements; Phytochemicals.

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Gallbladder and Gallbladder Disease

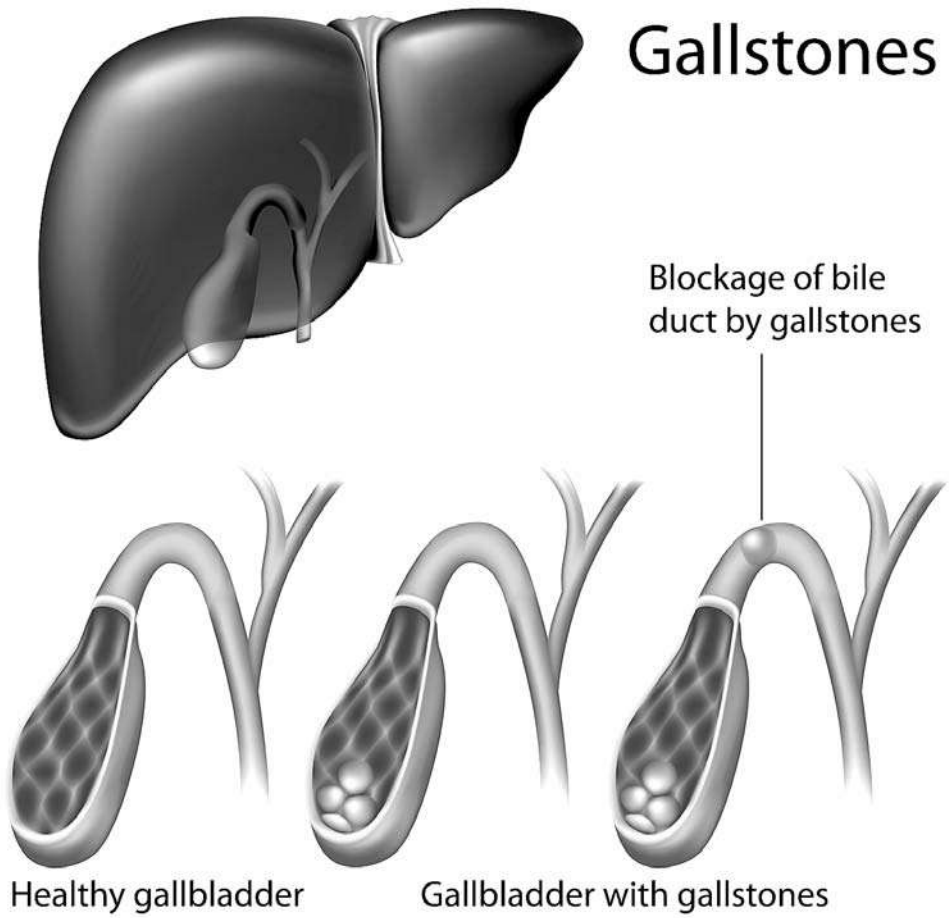
The gallbladder is a small sac located underneath the liver. Its functions are to store and concentrate the bile produced from the liver, and release the bile as needed for digestion. Shaped like a pear, this organ holds about a quarter cup of bile. When the small intestine senses the presence of food—which enters the small intestine after leaving the stomach—the intestine releases a hormone called cholecystokinin (CCK). Cholecystokinin causes the gallbladder to contract, squeezing bile into the bile duct. The bile duct transports the bile to the upper portion of the small intestine. Bile is composed of bile salts, electrolytes, bilirubin, and cholesterol and other lipids, including the phospholipid lecithin, and usually is a yellowish color. As the bile mixes with the contents entering the small intestine, it enables fat globules to be broken down into smaller particles, a process called "emulsification," which aids in digestion and absorption.

Gallbladder disease refers to any condition related to the dysfunction of bile ducts or the gallbladder. Gallbladder diseases include those caused by gallstones, gallbladder inflammation, and gallbladder cancer (a rare disorder). The most common disorders by far are those caused by gallstones. Approximately 20 to 25 million people in the United States have gallstones—about 10% to 15% of the adult population (Stinton & Shaffer, 2012). Several factors increase risk for gallstone formation, including obesity and rapid weight loss. As rates of obesity increase worldwide, the prevalence of gallbladder disease has increased as well. Several effective treatments are available to treat gallbladder disease caused by gallstones.

Gallstones

Gallstones accumulate when substances in the bile harden into particles as small as a grain of salt or as large as a tennis ball. There are two main types of stones; the first type is made of the cholesterol that the liver produces. Gallstones form when the liver releases too much cholesterol and there are insufficient bile salts in the bile to break down the cholesterol. Another cause of gallstones is the gallbladder not emptying, thus allowing the bile to concentrate and form a sludge that can develop into stones (Stinton & Shaffer, 2012).

The second type of gallstone, known as "pigment stone," is made of bilirubin. Bilirubin is a substance formed from the remains of hemoglobin derived from the



Comparison of healthy gallbladder and one with gallstones. A majority of gallstones are small and pass through the bile duct without notice. However, if a gallstone lodges and blocks a duct, severe pain results. Surgery may be necesssary for people with recurrent gallstones. (Alila07/Dreamstime.com)

breakdown of red blood cells. In comparison to cholesterol stones, they are smaller and darker. Pigment stones are classified as either brown or black. Black stones are more common in patients who have cirrhosis, a liver disease, or sickle-cell anemia, a blood disease. Brown stones have more cholesterol than calcium and can be caused by infection. Asian patients more commonly have brown stones. Although 70% of gallbladder patients usually have cholesterol stones, it is possible for patients to have both cholesterol and pigment stones (Simon & Zieve, 2013). Of the 10% to 15% of Americans who will develop gallstones, 80% might never actually suffer from discomfort or realize that they have stones (Stinton & Shaffer, 2012). For those who do experience discomfort, pain arises when gallstones block bile

ducts, preventing the gallbladder from draining. Gallstones can affect the pancreas because the pancreas duct empties through the same opening as the bile duct (Choi & Silverman, 2013).

Symptoms of Gallbladder Disease

When a gallstone becomes lodged in any of the bile ducts, medically described as "choledocholithiasis," an individual could feel discomfort or pain. Pain duration might last from minutes to hours, and usually affects the upper abdomen. Other symptoms include nausea, vomiting, and sweating. Pain attack severity is described as feeling like that of a heart attack. Symptoms of fever, jaundice, chills, and severe abdominal pain can indicate that the gallbladder is inflamed, a condition that also is known as "cholecystitis"; that a stone is blocking pancreatic juices from leaving the pancreas; or that something in the gallbladder is infected (Choi & Silverman, 2013).

Diagnosis for gallbladder disease first starts with the patient describing symptoms of a gallstone attack. The presence of gallstones and gallbladder disease can be detected through x-ray or ultrasound (Choi & Silverman, 2013). A doctor then can recommend further ultrasound testing or CT scans, which can detect whether a bile duct is swollen and thus blocking the passage of bile. Endoscopic ultrasound can detect whether a gallstone is forming and if there are any changes in the pancreatic or biliary duct system. Endoscopic retrograde cholangiopancreatography (ERCP) also detects whether the gallbladder or bile ducts are blocked, and also can remove small blockages. ERCP diagnosis techniques are slightly invasive (Cedars-Sinai, 2013). They only involve a small incision in which the surgeon can then insert an endoscope to diagnose the patient. The endoscope can also be inserted through the mouth (Cedars-Sinai, 2014).

Treatment of Gallbladder Disease

Treatment for gallbladder disease should be pursued only if the individual experiences significant pain. This can be done either through surgery to remove the gallbladder or gallstones, or via drugs. The removal of the gallbladder is called "cholecystectomy" and is considered to be a low-risk operation. There are two forms of cholecystectomy. The most common form is larcoscopic cholecystectomy, which involves several small incisions made to enable a small video camera and surgical tools to view the abdomen and remove the gallbladder. In this surgery, the patient is put under general anesthesia and most patients can leave the hospital the same day or day after their surgery. The patient usually can expect to recover in the course of a week. Another form of cholecystectomy is an open cholecystectomy, in which a single, larger incision is used. The open cholecystectomy requires a longer recovery time. Although either form of cholecystectomy has low risks for patients, complications can include bile leak; bleeding; blood clots; heart problems; infection; damage to the bile duct, liver, or small intestine; pancreatitis; pneumonia; and even death (Mayo Clinic Staff, 2013). Gallbladder surgery is

extremely successful, and because the gallbladder is a nonessential organ patients do very well after surgery. Some side effects of the surgery do include diarrhea and abdominal pain.

Other forms of gallbladder treatment include endoscopic retrograde cholangiopancreatography (ERCP) (described above), which is only slightly invasive. Intracorporeal electrohydraulic lithotripsy (EHL) is another treatment for gallstones that breaks up stones that are too big to be removed through a bile duct. A doctor also can prescribe drugs that can dissolve gallstones over the course of half a year. This method is intended for patients who for whatever reason are not candidates for surgery. This is the least-effective method, as new stones can form once the patient goes off the medication.

Risk Factors for Gallbladder Disease

Not everyone suffers from the presence of gallstones and, of those who do, not all require gallbladder removal. Gallstones are most commonly found in adults age 40 and older. Women are at a greater risk for gallstones because estrogen can increase the levels of cholesterol in bile, which can minimize gallbladder movement and create gallstones. Women who take oral contraceptives also have an increased chance of developing gallstones. Other risk factors include diabetes; a family history of gallstones; a high level of serum triglycerides; inactivity; low levels of HDL cholesterol; pregnancy; and rapid weight loss (Weight-control Information Network, 2013). Obesity—especially extra fat in the torso—is a strong risk factor for gallstone formation. Researchers think this is because obesity is associated with a higher cholesterol output by the liver, leading to more cholesterol in the bile, and a higher risk of stone formation. Diets high in cholesterol, fat, and carbohydrates have been associated with increased risk for gallstones; and higher intakes of fiber, coffee, unsaturated fats, vitamin C, and calcium, and moderate consumption of alcohol have been associated with lower risk (Stinton & Shaffer, 2012).

Nutrition and Diet Following Gallbladder Surgery

Diarrhea is a common symptom following gallbladder surgery. After the gallbladder is removed, the bile simply drains into the small intestine from the liver, rather than being concentrated and stored, and delivered when stimulated by the presence of food in the small intestine. The diarrhea usually resolves on its own after a few months. Patients coping with this symptom should try consuming smaller, more frequent meals, and gradually consume more water-soluble fiber such as psyllium (Nelson, 2012). People whose diarrhea symptoms do not improve, or who continue to experience pain or weight loss should seek medical advice.

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Research Issues

Obesity, especially excess visceral adipose tissue, stimulates increased rates of cholesterol and triglyceride production by the liver. Conversely, fasting and very low-calorie diets reduce bile flow, and can contribute to gallstone formation as bile builds up in the gallbladder.

If both obesity and weight loss increase risk for gallbladder disease, what is a person dealing with obesity supposed to do? Rapid weight loss significantly increases risk for gallbladder disease, so much so that some bariatric surgeons prophylactically remove the gallbladder when they perform a weight-loss surgery—although this procedure is questioned by some. Slower forms of weight loss, however, have a much lower risk of gallstone formation (Johansson, Sundstrom, Marcus, Hemmingsson, & Neovius, 2013). People with obesity who are considering weight-loss surgery or weight-loss diets must take into account their obesity-associated health problems along with treatment risks, and choose their treatment options accordingly.

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See Also: Digestion and the digestive system; Lecithin; The liver.

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Gamma Linolenic Acid

Gamma linolenic acid (GLA) is an omega-6 fatty acid found mainly in seed oils of borage, evening primrose, and black currant plants. These plant seed oils are sold as dietary supplement sources of gamma linolenic acid. Gamma linolenic acid also is found in human breast milk. The human body can make gamma linolenic acid from the essential fatty acid linoleic acid, which must be obtained from the diet. In humans, linoleic acid is obtained mostly from vegetable oils and egg yolks. Gamma linolenic acid is important for brain development, bone health, skin and hair growth, energy metabolism, and the health of the reproductive system. Gamma linolenic acid supplements are not needed by most people, because they can get more than sufficient linoleic acid from their diets and they are able to convert linoleic acid to sufficient quantities of gamma linolenic acid.

The human body uses gamma linolenic acid to manufacture prostaglandins, which are hormone-like substances that play important roles in many processes of the body. Prostaglandins help to control inflammation, make smooth muscles contract, and regulate body temperature. Although omega-6 fatty acids generally are thought to promote, rather than inhibit, inflammation, GLA might have anti-inflammatory effects, more commonly observed in the omega-3 fatty acids. Gamma linolenic acid has been promoted as a treatment for a variety of health problems, especially allergic skin conditions such as eczema, but evidence supporting a beneficial effect for eczema is fairly weak. A few small studies suggest that GLA might be somewhat helpful for the treatment of rheumatoid arthritis, hypertension, and diabetic neuropathy (Ehrlich, 2011)

Laboratory tests have shown that GLA can slow the growth of some types of human cancer cells in vitro, and GLA could enhance the effectiveness of some anticancer drugs (ACS, 2010). One interesting cell culture study found that gamma linolenic acid is able to stimulate apoptosis in leukemia K562 cells, and shows the capability of selectively inducing cell death in the cancer cells without causing damage to normal cells, which suggests that gamma linolenic acid someday might be an effective chemotherapeutic agent against cancer (Ge et al., 2009).

Fei Peng

See Also: Fatty acids; Linoleic acid.

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Garlic

Garlic, *Allium sativum*, is a bulb in the lily family. The bulb is segmented into smaller sections called "cloves." Around the world, garlic is used to flavor foods, and many people enjoy its pungent aroma and taste. A great number of cultures throughout time have also used garlic for medicinal purposes. Garlic has been shown to have multiple health benefits, including reducing the risk of cardiovascular disease, high blood pressure, and stomach and colon cancer. Garlic might help to prevent colds. Garlic has antifungal qualities when incorporated into a skin cream.

People in ancient Egypt used garlic medicinally, and buried pharaohs with garlic to give them health on their journey to the afterlife. Many cultures including the ancient Romans as well as modern European countries have used garlic poultices to prevent the infection of wounds. The well-known biologist Louis Pasteur was one of the first to demonstrate scientifically that garlic can kill bacteria. Garlic continues to be featured in folk remedies all over the world; many of these are gaining scientific support.

One of the active components of garlic is alliin. When garlic is crushed or cut, an enzyme is released that converts alliin to allicin and its derivatives. These contribute to garlic's strong odor and flavor. Although allicin is the most studied of garlic components, garlic contains many other compounds as well, including a number of trace minerals and essential fatty acids. For medicinal purposes, people use both raw and cooked garlic cloves as well as a variety of preparations, such as garlic powder and garlic oil formulas. Raw garlic exerts stronger physiological effects than garlic that has been cooked.



Garlic has been used as a health remedy around the world for thousands of years. It is a hardy plant that is relatively easy to grow. Garlic is usually grown by planting a single clove from a bulb of garlic. (U.S. Department of Agriculture)

Cardiovascular Effects: Blood Pressure and Artery Disease

When garlic is metabolized in the body hydrogen sulfide is released,

which relaxes blood vessels. This relaxation of blood vessels results in a decrease in blood pressure, which is good for overall heart health. In addition to its effects on blood pressure, garlic also might reduce the risk of artery disease, which can cause heart attacks and strokes. Arterial plaque is most dangerous when it becomes inflamed and ruptures, releasing debris that can block arteries and interrupt blood flow. Garlic appears to exert anti-inflammatory effects in the body, increasing the release of immune-signaling molecules associated with decreased inflammation levels. Garlic preparations also are associated with decreased oxidation of low-density lipoprotein (LDL). Oxidized LDLs are believed to contribute to plaque deposition in the artery walls, thus accelerating the process of artery disease. Garlic also appears to boost the activity of the body's own powerful antioxidant systems, at least in laboratory animals.

Stomach and Colon Cancer

Garlic has been associated with a variety of anticancer effects in vitro, when human cancer cells in a glass dish are exposed to garlic. The application of this evidence in living people has not been as promising, however, probably because garlic does not come into direct contact with cancer cells, except in the digestive tract. In humans, several studies have found that people who consume more garlic have a lower risk of stomach and colon cancer.

Antimicrobial Effects

Garlic appears to have antimicrobial effects when it comes into contact with a variety of microbes, including bacteria, viruses, fungi, and protozoa. This does not mean that garlic can serve as a systemic antibiotic. The garlic must make direct contact with the microbe. This could explain why garlic preparations can serve as an effective treatment for fungal infections on the skin, or reduce oral bacterial concentrations when consumed raw. A few well-controlled studies have shown that consuming garlic can lead to decreased incidences and duration of common colds.

Safety and Side Effects

Garlic appears to very safe when consumed raw, cooked, or in supplement form. Side effects can develop, however, when large volumes of garlic—especially raw garlic—are used. Some people have experienced stomachaches, heartburn, nausea, diarrhea, and other symptoms of gastrointestinal distress after consuming garlic. Difficulty sleeping also has been observed in a minority of people. Garlic applied topically can cause skin irritation; raw garlic also can irritate the mouth and throat. Because garlic can have a blood-thinning effect, people taking anticoagulants probably should avoid ingesting large doses of garlic.

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See Also: Allyl sulfides (organosulfurs).

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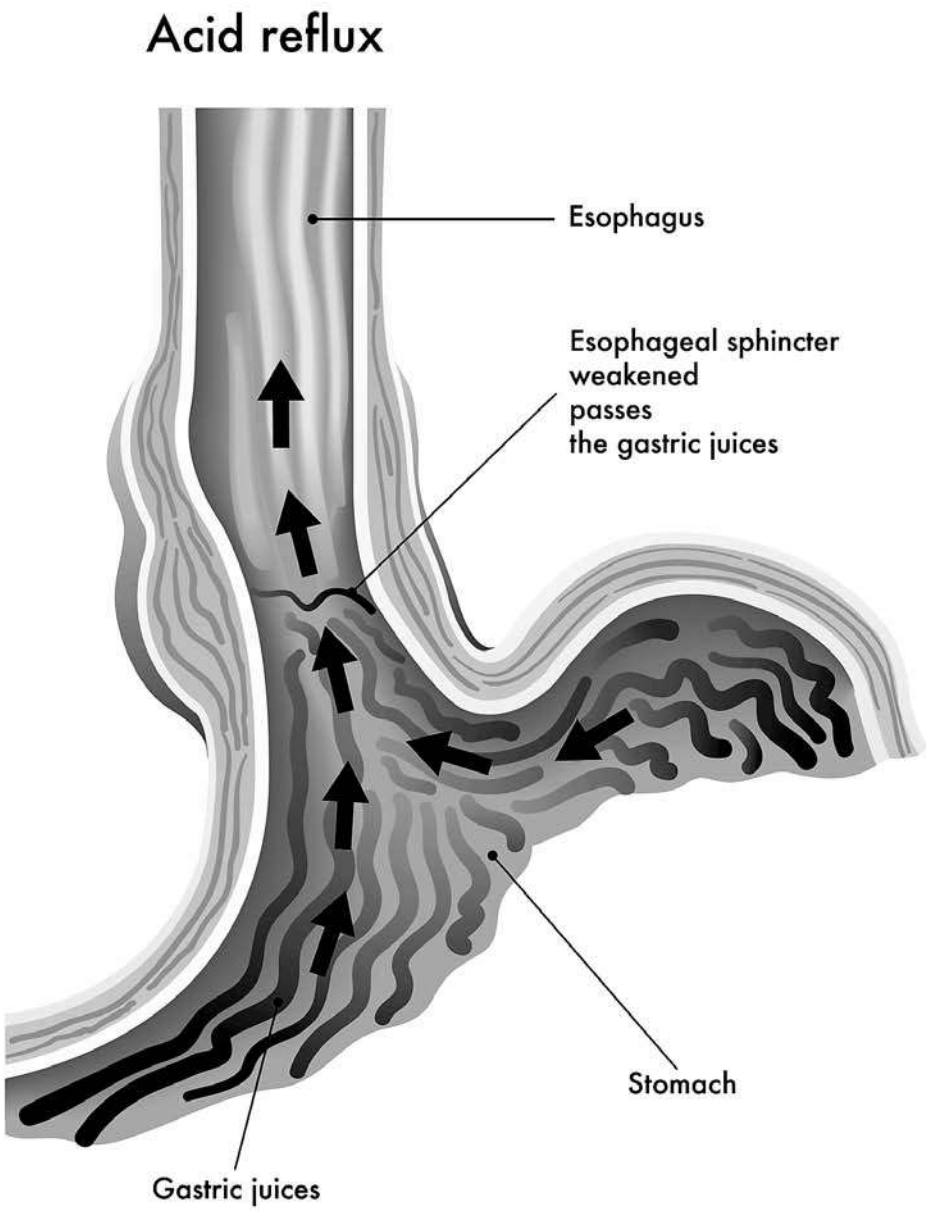
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Gastroesophageal Reflux Disease

Gastroesophageal reflux disease (GERD) is a digestive disorder that affects people of all ages. The esophagus is a muscular tube that transfers ingested food and liquids from the mouth to the stomach. Gastroesophageal reflux (GER) occurs when the stomach's acid-containing digestive juices regurgitate from the stomach back up into the esophagus. It is also referred to as "acid reflux" or "acid regurgitation" because patients with gastroesophageal reflux report tasting food or acidic liquid in the back of their mouth. Patients often report burning feelings in the middle of their chests, directly behind the breastbone, a symptom known as "heartburn." The reflux of the acid can inflame the lining of the esophagus and can damage the muscles of the lower esophageal sphincter, causing it to not close properly. This allows for the contents of the stomach to travel back into the esophagus more easily, causing the more chronic gastroesophageal reflux disease (GERD). If GER is occurring twice a week or more, it could be a symptom gastroesophageal reflux disease. People who suspect that they might have GERD should seek medical attention. If left untreated GERD can cause serious health problems, including esophagitis, esophageal bleeding and ulcers, and strictures, and can increase the risk of developing esophageal cancer. Treatments for GERD include lifestyle change, especially dietary change; weight loss (if overweight); medications; and surgery.

Anatomy and Physiology of Gastroesophageal Reflex Disease

The esophagus, stomach, and esophagogastric junction (where the esophagus and stomach join) comprise the crucial anatomy of the gastrointestinal tract that is involved in gastroesophageal reflux disease. The cervical, thoracic, and abdominal sections make up the three parts of the esophagus with inner circular and outer longitudinal muscular layers maintaining the structure. The proximal esophagus accommodates the upper esophageal sphincter and is composed of striated and smooth muscle. The thoracic esophagus travels into the abdomen through the esophageal



Gastroesophagel reflex refers to the movement of stomach contents up through the stomach and into the esophagus. The stomach has a specialized lining that prevents the acidic stomach contents from damaging the stomach. But the esophagus does not and is very vulnerable to damage caused by reflux. (Dreamstime.com)

Stomach Acid: A Good Thing or a Bad Thing?

"Heartburn" is a common name for "gastroesophageal reflux" (GER). When stomach contents are not digesting properly, fermentation begins, gas builds up, and the expanding stomach contents can press against the sphincter that separates the stomach from the esophagus. If this sphincter opens, the stomach contents, which are very acidic, can back up into the esophagus, causing pain, irritation, and even erosion of the esophageal lining.

Stomach acid actually is a good thing, thus the impulse to reach for antacids or proton pump inhibitors—drugs that reduce the stomach's production of hydrochloric acid and are marketed for GER—should be considered carefully. The highly acidic environment of the stomach disables many pathogens. Some research suggests that by reducing stomach acid, people are at increased risk for stomach cancer, initiated by the presence of bacteria in the stomach. Bacteria also increase risk of stomach ulcers.

Stomach acid increases the breakdown of food, facilitating separation of important nutrients so that they will be readily absorbed when they reach the small intestine. Stomach acid aids in the digestion of protein, for example. A highly acidic environment also helps calcium ions separate from food, thus making calcium more available in the small intestine. Studies suggest that people on long-term acid-reducing therapies decrease their absorption of calcium and thus increase their risk of osteoporosis.

Before reaching for products to reduce GER, it is important to try lifestyle measures first. Indigestion often is caused by eating too much too quickly, not chewing food enough, eating while feeling stressed, and consuming alcohol. Many people find that they have better digestion when they avoid high-fat meals, eat in a relaxing environment, chew their food thoroughly before swallowing, and consume smaller meals. Omitting alcohol can also aid digestion because alcohol can irritate the stomach. Meals should be consumed several hours before lying down so that gravity can assist stomach emptying. Some people also find relief with digestive enzymes such as papain and bromelain, which come from the fruits papaya and pineapple, respectively.

hiatus in the diaphragm, which creates a ring around the esophagus with right and left pillars. This allows for the esophagus to narrow when the diaphragm contracts. The phrenoesophageal ligament surrounds the esophagus at this level. The lower level of the phrenoesophageal membrane contains a fat pad on the anterior surface of the esophagus. The esophagogastric junction lies at the bottom of the esophagus in the abdomen, and contributes to the function of closure in the esophagus when intragastric and intra-abdominal pressures are at high levels.

The lower esophageal sphincter is a muscular valve between the esophagus and stomach that becomes strained or relaxed in individuals with gastroesophageal reflux disease. The lower esophageal sphincter is the most distal portion of the esophagus, ranging anywhere from 2 cm to 5 cm in length. The lower esophageal sphincter is responsible for keeping the top of the stomach closed and preventing the acidic contents of the stomach from traveling back up to the esophagus. Correct functioning of the lower esophageal sphincter is vital in preventing GERD.

Epidemiology

An estimated 7% to 10% of people in the United States experience GER symptoms on a daily basis, and 25% to 40% of Americans experience GERD symptoms at some point in their lives (Sawyer, 2013). Researchers believe that gastroesophageal reflux disease has become more common due to Western dietary habits, especially overeating, low intake of fruits and vegetables, and high alcohol intakes. It is as common in men as it is in women; however, white men are at a greater risk of Barrett esophagus and other adenocarcinomas than are other populations. GERD can occur in people of all ages, including infants. The prevalence of GERD is greater in people age 40 and older. Many individuals control symptoms with over-the-counter medications without consulting a medical professional, meaning that the actual number of people with GERD most likely is even greater.

Risk Factors

Several risk factors are associated with the development of GERD. Patients with asthma tend to have increased risk of developing GERD, as a relaxed lower esophageal sphincter causes asthma flare-ups. Asthma medications can worsen the acid regurgitation symptoms; however, it is not yet understood how or why. Reflux of the stomach's digestive acids also can worsen asthma symptoms by inflaming the lungs and airways. Irritated airways and lungs can trigger and cause more severe allergic reactions, because the irritation leaves people more sensitive to environmental conditions.

Abnormalities in the gastrointestinal system such as hiatal hernias also could be a casual factor. In hiatal hernias, part of the stomach is separated from the chest by the diaphragm. The upper part of the stomach pushes up into the chest and can slide through a gap (hernia) in the diaphragm. This opening is what can enable the stomach's digestive juices to travel back up through it, causing GERD. Other factors that could contribute to the development of gastroesophageal reflux disease are smoking, high alcohol intake levels, pregnancy, obesity, and certain medications such as calcium channel blockers, antihistamines, antidepressants, painkillers, and sedatives.

Signs and Symptoms

Common gastroesophageal reflux disease symptoms include regurgitation, heartburn, and dysphagia (difficult or painful swallowing). Excess and abnormal acid reflux can cause secondary esophageal symptoms such as bad breath, tooth cavities, sore throat, chest pain, wheezing, dry/chronic cough, asthma, nausea, vomiting, and otitis media (an infection of the middle ear). Long-term complications of GERD include esophagitis, strictures (a narrowing of the esophagus that causes difficulty swallowing), respiratory problems, and "Barrett's esophagus." Adults who have chronic forms of these complications can develop cancer of the esophagus. In the condition Barrett's esophagus, tissue of the intestinal lining replaces the

tissue originally lining the esophagus in a process known as "intestinal metaplasia." People who develop Barrett's esophagus are more susceptible to esophageal adenocarcinoma, a rare and lethal type of cancer.

Diagnosis

A gastroenterologist is a physician who specializes in digestive diseases and can diagnosis GERD. A GERD-specific test does not exist for diagnosis but secondary symptoms can be measured with several other tests aiding in the diagnosis. The most common exams are the upper GI endoscopy, manometry, and 24-hour pH study. The endoscopy can aid in the confirmation of a reflux diagnosis by determining effects of the reflux by evaluating the anatomy of the esophagus. The manometry exam determines the pressure of the lower esophageal sphincter. The 24-hour pH test helps to confirm GERD in patients by determining if the pH levels of the esophagus are more acidic than normal. Upper GI imaging also might be ordered for a diagnosis with contrast into the stomach to determine if the contrast passes back up into the esophagus.

Treatment

Treatment for gastroesophageal reflux disease can include lifestyle changes, medication, and surgery. Lifestyle changes alone often are effective at reducing GERD symptoms, and usually are the first treatment approach. Lifestyle change strategies include losing weight, if a person is overweight; wearing loose-fitting clothing (tight clothing can constrict the GI tract and increase reflux); avoiding lying down 2 to 3 hours after meals (maintaining an upright position makes GER less likely); avoiding smoking; decreasing alcohol intake; and raising the top half of the bed 6 to 8 inches using stilts. Dietary changes that can reduce GERD-induced acid reflux and heartburn symptoms include avoiding foods and drinks that worsen symptoms such as carbonated beverages and spicy foods. Other dietary changes include decreasing meal portions and increasing meal frequency.

Most GERD medications are available over the counter; however if symptoms worsen or persist, patients should seek further medical attention from a professional. Antacids, such as Riopan and Alka-Seltzer, are the medical professional's first line of treatment to treat heartburn and other GERD symptoms. Zantac 75 and Axid AR are H2 blockers and decrease acid production. Proton pump inhibitors (PPIs), including omeprazole and lansoprazole, are more effective than H2 blockers at relieving symptoms and healing the esophageal lining. Prokinetics are used to empty the stomach faster; however they sometimes have psychological side effects including depression and anxiety. Antibiotics, such as erythromycin, have fewer side effects than prokinetics and also improve gastric emptying.

Surgery might be recommended when patients with GERD cannot manage their symptoms with lifestyle changes or medication. A fundoplication is performed as the standard medical treatment for GERD and leads to long-duration regurgitation control. The operation entails sewing the top of the stomach around

the esophagus to the lower part of the esophagus, adding pressure that reduces regurgitation. Endoscopic techniques that sew and tighten the sphincter muscle are far less common and are less successful than the fundoplication.

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See Also: Digestion and the digestive system; Esophagus; Stomach.

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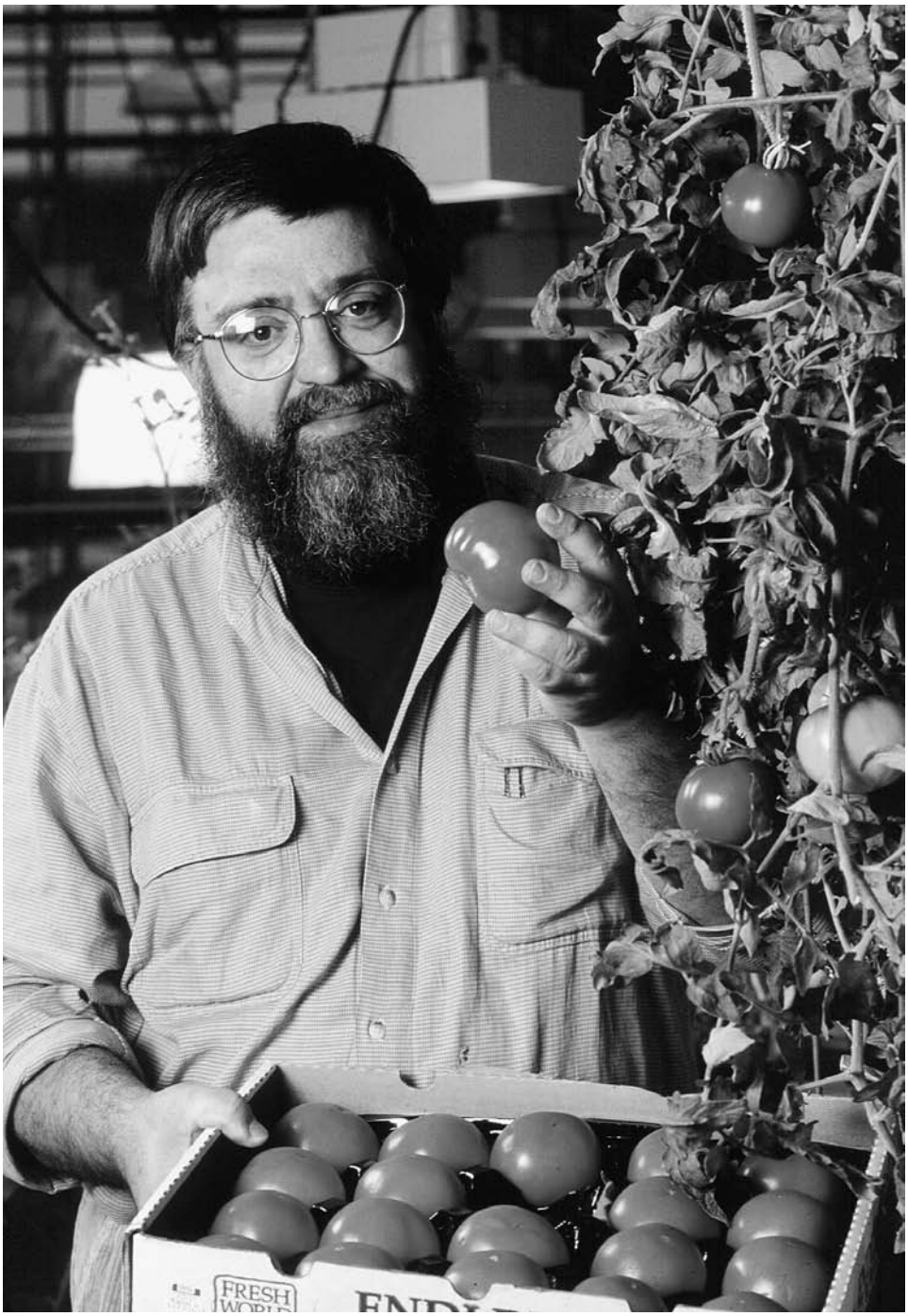
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Genetically Modified Organisms

Genetically modified organisms (GMOs) are plants and animals whose genetic material has been altered using genetic engineering techniques. Although people have been genetically modifying food for centuries through cross-pollination, grafting, and other forms of crossbreeding, biotechnology experts have developed tools that allow them to alter an organism's genetic makeup with more precision, including inserting genes not naturally found in the target organism. The goal of genetic modification is to improve an organism, for example making a plant more resistant to disease or drought. Opponents of genetic modification worry that the long-term safety of these procedures is unknown in terms of impact on the consumer in the case of genetically modified food, and regarding the environment.

To create a food, such as a tomato, using a more traditional breeding technique, the DNA from one type of tomato is crossed with the DNA from another type via pollinization, with the hope of creating a plant with desired traits, such as increased sweetness, pest resistance, or more durability for the long journey to the supermarket. This process transfers both desired and undesired genes, however, therefore it can take many generations before the ideal traits are achieved, if at all. Biotechnology offers a more precise way to modify an organism's DNA. Popularly called "genetic modification" (GM), the terms genetic engineering (GE) and recombinant DNA (rDNA) biotechnology are more precise. Genetic modification, GE, and biotechnology often are used interchangeably. Recombinant DNA biotechnology enables scientists to take a specific piece of DNA from one plant or animal and combine it with a strand of DNA from another plant or animal. Instead of sharing thousands of genes (as with traditional breeding), genetic engineering



A plant physiologist displays a genetically modified tomato. Genetically modified foods do not require labeling in the United States, although many states are enacting legislation to require such labeling. Over 60 countries around the world, including those in the European Union, require labeling of genetically modified foods. (Agricultural Research Service/USDA)

permits a single gene to be exchanged. It also allows for combinations of DNA from organisms that never could be combined before.

Two methods are used to modify DNA through genetic engineering. One method uses a gene gun to shoot DNA-coated pellets into tissue of the receiving organism, some of which are incorporated into the cell nucleus. The second method uses the microbe *Agrobacterium tumefaciens*. Agrobacterium lives in the soil and infects the roots of plants. The agrobacterium infects by injecting an organism with a circular portion of its DNA called a "plasmid." Genetic engineers can replace the agrobacterium's plasmid with one they have created. The bacterium then transfers this DNA to the organism that the scientists are trying to modify.

"Cisgenesis" is the term used for gene transfer between two compatible organisms. The changes might have happened eventually through crossbreeding or evolution, but cisgenesis speeds up the process considerably. Cisgenesis also is referred to as "close transfer." "Transgenesis" refers to gene modification between organisms that are not sexually compatible, creating changes that most likely never would have occurred without genetic engineering. For example, DNA from the arctic flounder was injected into tomatoes to encourage frost-resistance. The experiment worked, although the tomatoes were not sold commercially. Transgenesis also is referred to as "wide transfer." Plants can also be "tweaked," meaning that genes within the plant are changed to create new expressions (Lemaux, 2008). "Genetically modified organism" (GMO) is the name given to a plant or animal that has been created through any type of genetic-engineering process.

The Flavr Savr tomato was the world's first commercially available "genetically modified" food and was introduced to consumers in supermarkets in 1994. It did not prove to be profitable, but it opened the door to a new era of food production. With its advent arose enormous questions of how, why, and when to use GMOs, and GM foods in particular.

Genetically Modified Foods

The United States is the largest producer of GM crops. More than 90% of all cotton and soybeans planted in the United States are genetically engineered, as well as 88% of corn (Allen, 2013). Other common GM crops include canola, alfalfa, and sugar beets. Most of these crops are engineered to tolerate herbicide or fight off pests. For example, Roundup Ready® soybeans are tolerant to RoundUp® herbicide (both products are produced by the same corporation, Monsanto). Other crops, such as Bt corn, contain DNA from a microorganism, *Bacillus thuringiensis* (Bt), which produces chemicals toxic to insects. *Bacillus thuringiensis* corn therefore produces its own insecticide against the European corn-borer insect.

The major GM crops are used to produce animal feed and food ingredients, such as corn starch, corn syrup, cottonseed oil, soybean oil, and canola oil. These ingredients are then used to make soups, salad dressings, cereals, chips, and other processed foods. Whole foods such as fruits and vegetables are less commonly made with genetic engineering, although that could change with increased consumer support. More than 70% of Hawaii's papayas are genetically engineered to

resist the ringspot virus (Callis, 2013), and some varieties of disease-resistant squash, zucchini, and sweet corn also are on the market. In 1995, GM potatoes became available, but production ceased because the consumer market lacked interest. Several varieties of genetically engineered rice are in development, including "golden rice," which will include beta carotene, and rice that has been modified to contain the human enzymes lysostaphin and lysozyme, antibacterial agents that combat childhood diarrhea (Lemaux, 2008).

The most common use of genetic engineering among animals is for the creation of pharmaceuticals. In terms of foods, however, no meat, fish, or egg products created through GM are available for human consumption, although several have been or presently are being researched. In 1999, the University of Guelph in Ontario, Canada, developed a genetically engineered pig designed to create less pollution than conventional pigs. The project ended in 2012 because of lack of funding. Genetically modified rainbow trout and salmon also are being researched with the hopes of creating bigger, tastier fish in fish farms, thereby saving wild populations. Humans do consume milk that is the result of genetic engineering. Dairy cows are frequently given genetically engineered recombinant bovine growth hormone (rBGH) to increase milk production.

Regulation

Debate about GMOs frequently focuses on their regulation, which varies widely from country to country, and even from state to state within the United States because of new food labeling initiatives. In the United States, three federal agencies work in conjunction to regulate GMOs, the U.S. Food and Drug Administration (FDA), which is responsible for ensuring the safety of human and animal food; the U.S. Department of Agriculture (USDA), which is responsible for protecting agriculture from pests and disease; and the Environmental Protection Agency (EPA), which regulates food safety when connected with environmental concerns, such as pesticide use and crops that are genetically engineered to create their own pesticide, like Bt corn. Genetically modified foods must meet the same safety standards as traditional foods, as well as undergo tests for potential new toxins and allergens and any long-term risks from consumption. Nutrient levels between the GM crop and traditional crop also are compared.

Health Canada is the federal agency responsible for regulating GMOs grown and researched in Canada. Genetically modified foods have been sold in Canada since 1994, and all products must be approved before they can be marketed. More than 81 genetically modified foods have been approved, although not all are in commercial production.

The European Union (EU) has perhaps the most stringent GMO regulatory system. Few GM crops are grown in Europe, and those which are grown are predominately for research purposes. All GM crops require extensive testing, traceability, monitoring, and labeling, and many countries, such as Germany, have banned GM products altogether.

Arguments for and against GMOs

The genetic engineering of plants and animals is a complex issue with scientific, political, economic, and ideological implications. For every question answered, others are raised, and for every question raised, there are multiple answers. Some of the bigger issues are outlined in the table below, but the list is far from comprehensive in this ever-evolving debate.

Table 1. Genetically Modified Organisms

Issue	Arguments for GMOs	Arguments against GMOs
Risk to human health	• Substantial research shows that GM foods pose no health risks to humans. This position is supported by several large agencies, including the FDA, Health Canada, and the American Medical Association.	• Some research shows that there are risks to consuming GM foods. • Because this research is not positive regarding the corporations involved, it is hard to obtain funding and some researchers have lost their jobs because of their findings. • No studies can test the unknowns of new biotechnology. • GM foods only have existed for 20 years. Can research prove safe consumption for a lifetime when the products are so new?
Improved crop yield and pest resistance	• Plants genetically engineered to be disease resistant or herbicide resistant allow farmers to grow more per acre and use less pesticide, water, and fertilizer. Herbicide-resistant crops, for example, enable farmers to spray them with herbicide, which kills the weeds but not the crop.	• "Super weeds" have evolved that are herbicide resistant, causing more applications of herbicide rather than less. • The companies making the herbicide-resistant seeds also make the herbicide and are biased in their research and misleading in their marketing. • Increases in crop yields have not been significant.
Who benefits?	GM crops benefit everyone: • Farmers see increased profits • Food prices remain affordable • Developing countries are given resources to grow crops with improved nutritional value as well as crops more resistant to pests, disease, and extreme weather. • Technological innovation is nurtured by allowing corporations to patent their GM products.	• GM crops benefit the large corporations that develop them and patent their seeds. Farmers must buy patented seeds every year. Farmers have been sued by corporations for reusing patented seeds. • GM crops benefit large agribusinesses but not small farms or organic farms. • People in developing countries suffer from malnutrition because of lack of food. Food distribution must be improved, and not the food itself.

GMOs might spread to traditional plants and animals	• The risk of GMOs contaminating traditional plants and animals can be and has been managed effectively.	• There are numerous instances of GM crops contaminating GMO-free crops. Crops engineered to be weed-resistant, for example, cross-pollinate with the weeds, allowing the weeds to become resistant.
Regulation	• GM food is the safest food available because of the rigorous safety research required. • No food can ever be 100% safe.	• The FDA's regulation of GM foods is technically a voluntary consultation. • The GM food developers are the ones paying for the safety research. • Safety tests look for known risks; GMOs will have unknown risks.
Labeling	• Neither the United States nor Canada requires GM food to be labeled, although the FDA supports voluntary labeling of GM foods. • There is no reason to label because there is no real difference between GM foods and traditional foods. • Labels will cause uninformed consumers to think that GMO foods are unsafe.	• More than 60 countries require food made from genetically modified ingredients to be labeled. • If there is no risk to GM foods, why are companies afraid to label these products? • Consumers have a right to know what is in their food and make their own decisions about whether to buy it.
Additional Considerations	• Not all GMOs are the same and should be treated differently. • Not all GMOs are developed by large corporations. Many publically funded universities research and create GMOs. • Not all GMOs combine DNA from different species; some are combinations of similar species or even recombined DNA from the same species.	• All commercial varieties of GM crops are from the private sector, with the exception of papaya. • Tampering with the DNA of plants and animals changes evolution in a way that will have unexpected consequences. It could take a long time to know and understand the risks. Until more information is available, parties should proceed with caution—if at all.

Lisa P. Ritchie

Research Issues

Choose one of the arguments in Table 1 to investigate more thoroughly. Which side do you believe has the stronger argument?

See Also: Health Canada; Organic food and farming; Sustainable agriculture; U.S. Department of Agriculture; U.S. Food and Drug Administration.

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Ginger

Ginger is the rhizome, or underground stem, of the *Zingiber officinale* plant and is used as a spice and medicinal herb. Originally from Southeast Asia, the plant has been used since ancient times in India and China as a remedy for gastrointestinal distress, especially nausea. Ginger can be consumed in a variety of forms including fresh, dried, powdered, candied, pickled, and ground. The main bioactive ingredients in ginger are called gingerol compounds, more than 31 of which have been

Is Ginger Always a Healthful Food?

Ginger is sold in many forms. It is interesting to compare the labels of these products to evaluate ginger content, as well as note the presence of other ingredients. Ginger slices coated with sugar, for example, often are marketed as a healthy snack. This product, however, can contain a great deal of sugar, sometimes more than 30 g of sugar in 6 small slices of ginger, providing more than 125 kcals. This is equivalent to the amount of sugar in a 12-oz serving of some soft drinks.



Fresh and powdered ginger root are popular spices in many countries. Ginger root comes from the ginger plant, a perennial, herbaceous plant that grows in tropical climates. (Elena Elisseeva/Dreamstime.com)

isolated. The most-studied is [6]-gingerol, which is found in the rhizome's oleoresin, or oily resin (University of Maryland Medical Center, 2011). The concentration of gingerols and other bioactive substances vary widely based on the preparation, including in mass-produced supplement products where contents are not heavily standardized.

Ginger has been used for thousands of years in traditional medicine. Many scientific studies also have explored the efficacy of ginger for a variety of symptoms and disorders. Ginger is best known as an antinausea agent because of its ability to break up and get rid of intestinal gas. It has been suggested that its interaction with serotonin receptors has a role in its soothing qualities in the digestive tract (Bode, 2011). People experiencing nausea and vomiting induced by motion sickness and possibly from chemotherapy might benefit from ginger consumption. Ginger also helps relieve inflammation. A few studies have found that ginger supplements (250 mg, 4 times per day, for three days) can reduce pain associated with menstrual periods (National Institutes of Health, 2012). Similarly, some benefit has been found for knee pain associated with osteoarthritis. Although a small number of studies suggest that ginger can reduce muscle pain following exercise, other studies have not found a benefit. In animal models, ginger has been observed to suppress several forms of cancer by inducing cell death and serving as an antioxidant, although a lack of clinical trials in humans leaves its practical utility questionable at present.

The U.S. Food and Drug Administration (FDA) recognizes ginger as being safe overall, although generally it is suggested that adults ingest less than 4 g daily. Because ginger could affect blood sugar and blood pressure regulation, people taking medications for diabetes or hypertension should consult their health care providers before using ginger. Ginger also can have a blood-thinning effect, so people taking anticoagulant medications should consult their providers before taking ginger supplements. Ginger might be somewhat effective for the treatment of morning sickness (nausea and vomiting) associated with pregnancy. Pregnant women should check with their providers before taking ginger supplements, however, and should not take more than 1 g of ginger per day.

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See Also: Dietary supplements; Inflammation.

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Ginkgo Biloba

The Ginkgo biloba or "maidenhair" tree is native to China. Its leaves are used in alternative medicine, especially with the intent of improving memory and concentration. The tree is one of the oldest living species on the planet, and some individual trees are estimated to be more than 1,500 years old. The Gingko's leaves and nuts have been a part of traditional Chinese herbal medicine as far back as the Yuan dynasty (1280–1368 BCE) and have been used to treat a variety of maladies from pulmonary disorders to alcohol abuse (Birks & Grimley, 2009). The Ginkgo biloba tree is a resilient organism, immune to many diseases and pests, and can thrive in heavy pollution. Although few other living species survived, six Ginkgo trees are known to have lived through the 1945 atomic bomb in Hiroshima, Japan.

Contemporary medicine has seen the development of a widely used standardized Ginkgo leaf extract. The active components of this extract are its flavonoids and terpenoids, a pair of organic acid groups unique to plants. The flavonoid compounds have been shown to exert antioxidant effects. The terpenoids act to dilate

blood vessels and reduce platelet stickiness, thus improving blood flow. Gingko biloba preparations are available as supplements, are widely prescribed in many European countries, and have been the subject of an array of pre-clinical and clinical trials. Most studied has been the effectiveness of Gingko biloba supplements for the treatment of Alzheimer's disease and other forms of dementia. Although the Cochrane Database of Systematic Reviews has yet to affirm Ginkgo biloba as a clinically significant treatment for dementia or cognitive impairment, multiple trials have shown some improvement in cognitive symptoms in those with Alzheimer's and other dementias (Birks & Grimley, 2009). It is possible that the supplement could help a subgroup of dementia patients that is yet to be clearly identified.

The Natural Medicines Comprehensive Database (Gingko, 2014) rates supplements on their possible efficacy, based on the available scientific evidence. According to this group, Gingko biloba supplements are rated as "possibly effective" for Alzheimer's disease and other forms of dementia. Evidence suggests possible efficacy for improving cognitive ability in both young and old people. Ginkgo could improve circulation and relieve the pain associated with Raynaud's syndrome, a disorder characterized by severely reduced blood flow in the hands and feet. The supplement also might improve circulation and relieve the pain of peripheral vascular disease, such as intermittent claudication in the deep veins of the legs. Some studies suggest Ginkgo supplements have helped some with people with vertigo and dizziness. Ginkgo also might be effective in reducing symptoms associated with premenstrual syndrome (PMS).

The Gingko biloba leaf preparations generally are safe for most people, although reported side effects include upset stomach, headache, and skin rashes. Gingko supplements also might increase risk of bruising and bleeding, and should not be taken for several days before surgery. The roasted seed of the tree might be unsafe, and the fresh seeds are poisonous. Consumption of the fresh seed can lead to seizures and even death. Gingko biloba supplements appear to interact with a large number of prescription medications, so people on any kind of medication should check with their health care providers before taking gingko supplements (Ginkgo, 2014).

Patricia M. Cipicchio

See Also: Alzheimer's disease and nutrition; Antioxidants; Dietary supplements.

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Ginseng

Ginseng is a plant species used for a variety of pharmacological and clinical applications. It only grows in Eastern Asia and North America and its roots have been prized in China, Korea, and Japan for more than 2,000 years in traditional folk medicine. The ginseng root's gnarled appearance often is characterized by its human-like form. It is important to note that there are different kinds of ginseng which have different uses and effects. The most well-known ginseng plant is Panax ginseng, a name derived from the Greek word "panacea," which refers to a universal remedy. When the root is heated through sun drying or steaming, it becomes what is known as "Red ginseng," which typically is the form available for commercial distribution. Ginseng recently has gained wider acceptance in Western culture as one of the top 10 herbal dietary supplements in the United States, but is not as commonly used in food products because of its earthy, bitter taste (Chung, Lee, Rhee, & Lee, 2011). American ginseng, or *Panax quinquefolius*, is in the same genus but has different medicinal effects than Panax ginseng.



Ginseng root is used in Chinese and other herbal medicine traditions. The English word "ginseng" is derived from the Chinese words for "person" and "plant root," since the roots often resemble the human form. (Antaratma Images/Dreamstime.com)

The primary bioactive components of ginseng are a diverse group of compounds called ginsenosides. These substances might play a preventative role for certain types of cancer, as well as inhibit tumor growth and reduce metastasis (the breaking off and spreading of tumors) (Wee, Park, & Chung, 2011). Additionally, treatment of diabetic animal models and humans with ginseng, especially *Panax quinquefolius*, suggest that the plant could reduce blood glucose and prevent development of type 2 diabetes.

Memory and neurodegeneration also could be affected positively by ginseng by reducing programmed cell death and facilitating the formation and retrieval of memories (Wee, Park, & Chung, 2011).

In addition to reducing blood sugar, The Natural Medicines Comprehensive Database, as reported in Medline, rates American ginseng as "possibly effective" for the prevention of cold and flu symptoms. The database also rates Panax ginseng to be "possibly effective" for improvement of thinking and memory and treating erectile dysfunction (NIH, 2012). Panax ginseng supplements typically are formulated to contain 4% to7% ginsenosides, and are sold in 200 mg tablets. Therapeutic doses range from 200 mg to more than 2,000 mg per day. Some people also use raw ginseng, 1 g to 2 g daily during the treatment period. Ginseng is usually taken for only a 2- to 3-week period. Side effects are rare, although occasional cases of restlessness, sleeplessness, and hypertension have been reported. No toxicity level has been set, although users should exercise caution.

Patricia M. Cipicchio

See Also: Blood sugar regulation; Cancer and nutrition; Dietary supplements.

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Global Hunger and Malnutrition

Currently, the world produces enough food to feed 10 billion people (Gimenez, 2012), yet from 2011 to 2013, more than 842 million people—roughly 12% of the world's population—were estimated to be suffering from chronic hunger (FAO, 2013). Of the one in eight people experiencing hunger and its associated health implications—which include fat accumulation in the central region of the body, insulin resistance in adults, hypertension, poor mental development in children, and behavioral abnormalities—approximately 827 million live in developing regions of the world such as parts of Africa, Asia, Latin America, and Oceania (FAO, 2013).

In the context of malnutrition, hunger is defined as the discomfort or weakness caused by a chronic lack of food. Malnutrition, literally "bad nutrition," often is characterized by an inadequate food intake, resulting in nutrient deficiencies. Malnutrition also can occur with adequate energy (calorie) intake but insufficient

amounts of specific nutrients. Malnutrition generally is characterized by protein-energy deficiency or by vitamin-mineral deficiency. Protein-energy malnutrition (PEM) tends to be pervasive in resource-poor regions and essentially is the lack of energy and protein necessary for proper growth and development and for the maintenance of health. Commonly, PEM results in two similar but distinct diseases—marasmus and kwashiorkor—and their overlapping condition, marasmic-kwashiorkor. Marasmus refers to the chronic lack of energy needed to maintain body weight, and kwashiorkor is typified by the abnormal accumulation of fluid underneath the skin (edema), irritability, a distended abdomen, and an enlarged liver (FAO, 1997).

The second type of malnutrition—micronutrient deficiency—manifests in a variety of forms. The most prevalent form of malnutrition, iron deficiency, affects billions of people around the world and inhibits cognitive development. Vitamin A deficiency affects 140 million preschool children in 118 countries; increases the risk of dying from measles, malaria, and diarrhea; and is a leading cause of child blindness in developing countries. Iodine deficiency impacts 780 million people and results in mental developmental problems in newborns when women consume inadequate amounts during pregnancy. Zinc deficiency leads to weakened immunity in young children and contributes to about 800,000 child deaths per year (WFP, 2014).

Factors Influencing Global Hunger and Malnutrition

Chronic hunger and malnutrition can be caused by a wide variety of factors that limit people's access to food. These factors can grouped into four broad categories—availability, access, utilization, and stability.

Food availability describes the overall quantity of food for a given population supplied by domestic production and imports. Food production is dependent on a variety of factors including weather patterns, pest control, land management, and livestock management. Food importation is influenced by infrastructure, economic, political, and other factors.

As demonstrated by the fact that, in the early 1990s, 80% of all malnourished children lived in countries with food surpluses, access is a vital component to food security (FAO, 2002). Factors influencing access to food typically are divided into two categories—economic and physical. Economic access relies on disposable income, food prices, and sufficient social support. Physical access is determined by the availability of land resources; labor; inheritance; yields from agriculture, aquaculture, fisheries, and forests; and the ability of existing infrastructure such as roads, railways, communication, food storage facilities, and ports to facilitate market activity.

Poverty is a leading contributor to undernourishment and malnutrition. Market fluctuations due to policy changes, globalized trade, political conflict, and infrastructure management all potentially can impact a household or community's income and purchasing power, the local and regional allocation of food, and consequently the health of an entire area. Even if physical and economic accesses

are controlled, full access to food still might not be achieved due to the tendency for some to prioritize the purchasing of some goods and services over food. Furthermore, the intra-household distribution of food might not allow individual household members adequate access to food to meet their physiological requirements (IFPRI, 2012).

Often seen as the interface between food availability and human health, food utilization encompasses both anthropometric indicators of undernourishment and malnutrition, such as height for age scores, height for weight scores, weight for age scores, and other measurements. It also includes and is affected by the sanitary conditions and preparation of the food (FAO, 2013). Although increased availability and access to food could help to correct global, regional, and household conditions, it does not necessarily follow that food utilization on an individual level will adequately address symptoms of hunger and malnutrition. Hunger and malnutrition could be exacerbated by diseases, for example, such as malaria, AIDS, and tuberculosis, which prevent individuals and caregivers from obtaining, preparing, and consuming adequate food. Food utilization also is influenced by the handling, preparation, and storage of food. Prior to ingestion and dependent on access to clean water, the hygiene and nutritional quality of food must be adequately maintained to ensure good health and nutrition absorption.

Stability is the measure of the transitory and permanent vulnerability of a food system. Instability can result from changes in water supply (due to the uncertainty of drought); the ability of foreign exchange reserves to pay for food imports; local supply and production of food; and overall food prices. Volatility of food prices and supply can be strongly influenced by national and global institutions such as the U.S Department of Agriculture, the World Bank, the International Monetary Fund, and the World Trade Organization. Increasingly, however, unpredictable droughts, hurricanes, and flooding due to climate change could lead to substantial decreases in income and food production for smallholders, pastoralists, and poor consumers, especially in parts of the world such as Africa, Latin America, and the Caribbean, which have experienced the greatest variability in food supply since 1990 (FAO, 2013).

The Green Revolution

Serious efforts to address world hunger and malnutrition took place from the 1940s through the 1960s with "The Green Revolution." The Green Revolution is said to have begun in 1940 when an American scientist, Norman Borlaug, conducted research on disease-resistant high-yield varieties (HYV) of wheat in Mexico. The term was officially coined by a U.S. Agency for International Development administrator, and the Green Revolution picked up momentum through the 1950s due to its success in Mexico. Combining Borlaug's wheat with mechanized agricultural technologies, Mexico began producing more wheat than domestically needed, and by the 1960s was a leading exporter of the crop (IFPRI, 2002). During the mid-1960s, with widespread hunger and malnutrition still prevalent in Asia and back-to-back droughts in India, for example, Green Revolution technologies had room

to expand. The Rockefeller and Ford Foundations established an international agricultural research system to help adapt scientific advances in developing countries and began developing varieties of wheat and rice that would mature quicker, resist major pests and diseases, and retain desirable cooking and consumption traits (IFPRI, 2002).

By about 1990, 70% of wheat and rice in developing countries was converted to high-yield varieties (HYV), and by 1995 cereal production in Asia had doubled (IFPRI, 2002). Latin America also experienced significant gains, but Sub-Saharan Africa was only moderately impacted by the Green Revolution due to high transport costs, limited investment in irrigation, and market policies that made new technologies too expensive. A significant decline in global hunger and malnutrition, however, still is attributed to the agricultural growth of the Green Revolution (IFPRI, 2002). In many cases, raised incomes and reduced food prices that resulted from this rapid development have contributed to better nutrition. People have been able to consume added calories and a more diverse diet, as illustrated by increases in per capita consumption of vegetable oils, fruits, vegetables, and livestock products in Asia (IFPRI, 2002).

The Future

According to the Food and Agriculture Organization of the World Health Organization, 50% of the increase in crop yields in the recent years has come from irrigation and fertilizer and the other 50% has come from new seed varieties (FAO, 2010). Despite this yield increase and its ability to reduce poverty and hunger rates in developing countries, however, opponents of the Green Revolution argue that significant environmental and anthropological ramifications gradually have surfaced. When overused or used inappropriately, the high external inputs—namely fossil-fuel-based pesticides, fertilizers, and mechanization technologies—needed to ensure the production of HYVs in turn disrupt soil fertility, pollute waterways, kill beneficial wildlife, and poison agricultural workers (IFPRI, 2002).

The monocultures of wheat, soybean, corn, and rice cultivated by this process often require highly irrigated and high-potential rain-fed areas, resulting in an unquenchable reliance on groundwater, and economic and agricultural stagnation in areas with low rainfall. Moreover, this dependence on high-yield monocultures limits diet diversity, particularly the diets of poorer residents, by replacing a variety of nutrient-dense food crops from local food systems. The importance of biodiversity and the potential of wild crop varieties largely have been overlooked. The FAO estimates that throughout the 20th century, as much as 75% of crop diversity was lost. The FAO also has predicted that by 2055, 22% of the wild relatives of peanuts, beans, and potatoes will disappear due to climate change (FAO, 2010).

In response to issues regarding environmental quality and biodiversity, and subsequently human health and nutrition, methods of sustainable intensification have become more prevalent. Focused on increasing production, reducing food waste, moderating demand for resource-intensive foods, and improving the resiliency and efficiency of governance systems, many experts believe sustainable

intensification is an alternative framework through which to achieve food security (Garnett et al., 2013). It advocates for practices such as cover cropping (planting extra crops before or after the regular growing season to improve the soil), contour farming, organic farming, rain harvesting, zero-tillage farming, sheet mulching, and agroforestry. These practices produce higher yields from the same area of land and lessen environmental impacts such as soil salinization, desertification, and soil erosion (Godfray et al., 2010). Unlike industrialized agriculture strategies furthered by the Green Revolution—strategies that reduce biodiversity, limit ecosystem services, and contaminate natural resources—sustainable intensification offers a way in which to rethink food production. Whether it is through site-specific, hands-on land-management strategies; integrated pest management systems; or integrated livestock-waste management systems and their simultaneous interface with animal welfare, institutional priorities, economic systems, and social capital, sustainable intensification provides an alternative approach to the problem of world hunger and malnutrition.

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See Also: Climate change and global food supply; Food security and food insecurity; Sustainable agriculture.

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Glucosamine

Glucosamine is a natural compound present in human cartilage. Glucosamine is an amino monosaccharide, which is a sugar and protein composite. Glucosamine levels decline with age, causing researchers to question whether glucosamine supplements might help slow this decline, and perhaps even prevent the development of osteoarthritis (a condition marked by a loss of the cartilage that covers bones in the joints). Glucosamine sulfate often is taken with chondroitin—another component of cartilage—to relieve arthritis pain. Studies suggest it might not actually slow the process of osteoarthritis (which tends to worsen over time), but might be helpful for reducing pain, especially in people with moderate to severe knee pain caused by osteoarthritis.

Glucosamine injections initially were used in veterinary medicine in the 1970s as a treatment for larger animals that had joint pain, and treatments seemed to be successful. In the early 1990s, the Italian company Rottapharm combined glucosamine with sulfate to create the first supplemental form for humans. Several studies suggested that glucosamine supplements were helpful for many people with osteoarthritis (Towheed et al., 2009). The supplement came to the attention of the National Center for Complementary and Alternative Medicine—one of the centers that is part of the National Institutes of Health—which funded a well-controlled study of 1,583 people with osteoarthritis of the knee. This double-blind study was called the "Glucosamine Arthritis Intervention Trial" (GAIT). Researchers divided subjects into several groups and compared the effectiveness of glucosamine alone, chrondroitin alone, or the combination of both to a usual care group and a placebo group (Clegg et al., 2006). The researchers did not find much difference in pain levels among the groups, except for subjects in the glucosamine plus chondroitin group that had moderate to severe knee pain. Follow-up results did not show much difference between this group and the placebo group for arthritis progress; however, the placebo group had unusually slow progression, which could have muddied results (Clegg et al., 2006).

Glucosamine and chondroitin sulfate supplements did appear to be helpful for some subjects, with minimal side effects; therefore many experts suggest that patients suffering from arthritis pain should try using these supplements. Because

dietary supplements in the United States are regulated as foods rather than drugs, it is important to be sure the supplements come from a reliable source. Supplements used in research studies came from the Rotta Research Laboratorium in Europe. Glucosamine is sold in a variety of forms; the most effective form is glucosamine and chondroitin sulfate.

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See Also: Arthritis and nutrition; Dietary supplements.

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Glucose

Glucose is the most common simple carbohydrate compound (monosaccharide) in both plants and animals. In people, it is the primary source of energy for cellular metabolism. The term "blood sugar" refers to the glucose that is carried in the bloodstream. Blood glucose level is very important because cells in all body organs depend upon a reliable supply of glucose to carry out cellular functions. Glucose is the building block from which many other carbohydrates are made, including glycogen (the starch animals store in skeletal muscles and the liver) and many plant starches and fibers.

Extensive progress in understanding the structure of glucose occurred in the late 1800s in the laboratory of Hermann Emil Fischer in Germany. According to the scientist's autobiography, as a young man, Fischer was not very successful in his family's lumber business, wishing instead to study science. Fischer wrote that his father had declared that Fischer was not smart enough to succeed in business, so he had better be a student (Nobel Foundation, 1966). Fischer was an excellent student, received his doctorate in chemistry, and became a professor and researcher. He studied the chemical structure of a number of important molecules. Some of Fischer's most important work involved elucidating the structure of

several monosaccharides—including glucose—and synthesizing glucose and other molecules from glycerol (a component of fatty acids). Fischer received the Nobel Prize in Chemistry for his work in 1902.

Plants produce glucose with the process of photosynthesis, using energy from the sun to combine water and carbon dioxide. Plants also combine units of glucose to make a variety of starches and fibers; can convert glucose into other monosaccharides; and can combine monosaccharide units to form disaccharides (two monosaccharide units joined together). All disaccharides contain at least one unit of glucose. People obtain glucose from food containing carbohydrates, or the body converts other nutrients, such as amino acids (from proteins) and glycerol (from fats) into glucose. Glucose also is found in the diet as an ingredient in processed foods, where it is called "dextrose."

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See Also: Blood sugar regulation; Carbohydrates; Digestion and the digestive system; Hyperglycemia; Hypoglycemia.

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Glutamine

Glutamine is the most abundant amino acid in the human body and is produced primarily in muscle tissue, the lungs, and the brain. Because it is synthesized by the body by combining the molecules ammonia and glutamate, it is not considered essential. In high-stress circumstances, however, such as after extreme workouts or trauma, the body must consume outside sources of glutamine. Dietary sources of glutamine include meat, milk, ricotta and cottage cheese, raw spinach, parsley, and cabbage.

Glutamine serves to remove the waste product ammonia from the body and is heavily utilized by cells in the immune system, particularly by white blood cells known as "lymphocytes" and "macrophages." There also is high demand for glutamine in the gastrointestinal tract, where it can help to protect the lining of intestines. Glutamine levels in muscle and blood plasma are reduced after surgery and radiation treatment as well as injury and burns. Although moderate exercise can promote increased glutamine synthesis, heavy endurance exercise and excessive training depletes glutamine and slows synthesis over time (Agostini, 2010). Low

glutamine can compromise the functioning of the immune system and gut, leaving individuals vulnerable to more significant health issues.

Glutamine supplementation has proven beneficial in recovering from illness and surgery, leading to a reduced death rate in those with critical illness and trauma. Reduced levels of infection and shorter hospital stays also were found in a group that received glutamine following bone-marrow transplants. Patients considering glutamine supplementation should work with their health care providers, because excess amino acids can be harmful for people with reduced kidney function. In strenuous exercise, glutamine has been employed to boost the characteristically depressed immune system and to promote muscle growth and muscle glycogen stores (Gleeson, 2008). Although the supplement is well tolerated over time, clinical evidence is not sufficient to prove its efficacy in these areas. Protein supplements often include glutamic acid, an amino acid very similar in structure to glutamine. The body easily converts one form to another depending upon need.

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See Also: Amino acids.

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Glutathione

Glutathione is one of the body's most powerful antioxidants, low levels of which are associated with chronic illness and aging. Synthesized exclusively by the body and found in greatest concentrations in the liver, glutathione is a nonessential nutrient composed of the amino acids cysteine, glycine, and glutamine. Unlike most antioxidants, the molecule is located within nearly every cell, allowing it to directly scavenge free radicals and toxins. Glutathione not only neutralizes harmful reactive oxygen species directly, but it primarily is responsible for restoring the antioxidant potential of other useful antioxidants like vitamins C and E. Additionally, optimal levels of glutathione are important for supporting the activation of transcription factors that help control the expression of genes in cells.

Many factors can contribute to decreased glutathione levels, including poor diet, stress, and medications. Glutathione metabolism is regulated by several genes—some of which commonly are impaired in the general population. Many individuals are missing genes that regulate enzymes critical for making and recycling glutathione, for example, and this genetic profile (lacking the effective genes) might be associated with increased risk for certain diseases, such as several types of cancer (Yeh et al., 2010). Low levels of glutathione leave individuals less able to detoxify cells (Hyman, 2010). Research shows chronic diseases such as heart disease, cancer, autoimmune disease, diabetes, and arthritis nearly always are accompanied by glutathione deficiency. High-intensity exercise has been shown to immediately decrease plasma glutathione by increasing reactive oxygen species, therefore creating greater demand for the molecule's antioxidant properties (Elokda & Nielsen, 2007). Over time, however, exercise appears to increase plasma glutathione levels by increasing the ability of skeletal muscle to push glutathione into circulation, which increases its availability for the body (Kretzschmar & Muller, 1993).

Glutathione is present in most foods, especially protein foods. Supplementation has not proven beneficial, because the body breaks down the protein during digestion. Supplementation also has been associated with reduced endogenous production of glutathione. Instead, consumption of N-acetyl cysteine and alpha lipoic acid as well as folate, vitamin B6, and vitamin B12 could help boost glutathione levels (Hyman, 2010). High-quality whey protein also can provide the raw materials needed for glutathione production. (People allergic to milk products should avoid consumption of whey protein supplements.) The herb "milk thistle" helps to prevent depletion of the molecule in the liver (Das & Vasudevan, 2006).

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See Also: Antioxidants.

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Gluten-Free Diets and Foods

Gluten is a protein found in certain grains, including wheat, rye, and barley. Gluten-free diets refer to diets that contain minimal amounts of gluten (or none); gluten-free foods refer to foods that contain minimal or no gluten. Many gluten-free foods are naturally gluten-free, for example all vegetables, fruits, meats, and dairy products that have no added ingredients. Some food products—such as breads and baked goods that typically are made from wheat flour—can be made with wheat substitutes containing no gluten. Gluten-free foods often are consumed by people who must or who choose to avoid gluten, but who still wish to eat such products—which are very popular and common in the diet of most North Americans.



Gluten-free products on a grocery store shelf. In the United States, products labeled "gluten-free" have to contain less than 20 parts per million of gluten. (AP Photo)

People avoid gluten for a variety of reasons. In about 1% of the population, gluten elicits an autoimmune response, in which immune cells mistakenly attack the lining of small intestine. People with this autoimmune response and the accompanying damage to the small intestine are diagnosed with celiac disease, which is an inherited disorder. The only treatment for celiac disease is a lifelong gluten-free diet and avoidance of all gluten-containing foods, beverages, and medications, as no cure currently exists.

Some people avoid gluten because they are allergic to wheat. A wheat allergy is a type of food allergy. Allergic responses are characterized by a range of symptoms, from hives, rashes, and swelling to difficulty breathing and loss of consciousness. In severe cases, food allergies can be fatal. Wheat allergies are thought to affect about 0.1% of people in North America (Gaesser & Angadi, 2012).

Some people without celiac disease or wheat allergies could experience distressing symptoms, such as intestinal gas, bloating, pain, and constipation, as well as non-GI symptoms such as fatigue and headaches, when they consume gluten-containing foods, a condition known as non-celiac gluten sensitivity (NCGS). To receive a diagnosis of NCGS people must test negatively for celiac disease; experience the functional negative symptoms associated with celiac disease, such as bloating and pain after ingestion of gluten-containing foods; and show symptom improvement with a gluten-free diet. Recent research suggests that many people currently diagnosed or who have self-diagnosed themselves with NCGS actually could be sensitive to food components other than gluten, such as certain types of small carbohydrate groups common in grains (Biesiekierski et al., 2013; Catassi et al., 2013). These components have been called "FODMAPs," an acronym that stands for fermentable oligo- , di- , and mono-saccharides and polyols. FODMAPs are poorly absorbed in the GI tract of people with functional bowel disorders, such as irritable bowel syndrome. When the FODMAPs reach the large intestine, the microbes living there metabolize these molecules, releasing gas in the process. The gas increases feelings of bloating, pressure, and pain, and can interfere with normal colon motility. The elimination of gluten-containing foods concomitantly reduces intake of these FODMAP components, leading to an amelioration of NCGS symptoms.

People who suspect that they might have a gluten sensitivity of some sort should seek medical advice and be tested for celiac disease, rather than self-diagnosing this condition. Celiac disease is a serious illness that can compromise long-term health if untreated.

Gluten-free diets and foods have become popular even among people with no adverse GI reactions to gluten. One survey performed by a market-research company found that 30% of respondents expressed a desire to cut back on gluten consumption (Hamblin, 2013). This might be attributable to popular media that have sensationally painted gluten as a food ingredient responsible for everything from autoimmune diseases to brain disorders such as autism, anxiety, depression, and Alzheimer's disease. Although a few research studies have linked gluten

consumption to neurological disorders in animals and a small number of humans, especially people with celiac disease, the research is very preliminary at this point (Hamblin, 2013).

Even though gluten-free diets have been promoted as successful weight-loss strategies, evidence supporting this claim is lacking. Temporary weight loss often occurs when people eliminate foods from their diet. Several studies suggest that gluten and other components of gluten-containing whole grains could have important health benefits for people without celiac disease, wheat allergies, or NCGS, including better colon microbiome composition (beneficial bacteria in the gut) and protection from colon cancer. A diet high in cereal fibers appears to contribute to healthful blood pressure regulation, blood sugar regulation, and blood fat levels (Gaesser & Angadi, 2012). These observations suggest that eliminating wheat, barley, and rye from the diet of people without celiac disease, wheat allergies, or NCGS could have negative impacts on pubic health.

Food products must meet certain standards to make a gluten-free label claim. In the United States such claims are regulated by the Food and Drug Administration (FDA). According to FDA regulations, a product may claim to be gluten-free if it has less than 20 ppm of gluten (FDA, 2014). Consumers should note that gluten-free products such as baked goods are not automatically healthful foods, but actually can contain significant amounts of added sugars, salt, and fats.

Barbara A. Brehm

See Also: Celiac disease; Fiber; Food allergies and intolerances; Intestinal gas; Irritable bowel syndrome; Microbiota and microbiome.

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Glycemic Index and Glycemic Load

The glycemic index (GI) of a food is a measure of the food's impact on blood glucose level following its ingestion. Specifically, glycemic index is a measure of how quickly glucose appears and how high its level rises in the blood after a given portion of carbohydrate from that food is consumed, relative to the blood glucose response of a standard food such as pure glucose or white bread. Foods such as sugar, white bread, and instant white rice have a high glycemic index. The sugars and starches in those foods are digested and absorbed very quickly. Foods such as whole-grain breads, oatmeal, and berries have a lower glycemic index, which means it takes the body longer to digest and absorb the sugars and starches in these foods. Knowing a food's glycemic index is helpful for people who want to raise their blood sugar quickly, as would be the case for someone with hypoglycemia (low blood sugar). People who are trying to avoid high blood sugar, such as people with diabetes, also can benefit from knowing the GI of foods so they can avoid foods that might raise their blood sugar level too high.

In terms of chronic health issues, such as heart disease, the glycemic index of a particular food is not as important as a variable called glycemic load (GL), which represents the glycemic index multiplied by the grams of carbohydrate in the actual serving of food, divided by 100. Although GI is measured for a standard amount of carbohydrate, GL reflects the typical serving size of foods and better represents what people actually eat. For example, cooked beets have a relatively high glycemic index (64) but a fairly small amount of carbohydrate per serving, and thus a low GL (4). Macaroni has lower glycemic index (45) but quite a bit of carbohydrate per serving, and thus a high GL (22). Studies suggest that people consuming a relatively high-glycemic-load diet throughout their lives tend to have higher rates of chronic disease, especially heart disease (CQC, 2013). A high glycemic load is correlated with higher blood glucose levels after meals, which appear to be related to greater risk of disease progression, perhaps through higher levels of insulin and obesity.

Calculating Glycemic Index and Glycemic Load

Glycemic Index is calculated by measuring blood sugar changes in people after they consume standard amounts of specific foods. For example, to calculate the GI of apples, the subjects first might consume 50 grams of carbohydrate from pure glucose, the standard to which apples will be compared. Scientists monitor the subjects' blood glucose levels over time, noting how quickly and how high blood glucose levels rise, and how long it takes for blood sugar to return to normal. These measures are plotted on a graph, and the area under the curve is calculated. On a

separate occasion, the same participants would consume a portion of apples containing 50 g of carbohydrate under test conditions identical to the glucose trial. To calculate GI, the area under the apple curve is divided by the area under the glucose curve for each subject, and the results are averaged. The GI for apples is about 40. This means that the area under the curve for apples is about 40% of the area under the curve for pure glucose.

A number of different organizations have calculated the GI for various foods. The GI of a variety of foods can be found at www.glycemicindex.com, a GI database overseen by the University of Sydney, Australia. The GI of a given food can vary somewhat among databases, as some use different reference foods (for example, white bread rather than glucose) or a different variety of food being tested, such as different varieties of apples. This means that GI is simply a relative value rather than a precise number. In general, a GI of 55 or less is considered low; 56 to 69 is medium; and 70 or more is high.

To calculate the GL of an apple, multiply the GI, in this case 40, by the grams of carbohydrate present in a typical serving, 15 g, and then divide that number by 100 (to standardize values to a 100 g serving). This gives a GL of about 6.

$$\frac{40 \text{ X } 15 \text{ g}}{100 \text{ g}}$$

In general, a GL of 10 and under is considered low; 11 to 19, is medium; and 20 or greater is high. Some calculations of GL use 1,000 kJ (a measure of energy content equivalent to about 139 kilocalories) in the denominator to standardize for a food's energy value rather than its weight (CQC, 2013).

Factors That Influence Glycemic Index and Glycemic Load

Several factors influence a food's glycemic index and glycemic load. Of course, the food must contain carbohydrates, such as sugars or starches. Foods such as oils and meats that do not contain carbohydrate do not release glucose into the bloodstream; thus these foods do not have a GI.

The nature of the carbohydrates contained in a food influences that food's GI. The digestive system breaks down carbohydrates in foods and transports the resulting monosaccharides (basic carbohydrate structures), such as glucose and fructose, into the bloodstream. The liver converts fructose to glucose and releases some of the glucose back into the bloodstream. The speed of the digestion and absorption of a food depends upon the amount of simple carbohydrates (sugars) versus complex carbohydrates (starches) in the food, and the structure of the molecules. Some starch formations, for example, are broken down more quickly than others.

Additionally, the other structures in a given food influence the speed of digestion and absorption. Dietary fiber (especially water-soluble fiber) and fats slow down the digestion and absorption of carbohydrates. Interestingly, pasta has a fairly low GI, even though it has very high levels of carbohydrate. This is because the carbohydrate is bound up with a protein called gluten, found in wheat and some other grains, that makes the carbohydrate less accessible to digestive enzymes.

The composition of other foods consumed at the same time as the carbohydrate food impact digestion and absorption. A baked potato, for example, has a fairly high GI. If it is consumed with high-fat toppings such as chili, cheese, and sour cream, however, then the potato and its toppings stay in the stomach longer, and the digestion and absorption of carbohydrates from the potato occurs more slowly. (Carbohydrate digestion and absorption occur primarily in the small intestine; thus when food stays in the stomach longer, carbohydrate absorption slows.)

Applications

Epidemiological studies of dietary and lifestyle factors associated with chronic diseases and premature mortality are increasingly including glycemic load as a risk factor, as risk of all-cause mortality increases with GL (e.g., Baer, Glynn, Hu, et al., 2011). An international panel of experts suggests that reducing GL can be especially helpful for improving blood sugar regulation in people with type 2 diabetes, and for reducing risk of cardiovascular disease (CQC, 2013). This same group also suggests that low GL diets might reduce risk by decreasing insulin response, improving blood lipid levels, and reducing levels of systemic inflammation, although more research is needed to explain and quantify these relationships (CQC, 2013). Knowledge of a food's GI or GL alone is insufficient to guide dietary choices. Research on GL, however, generally reinforces other advice on healthful eating that urges people to consume healthful proteins and fats; choose whole grains rather than refined grains; consume a wide variety of carbohydrate foods, including fruits, nonstarchy vegetables, and legumes; and limit foods with added sugars and refined grains, especially soft drinks and dessert goods such as cookies and cakes.

Barbara A. Brehm

Research Issues

Knowing a food's glycemic index (GI) or glycemic load (GL) can be helpful for anyone trying to exert control over blood sugar levels, including athletes. Athletes sometimes speak of low- and high-glycemic-index foods as "slow" and "fast" carbohydrates. Fast carbohydrates (high GI) foods are helpful for coping with exertional hypoglycemia (low blood sugar that results from high levels of exercise) and replenishing depleted carbohydrate (glycogen) stores as quickly as possible. Athletes looking for ways to refuel during physical activity, for example, will find that high glycemic foods have a quicker impact on blood sugar. The same is true for athletes who exercise more than once per day; fast carbohydrates help restore glycogen and blood sugar levels between workouts or competitions. Fruit juices, sports beverages, and other high-sugar foods low in fat and fiber allow carbohydrate to enter the bloodstream quickly. Conversely, consuming high GI foods too soon before exercise can lead to a high insulin response, and then a drop in blood sugar levels that leave an athlete tired at the beginning of a workout or contest. Hundreds of food products—including sports drinks, bars, goos, and gels—have been designed for athletes seeking optimal glycogen and blood sugar levels.

See Also: Blood sugar regulation; Carbohydrates; Diabetes, type 1; Diabetes, type 2; Digestion and the digestive system; Fiber; Glucose; Insulin.

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Grains

Grasses that are cultivated for food have seeds which are called "grains." True grains belong to the Poaceae botanical family. Nutritionists generally include several other plants, such as amaranth, buckwheat, and quinoa in the "grain" family, as they are prepared and consumed in similar ways. Grains provide a significant portion of the daily energy intake in most countries around the world. The whole grain consists of three parts: the bran is the outermost layer that protects the grains from the environment, the endosperm is what provides food for the seedling, and the germ is the plant embryo. What makes whole grains whole is they have not been milled—a process that removes some or all of the bran and germ along with the nutrients and fiber found in those components. Grains can be consumed as whole or milled grains or when made into other products. Public health campaigns are encouraging consumers to replace some of the milled or refined grain products in their diets with whole grains and whole grain products, to improve diet quality.

Grains commonly cultivated and consumed include the following (Whole Grains Council, 2014; CDC, 2012).

- Amaranth: This grain usually is popped and eaten like popcorn and is especially high in fiber and protein. Like quinoa and buckwheat it is not a true grain.
- Barley: Barley often is used in soups and stews and is a great source of fiber.
- Buckwheat: This pseudo-grain is one the most heart-healthy choices because it is high in helpful phytochemicals and magnesium.

- Corn: Many people think of corn as a vegetable but it actually is a grain. Corn is high in fiber and beneficial phytochemicals.
- Millet: This grain often is served like rice and is high in magnesium, manganese, and phosphorous.
- Oats: Oats are one of the most popular grains, consumed whole, rolled, or in a variety of products. The soluble fiber in oats helps to lower blood cholesterol levels.
- Popcorn: Popcorn is a familiar grain to moviegoers. Once this whole grain is popped and drenched in fats and salts, its health benefits are reduced. Popping in healthful oils and adding small amounts of salt along with other herbs and spices can create a more healthful snack.
- Quinoa: This pseudo-grain offers more protein than any other grain, and the protein is complete, meaning that it has all nine essential amino acids.
- Rice: Brown rice (a whole grain) contains greater amounts of vitamins, minerals, and fiber than does white rice, which is polished to remove the outer covering.
- Rye: Rye usually is used in breads and is an excellent source of manganese.
- Teff: Teff is the smallest grain in the world.
- Triticale: The triticale grain is a hybrid of wheat and rye.
- Wheat: Many varieties of wheat are found in the food supply, including durum, bulgur, faro, spelt, and kamut. Wheat products include breads, pasta, and couscous, along with baked goods made from wheat flours.
- Wild Rice: Wild rice actually is not a type of rice, but is a grain that has a strong nutty flavor and is an excellent source of fiber and protein.

Nutritional Content

Whole grains contain many vitamins as well as dietary fiber. Whole grains offer a high concentration of B vitamins such as riboflavin, thiamin, and niacin, as well as minerals such as calcium, magnesium, and potassium. Whole grains also have significant amounts of fiber and protein. High antioxidant activity is associated with many of the phytochemicals found in whole grains. Common grain phytochemicals include lignans, phenolic compounds, tocotrienols (forms of vitamin E), tannins, enzyme inhibitors, and phytic acid.

Refined grains are grains that have been milled, a process that removes the bran and germ. Removing these components extends the shelf life of the grain product and creates a finer flour texture. Despite not being as healthful, refined grains and their products are popular in many countries. Refined grains include white flour and white rice. Grain flours are used to make white bread, cereals, crackers, pastries, and desserts.

Enriched and fortified grain products have added nutrients. Enriched means that nutrients typically removed during the milling process, such as B vitamins, are added back to the product. Fortified means extra nutrients, such as iron, that were not present in the original grain are added to the product. These added nutrients are listed on the labels of food products.

Grains and Health

Grains supply consumers with a rich source of complex carbohydrates. Although carbohydrates serve as an important fuel substrate for energy production, obesity can result if too many calories—including calories from carbohydrates—are consumed. Grain products such as donuts and dessert foods also can be high in added fats and sugars. Therefore, the health effects of grain consumption hinge on how grains are consumed.

Studies support the idea that a moderate consumption of whole grains prepared in healthful ways contributes to good health for people in energy balance, that is, people not consuming excess calories. Epidemiological studies suggest that the consumption of whole grains, rather than refined grains and grain products, is associated with a decreased risk of cardiovascular disease (CVD) (Jonnalagadda et al., 2011). Researchers believe the benefits of whole grains for cardiovascular health probably are attributable to the higher intake of cereal fiber. Other components in whole grains like antioxidants, lectins, and phytic acid also might reduce risk for CVD (Slavin, 2004).

Some studies indicate that consumption of whole grains is associated with reduced rates of gastrointestinal cancer and possibly other cancers. Whole grains contain selenium, vitamin E, and phytochemical antioxidants that might help slow carcinogenic processes in cells. Many phytochemicals found in grains, including digestive enzyme inhibitors, saponins, phytic acid, and phenolics could act as cancer inhibitors, as they might have the ability to prevent the formation of carcinogens as well as being able to block the interaction of carcinogens with cells (Slavin, 2004).

Rates of type 2 diabetes have been increasing dramatically in the United States and many other countries. This disease often can be controlled through lifestyle changes that produce weight loss, for those who are overweight, and prevent high blood glucose levels. Reducing consumption of carbohydrate foods often is part of type 2 diabetes treatment. Along with reducing carbohydrate intake, replacing the intake of refined grains with whole grains is recommended to increase fiber intake and diet quality. Researchers think that people consume fewer calories per day when their diets contain more fiber. It is possible that increasing dietary fiber content might help people eat less and could prevent weight gain.

Labeling of Whole Grain Products

The term "100% whole grain" means something different according to which agency is defining it. According to the U.S. Department of Agriculture Food and Nutrition Service, a food is considered whole grain when it meets one of three requirements: (1) it has 8 g of whole grain per serving; (2) it is 51% whole grain by weight; or (3) it has a whole grain as the first ingredient (Whole Grains Council, 2014).

Grains and Gluten

People with celiac disease, gluten intolerance, non-celiac gluten sensitivity, and wheat allergies must avoid foods that contain a protein called gluten. Gluten is found in all varieties of wheat and wheat products, barley, and rye. Other grains, including the pseudo-grains amaranth, buckwheat, and quinoa, do not contain gluten. Consumers should be aware, however, that these gluten-free grains can become contaminated with wheat and other gluten-containing grains during processing. Food labels can help consumers find out which products should be gluten free.

Improving Grain Choices

The *Dietary Guidelines for Americans* recommends that adults should consume at least half of their grains as whole grains. The purpose of this recommendation is to reduce the consumption of grain products of lower nutrient density, possibly reducing the consumption of dessert foods with added fats and sugars, and increase people's intake of cereal fiber. The consumption of whole grains is much lower than what is recommended; Americans on average have less than one serving of whole grains per day and 40% of adults don't have whole grains in their diet at all (Whole Grains Council, 2014).

How to Increase the Consumption of Whole Grains

One way to increase the consumption of whole grains is to simply substitute a refined-grain product with a whole-grain product, such as replacing white bread with whole-grain bread, or using brown rice instead of white rice, or whole-wheat pasta instead of white pasta. Whole-grain breakfast cereals are a good way to add more whole grains to the diet. Another easy way to increase whole grains in the diet is to eat popcorn, which itself is a whole grain; if it is air popped with very little salt and butter it is a healthful snack.

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Research Issues

Can grains be harmful to a person's health? Sensational book titles such as *Wheat Belly* and *Grain Brain* suggest that this can be the case. What is the evidence? Many people do consume too many calories, too many carbohydrates, and too much junk food, all of which elevate blood sugar. High blood sugar, in turn, damages arteries, thus increasing risk of heart disease, stroke, and dementia. High blood sugar and excess calories lead to too much adipose tissue, and the increased risk of developing the cardiometabolic syndrome and type 2 diabetes. When people eliminate grains from their diets, diet quality often improves if they replace grains with fruits and vegetables, and reduce intake of refined grain products with added fats and sugars. It is likely, however, that most people in energy balance can benefit from consuming small portions of whole grains.

See Also: Carbohydrates; Celiac disease; *Dietary Guidelines for Americans*; Enrichment and fortification; Fiber; Phytochemicals.

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Health Canada

Health Canada is Canada's federal department responsible for public health. Its mission statement highlights objectives to support scientific research and evaluation, as well as to ensure the quality of medical products and health care. Health Canada regulates and approves a wide range of products including food, consumer goods, medical devices, biologics, natural health products, pharmaceuticals, pesticides, and toxic substances. Health Canada promotes public health through a variety of educational programs.

Health care in Canada largely was privately funded and delivered before World War II. In 1957, the first specific set of health care services provided under universal coverage were outlined by the federal government in the Hospital Insurance and Diagnostic Act. These legislations eventually were consolidated to establish a system that was more accessible and comprehensive. Currently, Health Canada sets and administers principles and guidelines for the national health care system through the Canada Health Act.

Food safety and nutritional adequacy are key responsibilities for the promotion of public health. Health Canada establishes policies and standards for food safety and nutritional value as mandated by the Food and Drug Act. Surveillance of nutrition and food data informs many aspects of food safety, nutrition-related health outcomes, and nutrient intakes. Novel foods such as food additives, genetically modified foods, and biotechnology-derived foods are reviewed for approval by Health Canada. Before public distribution, companies producing novel foods are required to submit detailed scientific data for assessment. The organization is also responsible for providing safety warnings on food products currently in production. Potential food-related hazards are addressed in the Recalls and Safely Alerts Database, a regularly updated, comprehensive list of advisories and recalls.

As an authoritative voice in nutrition education, Health Canada focuses on the role of healthy eating in human development and disease prevention. Various public health programs and education initiatives are created through the Office of Nutrition Policy and Promotion and the Food Directorate. Topics addressed by the agency include prenatal nutrition and infant feeding as well as achieving healthy weight and activity levels in the general population.

Eating Well with Canada's Food Guide outlines information on nutrition and healthy eating. The guide is useful for learning basic nutrition facts, calculating individual energy requirements, and understanding recommended daily nutrient

intakes. Serving suggestions are provided for four food groups—vegetables and fruits, grain products, milk and alternatives, and meat and alternatives. Whole grains such as barley, quinoa, wheat, oats, and wild rice are recommended. To ensure the intake of a variety of micronutrients, Canadians are encouraged to eat at least one green vegetable and one orange vegetable per day. The food guide also suggests increased consumption of meat alternatives such as beans, lentils, and tofu in addition to two servings of low-mercury fish each week. Additional tools for nutrition support are found in the shopping tips, meal ideas, and recommendations for maintaining healthy habits. Interactive guides teach the importance of reading nutrition labels and understanding nutrition claims.

Ana Maria Moise

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Herbs and Herbal Medicine

An herb is a plant or plant part that is used for its flavoring, scent, and/or medicinal qualities. Botanists use the word "herb" to refer to seed-producing plants that do not develop woody branches (as do shrubs and trees), but which die after the growing season. The term also is used to mean any plant that provides desired components for food or medicine—which is the use that is discussed here.

Plants have provided the foundation of most human diets throughout the ages, and people in all cultures have developed ways to use plants for foods, medicines, and other purposes. Examples of popular herbs used in North America for health benefits include echinacea and ginkgo biloba. Garlic and ginger are examples of herbs that are used in the diet both to flavor food and as components of dietary supplements for health benefits. Soy products, such as edamame, provide nutrients and energy, along with flavors and health benefits.

Although herbs contain a range of chemicals that contribute flavor and health benefits when consumed, plant components also can be toxic and have been used intentionally as poisons in many cultures throughout time. Some plant compounds used for healing have both health benefits and risks. Kava, for example, can reduce feelings of tension and stress but has also been associated with liver damage. Current pharmacopeias—books with official lists of medical drugs' uses and compositions—contain many medical formulas taken directly from ancient herbalists. Herbs traditionally used in cooking are regulated as food. In the United States, food and drug regulations define and regulate herbal products as dietary supplements.

History of Herbal Medicine

The healing effect of herbs for numerous human diseases has been observed since before recorded history. One of the oldest known medical documents is the Edwin Smith Papyrus, and it documents the recommended use of herbal medicine over magic in Egypt in 1500 BCE. Other surviving papyrus documents from the period list more than 700 substances that mostly consist of plant derivatives. Information regarding herbal remedies spread from the ancient Near East along trade routes and disseminated into the medical practices of the ancient Greek world.

The ancient Greeks and Romans linked many of their gods and goddesses to specific herbs. Greek mythology, for example, documents the goddess Demeter being closely associated with barley water mixed with fresh mint through her asking for a glass of that concoction after the her nine-day search for abducted daughter Persephone (D'Andrea, 1982). Another example associates the myrtle plant with Venus, whereby it commonly became depicted as a symbol of marriage and indication of being a bride. Greek mythology hints at the power of herbal medicine as a life-saving remedy. Classical Greek medicine attributed the healing properties of herbs to their god Apollo and his son Asclepius, the herbalist of the gods.

The medical school of Alexandria, founded in 260 BCE, established an international reputation in its day as a top medical school. Medical treatises which included herbal remedies were translated and shared throughout the ancient world. Dioscorides, a surgeon in the Roman army, wrote a five-volume series on how to make drugs—primarily from herbs—and titled *De Materia Medica*. It became the prominent medical handbook of its century and spread throughout the Roman Empire.

Historical scholars claim Hippocrates (ca. 460 BCE–ca. 370 BCE) as the founder of Western modern medicine. Hippocrates was one of the first practitioners to abandon supernatural beliefs in the occult and turn his focus toward observation and scientific method, a major step that revolutionized the practice of medicine. Many of his remedies included pure herbs without alteration. Historical scholars also recognize Theophrastus (ca. 372 BCE–ca. 287 BCE) as the first scientific botanist. Theophrastus made a systematic analysis of herbs. His book, *Enquiry into Plants*, had a profound effect on herbal medicine during the medieval period and antiquity. Theophrastus outlined plant parts used, scientific and superstitious practices, and included expert advice from druggists and herbalists regarding the cultivation and use of herbs.

Through legend and education, the apparent healing effects of herbal medicine were passed down through generations. The three main influences on medieval medical botany in Europe were Greco-Roman school medicine; Christianity's interpretations of orthodoxy; and pagan folk beliefs, which incorporated the use of magic. After the fall of the Roman Empire, Christian monks preserved the knowledge of herbal medicine within their illuminated manuscripts.

Abd-Allah Ibn Al-Batir—a Muslim scientist and botanist of the 13th century—compiled a pharmacopeia titled *Simple Drugs and Food*, which became the most frequently translated book of the Middle Ages (Jorda, 2008). This

publication had far-reaching effects promoting herbal medicine beyond the Arab world into North Africa.

The use of herbs for both health maintenance and healing purposes has been central to many Asian medical traditions for thousands of years, including in Indian Ayurvedic medicine, traditional Chinese medicine, Tibetan medicine, and Japanese herbal medicine (known as "Kampo") (NCCAM, 2013).

Plants: Food and Phytochemicals

Plants can provide nutrients including carbohydrates, protein, fats, minerals, and vitamins. Plants also supply dietary fiber and and many other compounds, known as "phytochemicals." Phytochemicals include both primary and secondary metabolites. "Metabolites" are the intermediates and products produced during an organism's metabolism. Primary metabolites are substances that the plant requires to survive and are directly involved in the plant's normal growth, development, and reproduction. They include carbohydrates, fats, and proteins. Although not essential for survival, secondary metabolites are recognized as having beneficial effects upon an organism's health. Secondary metabolites include plant pigments that protect plants from too much sunlight, for example. When people consume these pigments, the pigments appear to exert helpful antioxidant activity in the human body. People also are able to utilize many of the secondary metabolites found in herbs for medicine and flavoring. Both primary and secondary metabolites are believed to have medicinal qualities, but the exact effects of many of these substances on the human body are largely unknown.

Ubiquity of Herbs and Herbal Remedies

Herbs continue to play a major role in the complementary and alternative treatment of ailments around the world. Traditional Chinese medicine, for example, still is popular today. It combines acupuncture and massage with prescriptions of herbal remedies. Naturopathy is another holistic approach to medicine focusing on noninvasive treatment and natural cures using herbs and herbal extracts. Homeopathy was established in 1876 with the premise of "like cures like." Homeopathic remedies are made from plants, minerals, and animal products. Allopathic medicine, also known as "modern biomedicine," treats chronic aliments by alleviating symptoms with drugs that often are extracted and refined from herbal sources. Aromatherapy uses extracts of essential oils from plants and herbs to alter a person's cognitive state, such as mood, in an effort to promote better health.

Regulation of Herbs

Primary metabolites as components of plants consumed as food have been part of the human diet throughout history. These foods and components therefore usually are unregulated as a result of their history of being harmless. Derivatives of these primary metabolites, however, can be artificially modified to create new forms

never before seen in the diet. The Dietary Supplement Health and Education Act (DSHEA) of 1994 currently classifies herbs as dietary supplements which are not subject to drug requirements of proof of efficacy and safety tests. Because herbs are deemed "natural" they often are assumed to be safe, but this is not always the case. Consumers should research herbal products—especially dietary supplements—before consuming any.

Jinan M. Martiuk

See Also: Dietary supplements; Phytochemicals.

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Heterocyclic Amines and Polycyclic Aromatic Hydrocarbons

Heterocyclic amines (HCAs) are chemicals that include an amine (nitrogen) group and a heterocyclic ring. A heterocyclic ring is a ring of carbons that includes an atom of an element that is not carbon, such as nitrogen, oxygen, or sulfur. Not all HCAs are harmful, but researchers and consumers have become concerned about a group of carcinogenic HCAs that are produced from cooking muscle meats such as beef, pork, fish, and poultry at high temperatures, particularly during grilling and frying. Polycyclic aromatic hydrocarbons (PAHs) are a type of chemical produced during the incomplete burning of organic substances such as meat, tobacco, and coal, and are composed of aromatic rings fused together. An aromatic ring is a closed chain of six carbons, each bonded to a hydrogen, as in a benzene ring. Heterocyclic amines and polycyclic aromatic hydrocarbons are capable of causing genetic mutations that can initiate the development of cancer. Although high exposure to HCAs and PAHs can cause cancer in animals, the link between humans and

HCA and PAH consumption still is unclear. Epidemiological studies have found an association between consumption of well-done meats and grilled meats, especially grilled processed meats such as hot dogs, and some types of cancer. Apart from avoiding consumption of grilled meats, using certain cooking techniques can reduce the risk of HCA and PAH formation. These include microwaving the meat or marinating meat before cooking it.

Heterocyclic amines are formed when amino acids, sugars, and creatine react at high temperatures. Formation is greater in well-done or medium-well-done grilled or barbequed chicken and steak. This is especially true for meats cooked at temperatures greater than 300°F. Polycyclic aromatic hydrocarbons in food usually are produced during the grilling of meats. Fats and other juices from the meat drip onto the coals beneath the meat being cooked, and produce PAHs. Flames and the smoke produced from the drippings carry the PAHs back up to the meat, where they adhere to the meat's surface. When enzymes in the body break them down, HCAs and PAHs become capable of damaging DNA. Both of these carcinogens usually are concentrated in the burnt or charred areas of the meat. When chicken is grilled or barbequed, the skin has more than eight times the amount of HCAs as the meat contains.

Research has found a link between the consumption of HCAs and certain forms of cancer. When HCAs are introduced to the diet of mice, the mice develop tumors in organs such as the colon, breast, and prostate (Sugimura, Wakabayashi, Nakagama, & Nagao, 2004). Although the amount of HCAs consumed by humans is less than the doses given to laboratory mice, human epidemiological studies have shown a positive correlation between preference for high-temperature cooked meat and an increased risk of cancer, including cancers of the prostate, pancreas, breast, colon, and rectum (American Association of Cancer Research, 2009; National Cancer Institute, 2010). In one study, 62,581 participants—including 208 people diagnosed with pancreatic cancer—were interviewed about their meat intake. Researchers found that the participants with a preference for well-done steak were about 60% more likely to develop pancreatic cancer than those participants who ate rare or medium rare steak, or did not consume steak (American Association of Cancer Research, 2009).

Research on the association between PAHs and cancer originated with studies of workers with occupational exposure to these chemicals. Workers in coal carbonization and gasification in 1936, for example, were found to have higher rates of lung cancer mortality (CDC, 2011). Animal studies have confirmed the carcinogenicity of PAHs, which appear to particularly increase risk of skin cancer, along with cancers in the pulmonary, gastrointestinal, renal systems (CDC, 2011).

There are several ways to prepare meat to lower consumption of HCAs and PAHs. Instead of grilling or barbequing, cooking meats on low heat using techniques such as steaming or stir-frying minimizes the formation of HCAs and PAHs. Microwaving the meat before grilling or pan-frying produces well-done meat without the prolonged exposure to high temperatures. Marinating meat before grilling also reduces production of HCAs and PAHs. Grilling vegetables does not produce

carcinogenic chemicals, therefore consuming dishes such as a shish kebab composed mostly or entirely of vegetables is less harmful than eating a large charbroiled steak.

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See Also: Cancer and nutrition; Nitrates and nitrites, dietary.

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High-Fructose Corn Syrup

High-fructose corn syrup (HFCS) is a common sweetener used in many food products. It is called "high fructose" because the syrup contains more fructose than regular corn syrup. Food engineers developed high-fructose corn syrup during the 1960s to serve as a sugar alternative. The abundance of corn has made HFCS cheaper than regular table sugar. High-fructose corn syrup became a popular ingredient in food products in the 1970s. Recently, consumers have questioned the safety of HFCS and other sugars in the diet, as studies show that too much sugar poses many health risks, including risk for obesity and type 2 diabetes.



Grain elevator with surplus corn pile in Nebraska. (Jeff Wilson/Shutterstock)

History

The process of converting starches to sugars was first developed in Japan in the 1800s using arrowroot (Cavette, 2009). The process became more popular in 1811, when Russian chemist Gottlieb Kirchhoff added sulfuric acid to starch and obtained starch-derived sweeteners. The method was brought to the United States in 1831 when chemist, physician, and inventor, Samuel Gutherie, explored the possibilities of creating sugar from potato starch (Warner, 2011). Americans soon adapted the new method to create cornstarch, and later began to derive glucose from corn. In 1866, a plant in Buffalo, New York, produced the first corn sweeteners. An enzyme-conversion method was discovered to yield high-fructose corn syrup in 1967.

The Market

Because of American agricultural subsidies, corn is both abundant and cheap, making high-fructose corn syrup one of the most common commercial sweeteners. Many American food manufacturers turned to corn syrup after 1977 when new tariffs and sugar quotas made importing sugar significantly more expensive (Goldstein, 2012). By 1996, 28 corn-refining plants existed in the United States, and about 25 billion pounds of corn were converted into corn syrups and other corn sweeteners (Cavette, 2009). Corn-based products provide more than 50% of nutritive sweeteners in the United States.

Processing

High-fructose corn syrup is mostly composed of fructose and glucose, but it also contains water and a small amount of other sugars. The two types of HFCS most commonly produced commercially are HFCS-42 and HFCS-55. The former consists of 42% fructose and 53% glucose; the latter consists of 55% fructose and 42% glucose. The percentage of fructose in the solution is positively correlated with the sweetness of the solution, as fructose is naturally sweeter than glucose. HFCS-42's sweetness is comparable to that of sucrose, whereas HFS-55 is sweeter than sucrose.

Not only is HFCS sweet, but it also can be used as a flavor and texture enhancer. High-fructose corn syrup also is used as a preservative, and it can help maintain levels of moisture in packaged foods. Although sugar derived from cane or beets undergoes a less complex process, corn syrup is more cost effective because of the availability of the corn crop. Therefore, the overall lower production cost yields greater profits for food producers.

Food manufacturers use high-fructose corn syrup in a variety of processed foods. HFCS appears most obviously in sweet foods, but it also is an ingredient in many savory products, which could account for the large quantities of HFCS that Americans today unknowingly consume. Corn syrup is used as a sweetener in foods like soft drinks, candy, baked goods, jams, sports drinks, pancakes, breads, fruit drinks, and flavored yogurt. HFCS is used as a flavor enhancer in products such as salad dressings, frozen pizza, macaroni and cheese, tonic water, and ketchup. High-fructose corn syrup also is used for added texture and prolonged shelf life.

Fructose Metabolism

Fructose, like glucose, is a six-carbon sugar. Although fructose is naturally occurring in foods such as fruit and honey, dietary fructose is not necessary for humans. Fructose metabolism occurs primarily in the liver, and favors the metabolic pathway leading to lipogenesis (formation of triglycerides). Several studies have found that a high-fructose intake increases circulating lipid levels; this happens with other sweeteners as well.

Health Risks

Although high-fructose corn syrup appears in a large number of food products that people consume, it is an ingredient that many people try to avoid. Because obesity rates increased during the same time period, researchers wondered if HFCS might be responsible. Several studies have found that excessive consumption of high-fructose corn syrup, like excessive consumption of other sugars, could pose many health risks, especially weight gain and the health problems associated with obesity. Rodent studies suggest that high-fructose corn syrup might cause greater weight gain than table sugar, and increase the risk of cardiometabolic syndrome. In

humans, a high consumption of HFCS has been associated with increased risk for the development of hypertension, kidney damage, type 2 diabetes, and cardiometabolic syndrome. But over time, researchers have found that the health risks associated with HFCS appear to be similar to those for other added nutritive sweeteners, including sugar (White, Foreyt, Melanson, & Angelopoulos, 2010). This is not surprising as cane sugar, beet sugar, and HFCS all are approximately 50% fructose.

Preliminary evidence suggests that fructose could fuel the growth of cancer cells (Boros et al., 2010). One research team observed pancreatic cells in vitro and found that pancreatic cancer cells given fructose grew faster than normal. The study revealed that—even though it is known that cancer cells use glucose to proliferate—they can just as readily use fructose, unlike other cells. More research is needed before these results can be applied in vivo. Fructose comes not only from HFCS and sucrose, but from fruits and vegetables as well. Public health experts recommend that all people limit their intake of food products with added sugars to prevent obesity and obesity-related health risks.

Environmental Impacts

The United States produces more corn than any other country. Corn is the biggest cash crop in the United States, occupying approximately 84 million acres of land (EPA, 2013). Many factors have led to corn being America's number one crop, including the introduction of high-fructose corn syrup. Monoculture corn production has a number of environmental impacts. Corn requires more synthetic fertilizers and pesticides than any other crop (Hartman, 2008). The fertilizers and pesticides are made from fossil fuels, and their hazardous chemical components are incorporated into runoff and subsequently contaminate the soil and bodies of water. Many consumers also are concerned about the prevalence of genetically modified corn in the United States and many other countries.

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See Also: Fructose; Obesity, causes; Sugar-sweetened beverages.

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Honey

Honey is made from the nectar of flowering plants, which honeybees break down into simple sugars and store in honeycombs. The shape of the honeycomb and the beating the bees' wings then cause much of the remaining moisture to evaporate, forming honey. Beekeepers remove frames of honeycomb from their hives and extract the honey. The honey then is strained, sometimes by using heat to speed the process, and bottled. Honey has different flavors, colors, aromas, sugar ratios, and antioxidant chemical content depending upon the flowers from which the bees collected the nectar. In North America there are more than 300 types of honey available, such as alfalfa, clover, and orange blossom. Humans have enjoyed honey's delicious flavor and sweetness throughout history. Honey also has been used for medicinal purposes in many cultures.

The honey produced by bees provides a source of energy for all of the bees in the hive. Nectar itself would ferment, and therefore does not serve as a suitable food source for use during the winter. To make honey, bees swallow the nectar as they collect it, storing it in an organ called the honey stomach. Enzymes in this organ act upon the nectar, converting the nectar's sucrose into glucose and fructose. The bees then regurgitate the product back at the hive, where other bees also ingest it, break it down further, and then regurgitate it. The honey then is stored in the honeycomb. After the water has evaporated, the honey maintains its nutritional qualities for extended periods of time.

Honey is predominantly composed of fructose and glucose. The fructose content gives honey a lower glycemic index than that of other popular sweeteners. Because it is concentrated, honey has more calories per tablespoon than granulated, powdered, or brown sugar. Honey also contains phenolics, peptides, organic acids, enzymes, and Maillard-reaction products which, combined, give honey its antioxidant capacity. Additionally, honey is a prebiotic; it contains a type of fiber that is not digested in the human digestive tract but instead feeds the beneficial bacteria that live in the intestines. A study in laboratory mice found that feeding the mice a food mix with honey led to a more beneficial mix of intestinal bacteria as compared to feeding them a food mix containing sugar (Ezz El-Arab et al., 2006).



A beekeeper examines a framed beehive panel. Many commercial beekeepers transport their bees to various locations around the country, freeing the insects in orchards so they can pollinate the crops. However, Colony Collapse Disorder poses a threat to the livelihood of migratory beekeepers, commercial growers, and U.S. consumers. (iStockPhoto.com)

The American Academy of Pediatrics recommends withholding honey from children younger than one year old, because spores from the Clostridium botulinum bacteria occasionally migrate from the soil into beehives. People older than one year have stronger immune systems and can cope effectively with the minute traces of the bacteria which occasionally occur in honey products, but infants could develop botulism infection.

All honey contains hydrogen peroxide, produced by bee enzymes in the honey-making process, and also has antimicrobial and antibacterial properties. Honey has been used on wounds to prevent infection, although that practice has become less common over time. Manuka honey, made from the pollen of the manuka bush in New Zealand, has been found to have antimicrobial, antibacterial, and antifungal properties, and has been made into a product called Medihoney, which was approved by the FDA in 2007.

Honey is a humectant, meaning it attracts and retains moisture. For this reason it often is used in moisturizers and to soothe and coat sore throats and suppress coughing. A couple of well-controlled studies have shown that honey might provide an effective treatment for cold symptoms. One study found that, as compared to a sweet placebo, honey increased sleep time and reduced nighttime coughing in

300 children 1 to 5 years old who had upper respiratory tract infections (Cohen et al., 2012).

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See Also: Glycemic index and glycemic load; Microbiota and microbiome.

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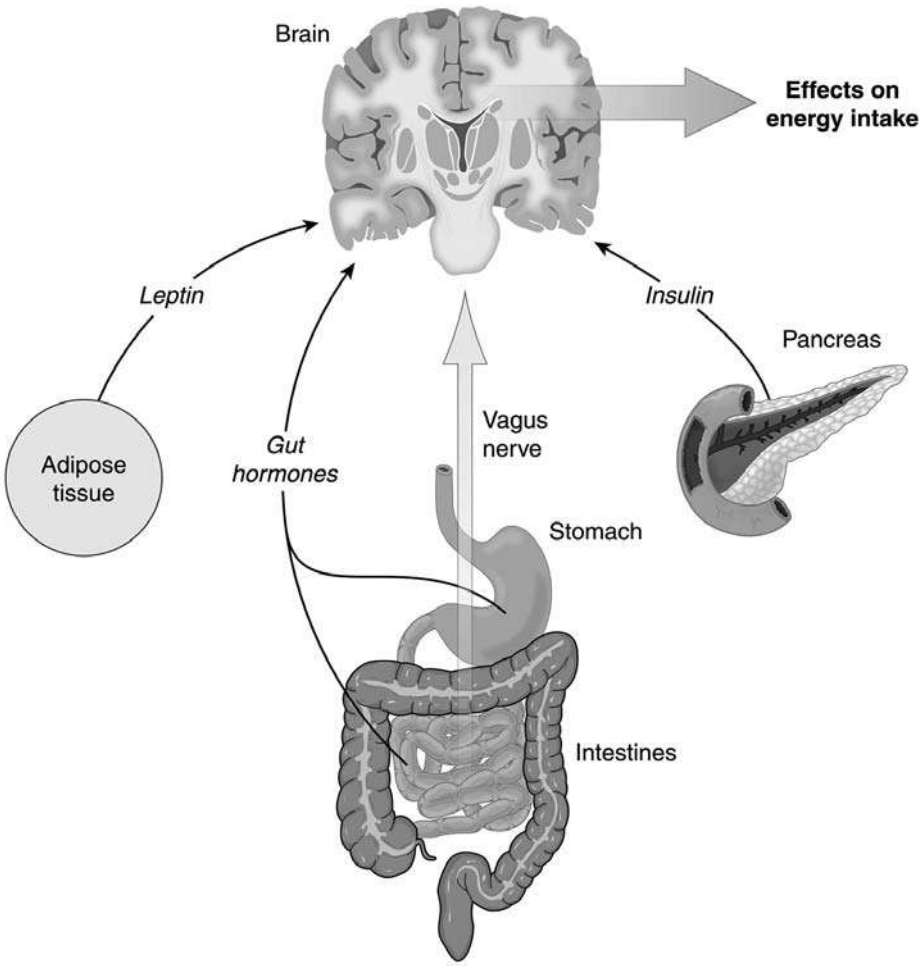
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Hunger, Biology of

Hunger is defined as the internal, physiological drive to find and consume food. Individuals often interchange the words "hunger" and "appetite." There is a key difference between these terms, however, and they are easily distinguishable. Hunger often is experienced as a negative, physical sensation when prolonged, and appetite is a psychological desire for food and often is a positive sensation. Hunger often begins with the sensation of an empty stomach or hunger pangs. The regulation of hunger also is controlled by an area in the brain called the lateral hypothalamus. Additionally, two important hormones—leptin and ghrelin—signal the brain when there is a lack of nutrients or when fullness is reached. There are believed to be more than 50 different chemicals, however, that play an integral part in regulating hunger and eating behavior (Insel, Ross, McMahon, & Bernstein, 2014).

Although hunger has a negative connotation and is thought of as something that must be "fixed" or "eliminated," hunger is an essential physical drive that ensures animals, including humans, obtain the food necessary for survival. This drive is helpful in many situations, but researchers are studying how hunger is related to overeating. It is important to know about the various regulations and the physiology of hunger because of the high rates of obesity worldwide. Understanding hunger and its physiological regulation could greatly improve the understanding and treatment of obesity.



Many factors affect the sensation of hunger. These include leptin levels, gut hormones, and the hormone insulin. (Legger/Dreamstime.com)

Biology of Hunger

The basic purpose of eating is to satisfy the body's need for nutrients and energy. Hunger typically is characterized by the aching and empty feeling that the stomach experiences. It is the body's first demand for essential nutrients. As the feeling persists and goes unsatisfied, the sensations grow into an uncomfortable pang, which most people call a "hunger pang." It can be distinguished as a growling stomach or a contracting pain in the abdominal area. This easily is relieved by ingesting food.

The hypothalamus plays a very important role in coordinating the chemicals that regulate hunger. The hypothalamus is located in the forebrain region, just above the brainstem and below the thalamus. There are three sections of the hypothalamus that are involved in the regulation of hunger; the lateral, the ventromedial, and the paraventricular. Damage to the ventromedial section of the hypothalamus produces a condition known as hyperphagia, which causes animals to overeat and gain enormous amounts of weight. Damage to the lateral hypothalamus produces aphagia and adipsia, which is the total lack of drive to eat or drink, respectively.

The hypothalamus regulates hunger through the release and monitoring of certain hormones. These specialized hormones circulate within the body and act as initiators or terminators of hunger. The lateral hypothalamus stimulates hunger. It produces the hormone orexin when blood sugar levels are too low. The ventromedial hypothalamus is responsible for controlling the amount of food consumed. When this area of the hypothalamus is stimulated, it reduces the feeling of hunger.

There are two mechanisms that influence the regulation of hunger—the short-term and long-term mechanisms. The short-term mechanism reflects daily energy balance, in which food intake is balanced with energy expenditure. The second mechanism, the long-term regulation, is the storage mechanism. Excess energy (calories) is stored so that it will be available for later use or use when emergency energy is needed spontaneously. This stored energy is in the form of fat within the adipose tissues and cells. The short-term mechanism generally is assumed to be closely related to monitoring blood glucose levels and when that level becomes too low, hunger is induced. The long-term mechanism involves monitoring the body's fat level and induces hunger when fat stores become too low.

Hunger Hormones

Neuropeptide Y is a major neurotransmitter that acts in the brain and in the autonomic nervous system. In the autonomic nervous system it is mainly produced by neurons of the sympathetic nervous system. Neuropeptide Y is produced in various locations in the brain, including the hypothalamus. In laboratory animals, elevating the activity of neuropeptide Y results in the increase of food intake.

Peptide YY is a short protein that is released by the cells in the ileum (the lower portion of the small intestine) and the colon. In humans, it appears to reduce hunger after a meal. Peptide YY works by decreasing hunger and increasing water and electrolyte absorption in the colon. Peptide YY works by slowing gastric emptying; it increases the effectiveness of the digestion process and nutrient absorption after a meal. Peptide YY signals the brain to sense that it is not hungry.

Leptin is a hormone produced by fat cells that appears to be involved with the long-term regulation of hunger. Increasing leptin levels appear to decrease the production of neuropeptide Y, thus decreasing hunger. Experiments on mice have revealed that leptin hormone levels are greater when more fat is present; however, other contributing factors—such as sleeping and eating patterns—also affect leptin levels. Additionally, it is possible for the body to become leptin-resistant. A person

who is leptin-resistant does not experience the normal increase in satiety and then stop eating after a filling meal. Leptin resistance is associated with excessive hunger and risk of obesity.

Ghrelin is released by the stomach and sends a signal to the brain that increases hunger. It has been shown that levels of ghrelin increase right before consuming a meal and decrease afterward. Ghrelin levels can be influenced by certain lifestyles and by stress. Studies have revealed a positive relationship with ghrelin and stress; thus, when stress rises and becomes significant, ghrelin levels also increase. Physical activities—such as weight lifting—have been shown to decrease ghrelin as well as food intake. Sleep deprivation has been associated with elevated ghrelin levels and therefore, increasing hunger (Adams, Greenway, Brantely, 2010).

Orexin, also known as "hypocretin," is produced by the hypothalamus. This neurotransmitter has various functions that include wakefulness, arousal, and appetite. Orexin increases feelings of hunger and has been shown to be inhibited by leptin and activated by ghrelin.

Hormones produced during the absorption of nutrients following digestion generally reduce feelings of hunger. These hormones include insulin, produced by the pancreas in response to elevations in blood sugar, and cholecystokinin, produced by the small intestine after a meal, in the presence of fats.

Prader-Willi Syndrome

Prader-Willi Syndrome is the most commonly known genetic cause of life-threatening obesity in children. It usually causes poor muscle tone, stunted growth, and a chronic feeling of hunger. It is a complex genetic disorder that causes the hypothalamus to dysfunction. This chronic feeling of hunger in turn causes the children to become obsessed with eating and with food. The amount that these children actually consume far exceeds physiological need. The lack of muscle tone results in the child only needing two-thirds of the normal calorie intake.

Sandy Wong

Research Issues

Dieticians and others who advise people on weight loss have been interested in research on hunger. Some popular weight-loss advice is based on the physiology of hunger. Dieters, for example, often are told to eat slowly so that hunger has time to fade. The fading of hunger is caused at least in part by the release of cholecystokinin by the small intestine when the organ detects the presence of fat. It takes at least 15 to 20 minutes for fat from a meal to reach the small intestine, which is why people are advised to eat slowly. Similarly, advice to get adequate sleep and manage stress is designed to reduce levels of the hormone "ghrelin."

See Also: Appetite; Obesity, causes.

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Hydrogenation

Hydrogenation is the process of adding hydrogen to a molecule, which then rearranges the molecule's chemical structure. Most often this occurs in organic molecules with a double bond between two carbons. The double bond becomes a single bond, leaving each carbon the opportunity to bind with an additional hydrogen atom. Although this phenomenon happens in nature, in the food industry it also occurs as part of a synthetic process using vegetable oils. Hydrogenated fats are desirable because their bonds are not as easily broken by oxygen; therefore shelf life is extended and taste is preserved longer. To initiate hydrogenation, oil typically must be heated to more than 300°F in the presence of hydrogen and a catalyst such as nickel, copper, or platinum. The level of hydrogenation can be controlled carefully through manipulation of temperature, pressure, agitation, and concentration of the catalyst. A by-product of hydrogenation is the creation of a fatty acid structure called a "trans fatty acid," or "trans fat"; during the process, a carbon-carbon double bond is not broken, but one of the hydrogens shifts position thus altering the shape of the fatty acid.

Increasing hydrogenation raises the boiling point of the oil and leads to a progressively more solid product when it reaches room temperature. As the oil becomes more hydrogenated, the concentration of mono- and polyunsaturated fats decreases and the concentration of saturated fats increases. Partially hydrogenated oil contains varying amounts of trans fat. Fully hydrogenated oil, such as margarine and shortenings, contains less trans fat. Due to the possible negative health effects of trans fat, the Food and Drug Administration now requires manufacturers to include all partially hydrogenated oils on the ingredient label, as well as the grams of trans fats contained in a serving of the product. Some products claim to be free of trans fat, but still list partially hydrogenated oils on their label. Although

misleading, this practice is legal because the FDA considers foods with less than 0.5g of trans fat per serving to be free of trans fat.

Patricia M. Cipicchio

See Also: Trans fatty acids.

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Hyperglycemia

"Hyperglycemia" is the scientific term for high blood sugar. Fasting hyperglycemia is characterized by a blood glucose level of more than 130 mg per deciliter following an 8-hour fast. Postprandial hyperglycemia occurs when an individual continually has a blood glucose level that is greater than 180 mg per deciliter following meals (American Diabetes Association, 2013). A normal fasting blood glucose level should be less than 100 mg/dl and a random-sample blood glucose level should be less than 150 mg/dl. Occasional episodes of hyperglycemia can be benign, but frequent hyperglycemia can have extremely detrimental long-term consequences.

Diabetes is the most common cause of frequent hyperglycemia. This is because people with diabetes have difficulties producing or responding to insulin, a hormone produced by the pancreas that helps to regulate the amount of glucose that is removed from the blood by the body's cells. Certain medications (such as corticosteroids and protease inhibitors) and critical illnesses can produce acute hyperglycemia as well (American Diabetes Association, 2013). Critical illnesses such as myocardial infarction, stroke, hyperthyroidism, pancreatitis, pancreatic cancer, Cushing's syndrome, and unusual tumors create acute stress and can induce hyperglycemia. Hyperglycemia also occurs naturally during times of infection and inflammation, and the resulting blood sugar increase varies based on the person and type of response.

Although hyperglycemia has a host of symptoms, the most typical symptoms comprise what is called the "classic hyperglycemic triad." The symptoms are polyphagia, polydipsia, and polyuria, which mean "frequent hunger," "frequent thirst," and "frequent urination," respectively. Unexpected weight loss is another major symptom. Temporary hyperglycemia often is benign and asymptomatic. Blood

glucose levels can rise well above normal for significant periods without causing any permanent effects or symptoms. Chronic hyperglycemia, however, spanning a period of years, can cause serious complications such as kidney, neurological, and cardiovascular damage, as well as damage to the retina. Acute hyperglycemia involving glucose levels that are extremely high is a medical emergency and can rapidly produce serious symptoms, including disorientation, mental confusion, dizziness, and (in severe cases) coma and even death.

Treatment of hyperglycemia begins with identifying its cause and, when possible, correctly the underlying problem. In people with diabetes—who are likely to experience hyperglycemia from time to time—treatment includes taking steps to improve glycemic control (control of blood sugar levels). People with diabetes must learn to recognize the symptoms associated with hyperglycemia and improve their glycemic control by increasing frequency of glucose testing, following a healthy diet, making lifestyle changes, and adjusting medications.

Lola Murray and Sonya Bhatia

See Also: Blood sugar regulation; Diabetes, type 1; Diabetes, type 2; Glucose; Hypoglycemia.

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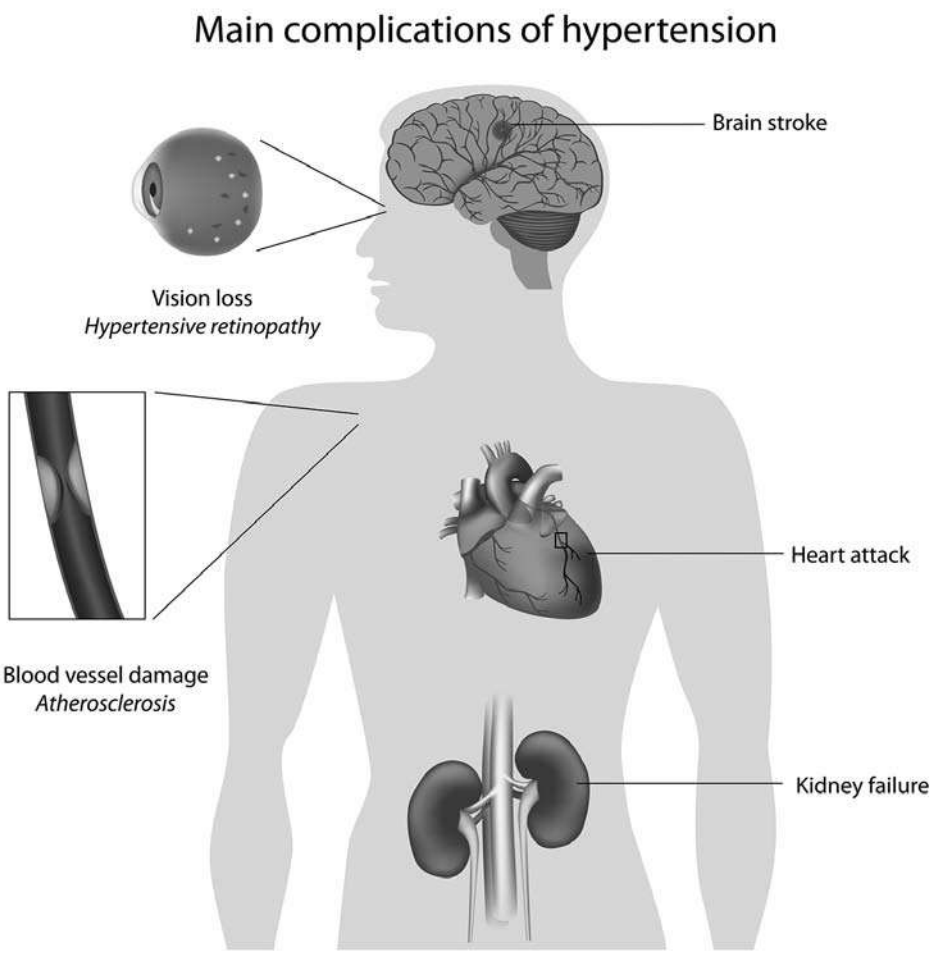
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Hypertension and Nutrition

"Hypertension" is the scientific term for high blood pressure. It is characterized by a person's resting blood pressure consistently being measured at 140/90 mmHg or greater while at rest. The normal resting blood pressure of a healthy individual is considered to be 120/80 mmHg or less. High blood pressure is the leading cause of strokes and heart failure, as well as one of the strongest risk factors for the development of heart disease. In 2008, these complications caused 7.5 million related deaths among adults worldwide, affecting about 40% of adults aged 25 and older



Hypertension is known as a "silent disease" because most people don't notice any symptoms. However, chronic, uncontrolled hypertension is associated with many health problems, including vision loss (hypertension retinopathy), blood vessel damage (atherosclerosis), heart attack, and kidney failure. (Shutterstock.com)

(WHO, 2014). The World Health Organization reports that the Americas had the lowest prevalence of high blood pressure readings, with about 35% of the population demonstrating an above-normal reading (WHO, 2014). The United States reports that hypertension affects about 30% of its adult population, with prevalence increasing with age and decreasing with education and income level (Keenan & Rosendorf, 2011).

Lifestyle change, including dietary change, is a central tool used in the prevention and treatment of hypertension. Increasing physical activity, reducing stress, and improving eating habits can reduce elevated resting blood pressure. One eating plan used to manage—and sometimes even reverse—hypertension is the DASH

(Dietary Approaches to Stop Hypertension) diet. The DASH diet emphasizes low salt intake with a high intake of vegetables and fruit and has been shown to lower blood pressure. Avoiding foods high in added fats and sugars also is beneficial to many people trying to reduce high blood pressure, as these foods can contribute to weight gain and increase the risk for high blood pressure.

Blood Pressure

Blood pressure is measured in millimeters of mercury, and is the measurement of the force exerted against the walls of the arteries as blood is pumped through them. The first number in a blood pressure measurement refers to systolic blood pressure, the pressure measured during systole, which is the contraction of the heart as it beats. The second number represents diastolic blood pressure, the pressure in the arterial system during diastole, the period between contractions. A number of factors influence blood pressure.

- Heart rate and the heart's force of contraction influence blood pressure. During exercise, for example, the heart must circulate a much higher volume of blood, thus the heart beats harder and faster and blood pressure rises; a normal and healthy response to exercise. Heart rate and the force of contraction also increase when a person feels stressed.
- The behavior of the arteries also influences blood pressure. The arteries have small muscles that alter their circumference, depending upon the need for blood in the tissues supplied by those arteries. During digestion, for example, the arteries that supply the digestive system become wider to accommodate increased blood flow. If the arteries do not widen appropriately, then the narrower artery passages create more resistance to blood flow, and blood pressure increases.
- Blood volume affects blood pressure. A greater blood volume increases blood pressure (when all other factors are equal). Fluid retention, such as that can resulting from a high intake of salt, can increase blood volume and blood pressure.

Blood pressure normally fluctuates throughout the day. Hypertension only is diagnosed when resting blood pressure is chronically elevated.

Physiological Effects of Hypertension

Over time, hypertension can lead to a number of harmful consequences. It contributes to artery disease because the greater pressure of the blood flowing through the arteries appears to cause damage to the artery lining. Hypertension seems to cause microscopic tears in the arteries that develop into scar tissue as the artery repairs itself. The scar tissue then can compromise the function of the artery lining, attracting substances such as LDL cholesterol that contribute to the formation of arterial plaque. Plaque buildup further worsens arterial function, increasing resistance to blood flow and thus increasing hypertension. Over time, plaque buildup causes arteries to become stiff

and less responsive to the chemical signals that regulate vasoconstriction and vasodilation. High blood pressure also can cause vulnerable arteries to bulge and tear, creating a hemorrhage; this process is responsible for hemorrhagic strokes. Worldwide, hypertension is considered the leading risk factor for the development of cardiovascular disease and mortality. People with hypertension have a greater risk of developing kidney disease; having a heart attack; and experiencing heart failure, a stroke, retinal hemorrhage, visual impairment, and even early death.

Causes and Risk Factors

In fewer than 10% of cases hypertension is secondary to another health problem, such as kidney disease. The vast majority of hypertension is not connected to one single cause, but rather is considered a multifactorial illness, meaning that many different variables—including both inherited and lifestyle factors—contribute to its development and severity. Hypertension not secondary to another health problem is known as "essential hypertension." The term "essential" has an interesting history. In the mid-1900s, physicians and researchers had observed that blood pressure increases with age. It was hypothesized that this increase was essential, because aging arteries were less elastic. Experts thought increased blood pressure was required to accomplish adequate blood circulation. This hypothesis later was discarded, as scientists observed that age was not associated with increased blood pressure in many areas of the world.

Many factors influence a person's risk of developing hypertension. Although some of these factors are out of a person's control, many can be modified to reduce risk. An unbalanced diet that includes excess calories, added sugars, and is high in added fats and processed foods is linked to many of the conditions that increase the risks for developing high blood pressure. The risk factors known to increase the chances developing high blood pressure are listed below.

- Obesity
- Sedentary lifestyle
- Stress and anxiety
- Overconsumption of alcohol (more than one drink a day for women and more than two drinks a day for men)
- Excess salt in diet
- Diet low in fruits and vegetables
- Smoking
- Family history of hypertension
- Diabetes
- African-American ethnicity

Symptoms

Hypertension is a condition that presents with no symptoms. Occasionally, people with hypertension experience headaches, nosebleeds, or dizziness, but

these symptoms are not reliable indicators of hypertension. Because hypertension typically has no symptoms, blood pressure is measured at most visits with health care providers, so that rising blood pressure can be detected and treated as early as possible.

Treatment

If resting blood pressure is only mildly or moderately elevated, patients might be able to reduce blood pressure significantly with lifestyle modification. Increasing physical activity and improving eating behaviors can help normalize blood pressure. If people are overweight, weight loss can also be beneficial. Learning to reduce feelings of stress that precipitate a fight-or-flight response can reduce the concentration of hormones that contribute to hypertension. When lifestyle measures alone do not lead to adequate control, or when people have difficulty implementing lifestyle change, medications can help reduce resting blood pressure.

Dietary Recommendations for Preventing and Treating Hypertension

Several dietary recommendations have been found to be helpful for preventing and treating hypertension, including the following.

Reduce Salt Intake

Greater salt intake has been associated with increased risk for hypertension in many studies. Research generally has found a modest but significant reduction in blood pressure when people with hypertension have decreased their salt consumption (He, Li, & MacGregor, 2013). Higher salt intakes also appear to contribute to increased blood volume.

U.S. public groups unanimously recommend fairly low salt intakes for the population at large. Myplate guidelines suggest that sodium intake not exceed 2,300 mg per day. People with hypertension—and those at high risk for the development of hypertension—are urged to keep sodium intake at less than 1,500 mg per day. Health Canada has similar recommendations (Government of Canada, 2012).

Increase Potassium Intake

Potassium, an important electrolyte mineral, is an essential component of the antihypertensive diet. Diets high in potassium have been shown to lessen the effects of sodium and thus aid in the control of blood pressure (American Heart Association, 2014). For this reason it is essential that foods rich in potassium be a component of a balanced diet. Potassium supplements, however, are not recommended because too much potassium can be harmful. The best way to achieve an adequate potassium intake is to consume plenty of vegetables and fruits, as

suggested in the DASH diet. The recommended intake of potassium is 4,700 mg per day. Foods high in potassium include potatoes, bananas, spinach, and broccoli—plus many other fruits and vegetables.

Increase Magnesium Intake

Magnesium is another important mineral in the control and reversal of hypertension. Magnesium helps to maintain the optimum functioning of the artery lining, and aids the mechanics of vasodilation and vasoconstriction. A diet rich in magnesium has been found to reduce blood pressure the most when combined with high potassium intake and low sodium intake (Houston, 2011). Moreover, magnesium also has been found to increase the effectiveness of all antihypertensive medications (Houston, 2011). The recommended intake of magnesium is 320 mg per day for women and 420 mg per day for men. Magnesium is found in many nuts, and in spinach, cocoa, beans, and quinoa.

Increase Calcium Intake

Calcium plays an important role in vasodilation and vasoconstriction. The recommended intake of calcium is 1,000 mg per day for adults, and 1,200 mg per day for people 50 years of age and older. Calcium is found in dairy products including milk and yogurt, and in sardines, dark green vegetables such as broccoli, sesame seeds, and calcium-fortified food products.

Dietary Approaches to Stop Hypertension

The Dietary Approaches to Stop Hypertension (DASH) diet was created to help people reduce, treat, and prevent hypertension and maintain a balanced and healthy diet. If followed correctly, the DASH diet can reduce systolic blood pressure by 6 to 12 points (Mayo Clinic Staff, 2013). The DASH diet emphasizes the reduction of sodium intake by encouraging the consumption of fruits; vegetables; low-fat dairy; moderate intake of whole grains; lean meat; fish; poultry; and nuts, seeds, and legumes. In a typical DASH diet the allowed daily sodium intake is 2,300 mg; however, a lower sodium DASH diet is available, and its sodium allowance is 1,500 mg per day (Mayo Clinic Staff, 2013). The chart below illustrates approximate daily servings for each food group, for a 2,000-calorie daily intake.

It is important to note the serving sizes for foods in each group. In particular, the serving size for the meat group is extremely small (1 oz of meat). Most meat portions are typically much larger. The DASH diet also recommends that consumers choose whole-grain foods in the grain group and limit alcohol consumption. Men should not consume more than two alcoholic drinks a day, and women no more than one drink a day, as alcohol intake is linked to higher blood pressure.

Table 1. The DASH Eating Plan

Food Group	Servings	Serving Sizes
Grains	6 to 8	1 slice bread 1 oz dry cereal ½ cup cooked rice, pasta, or cereal
Vegetables	4 to 5	1 cup raw leafy vegetable½ cup raw or cooked vegetable ½ cup vegetable juice
Fruits	4 to 5	1 medium fruit ¼ cup dried fruit ½ cup fresh, frozen, or canned fruit ½ cup fruit juice
Fat-free or low-fat milk and milk products	2 to 3	1 cup milk or yogurt 1 ½ oz cheese
Lean meats, poultry, and fish	6 or fewer	1 oz cooked meats, poultry, or fish 1 egg
Nuts, seeds, and legumes	4 to 5 per week	1/3 cup or 1 ½ oz nuts 2 Tbsp peanut butter 2 Tbsp or ½ oz seeds ½ cup looked legumes (dry beans and peas)
Fats and oils	2 to 3	1 tsp soft margarine 1 tsp vegetable oil 1 Tbsp mayonnaise 2 Tbsp salad dressing
Sweets and added sugars	5 or fewer per week	1 Tbsp sugar 1 Tbsp jelly or jam ½ cup sorbet, gelatin 1 cup lemonade

Source: U.S. Dept. Health and Human Services (2006). *Your Guide to Lowering Blood Pressure.* http://www.nhlbi.nih.gov/health/public/heart/hbp/dash/new_dash.pdf

Other Dietary Recommendations

Caffeine raises blood pressure temporarily. Many people with hypertension benefit from reducing caffeine consumption (Mayo Clinic Staff, 2013). People who have diabetes in conjunction with hypertension usually benefit from a lower intake of grains than that recommended by the DASH diet, replacing those calories with healthful fats such as avocadoes and olive oil. This reduces the glycemic load of the diet, resulting in lower blood sugar and insulin levels. The Mediterranean diet and a variety of low-fat diet recommendations also have been found to reduce resting blood pressure in people with hypertension (Toledo et al., 2013).

Paula Sophia Seixas Rocha

Research Issues

A number of nutrients, phytochemicals, and herbs have been studied to determine whether they might help to normalize high blood pressure. It is too early to say exactly which substances might be most helpful and will not have long-term negative consequences. Substances that hold some promise include Coenzyme Q 10 (CoQ 10), marine omega-3 fatty acids, dietary fiber, probiotics, chocolate, garlic, and cinnamon.

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See Also: Calcium; Cardiometabolic syndrome; Cardiovascular disease and nutrition; Electrolytes; Magnesium; Mediterranean diet; Potassium; Sodium and salt.

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Hypoglycemia

"Hypoglycemia" is the technical term for low blood sugar. The body normally maintains a blood glucose level between 70 mg/dL and 100 mg/dL through the action of a number of hormones including insulin, which stimulates body cells to take up glucose from the blood thus lowering blood sugar level, and glucagon, which raises blood sugar level by signaling the liver to release glucose into the blood stream. Hypoglycemia can result when this system causes too much glucose uptake and insufficient glucose release. Usually hypoglycemia can be corrected with the administration of foods that quickly raise blood sugar. In some cases, however, the disorientation and weakness that result from severe hypoglycemia can lead to injury. Recurrent severe hypoglycemia in people with diabetes can contribute to disturbance of the systems responsible for raising blood sugar, resulting in seizures and even death.

Symptoms of hypoglycemia include shakiness, disorientation, dizziness, irritability, hunger, anxiety, rapid pulse, and weakness. If blood glucose goes too low, hypoglycemia can even lead to coma and death. Episodes of hypoglycemia do not appear to cause long-term physical complications, unless the episodes are severe. One of the dangers for people with diabetes is over-treating hypoglycemia, which can result in a blood sugar level that is too high (hyperglycemia).

Hypoglycemia can be caused by several factors. People without diabetes can experience reactive hypoglycemia, which typically results from consuming a high-carbohydrate snack or meal that leads to a high insulin response. This high insulin response results in too much glucose being taken up by the cells, and not enough glucose remaining in the blood. Reactive hypoglycemia usually occurs about an hour after a high-carbohydrate intake, and can be prevented by reducing carbohydrate consumption and eating more frequently, being sure to include healthful fats and proteins in each meal or snack.

Fasting hypoglycemia indicates an abnormality in blood sugar regulation, sometimes because too much insulin is being produced even though no food has been consumed and blood sugar is low. Rarely, fasting hypoglycemia can indicate a tumor or other disorder of the pancreas. Exertional hypoglycemia occurs with physical exertion, when muscle glucose uptake exceeds glucose release from the liver. Exertional hypoglycemia can be prevented with exercise training and adequate feeding, so that the body improves blood glucose regulation during exercise, and the liver maintains a good level of glycogen. In the case of prolonged physical activity, foods and beverages can be consumed to avoid exertional hypoglycemia. Hypoglycemia also can be caused by several medications.

Hypoglycemia is most commonly observed in people with diabetes, usually occurring because too much insulin has been given. People with diabetes who experience frequent episodes of hypoglycemia can develop a condition known as hypoglycemia-associated autonomic failure (HAAF). With this condition, the systems responsible for activating glucagon and epinephrine release in the face of low blood sugar fail to respond as blood glucose levels drop (Seaquist et al., 2013). Because of the failure of the brain to respond to low blood sugar levels, people with HAAF do not even realize their blood sugar is getting too low, so they fail to respond.

Immediate treatment of hypoglycemia consists of administering a source of glucose to raise blood sugar levels. High-glycemic carbohydrates such as glucose tablets, sugar candies, and fruit juices that release glucose into the bloodstream quickly are best. If a person with hypoglycemia is unconscious or unable to eat, glucagon can be injected, or glucose can be given intravenously.

Preventing the recurrence of hypoglycemia begins with identifying its cause, and—when possible—addressing the underlying problem. In people with diabetes who are likely to experience hypoglycemia occasionally, treatment includes taking steps to improve glycemic control (control of blood sugar levels). People with diabetes must learn to recognize the symptoms associated with hypoglycemia, and improve glycemic control by increasing glucose testing, following a healthful diet, monitoring blood sugar response to exercise, and adjusting medications accordingly.

Barbara A. Brehm

See Also: Blood sugar regulation; Diabetes, type 1; Diabetes, type 2; Glucose; Hyperglycemia.

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Nutrition

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Nutrition

Science, Issues, and Applications

Volume 2: I–Z

Barbara A. Brehm, Editor

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This book discusses treatments (including dietary therapies, dietary supplements, medications, and mental health therapies) for a variety of symptoms and disorders, and a variety of organizations. The authors have made every effort to present accurate and up-to-date information. However, the information in this book is not intended to recommend or endorse particular treatments or organizations, or substitute for the care or medical advice of a qualified health professional, or used to alter any medical therapy without a medical doctor's advice. Specific situations may require specific therapeutic approaches not included in this book. For those reasons, we recommend that readers follow the advice of qualified health care professionals directly involved in their care. Readers who suspect they may have specific medical problems should consult a physician about any suggestions made in this book.

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Microbiota and Microbiome
Milk Thistle
Mindful Eating
Minerals
Molybdenum
Monoterpenes
Mood and Food
The Mouth
Multivitamin and Mineral Supplements
N-Acetylcysteine
National Weight Control Registry
Niacin
Nickel
Nitrates and Nitrites, Dietary
Nutritional Genomics
Nutritionists and Dietitians
Obesity, Causes
Obesity, Definition and Health Effects
Obesity, Treatment
Older Adults, Nutrition Needs
Omega-3 Fatty Acids. *See* Marine Omega-3 Fatty Acids.
Organic Food and Farming
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Osteoporosis
The Paleolithic Diet
Pancreas
Pantothenic Acid
Parenteral Nutrition
Peptic Ulcers
Phenylketonuria
Phospholipids
Phosphorus
Phytochemicals
Phytoestrogens
Polyphenols
Portion Size
Potassium
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Pyruvate and Pyruvic Acid
Quercetin
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Raw Food Diets

Raw Milk
Resveratrol
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Salivary Glands and Saliva
Salt. *See* Sodium and Salt.
Saponins
School Lunch Program
Seafood
Selenium
Slow Food Movement
Small Intestine
Sodium and Salt
Soybeans and Soy Foods
Spirulina
Sports Beverages
Sports Nutrition
Sports Supplements
St. John's Wort
Stevia
Stomach
Sugar Alcohols
Sugar-Sweetened Beverages
Supplemental Nutrition Assistance Program
Sustainable Agriculture
Taurine
Tea
Thiamin
Trans Fatty Acids
Triglycerides
Ulcers. *See* Peptic Ulcers.
Underweight
Upper Respiratory Tract Infections
U.S. Department of Agriculture
U.S. Food and Drug Administration
U.S. Pharmacopeial Convention and USP-Verified Mark
USP Verification Mark. *See* U.S. Pharmacopeial Convention.
Valerian
Vanadium
Vegetarian and Vegan Diets
Vitamin A
Vitamin B6
Vitamin B12
Vitamin C
Vitamin D
Vitamin E
Vitamin K
Vitamins
Water Needs; Water Balance
Weight Watchers
Wheatgrass
Whey Protein
Women, Infants, and Children, Special Supplemental Nutrition Program for
Yerba Mate
Zeaxanthin
Zinc

Guide to Related Topics

Diets, Dietary Guidelines, and Food Philosophies

The Atkins Diet
Daily Values
Detoxification
Dietary Guidelines for Americans
Dietary Reference Intakes
Enrichment and Fortification
Fad Diets
Fast Food
Fasting
Fermentation and Fermented Foods
The French Paradox
Functional Foods
Gluten-Free Diets and Foods
Glycemic Index and Glycemic Load
Herbs and Herbal Medicine
Ketosis and Ketogenic Diets
The Locavore Movement
Macrobiotic Diet
Mediterranean Diet
Mindful Eating
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The Paleolithic Diet
Portion Size
Public Policy on Nutrition
Raw Food Diets
School Lunch Program
Slow Food Movement
Supplemental Nutrition Assistance Program
Vegetarian and Vegan Diets
Weight Watchers
Women, Infants, and Children, Special Supplemental Nutrition Program for

Digestion, Absorption, and the Digestive System

Blood Sugar Regulation
Calorie
Celiac Disease
Cholesterol
Dental Caries (Cavities)
Detoxification
Diarrhea
Digestion and the Digestive System
Diverticular Disease
Enteral Nutrition
Enzymes, Digestive
Esophagus
Food Allergies and Intolerances
Gallbladder and Gallbladder Disease
Gastro-esophageal Reflux Disease
Glucose
Glycemic Index and Glycemic Load
Inflammatory Bowel Disease
Insulin
Intestinal Gas

Irritable Bowel Syndrome
Lactose Intolerance
Large Intestine
Lipoproteins
The Liver
Metabolism
Microbiota and Microbiome
The Mouth
Pancreas
Parenteral Nutrition
Peptic Ulcers
Prebiotics
Probiotics
Salivary Glands and Saliva
Small Intestine
Stomach
Water Needs; Water Balance

Environmental Issues

Arsenic
Bottled Water
Climate Change and Global Food Supply
Food Gardens
Food Security and Food Insecurity
Foodborne Illness and Food Safety
Genetically Modified Organisms
Global Hunger and Malnutrition
Insects as Food
Irradiation
Lead
The Locavore Movement
Mercury
Obesity, Causes
Organic Food and Farming
Sustainable Agriculture

Foods and Food Ingredients

Agave Syrup
Alcohol
Alternative Sweeteners (Sugar Substitutes)
Artificial Sweeteners
Caffeine
Carrageenan
Chamomile
Chlorella
Chocolate
Cholesterol
Coffee
Colostrum
Cordyceps Sinensis
Curcumin
Dairy Foods
Dietary Supplements
Echinacea
Energy Drinks
Fermentation and Fermented Foods
Fiber
Food Additives
Fructose
Functional Foods
Garlic
Ginger
Ginkgo Biloba
Ginseng
Grains
Herbs and Herbal Medicine
High-Fructose Corn Syrup
Honey
Hydrogenation
Insects as Food
Legumes
Margarine and Vegetable Oil Spreads
Marine Omega-3 Fatty Acids
Phospholipids
Prebiotics
Probiotics
Quorn
Raw Milk
Seafood
Sodium and Salt
Soybeans and Soy Foods
Spirulina
Stevia
Sugar Alcohols
Sugar-Sweetened Beverages
Taurine
Tea

Trans Fatty Acids
Triglycerides
Valerian
Wheatgrass
Whey Protein
Yerba Mate

Health Issues and Nutrition

Acne
Alcohol
Alzheimer's Disease and Nutrition
Arthritis and Nutrition
Attention-Deficit Hyperactivity Disorder and Nutrition
Autism and Nutrition
Blood Sugar Regulation
Caffeine
Cancer and Nutrition
Cardiometabolic Syndrome
Cardiovascular Disease and Nutrition
Celiac Disease
Cholesterol
Diabetes, Type 1
Diabetes, Type 2
Energy Drinks
Enteral Nutrition
Eye Health
Fetal Alcohol Syndrome and Disorders
Food Allergies and Intolerances
The French Paradox
Functional Foods
Gallbladder and Gallbladder Disease
Gastro-esophageal Reflux Disease
Glycemic Index and Glycemic Load
Hyperglycemia
Hypertension and Nutrition
Hypoglycemia
Inflammation
Inflammatory Bowel Disease
Insulin
Iron-Deficiency Anemia
Irritable Bowel Syndrome
Ketosis and Ketogenic Diets
The Kidneys
Lactose Intolerance
Lipoproteins
Megaloblastic Anemia
Nutritional Genomics
Obesity, Causes
Obesity, Definition and Health Effects
Obesity, Treatment
Osteoporosis
Peptic Ulcers
Phenylketonuria
Premenstrual Syndrome
Underweight
Upper Respiratory Tract Infections

Life Cycle

Adolescence and Nutrition
Breast-Feeding
Childhood Nutrition
Colostrum
Creatine
Electrolytes
Energy Drinks
Enrichment and Fortification
Female Athlete Triad
Fetal Alcohol Syndrome and Disorders
Infant Formula
Iron-Deficiency Anemia
Lactation
Older Adults, Nutrition Needs
Pregnancy and Nutrition
Premenstrual Syndrome

Nutrients

Alpha-Linolenic Acid
Amino Acids
Biotin
Boron
Calcium
Carbohydrates

Chloride
Choline
Chromium
Copper
Dietary Supplements
Electrolytes
Enrichment and Fortification
Fatty Acids
Fluoride
Folate and Folic Acid
Functional Foods
Glucose
Iodine
Iron
Linoleic Acid
Lipids
Magnesium
Manganese
Minerals
Molybdenum
Multivitamin and Mineral Supplements
Niacin
Nickel
Pantothenic Acid
Phosphorus
Potassium
Protein
Riboflavin
Selenium
Sodium and Salt
Thiamin
Triglycerides
Vanadium
Vitamin A
Vitamin B6
Vitamin B12
Vitamin C
Vitamin D
Vitamin E
Vitamin K
Vitamins
Water Needs; Water Balance
Zinc

Obesity

Adipose Tissue
Appetite
The Atkins Diet
Bariatric Surgery
Body Composition
Body Mass Index
Brown Adipose Tissue
Calorie
Cardiometabolic Syndrome
Diabetes, Type 2
Energy Balance
Fad Diets
Fast Food
The French Paradox
Hunger, Biology of
Ketosis and Ketogenic Diets
Metabolic Rate
National Weight Control Registry
Obesity, Causes
Obesity, Definition and Health Effects
Obesity, Treatment
Portion Size
The Poverty-Obesity Paradox
Public Policy on Nutrition
Sugar-Sweetened Beverages
Weight Watchers

Organizations and Programs

Academy of Nutrition and Dietetics
Health Canada
National Weight Control Registry
Nutritionists and Dietitians
School Lunch Program
Supplemental Nutrition Assistance Program
U.S. Department of Agriculture
U.S. Food and Drug Administration
U.S. Pharmacopeial Convention Verification Mark
Women, Infants, and Children, Special Supplemental Nutrition Program for

Phytochemicals and Other Compounds in Foods and Dietary Supplements

Allyl Sulfides (Organosulfurs)
Alpha-Lipoic Acid
Anthocyanins
Antioxidants
Arginine
Astaxanthin
Berberine
Beta-Carotene
Black Cohosh
Caffeine
Capsaicin
Carnitine
Carotenoids
Catechins
Choline
Coenzyme Q10
Creatine
Curcumin
Dietary Supplements
Ellagic Acid
Fiber
Functional Foods
Gamma Linolenic Acid
Glucosamine
Glutamine
Glutathione
Indoles
Inositol
Isothiocyanates
Lecithin
Lutein
Lycopene
Lysine
Marine Omega-3 Fatty Acids
Melatonin
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Monoterpenes
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Nitrates and Nitrites, Dietary
Phytochemicals
Phytoestrogens
Polyphenols
Pyruvate and Pyruvic Acid
Quercetin
Resveratrol
S-Adenosylmethionine
Saponins
St. John's Wort
Zeaxanthin

Psychological Issues

Appetite
Attention-Deficit Hyperactivity Disorder and Nutrition
Autism and Nutrition
"Brain Foods"
Cognitive Restructuring
Depression and Nutrition
Detoxification
Eating Disorders
Feeding Disorders
Female Athlete Triad
Food Addiction
Food Cravings
Hunger, Biology of
Mood and Food
Obesity, Causes
Obesity, Definition and Health Effects
Obesity, Treatment
Orthorexia
Premenstrual Syndrome

Sports Nutrition

Creatine
Electrolytes
Female Athlete Triad
Glycemic Index and Glycemic Load
Iron-Deficiency Anemia
Sports Beverages
Sports Nutrition
Sports Supplements

Toxins

Alcohol
Arsenic
Copper
Detoxification
Fluoride
Foodborne Illness and Food Safety
Heterocyclic Amines and Polycyclic Aromatic Hydrocarbons
Hydrogenation
Lead
Mercury
Nickel
Raw Milk
Trans Fatty Acids

I

Indoles

Indoles are a class of phytochemicals historically used in the fragrance industry that are increasingly being developed for medicinal applications. Although small amounts of the substance have a flowery scent, indoles are typically found in high concentrations in feces where they are responsible for the unpleasant odor. When not expelled in feces, indoles are processed by the liver and excreted in urine as indican. In urine, a high level of this chemical is indicative of impaired protein digestion and a possible imbalance between harmful and beneficial bacteria in the gut (Higdon & Drake, 2008). In addition to ingesting indoles in food, people also obtain them from conversion of the amino acid tryptophan by select bacteria in the intestines.

Indole-3-carbinol (I3C) is a type of indole found in cruciferous vegetables like broccoli and cabbage. I3C is readily converted into other indoles, particularly 3,3'-diindolylmethane (DIM) in the intestine (Wikoff et al., 2008). Both I3C and DIM have shown promise as antioxidants and anticarcinogens in human clinical trials, especially for breast and prostate cancers. The proposed mechanisms of action might be halting cell division in cancerous cells or repairing damaged DNA. Indole-3-carbinol also might help to regulate estrogen, converting it to weaker forms and thus potentially preventing cancer growth that is triggered by harmful forms of the hormone. Both indoles are available as dietary supplements, although concern exists about harmful effects that could result from consuming high quantities of these compounds. Some animal studies have found that I3C actually can promote the processes of carcinogenesis if carcinogens are introduced into animal models after giving them I3C (Higdon & Drake, 2008).

Indole-3-propionic acid (IPA) is another indole that could have protective properties. In the nervous system, IPA might be able to intervene against free radical–related damage in cells. In treating Alzheimer's disease, IPA could be effective for helping to slow accumulation of amyloid β-protein, thereby slowing brain degeneration. Several other indoles currently are being explored as part of potential treatment for Alzheimer's as well as other neurodegenerative diseases, although therapeutic applications have not yet been developed for humans.

Another indole currently under investigation is indolepropionamide (IPAM). Indolepropionamide could be helpful for maintaining the health of mitochondria, the cellular organelles where ATP is produced from fuel precursors. In vitro studies of isolated mitochondria suggest that IPAM might reduce the production of

reactive-oxygen species, which are thought to accelerate cellular damage and are the target of antioxidant therapies (Poeggeler et al., 2012).

Research on indoles—especially those in the form of concentrated supplements—suggests that it is too soon to recommend such supplements for humans. In addition to the few studies indicating potential cancer-enhancing effects in laboratory animals, I3C potentially could increase the risk of osteoporosis by reducing the activity of estrogens in the body. It is important to note that, although risks might be associated with specific indole supplements, the intake of cruciferous vegetables has been associated with beneficial health effects in a multitude of studies in humans.

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See Also: Phytoestrogens.

Further Reading

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Infant Formula

Infant formula is a manufactured food designed to provide infants with necessary nutrients for the first year of life. The three main types of infant formula are cow's milk, soy-based, and protein hydrolysate formulas. Commercial infant formulas are regulated in the United States through the Food and Drug Administration (FDA), which requires all formulas to contain at least the minimum—and no more than the maximum—recommended amount of nutrients for proper infant nutrition. The World Health Organization, the U.S. Centers for Disease Control and Prevention, the American Academy of Pediatrics, and other health organizations all recommend breast-feeding as the best source of nutrition for infants. Infant formula can be used, however, when breast-feeding is not an option for a mother or an infant. Inability to breast-feed can be due to a variety



Infant formula comes in a wide variety of product styles. Powdered formula must be mixed with the proper amount of clean water. If formula is mixed with contaminated water, babies may develop serious, even fatal, infections. (Hdevivo/Dreamstime.com)

of circumstances, including death of the mother during childbirth, adoption, and complications such as lactation failure. Additionally, many families choose formula feeding for a variety of other reasons, such as a mother's difficulty combining breast-feeding practices with job demands.

History

Use of formula dates back to 2000 BCE, with evidence of clay feeding vessels found in graves of newborn infants (Stevens, Patrick, & Pickler, 2009). Early feeding containers were difficult to clean, leading to the buildup of bacteria detrimental to infant health. In the early 19th century, dirty feeding devices and improper milk sterilization led to the death of one-third of all bottle-fed infants during their first year of life (Stevens, Patrick, & Pickler, 2009).

Animal's milk was the most commonly used food for bottle-feeding for infants until the 18th century. At that time, chemists began to analyze the composition of milk from a variety of mammals, including humans, and started to develop compounds that mimicked the composition of human milk. In 1865, chemist Justus

von Liebig developed and patented an infant food that originated in liquid form, and then was developed into a powdered form for preservation (Stevens, Patrick, & Pickler, 2009). This new formula was made from cow's milk, wheat and malt flour, and potassium bicarbonate. Many new products were developed in the following years, and by 1883, 27 brands of infant formula vied for consumer demand. These early products lacked some nutrients and were often not administered in a sanitary fashion, contributing to the deaths of many infants. The development of rubber nipples in 1912 and the introduction of iceboxes into many homes improved the safety of bottle-feeding.

Scientists began to develop non-milk-based formulas in the 1920s, designed for infants allergic to cow's milk. By the late 1920s, the American Medical Association began to approve the quality of infant formula products, and by the 1940s and 1950s, physicians promoted the notion that infant formula was a healthy alternative to breast-feeding (Stevens, Patrick, & Pickler, 2009). Breast-feeding in many countries declined significantly for several decades, until public health efforts in the 1970s began to promote the superiority of breast-feeding.

By the 1960s, the marketing tactics of formula companies sparked international debate. Sufficient evidence to support breast-feeding as the superior method of infant feeding had been gathered, and the World Health Organization (WHO) then deemed formula marketing campaigns to be unethical. The WHO developed international codes forbidding companies from claiming formula to be superior to breast milk. The code also prevented companies from providing free samples to pregnant women. The use of formula led to many health problems in areas where women could not afford to purchase the formula needed to feed their infants, or could not obtain safe water for the mixing of powdered formulas.

Types of Infant Formula

The chemical composition of infant formulas attempts to mimic the composition of human milk. Several types of infant formulas are available. Caregivers of infants are advised to work with their babies' pediatricians to determine the type of formula that would be best. Infants often are fussy, and caregivers frequently try a variety of formulas hoping to find one that leads to a more peaceful baby. Pediatricians, however, advise that fussiness often is due to factors unrelated to the type of formula a baby was fed.

Cow's Milk Formula

Most infant formula is made using cow's milk that is altered to resemble breast milk, giving the formula the right balance of nutrients that a baby needs for healthy growth. Cow's milk formulas contain whey and casein as protein sources, a blend of vegetable oils as the fat source, lactose as the carbohydrate source, and a mix of vitamins and minerals. The protein in the cow's milk–based formulas is heat treated, which enables infants to digest the formula easily.

Feeding Infants: Inappropriate Products

Cow's milk, other types of milk and milk products, and other types of beverages do not supply the nutrition needed by infants and can cause the development of health problems. It is important for caregivers to provide infants with good nutrition, and not use the following products in place of breast milk or infant formula.

- Whole cow's milk—Lacks some nutrients and is associated with gastrointestinal bleeding and blood loss in infants; stress on infant kidneys; and allergic reactions.
- Low-fat or nonfat cow's milk—Poses the same problems as whole cow's milk. These milk forms also are too low in fat.
- Evaporated cow's milk—Once popular as a source of infant nutrition, evaporated cow's milk presents the same problems as other forms of cow's milk.
- Sweetened condensed milk—Includes all of the problems associated with cow's milk and is very high in sugar, which is harmful to infants at such concentrations.
- Milk from other animals—Similar to cow's milks, milk from other mammals, such as goats, does not meet infant nutrition needs and also taxes the kidneys.
- Soy-based (soy milks), rice-based (rice milks), and similar beverages—Beverages made from soybeans, rice, almonds, coconut milk, and other foods do not provide the correct nutritional balance for infants. They generally lack the protein, fats, and calories needed by infants. Malnutrition and signs of starvation develop in infants nourished with these products.
- Other beverages—Infants should never receive fruit juice, fruit drinks, soda, or other beverages. These products do not meet infant nutrition needs but cause infants to take in less breast milk or formula, so they can become malnourished.

Blum-Kemelor, D., & Leonberg, B. (2009). Chapter 4: Infant formula feeding. In *Infant nutrition and feeding*. U.S. National Agricultural Library. Retrieved from http://www.nal.usda.gov/wicworks/Topics/FG/Chapter4_InfantFormulaFeeding.pdf

Soy-Based Formula

Soy-based formula is made from an easily digestible soybean foundation. Soy-based formulas often are chosen over cow's milk–based formulas if the parents wish to exclude animal protein from the baby's diet or if the baby might be lactose-intolerant. (Soy-based formula does not contain lactose, the sugar found in milk.) Soy formulas contain phytoestrogens, including a class of compounds called isoflavones. Phytoestrogens pose a theoretical negative effect on sexual development and reproduction, immune function, and thyroid function. Clinical studies of infant nutrition, however, raise no concerns on the effect of phytoestrogens in infant formula, and the FDA declares these compounds safe for consumption (Bhatia, 2008).

Protein Hydrolysate Formula

Caregivers of infants who are allergic to soy and cow's milk could elect to use protein hydrolysate formula. This formula contains protein that has been broken

down into smaller components (hydrolyzed). Smaller proteins are easily digestible compared to the proteins in cow's milk–based and soy-based formulas. Protein hydrolysate formulas are meant for babies who can't tolerate other types of formulas.

Preparation

Infant formula preparations are available in powdered, concentrated liquid, and ready-to-use forms. Powdered formula and concentrated liquid formula must be mixed with water. Formula must be prepared carefully to avoid harming an infant. Formula should be stored in a cool, clean, dry space to prevent bacterial growth.

Dry formula should remain covered when it is not being used, and should be discarded 30 days after the date of purchase. Warm water should be used when mixing the formula to ease digestion of the food; heating formula can affect its protein digestibility. Feeding bottles should be thoroughly sterilized prior to formula preparation. After feeding an infant, any formula that is not consumed should be discarded, as bacteria from the baby's mouth can contaminate the formula and bottle. Prepared formula can be refrigerated for 24 to 48 hours after its preparation if the bottle has not been used for feeding, but unused formula should be discarded after 48 hours.

Risks

Declining breast-feeding rates have been associated with serious infant health issues, such as type 1 diabetes mellitus and obesity. Type 1 diabetes mellitus has been associated with being breast-fed for less than 5 months and being fed cow's milk formula before 8 days of age. Evidence suggests that these factors can trigger pancreatic beta-cell autoimmunity, causing diabetes mellitus to develop (Stevens, Patrick, & Pickler, 2009). Formulas contain dense caloric content and increase

Probiotics and Other Additions to Infant Formula

Researchers continue to seek ways to improve the composition of infant formula so that it more closely replicates that of breast milk (Blum-Kemelor & Leonberg, 2009). Some infant formulas add extra ingredients not required by the FDA but which are hoped to improve formula quality, or at its least appeal to consumers. Some of these ingredients include long-chain fatty acids docosahexanoic acid and arachidonic acid, thought to improve brain and eye development; and nucleotides, the building blocks of DNA, RNA; and other important molecules. Prebiotics and probiotics are also added to some formulas. Prebiotics support the growth of helpful bacteria in the baby's digestive tract; probiotics are helpful bacteria. All of these ingredients are naturally present in breast milk.

Blum-Kemelor, D., & Leonberg, B. (2009). Chapter 4: Infant formula feeding. In *Infant nutrition and feeding*. U.S. National Agricultural Library. Retrieved from http://www.nal.usda.gov/wicworks/Topics/FG/Chapter4_InfantFormulaFeeding.pdf

insulin levels for digestion. Formula-fed infants have a different growth pattern. In particular, formula-fed babies gain more body fat and weight when they are 3 to 6 months old (and older) as compared to breast-fed infants, which increases the risk for type 2 diabetes mellitus and childhood obesity (Lönnerdal, 2014).

Breast-Feeding

Breast milk is the best nutritional option for an infant. Human milk is an optimal blend of all of the nutrients that a baby needs for growth and development, including carbohydrates, lipids, proteins, minerals, and vitamins. Breast milk also provides infants with helpful immune cells, growth factors, and microbiota; it also reduces the baby's risk for gastrointestinal illnesses, respiratory diseases, obesity, food allergies, and ear infections. Breast-feeding is associated with higher cognitive development scores in infants and children (Blum-Kemelor & Leonberg, 2009).

Victoria Brown and Allison M. Felix

See Also: Breast-feeding.

Further Reading

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Inflammation

Inflammation is part of the body's immune response. When the body is faced with an injury or infection, the immune system works to rid the body of harmful stimuli and damaged cells to begin the healing process. This is done through the inflammatory response, a complex cascade of cellular and molecular signals that alter

physiological responses and produce the common symptoms of pain, swelling, heat, and redness. The word inflammation comes from the Latin word "inflammo," meaning "I set alight, ignite." An inflammatory response initially is beneficial, but sometimes inflammation continues in response to a variety of conditions and becomes chronic.

Chronic inflammation is involved in a number of disease states. In these situations, inflammation is considered abnormal and does not benefit the body. Some diseases are inflammatory in nature, being caused primarily by malfunctioning inflammatory responses. These chronic inflammatory diseases include autoimmune disorders such as rheumatoid arthritis, inflammatory bowel disease, celiac disease, tendonitis, and type 1 diabetes. Chronic diseases, including neurodegenerative and cardiovascular diseases—which are not as closely associated with an altered immune response—also have inflammatory components. Examples include heart disease, cancer, Alzheimer's disease, stroke, and many metabolic diseases such as type 2 diabetes.

The Immune System and Inflammation

Inflammation is part of a person's innate immunity, which is different from the adaptive immunity that results from previous infection or vaccination and is quite specific to certain antigens. Acute inflammation is the body's natural response to infection or injury. At the site of injury, cells release molecular signals that cause a number of physiological changes to occur, including vasodilation (the widening of blood vessels), increased blood flow, and the influx of a number of proteins such as leukocytes (white blood cells). When a person receives a scratch that does not break the skin, for example, a red line might soon appear and turn red and puffy. This indicates that the arterioles have dilated and capillaries have filled with blood to become more permeable and allow fluid and blood proteins to move into the space between the tissues.

White blood cells—made from stem cells in the bone marrow—rush to the site of the injury. Neutrophils are the first leukocytes to appear, killing off invading pathogens as well as any adjacent cells, even healthy cells, using reactive oxygen species such as superoxide and hydroxyl radicals. These white blood cells also release cytokines, small proteins that relay information to other cells, including interleukin (IL)-1, IL-6, tumor necrosis factor (TNF-alpha), and gamma interferon (INF-gamma). Pro-inflammatory cytokines induce body-wide inflammatory responses, including fever and the increased production of white blood cells. In some cases, inflammation results in healing and then subsides, but sometimes inflammation is not able to adequately repair the damage, and chronic inflammation develops.

Chronic inflammation can result from an autoimmune reaction when the body fails to recognize its own constituent parts, when a viral or bacterial infection occurs, or from the persistent activation of inflammatory molecules. Monocytes, the largest leukocytes, are the primary motivators behind chronic inflammation. During the inflammatory process, these cells enter tissues from the bloodstream and turn into long-lived macrophages whose roles are both to engulf and digest pathogens

and tissues and to repair inflammation when necessary. Macrophages also release cytokines, including IL-1 and TNF-alpha that perpetuate the pro-inflammatory process, followed by the production of antibodies by other white blood cells called "lymphocytes." Reactive oxygen species and proteins that destroy the source of inflammation are released by macrophages. In abnormal situations, however, damage that occurs to the body's own tissues by macrophages results in the production of more inflammation. The destruction of tissue, thickening and scarring of connective tissue (fibrosis), and the death of cells or tissues are some of the outcomes from chronic inflammation. This process occurs, for example, with artery disease, when macrophages attempt to repair arterial damage but instead trigger more inflammation.

Epidemiology

Chronic diseases associated with a harmful inflammatory response are among the most common, costly, and preventable of all health problems in the United States (CDC, 2012). In 2005, 133 million Americans—almost 1 out of every 2 adults—suffered from at least one chronic illness, and 7 out of 10 Americans die each year from chronic diseases (CDC, 2012). Heart disease, cancer, and stroke comprise more than half of all deaths per year (CDC, 2012). In addition to higher mortality rates in diseases associated with a chronic inflammatory response, the quality of life for those suffering with these diseases is diminished. About one-fourth of people with chronic conditions have one or more limitations on their daily activities (CDC, 2012).

Symptoms and Diagnosis

The symptoms of chronic inflammation are silent as compared to those of the acute inflammatory response. Low levels of systemic inflammation can persist for years, only to contribute to a number of seemingly unrelated ailments. Chronic inflammation can manifest itself in many ways including weakening cholesterol deposits in the coronary arteries, leading to heart disease; triggering bronchial tubes in the lungs to swell, causing asthma; or kick-starting blood vessel formation to relay nutrients to abnormal cells so that they can proliferate and become invasive cancers.

There is one blood test that scientists think can detect this otherwise stealthy systemic inflammation. The cytokine interleukin-6 present during the inflammatory response is secreted by both macrophages and fat cells. This cytokine signals the liver to release C-reactive protein (CRP) into the bloodstream which binds to damaged cells to increase macrophage action. Acute levels of CRP can be measured using a blood test. Levels that are less than 1 mg/L are ideal, and levels greater than 3 mg/L indicate high levels of inflammation. Not all inflammation shows up on this test, however, and a higher-sensitivity version of the same test also can be used. People with inflammatory disorders could have CRP levels of 10 mg/L or more. The Centers for Disease Control and Prevention recommends

having the CRP test performed on a patient only if the patient is in a risk category, such as having a history of heart disease. Other health experts think that many more individuals should be tested.

Causes and Risk Factors

Just as there are many manifestations of chronic inflammation, there are numerous factors that play into the development of these diseases. Some gene variants can predispose certain people to the development of chronic inflammation. One known inherited condition, for example, results in a below-average number of interleukin-6 receptors on tissue cells of the body. In people who have the same traditional risk factors for the development of heart disease—diabetes, smoking, and high cholesterol—people with a lower-than-normal interleukin-6 receptor count were much less likely to develop the disease (Cool, 2013).

In coronary artery disease, a form of heart disease, LDL cholesterol is absorbed by the arteries and remains within the tissues, attracting immune cells to take care of the resulting damage. This creates inflammation that can cause the artery walls to swell and restrict blood flow. The predisposition to recruit more inflammation with an increased number of interleukin-6 receptors might exacerbate heart disease. The same inflammatory mechanism can occur in the development of neurodegenerative diseases. In Alzheimer's disease, beta-amyloid plaques develop in the brain and immune cells are recruited to contain the damage, specifically the pro-inflammatory cytokines interleukin-12 (IL-12) and IL-23.

That said, the development of chronic inflammation is caused in large part by lifestyle choices and a person's risk of developing the associated diseases can be reduced by following a variety of lifestyle-change recommendations. One of the main risk factors for the development of chronic inflammation is an excess of visceral fat. (Visceral fat refers to adipose tissue located in the abdominal cavity around the abdominal organs.) Stressed adipose cells release cytokines like interleukin-6 which increase systemic inflammation; visceral fat cells are much more biologically active than the same type of cells in other parts of the body. People with excess visceral fat or high body mass indices (BMIs) have higher resting levels of white blood cells than do lean individuals, and losing weight causes white blood cell levels to drop. Although there are some genetic components to fat deposition, managing one's lifestyle can cut the risk of developing both chronic inflammation and metabolic syndromes, such as type 2 diabetes (Cool, 2013).

Activity levels also are linked to the development of chronic inflammatory diseases. Those with an inactive lifestyle are more likely to develop these diseases, although the exact mechanism behind exercise and inflammation reduction still is being studied. People who exercise regularly have lower levels of CRP in their blood. This could be due to increased antioxidant activity that reduces levels of free radicals in the body (which are associated with prolonged inflammation). Muscles appear to produce chemical messengers that influence processes of inflammation. Exercise also can reduce stress; chronic stress is associated with inflammation and increased CRP levels. The inflammatory response in part is

regulated by the hormone cortisol. Cortisol is released in response to stress and, among other things, works to suppress the immune system. Prolonged stress alters the effectiveness of cortisol by decreasing tissue sensitivity to the hormone, altering its effectiveness to regulate inflammation (Carnegie Mellon, 2012).

Diet also is a significant contributor to a multitude of chronic inflammatory diseases, as well as pain associated with inflammation. Inflammation causes pain primarily by producing swelling that can push against sensitive nerve endings. One interesting study reported that eating sugars and high-glycemic index foods increased systemic inflammation, producing pain, overheating, redness, and swelling because more than 70% of immune cells are in the digestive system, making contact with the foods people consume every day (Daniluk, 2012). The immune system can be triggered by bacteria in food, can tag a particular food as an allergen, or can be stimulated by the imbalance of hormones such as insulin that set the stage for chronic inflammation. People with food allergies or intolerances should avoid consuming problematic foods.

Treatment and Prevention

Chronic inflammation can be reduced with both medications and a variety of lifestyle changes. Nonsteroidal anti-inflammatory drugs (NSAIDS) and corticosteroids are two common anti-inflammatory medications. NSAIDS block the cyclooxygenase enzyme, a precursor to inflammation, and include medications such as aspirin and ibuprofen. Corticosteroids are steroid hormones that are created naturally by the adrenal cortex, and also are produced in the laboratory to be added to medications. These hormones reduce the production of inflammatory chemicals to prevent further damage to cells. Another medication that is being used to treat rheumatoid arthritis, and might offer a new avenue of heart disease and other chronic inflammatory illness prevention, is interleukin-6 receptor blockers. Unfortunately, all of these medications have potentially dangerous side effects, so anyone considering using such medications should discuss the associated benefits and risks with their health care provider.

Chronic inflammation also can be reduced via lifestyle changes. Regular physical activity can help reduce markers of chronic inflammation. A minimum of 30 minutes of moderate physical activity most days of the week, with moderate strength training exercise twice a week, is recommended for healthy adults. Being active as well as engaging in mind-calming activities also reduces stress and aids in the reduction and prevention of chronic inflammation. Adequate restful sleep also reduces and prevents chronic inflammation. Maintaining a healthful weight and avoiding excess abdominal fat are important for preventing chronic inflammation.

Inflammation and Nutrition

A healthful diet could help prevent or reduce chronic inflammation. The basic suggestions include eating a variety of foods, especially of vegetables, and including

as much fresh food as possible, drinking enough water throughout the day, and minimizing consumption of processed and fast foods (Weil, 2014). Whole grains are less inflammatory than refined grains, and many herbs and spices appear to combat inflammation (Moore, 2013). Some dietary suggestions for reducing inflammation are listed below.

Carbohydrates

Reducing consumption of wheat flour and sugar—including packaged and processed foods, which are high on the glycemic index—is suggested, as is avoiding consuming high-fructose corn syrup. High amounts of dietary sugar increase the amount of advanced glycation end products (AGEs), which result when carbohydrates attach to protein molecules. The addition of the carbohydrate damages protein molecules. As the body tries to destroy the AGEs, immune cells secrete cytokines to increase the resulting inflammation. To slow carbohydrate digestion and decrease the likelihood of forming AGE, a diet should include whole grains which have intact grains, such as brown rice and bulgur wheat.

Consuming vegetables such as red radishes, sweet potatoes, purple cabbage, and dark green vegetables that are rich in antioxidants could help lessen inflammation. Antioxidants are molecules that help inhibit the oxidation of molecules, which produces harmful free radicals, and stop the creation of by-products such as AGEs. Although oxidation reactions are crucial for life, a lack of antioxidants can add oxidative stress that damages or kills cells and stimulates inflammation processes. Cruciferous vegetables, including broccoli, cauliflower, Brussels sprouts, and kale also are known to contain indole-3-carbionol, an antioxidant. Berries and cherries also contain inflammation fighting antioxidants.

Fats

Nutritionists generally recommend decreasing omega-6 fatty acid (the pro-inflammatory essential fatty acid) intake and increasing omega-3 fatty acid consumption (an inflammatory-neutral essential fatty acid) (Moore, 2013). Although the anti-inflammatory benefits of omega-3's (i.e., ALA, DHA, EPA) have good support, the exact mechanisms of action are not thoroughly understood. The pro-inflammatory nature of omega-6 has been revealed, however, because the body produces prostaglandins—the main hormones used to promote inflammation—from these precursors. In a typical Western diet, the ratio of omega-6 to omega-3 fatty acids is about 20:1, yet it is thought that humans evolved consuming a ratio closer to 1:1 (Drake, 2010). With the advent of the modern vegetable oil industry and the increased use of cereal grains as feed for livestock after the industrial revolution, intake of omega-6 fatty acids increased dramatically.

Nutrition experts suggest that people reduce intake of partially hydrogenated oils, saturated fats, and trans fats and opt for unsaturated fats. This can be done, for example, by using extra-virgin olive oil as a main cooking oil instead of using vegetable oils, such as corn oil. Olive oil, in addition to being a good source of

omega-3's, contains oleic acid, a powerful antioxidant that is associated with lower levels of LDL-cholesterol. Eating fish such as salmon, herring, and sardines can increase omega-3 levels, as well as eating omega-3–fortified eggs, plant foods, consuming hemp seeds and flaxseeds, or by taking fish oil supplements that provide both EPA and DHA. Other recommendations include consuming avocados and nuts, especially walnuts, cashews, almonds, and nut butters made from these specific nuts.

Proteins

A diet that includes lean meats and plant-based protein sources is recommended for reducing inflammation. Also suggested is decreasing consumption of animal protein, except for fish and high-quality natural cheese and yogurt. Red meat, including beef, pork, and lamb, contains a high amount of arachidonic acid, a polyunsaturated omega-6 fatty acid that can promote inflammation by forming prostaglandins. Eating more protein in the form of eggs or vegetables, especially from beans, soy foods, nuts and seeds, could decrease inflammation by providing antioxidants and some omega-3 fatty acids. As described, eating many types of fish will supply the body with omega-3 fatty acids in addition to protein.

Vitamins, Minerals, and Supplements

Several nutrients, including vitamin C, vitamin E, and the mineral selenium, serve as antioxidants; and diets should include foods high in these nutrients. Vitamin C is plentiful in many fruits and vegetables; vitamin E is found in wheat germ and nuts; and selenium is found in Brazil nuts, seafood, and many meats. A multivitamin and mineral supplement that provides close to the DRI for these nutrients can be helpful for people whose diets lack these nutrients. Some studies have called into the question the wisdom of antioxidant supplements. They might limit the body's own ability to strengthen endogenous antioxidant pathways. A few studies have found that supplementation with vitamin E or selenium even could increase cancer risk in some people.

Coenzyme Q10 (CoQ10) is a natural antioxidant that is present in every cell and participates in the metabolic chemical reactions that produce energy. CoQ10 prevents free radical formation and maintains the health of the cardiovascular system. Foods such as fish and meats, and oils from soybean and sesame seeds are good sources of this coenzyme.

Many herbs and spices including ginger, cinnamon, and turmeric appear to have anti-inflammatory properties. Turmeric works in the body by helping to turn off a protein called NF-kappa B, which regulates the immune system and triggers cytokine production. In preliminary experiments, ginger has been shown to reduce inflammation in the intestines when taken as a supplement.

An adequate amount of fiber in the diet decreases the immune cells' exposure to possible toxins in the gut by helping food move through the digestive system and preventing constipation. Increasing the intake of soluble fiber also lowers

blood glucose levels and blood cholesterol, which might aid in decreasing inflammatory processes. More fiber can be added to the diet by eating fruit, especially berries; legumes; vegetables; nuts; and whole grains. Fiber consumption should be coupled with drinking plenty of water.

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See Also: Alzheimer's disease and nutrition; Antioxidants; Arthritis and nutrition; Cancer and nutrition; Cardiovascular disease and nutrition; Food allergies and intolerances; The Paleolithic diet; Phytochemicals; Selenium; Vitamin C; Vitamin E.

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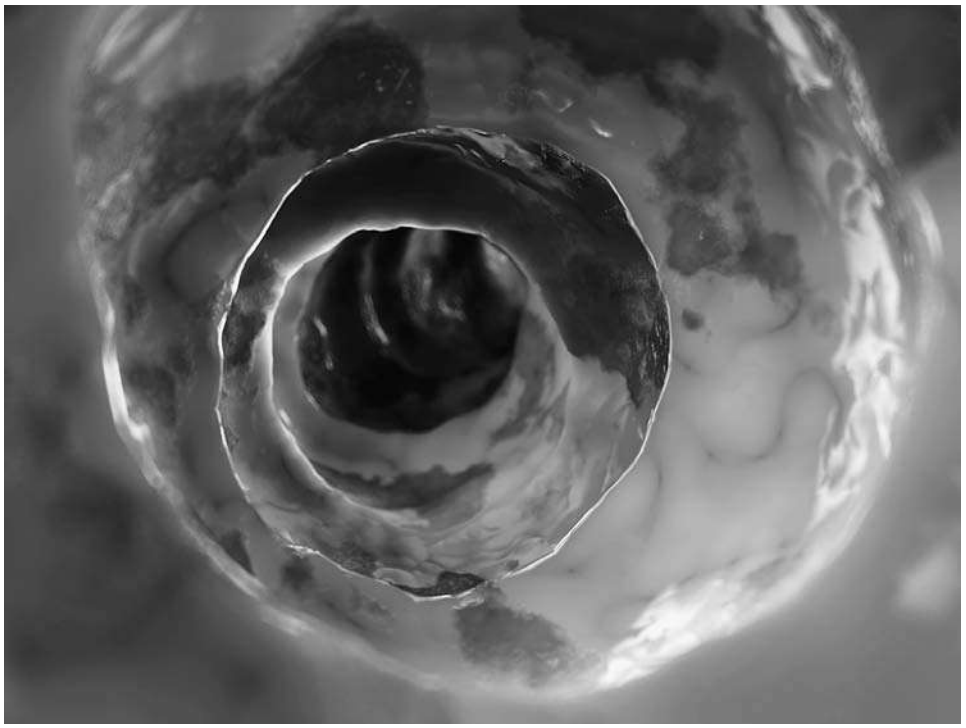
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Inflammatory Bowel Disease

"Inflammatory bowel disease" (IBD) is the name for conditions that involve chronic inflammation in the small or large intestines. The two most common forms of IBD are ulcerative colitis and Crohn's disease. Inflammatory bowel diseases generally are considered to be autoimmune disorders, meaning that they are caused by the body's immune system mistakenly attacking tissues of the body itself; in this case, the small or large intestine. When immune cells attack the intestinal lining they trigger an inflammatory response that causes tissue damage, including redness, swelling, open sores (ulcers), and bleeding. In some cases ulcers can lead to injury of the underlying tissues and the intestinal lining. Symptoms of IBD include abdominal pain, blood and mucus in the stools, and diarrhea, and most commonly appear in men and women between the ages of 15 and 30. The incidence of ulcerative colitis was estimated to be about 0.5 to 24.5 cases per 100,000



Inflamed colon. Inflammatory bowel disease is marked by redness, swelling, excess mucus production, and ulcers in the colon as well as other parts of the digestive tract. (Sebastian Kaulitzki/Dreamstime.com)

people worldwide; the rate for Crohn's disease is estimated to be about 0.1 to 16 cases per 100,000 people (CDC, 2012). Up to 1.4 million people in the United States are thought to have IBD (CDC, 2012).

Although the causes of IBD are unknown, a number of risk factors have been identified, including family history and ethnic background (rates are highest in those of Caucasian and Ashkenazic Jewish descent). Inflammatory bowel disease is more common in industrialized countries and urban environments. Cigarette smoking increases risk for the development of Crohn's disease. Stress does not cause IBD, but can worsen symptoms once IBD has developed. Symptoms of IBD range from mild to severe, and IBD often goes into remission for various periods of time. IBD is best managed with a combination of medical and lifestyle therapies.

Symptoms and Diagnosis

The symptoms of ulcerative colitis and Crohn's disease are similar. Symptoms of Crohn's disease tend to be more severe, and can occur in both the small intestine and the colon (large intestine), as well as in the mouth and rectum.

Ulcerative colitis occurs only in the colon and rectum. As its name indicates, ulcers form in one or both of these locations and can be detected through bloody stools or diarrhea. In severe cases, ulcers can deepen and destroy areas of the lining of the colon or rectum, creating a hole for intestinal fluids to flow into the abdominal cavity or bloodstream, which can lead to other serious health problems. Ulcerative colitis causes intense abdominal pain and cramping and the sensation of needing to go to the bathroom without actually being able to go. Both ulcerative colitis and Crohn's disease can lead to a loss of appetite and weight loss.

Unlike ulcerative colitis, which is somewhat concentrated, Crohn's disease can be found over a larger area of the body. The disease most commonly develops in the ileum, however, which is the portion of the small intestine closest to the colon, and the first part of the colon. Crohn's disease is marked by swelling, ulceration, and scar tissue buildup, all products of chronic inflammation. Swelling and scar tissue can narrow the infected part of the digestive tract, creating a stricture, which makes it difficult for food to pass through and leads to cramping and pain. The ulcers seen in Crohn's disease are open wounds that can penetrate deep into digestive tract tissue. Sometimes an ulcer permeates so deeply into the intestinal wall that it creates what is called a fistula, a link between the gut and other organs, such as the skin, bladder, or vagina. Bloody stools, diarrhea, and abdominal pain are the most common symptoms of Crohn's disease.

Inflammatory bowel disease typically is diagnosed after a patient seeks help for the gastrointestinal symptoms described above. Health care providers diagnose IBD using a number of strategies. An easy, preliminary way of detecting IBD is through a blood test that doctors examine for markers that point to inflammation. Blood tests showing anemia (low red blood cell count) can require further testing for IBD because anemia can indicate blood loss as well as poor iron absorption due to damage to the intestinal lining. Testing a stool sample for the presence of blood can assist in the diagnosis of IBD.

Endoscopies and colonoscopies are the most reliable ways of diagnosing IBD. An endoscopy is a procedure in which a tiny camera affixed to a bendable tube is inserted into the colon through the anus or into the small intestine by way of the mouth. Tissue samples are taken and put under the microscope for further examination. If inflammation is detected, then a form of inflammatory bowel disease is diagnosed. The instrument used to perform an endoscopy—the endoscope—is limited in length (10 to 20 feet), therefore a video capsule endoscopy might be used to view the portion of the small intestine that cannot be seen by performing a normal endoscopy. In a video capsule procedure, the patient swallows a camera the size of a large vitamin tablet. The camera then travels through the intestinal tract for four to eight hours and takes thousands of images that are examined for signs inflammation. A colonoscopy is a type of endoscopy that examines the colon, specifically, for signs of inflammation and ulceration.

Radiographic tests are also used to diagnose IBD and can be preferable to endoscopies and colonoscopies because they are noninvasive and can show areas that endoscopies and colonoscopies cannot. Regular x-rays, computerized tomography

(CT) scans, and magnetic resonance imaging (MRI) tests all can be helpful for diagnosing IBD.

Medical and Lifestyle Treatments

Inflammatory bowel disease is a chronic health problem, which means that no cure is available. Instead, treatment goals consist of reducing inflammation, correcting nutritional deficiencies that develop because of damage to the gastrointestinal tract, and managing symptoms such as pain and diarrhea. Inflammation generally is managed with a wide variety of medications, including drugs that suppress immune system activity. Some drugs, known as "biologics," target specific immune system messengers that contribute to inflammation. Infections are managed with antibiotics, and a variety of drugs can help reduce pain. Medications for diarrhea also are helpful for some people.

When medication is ineffective or harmful to the patient, surgery might be suggested to repair or remove the diseased part of the intestinal tract. About 25% of people with ulcerative colitis undergo surgery (CDC, 2012). Because ulcerative colitis occurs only within the large intestine, complete removal "cures" a person of the condition. Conversely, because Crohn's disease can show up anywhere along the digestive tract, surgery does not guarantee recovery (CDC, 2012). Eventually about 75% of people with Crohn's disease have surgery to remove damaged tissue (CDC, 2012).

Lifestyle changes can improve both general and digestive health. People with IBD often find that some foods—such as beans, caffeine, and soft drinks—are more likely than others to cause discomfort and must be avoided. People with IBD usually are advised to consume adequate fluids, eat smaller meals, and avoid the additive carrageenan, which can cause tissue damage. Increasing water-soluble fiber, such as psyllium, improves symptoms for some, and decreasing fibrous foods and consuming cooked rather than raw vegetables helps others. A multivitamin and mineral supplement, probiotic foods, and supplements often are recommended. Living with IBD can be very stressful, and stress can exacerbate IBD symptoms. Physical activity, recreational pursuits, biofeedback, and other relaxation techniques such as meditation and yoga are effective for reducing stress and can help people better manage IBD symptoms and maximize their quality of life.

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See Also: Digestion and the digestive system; Inflammation; Large intestine; Small intestine.

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Inositol

Inositol once was thought to be an essential B vitamin, and is still informally known as vitamin B8, but researchers now believe that most of the time people do not need to obtain inositol from the diet. Inositol is found in all body tissues and is especially concentrated in the heart and brain. Glucose is one of inositol's many isomers, meaning the molecules share the same molecular formula but have different structural formulas. Humans can synthesize inositol from glucose. There are nine forms of inositol in nature, but myo-inositol is the only form known to participate in human metabolic processes. Inositol is a component of cell membrane phospholipids, and appears to perform a variety of roles in the body. Inositol phospholipids serve as precursors to eicosanoids, compounds that work like neurochemicals in the human body. Inositol also helps the liver process lipids.

Inositol often is classified as a "conditional nutrient," meaning that people typically seem to make enough from the food they consume but occasionally—especially in cases of illness or inherited metabolic errors—the nutrient must be obtained more deliberately from the diet. Inositol is generally plentiful in nuts, seeds, beans, whole grains, cantaloupe, and citrus fruits. These foods contain inositol as a component of phytic acid (inositol hexaphosphate, or IP6). The diets of people in the United States and Canada typically supply about 1,000 mg of inositol/day.

Interesting research suggests that supplemental myo-inositol could have several therapeutic applications, although research still is preliminary. Myo-inositol has been studied as an intervention for multiple psychiatric disorders. It seems to be a crucial precursor molecule for a second messenger system for serotonin receptors in the brain, which helps to transmit signals from receptors on the cell membrane to a specific target inside the cell. Myo-inositol has been found to mimic the action of selective serotonin reuptake inhibitors, which are utilized for treatment of depression as well as panic disorder and obsessive-compulsive disorder (Levine, Mishori, Susnosky, Martin, & Belmaker, 1999).

Studies have produced mixed results regarding the effectiveness of myo-inositol for relieving the pain caused by diabetic neuropathy (EBSCO CAM Review Board, 2012). Small studies have found myo-inositol to improve some of the symptoms of polycystic ovary syndrome, including fertility (myo-inositol administration increased the frequency of ovulatory cycles) (EBSCO CAM Review Board 2012). An interesting study of 80 post-menopausal women with metabolic syndrome suggests that myo-inositol has several beneficial effects for this population. The women were divided into two groups. Both groups received standard

dietary recommendations, focusing on calorie restriction and weight loss. One group also received myo-inositol supplements (2g/day) and the other group received placebo pills. After six months, the group receiving myo-inositol supplements was found to have improved blood cholesterol and triglyceride levels, better blood pressure, and improved blood sugar regulation (Giordano et al., 2011).

In vitro and animal studies of another form of inositol, inositol hexaphosphate, suggest that this supplement inhibits cancer development and also might alleviate the side effects of chemotherapy (Memorial Sloan-Kettering Cancer Center, 2013). Though inositol might be worthy of continued exploration, its status as a naturally occurring molecule makes it difficult to patent and therefore a less attractive option for drug companies. There is little information regarding the safety of inositol supplements, but one study found 12 g of myo-inositol daily resulted in only mild side effects like nausea, flatulence, and diarrhea (Carlomagno & Unfer, 2011).

Patricia M. Cipicchio

Research Issues

Phytic acid has been called an "anti-nutrient," because it aggressively binds with many minerals—such as calcium and iron—in the digestive tract, making important minerals unavailable for absorption into the bloodstream. Yet phytic acid also appears to have many beneficial health effects, partly as a supplier of inositol. Populations consuming low amounts of essential minerals might not benefit from increasing consumption of high-phytate foods, such as whole grains and beans, but cultures with a plentiful intake of iron, calcium, and other minerals could benefit from a higher phytic acid intake.

See Also: Cardiometabolic syndrome; Depression and nutrition.

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Insects as Food

Entomophagy—the practice of eating insects—commonly is utilized by many animals such as birds, fish, lizards, spiders and other insects. Human entomophagy is practiced by at least 2 billion people worldwide. Of the 1.5 million documented species of animals on earth, many of which are entomophagous, 1 million are insects and 1,900 of these species are considered edible (FAO, 2013).

Defined as a class of animals with a chitinous exoskeleton, three-part body, and six jointed legs, insects are cold-blooded, undergo metamorphosis to adapt to seasonal variation, reproduce quickly, and often have large populations. The most commonly consumed insects are beetles (*Coleptera*), 31% of all insects consumed; caterpillars (*Lepidoptera*), 18% of all insects consumed; bees, wasps, and ants (*Hymenoptera*), 14% of all insects consumed; grasshoppers, locusts, and crickets (*Orthoptera*), 13% of all insects consumed; and cicadas, leafhoppers, planthoppers, scale insects, and true bugs (*Hemiptera*), 10% of all insects consumed (FAO, 2013). In most cases these insects are eaten in tropical, rather than temperate, regions of the world due to their year-round presence (in colder areas, insects hibernate to survive winters), their tendency to congregate in swarms at certain points in the day or season, and their typically larger body sizes facilitated by the faster diffusion of air through their respiratory systems at higher temperatures (FAO, 2013).



Deep-fried insects for sale in Thailand. People in many cultures have consumed the eggs, larvae, pupae, and adults of many insect species since prehistoric times. (Thor Jorgen Udvang /Dreamstime.com)

Compared to the virtually nonexistent consumption of insects in Western diets—aside from the permissible and unavoidable insect contamination allowed by food regulation (e.g., the U.S. Food and Drug Administration permits 150 insects fragments per 100 g of wheat flour)—an estimated 96 species of insects are eaten in the Central African Republic (FAO, 2013) and between 150 and 200 species are consumed in Southeast Asia (FAO, 2013). In the Democratic Republic of Congo, households in Kinshasa consume an average of 300 g of caterpillars per week, and insect consumption in the entire country represents 40% of the total animal protein consumed (FAO, 2013). Figures like these, however, are unheard of in Westernized societies due to the cultural aversion to insects. The role of insects in nutrition often is forgotten, despite the positive economic and ecosystem services provided by insects—1.2 million tons of honey generated by honeybees yearly, carmine dye extracted from cochineal beetles, and the pollination of 80% of plant species (FAO, 2013).

In regions having a more pervasive cultural acceptance of entomophagy, bugs are harvested and prepared in a variety of ways and ultimately offer an additional means of food security. Although the domestication of insects—with the exception of honeybees, silkworms, and cochineal beetles—is a difficult (albeit underutilized) method, the process of semi-cultivation, a practice that promotes the growth of an organism by skill and labor, has been undertaken by many societies.

Palm weevil larvae, for example, are semi-cultivated in South America, Africa, and Southeast Asia by the deliberate felling of palm trees at a specific location and time. One to three months later the larvae are ready to be harvested from the palm trunks. Making use of a far different approach, caterpillars in Malawi are semi-cultivated by a fire-management tactic in which landscapes are set afire between June and July to decrease the number of moth egg predators and promote the growth of young leaves on which the caterpillars feed (FAO, 2013). Additionally, local products in Togo are exclusively used for the semi-cultivation of termites. Inner mound conditions are created by providing a combination of humidified cellulose and soil in a cool, dark environment (FAO, 2013). In other regions of the world, such as Mexico, Colombia, and Ecuador, insects are harvested using the indigenous knowledge of plant life cycles, moon cycles, migration, and seasonal weather patterns (FAO, 2013).

Although each of these harvesting techniques reflects a specific and indigenous entomological understanding, little taxonomic knowledge of insects exists in comparison to vertebrates and plants. Without the knowledge of conservation and management requirements, the population dynamics and life cycles of insects can become disrupted by deforestation, forest degradation, overexploitation, pollution, and pesticide use (FAO, 2013). Subsequently, the importance of insects often can be misunderstood or undervalued, which leads to disruption of entire ecosystems. In places where this balance is maintained, however, entomophagy represents a viable contribution to food security.

Whether they are fried, steamed, boiled, turned into flour, sun-dried, candied, or eaten raw, insects provide an additional—and generally sustainable—food

source. Due to their cold-blooded nature, which means that they don't require feeding to maintain body temperature, insects have a far more practical feed-to-meat conversion rate than that of farm animals. Compared to chicken, pigs, and cattle, which in a typical North American food production system require 2.5 kg, 5 kg, and 10 kg of feed to produce 1 kg of animal weight, respectively, crickets are able to turn 1.7 kg of feed into 1 kg of animal weight (FAO, 2013). These figures become even more significant when one takes into account the fact that 80% of crickets, 55% of chicken, 55% of pigs, and 40% of cattle are edible and digestible. Further, insects can be reared on biowaste, which helps to make insect farming a more ecologically productive and profitable initiative.

Although insects can be seen as a sustainable food option due to their feed-to-meat conversion rates, as well as their low greenhouse gas emissions, low waste outputs, and low water inputs, they also provide a variety of nutritional benefits. Depending on metamorphic stage of the insect, its location, and its diet, edible insects represent a satisfactory source of protein, fat, minerals, vitamins, and fiber. In comparison to cattle and tilapia, which range from 19 g to 26 g and 16 g to 19 g of protein per 100 g of fresh weight, locusts and grasshoppers larvae, adult locusts and grasshoppers, chapulines (Mexican grasshoppers), yellow mealworms, and termites contain 14 g to 18 g, 13 g to 28 g, 35 g to 48 g, 14 g to 25 g, and 13 g to 28 g of protein, respectively (FAO, 2013). In regards to fat content, termites' and African palm weevils' dry weights are made of roughly 50% fat and contain a variety of monounsaturated, polyunsaturated, and saturated fatty acids (FAO, 2013). Iron and zinc content, depending on the diet, also can be adequately provided by insects. The mopane caterpillar, for example, provides 31 mg to 77 mg of iron per 100 g of dry weight, and the palm weevil larvae provides 26.5 mg of zinc per 100 g of dry weight; cattle supply only 6 mg of iron and 12.5 mg of zinc per 100 g (FAO, 2013). Although insects generally are not the best source of vitamin B12 and vitamin A, and more research is needed to identify insects rich in these and other vitamins, certain species produce sufficient amounts of vitamins B1, B2, and E. Lastly, research suggests that chitin—an insoluble fiber derived from exoskeletons—despite its indigestibility has been found to remediate asthma symptoms when administered as chitin microparticles.

Risks of entomophagy include the ingestion of poisonous species, improper preparation of insects (neglecting to remove various body parts that are indigestible or toxic), contamination of insects through the bioaccumulation of harmful metals and pesticides, and allergic reactions (FAO, 2013).

Tyler L. Barron

See Also: Food security and food insecurity.

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Insulin

Insulin is a hormone secreted primarily by the beta cells in the islets of Langerhans in the pancreas. Insulin plays a pivotal role in the regulation of glucose level in the bloodstream. When glucose level is high, insulin is released into the bloodstream and carried throughout the body. Insulin then binds to cell membranes and stimulates the cells to take up glucose. Insulin also signals muscle and liver cells to convert excess glucose into glycogen, a form of energy storage. Insulin signals cells to convert glucose into triglycerides, the primary form of fat storage. When blood glucose level is low, insulin secretion stops, and the pancreas releases another hormone, glucagon, which signals the liver to break down glycogen and release glucose into the bloodstream. Thus, insulin is regulated by negative feedback; after the release of insulin into the bloodstream, glucose level starts to decrease as cells take up glucose. As the amount of glucose decreases, the insulin secretion decreases and eventually stops.

When the pancreas does not produce sufficient amounts of insulin, or when the cell membrane receptors fail to respond appropriately to the presence of insulin in the bloodstream, diabetes mellitus results. Type 1 diabetes develops when the beta cells of the pancreas are destroyed and insulin no longer is produced. Type 2 diabetes results initially from a defect at the cell receptor level; in the later stages of diabetes, however, insulin production can decline as well.

Until the discovery of insulin, diabetes was a mysterious and deadly disease. In an effort to learn more about diabetes, a surgeon named Frederick Banting and a medical student named Charles Best conducted a series of experiments. The experiments resulted in a better understanding of the pancreas and the discovery of insulin (Nobel Media, 2009). In the summer of 1921, Banting and Best started their experiments on dogs. They first removed the pancreas from a dog and then, utilizing that pancreas, they filtered out a substance which they called "isletin" after the islet cells thought to produce the chemical. The researchers then injected the filtered substance into the dog from which the pancreas had been removed. After the injection, the dog, which had developed diabetic symptoms after removal of its pancreas, became better and the symptoms started to disappear. The isolated substance later was renamed "insulin" by Professor John Macleod at the University of Toronto, who had provided the resources for the experiment.

In 1922, after testing the insulin extract on themselves, Banting and Best injected the new drug into a 14-year-old boy named Leonard Thompson, who was

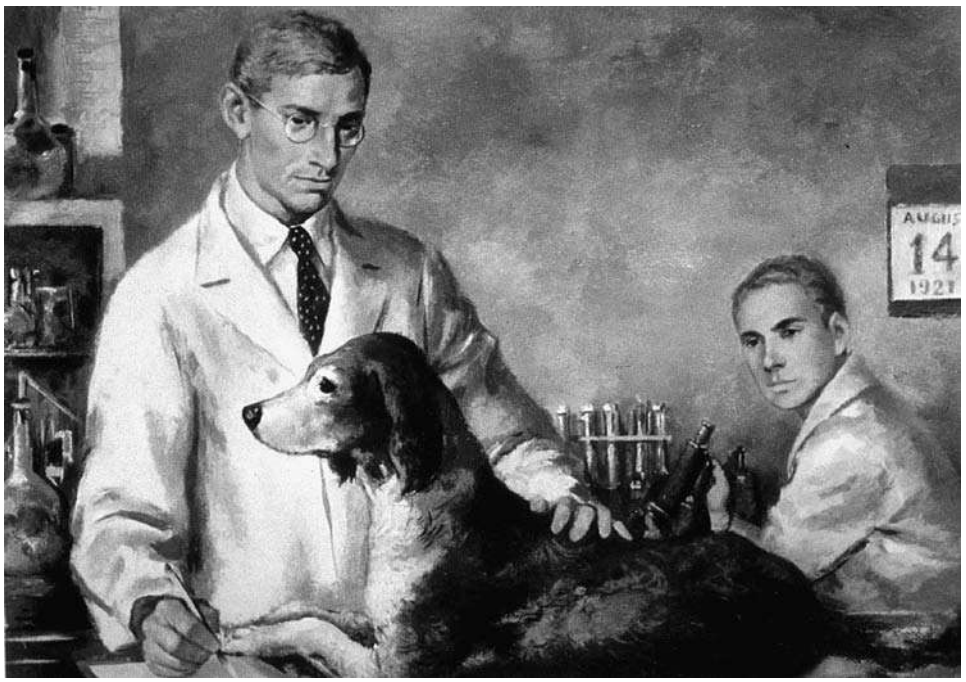


Illustration of Dr. Frederick Banting and Dr. Charles Best in the laboratory at Toronto University, with one of the first diabetic dogs to receive the insulin hormone, 1921. In 1923, two members of the Toronto team, Canadian physiologist Frederick Banting and British physiologist J. J. R. Macleod, shared the Nobel Prize in physiology or medicine for the discovery. (National Library of Medicine)

near death because of his diabetes. The injections reversed Thompson's symptoms and he regained his health. The insulin extract then was given to other volunteers, whose conditions improved in a similar fashion. In 1923, Banting and Macleod were awarded the Nobel Prize in Physiology or Medicine for the discovery of insulin (Nobel Media, 2009).

Since the 1920s, commercial insulin has been produced to help treat diabetic patients who lack sufficient insulin secretions. Insulin structure varies somewhat among species. The initial source of commercial insulin mainly was the pancreases of cattle or pigs, which produce insulin most similar to human insulin. Since 1983, however, bacteria have been used to produce commercial insulin. The human gene for insulin production is inserted into bacteria, which stimulates the bacteria to produce human insulin.

Recent research has shown that there might be a connection between brain insulin resistance and Alzheimer's disease (Correia et al., 2011). Glucose is the primary energy source for the brain, and because the brain does not store glucose it must rely on blood sources. Most of the insulin in the brain appears to come from peripheral circulation, although some insulin also might be made in the brain itself.

Fei Peng

Research Issues

Insulin's best-understood role is the part it plays in blood sugar regulation. Less understood are the intracellular signaling mechanisms stimulated when insulin binds to cell receptors. In addition to causing glucose uptake, insulin stimulates a number of anabolic functions that science is only just beginning to understand.

See Also: Alzheimer's disease and nutrition; Blood sugar regulation; Diabetes, type 1; Diabetes, type 2; Pancreas.

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Intestinal Gas

Intestinal gas is a natural by-product of digestion and swallowing air. The primary source of gas is the large intestine, where bacteria break down carbohydrates for energy and emit gas as a metabolic waste product. The main components of intestinal gas are nitrogen, oxygen, hydrogen, carbon dioxide, and methane (NIH, 2012). The unpleasant odor is attributed to trace sulfur-containing gases that make up only 1% of total gas content. Gas typically is expelled through the anus or the esophagus, although it can build up in the gut for a variety of reasons. The small intestine is less equipped to bear high gas loads, resulting in greater abdominal discomfort if buildup occurs. People pass gas on average about 13 to 21 times per day (Bharucha, 2007).

A diet high in carbohydrates that can be incompletely absorbed leads to more intestinal gas. Foods that lead to excess intestinal gas vary somewhat from person to person; people with food intolerances, such as lactose intolerance, experience more excess gas than others. In general, lactose in dairy products, fructose in fruit, and raffinose and stachyose in vegetables are the largest contributors to carbohydrate fermentation in the large intestine. Foods most associated with excess gas include beans; vegetables such as broccoli, cabbage, cauliflower, onions,

asparagus, and mushrooms; whole grains, such as whole wheat and bran; soft drinks and fruit drinks, especially those containing high-fructose corn syrup; and milk and dairy products. Symptoms of excess gas caused by fermentation include malodorous gas and nocturnal gas emission. Many people complain of abdominal bloating, but this symptom is not always caused by excess gas. Instead it could be the result of a sensitive GI tract, often accompanied by irritable bowel syndrome (IBS) or constipation. In IBS, motor dysfunction in the gut can impair the ability to move gas through the gut, resulting in increased distension, or abdominal bloating. In this case, even a normal amount of gas can cause pain (NIH, 2012). Excessive belching typically is caused by swallowing too much air. People can swallow too much air if they eat too quickly; talk while eating and swallowing, chewing gum, or sucking on candy; or by drinking fizzy (carbonated) drinks.

Many people self-treat problematic intestinal gas by keeping a food diary to determine which foods they should avoid. Over-the-counter products can aid in the digestion of problematic carbohydrates. Lactase can help people better digest dairy products, and the enzyme alpha-galactosidase (as found in the product "Beano") breaks down the carbohydrates found in beans and other vegetables. People should consult a health care provider if symptoms become problematic. People older than age 40 who experience a sudden change in symptoms should consult a provider, especially if intestinal gas is accompanied by weight loss, constipation, or diarrhea.

Patricia M. Cipicchio

See Also: Digestion and the digestive system; Irritable bowel syndrome.

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Iodine

Iodine is a nutrient necessary for the production of two important hormones, triiodothyronine (T3) and thyroxine (T4). Produced by the thyroid gland, these hormones help to regulate body temperature, basal metabolic rate, growth, and reproduction. Iodine is found predominantly in oceans and is the second-heaviest element used widely for biological functions. Iodine also is present in some



Dembele Terefe Gendo, 48, foreground, and her daughter Rome Berinhun, 16, right, outside their home in Nedjo, Ethiopia, February 27, 2008. Gendo has had a goiter since she was a young girl. Her daughter has also developed one, and her son says he feels the beginning of one, as well. The 16-year-old is among some 80% of Ethiopians suffering from an easily preventable deficiency of iodine, an essential nutrient that was readily available from Eritrea until the 1998–2000 war halted all trade between the countries. (Anita Powell/AP Photo)

groundwater. Iodine levels in plants reflect the soil content—and much of North America's soil is considered to be iodine deficient.

Insufficient iodine is the second most common dietary deficiency, behind iron, and is estimated to impact about 2 billion people worldwide. Diets including seafood, kelp, eggs, and dairy products will provide the highest concentrations of iodine. Iodine is added to livestock feed, and organic farmers often utilize iodized salt licks for grass-fed cows and chicken feed with kelp additives to maintain healthy iodine levels in the animals. Iodized salt was introduced in the United States in 1924 to address iodine deficiency, which was still common in the North American population in the early 1900s.

Table 1. Selected Food Sources of Iodine

Food	Approximate Micrograms (mcg) per Serving	Percent Daily Value*
Seaweed, whole or sheet, 1 g	16 to 2,984	11% to 1,989%
Cod, baked, 3 oz	99	66%
Yogurt, plain, low-fat, 1 cup	75	50%
Iodized salt, 1.5 g (approx. 1/4 teaspoon)	71	47%
Milk, reduced fat, 1 cup	56	37%
Fish sticks, 3 oz	54	36%
Bread, white, enriched, 2 slices	45	30%
Fruit cocktail in heavy syrup, canned, 1/2 cup	42	28%
Shrimp, 3 oz	35	23%
Ice cream, chocolate, 1/2 cup	30	20%
Macaroni, enriched, boiled, 1 cup	27	18%
Egg, 1 large	24	16%
Tuna, canned in oil, drained, 3 ounces	17	11%
Corn, cream style, canned, 1/2 cup	14	9%
Prunes, dried, 5 prunes	13	9%
Cheese, cheddar, 1 oz	12	8%
Raisin bran cereal, 1 cup	11	7%
Lima beans, mature, boiled, 1/2 cup	8	5%
Apple juice, 1 cup	7	5%
Green peas, frozen, boiled, 1/2 cup	3	2%
Banana, 1 medium	3	2%

*DV = Daily Values were developed by the U.S. Food and Drug Administration (FDA) to help consumers compare the nutrient contents of products within the context of a total diet. The DV for iodine is 150 mcg for adults and children 4 years of age and older. The FDA, however, does not require food labels to list iodine content unless a food has been fortified with this nutrient. Foods providing 20% or more of the DV are considered to be high sources of a nutrient.

Source: National Institutes of Health. Office of Dietary Supplements. (2011). *Iodine*. Dietary Supplements Fact Sheet. Retrieved from http://ods.od.nih.gov/factsheets/Iodine-HealthProfessional/

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In adults iodine deficiency leads to an enlargement of the thyroid gland known as "goiter." Iodine deficiency most typically results from a diet's insufficient iodine. Because the mineral selenium is essential for the production of thyroid hormones, however, a selenium deficiency also can cause symptoms of iodine deficiency.

Adequate iodine intake is especially critical for pregnant mothers and infants. Early physical and mental development is driven by thyroid hormones, leaving neonates, infants, and children most vulnerable to hypothyroidism caused by inadequate iodine intake. During all fetal stages, myelination of the central nervous system is especially affected by thyroid hormone. Pregnant mothers with inadequate iodine have an increased risk of miscarriage and of having babies with low birth weight, and their children have lower survival rates. Iodine deficiency also is the world's most common preventable cause of brain damage and mental retardation. It can result in a condition known as "cretinism," with an estimated loss of 15 to 20 IQ points. Irreversible impairment of neurologic function, including low performance in motor and perceptual skills, can occur even with moderate iodine deficiencies during pregnancy.

Iodine and selenium appear to exert a protective antiproliferative effect on thyroid tissue. In other words, these minerals prevent cells from continuing to divide in harmful ways. Preliminary in vitro evidence suggests that the mineral combination could have a similar effect on breast tissue. In a few small studies, iodine has been found to be somewhat useful for the treatment of fibrocystic breast disease. Animal studies suggest that iodine might be useful for the prevention of breast cancer, although it is too early to recommend iodine supplements for this purpose. The body is unable to store iodine for long periods, resulting in a need for a regular intake. The DRI for adult men and women is 150 mcg/day. Iodine is toxic at high doses, and the Tolerable Upper Intake Level is 1,100 mcg/day for adults.

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Research Issues

Iodine deficiency is a leading cause of intellectual disability (formerly known as "mental retardation") worldwide. This form of intellectual disability, which develops during pregnancy in iodine-deficient mothers, is preventable with the use of iodized salt. The International Council for Control of Iodine Deficiency Disorders publishes a quarterly newsletter that provides information on global efforts to eradicate iodine deficiency (http://iccidd.server295.com/pages/idd-newsletter.php).

See Also: Cancer and nutrition; Minerals.

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Iron

Iron is an essential mineral that is found in every cell in the human body. This mineral enables the body to make hemoglobin and myoglobin. Hemoglobin is a protein in red blood cells that transports oxygen, and myoglobin is a protein that serves a similar function in muscles. Many enzymes require iron to function properly, and iron is essential for immune system and brain function, and for producing the energy molecule ATP. Dried beans, dried fruit, eggs (especially egg yolks), beef, poultry, salmon, tuna, and whole grains provide dietary iron. Adults are recommended to have 8 mg of iron per day. The recommended daily intakes for women of childbearing age and pregnant women are much higher. Women of childbearing age require 18 mg per day, and pregnant women need 27 mg per day.

Dietary Sources

Dietary iron exists in two forms in foods, "heme" and "nonheme" iron. Nonheme iron is found in plant sources, dairy products, eggs, iron supplements, and iron-fortified food. Heme iron is located within hemoglobin, therefore it only is found in meat sources—but meats also contain nonheme iron. Meats such as chicken, beef, and fish, for example, contain approximately 60% of their iron as nonheme iron. Heme iron is more readily absorbed in the body; however, a majority of the iron supplied by the typical diet is nonheme.

Iron Absorption and Storage

Iron absorption is carefully regulated by the body, as too much iron can be toxic. The absorptive cells on the microvilli of the small intestine are the site of iron absorption. These cells contain a protein called "transferrin," which binds to iron. If body iron stores become low, then more transferrin is made. Transferrin also carries iron into the bloodstream, taking it from the absorptive cells to tissues throughout the body. Iron is used by all cells to make important enzymes.

The tissues can store iron in several ways. Iron sometimes becomes part of a soluble protein complex called "ferritin," and at other times it is incorporated into an insoluble complex known as "hemosiderin." Both ferritin and hemosiderin stores are especially high in bone marrow and the spleen (where red blood cells are made), the liver (the primary site of iron storage), and in skeletal muscles (where iron is incorporated into myoglobin).

Hemochromatosis (Iron Storage Disease)

Although people with iron-deficiency anemia look for foods fortified with iron to meet their iron needs, people with the genetic disorder hemochromatosis must be careful to limit iron consumption. The Centers for Disease Control and Prevention provide the following facts about hemochromatosis.

Hemochromatosis (iron-storage disease) occurs when the body absorbs too much iron from foods and other sources such as vitamins containing iron. This disease causes extra iron to gradually build up in the body's tissues and organs, causing iron overload. If this iron buildup is not treated, then over many years it can damage the body's organs. Not all people with this gene mutation develop iron overload, and not all people with iron overload develop the signs and symptoms of hemochromatosis.

Signs and Symptoms

Symptoms can be different for men and women. Although most people reach middle age before they have symptoms of hemochromatosis, some people can develop symptoms at a younger age.

Early symptoms include the following.

- Fatigue
- Weakness
- Weight loss
- Abdominal (belly) pain
- Joint pain

As iron builds up, the following symptoms can occur.

- Loss of menstrual periods or early menopause
- Loss of sex drive or impotence
- Loss of body hair
- Shortness of breath

Although not a physical symptom, another indication of hemochromatosis is an elevated liver enzyme test result.

Advanced Symptoms

- Arthritis
- Liver problems, such as cirrhosis and liver cancer
- High blood sugar and diabetes
- Constant abdominal (belly) pain
- Severe fatigue
- Heart problems
- Heart failure
- Gray-colored or bronze-colored skin

Risk Factors and Causes

Although it can have other causes, in the United States hemochromatosis usually is caused by a genetic disorder. The genetic defect of hemochromatosis is present at birth, but symptoms rarely appear before adulthood.

Diagnosis

The iron overload associated with hemochromatosis can be diagnosed through two blood tests performed in a doctor's office. If the disease is not diagnosed and treated early, it can cause serious problems.

Treatment

Treatment consists of taking blood from the arm, much like when giving blood. The treatment is safe and effective. Patients can expect a normal life span if they start treatment before organ damage has begun.

Centers for Disease Control and Prevention. (2011). *Hemochromatosis (Iron Storage Disease)*. Retrieved from http://www.cdc.gov/ncbddd/hemochromatosis/facts.html

Iron absorption varies widely from person to person. People absorb about 15% to 35% of heme iron, and anywhere from 2% to 20% of nonheme iron (ODS, 2007). Absorption of heme iron is influenced primarily by need: Women of childbearing age absorb more iron than men, and absorption increases even more during pregnancy. Absorption of nonheme iron is influenced by meal composition. Some dietary components decrease nonheme iron absorption because they bind with iron to form complexes that are not bioavailable. These components include phytates (present in whole grains and legumes); tannins (in tea, coffee, and wine); oxalates (found in many vegetables such as spinach); and polyphenols (present in tea, coffee, and many other plants).

Many components—such as vitamin C, amino acids (proteins), citric acid, and hydrochloric acid—chelate with nonheme iron and enhance its bioavailability. Hydrochloric acid is produced by special glands in the stomach, but production decreases with age, therefore older adults can develop iron deficiency because of poor absorption. Absorption of iron from plant sources is improved if plants and meat are eaten at the same meal or if vitamin C is consumed along with the nonheme iron. Calcium, iron, and zinc each can inhibit absorption of the other. People taking these minerals as supplements should take them at separate times to avoid competition for absorption.

Health Problems Associated with Iron Intake

Low iron intake can result in iron-deficiency anemia, in which a lack of iron results in an inadequate number of healthy red blood cells. Iron-deficiency anemia causes low oxygen levels in tissues throughout the body, and results in a number of symptoms including extreme fatigue, shortness of breath, difficulty regulating body

Table 1. Dietary Sources of Iron

Food, Standard Amount	Iron (mg)	Calories
Clams, canned, drained, 3 oz	23.8	126
*Fortified dry cereals (various), about 1 oz	1.8 to 21.1	54 to 127
Cooked oysters, cooked, 3 oz	10.2	116
Organ meats (liver, giblets), cooked, 3 oz	5.2 to 9.9	134 to 235
*Fortified instant cooked cereals (various), 1 packet	4.9 to 8.1	Varies
*Soybeans, mature, cooked, ½ cup	4.4	149
*Pumpkin and squash seed kernels, roasted, 1 oz	4.2	148
*White beans, canned, ½ cup	3.9	153
*Blackstrap molasses, 1 Tbsp	3.5	47
*Lentils, cooked, ½ cup	3.3	115
*Spinach, cooked from fresh, ½ cup	3.2	21
Beef, chuck, blade roast, cooked, 3 oz	3.1	215
Beef, bottom round, cooked, 3 oz	2.8	182
*Kidney beans, cooked, ½ cup	2.6	112
Sardines, canned in oil, drained, 3 oz	2.5	177
Beef, rib, cooked, 3 oz	2.4	195
*Chickpeas, cooked, ½ cup	2.4	134
Duck, meat only, roasted, 3 oz	2.3	171
Lamb, shoulder, cooked, 3 oz	2.3	237
*Prune juice, ¾ cup	2.3	136
Shrimp, canned, 3 oz	2.3	102
*Cowpeas, cooked, ½ cup	2.2	100
Ground beef, 15% fat, cooked, 3 oz	2.2	212
*Tomato puree, ½ cup	2.2	48
*Lima beans, cooked, ½ cup	2.2	108
*Soybeans, green, cooked, ½ cup	2.2	127
*Navy beans, cooked, ½ cup	2.1	127
*Refried beans, ½ cup	2.1	118
Beef, top sirloin, cooked, 3 oz	2.0	156
*Tomato paste, ¼ cup	2.0	54

Food sources of iron are ranked by milligrams of iron per standard amount; also calories in the standard amount. (All amounts listed provide 10% or more of the Recommended Dietary Allowance (RDA) for teenage and adult women, which is 18 mg/day.)

*These are nonheme iron sources. To improve absorption, eat these with a vitamin C–rich food.

temperature, pale skin, and weakness. Other symptoms include rapid heartbeat, and reduced concentration and cognitive performance.

Though iron is essential for proper body function, this mineral is toxic in high doses. It is rare that people have too much iron in their diets unless they consume too many supplements. Importantly, however, iron overdose from overconsumption of

dietary supplements is one of the leading causes of fatal poisoning of children living in North America. People also can acquire too much iron if they have a disorder known as "hemochromatosis." Hemochromatosis comes in two forms, primary and secondary. Primary hemochromatosis is a genetic disorder in which the body absorbs too much iron and this causes a buildup of iron in the liver and other places in the body. Secondary hemochromatosis develops in conjunction with certain blood-related and other disorders, as well as with long-term alcoholism.

Iron can act as an oxidant in the body, generating free radicals which can damage DNA, cell membranes, and other cellular components. For this reason, iron supplements should not be taken except during pregnancy or if iron deficiency has been diagnosed by a health care professional. Iron supplements often cause constipation and are poorly tolerated by many people.

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See Also: Iron-deficiency anemia.

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Iron-Deficiency Anemia

Iron-deficiency anemia (IDA) is the most severe stage of iron deficiency and is marked by a decrease in red blood cell size and number. It is diagnosed when hemoglobin and hematocrit levels, measured with a blood test, drop below desirable levels. Hemoglobin is the compound in red blood cells that gives blood its color and transports oxygenated blood throughout the body. Hematocrit is the ratio of the volume of red blood cells to the total blood volume. Without enough available iron, the body does not produce adequate amounts of hemoglobin and, thus, not enough red blood cells.

Iron deficiency is the most common nutrient deficiency worldwide, and iron-deficiency anemia is the most common form of anemia. Iron deficiency can result from inadequate dietary iron, increased iron requirements, blood loss, problems with iron absorption, or a combination of these factors. A variety of infectious diseases can contribute to impaired iron absorption or red blood cell production. Consequences of IDA range from mild to life threatening. In children, severe anemia can lead to impairments in physical growth and mental development,

including deficits in motor control, memory, and attention span. Treatments include increasing iron intake and addressing the cause of the IDA.

The World Health Organization (WHO) estimates that IDA affects nearly 2 billion people—more than 30% of the world's population (WHO, 2012). Rates are generally lower in high-income countries. Groups most affected include young children, women of childbearing age, pregnant women, and older adults. In the United States and Canada, nursing home residents have the highest rates of IDA, nearly 20%, although much of this could be due other health problems (CDC, 2013; Cooper et al., 2012). Rates for young women also are fairly high, approximately 10% to 15%. In the United States, children ages 1 to 2 years have especially high rates of anemia, about 14% (CDC, 2013). Children from low-income areas are most vulnerable. Rates for children in Canada are much lower.

Iron Deficiency: Stages and Diagnosis

Stage 1

The first stage of iron deficiency is a gradual decline in iron stores. Iron is stored in two compounds, ferritin and hemosiderin. Both ferritin and hemosiderin stores are especially high in bone marrow and the spleen (where red blood cells are made), the liver (the primary site of iron storage), and in skeletal muscles (where iron is incorporated into myoglobin, an oxygen-binding compound). Serum (blood) ferritin levels reflect general levels of iron storage. Low serum ferritin levels can be diagnosed with a blood test, and indicate low iron stores.

Stage 2

The second stage of iron deficiency is depletion of transport iron, the iron that is being transported in the bloodstream for use by the cells. Transferrin is a compound that helps to transport iron in the bloodstream. Transferrin also aids the absorption of iron during digestion, transporting iron from the digestive mass into the intestinal cells, and then into the bloodstream. Low transport iron indicates more serious anemia. Transport-iron levels can be measured in several ways. Transferrin saturation measures indicate the extent to which serum transferrin has empty binding sites. Empty binding sites indicate low iron. This measure is referred to as total iron binding capacity (TIBC). Transport iron also can be measured using protoporphyrin levels. Protoporphyrin combines with iron to make hemoglobin, therefore high protoporphyrin levels are a sign that not enough iron is available to make hemoglobin. Physical symptoms at this stage are fairly mild. Athletes could experience a decline in sport and exercise performance.

Stage 3

The final stage of iron deficiency is iron-deficiency anemia. In this stage, red blood cells could be pale, smaller than normal, and fewer than normal in number.

Hemoglobin and hematocrit levels are low. Mean corpuscular volume, an indication of the average size of the red blood cells, also can be measured. (Larger than normal red blood cells can indicate megaloblastic anemia, caused by folate and vitamin B12 deficiency, and smaller than normal cells, in combination with other measures, indicate IDA.) Symptoms of iron-deficiency anemia include extreme fatigue, weakness, light-headedness, rapid heartbeat, shortness of breath, pale skin, difficulty concentrating, irritability, and mental confusion. Active people experience a decline in ability to participate in vigorous physical activity.

Causes

Iron-deficiency anemia results from a variety of causes that fall into four general categories: inadequate iron in diet, problems with iron absorption, increased iron loss, and increased iron requirements. In children and young adults, IDA most commonly results from inadequate levels of iron in the diet. Dietary iron exists in two forms in foods, heme and nonheme iron. Nonheme iron is found in plant sources, dairy products, eggs, iron supplements, and iron-fortified food. Heme iron is located within hemoglobin, and therefore it is found only in meat sources; however, meats also contain nonheme iron. Meats such as chicken, beef, and fish, for example, contain approximately 60% of their iron as nonheme iron. Heme iron is more readily absorbed in the body, but a majority of the iron supplied by the typical diet is nonheme. A lack of heme iron sources in the diet greatly reduces overall iron intake and absorption, as nonheme iron is best absorbed when consumed in a mixed diet (a diet including both animal and plant foods).

The amount of iron absorbed from the diet depends on many factors in addition to iron intake. Some foods such as tea, coffee, whole grains, legumes, and milk or dairy products contain substances that decrease the amount of nonheme iron absorbed. Calcium supplements also can decrease the amount of iron absorbed at a meal. Intestinal disorders can affect the body's ability to absorb iron from food into the bloodstream. Celiac disease, for example, reduces the ability of the small intestine to absorb nutrients. Pathogens such as hookworm and schistosomiasis, which commonly are found in many middle- and low-income countries, increase a person's risk of developing anemia by decreasing iron absorption.

Blood loss can result in IDA. Chronic blood loss can develop from an ulcer, hernia, gastrointestinal bleeding, or menstrual blood loss. Any illness that increases blood loss increases the risk of IDA. Women who have heavy menstrual bleeding have an increased risk for developing IDA.

Iron needs increase during several periods of the life cycle. Children experience a rapid rate of growth and the production of new blood cells during the first few years of life. The iron requirements of infants vary with prenatal environment. If mothers have sufficient iron status during pregnancy, then infants can store enough iron for the first six months of life. Breast milk has fairly low levels of iron, although it is more bioavailable to infants than the higher levels

of iron found in formula. After six months, infants and young children need iron-rich foods. When mothers are iron deficient during pregnancy, infant iron stores are compromised and these babies are at a high risk of developing iron deficiency.

During pregnancy a woman's blood volume increases by about 50% to carry oxygen and nutrients to the uterus, placenta, and developing fetus. Iron deficiency during pregnancy induces both maternal and fetal stress, which increases rates of maternal mortality during childbirth, and can create long-term cognitive and behavioral problems in childhood.

Iron needs increase with the onset of puberty for both boys and girls. Boys and girls need more iron for their growth and development. Girls require even more dietary iron with the onset of the menses and monthly blood loss.

Long-Term Complications

If left untreated, iron-deficiency anemia can lead to health complications over time, especially if severe. Adults can develop an irregular heartbeat and even heart failure, because the heart is required to pump more blood to compensate for the blood's low oxygen content. For infants and children, IDA has been associated with adverse physical, cognitive, and emotional development.

Treatment

Successful therapy for IDA involves determining and, if possible, correcting the cause of iron deficiency and increasing iron intake. Overloading the body with iron can be dangerous because excess iron accumulation can damage the liver and cause other complications; therefore people should not self-diagnose or add iron supplementation. Patients should collaborate with their health care providers to be sure to verify the existence of an iron deficiency and, if it is diagnosed, then identify a tolerable daily iron dose, formulation, and regimen.

An iron-rich diet is vital for the treatment of IDA. Foods rich in heme iron such as red meat, liver, chicken, and oily fish are most helpful. Foods containing heme iron enhance iron absorption from foods that contain nonheme iron, such as iron-fortified cereals, beans, and spinach. Vitamin C is plentiful in many fruits and vegetables and increases iron absorption. Cooking with cast-iron pots and pans adds iron to food. People with IDA usually must take iron supplements to replenish the body's iron stores. Dosing cycles for iron replacement depend upon the tolerated daily dose and the total iron deficit for an individual. Unfortunately, many people experience some stomach upset and constipation when taking iron supplements. When IDA is severe, blood transfusions sometimes are required.

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Research Issues

The World Health Organization has identified iron-deficiency anemia (IDA) as a serious public health problem, especially in resource-poor areas, where about 50% of pregnant women and 40% of preschool children are anemic (WHO, 2012). Iron-deficiency anemia is embedded in the cycle of poverty, in which inadequate diets, infectious disease, and IDA create poor maternal health, and then results in babies and children who are unable to reach their potential because of stunted growth and development. The World Health Organization has organized a public health campaign for countries with high rates of IDA to reduce the disease burden of this treatable illness. Preventing and treating IDA requires more than simply supplying people with iron supplements. Indeed, iron supplements can be harmful to children and adults who are not iron-deficient. Although the best practice would be to test every person before supplementing with iron, this approach is not always economically feasible. Iron-deficiency anemia seems to be somewhat protective against malaria for children in countries with high rates of this infectious disease, so controlling malaria also must be a priority, along with establishing the most effective IDA treatment guidelines for children and adults in these locations (Pasricha et al., 2013).

See Also: Iron.

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Irradiation

Food irradiation is a technology used to eliminate bacteria, parasites, and other microorganisms which can cause spoilage or disease. The tightly controlled process exposes food to ionizing radiation utilizing one of three different irradiation methods: electron beams, x-rays, or gamma rays. High-energy electron beams are emitted from a gun directly onto food and produce no radiation, but only penetrate to shallow depths. X-ray irradiation is an emerging technology that consists of passing an electron beam through a plate of metal and onto foods where it can enter foods to greater depths. When using gamma rays, the radioactive forms of cesium or cobalt are contained with food in an enclosure lined with concrete. Photons given off by these radioactive elements are able to penetrate deep into food. This technique also is used to sterilize medical equipment and household products, as well as for cancer radiation treatment. The energy given off by these methods is transferred to harmful microbes and damages their DNA.

The Centers for Disease Control and Prevention cites nutritional changes that accompany food irradiation to be negligible. The vitamin thiamine is the only known nutrient to decrease after treatment, and changes only by a minimal amount. Although these methods kill all remaining live cells in food products, thus extending shelf life, irradiated foods still need to be cooked and handled as if they were



A microbiologist with the U.S. Department of Agriculture vacuum-seals hot dogs in preparation for irradiation. Food irradiation is a safety technology that uses ionizing radiation to kill disease-causing organisms in such foods as raw meat, raw poultry, and fresh produce. (Stephen Ausmus/U.S. Department of Agriculture)

not treated. In the United States, irradiation is approved by the Food and Drug Administration for use on fruits and spices, most meats, vegetables, and wheat products, and can be identified by the presence of the Radura logo on the packaging of any irradiated foods. The treatment process does produce free radicals in food, but the majority of these decay almost immediately. Irradiation has been examined extensively for safety, and repeated long-term studies reveal no substantial evidence for adverse effects. Irradiation is not permitted in organic foods, as organic advocates are concerned about nutritional and chemical changes caused by irradiation, called "radiolytic products," and also worry that the long-term safety of the practice has not been satisfactorily confirmed in humans.

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Research Issues

Food manufacturers in North America have been slow to adopt food-irradiation technology because they fear consumer rejection. Media reports of deaths and illness caused by food-borne pathogens, however, have increased public awareness of the importance of food safety. As consumers become more worried about food-borne pathogens such as *E. coli*, salmonella, and campylobacter, they could become more open to purchasing irradiated products.

See Also: Foodborne illness and food safety.

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Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is a chronic disorder of the gastrointestinal tract (GIT) associated with abdominal pain and altered bowel activity. The condition is poorly understood and has no cure or consistently effective treatment. The disorder is characterized by a mixture of both diarrhea and constipation, with one condition usually being predominant. Symptoms also can include mucus in the stools and feelings of incomplete bowel movements. Additional symptoms include

headaches, backaches, fatigue, bloating, and gynecological problems. IBS is a fairly common disorder, affecting about 10 % to15% of North Americans (NDDIC, 2012). Irritable bowel syndrome tends to affect women twice as often as men and is most likely to occur in people younger than age 45. Signs of IBS usually first appear in childhood, then increase in young adults, and decrease in mature adults. As a chronic condition, sometimes IBS symptoms improve or disappear completely. Symptoms usually are aggravated after a meal, during stressful events, or during menstruation, with the pain usually reduced after a bowel movement occurs. Unlike other gastrointestinal disorders, such as Crohn's disease and celiac disease, IBS causes no perceptible damage to the colon. Nevertheless, its symptoms can be stressful and debilitating, and interfere significantly with participation in activities and quality of life.

Irritable Bowel Syndrome Diagnosis and Classification

No specific laboratory test for the diagnosis of IBS currently exists. Instead, patients are tested for conditions that produce IBS-like symptoms, ruling out parasitic infections, lactose intolerance, celiac disease, inflammatory bowel diseases, and other possible causes. After other potential causes have been eliminated, and when specific gastrointestinal (GI) symptoms have been present for at least three days per month for three consecutive months, and if the symptoms do not seem to be caused by another disorder, then IBS is diagnosed. Patients must have abdominal discomfort or pain with at least two of the following symptoms: a change in the frequency of bowel movements; a change in the appearance of the stools, either becoming more watery or harder than usual; or a reduction in discomfort after a bowel movement.

The three primary classifications of IBS are IBS-Constipation (IBS-C), IBS-Diarrhea (IBS-D), and IBS-Mixed (IBS-M). These are based upon the symptoms.

- IBS-C is classified as constipation-predominant IBS. This subgroup is most commonly composed of women and is the diagnosis in about one-third of all IBS cases. It is characterized by having hard stools more than 25% of the time and loose stools less than 25% of the time.
- IBS-D is classified as diarrhea-predominant IBS. This subgroup is most common in men and comprises up to one-third of all IBS cases. It is characterized by having loose stools more than 25% of the time and hard stools less than 25% of the time.
- IBS-M is a mixed form of bowel habits characterized by periods of both constipation and diarrhea. IBS-M patients cycle between patterns of hard and soft stools more than 25% of the time.

Causes

The exact cause of IBS is unknown, however symptoms are thought to be due to abnormal GIT contractions. The intestinal walls are lined with layers of muscle

that contract and relax to facilitate the flow of food from the stomach through the intestinal tract and to the rectum. For IBS-D patients, GIT contractions can be stronger and last longer than normal. This forces food through the colon quickly, causing gas, bloating, and diarrhea. Faster movement of food through the intestine can result in a nutritional deficiency, as the food might not have adequate time to be absorbed. In IBS-C patients, the opposite situation occurs; food passage is slowed and stool hardens and dries in the colon.

But what causes the abnormal GIT contractions? Researchers are not sure what causes the development of IBS. Once IBS has developed, individuals can react strongly to certain foods, stress, or hormone stimuli. These stimuli are referred to as "triggers." Although triggers do not appear to cause IBS, they can make the symptoms worse. The IBS triggers vary from person to person, but the most commonly reported trigger foods associated with IBS are chocolate, milk, and alcohol, which could cause constipation or diarrhea. Carbonated beverages and fruits also are reported to cause bloating and discomfort. Stress is another commonly reported trigger. Patients report heightened or more frequent symptoms during stressful periods. Hormonal triggers are also thought to be associated with IBS, particularly for women. Women diagnosed with IBS report increased IBS symptoms during menstruation.

Many researchers believe that the abnormal GIT contractions of IBS result, at least partly, from dysfunctional communication between the nerves that regulate the digestive system and the central nervous system. The nerves regulating the digestive system are known as the enteric nervous system. The central nervous system consists of the brain and the spinal cord. Digestive processes operate best when people feel relaxed. Conversely, when the brain perceives a need to respond to stress, the fight-or-flight response activates the physiological systems most essential for immediate survival: the cardiovascular, respiratory, and musculoskeletal systems. Proper digestive system function is interrupted.

People with IBS often suffer from emotional health disorders such as anxiety, depression, panic disorders, and post-traumatic stress disorder. It is possible that a state of over-arousal or other dysfunction in the central nervous system could result in communication with the enteric nervous system that causes IBS symptoms. It is important to note that IBS symptoms themselves can increase feelings of anxiety, stress, and other emotional health problems.

Treatment

Treatment of IBS focuses on symptom management to help patients maintain daily functioning and improve their quality of life. The goal of treatment is to normalize gastrointestinal movement based on the predominant symptoms of diarrhea, constipation, or mixed IBS. A majority of people with IBS respond well to dietary and other lifestyle changes. Alternative therapies often are helpful for IBS. Over-the-counter and prescription medications also can help with symptom relief.

Lifestyle remedies are an inexpensive and noninvasive way to alleviate pain and symptoms associated with IBS. Dietary recommendations include increasing

intake of fluid and soluble fiber. Soluble-fiber foods and supplements are recommended for both diarrhea and constipation, as they help normalize stool consistency. Probiotic foods (such as yogurt) and supplements are often recommended for people with IBS, although it is not clear exactly which organisms are most therapeutic. People with IBS must learn to identify and avoid trigger foods, usually through trial and error. Fatty foods and gas-producing foods trigger IBS symptoms in many people. Caffeine, alcohol, and foods containing fructose or sorbitol (a sugar-alcohol often used as a sugar substitute) also can be problematic.

Many people find relief from alternative remedies. Herbal medicines—especially those with peppermint oil—often are used for IBS. Alternative therapies that have shown promise for the treatment of IBS include acupuncture, hypnosis, therapeutic yoga and other body work, and many types of relaxation techniques.

Over-the-counter and prescription medications can help to control diarrhea and constipation. Over-the-counter medications should be used with caution, as the body can develop a dependency on them for normal bowel function. Additionally, these drugs can have side effects if taken too often or for too long. Similar cautions apply to the prescription drugs for IBS. The two most commonly prescribed pharmacological approaches are Alosetron (Lotronex) and Lubiprostone (Amitiza) (Mayo Clinic, 2012). Alosetron is intended for severe cases of IBS-D in women who have not responded to other treatments. It works by using a nerve receptor antagonist that relaxes the colon to slow the muscle contractions causing diarrhea. Alosetron is not approved for use by male patients. Lubiprosterone is a laxative prescribed to adult women and men with severe IBS-C who have not responded to other treatments. Lubiprosterone increases fluid secretion in the small intestine to facilitate the passage of stool. People with IBS sometimes respond well to antidepressant medications, as these act on the enteric nervous system as well as on the central nervous system.

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Research Issues

Researchers have suggested that people with Irritable Bowel Syndrome might respond differently to pain than people without IBS. This theory proposes that, in IBS patients, the brain overreacts to gastrointestinal tract (GIT) sensations, interpreting stimuli as painful. As the brain "learns" to pay attention to painful input, and interpret sensations as painful, perceptions of pain increase. If this theory is true, then pain education for people with IBS—in conjunction with other forms of treatment—might be helpful in reducing stress arousal in response to perceived pain. If people with IBS can learn to relax even when some discomfort is present it could enhance gastrointestinal tract function and reduce IBS symptoms.

See Also: Digestion and the digestive system; Large intestine.

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Isothiocyanates

Isothiocyanates are phytochemicals that are thought to have cancer-prevention effects. These compounds are released during the breakdown of glucosinolates by a group of enzymes called myrosinases. These enzymes become active when something causes the structural components of plant cells to be disrupted, such as chewing. Fresh cruciferous vegetables are the primary source of glucosinolates, especially broccoli, kale, brussels sprouts, turnips, and cabbage. A variety of isothiocyanates exist, all of which hold different valuable applications in the body, industry, and medicine. Phenethyl and benzyl isothiocyanate, for instance, show promise for preventing certain enzymes from activating carcinogen precursors (leading to cancer). Horseradish, wasabi, and mustard owe their distinctive tastes to allyl isothiocyanate, which is isolated for use as a flavor additive in the form of volatile oil of mustard. One of the glucosinolates in broccoli is glucoraphanin, which is a precursor of the isothiocyanate sulforaphane.

In the intact plant cell, myrosinase and glucosinates are physically separate. When an insect chews on the plant and breaks the cell wall, myrosinase then transforms the glucosinates into isothiocyanates, which repel the insect. Cooking inactivates myrosinase; bacteria in the human digestive tract also have myrosinase and thus make can isothiocyanates available to the human host. Raw cruciferous vegetables provide the highest concentration of isothiocyanates, but cooked cruciferous vegetables still offer significant amounts of this helpful chemical family. The method of cooking cruciferous vegetables—particularly boiling them or microwaving them on high heat—can decrease the availability of isothiocyanates. Some dietary supplements contain cruciferous vegetable extracts, however the isothiocyanates ingested through this medium might not be in a form that is readily available to the body.

Research in animal models has shown that cancers of many digestive organs, the lungs, and mammary glands are reduced by isothiocyanates, with implications for positive effects in humans as well. Isothiocyanates are thought to act by suppressing tumors and helping to rid the body of potential cancer-causing agents by activating anticarcinogenic enzymes (Zhang, 2012). Isothiocyanates might help support normal cell cycles by controlling inflammation, which appears to inhibit appropriate cell death (apoptosis). To avoid replicating harmful mutations, isothiocyanates also can halt cell division temporarily if DNA is damaged to allow time for repair (Higdon, 2005). Several studies in humans have found an association between consumption of cruciferous vegetables and reduced cancer rates, but few studies have examined whether this effect is attributable to isothiocyanates or other variables. One interesting prospective study in Chinese men measured urinary isothiocyanates, and then followed the men for 10 years. The men with detectable levels of isothiocyanates at the beginning of the study had significantly lower rates of lung cancer than subjects with undetectable levels (London et al., 2000).

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See Also: Cancer and nutrition; Phytochemicals.

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Ketosis and Ketogenic Diets

Ketosis refers to a metabolic state in which the body is producing greater than normal levels of compounds called "ketones." A ketogenic diet is a very low-carbohydrate diet designed to stimulate the body to burn increased amounts of ketones for energy. The body increases its manufacture of ketones when its supply of carbohydrate is low. Many people regard ketosis as a potentially dangerous state, because when ketone levels are very high—as can occur with untreated or poorly controlled type 1 diabetes—a state known as "diabetic ketoacidosis" results and the blood becomes very acidic. Diabetic ketoacidosis can result in dehydration, nausea, vomiting, and, in extreme cases, even coma and death.

A ketogenic diet that is properly monitored and controlled, however, was shown to be helpful in the treatment of epilepsy in young children. A ketogenic diet also could be helpful in the treatment of several other disorders, although it is possible that a low-carbohydrate diet, without the production of excess ketones, might be beneficial for some of these disorders as well. A ketogenic diet has been promoted as a way to lose weight, but the weight-loss benefits of such diets usually are short-lived, and ketogenic diets potentially can have negative side effects, especially if the diet is followed for an extended period.

Conditions under which ketosis most commonly is observed include those associated with very low blood glucose levels and glycogen depletion. (Glycogen is the molecule the body produces to store carbohydrates, primarily in the liver and in skeletal muscles.) These conditions include starvation, fasting, and adherence to a very low-carbohydrate (ketogenic) diet, as well as with type 1 diabetes, as described above.

The human body is able to generate energy molecules (ATP) from carbohydrates, fats, proteins, and alcohol. When the body metabolizes fats for fuel, it breaks down triglycerides into a glycerol unit and three fatty acid chains. Through a process known as "beta oxidation," the fatty acid chains are broken down into two-carbon units that can enter the Kreb's cycle (citric acid cycle) as acetyl coenzyme A (acetyl CoA). Acetyl CoA enters the Kreb's cycle by binding with an intermediary called "oxaloacetate." When carbohydrate levels become too low, the body uses oxaloacetate to make glucose, oxaloacetate levels drop, and acetyl CoA is unable to enter the Krebs cycle. When levels of acetyl CoA rise, the body produces ketones, including acetoacetate, acetone, and beta-hydroxybutyrate (the latter technically is not a true ketone, as the carbonyl group has been reduced).

Ketones can be used to produce ATP in many types of cells, including cells in the brain, liver, and kidney. As the body becomes accustomed to ketosis, its ability to use ketones for energy improves.

Applications

Ketogenic diets have been used with significant success in young children (usually younger than age 10) who have epilepsy. Epilepsy is marked by seizures of varying severity, which are thought to be caused by sudden electric activity in certain areas of the brain. Ketogenic diets usually are medically administered and supervised, because these diets can be difficult to follow and can have negative consequences, especially in young children. The diet often is worth a try, however, as about a third of the children who follow the diet become seizure-free or almost seizure-free, with another third experiencing at least significant improvement (Epilepsy Foundation, n.d.). Researchers do not yet understand how the diet influences brain activity. Researchers theorize that ketosis can lead to changes in neurotransmitter activity in the brain (Paoli, Rubini, Volek, & Grimaldi, 2013) (neurotransmitters are the chemicals that enable nerve cells to communicate with one another).

Ketogenic diets also have demonstrated beneficial effects on blood lipid levels, especially in people with type 2 diabetes, in which the body's cells do not respond strongly enough to insulin, a condition known as insulin resistance. In other words, while insulin is present in the bloodstream the cells do not bind with the insulin, and thus do not allow glucose to enter as readily as normal cells. People with type 2 diabetes often have abnormally high levels of blood triglycerides and LDL cholesterol, and levels of HDL cholesterol that are too low. A ketogenic diet can improve these numbers, probably by reducing levels of insulin, as insulin stimulates the liver to produce more cholesterol and triglycerides.

Preliminary research also suggests that a ketogenic diet could be beneficial as part of a treatment plan for acne (Paoli, Rubini, Volek, & Grimaldi, 2013). A high-glycemic-load diet appears to stimulate acne development; thus, a ketogenic diet could have the opposite effect, although more research is needed to clarify the exact biological mechanisms through which these effects occur. Polycystic ovary syndrome is an endocrine disorder characterized by abnormal sex hormone levels and ovarian dysfunction. It shares many symptoms with type 2 diabetes, including obesity and insulin resistance. A ketogenic diet could help to improve blood lipid levels and insulin sensitivity for women with this disorder.

Animal studies have suggested that a ketogenic diet could help to reduce the size of certain types of cancer tumors. Theoretically, this could be due to the fact that some cancer cells are less able to use ketones (as opposed to glucose) for fuel. No studies have yet confirmed that ketogenic diets are helpful for people with cancer, although a few case studies suggest further research in this area is warranted. Ketogenic diets have shown similar promise for neurological diseases such as Alzheimer's disease and Parkinson's disease.

It should be noted that, in some cases, the benefits of a ketogenic diet might be due simply to its low carbohydrate content rather than to the presence of ketones

per se. Future research on the benefits of ketogenic diets should compare ketogenic diets to other types of low-carbohydrate diets that are not low enough in carbohydrate to induce ketosis.

Negative Effects

Ketogenic diets are extremely difficult to follow, as they generally allow fewer than 50 grams of carbohydrate per day, and this is not how most people eat. Most nutrition guidelines recommend at least 130 grams of carbohydrate per day for adults, to avoid the symptoms of low blood sugar, such as dizziness, nausea, confusion, and fatigue. Most adults consume at least 250 grams of carbohydrate per day. For example, 15 grams of carbohydrate are found in a small piece of fruit, a slice of bread, or 1/3 cup of rice (American Diabetes Association, 2014).

Ketogenic diets limit consumption of fruits and vegetables. A high intake of fruits and vegetables generally is associated with many positive health benefits, therefore nutritionists are concerned that a very low-carbohydrate diet could lack healthful phytochemicals (plant components). People must take a multivitamin and mineral supplement when following a ketogenic diet, because the diet lacks many nutrients. A low intake of plant foods means that people on the diet have a low fiber intake, and constipation is a common side effect. The long-term safety of a ketogenic diet is unknown, as most people only follow the diet for a few months or years.

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See Also: Blood sugar regulation; Diabetes, type 1; Insulin; Triglycerides.

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The Kidneys

The two bean-shaped kidneys are the functional core of the urinary system. They rid the body of many waste products, maintain a healthy water and chemical balance, oversee the composition of electrolytes, regulate blood pressure, and secrete several important hormones. Good nutrition—and special diets for people with different types of kidney disorders—is essential for kidney function and good health. Enough water intake, or hydration, is especially important for kidneys, although excessive fluid intake also can be a problem for kidney function.

The kidneys are located on either side of the spine toward the back, just underneath the rib cage. The right kidney is slightly lower than the left to make room for the liver. In an average adult, each kidney measures about 5 inches long, 3 inches wide, and 1 inch thick, and weighs about 5 ounces. Three layers of tissue encase and protect each kidney. The renal (another word for kidney) capsule, a smooth fibrous membrane, forms the innermost layer. It is surrounded by the adipose capsule, a layer of fatty tissue. The outermost layer, the renal fascia, is composed of connective tissue that holds the kidney to the abdominal wall.

The outer portion of the kidney is called the cortex. In the center of the kidney is the medulla, which contains 10 to 15 cone-shaped collecting ducts called "renal pyramids." The renal pyramids drain urine into cup-shaped receptacles called "minor calyces." From here, the urine flows into larger openings called "major calyces," through the funnel-shaped renal pelvis, and on to the ureter and bladder. The kidneys have three main functions, homeostasis, waste removal, and hormone secretion.

Functions

Homeostasis

The primary function of the kidneys is homeostasis—maintaining a balance of fluids within the body. The body takes in about 2.5 quarts (2,500 millimeters) of water every day through food and beverages. What goes in must equal what goes out, and the body has several routes by which fluid can exit the body—the kidneys (urine), skin (perspiration), lungs (breath), and intestines (feces). When a malfunction in the water-removal process occurs, the body becomes overly saturated or parched. Too much water in the blood can force the heart to work harder and dilute essential chemicals in the system. Dehydration, or too little water, can lead to low blood pressure or shock and is potentially fatal. The kidneys help to balance the fluid in the body by reabsorbing liquid into the bloodstream when levels get too low, or by eliminating excess fluids when levels rise too high. These processes are overseen by the hypothalamus, the part of the brain that also regulates metabolism, body temperature, blood pressure, and hormone secretion.

Waste Removal

As food moves through the stomach and intestines, digestive enzymes break the nutrients into smaller particles to be used by the body. This breakdown process

releases several toxic waste products into the bloodstream, urea, uric acid, ketone bodies, and creatinine.

- Urea is formed when amino acids derived from protein metabolism are broken down in the liver, in which the by-product ammonia is formed. Ammonia is too poisonous for the body to process, so the liver converts it into the less-toxic urea for removal.
- Uric acid is formed by the breakdown of purines (components of foods) in the tissues.
- Ketone bodies are produced by the breakdown of excess fatty acids in the liver.
- Creatinine is a by-product of muscle metabolism.

If any of these wastes are allowed to build up in the blood, they eventually poison the blood and cells. The kidneys filter out dissolved wastes from the bloodstream to form urine, which eventually is excreted from the body.

Hormone Secretion

The kidneys either secrete or activate three essential hormones: erythropoietin, which stimulates the production of red blood cells in bone marrow; calcitriol, which promotes bone growth by increasing the levels of calcium and phosphorous in the blood; and aldosterone, which regulates blood pressure and sodium balance by increasing the filtration of blood in the kidneys, increasing water reabsorption, and decreasing the amount of sodium that is lost. The kidneys do not actually produce aldosterone, but they do control its production by secreting renin, an enzyme that converts a protein in the blood called "angiotensin."

Kidney Diseases

Kidney diseases can include cancer, kidney infections, cysts of the kidney, kidney stones, and chronic kidney disease, and is any condition that causes reduced kidney function over time. Kidney failure is diagnosed through the use of blood and urine tests, kidney ultrasounds (a type of diagnostic imaging), and the monitoring of urine output. Kidney function could return after treatment of the illness that caused the failure. Medications can be used to control blood levels of potassium and calcium and to reduce high blood pressure. Diets with limited proteins and low-potassium foods can reduce toxins in the blood. Monitoring intake of fluids and salt might be recommended (Mayo Clinic Staff, 2012a).

Diabetes and high blood pressure are the two leading causes of chronic kidney disease in the United States. A person's eating habits can increase or decrease diabetes and blood pressure risks. Diabetes is the most common cause of kidney failure, accounting for nearly 44% of new cases (United States Renal Data System, 2007). Even when diabetes is controlled, the disease can lead to chronic kidney disease and kidney failure. Most people with diabetes, however, do not progress to kidney failure. Nevertheless, nearly 24 million people in the United States have diabetes (National Institute of Diabetes and Digestive and Kidney Diseases, 2008)

and nearly 180,000 people are living with kidney failure as a result of diabetes (United States Renal Data System, 2007).

African-Americans are especially at risk of developing kidney disease. The National Kidney Foundation (2014) lists the following important findings.

- African-Americans suffer from kidney failure at a significantly higher rate than Caucasians—more than three times greater.
- African-Americans constitute more than 32% of all patients in the United States receiving dialysis for kidney failure, but only represent approximately 13% of the overall U.S. population.
- Diabetes is the leading cause of kidney failure in African-Americans. African-Americans are twice as likely to be diagnosed with diabetes as Caucasians. Approximately 4.9 million African-Americans who are 20 years of age and older are living with either diagnosed or undiagnosed diabetes.

African-Americans might be more susceptible to kidney diseases, including diabetes, due to such factors as unhealthy diet including much fat and sodium; low income leading to lack of affordable, good food choices; stress; lack of medical care; obesity; and lack of exercise.

Kidney failure that poses a severe health threat could require dialysis. Dialysis is a procedure in which machines act as artificial kidneys and filter wastes and excess fluids from the blood. Blood is passed through the dialysis machine and returned to the body. Another form of treatment for renal failure is a kidney transplant, in which a kidney from a matched donor is surgically placed into the body of the person with kidney disease. Transplanted kidneys can come from live donors, who have one kidney surgically removed to be donated, or from deceased donors. Kidney donors usually function well with their remaining healthy kidney.

Diabetes and Nutrition

Controlling blood glucose, also called "blood sugar," and blood pressure through healthy food choices are crucial steps toward slowing or stopping the progression of diabetes. People with either type 1 or type 2 diabetes must choose foods carefully to control their blood glucose, the body's main source of energy. Following a meal plan to keep blood glucose at a healthy level could prevent chronic kidney disease from developing.

People with diabetes must learn from a health care professional how often to check their blood glucose level. The results from these blood glucose checks indicate whether a person's meal plan is helping to keep diabetes under control. According to the National Kidney and Urologic Diseases Information Clearinghouse (2014), following daily habits can help maintain healthy blood glucose levels. Such habits include the following.

- Eating about the same amount of food each day.
- Eating meals and snacks at about the same times each day.
- Not skipping meals or snacks.

- Taking medicines at the same times each day.
- Participating in physical activity every day.

Chronic Kidney Disease, High Blood Pressure, and Nutrition

As blood pressure rises, the risk of damage to the arteries, heart, brain, and kidneys increases. Controlling blood pressure through good food and regular physical activity can delay or prevent the development of chronic kidney disease.

Normal blood pressure is 120/80 millimeters of mercury (mmHg). According to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDKD), people with chronic kidney disease should try to keep their blood pressure below 140/90 mmHg. The National Kidney and Urologic Diseases Information Clearinghouse from the NIDDKD also describes the Dietary Approaches to Stop Hypertension (DASH) diet, which controls helps to control high blood pressure.

The National Heart, Lung, and Blood Institute has supported research that compared a typical American diet with the Dietary Approaches to Stop Hypertension (DASH) eating plan. The DASH diet is lower in saturated fat, cholesterol, and total fat, and emphasizes eating fruits, vegetables, and low-fat dairy foods. People who followed the DASH eating plan were able to reduce their blood pressure more than those who ate a typical diet. The DASH eating plan also includes whole-grain products, fish, poultry, and nuts. Limiting sodium (salt) is another important feature of the plan. A dietitian can help find low-salt or salt-free alternatives to foods that are high in salt (National Kidney and Urologic Diseases Information Clearinghouse, 2014).

If chronic kidney disease worsens, then doctors might also recommend limiting potassium, phosphorus, and fluids (American Kidney Fund, 2014).

Potassium

A mineral that is essential to many functions of the human body, including the kidneys, potassium might have to be reduced due to certain types of kidney disease. Lower-potassium foods include fruits such as apples, cranberries, grapes, pineapples and strawberries; vegetables including cauliflower, onions, peppers, radishes, summer squash, and zucchini squash, lettuce; breads made from refined flour rather than whole grains; white rice; and beef and chicken.

Phosphorus

A mineral that works with calcium and vitamin D to promote healthy bones, phosphorus might not be controlled correctly if the kidneys are not maintaining the right balance of phosphorus in the body. If the kidneys are not working properly, phosphorus can build up in the blood, leading to weakening of the bones. Low-phosphorous foods include Italian, French, or sourdough bread; corn or rice cereals and cream of wheat; unsalted popcorn; some light-colored soft drinks and lemonade (instead of dark soft drinks, especially colas).

Fluids

People with kidney disease might not need as much water as people with normal kidney function, because the unhealthy kidneys cannot remove extra fluid in the body as well as normal kidneys do. Too much fluid can cause high blood pressure, swelling, and heart failure. Extra fluid also can build up around the lungs, making it difficult to breathe. Some doctors recommend that people with kidney disease limit protein or change their source of protein. This is because a diet very high in protein can make the kidneys work harder and could cause more damage.

Kidney Stones

Some people develop kidney stones, which are small, hard deposits that form inside the kidneys and are made of mineral and acid salts. Kidney stones have a number of causes and can affect any part of the urinary tract, from the kidneys to the bladder. They can cause extreme pain when moving through the urinary system (Mayo Clinic Staff, 2012b). Nutritional remedies depend on the type of kidney stone a person has. If the kidney stones are calcium oxalate, which are the most common, a doctor will recommend a low-oxalate diet. This diet includes fewer high-oxalate foods such as spinach, nuts, tea, and chocolate. Other types of kidney stones are calcium phosphate stones and uric acid stones. All people with kidney stones are recommended to limit animal protein. Foods including legumes, which can provide protein, are recommended. Legumes are a class of vegetables that include peas, beans, and lentils. Other legumes include red beans, black beans, chickpeas, black-eyed peas, edamame, kidney beans, lima beans, and fava beans.

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See Also: Diabetes, type 1; Diabetes, type 2; Hypertension and nutrition; Phosphorus; Potassium; Sodium and salt.

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Lactation

Lactation refers to the processes of making and secreting milk. Human milk contains an excellent balance of nutrients and other compounds, and usually is the best choice of nourishment for infants. Human milk also complements the feeding of solid foods for young children. Milk production is energetically demanding. A woman who is lactating must consume extra calories to support milk-production processes, as well as all of the nutrients that go into the milk. During breast-feeding, good nutrition is essential to support a woman's health and milk production.

Anatomy and Physiology of Lactation

The breasts are the site of milk production. Externally, the breast contains the areola (darkened skin around the nipple), nipple, and Montgomery's tubercles, small bumps on the skin of the areola that produce oily secretions to lubricate and protect the skin of the nipple. Internally, the breast contains fat cells, connective tissue, lactiferous ducts which control milk movement of milk through the breast, and alveoli (the sites that create milk). Alveoli are made of lactocytes, the cells that create milk, and myoepithelial cells that act as smooth muscle to contract the milk through the lactiferous ducts and eject it out of the nipple. As the body prepares for breast-feeding, the areola darkens. The hormone prolactin, secreted by the pituitary gland, controls the movement, synthesis, and amount of milk produced in the breasts. The infant's suckling triggers nerves in the breast and stimulates oxytocin release by the pituitary gland into the bloodstream, causing the "let-down reflex," or descending of milk down the breast. Oxytocin also expands the diameter of the milk ducts to increase milk flow to the infant (Pollard, 2011).

Colostrum is a yellow substance present in the breast during the first days after delivery (typically during the first four days, though this can vary). Colostrum has a different chemical composition than mature breast milk. It is full of live cultures, healthy bacteria, immune cells, growth factors, minerals, and whey proteins that coat the infant's gut to prepare it for digestion. Carbohydrate, fat, and vitamin contents are low in colostrum. Synthetically produced colostrum does not contain the essential immunoglobulins, or antibodies, that are present in human milk.

Lactogenesis is the process by which milk is produced and involves two stages. During stage 1, milk ducts expand and prepare for milk production. During stage

2, the nipple secretes colostrum, transitional milk, and mature milk (Riordan, 2005).

Breast-Feeding Nutrition

During breast-feeding, women depend on good nutrition to fortify their breast milk and support their own health. Needs for many nutrients are higher for lactating women than for non-lactating and nonpregnant women of the same age (*see* Table 1). Some of the most important nutrients supporting lactation include those listed below.

- Water: The recommended water intake during lactation is approximately 2 liters (about 8 cups) per day. This amount can be composed of water and other fluids, including milk. Nutrient-dense fluids and water are preferred to empty-calories beverages such as soft drinks. During each infant feeding, 8 ounces of water (or other fluids) should be consumed to ensure the mother's hydration.
- Energy: The energy to support lactation comes partly from the diet and partly from the metabolism of the mother's fat stores. In general, breast-feeding women need to consume at least 1,800 kcal per day (Insel, Ross, McMahon, & Bernstein, 2014). This level will be too low, however, for many women. The exact calorie recommendation varies with the mother's size and activity level.
- Protein: Lactating women should consume an extra 25 grams of protein per day over prepregnancy needs, or about 1.3 g/kg per day.
- Calcium: A significant amount of calcium goes into breast milk. The calcium is taken from the bloodstream. If dietary intake of calcium is not adequate to maintain necessary blood calcium levels, then the mineral is drawn from the mother's bones. (This is true for women in both lactating and non-lactating states.) It therefore is imperative that lactating women ingest adequate calcium. The DRI for calcium is no higher for lactating women than for non-lactating women (1,000 mg/day), (except for lactating women 18 years old and younger, who are recommended to consume 1,300 mg per day). Lactating women usually lose up to 3% to 5% of their bone mass, although this usually is recovered within the first year following weaning (NIH, 2012). Adolescent mothers and mothers older than age 40 can have a higher risk of osteoporosis or bone loss after breast-feeding. Women at risk for osteoporosis might want to consume somewhat more calcium than recommended, and consult their health care providers regarding possible supplementation for the prevention of osteoporosis.
- Vitamin D: Vitamin D is required for the proper utilization of calcium and other minerals, for both mother and infant. The vitamin D level in breast milk reflects the mother's vitamin D status, which often is low in North Americans.
- Other vitamins and minerals: The need for many vitamins and minerals is slightly greater for women during lactation, but few are problematic in well-fed women. Interestingly, the recommendation for iron is somewhat lower during lactation, as many women do not experience menstrual blood loss during the first few months of lactation.

Table 1. Dietary Reference Intake Recommendations for Lactating and Non-Lactating Women, Ages 19 to 30 Years.

Nutrient	**Lactating**	**Non-Lactating**
Carbohydrate (g)	210	130
Protein (g)	71	46
Fiber (g)	29	25
Fat	Not determinable	Not determinable
Linoleic Acid (g)	13	12
Vitamin A (µg)	1300	700
Vitamin D (IU)	600	600
Vitamin E (mg)	19	15
Vitamin K (µg)	90	90
Thiamin (mg)	1.4	1.1
Riboflavin (mg)	1.6	1.1
Niacin (mg)	17	14
Pantothenic Acid (mg)	7	5
Biotin (µg)	35	30
Vitamin B6 (mg)	2	1.3
Folate (µg)	500	400
Vitamin B12 (µg)	2.8	2.4
Vitamin C (mg)	120	75
Choline (mg)	550	425
Sodium (g)	1.5	1.5
Potassium (g)	5.1	4.7
Chloride (g)	2.3	2.3
Calcium (mg)	1,000	1,000
Phosphorus (mg)	700	700
Magnesium (mg)	310	310
Iron (mg)	9	18
Zinc (mg)	12	8
Selenium (µg)	70	55
Iodine (µg)	290	150
Copper (µg)	1,300	900
Manganese (mg)	2.6	1.8
Fluoride (mg)	3	3
Chromium (µg)	45	25
Molybdenum (µg)	50	45
Water (L)	3.8	2.7

Additional Nutrition Issues

- Caffeine: Suggested caffeine intake is no more than 1 to 2 cups of a caffeinated beverage per day. If ingested in greater amounts, caffeine can cause discomfort for the infant, apparent through fussiness, irritability, crankiness, or symptoms of colic (episodes of crying in otherwise healthy infants, commonly attributed to gastrointestinal symptoms). Other baby behaviors that can result from a mother's caffeine intake include jitters or wakefulness. Caffeine also might worsen an infant's sleep quality (NIH, 2012).
- Alcohol: Women should avoid breast-feeding for 2 to 3 hours after alcohol consumption when the alcohol content in the breast milk is highest. Alcohol is not considered safe for infants (Mayo Clinic Staff, 2012).
- Dietary supplements: Other than the recommended daily prenatal or multivitamin and multi-mineral supplements, most dietary supplements have not been tested in lactating mothers.
- Vegetarian diet during lactation: Breast-feeding vegetarians, especially vegans, must consume foods rich in calcium, protein, vitamins B12, vitamin D, and iron, all the nutrients which are likely to be low on such diets.
- Toxic substances: Breast-feeding women should limit consumption of large fish, as these contain higher than recommended levels of mercury which has neurotoxic effects, especially in infants and children.

Infant Allergic Reactions, Colic, and Fussiness

If an infant experiences allergy symptoms, such as a rash or congestion, soon after feeding, then it is possible that the baby is allergic to a substance in breast milk (Mayo Clinic Staff, 2012). In such cases, breast-feeding women should work with their health care providers to monitor their consumption of common allergens, such as wheat, eggs, fish, soy, cow's milk, peanuts, or tree nuts to see if there is link between the infant's symptoms and the mother's foods. If an infant suffers from colic, then the mother might wish to keep a food diary to see if any foods are associated with the fussy behavior. Although vegetables from the cabbage family, such as broccoli, kale, and cauliflower, often are blamed for infant fussiness, evidence to support this notion is lacking (Mayo Clinic Staff, 2012). Women often find that reducing caffeine consumption reduces baby fussiness as well.

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See Also: Breast-feeding; Colostrum; Mercury; Osteoporosis; Pregnancy and nutrition.

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Lactose Intolerance

Lactose intolerance is the inability to digest lactose—the sugar found in milk—due to a deficiency in the enzyme lactase-phlorizin hydrolase, also known as "lactase." Lactose intolerance, also known as "lactase deficiency" or "hypolactasia," can result in symptoms such as gas, bloating, and diarrhea. With inadequate levels of lactase, lactose (a disaccharide) cannot be broken down into its component monosaccharides, glucose and galactose, in the digestive system. The undigested lactose then passes into the colon. Fermentation takes place as bacteria in the colon metabolize the lactose.

Types

There are three classifications of lactase deficiency. "Primary lactase deficiency" is genetic and is the most common cause of lactose intolerance. Primary lactase deficiency is caused by deficient levels of the enzyme lactase in the lining of the duodenum of the small intestine. Although lactase levels naturally decrease after weaning, levels sometimes decrease enough to elicit symptoms of lactose intolerance (Lomer, Parkes, & Sanderson, 2008). Lactase levels often decline when the diet changes to include more variety and becomes less dependent on milk. Many people produce some lactase, but not enough to avoid symptoms following milk consumption. Primary lactase deficiency usually manifests by the time a person 20 years old.

"Secondary lactase deficiency" can be caused by trauma to the small intestine that causes damage to the intestinal mucosa, or by medical conditions including Crohns disease, ulcerative colitis, chemotherapy, celiac disease, and gastroenteritis. Secondary lactase deficiency can be temporary. If the deficiency is caused by a chronic illness, however, then the lactose intolerance is likely to be long term.

"Congenital lactase deficiency" is an autosomal recessive genetic disorder that limits the digestion of milk from birth. In this case, the small intestine never produces any lactase. This is a very rare disorder.

Symptoms of Lactose Intolerance

The symptoms of lactose intolerance vary in severity among individuals and among types of lactase deficiency. Symptoms usually appear within 30 minutes to 2 hours of ingestion of lactose. The severity of the symptoms depends on the amount of lactose ingested and the degree of lactase deficiency. Symptoms include the following.

- Abdominal cramps and bloating—The digestion of lactose by bacteria in the colon creates short-chain fatty acids, hydrogen, methane, and carbon dioxide as by-products, resulting in an increase in bloating and intracolonic pressure (Lomer, Parkes, & Sanderson, 2008).
- Diarrhea—Undigested lactose in the colon results in a high osmotic (nonabsorbable) load, and acidification of the colonic contents. This causes an increase in secretions of electrolytes and fluid into the colon, as well as a faster transit time, resulting in frequent and watery stools (Lomer, Parkes, & Sanderson, 2008).
- Flatulence—Bacterial fermentation that takes place in the colon produces large amounts of gas as a by-product that results in flatulence.

In some cases, constipation as a result of methane production can occur, as well as nausea and vomiting. For infants with congenital lactase deficiency, the diarrhea can be fatal. Due to their inability to produce lactase, these infants are unable to consume breast milk for adequate nutrition and must be given lactose-free formula.

Diagnostic Testing

Once symptoms of lactose intolerance have been detected, a lactase deficiency can be diagnosed using several methods.

Hydrogen Breath Test

Patients are asked to ingest a lactose-containing beverage. Every 15 minutes, for 2 hours, a sample of the patient's breath is taken. A by-product of the lactose fermentation occurring in the digestive system is hydrogen, which is detectable in the breath samples.

Stool Acidity Test

When lactose goes undigested it passes into the colon. Fermentation caused by bacteria in the colon produces fatty acids which can be detected in the stool. This test usually is reserved for infants and young children (NIDDK, 2012).

Blood Test

Normally, when lactose is ingested it is broken down and blood glucose levels increase. To test a patient's glucose levels, a blood sample is drawn following a

fasting period. A lactose solution then is given to a patient. Blood is drawn again at varying intervals. If blood glucose levels do not increase following lactose ingestion, then the lactose has not been digested, indicating lactose intolerance.

Risks and Prevalence

Lactose levels naturally decrease after weaning. Babies born prematurely are more likely to develop lactose intolerance than are babies born at full term. Women sometimes develop lactose intolerance during pregnancy. In the case of secondary lactose intolerance, bowel surgeries and intestinal diseases can initiate symptoms.

Rates of lactose intolerance are highly variable with ethnicity (Insel, Ross, McMahon, & Bernstein, 2014). Rates of lactose intolerance are lowest in people of Northern European descent. Only about 12% of Caucasian North Americans are lactose intolerant. The rate of lactose intolerance is about 95% in African-Americans, and ranges from 20% to more than 90% in African populations. Chinese populations are more than 80% lactose intolerant. In some Asian countries, such as Thailand, lactose intolerance rates are as high as 98%.

Management and Treatment

Lactose intolerance typically is not life threatening and requires only dietary management. The amount of lactose that can be tolerated varies from individual to individual. Some individuals with mild lactose intolerance can drink small amounts of milk and have no symptoms. Others can consume yogurt and cheese, but not milk. Lactase pills and drops, taken prior to lactose consumption, also are available and are helpful to some people. People with severe symptoms might find that avoiding lactose-containing products is best. There is lactose in dairy products and dairy-containing foods. When treating lactose intolerance with dietary avoidance, consulting food labels is critical. For a person who is lactose intolerant, the most reliable way to obtain the nutrients in dairy is to select lactose-free milk products or fortified foods and beverages.

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See Also: Digestion and the digestive system.

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Large Intestine

The large intestine is the last section of the gastrointestinal tract, and it plays a vital role in the absorption of water and sodium before food finally is eliminated as waste. "Colon" and "large intestine" often are used interchangeably, but the large intestine actually consists of the cecum, the colon, and the rectum. The colon itself is made up of the ascending colon, the transverse colon, the descending colon, and the sigmoid colon. The remains of the digestive mass (which once was food) pass into the cecum from the small intestine. This matter moves through the colon, is stored in the rectum, and is excreted through the anus.

The four sections of the colon are named for their shape and orientation. Waste moving through the ascending colon travels upward on the right side of the abdomen, then across through the transverse colon, downward through the descending colon on the left side of the abdomen, and finally through the curved, C-shaped sigmoid colon, after which it moves into the rectum. The end of the large intestine and the gastrointestinal tract is the anus.

The colon, or large intestine, has a diameter of about 6.5 cm, and its width is the source of its name. It is only about 1.5 meters long, which is small in comparison to the 3-meter-long small intestine. The small intestine is connected to the ascending colon by the cecum, and the boundary between the small intestine and the cecum is the ileocecal valve. Watery digestive matter passes through the valve from the small intestine. The ileocecal valve closes after material enters the cecum, to prevent the backflow of material into the small intestine.

The colon does not produce digestive enzymes, but it is lined with mucous-secreting cells. These cells lubricate the colon with mucous that protects the internal lining from acids produced by fermenting bacteria. The inside of the colon is mostly smooth, and has a smaller surface area than the small intestine. The large intestine absorbs water, vitamin K, and some electrolytes (especially sodium, chloride, and potassium) from the digestive mass through diffusion (both passive and facilitated diffusion depending on the product). These processes turn waste from a liquid into a semisolid called stool (or feces), which consists of 60% solid material and 40% water. Waste products include undigested food, older cells from the gastrointestinal tract, and bacteria.

The colon has three bands of smooth muscle, called taeniae coli, which move material through the large intestine. The three bands are known individually as the mesocolic, free, and omental coli. The taeniae coli run throughout the outside of the large intestine, and they cause the outside of the colon to appear as if it is covered in small pouches. The pouches are called haustra, and contractions of the taeniae coli can cause them to change position slightly. Haustral contractions occur

a few times every hour in regional spots on the colon, causing the liquid to move back and forth between the haustra and aiding in the slow absorption of water and electrolytes.

Several times a day, the ascending and transverse colon contract together, which moves the stool into the descending colon. From there the stool passes to the sigmoid colon and then into the rectum. The synchronized contractions and passing of the fecal matter from one region to another is called a mass movement, and these typically occur after meals.

Contractions also can be triggered by the gastrocolonic reflex, causing food to move from the small intestine to the large intestine, and from the colon to the

Hemorrhoids

Hemorrhoids, or "piles," are swollen and often painful veins in the lower anus or rectum. They are a common condition, occurring in nearly 50% of adults in the United States at some point in their lives. The condition usually can be treated with over-the-counter corticosteroid creams (to reduce inflammation and itching) and stool softeners (to reduce constipation), and through dietary adjustments. Hemorrhoid symptoms include itching and pain in the area, especially when sitting and during bowel movements; blood in the stool; and tender lumps near the anus. Constipation and subsequent straining during bowel movements are the greatest risk factor for hemorrhoids. Any other state in which extreme pressure is placed on anorectal veins also can cause hemorrhoids, such as pregnancy, childbirth, and performing sudden heavy lifting. Some evidence suggests that obesity and a sedentary lifestyle can increase risk for the development of hemorrhoids. The Goligher classification system is a universal scale used to grade severity of hemorrhoids; first-degree as internal hemorrhoids and bleeding only, and fourth-degree is fully prolapsed, or external, hemorrhoids that are hanging outside of the anus.

Good hydration (getting enough water) and a high-fiber diet that includes fruits, vegetables, and whole grains help to prevent hemorrhoids by preventing constipation. Foods such as peppers, coffee, and alcohol might contribute to irritation of existing hemorrhoids, but evidence is not conclusive. Moderate exercise is beneficial for reducing constipation, promoting blood circulation, and relieving discomfort; however heavy exercise has the potential to aggravate hemorrhoids and increase bleeding. A variety of surgical and nonsurgical interventions exist for hemorrhoids that cannot be managed with mild treatment. Rubber band ligation is a frequently used outpatient method that involves tying off the hemorrhoid and cutting off its blood supply so that it detaches after two to seven days. A hemorrhoidectomy—sealing blood flow and cutting the hemorrhoid out—is the most common surgical treatment and provides least chance of reoccurrence, although a greater chance for complications exists with operative measures (Lohsiriwat, 2012).

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rectum. The rectum is about 15 cm long, and it stores the waste until the body is ready for defecation. The defecation reflex is the final step in eliminating waste, and it begins with the simultaneous contraction of the sigmoid colon and the rectum, and pushes the waste toward the external anal sphincter. About 500 ml (15 fl. oz.) of liquid enters the large intestine. Only about 350 ml (10.5 fl. oz.) are absorbed and the rest exits as waste. Control of the anal sphincter is voluntary in most healthy individuals. When people perceive the urge and decide to defecate, a bowel movement occurs and stools are expelled through the anal sphincter. In a healthy individual, bowel movements usually occur once or twice per day.

Billions of bacteria and other microbes coat the intestinal walls of the colon. Most of these bacteria perform useful functions, such as synthesizing vitamins such as biotin and vitamin K (it is unknown how much biotin actually is absorbed and used by the body), processing waste products and food particles, and protecting against harmful bacteria. There are more than 400 different bacterial species in the colon, many of which are responsible for the breakdown of fecal matter. Populations of bacterial flora change not only along the length of the colon, but also cross-sectionally with regard to the mucosal surface. The large intestine generally contains some pathogenic bacteria, such as *Clostridium difficile*, however populations of these bacteria tend to be generally small. Overpopulation by pathogenic bacteria—such as *Vibrio cholerae* and toxic *Escherichia coli* strains, which colonize the upper bowel—can cause watery diarrhea. These bacteria produce an enterotoxin (a protein that is frequently cytotoxic) that stimulates mucosal cells to secrete fluid. Invasive bacteria such as *Shigella* and *Campylobacter*, which penetrate the intestinal mucosa, can cause diarrhea and a bloody, mucoid diarrheal stool.

Diarrhea—which is a very common condition and usually is not a grave illness—can be described as stools that are both loose and watery. Diarrhea typically lasts two to three days. Treatment for this problem includes limiting food intake to liquids or nonirritating foods (such as bananas and rice) and drinking plenty of fluids. As described above, diarrhea can be caused by a pathogenic bacterial infection; however, it also can be caused by viral and helminthic infections. Diarrhea caused by a pathogenic infection is called "secretory diarrhea," because the body is secreting water into the colon. Other types of diarrhea are "exudative diarrhea" and "osmotic diarrhea." Exudative diarrhea refers to the presence of blood in the stool, usually caused by inflammatory diseases such as Crohn's disease or ulcerative colitis. People also can develop diarrhea as part of irritable bowel syndrome, which can result from improper colon function. Osmotic diarrhea is caused by the presence of substances in the stool that draw water into the large intestine. The sugar substitute "sorbitol," for example, can have this effect on some people.

Constipation is characterized by difficulty passing stools and less frequent bowel movements. Stools can be dry and hard. Constipation is a common ailment, and can be caused by a poor diet, stress, pregnancy, depression, or not taking enough time to empty the bowels. Persistent constipation can be indicative of a more serious disease, such as colon cancer. Lifestyle change measures, including dietary changes, usually are enough to treat occasional constipation. If left

Constipation

Constipation is a condition in which a person has fewer than three bowel movements a week or has bowel movements with stools that are hard, dry, and small, making them painful or difficult to pass. People might feel bloated or have pain in the abdomen. The National Digestive Diseases Information Clearinghouse offers the following information on constipation.

Most people become constipated at some point in their lives. Constipation can be acute, which means sudden and lasting a short time; or chronic, which means lasting a long time, even years. Most constipation is acute and is not dangerous.

Causes of Constipation

Constipation is caused by stool spending too much time in the colon. Common factors or disorders that lead to constipation include diets low in fiber; lack of physical activity; medications; life changes or daily routine changes; ignoring the urge to pass a bowel movement; neurological and metabolic disorders; GI (gastrointestinal) tract problems; or functional GI disorders.

Treating Constipation

First-line treatments for constipation include changes in eating, diet, and nutrition; exercise and lifestyle changes; and laxatives. People who do not respond to these first-line treatments should talk with their health care provider about other treatments.

Eating, Diet, and Nutrition

The Academy of Nutrition and Dietetics recommends that adults consume 20 g to 35 g of fiber per day. Americans consume only 15 g per day on average. People often eat too many refined and processed foods from which the natural fiber has been removed. A health care provider can help plan a diet with the appropriate amount of fiber. Examples of good sources of fiber include navy, pinto, kidney, and other such beans; bran muffins or bran cereal; fruits such as apples, pears, raspberries, and prunes; and vegetables including squash, sweet potatoes, peas, broccoli, and cooked greens.

Drinking water and other liquids, such as fruit and vegetable juices and clear soups, could make fiber in the diet more effective in normalizing bowel function and maintaining regularity. A health care provider can give advice about how much a person should drink each day based on the person's health and activity level and where the person lives.

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untreated for a prolonged period, however, constipation can cause diverticulitis or sepsis.

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See Also: Diarrhea; Digestion and the digestive system; Diverticular disease; Foodborne illness and food safety; Inflammatory bowel disease; Irritable bowel syndrome; Microbiota and microbiome; Small intestine.

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Lead

Lead is a naturally occurring element found in rocks and soils. It has been used most commonly throughout history in the construction of pipes and paint, and later was added to gasoline for motor vehicles. Lead poses a significant risk of

Lower the Chances of Exposure to Lead

Important information from the U.S. Environmental Protection Agency (EPA) website discusses how to prevent home lead exposure. Simple steps such as keeping the home clean and well maintained go a long way in preventing lead exposure. The chances of exposure to lead in the home—now and in the future—can be reduced by taking these steps.

- Inspect and maintain all painted surfaces to prevent paint deterioration.
- Fix water damage quickly and completely.
- Keep the home clean and dust-free.
- Clean around painted areas where friction can generate dust, such as doors, windows, and drawers. Wipe these areas with a wet sponge or rag to remove paint chips or dust.
- Use only cold water to prepare food and drinks.
- Flush water outlets used for drinking or food preparation.
- Clean debris out of outlet screens or faucet aerators regularly.
- Wash children's hands, bottles, pacifiers, and toys often.
- Teach children to wipe and remove their shoes and wash their hands after playing outdoors.
- Ensure that family members eat well-balanced meals. Children with healthy diets absorb less lead. See the EPA publication *Lead and a Healthy Diet, What You Can Do to Protect Your Child.*
- If home renovation, repairs, or painting are being done, make sure contractors are "Lead-Safe Certified" and make sure they follow lead-safe work practices.
- Determine whether your family is at risk for lead poisoning by reading the EPA's *Lead Poisoning Home Checklist.*

Environmental Protection Agency. (2013). *Lower your chances of exposure to lead*. Retrieved from http://www2.epa.gov/lead/learn-about-lead#lower

poisoning for people who come in contact with it. Symptoms of lead poisoning include fatigue, nausea, headaches, muscle weakness, and seizures. Elevated blood lead levels—a marker for lead toxicity—result in permanent and irreversible problems. In children damage can include reduced IQ and increased incidence of learning disabilities and behavior problems. In adults, lead toxicity contributes to cardiovascular, kidney, and brain damage. This is because of lead's dangerous ability to mimic essential minerals, such as iron, calcium, and zinc, in the body. The body attempts to use lead instead of those nutrients for body processes. The FDA has set limits on the amount of lead allowed in emissions and in food, but research has shown more restrictions might be necessary for the safety and health of vulnerable populations.

Lead is as useful as it is dangerous. It has been used since ancient times for various purposes. Ancient Romans began using lead in 3000 BCE as material for pipes and the linings of baths. Unlike steel and copper, lead does not succumb easily to wear and rust. Lead was used for coins in ancient China. Some scholars suspect that lead poisoning and toxicity could have contributed to the downfall of the Roman Empire, because the Romans consumed lead as a food additive. Lead also leached into their foods and beverages from lead pipes, pots, and kettles. Over time, people expanded the uses of lead to include molding for windows, spices for food, and the base of many paints. Lead made a great historical appearance in the first printing press of the 1500s, which contained movable lead letter blocks. Fortunately, lead's harmful effects were quickly discovered. There is evidence found in literature as far back as the 1600s of terms such as "plumberism" or "painting madness." These are suspected euphemisms for the nerve damage caused by the widespread lead poisoning of plumbers and painters. In 1922, lead began to be added to the gasoline fuel used by motor vehicles to improve vehicle performance. In the 1970s, the United States began to enact legislation to reduce lead levels in emissions, and to ban or reduce the use of lead in products such as paint and gasoline. Lead safety standards have been improving drastically since that time, with average blood lead levels of the general population dropping from 13 mcg/dL in the 1970s to 1.12 mcg/dL in 2010 (Chen, 2013).

There are many reasons for concern about lead's presence in food. Lead has no beneficial properties and is not a nutrient. It is indestructible, and accumulates in the bones and soft tissues. Lead wreaks havoc on the body by interrupting the paths of nutrients. Lead is chemically similar to iron, calcium, and zinc in that it is a cation with two positive charges. Because of this similarity, lead is able to displace these essential nutrients from the metabolic sites they normally occupy. Lead competes with iron in the blood, but cannot carry oxygen. It competes with calcium in the brain, but cannot signal nerve cells. Fortunately, there are several other nutrients that can combat the effects of lead. For example, vitamin C and folic acid improve iron absorption and help to reduce the damage caused by lead in the blood. Children with healthful diets tend to experience fewer symptoms of lead toxicity than children who are less well fed, even at similar levels of lead exposure (EPA, 2013).

Many countries—including the United States and Canada—have enacted legislation aimed at reducing elevated blood lead levels, especially in children. Lead levels in the bloodstream rise because of lead ingestion. Lead can be ingested when people drink water that has been contaminated by lead plumbing. Inhaling or ingesting lead contained in the dust from deteriorating lead-based paint is another common source of high blood lead levels. Anything that can come in contact with soil containing lead holds a risk of poison for humans. Children age 6 and younger are at highest risk for lead poisoning, for two reasons. Children develop at a very rapid rate. If the nutrients needed for that development are being replaced with lead, then lead toxicity damage can result. Children also are at a higher risk because of their behaviors. Because children play closer to the ground and have less conception of what is dirty, they have a better chance of ingesting lead-infected soil or dust. Lead toxicity is more common in areas with higher poverty rates. Such areas generally contain greater levels of lead in soils and dust, as they tend to be located closer to highways, incinerators, and power plants. (Lead from past and previous emissions ends up in soil and dust.)

Food and beverages can acquire lead through contamination of any of the ingredients used in the manufacture of food products, the containers in which the food is prepared, or the food wrappers. Foods recently noted to contain lead are imported candies and some fruit juices.

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See Also: Arsenic; Mercury.

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Lecithin

Lecithin refers to a group of several different phospholipid compounds. Phospholipids are similar in structure to triglycerides, but with a phosphate group in place of one of the fatty acid chains. In animals and plants, lecithin is a naturally occurring phospholipid also known as "phosphatidylcholine." In this form, lecithin is a primary component of cell membranes and the myelin sheath of nerve cells. Lecithin also refers to phospholipid compounds derived primarily from egg yolk and soybeans, used widely by the food industry. Dietary lecithin supplements usually are composed of a mixture of phospholipids, mainly from soybeans. Lecithin developed primarily from plant sources also is widely used in the textile, rubber, chemical, automotive, and other industries. Lecithin is not an essential nutrient, although lecithin as phosphatidylcholine is a source of choline, an essential vitamin-like compound. Lecithin is found in many foods including egg yolk, soybeans and other legumes, seafood, liver, wheat germ, broccoli, and Brussels sprouts. There is no dietary intake requirement for lecithin and information regarding excessive lecithin intake is not available.

Lecithin was the first phospholipid to be discovered. The discovery generally is attributed to the French Chemist Theodore-Nicolas Gobley in 1846 (Sourkes, 2004). Gobley isolated an orange-colored substance from egg yolks and named it after lekithos, the ancient Greek word meaning "egg yolk." He established the complete chemical formula of phosphatidylcholine many years later.

Lecithin's emulsification properties have been utilized in home kitchens for centuries. Eggs or egg yolks often are added to recipes to enhance the mixing of unlike ingredients. The lecithin in egg yolks, for example, enables the liquid ingredients in a cookie recipe to combine with the lipid ingredients, such as butter and oils. (Water and oil do not mix well, they separate when combined.) This emulsification property combined with lecithin's ready availability in cheap sources (soybeans) has led to its widespread use in commercial food preparation. Lecithin also is a lubricant, improving food texture. Lecithin frequently is added to high-fat powdered products such as dry milk and coffee creamers; baked goods; salad dressings, sauces, and soups; and even chewing gum, to prevent gum from sticking to the teeth. As a food additive, lecithin is generally recognized as safe (GRAS) by the U.S. Food and Drug Administration. People with soy allergies usually, although not always, can consume products containing soybean-derived lecithin, because the soy proteins—the actual allergens—generally are removed during processing (Martin, 2012).

Researchers have investigated the use of lecithin supplements for a wide range of health benefits. Preliminary research suggests lecithin supplements might improve symptoms of multiple sclerosis, as lecithin is a component of the myelin sheath that is attacked in this autoimmune disorder (Weil, 2007). A couple of small studies have found that subjects with ulcerative colitis—an inflammatory bowel disorder—experienced greater symptom relief when taking 2 g to 4 g per day of lecithin supplements, as compared to a placebo condition (EBSCO, 2012). Although lecithin is widely promoted as a treatment for obesity, heart disease, and

high cholesterol, research results do not currently support lecithin's effectiveness for these disorders.

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See Also: Choline; Lipids; Phospholipids.

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Legumes

Legumes are a group of plants in the pea family that produce pods that contain the plants' seeds. Edible seeds from these legumes include beans, peas, lentils, soybeans, and peanuts. The legume family also includes ornamental plants and plants that provide ingredients for dyes, drugs, resins, and perfumes. Some legume plants, such as clover and alfalfa, are used to feed animals and are planted as forage crops for grazing animals. Legumes belong to the family *Leguminosae* and thousands of species have been identified. Legumes grow on every continent and have been consumed and cultivated for centuries. When grown naturally, the pods split open on both sides as they ripen and dry out. This releases the seeds and allows the plant to spread. Sometimes the seeds are projected out of the pod, which spreads them farther. Legumes can be annual, biennial, or perennial and include low shrubs and trees.

The high protein content of legumes is due to the tubercles on legume roots that hold nitrogen-fixing bacteria. Legumes are nitrogen fixers, which means that they pull nitrogen from the atmosphere into the soil. Doing so makes the nitrogenous materials available to the plants and also helps restore nitrogen-depleted soil. Because of this, legume plants often are included in crop rotation and are planted with vegetables to ensure optimal soil nitrogen levels.

When legumes are dried, they are referred to as "pulses" in English-speaking countries and also "legumes" in the United States. Legumes have low water content and have seed coats that make them able to endure long periods of storage. Legumes are fairly easy to grow, mature rapidly, and are very nutritious. They are an excellent source of protein and low-glycemic index carbohydrates, and are rich

in fiber, folate, and other B vitamins, and the minerals iron, magnesium, and potassium. Legumes contain a variety of phytochemicals thought to influence health. One group of these chemicals, the phytoestrogens, could exert hormone-like effects in the body, and influence processes associated with the prevention or development of hormone-related cancers, such as some cancers of the breast and prostate. Because legumes are relatively high in protein, they are commonly consumed in vegetarian diets and can be substituted for dietary animal protein. Substituting legumes for foods that are high in processed fats and refined carbohydrates could lower risk of cardiovascular disease and type 2 diabetes mellitus. Many health organizations, including the American Heart Association, Health Canada, and the American Diabetes Association recommend that people replace some animal protein sources with several servings of legume foods each week.

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See Also: Fiber; Phytochemicals; Phytoestrogens; Soybeans and soy foods; Vegetarian and vegan diets.

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Linoleic Acid

Linoleic acid (LA) is an essential omega-6 fatty acid, which means people must obtain this nutrient from their diets, because the body is not able to manufacture it. This acid is composed of an 18 carbon chain with 2 carbon-carbon double bonds. It is plentiful in seeds, nuts, and many vegetable oils such as poppy seed, safflower, sunflower, and corn. The dietary reference intake for linoleic acid is 17 g per day for men 19 to 50 years old, and 12 g per day for women ages 19 to 50. Linoleic acid deficiency is rare; when it does occur, it is associated with scaly skin rashes, underdevelopment in children, and slowed wound healing. The term "linoleic" is derived from the Greek words "linon" (flax) and oleic meaning related to oleic acid (linoleic acid produces oleic acid when its omega-6 double bond is saturated). It is found in the lipids of cell membranes and is used in the biosynthesis of arachidonic acid, another fatty acid. Arachidonic acid is converted into important cell signaling molecules, including prostaglandins, leukotrienes, and

thromboxanes. These molecules direct cell activities, influencing processes such as inflammation and blood clotting.

Researchers have been exploring the health benefits and risks of diets with various fatty-acid profiles since the 1960s. Scientists initially believed that saturated fats were associated with increased risk of artery disease, and people at risk for cardiovascular disease were frequently advised to replace foods high in saturated fats with those high in polyunsaturated fats. Many people began to replace butter and other animal fats, for example, with margarines and vegetable oils. A study done in Sydney, Australia, examined the effect of this dietary counsel (Ramsden et al., 2013). Researchers recruited 458 men, from age 30 to 59 years old, who had recently experienced a coronary event, such as a heart attack. Half of the men were instructed to increase their intake of polyunsaturated fatty acids, primarily linoleic acid, to 15% of daily calories, and decrease the intake of saturated fats to less than 10% of daily calories. Men in the first group were given safflower oil and safflower oil margarine. Safflower oil is high in linoleic acid. Contrary to expectations, the group receiving a high intake of linoleic acid experienced higher death rates than the control group: 17.6% versus 11.8%. The researchers concluded that the advice to replace saturated fats with linoleic acid might not be prudent (Ramsden et al., 2013).

Such studies illustrate that when evaluating the health risks and benefits of linoleic acid, it is important to consider it in the context of an entire diet. Some researchers have proposed that increased intakes of the omega-6 fatty acids, such as linoleic acid, tend to promote inflammation and more rapid blood clotting, which might explain the greater rates of cardiovascular and other causes of death in the Sydney Diet Heart Study. Other researchers, however, argue that evidence for this is lacking (Johnson & Fritsche, 2012).

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See Also: Fatty acids.

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Lipids

Lipids are a category of molecules that generally are insoluble in water but are soluble in fat and organic solvents. Lipids include fatty acids, triglycerides, phospholipids, and sterols. All of these chemicals are found both in the diet and in the body. In the diet lipids often are referred to as fats and oils; fats are solid at room temperature and oils are liquid at room temperature.

Fatty Acids

Fatty acids are composed of hydrocarbon chains with a carboxyl (acid) group (-COOH) and a methyl group ($-CH_3$). They are called "free fatty acids" when they are not attached to other compounds. Fatty acids are distinguished according to their chain length. A chain length refers to the number of carbons present in a given chain. Fatty acids have between 4 and 24 carbons, and that number almost always is even. Short-chain fatty acids have between 2 to 4 carbons, medium-chain fatty acids have 6 to 10 carbons, and long-chain fatty acids have 12 or more carbons.

Fatty acids can be saturated, unsaturated, monounsaturated, or polyunsaturated. Saturated fatty acids contain all single bonds between carbons, with the other bonds filled by hydrogen. Substances that are composed primarily of saturated fatty acids tend to be more solid at room temperature. Unsaturated fatty acids contain one or more carbon-carbon double bonds; monounsaturated fatty acids contain one carbon-carbon double bond. Polyunsaturated fatty acids contain more than one carbon-carbon double bond. The location of the double bond is used in naming fatty acids. For example, omega-3 fatty acids have a carbon-carbon double bond between the third and fourth carbon from the methyl end of the fatty acid.

Fatty acids can vary in shape, depending upon the location of the carbon-carbon double bonds. A "cis fatty acid" is an unsaturated fatty acid with a bent carbon chain. Cis fatty acids are naturally occurring fatty acids. Trans fatty acids also are unsaturated fatty acids, but they take the shape of a straight carbon chain. Trans fatty acids usually result from hydrogenation, a process that adds hydrogens to an unsaturated fatty acid making it more saturated, which makes the food products to which it is added more stable, and gives them a longer shelf life.

Essential fatty acids refer to those that must be obtained through the diet; non-essential fatty acids can be produced by the body. Humans need to consume linoleic acid and alpha-linolenic acid in their diets. Food sources for linoleic acid include seeds, nuts, and many vegetable oils such as poppy seed, safflower, sunflower, and corn. Food sources for alpha-linolenic acid are flaxseed, canola, soy,

walnuts, chia seeds, and pumpkin seeds, with flaxseed being the richest. Alpha-linolenic acid also is found in some dairy foods and red meat.

Triglycerides

Triglycerides are made when three fatty acids attach to a glycerol backbone. Diglycerides have two fatty acids attached to glycerol, and a monoglyceride has one fatty acid attached to glycerol. Triglycerides are the primary molecule for fat storage in the body. Triglycerides are stored in adipose cells. Triglycerides are also stored in muscle, liver, and other types of cells. In the diet, triglycerides are the primary form in which fat is ingested. Triglycerides provide the feeling of satiety, give flavor to food, serve as an energy source for the body, and act as carriers for fat-soluble compounds such as vitamins A, D, E and K, and many phytochemicals.

Phospholipids

Phospholipids have a similar structure to triglycerides. Instead of having three fatty acid groups, however, phospholipids have two fatty acid chains and one phosphate group with a nitrogen-containing compound attached to a glycerol. This nitrogen-phosphate group is soluble in water and attracts water-soluble substances; the diglyceride area attracts fat-soluble substances. For this reason phospholipids act as emulsifiers, that is, they can keep water and oils mixed together. Phospholipids are crucial components of cell membranes, forming a phospholipid bilayer. This allows fatty and water-soluble substances to move in and out of cells.

Sterols

Sterols are hydrocarbons and form multiple-ring structures. Cholesterol is an important sterol, and is an essential structural component of cell membranes and nervous tissue. Cholesterol is a precursor to many important compounds, including vitamin D, bile, and several hormones, including testosterone, estrogen, and the corticoid hormones.

Paula Sophia Seixas Rocha

See Also: Alpha-linolenic acid; Cholesterol; Fatty acids; Linoleic acid; Lipoproteins; Phospholipids; Trans fatty acids; Triglycerides.

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Lipoproteins

Lipoproteins are large compounds composed of triglycerides, cholesterol, phospholipids, and proteins. The lipid components form the core of the lipoproteins, with phospholipid and protein groups coating the exterior. Lipoproteins are manufactured by the body and are used as transport molecules. Lipoproteins allow lipids, including triglycerides and cholesterol, which do not dissolve in water, to travel through the aqueous environment of the circulatory system. There are many varieties of lipoproteins, and they are classified by their density—the lower the density, the higher the relative amount of triglycerides. Serum lipoprotein levels are used to calculate an individual's risk for artery disease, with higher levels of low-density lipoprotein (LDL) cholesterol indicating greater risk. Higher levels of high-density lipoprotein (HDL) cholesterol are associated with a reduced risk of artery disease. Lowering serum LDL levels often is a therapeutic goal for people at elevated risk for heart disease. Lower LDL levels can be achieved through lifestyle measures such as dietary change, physical activity, and weight loss, and with medications. High-density lipoprotein cholesterol levels can be raised by engaging in regular physical activity.

Chylomicrons

Chylomicrons are a type of lipoprotein that form in the digestive tract during the absorption of fats. Chylomicrons are about 90% triglyceride. From the digestive tract, chylomicrons are absorbed into the lymphatic system and travel from there to the circulatory system. In the circulatory system, an enzyme called "lipoprotein lipase," found on the capillaries, removes triglycerides from the chylomicrons, so that the triglycerides can be stored in various areas of the body or used for energy. After about 10 hours, chylomicrons have lost a majority of their triglycerides.

Very Low-Density Lipoproteins

The liver and intestines transform the chylomicron remnants into very low-density lipoproteins (VLDLs). These VLDLs are approximately two-thirds triglyceride. As VLDLs circulate in the bloodstream, lipoprotein lipase removes triglycerides and transforms VLDLs into intermediate-density lipoproteins (IDLs). The intermediate-density lipoproteins are about 40% triglyceride. As IDLs circulate through the liver, the liver takes the intermediate-density lipoprotein and changes it into low-density lipoprotein.

Low-Density Lipoproteins

Low-density lipoproteins are only about 6% triglyceride and are more than 50% cholesterol. The LDLs deliver cholesterol to the cells of the body, where the cholesterol is used in the manufacture of cell membrane structures and a variety of chemicals, include the steroid hormones. Apoprotein B, found in low-density

lipoproteins, is a protein that binds to receptors on the surface of body cells and allows for the induction of cholesterol. When a cell requires cholesterol, a gene transcription cascade results in the assembly of protein receptors that are anchored on the outside of the cell membrane. These receptors are able to bind to apoprotein B and spur endocytosis of the entire lipoprotein into the cell, where it is digested and the freed cholesterol is incorporated into the cell membrane.

High levels of LDL are associated with increased risk for artery disease. When there are more low-density lipoprotein complexes in the bloodstream than there are receptors for apoprotein B, the excess LDLs accumulate in the arteries. These lipoproteins are vulnerable to oxidation, which increases the likelihood of an immune response and the formation of plaques, or buildups of white blood cells, along the artery walls. Receptors lining the arteries have an affinity for oxidized LDL particles, which bind to the artery lining, stimulating a cascade of events that lead to the buildup of arterial plaque. Genes responsible for the proper function of the apoprotein B receptor are known to have inheritable mutations that interfere with the endocytosis of LDLs, increasing the LDL blood count and the risk of coronary artery disease. Some mutations seem to hinder the anchoring of receptors to the cell membrane, and others have been shown to affect its binding affinity to apoprotein B. Its association with increased risk for coronary artery disease is responsible for LDL's moniker, "bad cholesterol."

High-Density Lipoproteins

High-density lipoprotein is manufactured in the liver, and is only about 5% triglyceride and 20% cholesterol. It contains a form of protein known as "apoprotein A." As high-density lipoprotein travels in the bloodstream, it picks up cholesterol from arterial plaque. The HDLs also interact with transporters on the surface of body cells, initiating the removal of cholesterol from the cell and its uptake into the lipoprotein. The complex then travels through the bloodstream and is directed to bind to endocrine and liver cells by apoprotein A, depositing cholesterol for the production of bile salts and steroid hormones. High-density lipoprotein also appears to transfer cholesterol to intermediate-density lipoproteins, which carry the cholesterol to the liver. Higher levels of HDL are associated with decreased risk for artery disease, earning it the nickname "good cholesterol."

Lipoproteins and Health

High levels of LDLs and low levels of HDLs contribute to an atherogenic blood lipid profile (*see* Lipoproteins sidebar). This profile has also been linked to increased risk for stroke, cardiometabolic syndrome, and Alzheimer's disease. The elevation in LDL levels that has been shown to correspond to an increased threat of artery disease is a target for the reduction of heart disease and its death toll. Most treatments aim to limit the levels of cholesterol in the blood available to form LDLs. Lifestyle changes generally are used for patients with low to

moderate risk of heart disease and involve avoiding tobacco products, increasing exercise, losing weight (if overweight), and improving diet. Smoking increases the oxidation of LDLs and makes it far more likely that plaques form, even when LDL levels are normal. Overweight and obesity have been associated with high LDL and low HDL levels, though the mechanism is not yet fully understood. Physical activity increases HDL levels and contributes to a healthful body size. Dietary changes to improve blood lipid profile include increasing consumption of fruits, vegetables, and whole grains; reducing intake of refined grain products, added sugars, and added fats; and limiting calorie intake to achieve a healthful body composition. Many medications are available to control serum cholesterol levels, including a family of drugs known as statins. Statins inhibit the rate-limiting step in the synthesis of cholesterol in the liver. Pharmaceuticals are especially helpful to patients who likely have a genetic control increasing their LDL levels and whose diet already reflects the standard recommendations.

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Research Issues

Each class of lipoprotein is actually a group of compounds. There are several types of low-density lipoprotein (LDL), for example, that vary in composition. One class of LDLs is known as small dense LDLs (sdLDLs). These particles appear to have a strong association with the development of arterial plaque. They seem to be more susceptible to oxidation than are other types of LDLs. Small dense LDLs also appear to cling to and absorb more easily into the endothelial cells of the artery lining. They seem to have a reduced binding capacity to LDL receptors, which suggests that sdLDLs are less likely to shed their triglycerides, but remain in circulation longer, thus enabling them to do more damage to artery linings.

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See Also: Alzheimer's disease and nutrition; Cardiometabolic syndrome; Cardiovascular disease and nutrition; Cholesterol; Lipids; Mediterranean diet.

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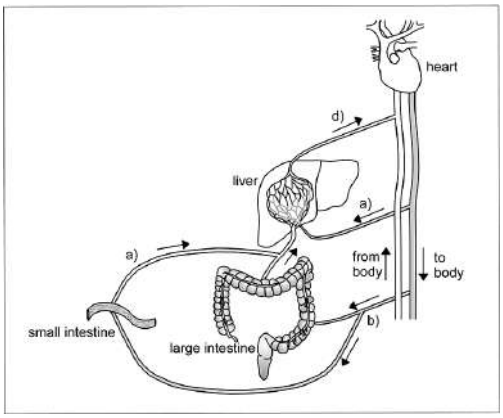
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The Liver

The liver is an organ of the digestive system that plays a vital role in the digestion, absorption, and metabolism of nutrients. It also helps to metabolize and excrete certain waste products, such as alcohol, medications, and dead blood cells, removing them from the body. The liver produces most of the cholesterol needed by the body, and converts excess calories into triglycerides; thus, the liver plays a central role in the production of the lipids associated with metabolic syndrome and cardiovascular disease. This important organ is especially vulnerable to excessive alcohol consumption, obesity, and toxic chemicals. Toxic chemicals include not only over-the-counter, prescription, and illegal drugs, but also a variety of herbs, dietary supplements, and other substances.

The best way to maintain liver health is by consuming a healthful diet; limiting alcohol consumption; avoiding unnecessary medications, risky herbs, and dietary supplements; and limiting the consumption of excess calories. Daily physical activity helps to prevent or reverse obesity and the metabolic syndrome and thus, promotes liver health and slows or reverses nonalcoholic fatty liver disease. No evidence currently supports the notion that programs claiming to "cleanse" the liver by fasting or consuming large amounts of substances such as lemon juice, vinegar, or Epsom salts are necessary or help to promote the health of the liver.



Hepatic circulatory system. Blood leaving the heart may proceed directly to the liver (a) or to the intestines (b) by way of arteries. However, nutrient-rich blood from the intestines first returns to the liver (c) where nutrients are filtered before the blood returns to the heart (d). (Sandy Windelspecht)

Anatomy

The liver is the largest of the internal organs, weighing about 1.5 kilograms in an adult. It lies just under the diaphragm toward the right side of the body. The liver is a red-brown color, mostly due to the fact that it is an extremely vascular organ, meaning that it has a very rich blood supply to support its many functions. There is a small duct called the "common hepatic duct" connecting the liver and the gallbladder, whose function is to store bile produced by the liver to be secreted as needed. Also connected to the liver is the hepatic artery, which brings oxygenated blood indirectly from the aorta

to the liver, to keep the liver functioning. The hepatic portal vein carries nutrient-rich blood to the liver from the gastrointestinal tract. The liver can break down, absorb, recycle, or send out these nutrients to other tissues, depending on what the body needs. A third vessel, the hepatic vein, takes deoxygenated blood away from the liver back to the heart to be oxygenated again.

The cells of the liver, called "hepatocytes," are specialized for their function in this organ. These cells are arranged into hexagonal lobules, whose center is a vein which drains into the hepatic vein. On the perimeter of the lobules are the hepatic artery and hepatic portal vein, bringing oxygenated and nutrient-rich blood to the liver cells.

Physiology

The functions of the liver are extensive, oftentimes complex, and essential for everyday life. These functions include the following.

- Removes wastes that come from metabolic processes or outside sources (i.e., drugs and alcohol) by alteration of these substances by enzymes, so that they can be safely excreted.
- Produces proteins that aid in immune response to fight off microbes, reduce inflammation, and repair damaged tissues.
- Synthesizes plasma proteins, which are responsible for blood clotting, regulation of osmotic pressure, and transportation of some minerals.
- Produces bile, a yellow-green, non-enzymatic solution secreted by hepatocytes, made up primarily of bile salts, bile pigments, and cholesterol and other lipids.
- Synthesizes cholesterol (found in bile), which is used structurally in cell membranes and as a precursor to steroid hormones such as estrogen and testosterone.
- Produces lipoproteins from precursor chylomicrons, for the transport of cholesterol and lipids in the bloodstream.
- Excretes bilirubin, which begins as a toxic by-product of red blood cell breakdown, but is turned into a bile pigment when mixed with bile. The bile pigment then is excreted in urine.

The list does not end here, however, because the liver also has numerous functions that are more specifically related to its role as a major organ of the digestive system.

Physiology and Nutrition

From a nutrition standpoint, the liver has a major role in metabolism, because it aids in the absorption, breakdown, storage, and utilization of nutrients obtained in the diet.

- Fats: Digestion and absorption of lipid molecules in the intestine is prefaced by the lipids being broken down by bile, which is produced by the liver. Bile

coats the surface of lipid droplets and breaks them into smaller parts, so that it becomes easier for the lipids to be digested further by enzymes in the small intestine. From the small intestine these lipid derivatives are absorbed by intestinal cells. Additionally, the liver helps to synthesize cholesterol and phospholipids, two lipid-based molecules which help form the structure of cell membranes. Without the liver—especially its bile excretion—fat metabolism would be extremely difficult, and the benefits of fat—as an energy source or a structural component—would be lost.

- Proteins digested from food are sent to the liver as amino acids, which are utilized in several different ways. New proteins can be synthesized in the liver using the amino acid components; the amino acids can be sent elsewhere in the body to build new proteins; amino acids can be converted to glucose or triglycerides for energy; and excess nitrogen groups from some amino acids are excreted as urea, which the liver has converted from the toxic substance, ammonia.
- Glucose, the primary monosaccharide of carbohydrates, is absorbed by the liver and either used for immediate energy, or stored as a carbohydrate compound called "glycogen." The liver then works in conjunction with the pancreas, which releases insulin when the liver must break down glycogen to glucose for energy, and glucagon when the liver must build glycogen from glucose for storage. Additionally, excess glucose is converted to triglycerides.
- Vitamins: Fat-soluble vitamins A, D, E, and K are absorbed and stored by the liver. The liver also works with the kidneys to convert vitamin D precursors into active vitamin D.
- Minerals: Iron and copper are stored by the liver and released as needed.

In short, because of its ability to metabolize these nutrients, the liver is able to fulfill many major functions that keep the body working properly. It can create energy, store substances for later use, remove waste products from the body, and build new structures with old materials, all using nutrients that have come from the diet.

Liver Health and Nutrition

Many of the disorders and diseases that develop in the liver are directly related to diet and lifestyle. One concern, especially in recent decades, is the effect of obesity on the liver because of the liver's major role in nutrient digestion and absorption. Nonalcoholic fatty liver disease is associated with the metabolic syndrome and visceral obesity. Excess calorie consumption stimulates triglyceride, cholesterol, and lipoprotein synthesis in the liver. High volumes of triglycerides, cholesterol, and lipoproteins not only raise the levels of harmful blood lipids, but increase deposition of triglycerides in the liver itself, interfering with healthy liver function. Maintaining energy balance with a healthful diet and daily physical activity can prevent the positive energy balance (consuming more calories than one expends) that contributes to the prevention of metabolic syndrome and nonalcoholic fatty liver disease.

In addition to issues caused by food intake, the liver also is greatly harmed by excessive alcohol consumption. Fatty liver disease (not to be confused with nonalcoholic fatty liver disease), for example, is the accumulation of fat in liver cells because of excessive alcohol. This disease causes the liver to become enlarged and painful. Additionally, alcoholic hepatitis is a condition characterized by damage to, and often destruction of, the liver cells, causing symptoms such as inflammation, nausea, tenderness, fatigue, jaundice, and weight loss. Both fatty liver disease and alcoholic hepatitis can lead to a more serious and chronic liver disease, due to repeated abuse of the liver through alcohol consumption, and excessive liver cell damage. This chronic damage is referred to as "cirrhosis"; it causes the liver cells to be replaced by tough, fibrous scar tissue, which cannot carry out the normal functions of liver cells.

The liver can also be damaged by a variety of toxic chemicals. Toxic chemicals include not only over-the-counter, prescription, and illegal drugs, but also a variety of herbs, dietary supplements, and other substances. For example, acetaminophen (Tylenol) can cause liver disease when taken in only slightly higher than recommended doses, especially when combined with alcohol. The herbs chaparral, comfrey, kava, and mistletoe (among others) also have been associated with liver damage in some people.

Liver cleanse supplements or diets claim to improve liver function by "cleansing" this vital organ. Most experts are skeptical of cleansing practices—which frequently include fasting, enemas, and very restrictive diets. The best way to maintain liver health is to avoid toxins on a daily basis, rather than "cleansing" a few times a year. It is prudent to reduce or eliminate intake of toxins such as alcohol, unnecessary medications, and risky herbs and supplements, and to avoid environmental toxins such as household cleaning chemicals. Consumers should incorporate the best practices of liver cleanse regimens into one's daily lifestyle: Drink more water, consume more fruits and vegetables, and eat fewer processed foods high in added fats and sugars.

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See Also: Alcohol; Detoxification; Gallbladder and gallbladder disease; Obesity, definition and health effects.

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The Locavore Movement

The locavore movement is an effort in which participants choose to eat food that has been grown locally, that is, food produced within a determined distance of where participants live. The word "locavore" is derived from the word "local" and the Latin word "vorare," which means to swallow or devour, and is analogous to the terms omnivore, herbivore, and carnivore. Proponents for the cause argue that the locavore diet tastes better, promotes crop biodiversity, boosts local economies, and saves energy, therefore reducing the environmental impact of food production and shipping. Points counter to the locavore movement include the fact that in many places—especially those in colder climates—people are unable to grow food outside year-round. Nevertheless, the locavore diet has grown in popularity as its implications and motives are both embraced and criticized.

Of course, throughout time people around the world have consumed food produced locally, as that was the only food available until relatively recently in human history. In the mid-20th century, technologies in food preservation and transportation were developed that enabled food to be transported long distances and sold thousands of miles from the location in which it was grown or produced. "Back to the land" movements beginning in the 1960s featured many groups of people learning to grow their own food on farms or in gardens, often as part of counterculture efforts to flee urban living and promote intentional communities. At the beginning of the 21st century, increasing concerns about issues related to climate change and energy conservation prompted more consumers to examine food-buying and food-consumption patterns.

The locavore movement took off in earnest in San Francisco in 2005, when four residents designated August of that year as the "Eat Local Challenge" and launched an accompanying website. The event had been inspired by ecologist Gary Paul Nabhan's book *Coming Home to Eat*, originally published in 2001, in which he restricts himself to eating foods produced within a 100-mile radius of his home in Arizona (Nabhan, 2009). Similar challenges, most a week in length, began surfacing across the United States in the following years. Although most of the challenges initially began in the summer months, eventually all months of the year began to be embraced, including week-long challenges in the heart of Vermont and Minnesotan winters (Burros, 2007). In her book *Animal, Vegetable, Miracle*, Barbara Kingsolver (2007) described the challenges and benefits of a locavore diet, as her family of four followed a primarily locavore diet for one year. Her popular book introduced growing numbers of people to the locavore movement.

Locavores have cited many reasons for their diet. Some are quick to mention taste, as many of the local foods are fresh, because they go right from the farm to the locavore's plate. One of the primary motivations for locavores, though, is the environmentally friendly nature of the diet. The appeal of the "100-mile diet" (eating only food sourced from within a 100-mile radius of one's home) is that it greatly reduces the carbon footprint related to food. Today, the average distance that any given food item has travelled to get from source to plate is 1,500 miles—a distance that has substantial fossil fuel costs (Bennett, 2007). A benefit of the

locavore diet is that participants can pick a food radius that best suits them, such as consuming food produced within 10, 100, or 250 miles, or only from in-state sources.

Another oft-cited benefit of the locavore diet is the inherent community building and boost to the local economy that occur. As people seek out local food providers, they frequent farmers markets and local stores, meet neighbors, and support local growers and producers.

The rise of the locavore movement is beginning to be recognized by the government and big businesses. In the 2008 Farm Bill, for instance, $2.3 billion dollars was set aside for specialty crops produced by small, mainly organic farmers—a significant increase from the $100 million allotted in the previous legislation (Gogoi, 2008). Major U.S. supermarket chains such as Wal-Mart, Kroger, and Whole Foods have designated portions of their produce aisles for local farmers, although executives to the businesses admit that the seasonality of fruits and vegetables make it impossible for them to supply their shelves with only local produce (Gogoi, 2008).

One state that has widely embraced the locavore movement is Vermont. Although its population is fewer than 622,000 residents, Vermont boasts 99 farmers markets and 164 community-supported agriculture ventures (CSAs)—one of the highest rates in the country (Rathke, 2012). What started as weeklong local challenges has developed into a movement that many Vermonters embrace, especially in rural areas of the state. Hit hard by the recession, the locavore movement has helped create jobs in Vermont. Journalists have noted that farmers markets often bring people together and inspire feelings of community (Rathke, 2012).

Although there are many proposed benefits to the locavore diet, critics have voiced concerns about the movement. Some believe that the locavore diet is elitist, because the prices of locally sourced, organic foods can be much greater than those of imported, mass-produced foods (Burros, 2007). Another point of contention is the definition of "local" within the movement. Because there is little regulation and no official definition of local, supermarkets can label a food "local" even if has come from more than 100 miles away (Rathke, 2012). Michael Pollan, author of *The Omnivore's Dilemma,* believes that "local means local in season," meaning, for instance, that residents of New England would have to learn to embrace long winters subsisting on root vegetables and canned summer vegetables, foregoing lettuce and tomatoes until spring and summer (Bennett, 2007).

The environmental benefits of the locavore movement also have been contested. In winter, it takes much less energy to grow produce at locations in warm climates versus in the heated greenhouses available in cold climates, and many wonder whether the energy cost of transporting produce truly outweighs the cost of the energy required to warm greenhouses. Such factors make "food miles" (the distance a food product has travelled from farm to table, which some locavores think should be included on labels) an inconsistent measure of true energy consumption.

Animal husbandry, which has been promoted by some in the locavore movement, has also been met with opposition from critics. Many inexperienced locavores

take on backyard farm animals, believing this to be more environmentally sustainable and less cruel than subjecting animals to factory-farm settings. Individuals who have no farming experience, however, could unknowingly subject animals to subpar living conditions. Animals slaughtered by inexperienced people are also apt to suffer greatly, which has led some critics of the locavore movement to speak out against the deregulation of animal slaughter (McWilliams, 2011).

Despite these criticisms the locavore movement continues to grow in size and popularity. Some believe that the locavore movement could be part of a critical effort to revive small American cities, which recently have seen significant downsizing. Land availability near smaller cities could give them an advantage to help supply the growing locavore movement, and also could provide jobs and build communities in struggling areas. The importance of making the locavore movement more accessible to low-income, urban communities also is discussed frequently. For many people who live in urban "food deserts," farmers markets and grocery stores selling local food are not readily accessible, and farmers and community workers need to reach out to include these communities in the growing locavore movement.

Hannah E. Underwood

Research Issues

What would your diet be like if you restricted your intake to foods produced within 100 miles of your home? Investigate local food growers and producers to learn what is grown in your area.

See Also: Food gardens; Organic food and farming; Sustainable agriculture.

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Lutein

Lutein is a carotenoid, which is a group of organic pigments found in plants. It accumulates in the eye and plays a critical role in vision. In 1945, George Wald dissected 10 human retinas and was the first to suggest the presence of carotenoids in the fovea, a small area of the retina responsible for acute vision. Along with zeaxanthin, the presence of lutein in eye tissues was confirmed in the mid-1980s using high-performance liquid chromatography. The yellow-tinted macular pigment serves to filter blue light in the eye. Lutein's primary location in the Henle fiber layer of the inner portion of the retina allows it to effectively diminish harsh blue light before it reaches photoreceptors and other sensitive structures in the eye. It is also found in lesser concentrations in the outer layer and other eye tissues. As a dietary antioxidant, lutein is thought to decrease damage to the retina caused by reactive oxygen species, in addition to its role in shielding it from high-energy blue light. Studies have shown that a high intake of leafy green vegetables is associated with lower incidence of age-related macular degeneration.

Lutein is consumed from fruits and vegetables, particularly leafy vegetables like kale and spinach, broccoli, collard greens, and turnip greens. Eggs also provide lutein. The lutein content of foods is sensitive to cooking methods, therefore serving vegetable sources raw or lightly steamed is recommended. Lutein supplements are available, but its bioavailability from this source has not been established. Although there are no daily intake recommendations for lutein, long-term deficiency can leave individuals vulnerable to cataracts and macular degeneration—a disorder resulting in the loss of sight to the center of vision.

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See Also: Eye health; Zeaxanthin.

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Lycopene

Lycopene is a fat-soluble compound that belongs to a family of compounds known as "carotenoids." A carotenoid is a type of pigment that is generated in plants and other photosynthetic organisms. Carotenoids help protect chlorophyll from photodamage, and help the plant absorb light energy to be used for photosynthesis. Carotenoids such as lycopene are responsible for a variety of plant coloration. Lycopene gives plants and fruits such as red peppers, watermelons, and tomatoes their red hue. Most commonly found in tomatoes and tomato products such as tomato juice and tomato sauce, lycopene has received a lot of attention for its antioxidant properties that could be associated with health benefits.

The antioxidant properties of carotenoids stem from their ability to quench singlet oxygens ($^1O_2$) and trap peroxyl radicals, inevitable by-products of metabolism. This means that carotenoids absorb energy from overexcited oxygen molecules and dissipate that energy before the excited oxygen can damage surrounding systems, such as cellular DNA or cell membranes. Lycopene appears to have the most effective singlet oxygen-quenching properties of the carotenoids.

Lycopene is a straight chain hydrocarbon, which means it is composed solely of carbon and hydrogen atoms. In nature it generally is found in its trans-state, as are most carotenoids, but processing the molecule transforms it to its cis-conformation. This means that when lycopene is consumed in the form of processed or cooked tomatoes or sauces, the molecule goes from its trans-conformation to its cis-form. Interestingly, the cis-formation of lycopene is the conformation of the molecule required for the human body to make use of it. Additionally, the cis-formation is more stable, making the molecule a stronger antioxidant. Because lycopene is composed entirely of hydrocarbons, it is a hydrophobic molecule. As a result, lycopene does not mix well with polar molecules such as water, and prefers to associate itself with lipids or fats. Research has shown that carotenoids are absorbed much more efficiently in the body when they are eaten with a source of fat, such as oil or avocado.

Lycopene exhibits antioxidant and antiproliferative properties in vitro and in laboratory animals. As is often the case, studies in humans regarding lycopene health benefits have shown mixed results. In some studies, higher dietary consumption of lycopene-containing foods—primarily tomatoes and tomato products—was associated with reduced risk of certain cancers, such as prostate cancer. Other studies, however, have failed to support this association. Additionally, in studies finding an association between consumption of tomato products and health effects, it is unclear whether lycopene or other substances in the tomato products or diet are responsible. In one interesting study of more than 1,000 Finnish men, the subjects with the highest serum lycopene levels had fewer than half the number of strokes that subjects with the lowest serum lycopene levels had (Karppi, Laukkanen, Silvenius, Rondainen, & Kurl, 2012). Researchers speculate that lycopene might exert beneficial effects on the cardiovascular system by reducing the oxidation of LDL cholesterol, thus slowing the process of artery disease. Lycopene also might reduce inflammation and blood clotting rate (Godman, 2012).

As is the case for studies linking tomato consumption with health benefits, however, high serum lycopene levels also could be markers for other factors influencing health, such as a generally greater consumption of fruits and vegetables.

Taking a dietary supplement with high levels of a single carotenoid does not appear to offer health advantages, and even might lead to negative health effects, as has been the case with beta-carotene supplementation. Current recommendations for maximizing the beneficial effects of lycopene suggest consuming lycopene-rich foods such as tomato juice as part of a balanced diet that includes several servings of fruits and vegetables each day.

Rachael Ann Gainer and Barbara A. Brehm

See Also: Antioxidants; Beta-carotene; Dietary supplements; Phytochemicals.

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Lysine

Lysine is an essential amino acid that plays a role in helping the body absorb calcium. As an essential nutrient, the body cannot synthesize lysine and it must be taken in through the diet. The best sources of lysine are protein-rich foods such as meat, cheese, nuts, eggs, and soybeans, as well as some fish (UMMC, 2011). Vegans can look to legumes such as beans and lentils for their source of lysine. Those who do not take in enough lysine over a long period might experience fatigue, loss of appetite, dizziness, anemia, and reproductive issues. For adults, about 30 mg/kg of lysine per day is recommended by the World Health Organization (2007).

The most promising medicinal application of lysine is in the treatment of herpes simplex virus. Lysine supplements and topical creams might help to curb outbreaks of the virus that lead to cold sores and blisters. It is thought to work by preventing the action of arginine, which facilitates replication of the virus (UMMC, 2011). Lysine helps the body to absorb calcium, and appears to influence the activity of osteoblasts, the cells that form new bone tissue, in vitro. More research



The Herpes Virus is transmitted by respiratory and oral secretions. After the initial infection, the virus remains dormant in nerve cells, but may become active again, especially with stress, sunlight, or other changes to immune function. A diet with a high lysine–arginine ratio may help prevent reactivation of the virus. (Kuhar/Dreamstime.com)

is needed, however, to support this observation in humans. The nutrient also is needed in the formation of collagen—which can be found in ligaments, tendons, skin, and elsewhere in the body—to provide structure within the body. Although research still is inconclusive to support the practice, some take lysine as a supplement for improved athletic performance. It is a crucial nutrient for the production of carnitine, which contributes to fatty-acid metabolism. Excessive intake of lysine can result in stomach pain, diarrhea, and increased cholesterol levels. Chronically high levels also have been associated with gallstones and renal dysfunction.

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See Also: Amino acids.

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M

Macrobiotic Diet

Macrobiotics is a way of eating and living that emphasizes natural, unprocessed foods combined with efforts to live in harmony with nature and natural forces. The macrobiotic diet refers to the dietary principles and guidelines that are part of the macrobiotic lifestyle. More than a list of what foods to eat, the macrobiotic diet emphasizes developing a diet that takes into consideration climate, season, age, activity level, individual disposition, and health concerns. A central feature of macrobiotics is choosing foods to balance "yin" and "yang" elements and energies. The concept of yin-yang balance evolved from Asian spiritual traditions emphasizing the interconnectedness of opposing forces, such as light-dark, male-female, and warm-cool. Practitioners of macrobiotics seek to balance the yin and yang forces in their lives not only through food choice, but with methods of food combination and preparation along with other lifestyle factors.



Brown rice is a staple in a macrobiotic diet. Within the rice family, long and medium grain rices are more yin while short grain rices are more yang. (Hlphoto/Dreamstime.com)

There is no single "macrobiotic diet" but, in general, macrobiotic diets feature daily consumption of whole grains, vegetables, legumes, and sea vegetables. Plant foods comprise the bulk of the diet, but animal foods such as fish also are allowed, depending upon one's needs. The macrobiotic diet includes whole, preferably organic foods and discourages the consumption of processed foods, along with sugars, and stimulants such as coffee, black tea, and alcohol. Well-planned

macrobiotic diets tend to be adequate in most vitamins and minerals, with the exception of iron, calcium, and vitamin D and vitamin B12 (if few animal foods are consumed). These diets are high in fiber and low in cholesterol, saturated fats, and sugar. Extreme forms of the diet—in which people consume only whole-grain brown rice and water—no longer are widely promoted and are not recommended. Macrobiotic diets can be manipulated to suit the needs of most people, including children, and women who are pregnant or breast-feeding. Although macrobiotic diets have not been subjected to the scrutiny of medical research, nutrient composition analyses suggest that the diet should be helpful for the prevention and treatment of chronic diseases such as obesity, type 2 diabetes, hypertension, and artery disease. Macrobiotic diets usually are high in healthful phytochemicals (plant compounds) that could help to prevent cancer. Although macrobiotic diets have been promoted as a means to cure cancer, evidence for this effect is lacking.

The History of Macrobiotics

Promoters of macrobiotic diets claim that the history of macrobiotics has is roots in the philosophy of ancient Greece (Kushi & Blauer, 2004). Hippocrates was the first person to use the term "macrobiotics" as a way of describing people who were healthy and long-lived. "Macro" translates to "large" or "great" and "bios" means life. The word macrobiotics appeared again in the late 18th century, in the title of a book by German physician Christoph Wilhelm Hufeland, *Macrobiotics: The Art of Prolonging Human Life* (Aschoff, 1998). Hufeland recommended good sleep habits, fresh air, adequate light, and a modest diet to promote good health.

Today's macrobiotic philosophy grew more directly out of work on nutrition and health published at the turn of the last century by the Japanese physician Sagen Ishitsuka, and later by Yukikazu Sakurazawa, who studied with disciples of Ishitsuka. Sakurazawa and colleagues combined traditional Asian medicine and Eastern philosophy with Judeo-Christian teachings, and supplemented the foods which were part of their beliefs with a diet of brown rice, miso soup, and sea vegetables as a way to cure themselves of illnesses. Sakurazawa believed he cured himself of tuberculosis by following a diet of whole, living, natural, seasonal foods. He moved to Paris in the 1920s and changed his name to George Ohsawa. Ohsawa began promoting his food and lifestyle philosophy, which he called "macrobiotics," in the 1930s, bringing his teachings to the United States in the 1960s. Ohsawa's spiritual perspective and theory that a macrobiotic lifestyle could help heal disease, protect the environment, and promote world peace quickly took hold in the counterculture movement—especially among young people disenchanted with what they saw as an American emphasis on production and consumerism, and who were opposed to the Viet Nam War. Michio Kushi, a student of Ohsawa's, adopted the macrobiotic lifestyle, expanded its ideas, and in 1978 created the Kushi Institute in Boston. Additionally, he started the Erewhon company—one of the first businesses to specialize in macrobiotic and natural foods.

The Macrobiotic Lifestyle

Along with a belief system and food guidelines, many lifestyle changes complement the macrobiotic diet (Kushi, 2013). Macrobiotic principles state that the preparation of food and one's eating habits are just as important as the actual foods consumed. People should only eat or drink when hungry or thirsty, but there is no limitation on the amount people should eat as long as they are listening to the body's signals. People are encouraged to chew slowly to allow time for the food to mix with digestive enzymes. Some believe in a precise count of chewing 50 or more times for each bite of food, but more modern macrobiotic followers are more lenient. No mineral or vitamin supplements are recommended; the diet should provide ample quantities of nutrients. A person should stop eating at least three hours before bedtime.

Limiting stress is a key lifestyle factor in macrobiotics. Other lifestyle changes include using natural products for personal hygiene and for home and garden care. The macrobiotic philosophy recommends avoiding long, hot baths and showers; using only natural fiber materials for clothing, carpets, and bedding; and avoiding overuse of air conditioning or heating. Physical activities such as yoga, stretching, and walking are recommended.

Yin-Yang Balance

Striving for yin-yang balance is a basic principle of macrobiotics. Yin represents energy or movement with outward direction, which results in expansion; yang is energy with an inward direction, resulting in contraction. According to macrobiotic philosophy, these "food energies" are absorbed in waves and vibrations that influence a person's body and consciousness when eaten. Every food contains both yin and yang energy, but most contain more of one than the other. Yin foods, for example, are cooler, moist, sweet, and upward growing; foods with more yang energy are more compact, dry, warm, and downward growing. Thus, root vegetables have more yang energy than do leafy green vegetables, for example. People are encouraged to choose foods higher in yin or yang to accommodate factors such as climate and season. In hot summer weather, for instance, a macrobiotic diet would feature more cooling, yin foods, and in the cold winter months, more yang foods would be chosen. Foods thought to have the most yin-yang balance are whole grains, sea vegetables, root vegetables, and legumes. The macrobiotic diet discourages consumption of vegetables and fruit from the nightshade family, however, including potatoes, eggplants, peppers, and tomatoes.

Cooking methods also contribute to yin-yang balance. For example, stir-frying, sautéing, and lightly steaming enhance a food's yin quality, leaving it crisp and fresh. Stewing, boiling, and baking contribute to a food's yang quality, creating food that is warmer with blended flavors. People following a macrobiotic lifestyle use cookware made of more natural materials, such as stainless steal, enamel, and glass. They do not use microwave or electric ovens.

Dietary Guidelines

Aside from working with the yin and yang life forces of foods, the macrobiotic diet does offer some general food guidelines. Daily intake consists of about 50% of food (by weight) from whole grains (e.g., brown rice, barley, quinoa), 30% from vegetables (mostly cooked, but some could be raw), 5% to 10% from legumes (lentils, beans, and soy foods such as tempeh and natto), and 5% to 10% from sea vegetables (kelp, kombu, nori,). Soup is a common dish, and one or more cups of soup—often made with miso—are consumed each day. Fermented foods such as miso can be included in small amounts, even though they have high yang energy. They also contain beneficial probiotic bacteria and help with digestion. Other foods, such as locally grown, seasonal fruits, seafood, nuts, seeds, and natural sweets (such as dried fruits and desserts made with rice syrup and barley malt) are added to the basic diet as needed. Dairy, eggs, poultry, and red meat are less frequently consumed, although their use is allowed in some diets, depending upon individual need. In temperate climates, such as in much of the United States and southern Canada, tropical fruits also are avoided.

Health Benefits and Risks

A well-planned macrobiotic diet is similar to a good vegetarian diet, as endorsed by the Academy of Nutrition and Dietetics (ADA, 2009). Adequate protein can be obtained from whole grains and legumes, along with fish, seeds, and nuts. Macrobiotic diets usually are low in cholesterol and animal fats, thus following most dietary guidelines in this area. Macrobiotic diets offer an adequate intake of almost all vitamins and minerals, with some exceptions depending upon diet composition. Vitamin B12, for example, comes only from animal sources, so vegan macrobiotic diets are low in this important vitamin—which is why most people following a macrobiotic diet include some seafood. People regularly exposed to sunshine might make enough vitamin D, but people in more northern latitudes could benefit from supplementation or by consuming foods with vitamin D added, such as dairy products. Some people have wondered whether a macrobiotic diet contributes enough calcium. Calcium is found in many vegetables, seeds, and nuts. People with high calcium needs, such as growing children and women at risk for osteoporosis, also should consume some dairy products; small amounts of yogurt and kefir are included in many macrobiotic diets for this reason. Young women must be especially careful to include foods with adequate iron, such as dark green vegetables, legumes, and sea vegetables. A macrobiotic diet might not contain enough iron to address the needs of people with iron-deficiency anemia.

The composition of a typical macrobiotic diet suggests that it conforms in several areas to diets recommended for the prevention and treatment of many chronic diseases. Rich in whole grains and vegetables, the diet is low in cholesterol, saturated fats, and trans fats. It also is low in sugars, thus it is less likely to cause obesity and type 2 diabetes. It is high in helpful minerals such as potassium that reduce risk of hypertension. The diet's high fiber content reduces risk of

digestive problems such as constipation, hemorrhoids, and diverticular disease. Fermented foods also might help to alleviate digestive problems. Foods such as miso, tempeh, tamari, umeboshi, sauerkraut, and pickles might contribute to a healthy composition of microbes in the digestive tract, and correct the balance between digestive bacteria and potentially harmful bacteria.

The composition of the macrobiotic diet suggests that it might be helpful for the prevention of cancer. Its low-fat, high-fiber foods could reduce inflammation levels; the high intake of plant foods supplies helpful phytochemicals. Advocates of the macrobiotic diet have suggested that the diet could be helpful for the treatment of cancer, but medical experts strongly object to this claim. No evidence suggests that cancer can be reversed by a macrobiotic lifestyle, and experts worry that people putting all their hope on macrobiotics might delay seeking medical treatment that might be more helpful. Dietary changes can inhibit the effectiveness of some chemotherapy treatments. Additionally, weight loss—a common consequence of the diet—could be harmful for cachexic cancer patients.

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Research Issues

Explore the websites listed in the Further Reading section to learn more about the macrobiotic diet and lifestyle. Which dietary recommendations seem to be most in line with public health guidelines, such as the *U.S. Dietary Guidelines for Americans* and Canada's *Food Guide*?

Read about the Ayurvedic diet, Chinese food therapy, and vegetarian and vegan diets. How does the macrobiotic diet compare to these? What are the similarities and differences, both in terms of recommended food intake and guiding philosophies?

See Also: Mindful eating; Vegetarian and vegan diets.

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Magnesium

Magnesium is an essential mineral in the human body. It is needed for more than 300 biochemical reactions in the body. For example, magnesium helps to maintain normal nerve and muscle function; supports a healthy immune system; keeps the heart beat steady; helps bones remain strong; helps regulate blood glucose levels; and aids in the production of energy and protein (National Institute of Health [NIH], 2014a). Magnesium has important roles in both preventing and managing high blood pressure, heart disease, and diabetes. Individuals with high blood pressure are at an increased risk for heart disease and stroke.

The recommended intake of magnesium depends on one's age and gender. For adult men from 19 to 30 years old the recommended intake is 400 mg per day, and men more than 30 years old should consume 420 mg per day. The recommended dietary reference intake for women from 19 to 30 years old is 310 mg per day, and women age 30 and older need 420 mg per day. Good food sources of magnesium are whole grains, green leafy vegetables, fruits, nuts, seeds, beans, and soy products (NIH, 2014b). Dark chocolate also contains magnesium.

Magnesium Deficiency

There are two categories of people that have low magnesium intake. The first category consists of healthy individuals with a low intake over a short time. People in this category might not even notice any symptoms of deficiency. Getting too little magnesium in the short term does not lead to obvious symptoms because the kidneys recognize the low intake of magnesium and retain the magnesium by limiting the amount lost in urine (NIH, 2014b). Some of the early symptoms include anorexia, apathy, confusion, fatigue, insomnia, irritability, muscle twitching, poor memory, and reduced ability to learn (NIH, 2014a).

The second category consists of people with low intake over a long period—and they could experience magnesium deficiency. Symptoms of magnesium deficiency include loss of appetite, nausea, vomiting, fatigue, and weakness (NIH, 2014b). Individuals with extreme magnesium deficiency could experience numbness, tingling, muscle cramps, seizures, personality changes, and abnormal heart rhythm (NIH, 2014b). Severe symptoms can include continued muscle contractions, delirium, numbness, tingling, and hallucinations (2014a).

Some individuals have medical conditions where the body excretes an increased amount of magnesium due to the body having problems absorbing magnesium. Individuals with gastrointestinal diseases and type 2 diabetes are likely to have insufficient amounts of magnesium. Individuals who are dealing with long-

term alcoholism also most likely are not getting enough magnesium. This is especially true for older adults (NIH, 2014b).

Dietary Supplements

Diet alone might not provide a sufficient amount of magnesium for most individuals in the United States. This is especially true for men 70 years old and older, and teenage girls 14 to 18 years old (NIH, 2014b). Different forms of magnesium are available as dietary supplements, and some are more easily absorbed in the body than others. Four of the more easily absorbed forms of magnesium are magnesium aspartate, magnesium citrate, magnesium lactate, and magnesium chloride (NIH, 2014b).

Health Benefits of Magnesium

Some research shows that magnesium supplements can help with decreasing a person's blood pressure. Consuming a diet with more magnesium and taking supplements could reduce the risk for some types of heart disease and stroke. Due to other nutrient interactions in the body, however, it is difficult to prove that the greater intake of magnesium reduces the likelihood of heart disease and stroke (NIH, 2014b).

For individuals with type 2 diabetes, magnesium helps the body break down sugars and use insulin properly. Individuals with higher intake of magnesium have greater bone mineral density, and with healthier bones there is a lesser chance of bone fractures and osteoporosis. Individuals who have migraine headaches might want to consult with their health care providers to see whether magnesium supplements might be an appropriate treatment to reduce the frequency of the migraines (NIH, 2014b).

Toxic Upper Intake Level

Magnesium found naturally in food is not harmful. Magnesium in dietary supplements, however, does have an upper limit. Children from 9 to 18 years old and adults older than age 18 should not ingest more than 350 mg of magnesium from supplements. Consuming more than the upper limit of magnesium in the form of supplements can cause diarrhea, nausea, and abdominal cramping. Heartbeat and cardiac arrest can result from consuming extremely high doses of magnesium (NIH, 2014b).

Susana Leong

See Also: Minerals.

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Manganese

Manganese is a trace mineral and an essential nutrient involved in many chemical processes in the human body. It also is important for the industrial production of iron and steel, as well as glass, ceramics, dyes, and fertilizers. In the body, manganese functions as a cofactor in many enzyme systems and is needed for normal growth and health. The body does not store manganese, and only contains about 10 to 20 milligrams of the nutrient, most of which is located in organs such as the liver, pancreas, brain, and bones. Manganese deficiency is rare, as the mineral is common in the food supply. Excess manganese normally is excreted from the body in the bile produced by the liver, but manganese toxicity can occur, especially in foundry workers and others experiencing significant exposure to airborne manganese dust.

Manganese was first considered an essential element in 1931. It a naturally occurring element found almost everywhere in water, air, and soil. In the human body, manganese is involved in energy metabolism, especially the production of energy from carbohydrates and lipids. It also activates enzymes responsible for the utilization of several nutrients such as biotin, thiamin, ascorbic acid, and choline. Manganese is required for the formation of cartilage and bone, for blood clotting factors, and for normal brain and nerve function. Manganese is a component of the enzyme superoxide dismutase, which helps the body neutralize free radicals and prevent the harmful oxidation of cellular components such as DNA and cell membranes.

Manganese deficiencies rarely are observed in healthy people. Deficiency symptoms found in several clinical cases have included abnormal bone development, impaired growth, and reduced glucose tolerance. In animal studies, manganese deficiency produces profound effects, including impaired growth and development, reduced fertility, abnormal bone development, and disruption of carbohydrate and lipid metabolic pathways.

Manganese is plentiful in a variety of foods, including tea, nuts, seeds, whole grains, legumes, and leafy green vegetables. Because manganese deficiencies are rare, scientists do not have enough information to establish a firm Recommended Dietary Allowance (RDA), therefore the DRI for manganese is given as an Adequate Intake value, based on levels generally consumed by healthy individuals. The DRI for adult women is 1.8 mg per day, and for adult men is 2.3 mg per day. The body's absorption of manganese is very low, about 1% to 15%, which might serve as protection against toxicity. Significant amounts of manganese can be lost

during food processing such as the cooking of beans or the milling of whole grains. Because there is little storage of manganese in the body, most excess manganese is excreted in bile.

As a dietary supplement, manganese usually appears along with other minerals in preparations specific to several disorders. Manganese is sometimes combined with calcium, zinc, and copper and taken for the treatment of osteoporosis. Manganese often is included with chondroitin sulfate and glucosamine hydrochloride in products used to relieve the pain of osteoarthritis. The efficacy of these preparations is unclear, although a few small studies suggest possible benefits.

The UL of manganese is 11 mg for adults per day. Manganese toxicity is a greater threat to one's health than manganese deficiency. Toxicity often is due to inhalation, and not food or water consumption. Most cases are found in industrial workers who are exposed to the metal and who inhale manganese dust on a daily basis. Symptoms include impaired memory and motor coordination, with shaking and tremors that can resemble Parkinson's disease. People with impaired liver function also are at risk of manganese toxicity if they take too many supplements containing manganese.

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See Also: Minerals.

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Margarine and Vegetable Oil Spreads

Margarine is a spread made from vegetable oils, originally invented as a butter substitute. Soybean oil is the most common base in U.S. margarines, but sunflower, corn, palm, safflower, cottonseed, peanut, and canola oils also are used. Margarine's popularity in America soared in the second half of the 20th century when a focus on cholesterol and heart health touted margarine as a healthy alternative spread. The trans fats in margarine are now thought to be a serious health threat,

however, and are being progressively controlled by the U.S. Food and Drug Administration (FDA). Although still popular in other varieties, stick margarine has become a thing of the past. Similar products known as vegetable oil spreads can be produced without the creation of harmful trans fats, and these remain popular consumer choices.

History

Hippolyte Mège-Mouriès, a French chemist, first created margarine in 1869 when Emperor Louis Napoleon III wanted a cheaper fat substitute to mimic the taste and texture of butter (Dalton, 2004). Mège-Mouriès created oleomargarine, a combination of beef fat, milk fat, and water, and named it after one of the components: margaric acid. German and French chemists later discovered the process of hydrogenation, which became used in margarine production. Hydrogenation converts monounsaturated and polyunsaturated fats into saturated fats, allowing the vegetables oils to solidify at room temperature. Consistency and shelf life are dependent on the amount of hydrogenation involved.

From its inception, margarine was cheaper than butter. Dairy businesses felt threatened by margarine's presence in the marketplace, and successfully lobbied Congress to pass the Margarine Act in 1886, which added a two-cent tax to margarine and mandated licenses for its manufacturing and sale (Dalton, 2004). A majority of states forbade coloring the naturally white margarine yellow to look like butter, hoping this would reduce margarine's appeal to consumers. The last coloring law was repealed in 1967, by which time U.S. households were consuming more margarine than butter. (Dyed margarine was contraband in Quebec, Canada, until 2008.) Its popularity increased in the 1970s when public health efforts promoted the notion that margarine was healthier than butter due to its lower saturated fat content and its lack of cholesterol. Research has since shown that the trans fat in margarine could be more harmful than the saturated fats in butter, but the average American today eats almost twice as much margarine-type products as butter.

Ingredients and Health Effects

Although margarine has been thought to be more healthful than butter, the hydrogenation needed to create a spreadable consistency creates trans fatty acids. Trans fats increase "bad" low-density lipoprotein (LDL) cholesterol, tend to lower "good" high-density lipoprotein (HDL) cholesterol, and are associated with a greater risk of heart disease. The Centers for Disease Control estimate that decreasing trans fat consumption in America could prevent up to 20,000 heart attacks and 7,000 deaths each year (Tozzi, 2013). For these reasons, the FDA required trans fat to be listed on nutritional labels starting in 2006 and, as of 2013, partially hydrogenated oils were no longer "generally recognized as safe." This marked the beginning of the end for stick margarine, which contains between 2 and 3 grams of trans fat.

The more solid the margarine is at room temperature, the more trans fat it contains, so the FDA ban will leave room for tub margarine or other varieties. There has been a rise in "light," "soft," "whipped," "squeeze," "spray," and "spread" products, which do not fit the legal definition of margarine and are referred to as "vegetable oil spreads." They contain more liquid oil and water and less partially hydrogenated oil. They typically have fewer calories, less saturated fat, and no cholesterol. Some include canola or olive oil and indicate that they contain "no trans fatty acids" or hydrogenated oils, making them a healthier alternative.

Several spreads also contain plant sterols or stanols that reduce intestinal absorption of cholesterol. Stanols resemble cholesterol in structure and, when ingested, compete with and inhibit cholesterol absorption. Some studies have shown that the consumption of stanols helps reduce total blood cholesterol and LDL cholesterol levels and increase HDL cholesterol levels. Margarines such as "Benecol" and "Take Control," which contain plant stanol and sterols, might be modestly beneficial for people with high cholesterol.

Colleen Irby and Emily Ohrtman

Research Issues

Which is more healthful, butter or margarine/vegetable spreads? Opinion on this question continues to shift as scientists learn more about the health effects of the many types of fatty acids. There are many types of saturated fatty acids, and research suggests that not all of these contribute to the harmful blood lipid profile that increases risk for heart disease. A recent meta-analysis performed by researchers on 72 studies and published in March 2014 *Annals of Internal Medicine* could not find that reducing saturated fat consumption reduced the risk of heart disease. This finding led to many happy comments in popular news media about people being able to resume consumption of butter and other sources of saturated fats. Dr. Walter Willett, the chair of the Department of Nutrition at the Harvard School of Public Health, however, criticized the study as having misleading conclusions. Dr. Willett pointed out that one issue is that, in some of the studies, people who were eating unsaturated fats also were eating highly refined carbohydrates, which also leads to a risk of heart disease.

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See Also: Cardiovascular disease and nutrition; Cholesterol; Fatty acids; Lipids; Transfatty acids.

Further Reading

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Marine Omega-3 Fatty Acids

Oily fish are the major sources of two essential long-chain omega-3 fatty acids called "docosahexanoic acid" (DHA) and "eicosapentaenoic acid" (EPA). These acids have been shown to be important for healthy aging and could play a role in the prevention and treatment of a variety of diseases and disorders. Marine omega-3 fatty acids can be found in fish, such as salmon, tuna, halibut, sardines, and fish supplements and other seafood including algae, krill, some plants, and nut oils, with about 1 gram of omega-3 fatty acids per 3.5 grams of fish (Medline Plus, 2013). Dietary surveys in the United States indicate that the intake of EPA and DHA for an average adult range from 0.04 to 0.07 g per day and 0.05 to 0.09 g per day, respectively, and is about 10 times less than the intake of omega-6 fatty acids



Seafood, especially oily cold-water fish such as salmon, mackerel, sardines, and herring, are good sources of marine omega-3 fatty acids. Fish oil supplements are also manufactured from krill and calamari oil. (Corel)

(Higdon, Drake, & Jump, 2009). The American Heart Association and other public health authorities generally recommend eating at least two servings of fish per week (Medline Plus, 2014).

History

Interest in omega-3 fatty acids, fish oils, and their possible protection against disease gained momentum in the 1970s when surprising research highlighted the unusually low incidence of cardiovascular disease among the Greenland Inuits whose diets contained more than 70% fat (Jump, 2012). The primary source of this fat was found to be from fatty cold-water fish and marine mammals, and the research emphasized that the type of marine fat the Greenland Inuits were consuming protected them against cardiovascular disease. This research was surprising to scientists at the time, because a high-fat diet was thought to cause artery disease.

Biology

Omega-3 fatty acids are polyunsaturated fatty acids (PUFAs), meaning they contain more than one double bond, with the first double bond between the third and fourth carbon atoms from the methyl end of the fatty acid (omega-3). Humans and many mammals lack the enzymes necessary to insert this double bond, thus omega-3 fatty acids are essential nutrients and only can be obtained from the diet. The "parent" fatty acid of the omega-3 series is the short-chain, essential alpha-linolenic acid (ALA) that can go through a series of desaturation (addition of a double bond) and elongation (addition of two carbon atoms) reactions to synthesize the long-chain omega-3 fatty acids, EPA and DHA which contain 20 and 22 carbons, respectively. This process occurs in many mammals, including humans. The rate of this process is fairly slow in humans, however, so to significantly increase the level of EPA and DHA in the body, these fats should be consumed in the diet.

Omega-3 PUFAs are important structural components of cell membranes, affecting cell properties such as fluidity, flexibility, and permeability and the action of membrane-bound enzymes. DHA is found is high concentrations in retinal cell membranes, playing a role in the regeneration of the visual pigment rhodopsin, and postsynaptic neuronal cell membranes, especially in the brain's gray matter where research has shown learning and mood changes with differing DHA concentrations (Higdon, Drake, & Jump, 2009).

Eicosapentaenoic acid and arachidonic acid (AA)—another essential long-chain PUFA that is an omega-6 fatty acid—that are within cell membranes also can be converted to potent chemical messengers called "eicosanoids" during an inflammatory response by enzymes (known as "cyclooxygenases" and "lipoxygenases") to form prostaglandins and leukotrienes, respectively (Higdon, Drake, & Jump, 2009). In general, EPA-derived eicosanoids are less potent inducers of inflammation, blood vessel constriction, and coagulation (blood clotting) than are eicosanoids derived from AA. Which long-chain PUFA is converted into eicosanoids is determined by the concentration found within cell membranes, and

increasing omega-3 fatty acid intake (especially of the long-chain variety) increases the EPA content of cell membranes. Preliminary research has shown that long-chain PUFAs can modulate expression of many genes, including those involved in inflammation (Higdon, Drake, & Jump, 2009). The transcription factor nuclear factor kappa beta (NFkB) is involved in regulating the expression of multiple genes involved in inflammation, and omega-3 PUFAs suppress NFkB content in the nucleus and thus inhibit the production of inflammatory eicosanoids and cytokines (pro-inflammatory cell signaling molecules) (Higdon, Drake, & Jump, 2009).

Health Benefits

Research has shown that increasing intakes of EPA and DHA, either through dietary intake or with supplements, decreases inflammation. This can decrease the risk of cardiovascular disease by preventing arrhythmias that can lead to sudden cardiac death, decreasing the risk of thrombosis, or clot formation, that can lead to heart attacks or stroke, and lowering blood pressure. EPA and DHA also have been shown to decrease serum triglyceride levels, slow the growth of atherosclerotic plaques, and improve the function of blood vessel walls.

Cardiovascular diseases also are the leading causes of death in individuals with diabetes, and a number of randomized controlled trials have found that fish oil supplementation significantly lowered serum triglyceride levels in these individuals. Symptoms of inflammatory diseases such as arthritis and inflammatory bowel disease have been shown to respond to an increased intake of omega-3s, and EPA/DHA consumption even might provide a reduced requirement for anti-inflammatory medications in some people (Higdon, Drake, & Jump, 2009).

Although some studies have found that long-chain omega-3 PUFA intake does not significantly reduce the risk of total mortality or cardiovascular events, recent studies have shown just the opposite (Higdon, Drake, & Jump, 2009). Research methods that do not take into account the use of prescription medications can confound the possible effects from EPA and DHA, masking their effects. The results of randomized controlled trials in individuals with coronary heart disease (CHD) who consumed EPA and DHA from fish or fish oil supplements suggest a beneficial effect, and the American Heart Association recommends that individuals with documented CHD consume approximately 1g per day of EPA and DHA (Higdon, Drake, & Jump, 2009).

EPA and DHA also might have implications for brain health, but larger clinical trials are needed to determine therapeutic efficacy. Data from studies in different countries suggest a correlation between seafood consumption and the national rates of major depression and bipolar disorder (Medline Plus, 2014). Smaller studies also have found lower omega-3 fatty acid concentrations in the blood plasma and adipose tissue of those suffering from depression (Medline Plus, 2014). According to some epidemiological studies, decreased risk of impaired cognitive function, dementia, schizophrenia, and Alzheimer's disease (AD) even could be aided by a high-fish diet. DHA, which is the major fatty acid in the brain, appears to be

protective against AD with observational studies showing that lower serum DHA levels are associated with an increased risk of AD and some types of dementia.

Small studies have suggested that marine omega-3 fatty acids might help prevent macular degeneration, an eye disease marked by the destruction of the retina. EPA and DHA also might slow the progression of osteoporosis in older adults, perhaps because inflammation reduces the production of osteoblasts, the cells that help to manufacture and remodel healthy bone tissue (Medline Plus 2013).

Health Risks

No serious adverse effects have been reported for individuals consuming marine omega-3 PUFAs or fish-oil supplements, and no official upper intake level has been set (Higdon, Drake, & Jump, 2009). The most common adverse effect of fish-oil supplements is the fishy aftertaste, with high doses possibly causing nausea and loose stools. There are potential health risks, however, that have been well studied. Prolonged bleeding times after injury have been observed in Greenland Eskimos with very high intakes of EPA and DHA (6.5 g/day), which could be due to the high EPA-derived eicosanoids that hinder blood clot formation (Higdon, Drake, & Jump, 2009). Also, omega-3 PUFA suppression of inflammatory responses could decrease the potential of the immune system so much so that it becomes inadequate at destroying pathogens in healthy individuals without inflammatory or autoimmune diseases. The FDA has ruled, however, that intakes of up to 3 g per day of EPA and DHA are generally safe and that lesser intake levels are unlikely to result in either of those potential health risks (Higdon, Drake, & Jump, 2009). However, people taking anticoagulant prescription drugs should be cautious when taking fish oil or DPA/EPA supplements and should be monitored by a physician.

The presence of environmental contaminants such as methylmercury, an organic mercury compound that is toxic, with excessive exposure possibly causing brain and kidney damage; and polychlorinated biphenyls (PCBs), which are neurotoxic, are also of concern when increasing fish and marine life intake. In general, larger predatory fish, such as swordfish, tend to contain the highest levels of these contaminants. Removing the skin and fat from fish prior to cooking decreases contaminant exposure, but methylmercury is found throughout the muscles of fish and these cooking precautions will not reduce exposure. Fish oil and other marine-n3 supplements, however, generally are free of these contaminants because they are free of muscle tissue and are generally made with fish body oils that contain lower levels of PCBs and other fat-soluble contaminants than fish liver oils (Higdon, Drake, & Jump, 2009).

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See Also: Alzheimer's disease and nutrition; Arthritis and nutrition; Attention-deficit hyperactivity disorder and nutrition; "Brain foods"; Cancer and nutrition; Cardiovascular disease and nutrition; Depression and nutrition; Eye health; Fatty acids; Inflammation; Lipids; Mercury; Mood and food; The Paleolithic diet; Seafood.

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Mediterranean Diet

The Mediterranean diet refers to a pattern of food consumption based on the traditional diets of the countries found in the Mediterranean region. Traditional diets from this region typically are high in fruits, vegetables, whole grains, legumes, fish, red wine, and olive oil, and relatively low in refined carbohydrates, sugar, and red and processed meats. Early epidemiological studies examining the relationship between diet and health in countries around the world found that people in the Mediterranean region had relatively low rates of cardiovascular disease despite consuming diets relatively high in fat. This discovery was interesting because at the time, dietary fat was suspected to contribute to greater rates of cardiovascular disease. Over time, subsequent research has explored Mediterranean diet patterns and components of the diet and their associations with a variety of health effects. Compared to a Western diet—with higher intakes of meat, refined grain products, and sugar—the Mediterranean diet appears to reduce risk of many chronic illnesses, including cardiovascular disease, type 2 diabetes, cancer, Alzheimer's disease, and depression.

Mediterranean Diet Composition

General recommendations for a healthful Mediterranean diet include the following (Mayo Clinic Staff, 2013).

- Base most meals on plant foods, including fruits, vegetables, whole grains, legumes, nuts, seeds, herbs, spices, and olive oil
- Replace butter and spreads with olive oil, preferably extra virgin olive oil



Example of a meal prepared in the Mediterranean diet fashion. Foods often featured in this diet include olives, garlic, fresh vegetables and herbs, and red wine. (Jose Fuente/Dreamstime.com)

- Consume seafood at least twice a week
- Consume moderate portions of poultry, eggs, cheese, and yogurt
- Limit consumption of red meat, processed meats, and sweets
- Season foods with herbs and spices rather than salt
- For people who habitually drink alcohol, consume red wine in moderation

Experts often recommend combining general Mediterranean diet advice with scientific knowledge. Mediterranean diet researchers Estruch and Salas-Salvadó, for example, advise consumers to choose extra virgin olive oil rather than processed olive oil (2013). Virgin olive oil is extracted mechanically from olives, without the use of solvents. Extra virgin olive oil is the highest in helpful compounds called polyphenols of all forms of olive oil. Experts advise that people striving to eat well should try to limit sodium intake; the USDA suggests 2,300 mg or less per day. Choosing a wide variety of healthful vegetables and fruits contributes to the health benefits of this diet.

Health benefits from consuming a Mediterranean diet are most likely to occur when calorie intake matches calorie expenditure, so that no weight gain occurs. (The exception to this is for people initially underweight who might benefit from

some weight gain.) People who add healthful components of the Mediterranean diet onto their previous Western-style diet might end up consuming too many calories. For example, adding a handful of nuts to one's daily food intake without reducing calorie intake from other sources could lead to weight gain. Adequate levels of physical activity are recommended for a variety of health benefits, as well as to promote a healthful body weight.

Research on the health benefits of the Mediterranean diet suggest that, in addition to the foods consumed on this eating plan, the eating style in this region contributes to good health. Meals are usually consumed slowly, with family and friends, and food is enjoyed. People value fresh ingredients, flavorful food, and culinary skill.

Despite the word "diet" in the term, the Mediterranean diet does not refer to a weight-loss plan. Diet simply refers to dietary pattern. People desiring to lose weight can still follow a Mediterranean diet, but must limit calorie intake more strictly.

Health Benefits

The Mediterranean diet is best known for its association with reduced risk for cardiovascular disease. Some research on the health benefits of a Mediterranean diet has come from a clinical trial known as the PREDIMED trial in Spain. The acronym stands for "PREvención con DIeta MEDiterránea" ("Prevention with Mediterranean Diet"). Ramón Estruch and colleagues tested the Mediterranean diet against a control diet to determine which diet was more effective for heart disease prevention in a study that spanned over five years (Estruch, Ros, Salas-Salvadó, et al., 2013). The study followed rates of heart attack, stroke, and heart disease–related death. The subjects were randomly assigned to one of three groups, two experimental groups that were instructed to follow the Mediterranean diet (one group was supplemented with extra virgin olive oil, and the other was supplemented with nuts as a source of fat), and a control group (participants were instructed to follow a low-fat diet, but many participants failed to strictly follow the diet or dropped out) (Estruch et al., 2013). After five years, the researchers found that the experimental groups had significantly lower death rates from cardiovascular diseases than the control group. The experimental groups showed an overall 30% (the group consuming extra virgin olive oil) and 28% (nuts) lower risk of having a heart attack, a stroke, or dying of heart disease after five years, than the risks of the control group (Estruch et al., 2013). Subsequent research by this group suggests that the Mediterranean diet could slow or even reverse the buildup of plaque in the carotid arteries (the main arteries in the neck that supply the brain with blood) (Casas et al., 2014).

Evidence suggests the Mediterranean diet is associated with reduced risk of stroke, dementia, and depression (Psaltopoulou, Sergentanis, Panagiotakos, et al., 2013). It appears to slow the loss of physical function with aging (Samieri et al., 2013). The Mediterranean diet also might reduce cancer risk (Giacosa et al., 2013). The diet is associated with lower rates of type 2 diabetes and more healthful blood lipid levels (Sofi, Abbate, Gensini, & Casini, 2010).

Proposed Mechanisms Explaining Health Benefits

The health benefits associated with long-term consumption of a healthful Mediterranean diet might be explained by a number of interacting factors, including the following.

- Reduced levels of inflammation—Lower levels of C-reactive protein and interleukin-6, markers of excess systemic inflammation, have been found in subjects consuming a Mediterranean diet (Casas, et al., 2014). Lower levels of inflammation are associated with reduced risk of Alzheimer's disease, heart disease, stroke, and cancer.
- Less oxidative stress—A high intake of antioxidants from plant foods, olive oil, and red wine, might reduce the level of harmful free radicals in the body.
- Slower blood clotting rates—The fatty acid profile of the diet is associated with slower blood clotting rates, reducing risk of thrombosis, which is the formation of blood clots in the vascular system, and can cause a heart attack or stroke.
- Better blood lipid levels—The Mediterranean diet is associated with lower levels of LDL cholesterol, and higher levels of HDL cholesterol.
- Lower risk of hypertension—Lower rates of hypertension (high blood pressure) reduce risk for heart attack and stroke. Lower rates of hypertension could be the result of lesser rates of type 2 diabetes and cardiometabolic syndrome, a healthful intake of minerals such as potassium and magnesium, a low intake of sodium, as well as improved endothelial function.
- Improved endothelial function: Less inflammation and plaque buildup, along with reduced blood pressure, are associated with improved endothelial function. The endothelium is the artery lining, responsible for regulating the opening and closing of individual arteries in response to blood flow needs.

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Research Issues

Which is the best diet for reversing artery disease? People who already are experiencing health problems associated with plaque deposition in the arteries want to know what the best diet is for the stabilization and regression of plaque. People who already have suffered a heart attack usually are advised to follow a very low-fat, plant-based diet, such as that recommended by cardiologist Dean Ornish, enrollment in whose programs are now covered by a number of insurance programs, including Medicare.

Good evidence is accumulating for the Mediterranean diet, however. This diet also generally is perceived to be more palatable to people in North America. The PREDIMED trial (PREvención con DIeta MEDiterránea; "Prevention with Mediterranean Diet"), a research trial conducted in Spain, initially set out to compare the Mediterranean diet to a low-fat diet. The low-fat dieters, however, failed follow their diet recommendations, therefore the comparison could not be made. It also is likely that individuals might respond differently to the two diets. Perhaps, in the future, genetic testing can help inform diet recommendations. It is hoped that

future research will help guide people who are interested in reversing artery disease to understand which eating plan would work best.

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See Also: Alzheimer's disease and nutrition; Cardiometabolic syndrome; Cardiovascular disease and nutrition; Depression and nutrition; Diabetes, type 2; Fatty acids; Inflammation; Marine omega-3 fatty acids; Polyphenols.

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Megaloblastic Anemia

Megaloblastic anemia is a type of anemia that usually is caused by a deficiency of folate or vitamin B12. These vitamins are required for DNA synthesis, and when they are lacking, red blood cells continue to grow and are unable to divide. Megaloblastic anemia is characterized by large red blood cells with an oval shape as opposed to a normal round shape. The cell's nucleus is not fully developed and the bone marrow might not produce as many red blood cells as normal. Megaloblastic red blood cells also can have a life span of less than 120 days, which is the typical life span of a red blood cell.

Reduced levels of folate and vitamin B12 can be caused by several different factors. Inadequate dietary intake occasionally is the problem. Vitamin B12 only is found in animal products, therefore people who do not consume animal products must be sure to consume foods fortified with B12. More often, a deficiency in folate or B12 is caused by problems with vitamin absorption. Digestive problems that can interfere with the absorption of folate and B12 include several autoimmune disorders. One such problem is celiac disease, in which the body's immune system mistakenly destroys the absorptive cells of the small intestine. Another example is a disorder in which the immune system destroys the stomach's parietal cells. The parietal cells produce intrinsic factor, a compound that is required for the absorption of vitamin B12 in the small intestine. When this is the case, the resulting anemia is called "pernicious anemia." Pernicious anemia is one type of megaloblastic anemia.

Crohn's disease and ulcerative colitis are autoimmune diseases in which inflammation is triggered in the gastrointestinal tract. This inflammation can interfere with physiological function, including vitamin absorption. Alcohol abuse can interfere with vitamin absorption, as can many medications, including chemotherapeutic drugs for cancer. Digestive parasites such as tapeworms can reduce folic acid levels. Several inherited disorders also can interfere with vitamin absorption, as can gastrointestinal-tract surgeries.

Symptoms of megaloblastic anemia can be physical or psychological. Physical symptoms include paleness of the skin, fatigue, memory loss, wobbly gait, numbness in the hands and feet, bleeding of the mouth and gums, a smooth and sensitive tongue, and infertility. Psychological effects include dementia, depression, and even personality changes.

Megaloblastic anemia usually is diagnosed with a blood test. Further tests often are required to uncover the source of the problem. Treatment involves correcting the cause of vitamin deficiency. Patients might receive vitamin B12 injections and folate supplements. People with megaloblastic anemia usually are encouraged to consume foods high in folate and vitamin B12. Folate is available in leafy dark green vegetables, lentils, oranges, liver, peanuts, and wheat germ. Vitamin B12 is supplied by animal products such as eggs, meat, and milk, and by fortified cereals.

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See Also: Folate and folic acid; Vitamin B12.

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Melatonin

Melatonin is a hormone produced by a pea-sized gland in the brain called the pineal gland. The hormone helps regulate an individual's circadian rhythm in a complicated process involving light. Because melatonin is found in foods such as fruits, vegetables, grains, and meats, it can be purchased over the counter and taken as a supplement to treat conditions such as sleep issues or jet lag. Melatonin plays many significant roles in the body and shows some promise as a therapeutic agent in the treatment of a number of disorders.

In the 1500s, the father of modern philosophy and French mathematician and scientist, Rene Descartes, claimed that "the seat of the soul" was the pineal gland, where the body, mind, and soul were united. The pineal gland was viewed as vestigial for hundreds of years. In 1958, however, dermatologist Dr. Aaron B. Lerner isolated melatonin from cows' pineal glands at Yale University. Soon after, Lerner discovered that it was a hormone produced in the gland by specific enzymes from serotonin. Serotonin is a neurotransmitter that plays a role in many functions of the central nervous system, such as regulating appetite and mood. Researchers observed that the melatonin in lower animals had a certain relationship with light such that melatonin levels increased at night and decreased throughout the day. Years later, researchers hypothesized that melatonin actually controlled an animal's day and night patterns. The hormone then gained much attention throughout the 1980s and 1990s in the form of new studies and references in the popular media. It was discovered that melatonin causes drowsiness and is present in high levels in carrots, nuts, and tomatoes. Consequently, it became available as a dietary supplement in the 1990s.

Melatonin plays a significant role in the sleep-wake cycle of the body—also called the "circadian rhythm"—as an internal, biological clock. Scientists have just begun to understand exactly how this clock works and how it is affected by exposure to daylight and darkness. When the body is exposed to light, a nerve pathway from the eye's retina to the hypothalamus located in the brain is stimulated. In this area of the brain, a small group of brain cells called the "suprachiasmatic nucleus"

(SCN) sends signals to various parts of the brain regulating body temperature, hormones, and other functions that cause feelings of alertness or drowsiness. By initiating all of these activities, the SCN acts as the body's "clock." The clock starts to increase body temperature, release hormones, and hinder the release of melatonin and other hormones when the body is exposed to the first light of the day.

Thus, in daytime the pineal gland remains inactive. When darkness falls the SCN activates the gland, usually at around 9 p.m. (National Sleep Foundation, 2014). When the pineal gland is "turned on," melatonin is produced and released into the bloodstream, causing feelings of drowsiness. The hormone's levels in the blood decrease back to the hardly detectable daytime levels about 12 hours later. Therefore, bright light not only regulates the SCN clock, it also hinders the release of melatonin. Such activation requires that the body be exposed to little or no light, including both sunlight and indoor lights. Indoor lighting can be bright enough to inhibit melatonin's release into the bloodstream and disrupt the hormone's cycle.

The intricately delicate relationship between melatonin and light—in which light affects the amount of melatonin produced—can easily be disrupted, and such disruption can affect an individual's health in different ways. Melatonin production can be disturbed by any number of factors involving light, such as poor vision, jet lag, shift work, and even seasonal transition. In the winter, for example, the days are shorter with fewer hours of sunlight. This can cause the body to make melatonin later or earlier every day, altering its normal levels in the blood. Because the level of melatonin in the blood can affect an individual's mood, this shift in the timely production of melatonin sometimes causes an individual to develop symptoms of winter depression, more commonly known as "seasonal affective disorder" (SAD). Further, low melatonin levels due to disruption in the hormone's relationship with light can disturb peaceful sleep, which has various consequences on a person's physical and emotional health by causing sleep disorders such as insomnia and mood disorders such as depression.

Melatonin also has many other functions that are not related to sleep. For example, melatonin assists in the regulation of other hormones, such as female reproductive hormones. It contributes to both the timing and release of these hormones and therefore plays a role in women's menstrual cycles. Melatonin helps determine when a woman begins menstruation, how often menses occurs, how long the menstrual cycles last, and when the woman will experience menopause (Ehrlich, 2013).

Low melatonin levels have been associated with increased risk of hormone-related cancers, including breast and prostate cancers. Melatonin has antioxidant properties, and researchers have found evidence suggesting that it contributes to the strength of the body's immune system and prevents cellular damage by acting on free radicals.

Research suggests melatonin dietary supplements or medication could have potential benefits for numerous conditions. Researchers have found strong evidence for melatonin's ability to reset the body's biological clock—several clinical studies reveal melatonin's effectiveness in decreasing sleep latency, increasing sleep duration, and, as a result of improved sleep, heightening a person's alertness during the day. Other convincing evidence concerning melatonin as a treatment for

sleep issues suggests its promising benefits for Delayed Sleep Phase Syndrome (DSPS), insomnia in the elderly, and sleep disturbances in children and adolescents who have neuropsychiatric disorders, mental retardation, and autism.

Some studies suggest that melatonin might decrease the damaging effects of Parkinson's disease. Preliminary evidence suggests melatonin could have possible benefits for the treatment of stroke, high blood pressure, preoperative sedation, smoking cessation, ultraviolet light skin damage, benzodiazepine tapering, chemotherapy side effects, and menopausal psychological symptoms (NIH, 2014). Researchers are investigating the possible use of melatonin as a form of birth control and for treating epilepsy, migraine headaches, idiopathic stabbing headaches, tinnitus, osteoporosis, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, and various other conditions (NIH, 2014).

Although research shows that melatonin might help improve a number of conditions, further evidence is needed to demonstrate that it actually can treat the conditions and whether doing so is safe and effective. Melatonin supplements are available as tablets, capsules, creams, and lozenges. Presently, most people take melatonin as a supplement to treat sleep disorders such as shift-work sleep disorders, circadian rhythm disorders, early morning awakenings, and jet lag. Although consulting a physician is strongly recommended, melatonin is available over the counter in the United States and Canada. In other countries, either a prescription is required or melatonin is not available at all. In fact, melatonin is the only hormone in the United States that does not require a prescription because it is considered a dietary supplement rather than medication and it can be found in some foods. Most commercial melatonin is sold in dosages that can increase melatonin content in the blood to 1 to 20 times the normal level, which could render it ineffective or lead to complications. Additionally, widely accepted dosages of the hormone for people of differing ages and with varying conditions have not been established, although research suggests that an effective dosage is 0.3mg to 1.0 mg. Synthetic or pharmacy-grade melatonin is recommended rather than natural and animal- or bovine-grade melatonin—which consists of extracts from an animal's pineal gland and therefore could contain proteins or viruses that can trigger an antibody response.

Melatonin medications can have many side effects including depression, headaches, nausea, morning grogginess, hormone fluctuations, vivid dreams and nightmares, stomach cramps, irritability, gynecomastia, ataxia, confusion, skin rash, and increased urination. Melatonin must be taken at the right time of day and in the correct dosage for it to be effective. Melatonin supplements have not been demonstrated to be safe for pregnant women or for children.

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See Also: Dietary supplements.

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Mercury

Mercury is silvery-white, heavy metal found as a liquid at room temperature (Winter, 2014). Exposure to very low concentrations of environmental mercury can significantly impact a person's health. These effects of exposure range from minor problems to long-term debilitating illness, depending on the dose and the duration of exposure. Although exposure to mercury is widespread due to the ubiquitous nature of mercury in the environment, many steps can be taken to reduce exposure and minimize impacts on human health.

Types and Sources of Exposure

Mercury is omnipresent in the environment. Many sources contribute to its prevalence—both anthropogenic and naturally occurring events play a role. Mercury can be released into the environment by natural events, for example, volcanic explosion, and through pollution resulting from a variety of industrial processes. Several forms of mercury are present in nature and can impact human health.

Elemental mercury naturally occurs in rocks, air, soil, and living things. Mercury does not typically present a major exposure risk in the elemental form. When elemental mercury is spilled and exposed to air it generally vaporizes slowly. If spilled in a warm environment, however, it vaporizes at a much quicker rate and can produce high levels in indoor air. In the vapor form, mercury is extremely toxic when inhaled. Vaporized mercury can travel great distances and can remain in the atmosphere for a long time. Prolonged exposure to even a small amount of mercury in the vapor state can negatively affect a person's health.

Elemental mercury also can be found in many everyday items, including thermometers, some gold jewelry, and dental amalgam (fillings). Humans can be exposed to mercury when these products are not handled responsibly. There have been many reported cases of children breaking mercury-filled thermometers in their mouths, for instance. The prevalence of these types of accidents has led to the production of safer products, such as alcohol-filled thermometers.

Reducing Seafood Mercury Exposure

The Environmental Protection Agency offers the following advice on limiting mercury intake from seafood, which is especially important for pregnant women and young children.

Fish and shellfish are an important part of a healthy diet. Fish and shellfish contain high-quality protein and other essential nutrients, are low in saturated fat, and contain omega-3 fatty acids. A well-balanced diet that includes a variety of fish and shellfish can contribute to heart health and to children's proper growth and development. Women and young children, in particular, should include fish or shellfish in their diets due to the many nutritional benefits. Nearly all fish and shellfish, however, contain traces of mercury.

By following the three recommendations listed below for choosing and eating fish or shellfish, women and young children can receive the benefits of eating fish and shellfish but avoid exposure to harmful effects of mercury.

- Do not eat shark, swordfish, king mackerel, or tilefish, all of which contain high levels of mercury.
- Eat up to 12 ounces (2 average meals) per week of a variety of fish and shellfish that have lesser mercury levels, including shrimp, canned light tuna, salmon, pollock, and catfish.
- Albacore ("white") tuna has more mercury than canned light tuna. Therefore, when choosing two meals of fish and shellfish, only eat up to 6 ounces (one average meal) of albacore tuna per week.
- Check local advisories about the safety of fish caught in local lakes, rivers, and oceans. If no advice is available, eat up to 6 ounces (one average meal) per week of fish caught in local waters, but don't consume any other fish during that week.

Follow these same recommendations for feeding a young child, but serve smaller portions.

Source: United States Environmental Protection Agency. (2013). *What you need to know about mercury in fish and shellfish*. Retrieved from http://www.fda.gov/food/resourcesforyou/consumers/ucm110591.htm

A more significant threat to the health of humans is exposure to methylmercury. The most common source of exposure in this form is through the ingestion of fish or seafood that contains mercury. Elemental mercury in the soil and sediment can be methylated and converted to methylmercury by certain bacteria living in aquatic environments such as rivers, streams, and oceans. These bacteria containing methylmercury in turn are consumed by small aquatic animals or plants, which then are consumed by larger plants and animals. Through this process, known as "bioaccumulation," animals consume greater concentrations of mercury at each successive level of the food chain.

The concentration of methylmercury that bioaccumulates in fish depends on several criteria, including the pH and temperature of the water; the organismal community within the environment; and the amount of dissolved solids and organic matter present. Due to the many factors that influence bioaccumulation, the concentrations of methylmercury vary from one body of water to another.

Mercury also occurs as an organic compound or as several inorganic salts. In this form, mercury can be used as an ingredient in fungicides, antiseptics, and disinfectants. It also can be found in some preservatives of medicines.

Effects of Exposure

Mercury is classified as a neurotoxin—a substance that alters the activities of nerves, preventing them from functioning. When nerves do not function properly, major damage can be done to the nervous system (both peripheral and central), including the brain. Methylmercury is the only significant neurotoxic form of mercury. The consumption of mercury inhibits amino acid and glutamate transport, leading to excitotoxic effects, or the damage of interneurons. Excitotoxins can cause neurons to fire impulses rapidly for an extended period, leading to a state of exhaustion. Sometimes this exhaustion can lead to neuron death. Mercury exposure also can harm the heart—a correlation between mercury exposure and increased risk for heart attacks has been established. Buildup of mercury in the liver and kidneys can lead to abnormalities in function or disease. Mercury also suppresses the immune system, making the body susceptible to infection. Nerve damage as a result of mercury poisoning generally starts with the loss of sensitivity in hands and feet, difficulty in walking, and slurred speech.

Mercury is especially detrimental to the health of neonates. In many cases mercury exposure goes unnoticed in a pregnant mother, but becomes evident after a child is born and shows symptoms of mercury poisoning. Methylmercury can cross the placenta and poison a fetus—the levels of mercury in fetuses can be up to 30 times greater than that in the mother (Finch & Raines, 2001). Fetal exposure can result in problems with thinking, memory, motor skills, and language. Blindness, hearing loss, seizures and low birth weight can also occur.

Mercury is not only a major threat to the health of humans, but also can have many ecological effects. The fish that consume methylmercury suffer many health consequences, as do fish-eating predators. Harmful effects range from stunted growth and development to reduced levels of reproduction and even death.

Many factors influence the severity of the effect of exposure to mercury, including the chemical type of mercury, the dose and duration of the exposure, the age of the person who is exposed, and the route of exposure. High-level exposure for a short of time, for example, can elicit a multitude of symptoms, including skin rashes, diarrhea, and respiratory distress. Those symptoms differ from the effects of long-term exposure at low levels. This circumstance can result in muscle tremors, irritability, personality changes, and rashes (Minnesota Department of Health, 2013).

Instances of Widespread Exposure

In 1971, Iraq experienced a terrible drought that led to major food shortages. The United States sent Iraq excess grain that had been treated with mercury fungicide to aid in crop production. The grain was supposed to be planted because, although

the fungicide is beneficial to the growth of the crops, it is far too toxic to be consumed directly. Due to a lack of communication concerning the health risks, farmers in Iraq used the grain sent from the United States to make bread. The ingestion of the mercury-permeated bread led to many illnesses and fatalities. More than 40,000 people were poisoned as an effect of the 1971 Iraq Poison Grain Disaster (Foley, 2013).

Japan also experienced widespread mercury poisoning starting in 1956. The poisoning in Japan was an effect of bioaccumulation of mercury in seafood in the Minamata Bay and Shiranui Sea. Methylmercury was released into the bodies of water from the Chisso Corporation's chemical factory. People and animals living in Minamata that consumed seafood began to display irregular behavior due to the mercury poisoning. "Minamata disease" acquired its name from this event and refers to a neurological syndrome that is an effect of mercury poisoning. Common symptoms of Minamata disease include ataxia (loss of balance), speech disturbance, muscle weakness/cramps, and loss of hearing (Allchin, 2014).

Prevention and How to Avoid Exposure

The Environmental Protection Agency (EPA) plays a fundamental role in the regulation of public policy regarding mercury contamination. The Mercury and Other Toxics Standards (MATS) together with other EPA regulations require power plants to limit their emissions of toxic pollutants, including mercury.

The government provides a great amount of information concerning the dangers of mercury exposure to the public. Fish consumption advisories, for example, are released when measured mercury levels in seafood are high. There is an abundance of information regarding mercury exposure, found in all types of media—from health pamphlets to scientific articles.

There are several ways to reduce the chances of mercury poisoning: avoid purchasing products that contain mercury; dispose of mercury and products that contain mercury properly; and only eat large, long-lived fish (shark, swordfish, king mackerel, tilefish) in moderation and in accordance with advisories.

Sophie Dilek

Research Issues

Governments around the world are working to reduce the release of mercury into the environment. The U.S. Environmental Protection Agency, for example, works with local governments, industries, and international organizations. You can explore this work by visiting the EPA's website, listed in the "Further Reading" section.

See Also: Pregnancy and nutrition.

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Metabolic Rate

Metabolic rate refers to the energy expenditure of an organism, and is the energy that is required to sustain metabolism in a given period. Metabolism refers to the entire collection of biochemical processes that occur in the body, many of which require energy. Metabolic rate at any moment depends on the size of the organism and the biochemical processes occurring in the body. These biochemical processes are influenced by the signals that cells receive. Signaling occurs through the action of hormones and other chemical messengers. In animals—including humans—metabolic rate usually is measured in terms of energy units, such as joules or kilojoules. In the United States and a few other countries metabolic rate is also expressed in calories or kilocalories. Basal metabolic rate (BMR) refers to the energy required just to stay alive in a resting state and is measured while a person is awake but resting and lying down. For most people, BMR contributes significantly more than half of the calories expended in a 24-hour period.

Factors That Influence Metabolic Rate

Many factors influence cellular and organism metabolic processes and, thus, metabolic rate. Factors that influence metabolic rate include the following.

Size and Body Composition

Size exerts the greatest influence on BMR, as more cells carrying on metabolic processes result in higher total energy utilization. This is why larger people need to consume more calories than do smaller people. In addition to size, body composition also affects BMR, as fat cells have a significantly lower metabolic rate than most other cells. Muscle is one of the most metabolically active tissues, so a

relatively muscular person will have a higher BMR than an obese person of the same size. If a person's size decreases as a result of weight loss, that person's BMR decreases as well.

Endocrine Hormones and Other Signaling Molecules

The endocrine system refers to the network of glands in the body that produce substances called hormones. These important chemicals travel throughout the body, directing cellular activities in various locations. The pancreas, for example, produces the hormone insulin in response to increasing blood sugar, which usually occurs after a meal. Insulin signals the cells not only to take up sugar (glucose) from the blood, but also to transport protein building blocks (amino acids) into the cells. This initiates a number of other metabolic activities, such as making proteins to repair cells.

The thyroid gland, located in the front of the neck, produces thyroid hormones that exert significant effects on metabolic rate. Too much thyroid hormone (thyroxine) activity results in a condition known as "hyperthyroidism," which causes an elevated metabolic rate. Symptoms of hyperthyroidism include weight loss, rapid heart rate, anxiety, and increased body temperature. Too little thyroxine causes "hypothyroidism," which slows metabolic rate. Symptoms of hypothyroidism include fatigue, low body temperature, constipation, and weight gain.

Hormones produced as part of the body's stress response also influence metabolic rate. For example, epinephrine and norepinephrine are produced by the adrenal glands, which are located on top of the kidneys. These hormones help to stimulate the body's "fight-or-flight" response, also known as the "stress response." Metabolic rate increases during the stress response, as heart and breathing rates increase and muscles contract in preparation for a physical response to an emergency. During stress, biochemical processes increase the availability of blood glucose escalate, contributing to the rise in metabolic rate. Other stress hormones, such as cortisol, contribute to the metabolic processes associated with the stress response. One might suppose that people would lose weight with chronic elevation of the stress response. Although this sometimes is the case, people often overeat when feeling stressed and therefore weight loss might not occur.

Signaling molecules other than endocrine hormones also appear to influence cellular metabolism and metabolic rate—for example, immune cells produce messengers called "cytokines"; adipose tissue produces "adipokines"; and muscles produce "myokines." These protein molecules communicate with a variety of cells throughout the body and influence the cell's manufacture of proteins and other cellular activities, and thus influence the metabolic rate of the organism.

Drugs

Many substances influence metabolic rate. Some drugs, such as caffeine and nicotine, have effects similar to those of the stress response, and thus increase

BMR. Amphetamines have the same effect. Amphetamines have been used in weight-loss medications, although long-term effectiveness for this purpose has not been demonstrated. Anabolic steroids increase BMR, as they stimulate anabolic processes that require energy.

Physical Activity

Physical activity requires muscle contraction, which in turn requires energy. Metabolic rate increases during physical activity. Low- to moderate-intensity activities such as walking or performing household chores can double or triple metabolic rate. More vigorous activity could increase metabolic rate ten or more times above resting level. The greater the exercise intensity, the greater the metabolic rate. Metabolic rate during exercise also is a function of the amount of muscle tissue actively working. An activity using both arms and legs, such as Nordic skiing, for example, expends more energy than activities using fewer muscles, such as walking. Physical activity that is especially prolonged or of high intensity results in a small elevation in metabolic rate during the post-exercise period, as body temperature and metabolic processes return to resting levels.

Even minor physical activity, such as fidgeting in one's chair, chewing gum, and doing household chores increases metabolic rate during the period of the activity. Similarly, metabolic rate during inactivity is relatively low. Metabolic rate reaches its lowest levels during quiet sitting and sleeping. One might think that reducing sleep time would enhance weight-loss efforts by increasing daily energy expenditure. People seem to experience greater levels of hunger and greater daily calorie intake when sleep-deprived, however, therefore reducing sleep hours does not appear to enhance weight-reduction efforts.

Age

Basal metabolic rate varies with age. Metabolic rate increases during periods of growth, such as during childhood and adolescent growth spurts. Metabolic rate tends to decline as people age. Much of this decline is attributed to loss of muscle mass, but some of the decrease could be related to a decline in the functional level of other organs. Hormone levels that change with age also could help explain the age effect on metabolic rate.

Sex and Menstrual Cycle Effects

Men tend to have slightly higher metabolic rates than women, even when size and body composition are taken into account. The difference might be explained by variation in the action of the sex hormones. In young women, metabolic rate also varies with menstrual cycle phase. Metabolic rate is lowest about one week before ovulation and highest during the week before the menstrual period begins.

Eating Behavior

Metabolic rate increases after eating, as energy is required for digestion and absorption. Spicy foods raise BMR slightly. Calorie restriction—especially severe calorie restriction—reduces BMR and also can lead to physiological suppression of a variety of metabolic functions in an effort to conserve energy in the face of starvation. For example, body temperature could fall. Some women stop menstruating when calories are severely restricted. People also could experience fatigue and can conserve energy by reducing levels of physical activity.

Measuring and Estimating Metabolic Rate

Metabolic rate can be measured in several ways. Performing such measurements requires specialized equipment and supplies, making them quite expensive to perform. Such measurements therefore are used primarily in research and clinical settings. Several formulas have been devised to estimate basal metabolic rate and daily energy expenditure.

Direct Calorimetry

Direct calorimetry measures the heat loss of an organism. Heat loss is proportional to metabolic rate, as heat is a by-product of metabolism. For direct calorimetry measurements, a person (or other organism) is placed in a sealed chamber that is surrounded by a water "jacket." The water captures the heat that the organism releases while inside the inner chamber, and the water temperature increases. The increase in water temperature is measured and then used to calculate metabolic rate. The chambers required for performing direct calorimetry are expensive; therefore other methods of measuring metabolic rate are used more commonly.

Indirect Calorimetry

Indirect calorimetry estimates metabolic rate by measuring an animal's oxygen utilization and carbon dioxide production. Special chemical bonds in fuel substrates, including carbohydrates, proteins, and fats (and alcohol), are used to produce energy through metabolic pathways. Oxygen is used in this process, and carbon dioxide is produced. Indirect calorimetry involves measuring the oxygen and carbon dioxide concentrations in an organism's inspired and expired gases. The volume of inspired air also must be measured. Indirect calorimetry instrumentation is available in many clinical facilities and kinesiology laboratories.

Doubly Labeled Water

The "doubly labeled water" technique involves the administration of water containing two "labels." The label refers to an isotope—a form of an element with a greater than normal atomic mass. In the case of doubly labeled water two

isotopes are used. One is the hydrogen isotope, deuterium (^{2}H), and the other an oxygen isotope, oxygen-18 (^{18}O). Both of these isotopes are nonradioactive and occur in nature. The replacement results in $^{2}H_2O$ and $H_2{}^{18}O$. A blend of these two waters is given to the person or laboratory animal.

Doubly labeled water can be used to measure energy expenditure and, thus, metabolic rate. The atoms in the labeled water make their way—via metabolic processes—into carbon dioxide and all of the body's water compartments. Carbon dioxide produced by the organism then contains some of the labeled oxygen; the labeled hydrogen and the labeled oxygen appear in body water. Measuring where the labels end up enables calculation of carbon dioxide production in a given period and, thus, metabolic rate. The labeled water, collection procedures, and instruments for analyzing isotope presence in water and carbon dioxide are expensive, therefore this technique primarily is used in clinical and research settings. Additionally, the doubly labeled water technique only can provide an average metabolic rate for a relatively long period, typically 14 days.

Estimation Formulas

A number of prediction formulas for estimating metabolic rate have been developed. One of the most widely used is the Mifflin-St. Jeor equation (Frankenfield, Roth-Yousey, & Compher, 2005; Kelly, 2012). To use these equations, the subject's weight in kilograms (lbs / 2.2); height in centimeters (inches x 2.54); and age in years.

Males: (9.99 x wt) + (6.25 x ht) – (4.92 x age) + 5 = BMR in kcals/day
Females: (9.99 x wt) + (6.25 x ht) – (4.92 x age) – 161 = BMR in kcals/day

Although these formulas provide a decent approximation of 24-hr BMR, an individual's BMR could be more than 10% greater or less than the calculated figure, therefore results should be applied with caution.

Barbara A. Brehm

Research Issues

People trying to lose weight or prevent obesity could focus on various strategies for increasing metabolic rate. Interesting laboratory research suggests, however, that lower metabolic rate is related to a longer life expectancy. Research on insects, rodents, dogs, and other organisms suggests that animals whose basal metabolic rate (BMR) is lower live up to 30% longer than control subjects with normal BMRs. Lower metabolic rate is achieved in laboratory settings by a sizeable reduction in calorie intake (usually a 25% to 30% reduction). Researchers have speculated that reducing metabolic rate reduces the oxidative damage associated with metabolism, because metabolic processes generate a number of harmful chemicals as a by-product of their reactions. Would calorie restriction and a lower BMR extend life in humans? Some research groups are studying this question, examining the metabolic changes that occur in humans voluntarily reducing energy intake (Gertner, 2009).

At present, a link between food restriction, lower BMR, and longevity has not been established in humans. The calorie restriction and consequent weight loss have been associated with some health improvements, however, most notably a reduced risk for type 2 diabetes. Of course, the diet is very hard to follow, and theoretically could initiate or contribute to the development of eating disorders in vulnerable individuals. Frail elders and older adults with low muscle and bone mass also could be harmed by this type of diet.

See Also: Calorie; Energy balance; Metabolism; Obesity, causes; Obesity, treatment.

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Metabolism

Metabolism refers to all of the physiological and biochemical processes that take place in an organism. These processes include both those that build up molecules and material substance, as well as those that break down substances—both enable an organism to maintain life. "Anabolism" refers to processes that build smaller compounds into larger substances. The processes that break down larger substances into smaller units are referred to as "catabolism." Additionally, metabolism includes the processes of converting energy from one form to another—a primary characteristic of living things. In humans, metabolism includes the processes that build new cellular components, cells, and tissues; that break down and remodel substances such as cellular components and larger structures such as muscle and bone; and the cellular biochemical reactions that produce energy. To execute all of the metabolic processes in the human body, thousands of chemical processes occur at every moment.

The word "metabolism" also refers to specific biochemical pathways, or the pathways that involve a particular substrate or substance. Nutritionists refer to

"carbohydrate metabolism," for example, to refer to how the body breaks down the carbohydrate molecules in food into smaller components, and how those components are used in the body to produce energy, are made into other substances, or are excreted.

In animals—including humans—some of the most important metabolic processes are those that capture energy from the chemical bonds in the carbohydrate, protein, and fat molecules found in food, and store that energy in special high-energy phosphate bonds. All fuel substrates are broken down by similar processes that produce the molecule adenosine triphosphate (ATP) from adenosine diphosphate (ADP). The cells of the body then use the energy stored in ATP to do everything—including producing hormones and neurotransmitters, contracting muscle fibers, and repairing a bone fracture. Other high-energy bond carriers also are found in the body. These include phosphocreatine and guanosine triphosphate. The use of ATP in the body results in energy expenditure. When energy expenditure is expressed per unit of time it is known as "metabolic rate." Metabolic rate can be measured in calories per unit of time, such as calories per minute.

Metabolic pathways are aided by the action of enzymes, special catalysts that help biochemical reactions occur at a reasonable pace. Enzymes are large protein molecules whose shape helps to bring two substances together so that they can form a chemical bond. The enzyme's shape also can help to bring one substance into contact with another substance that causes the first to break into smaller pieces.

Cellular metabolic activities are influenced by a number of factors. Some of these factors are part of the cell itself—for example, receptors in the cell membrane and intracellular signaling molecules help to direct many cellular metabolic processes. Hormones released by special glands that comprise the endocrine system also influence metabolism. Thyroxine from the thyroid gland, for example, helps to regulate the speed of energy use and production. The pancreas releases the hormones insulin and glucagon that tell cells whether to take up glucose from the blood and make it into storage molecules such as glycogen (a form of starch) or triglyceride (a form of fat), or break down these molecules and release glucose into the blood to help raise blood glucose level.

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See Also: Calorie; Energy balance; Metabolic rate.

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Microbiota and Microbiome

In terms of human nutrition, the "microbiota" refers to the collection of microbes living on and within the human body. It is estimated that the number of cells belonging to microbes inhabiting a person's body outnumbers the number of human cells by ten to one. The collective genome of the microbiota is referred to as the "microbiome" (The Human Microbiome Project Consortium [HMP], 2012). Various types of microbes inhabit humans; some are "commensals," meaning they neither harm nor benefit their host; some are "mutualists," meaning that they live symbiotically with their host, and a few are potentially harmful pathogens. In addition, the microbiota is not composed solely of bacteria. The microbe population in the gut, for instance, consists largely of bacteria, but also includes some archaea, viruses, protozoa, and fungi (He, Marco, & Slupsky, 2013).

Although the microbiota inhabits most of the body, research to date has focused on four main habitats, oral, gut, skin, and vagina. The diversity and populations within these habitats is quite variable, but a relatively distinct community characterizes each one (HMP, 2012). Interestingly, variations in microbe communities of different habitats are so pronounced that samples taken of the same habitat from two different individuals will have more similar microbe communities than samples taken from two different habitats on one individual (HMP, 2012).

Even though similarities in microbe communities exist within habitats, there still is an incredibly broad range of microbial species observed within healthy individuals. In other words, there is an enormous range of "healthy" microbiota populations. All microbial communities—regardless of how varied in species composition—seem to perform essentially the same basic functions. Thus, research suggests that the microbiota cannot be characterized by a core species population, but can be characterized by a core set of functions, that is, a core microbiome (Lozupone, Stombaugh, Gordon, Jansson, & Knight, 2012).

Development and Changes

An individual's microbiota typically grows and develops over the first three years of life and then becomes relatively stable (Lozupone et al., 2012). An infant has no microbiota when it is in the womb, but microbe colonization begins immediately upon birth. After birth, an infant's microbiota continuously propagates and diversifies in response to changes, such as the introduction of solid food to the diet. Research has found that mode of delivery, vaginal versus C-section, has a significant effect on infant colonization. Specifically, babies born vaginally are colonized by their mother's vaginal microbiota whereas babies born via C-section are colonized less optimally by their parents' skin microbiota.

One of the most marked differences between an infant's developing microbiota and that of an adult is the high proportion of bifidobacteria regularly observed in infants (Lozupone et al., 2012). Breast milk contains a complex carbohydrate, "oligosaccharide," which an infant's GI tract cannot digest; yet the bifidobacteria in the infant's microbiota can digest oligosaccharides. Hence, breast milk promotes

the proliferation of bifidobacteria in an infant's GI tract, which serves to crowd out potentially harmful microbes and to nurture the gut epithelium. This in turn helps prevent infections and inflammation.

Factors believed to influence microbiota development include daily diet, environment, host genetics, and the host's early microbial exposure (HMP, 2012; Lozupone et al., 2012). After initial colonization, however, the microbiota of an individual is relatively stable. One study compared samples of an individual's microbiota taken at different times with samples taken from other individuals. It found that the samples varied less within the individual over time than they varied between individuals. Moderate changes can occur in an individual's microbiota, however those changes typically are less distinct than variations seen between individuals and thus are not considered significant. In general, the microbiota's stability can be attributed to a strong resistance to colonization by "new" microbe species (Lozupone et al., 2012).

An individual's microbiota though typically stable is not completely unchangeable. Antibiotic use and a drastic transformation in diet can significantly alter the microbiota; in the absence of such factors, the microbiota only exhibits insignificant variation. Studies suggest that one course of antibiotics can significantly change the state of one's microbiota for years. In particular, a course of antibiotics can increase the amount of antibiotic-resistant genes in the microbiome (Lozupone et al., 2012). Additionally, a substantial change in diet (for instance replacing a Western diet with a diet consisting primarily of whole foods) can alter the stable state of an individual's microbiota in a few as three to four days (Feltman, 2013).

The ability of diet to affect microbiota composition is demonstrated by the fact that there exists a definite relationship between plant-based versus meat-based daily diets and gut microbe communities. People consuming a largely plant-based and fiber-rich diet generally have a high proportion of *Prevotella* bacteria in their gut microbiota. Conversely, individuals living on a diet more abundant in meat typically have microbiotas exhibiting a high proportion of *Bacteroides* bacteria (Lozupone et al., 2012). Additionally, research suggests that the Western diet is harmful to gut microbiota due to the predominance of processed foods. By the time easily digested processed food reaches the further end of the intestine the food has been stripped of virtually all nutritional value, and leaves the microbiota that inhabit the later stages of the GI tract malnourished.

Remarkably, culture and community have been shown in multiple studies to have strong correlations to microbiota composition and function. Most notably there is a vast difference between the microbiota and microbiomes of (Western) urbanites and people living in rural locations. These differences could be due to dietary patterns. Differences in antibiotic use, intake of processed food, and in day-to-day exposure to bacteria, however, all are likely contributors to discrepancies as well (He, Marco, & Slupsky, 2013).

Evolutionary Theory

Theory suggests that humans did not evolve to perform the tasks of the microbiome themselves due to the high adaptability of microbes; they have an ability to

adjust to changes in their environment much faster than humans can. The microbiota plays an essential role in optimal nutrient and energy absorption from food. Historically, the diets of hunter-gatherers could shift dramatically within a short time. Consequently, from an evolutionary standpoint it makes more sense for humans to rely on readily adaptable microbes for ideal nutrient and energy extraction than it does for them to rely on their own bodies (Feltman, 2013).

Additionally, the microbiota has the advantage of "gene trading"; a characteristic not possessed by humans. Simply put, bacteria can transfer genetic material (and thus, traits) between each other. Before food hygiene became as prevalent as it is today, the ingestion of food included the ingestion of the microbes living on food. The microbes living on certain food are able to sustain themselves by digesting that food. Thus, when food and its indigenous microbes are consumed, there is the possibility that the food microbes will transfer their digestive capabilities to the GI microbiota of the person eating the food. By this mechanism humans can gain the ability to digest previously indigestible foods, such as seaweed (Discover, 2010).

Interactions with Host

Some key interactions between the microbiota and host occur in the digestive tract and influence both digestion and immune function. In terms of digestion, the microbiota is responsible for the breakdown of specific compounds that the human body cannot digest (Lozupone et al., 2012). Microbial activity in the GI tract aids in the efficiency of harvesting energy from food and also impacts synthesis; bioavailability; and function of nutrients, vitamins, and drugs. The majority of microbial metabolic activity takes place in the colon. One example of important colonic microbial metabolic activity is the digestion of polyphenols. Only after microbial metabolic processing can the metabolites derived from polyphenols be absorbed by the body. The absorption of polyphenol metabolites, as well as other metabolites, contributes beneficially to an individual's health and metabolism (He, Marco, & Slupsky, 2013; Ramakrishna, 2013).

The microbiota not only provides digestive benefits, but also plays a key role in immunity. The gut microbiota protects against enteropathogens, for instance, by crowding out potentially harmful microbes (Lozupone et al., 2012). Gut microbiota also help protect immune function by nourishing the gut epithelium. Significant disruptions in the gut microbiota impair its ability to properly nourish gut epithelium, which results in increased gut permeability. Endotoxins are a by-product of bacteria and increased gut permeability allows those endotoxins, as well as proteins, to enter the bloodstream. In response to the presence of foreign bodies in the bloodstream, the immune system mounts a body-wide immune response known as low-grade inflammation. Multiple studies have demonstrated the negative health effects of low-grade inflammation by linking it to chronic diseases and metabolic syndrome (Pollan, 2013).

Popular Research Areas

One particularly popular topic of microbiota research is exploring the relationship between the microbiota and obesity. High proportions of two types of gut bacteria in the microbiota have been linked to obesity. These specific bacteria have the ability to send hunger signals to the brain and can also affect fat storage. A study on mice indicated that the microbiota of genetically obese mice include a type of bacteria which could digest otherwise indigestible polysaccharide chains into short-chain fatty acids that the mice then stored as complex lipids. In short, the obese mice digested polysaccharides that were indigestible to lean mice and then stored the extra energy from the polysaccharides as additional body fat, thereby contributing to their obesity (Turnbaugh et al., 2007).

Some research has demonstrated that simply looking at an individual's microbiota is a 90% accurate method of predicting leanness versus obesity (Lozupone et al., 2012). The microbiota of obese individuals is characterized by a distinct lack of microbe diversity. In particular, the microbiota of obese individuals usually is associated with a depletion of "Bacteroidetes" and an excess of "Actinobacteria" as compared to a lean person's microbiota. Researchers hypothesize that gut microbiota affect an individual's energy homeostasis, fat storage, energy extraction from food, as well as other processes related to weight. Fortunately, differences between lean and obese gut microbiota have proven useful in treating metabolic syndrome. A Swedish study found that implanting a lean individual's microbiota into an individual with metabolic syndrome had a beneficial effect on the recipient's metabolic health (Pollan, 2013).

Abigail Mosca

Research Issues

Another recent area of interest to researchers is probiotics: substances that supposedly promote microbiota health. Currently, the understanding is that probiotics could affect the microbiota in one of two ways: through interaction with the intestinal epithelium (from which the microbiota derives some of its nutrition) and immune cells, or through direct interaction with the microbiota (He, Marco, & Slupsky, 2013; Ramakrishna, 2013). The idea is that probiotics have the ability to produce antimicrobial compounds that could help "good" bacteria outcompete "bad" bacteria. For instance, some bacteria produce a peptide called bacteriocin. Bacteriocin simultaneously promotes the growth of beneficial bacteria and inhibits the growth of potentially harmful bacteria, such as E. coli, and therefore has potential as a probiotic (Angelakis, Merhej, & Raoult, 2013).

Research has not yet fully determined the mechanisms leading to the benefits of probiotics. Positive results have been observed in the use of probiotics as treatment for traveler's diarrhea, antibiotic-induced diarrhea, and to prevent relapse diarrhea in individuals with *C. difficile* infections. Long-term safety has not yet been scrutinized, however, and there exist very few studies exploring potentially adverse effects of probiotic use (Angelakis, Merhej, & Raoult, 2013).

See Also: Digestion and the digestive system; Large intestine; Prebiotics; Probiotics.

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Milk Thistle

Milk thistle, *Silybum marianum*, is a flowering herb that produces round purple flowers. Remedies produced from the milk thistle fruit and seeds commonly are used to treat a variety of liver and gallbladder disorders. The active flavonoid component of milk thistle, "silymarin," is composed of three compounds, silybin, silydianin, and silychristin. Silymarin exhibits antioxidant activity and could thus help protect cells from free radical damage. Additionally, laboratory studies show that silymarin could prevent toxins such as acetaminophen from binding to liver cell receptors and causing liver damage. Silymarin also appears to interact with the immune system, influencing processes of inflammation. Preliminary research suggests that milk thistle remedies might be somewhat helpful for chronic liver

diseases caused by alcohol or other toxins. Milk thistle products also have shown some potential benefit for the treatment of seasonal allergies.

Native to the Mediterranean region, milk thistle now also is grown in North America and South America, as well as in South Australia (Abenavoli, Capasso, Milic, & Capasso, 2010). Milk thistle's name is thought to come from the legend that a drop of the Virgin Mary's milk caused white veins to appear on a milk thistle leaf. According to the Bible story, as Mary searched for a place to sit and nurse the baby Jesus, the only shelter she could find was a bower formed by the prickly milk thistle. This plant is also known as "Mary thistle," "holy thistle," and by a host of other names. Blooming from July to August in northern countries, milk thistle has been used for more than 2,000 years by ancient physicians and herbalists worldwide for liver and gallbladder disorders, especially hepatitis, cirrhosis, and jaundice. Milk thistle also has been used for the treatment of poisoning, such as poisoning from mushrooms.

Many cell-culture and laboratory studies support the beneficial biological activity of milk thistle (Abenavoli et al., 2010), making the remedy worthy of further study. Its usefulness in the treatment of liver disease caused by the hepatitis C virus, however, has been questioned. Two well-designed large-scale studies suggest that milk thistle offers only limited benefits for people with this serious disorder. One study enrolled people with chronic hepatitis C who had not responded to standard treatment with antiviral medications. Subjects taking higher than normal doses of silymarin and people taking a placebo had similar liver function results, demonstrating that milk thistle conferred no benefit in this group (NCCAM, 2012). An earlier study on patients with the hepatitis C infection examined the time course for the development of cirrhosis in patients taking silymarin or a placebo. Researchers found no difference in viral activity or the severity of liver disease in the two groups, although the patients who took silymarin experienced milder symptoms of liver disease and a better subjective quality of life (NCCAM, 2012). Both groups showed similar progression to cirrhosis (a condition in which nonfunctional fibrotic tissue replaces health liver tissue). Although this study did not support the effectiveness of milk thistle for patients with severe hepatitis C, it still is possible that milk thistle could be helpful for other disorders, including other liver diseases and less-severe liver infections.

Milk thistle supplements appear to be fairly safe. Some people have reported gastrointestinal side effects when taking milk thistle supplements. Others have developed allergic reactions; most commonly the people who are allergic to ragweed, chrysanthemum, marigold, and dandelion, because milk thistle belongs to the same family as these plants. It has also been found that milk thistle sometimes reduces blood sugar levels, which might be problematic for people with diabetes who are taking medications to regulate blood sugar levels. Milk thistle might interact with the metabolism of cholesterol-lowering drugs such as statins.

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See Also: The liver.

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Mindful Eating

Mindful eating is a practice derived from Buddhist teachings that involves eating with present-moment awareness. The technique attempts to transform one's relationship with food to develop a greater sensory awareness of the eating experience, while responding to the body signals of satiety and hunger. These practices are said to help with unhealthy eating habits and could lead to a greater sense of well-being and self-acceptance.

Mindful Eating Practice

This exercise asks a person to focus mindfully on eating, trying to keep attention focused on the food and the act of eating. Mindfulness means simply observing with awareness the sensations, feelings, and thoughts in the present moment. Try to observe the experience without judging or analyzing it. Readers might wish to try this exercise with a friend, so one person can read the instructions aloud and the other perform the exercise.

Begin by taking a raisin or other small piece of food that you enjoy. (If you don't like raisins, try a piece of chocolate or a slice of an apple or other fruit.) Hold the food in your hand and notice its appearance. Sense the weight of the food and raise it to your noise to smell it. After observing the food, place it in your mouth. Observe any sensations associated with this action, such as the weight of the food on your tongue or the release of saliva into your mouth. Begin to slowly chew the raisin, observing its taste and texture and the feeling of chewing. Notice the impulse to swallow; as you swallow, focus on the sensations of swallowing the food and the way your mouth feels after you swallow.

A variation of this exercise is to try eating an entire meal in this same mindful fashion, focusing on the food and the process of eating. Do not read, talk, or watch TV while eating the meal. Chew each bite thoroughly and pay attention to levels of hunger and fullness. When your mind starts to wander, simply bring your focus back to your food and the process of eating. Observe the shapes, colors, aroma, flavors, and textures of the food. Pay attention to the sensations of tasting, chewing, and swallowing. Enjoy the pleasure of eating delicious food. Stop eating when you feel like you have had enough food.

Mindfulness refers to the practice of deliberately paying attention and cultivating awareness in the present moment. Mindfulness practice also includes detaching oneself from identification with one's beliefs, thoughts, and emotions, and being open and accepting to all experiences as they occur. Mindful eaters focus not just on what they are eating, but how they are eating—paying close attention to the total eating experience. This practice encourages paying attention to flavors, colors, textures, smells, temperatures, sounds, and the origins of the food. Habits of self-criticism and distractions are observed with detachment, and feelings of gratitude and appreciation for the meal are encouraged.

Mindful eating can become a helpful antidote for mindless eating, which often is caused by eating in a rush, eating with a distracted or judgmental mind, or eating without awareness of when the stomach is full. Mindless eating is especially prevalent for people whose lives move at a fast pace with significant levels of distraction and stimulation. Many people, for example, eat while working at their computer, watching television, or driving in a car. Distractions can result in a less satisfying eating experience, and can contribute to a compulsive pattern of eating more because of a lack of satisfaction.

Additionally, a stressful eating environment interferes with digestive processes. The branch of the nervous system known as the "parasympathetic nervous system" governs the "rest and digest" functions; it is active when a person is relaxed. Any type of stress or preparation for physical activity activates the sympathetic nervous system, which inhibits the parasympathetic nervous system and thus, digestion. The sympathetic nervous system is especially aroused during the stress response; feelings of stress can interfere with digestion and even cause or worsen digestive disorders such as irritable bowel syndrome. Eating mindfully can activate the parasympathetic nervous system, and often reduces problems such as excess intestinal gas, bloating, stomach aches, and bowel irregularities.

Mindful eating can help prevent overeating. Not only is eating more satisfying, but the signals of hunger and satiety become clearer, as a person takes the time to pay attention to these feelings. (Satiety refers to the feeling of having had enough to eat.) It takes about 20 minutes for the hormonal signals indicating that one has had enough to eat to stimulate the feeling of satiety. When people eat quickly, they can eat more than they actually need to eat, so their chances of overeating increase.

Studies suggest that eating mindfully could be related to eating less. One study for example, divided 29 female college students into three groups, which consumed a standard meal under three conditions (Higgs & Donohoe, 2011). In the first condition, subjects ate while listening to a recording that guided them to focus on the sensory characteristics of the food they were eating and the process of eating. The second group read a newspaper article about food. Subjects in the third group simply were asked to eat their meal and were given no other direction. Later in the afternoon, subjects were presented with three plates of cookies and allowed to eat as many as they wished. The study found that subjects who ate mindfully chose significantly fewer cookies later in the day. They also had more vivid memories of their lunch foods than subjects in the other two groups.

The authors suggest that memory of previous meals could influence food intake later in the day and that eating mindfully enhances memory (Higgs & Donohoe, 2011). Eating when distracted could lead to more eating later in the day. Another study performed by the same research group, for example, found that women who watched television during a meal ate more for their afternoon snacks than women who did not watch television during a meal (Higgs & Woodward, 2009).

Although mindful eating might be beneficial for the general population, it could be especially helpful for people with disorders characterized by overeating, such as binge-eating disorder (BED) and bulimia nervosa, an eating disorder characterized by both overeating and harmful purging behaviors. Mindfulness has been used to help people become more detached from the strong emotional responses often linked to eating, and provides awareness for signals of satiety. Clinical studies suggest that eating-specific mindfulness trainings can increase awareness of hunger and satiety, reduce feelings of anxiety and depression, and reduce binge-eating behavior (Kristeller & Wolever, 2011).

Multiple tips and techniques have been developed to improve mindful-eating habits (*see* Mindful Eating Exercise sidebar). Some suggestions include beginning a meal with some type of spoken or silent grace that helps one cultivate a grateful attitude; taking one's first few bites of food with full attention; enjoying the first five minutes of a family meal in silence; setting a kitchen timer to make sure a normal-sized meal lasts for at least 20 minutes; and eating one meal a week mindfully and alone. Meals should be consumed without television, reading, or other distractions. Many people find that creating a pleasant eating environment with an attractive table, including items such as candles and flowers, encourages mindful eating.

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See Also: Binge-eating disorder; Bulimia nervosa; Digestion and absorption; Irritable bowel disorder.

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Minerals

Minerals are inorganic substances found in nature. Many minerals are required by the human body and perform a variety of essential roles. In the human diet, minerals are elemental atoms or ions, unlike carbohydrates, vitamins, proteins, or fats, which are organic compounds. Minerals are fairly stable elements and remain unchanged by surrounding or environmental factors such as heat, light, or pH (acidity or alkalinity). That is, minerals found in the body—such as iron in hemoglobin—retain the same chemical structure and are unchanged, unlike carbohydrates and proteins.

Minerals are considered micronutrients, meaning that they are needed in the body in minute amounts, at no more than a few grams or milligrams per day. They are further subdivided into major minerals and trace minerals (sometimes called "microminerals"). Major minerals must be consumed in the diet and are found throughout the body and in larger amounts. Trace minerals are found in the body and are needed in the diet in minute amounts.

More than 20 minerals are thought to be essential to health. Some appear in the body, but researchers are not sure what role they play. Arsenic, for example, occurs in the body in very small amounts, but its function in the body—if any—is unknown. Vanadium is thought to be essential in very small amounts, although its roles in the body are unclear.

Major minerals include calcium (Ca), chloride (Cl), magnesium (Mg), phosphorus (P), potassium (K), sodium (Na), and sulfur (S). Trace minerals include copper (Cu), chromium (Cr), fluoride (F), iodine (I), iron (Fe), manganese (Mn), molybdenum (Mo), selenium (Se), and zinc (Zn).

Minerals can be found in all of the food groups, including meats, eggs, dairy products, fruits, vegetables, nuts, legumes, seeds, and grains. Minerals also are found in water and beverages. The mineral content of plants is contingent upon the minerals in the soil in which the plants were grown, thus richer soils produce mineral-rich plants. Moreover, the time of harvest and plant maturity also influence mineral content of plants. The mineral content of water varies with the environment in which the water is found.

Mineral absorption occurs in the gastrointestinal (GI) tract; many minerals are absorbed in small amounts. The amount of minerals absorbed from the GI tract is dependent on many factors, including the amount of the specific mineral in the GI tract and the amount of other minerals in the GI tract at a given time. Absorption varies because some minerals, such as calcium, iron, zinc, and

magnesium all have very similar chemical characteristics, which causes them to compete for absorption. For this reason, it is important to avoid consuming too much of one mineral; the body often has difficulties expelling the extra amount, and too much of one mineral can inhibit the body's absorption of other minerals. The presence of dietary fibers and other constituents, such as oxalate and phytate (organic acids commonly found in foods) that can bind to minerals reduce mineral absorption in the small intestine. The presence of certain substances such as vitamin C enhances absorption. Absorption also varies with a person's need for a given nutrient. Absorption often increases during pregnancy, for example, when more iron, calcium, and other minerals are required. People with iron-deficiency anemia require greater amounts of iron, so they usually absorb iron more readily.

Minerals have a wide range of health effects and functions in the human body. Sodium is involved in cellular regulation and impacts the amount of fluids in the body. Excess sodium also is linked to an increase in blood pressure, which can lead to hypertension. Potassium is involved in signal transduction pathways, muscle contraction, and blood pressure regulation. Chloride helps maintain the body's fluid balance and is a component of stomach acid. Calcium is essential to bone health, nerve function, cellular metabolism, muscle contraction, and blood clotting. Phosphorus is a component of bone tissue and energy production compounds and is responsible for various enzyme-activating processes. Magnesium also is found in the bones and is present in more than 300 enzyme reactions, such as DNA and protein synthesis, blood clotting, muscle contraction and production of ATP. Sulfur is part of organic nutrients, such as vitamins, and helps maintain protein shape and structure.

Some minerals in the diet, such as lead and mercury, are harmful to health. Like all minerals, they can accumulate in the body. To prevent negative health effects, these are best avoided. Public health agencies, such as the Environmental Protection Agency, often enact regulations to reduce human exposure to these harmful agents.

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See Also: Arsenic; Calcium; Chloride; Chromium; Copper; Fluoride; Iodine; Iron; Iron-deficiency anemia; Lead; Magnesium; Mercury; Molybdenum; Phosphorus; Potassium; Selenium; Sodium and salt; Vanadium; Zinc.

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Molybdenum

Molybdenum is a mineral that is essential for both plant and animal metabolism. It serves as a cofactor for at least three important enzymes that promote oxidation in the human body. A cofactor is a compound that enables an enzyme to be active. Plants obtain molybdenum from the soil and animals obtain the mineral from plants, or from animals that have eaten plants. Molybdenum deficiencies rarely are found, and excess molybdenum does not appear to have any beneficial effects in terms of health promotion or disease prevention. Molybdenum levels in the food supply are highest in legumes, grains and grain products, and nuts.

Molybdenum deficiencies rarely are found in North America in people who consume a varied diet, as soil levels of molybdenum are good. Symptoms of molybdenum deficiency are observed in people with a rare genetic disorder—molybdenum cofactor deficiency—which interferes with the production of sulfite oxidase, an enzyme found in the mitochondria that is required for the metabolism of the sulfur-containing amino acids, cysteine and methione. This disorder causes severe neurological symptoms, brain damage, and death. Although the disorder is not caused by a molybdenum deficiency, it illustrates what a total molybdenum deficiency would be like. Molybdenum deficiency once was observed in a patient on total parenteral nutrition (all nutrients supplied through an intravenous solution) when molybdenum was absent from the parenteral solution (Higdon, 2001). The symptoms of molybdenum deficiency included night blindness, muscle weakness, and mental disorientation. Once the cause of his symptoms was discovered, and molybdenum added to the feeding solution, the patient recovered.

Although several therapeutic claims have been made for molybdenum supplements, they have little research support. Research on medical applications for cancer patients suggests that, because molybdenum interferes with copper absorption and because copper is required for making new blood vessels, molybdenum drugs might slow cancer growth by inhibiting angiogenesis (Molybdenum, 2011). Only a handful of studies have looked at molybdenum-based therapies of this nature in humans, however, and a strong effect has not yet been observed.

The U.S. Dietary Reference Intake (DRI) for molybdenum is 45 mcg per day for adults. Humans absorb 80% to 90% of the molybdenum in their food and, unlike the absorption of many other minerals, absorption of molybdenum is not inhibited by dietary fibers or phytates. Molybdenum toxicity does not occur very often. In one report of an adult male ingesting between 300 mcg and 800 mcg of molybdenum per day over an 18-day period, acute psychosis with seizures and other neurological symptoms were observed (Higdon, 2001). In another study, however, four healthy young men demonstrated no acute symptoms with molybdenum intakes of 22 mcg to 1,490 mcg per day (Turnlund, Keyes, & Peiffer, 1995). In grazing animals, copper and molybdenum interact, so that high levels of molybdenum intake cause copper deficiencies, and low levels of molybdenum in the grasses lead to copper toxicity. Researchers are investigating optimal levels and

balance of these two minerals in grazing animals (Zhang et al., 2012). At present, however, this balance appears to be less critical in humans. The tolerable upper intake level set by the U.S. Food and Nutrition Board is 2,000 mcg per day.

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See Also: Minerals.

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Monoterpenes

Monoterpenes are 10-carbon molecules that are found in the oils of many plants and often are utilized in alternative medicine. The flavor of most fruits, spices, vegetables, and herbs can be attributed to one of the more than 2,000 aromatic monoterpene compounds presently known. Monoterpenes are found in many foods, including citrus fruits, garlic, carrots, celery, cilantro, parsley, potatoes, peppers, caraway seeds, sage, dill, basil, and mint. The close analysis of monoterpene content in grapes is significant for winemaking. Monoterpenes also are critical components of many perfumes and artificial food flavorings. The mass production of monoterpenes through the metabolic engineering of yeast strains is an area of heavy research, with implications for industrial and medicinal applications (Fischer, Meyer, Claudel, Bergdol, & Karst, 2011).

Monoterpenes are employed in a variety of medicinal areas. Monoterpenes are the basis of aromatherapy, in which essential oils are proposed to have several healthful and mood-enhancement effects. Although only a few well-controlled scientific studies have evaluated aromatherapy, preliminary results suggest certain monoterpenes do exert measurable effects. One study, for example, found that a treatment consisting of lavender oil suffused into the air of a hospital ward for dementia patients was associated with lower levels of agitation in the patients than was a placebo condition (EBSCO, 2013a). Essential oils containing

monoterpenes also can enhance the effects of massage when incorporated into the massage treatment. How does aromatherapy work? Monoterpenes from the oils might be absorbed into the lungs or, in the case of massage, through the skin. Monoterpenes also might exert an effect by activating the olfactory centers in the brain.

Some monoterpenes appear to have therapeutic effects when ingested. Eucalyptus oil and its associated monoterpenes frequently are found in cough drops and syrups. Essential oil therapies containing the monoterpenes cineole, d-limone, and alpha-pinene have shown promise for treating respiratory conditions such as acute and chronic bronchitis, as well as sinus infections. Of great interest are the monoterpenes limonene and perillyl alcohol, derived primarily from orange peel and lavender oil, respectively. Their mechanism of action is not known, but a few possibilities exist. These monoterpenes administered in high therapeutic doses might inhibit cholesterol synthesis, which in turn reduces cholesterol's contribution to tumor formation. They also might increase certain detoxifying liver enzymes, which could prevent cellular damage. Further, these compounds could trigger apoptosis (programmed cell death) in cells with damaged DNA and have even greater protective effects. It should be noted that these results only have been tested in animal models, and it is too soon to recommend monoterpene therapies for cancer treatment in humans.

Monoterpene supplements come in many varieties. The essential oils do not appear to have serious side effects when used as directed, although some of the topical oils cause skin sensitization or eye irritation. Because of the limited research, these supplements probably should be avoided by people with compromised kidney or liver function, as well as by pregnant women.

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See Also: Beta-carotene; Lycopene.

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Mood and Food

Research supports the common-sense notion that the food one consumes and one's mood are interrelated. Psychologists use the word "mood" to refer to how a person feels psychologically. Some researchers distinguish mood from emotion using the word "emotion" to refer to shorter, more intense feelings experienced in response to a specific stimulus, such as something perceived to be disgusting or frightening. "Mood" generally is used to refer to more diffuse and longer-lasting feelings that might or might not be triggered by something in particular. Moods also could reflect underlying mood disorders, as when people with depression are likely to experience depressed moods. People's moods can influence what types of food they choose to eat, such as when a person is feeling stressed and reaches for "comfort food." The opposite is true, as well; peoples' moods can be influenced by what they eat.

Reward Sensitivity

The choice of food that a person makes often comes from the anticipated pleasure he or she expects to feel by eating something in particular; people select foods that they enjoy eating. Several factors impact which foods are remembered as pleasurable, including past experiences, hunger level, a food's sensory properties, and physiological needs. Individuals have different levels of reward sensitivity that they receive from consumption of particular foods. Those who are more sensitive to reward will experience the pleasure of eating foods more quickly and frequently. Research has shown that people with high reward sensitivity are more likely to experience food cravings, binge eating, body weight, and preference for foods high in fat (Griffiths, 2013).

Stress

Chronic stress can cause the craving for "comfort foods," which often are high in calories, fats, sugar, and salt. From a psychological perspective, the craving for specific comfort foods could stem from memories of feeling comforted when eating these foods earlier in life. Stress can cause the brain's reward system to crave more sugar and fat. Additionally, when stressed, there is less motivation to think about the healthier choice, which makes comfort foods more appealing. Several studies have found that stress—both perceived and chronic—causes an increase in the drive to eat high-calorie fatty foods (e.g., Groesz et al., 2012). Research has shown that women are more likely than men to engage in overeating behaviors when feeling stressed, anxious, depressed, or lonely (Griffiths, 2013).

One interesting study suggests that certain nutrients or foods might influence mood, even without the "comfort" associations. The study examined the effect of fatty acids combined with a "sad" stimulus. Subjects in the trial received either a fatty acid infusion (to eliminate any conceived notions about comfort foods) or a

saline infusion. Then they were exposed to a neutral or sad stimulus (subjects viewed photographs). The subjects rated their mood, and their brain activity was tracked using MRI scans. The results of the study revealed that the fatty acid infusion attenuated the effect of sad emotions as compared to the saline placebo (Van Oudenhove et al., 2011). In other words, when people had some fat in their stomachs, they did not feel as sad when viewing the sad content. The researchers proposed that communication between the digestive system and the brain influences people's experiences of mood. This could help explain why many people are motivated to eat in response to certain moods.

Tryptophan and Carbohydrates

There has been much research examining the link between foods high in tryptophan and mood elevation. Tryptophan is an important amino acid that the human body cannot produce on its own. Tryptophan aids in the production of melatonin, serotonin, and niacin. Serotonin is an essential mood regulator. This neurotransmitter helps decrease feelings of depression and anxiety. Some foods high in tryptophan include yogurt, milk, cheese, turkey, chicken, shellfish, eggs, lentils, brown rice, almonds, seeds, mangos, bananas, and chocolate. Studies examining the relationship between acute tryptophan depletion (ATD), serotonin levels, and mood show that people with clinical depression experience decreased mood after acute tryptophan depletion (ATD), thus showing a plausible link between low tryptophan levels and depressed mood. Tryptophan depletion is induced in these studies by feeding subjects a meal without tryptophan. In one study, subjects receiving tryptophan supplements showed an increase in agreeableness and decrease in quarrelsomeness (Young & Leyton, 2002).

Tryptophan enters the brain more easily (crossing the blood-brain barrier) when carbohydrates are consumed concurrently. Studies have shown that higher glycemic index foods can elevate mood in some people. One research group, for example, conducted a study to analyze the effect of a moderate glycemic index (MGI) energy bar on professional dancers. The experimental group ate the MGI bar and the control group had only water. The experimental group had significantly higher pleasure scores than those of the control group (Brown & Wyon, 2014).

Omega-3 Fatty Acids

Researchers have found a strong link between regular consumption of omega-3 fatty acids and depression. Omega-3 fatty acids are found in foods such as fish, walnuts, kidney beans, cauliflower, broccoli, and seeds. Omega-3 fatty acids appear to influence the activity of neurotransmitters in the brain. For example, one interesting study tested omega-3 supplements over a short period in people with major depressive episodes. The subjects taking omega-3 supplements had reduced depression symptoms as compared to those subjects taking placebos (Lespérance et al., 2011).

Chocolate

A popular belief often promoted in the media is that chocolate improves mood. Cocoa contains low levels of several types of psychoactive chemicals, including anandamides, tyramine, and theobromine. These chemicals influence the neurotransmitters serotonin, dopamine, and endorphins, which alter mood, behavior, and perception. Several studies have shown that, for many people, chocolate reduces negative mood.

It is likely that chocolate-cravers notice this association and develop motivation to consume chocolate when experiencing negative moods. The idea that chocolate can elevate mood was examined in a study that required people with high cravings for chocolate and people with low cravings for chocolate to follow a two-week chocolate-deprivation trial. The results showed that individuals in the high chocolate-craving group generally were more likely to experience greater levels of anxiety (Moreno-Dominguez, Rodríguez-Ruiz, Martín, & Warren, 2012).

Caffeine

Evidence shows that caffeine is easily absorbed into the body tissues, especially into the brain. Caffeine is found in various foods and beverages, including coffee, tea, chocolate, cocoa powder, coffee ice cream, and some soft drinks and energy drinks. People vary widely in their response to caffeine. Caffeine improves alertness and attention, and commonly is experienced as improving mood. Too much caffeine, however, can cause feelings of anxiety and restlessness. For some people, any amount of caffeine is associated with negative moods.

Fruits, Vegetables, and Diet Quality

Several studies have indicated that greater intakes of plant foods (fruits, vegetables, legumes) and healthful fats along with reduced intakes of refined grains, added sugars, artificial fats, and dessert-type foods are associated with a decreased incidence of mental disorders, nervousness, depression, and with elevated levels of happiness, quality of life, and mental well-being. One study, for example, found an association between intake of fruits and vegetables to subjects' reports of feeling more energetic, calm, and happy. Researchers White and colleagues (2013) had 281 students keep a food diary for 21 consecutive days. The students recorded how they felt, what they ate, and how many servings of vegetables, fruit, and unhealthy snacks were eaten each day. The results showed a correlation between high intake of fruits and vegetables and positive moods (White, Horwath, & Conner, 2013).

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See Also: "Brain foods"; Depression and nutrition; Marine omega-3 fatty acids.

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The Mouth

The mouth, or oral cavity, is the opening to the lower half of the human face and is the gateway to the gastrointestinal tract. Digestion begins here as the mouth chews, lubricates, and swallows ingested food.

Starting with the muscular lips, food is manipulated and brought into the oral cavity. Subject to an adducting and abducting mandible and along with 32 teeth, including the cutting incisors and grinding molars, the food is mechanically broken down through the process of mastication (chewing). Aided by the salivary glands located below the jaw, next to the jaw, and in front of the ear, food is moistened and the mouth is lubricated to facilitate the passage of the bolus—the rounded food mass—down the esophagus. The primary organ of taste, the tongue, also serves a vital role in food "deglutition," which is the act or process of swallowing. Stemming from the floor of the mouth, the tongue is a muscular, mobile organ. When the tongue elevates and retracts against the hard palate, it forces the bolus past the soft palate and uvula, into the pharynx.

Swallowing Disorders (Dysphagia)

Most people take the act of swallowing food for granted. Swallowing, however, is a complex action that requires the coordination of several muscle groups. Difficulty swallowing is a condition known as "dysphagia." Excerpts from information on dysphasia from The National Institute of Neurological Disorders and Stroke are provided below.

Swallowing Disorders

Trouble with swallowing (dysphagia) is a symptom with many neurological disorders. The problem can occur at any stage of the normal swallowing process as food and liquid move from the mouth, down the back of the throat, through the esophagus, and into the stomach. Difficulties can range from a total inability to swallow, to coughing or choking because the food or liquid is entering the windpipe, which is referred to as "aspiration." When aspiration is frequent, a person can be at risk of developing pneumonia. Food can get "stuck" in the throat, or individuals might drool because they cannot swallow their saliva.

Neurological conditions that can cause swallowing difficulties include stroke (the most common cause); traumatic brain injury; cerebral palsy; Parkinson's disease and other degenerative neurological disorders such as amyotrophic lateral sclerosis (ALS, also known as Lou Gehrig's disease), multiple sclerosis, progressive supranuclear palsy, Huntington disease, and myasthenia gravis. Muscular dystrophy and myotonic dystrophy are accompanied by dysphagia, which also is the cardinal symptom of oculopharyngeal muscular dystrophy, a rare, progressive genetic disorder.

Treatment

Changing a diet by adding thickeners helps many people, as does learning different ways to eat and chew that reduce the risk for aspiration. Occasionally drug therapy can help dysphagia. In some people, botulinum toxin injections can help when food or liquid cannot enter the esophagus to get to the stomach. More severely disabled individuals could require surgery or feeding tubes.

Prognosis

The prognosis depends upon the type of swallowing problem and the course of the neurological disorder that produces it. In some cases, dysphagia can be partially or completely corrected using diet manipulation or noninvasive methods. In other cases, it might require aggressive intervention such as a feeding tube. For those with progressive degenerative neurological disorders, dysphagia is only one in a cluster of symptoms and disabilities that require treatment.

National Institute of Neurological Disorders and Stroke. (2014). *Swallowing disorders information page*. Retrieved from http://www.ninds.nih.gov/disorders/swallowing_disorders/swallowing_disorders.htm

Covering the entirety of the mouth—and much like the skin which forms a physical barrier from the environment—is the oral mucosa. Composed of a surface epithelium that protects the underlying connective tissue, the oral epithelium is lubricated by mucous secretions, hence the term "oral mucosa." Each defined by

their differing functions and regions, the oral mucosa can be divided into three main types, masticatory, lining, and specialized mucosa. Characterized by its tough keratinized epidermis layer, the masticatory mucosa of the hard palate and gingiva (gums), are tightly bound to the underlying bone so as to resist abrasion and masticatory forces. Areas of the oral mucosa such as the cheeks, lips, ventral surface of the tongue, soft palate, and floor of the mouth comprise the lining mucosa. In each of these mucosal regions, the epithelium is non-keratinized to allow for mobility and distension and is thicker than the masticatory mucosa. Lastly, due to its unique lingual "papillae" (small hair-like structures that have both mechanical and sensory functions), the dorsal surface of the tongue is neither classified as masticatory nor lining mucosa; it is known as the "specialized mucosa."

The oral cavity is a dynamic environment—with turnover rates of about 14 to 20 days for the lining mucosa, and 24 days for the masticatory mucosa (Squier & Kremer, 2001). It is home to a complex and flourishing microbiota in which 6 billion microbial cells consisting of roughly 500 bacterial species found on the tongue, cheeks, gingiva, and teeth, along with species of viruses and yeasts, are produced every 1 to 2 hours. In the presence of both commensal and pathogenic bacterial communities, the oral cavity and mucosa must serve as a physical barrier to the external environment, as well as provide biochemical and immunological functions (Rouabhia, 2002).

A dynamic equilibrium generally exists between the oral flora—free-floating microorganisms, and dental plaque bacteria—and its host. Changes in pH, diet, drug use, radiation exposure, and dental hygiene can result in imbalances in this homeostasis maintained between the host and oral microbial communities, manifesting as diseases such as gingivitis in which the local bacteria growth exceeds a certain limit resulting in gingival inflammation. Likewise, in children afflicted by the protein-calorie deficiency disease known as "Kwashiorkor," the previously commensal microbiota of the mouth can begin to adversely affect the oral cavity by invading the muscosal tissue and resulting in an infectious condition called "cancrum oris." The interaction between the host and its microflora, however, if met with positive hereditary, hormonal, and nutritional factors, establishes a protective state whereby the bacterial communities create and maintain an effective host-defense barrier.

Sometimes described as a mirror that reflects an individual's health (Rouabhia, 2012), research suggests that the oral cavity and mucosa can evidence early signs and symptoms of nutritional deficiencies or systemic disease (Thomas & Mirowski, 2010). Some of these signs and symptoms can be caused by relationships between the oral microbiota and nutrition. Diets that are rich in fermentable carbohydrates, for example, can lead to the accumulation of bacterial plaque and gingival inflammation through bacterial processes that exacerbate the cohesion of plaque and facilitate its cohesion to the gingiva. Thus, nutrition can also have direct—yet sometimes difficult to identify and isolate—impacts on the oral mucosa. Poor nutrition can lead to atrophy of the epithelium, causing a reduction in the number of epithelial layers and size of individual cells. In high-income countries where high caloric intake is common, arteriosclerosis and obesity are indicated by excess

deposits of adipose tissue in the oral mucosa. Other nutritional complications such as vitamin A, vitamin B3, and vitamin C deficiencies are reflected in the oral cavity by reduced resistance to infections and symptoms of dry mouth (xerostomia); burning mouth, reds bands along the gingiva (erythema of the gingiva), and dental caries (cavities); and gingival bleeding, swollen gingiva, and infections, respectively (Thomas & Mirowski, 2010).

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See Also: Digestion and the digestive system; Salivary glands and saliva.

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Multivitamin and Mineral Supplements

Multivitamin and mineral (MVM) supplements contain three or more vitamins and minerals at a dose below the tolerable upper level regulated by the Food and Drug Administration's (FDA) Center for Food Safety and Applied Nutrition. These supplements commonly are referred to as "multis," "multiples," and "vitamins." They can be taken in the form of tablets, capsules, pastilles, powders, liquids, and injections.

History

The word "vitamin" was introduced in 1912 as an abbreviated term for the important factors in the diet, or "vital amines." The identification, isolation, and purification of nutrients in the early 20th century raised the possibility that optimal health outcomes could be achieved through nutrient supplementation (Lichtenstein & Russell, 2005). The fortification of diets began in the United States in 1924, with the addition of iodine to table salt to prevent goiter. Diet fortification continued with the addition of vitamin D to milk in 1933 to prevent rickets, and the addition

of thiamin, riboflavin, niacin, and iron to flour in 1941. In the early 1940s, the first MVM tablet was introduced.

Prevalence

The use of nutritional and dietary supplements in the United States is highly prevalent, with about one-third of adults using MVMs regularly (ADA, 2009). Although it is largely uncommon in the United States to have a clinical deficiency of vitamins and minerals—with the exception of iron—supplement use continues to grow in popularity. The U.S. supplement industry continues to grow in the sale of MVMs, reaching $28 billion in annual sales in 2010 (Guallar, Stranges, Mulrow, Appel, & Miller, 2013). Contributing to industry growth is the aging of the population and desire to achieve optimal health. Data suggest that individuals using dietary supplements tend to be older, white, well educated, affluent, and more likely to consume a healthy diet, and have lesser rates of smoking (Lichtenstein, & Russell, 2005).

Targeted Supplementation

Targeted recommendations for the supplemental use of multivitamin and mineral supplements primarily benefit certain population segments that require additional nutrients to prevent deficiencies. The *Dietary Guidelines for Americans* (DGA) state that such supplements could be useful when they fill a specifically identified nutrient gap that cannot or is not otherwise met by the individual's food intake (DGA, 2010). Among the groups most likely to benefit from MVM supplementation are the following.

- Women of childbearing age who might become pregnant
- Pregnant women recommended by the DGA to consume folic acid from supplements and fortified foods to reduce the risk of neural tube defects
- Women who are breast-feeding
- Older adults (the ability to absorb nutrients can decline with age)
- People of all ages with irregular dietary patterns such as people with food allergies, vegans, or people who diet or restrict calories

Effectiveness

Although multivitamin and mineral supplementation can assist in meeting RDAs, research has not found them to be very effective in preventing heart disease or cancer. A 2013 study in the *Annals of Internal Medicine* found that MVM supplementation provided only a borderline-significant benefit in the reduction of cancer risk, and only in men (Fortmann, Burda, Senger, Lin, & Whitlock, 2013). Researchers in another study found that MVMs did not slow cognitive decline among men age 65 and older compared to participants taking placeboes (Grodstein et al., 2013). A study specifically examining MVM role in preventing another heart

attack found no difference in rates of another heart attack, chest pain, the need for hospitalization, cardiac catheterization, or rates of stroke and early death between people taking vitamins and those taking placeboes (Lamas et al., 2013). A reoccurring issue in clinical studies is that many participants take the pills inconsistently, stop taking the pills, or do not take the pills as often as is recommended. It also is possible that, in some studies, individuals who develop health problems could start taking MVM supplements, artificially strengthening the association between MVM supplements and illness, thus making it difficult to draw firm conclusions about the actual benefit of MVM supplements.

Complications

Supplement users who exceed the recommended tolerable upper intake limits (ULs) for nutrients, increase the risk of adverse health effects. The upper limits can be exceeded when the individual takes a high-dose supplement, takes multiple products having the same ingredients, or consumes a diet rich in fortified foods. The ingestion of a large amount of nutrients can cause metabolic interferences of other nutrients and can prevent absorption.

Nutritionists agree that a balanced diet of foods having abundant vitamins and minerals is the best strategy to meet nutrient needs. Natural food sources such as fruits, vegetables, whole grains, beans, nuts, and seeds provide nutrients beyond vitamins and minerals, including fiber, phytochemicals, and fatty acids. Data suggest that positive health outcomes are more closely related to dietary patterns than to the intakes of individual nutrients.

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See Also: Dietary supplements; Minerals; Vitamins.

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N-Acetylcysteine

N-acetylcysteine (NAC) is a special form of the nonessential dietary amino acid cysteine. It does not occur naturally in the diet, but is manufactured in the laboratory. N-acetylcysteine stimulates the body's production of glutathione, a small protein composed of three amino acids. Glutathione is found in most cells; it acts as an antioxidant and is vital to the body's constant process of free-radical scavenging. Glutathione acts as a cofactor for some important enzymes, appears to stimulate the immune system, and has other biological activities as well. (Glutathione supplements do not increase glutathione levels in the body, as the small protein is quickly broken down during digestive processes.) N-acetylcysteine is used clinically to help treat a number of serious health problems, including liver failure, heart disease, and chronic bronchitis. It also is marketed as a daily antioxidant supplement, although its value to human health still is under investigation.

N-acetylcysteine appears to act through two main biochemical pathways, it helps facilitate cellular glutathione biosynthesis, increasing bodily reserves of the vital antioxidant glutathione; and it scavenges for potent free radicals by providing molecular groups with which those radicals can bond. Throughout the body's normal metabolic conversion of molecular oxygen to water, unpaired oxygen atoms—also known as "free radicals"—frequently are produced as a by-product. Due to the presence of unpaired electrons, these free radicals are intensely reactive and can cause irreparable harm to cell parts, including to the DNA in still-replicating cells. The body's main defense mechanism against such harm from free radicals is antioxidant protection—particularly from glutathione, whose lone thiol group provides electron pairs to free radicals, eliminating their previous reactivity. A growing body of data suggests that the oxidative stress caused by an imbalance between cell-destroying free radicals and cell-defending glutathione could be a leading contributor to several health problems.

In clinical settings, NAC has been in common use for more than 50 years, most notably as an antidote for toxic acetaminophen (a common over-the-counter pain medication; the brand name is Tylenol) overdose. In such cases, NAC can replenish glutathione levels and bind with the acetaminophen metabolites to speed their excretion. N-acetylcysteine also has been used pharmaceutically to treat a life-threatening condition called "acute respiratory distress syndrome," in which people experience difficulty breathing. This disorder is most likely to occur in people who have chronic lung diseases, such as chronic bronchitis and emphysema.

N-acetylcysteine also appears to enhance the effectiveness of nitroglycerin treatment for chest pain with coronary heart disease (disease that leads to inadequate blood flow to the heart muscle). It is important to note that the health problems described herein are serious and sometimes life threatening; people should not attempt to treat these conditions solely with dietary supplements and should seek emergency medical care immediately.

N-acetylcysteine has shown some preliminary results in the treatment of infertility in women with polycystic ovary syndrome. Additionally, NAC might reduce respiratory symptoms in people with lung disease, and could be helpful for the treatment of a psychological disorder known as "hair-pulling," and possibly for other obsessive-compulsive behaviors and addictions. It could be helpful in the treatment of some cancers, although its antioxidant behavior might protect cancer cells as well as normal cells (Memorial Sloan-Kettering Cancer Center, 2013).

N-acetylcysteine is marketed as an antioxidant supplement that promotes health, prevents serious diseases, and provides general liver protection. Evidence for these claims presently is fairly weak. One interesting double-blind, placebo-controlled study found that daily administration of NAC reduced influenza symptoms in a group of older adults (De Flora, Grassi, & Carati, 1997). Subjects took 600 mg of NAC or a placebo twice a day for 6 months. During this period, 25% of people in the NAC group experienced flu-like symptoms, and 79% of volunteers in the control group experienced symptoms. Of note is that the level of flu antibodies in the blood of the participants was the same for both groups, indicating that influenza infection rates probably were similar. Researchers speculated that NAC could have exerted an effect by strengthening immune response (De Flora, Grassi, & Carati, 1997). N-acetylcysteine supplements appear to be fairly safe, although they might cause headaches in people who take them together with nitroglycerin medication.

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See Also: Antioxidants.

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National Weight Control Registry

The National Weight Control Registry (NWCR) is the largest and longest-running prospective study of successful long-term weight-loss maintenance. The NWCR was established in 1994 by obesity researchers Rena R. Wing and James O. Hill. The NWCR solicits information from individuals who have lost at least 30 lbs. and have kept the weight off for at least one year. Early studies from the center included 629 women and 155 men who had lost on average more than 66 lbs. and kept the weight off for at least five years (Klem, Wing, McGuire, Seagal, & Hill, 1997). Since the NWCR's establishment, the sample has grown to more than 10,000 people, 3,000 of whom have been in the registry for more than 10 years. For this 10-year group, the average weight-loss maintenance is 51 lbs. (maintained for 10 years) (NWCR, 2014). The National Weight Control Registry is a groundbreaking initiative that identifies factors that contribute to successful weight-loss maintenance to provide beneficial suggestions regarding effective weight management.

History of the National Weight Control Registry

Obesity is recognized as a chronic disease with no known successful universal treatment. Obesity rates in North America and around the world continue to climb and are contributing to skyrocketing health care costs and declining health. For decades, researchers primarily have focused on comparing methods of weight loss rather than long-term weight management, the greatest challenge in treating obesity. Evidence suggests, however, that short-term dieting instead of permanent healthy lifestyle alterations has had little to no impact on obesity rates.

Prior to the creation of the National Weight Control Registry, research on weight-loss maintenance had examined only small samples of individuals from one study or treatment program. Because commercial programs typically do not publish or gather data from participants, very little was known about how people could successfully maintain weight loss. The lack of information along with disparity on how successful weight loss was defined, led to the idea that 95% to 99% of people fail at long-term weight loss (Wing & Hill, 2003). The results of small studies containing only participants from one treatment program often are applied to the general population. The 1959 Stunkard & McLaren-Hume study, for example, which followed 100 obese individuals in a nutritional weight-loss program still frequently is cited for its finding that—two years after the program—only 2% had maintained a 20-lb weight loss (Wing & Hill, 2001). Similar studies had tried to correct common flaws by including a larger sampling, developing a universal definition of weight loss, and including individuals who lost weight on their own.

In 1993, obesity researchers Rena R. Wing and James O. Hill set out to learn from the rare individuals who were successful at long-term weight-loss maintenance in a self-selecting, longitudinal study that would become known as the National Weight Control Registry. The goal was to identify the factors associated with successful weight-loss maintenance (Wing & Hill, 2003). The Registry,

Table 1. Reports on Diet by National Weight Control Registry Participants

Behavior Information	
Modifying both diet and exercise	89% of participants
Modifying diet alone	10% of participants
Restricting intake of type of food	88% of participants
Limiting quantity of food	44% of participants
Counting calories	44% of participants
Lost weight on their own	45% of participants
Used a commercial weight-loss program	55% of participants
Food Information	
Average (reported) intake	1,381 kcal/day 24% kcals from fat 19% kcals from protein 56% kcals from carbohydrates
Average meals/snacks	4.87
Average fast food per week	0.74
Average restaurant meals per week	2.5
Eat breakfast daily	78%

Source: Data taken from Successful Weight Loss Management, by R. R. Wing & J. O. Hill (2001), *Annual Reviews Nutrition,* p. 327.

Table 2. Reports on Physical Activity and Behavior by National Weight Control Registry Participants

Behavior Information	
Weigh themselves daily	44% of participants
Weigh themselves at least once a week	31% of participants
Report improved quality of life	95.3% of participants
Report increased level of energy	92.4% of participants
Lost weight using physical activity alone	1% of participants
Calories expended by exercise: female	2,545 kcal/week (approx. 1 hr/day)
Calories expended by exercise: male	3,293 kcal/week (approx. 1 hr/day)
Report walking plus other activity	49%
Report solely walking	28%
Report other regular exercise	14%
Incorporate regular weight lifting: male	24%
Incorporate regular weight lifting: female	20%

Source: Data taken from Successful Weight Loss Management, by R. R. Wing & J.O. Hill (2001), *Annual Reviews Nutrition,* p. 327

managed at Brown Medical School and The Miriam Hospital Weight Control & Diabetes Research Center in Providence, Rhode Island, has generated a great deal of interesting results and dozens of scientific publications.

Inclusion Criteria and Participants

Participants in the NWCR must be 18 years of age or older and maintain a 30-lb or greater weight loss for at least one year. Wing and Hill define successful weight loss as an intentional reduction of 10% body weight, because this modest weight loss is associated with a reduction in the risk for diabetes and cardiovascular disease. By this definition, more than 20% of overweight individuals are successful at losing weight (Wing & Hill, 2001). In addition to signing paperwork giving informed consent to participate in the study, participants receive a packet of questionnaires inquiring about their weight history, family history, demographic information, method of weight loss, and behaviors associated with their long-term weight-loss management, including diet and exercise regimen. These surveys are distributed annually with an 80% return rate—a rate comparable to that of similar studies. Additionally, 83% of participants provide some type of documentation verifying weight, and all are required to identify a physician who can provide verification (Wing & Phelan 2005).

The database created by the NWCR contains a somewhat diverse group of individuals in terms of behaviors associated with weight loss, but not a representative sampling in terms of the national population. Statistically speaking, 77% of participants are women, 82% are college educated, and 95% are Caucasian (Wing & Phelan, 2005). The average woman in the study is 45 years old and weighs 145 lbs. The average male is 49 years of age and weights 190 lbs; within these groups, however, there are extremes. Participants have lost between 30 lbs and 300 lbs and have maintained it for up to 66 years (NWCR, 2014). Genetics and family history—factors that take much of the blame associated with obesity—are supported by the National Weight Control Registry as playing a significant role in determining obesity in adulthood. The study reported that 46% of participants were overweight by age 11 years and another 25% became overweight between ages 12 to 18. The majority of participants have a genetic predisposition to obesity, an observation supported by the finding that 75% of participants have at least one overweight parent (Wing & Hill, 2003).

Results: Methods of Weight Loss and Maintenance

Surprisingly, only 55.4% of participants received assistance in their weight loss from a commercial program, physician, or nutritionist; the rest report self-help methods of weight loss (Wing & Phelan, 2005). Of the 4,902 people who registered between 1994 and 2006, 105 reported undergoing bariatric surgery, such as gastric bypass or gastric banding. Although faster initial weight loss is typically associated with surgical patients, surgical and nonsurgical patients report similar minimal weight regain after one and two years. Interestingly, patients of bariatric

weight loss generally report higher levels of stress, depression, diets that are higher in fat, and less physical activity (Bond, Phelan, Leahey, Hill, & Wing, 2009).

The most common behavioral patterns associated with success in the study include eating a low-fat, high-carbohydrate diet; eating breakfast every day; frequently self-monitoring weight; having a consistent eating pattern; and participating in a high level of physical activity (Wing & Hill, 2003)..

Criticism and Response

The National Weight Control Registry is not without critics. One group criticizing the NWCR is an organization of doctors and dietitians that subscribe to the Health at Every Size (HAES) approach to weight management. The HAES group points out the significant lack of diversity within the study because most participants are well-educated white women (Ikeda et al., 2005). The NWCR creators, however, have responded by recognizing this as an unavoidable issue that arose in the self-selecting study (Hill, Wyatt, Phelan, & Wing, 2005). The HAES criticism also argues that representing individuals in the NWCR as "typical" and projecting the idea that "if they can do it, you can do it" onto every overweight individual perpetuates false optimism that anyone can achieve long-term weight loss. The HAES group also argues that research supports the observation that individuals can reduce their risk for developing chronic diseases by eating a nutrient-dense diet and increasing physical activity without a focus on weight (Ikeda et al., 2005). These points, although arguably valid, don't contradict the NWCR's mission to help those who decide to lose weight also achieve long-term success.

The Adolescent Weight Control Registry

The Adolescent Weight Control Registry (AWCR), created in 2010, is one of the latest initiatives of Rena Wing, the cocreator of the National Weight Control Registry. The AWCR seeks to identify the factors that lead to successful weight loss in adolescents including parental involvement, social interactions, and dietary choices. People who are 14 to 21 years old and have maintained at least a 10-lb weight loss for a year or longer qualify for participation in the AWCR (AWCR, 2014). As a part of the study, the parents and the adolescent both are sent annual questionnaires. Wing and colleagues hope that results from the AWCR will be able to provide teenagers and their parents with advice for promoting successful weight loss.

Conclusion

Studies on weight-loss success still are fairly dismal. The majority of people who lose weight regain the lost weight—and sometimes more—within a few months of stopping their weight-control programs. Research by Wing, Hill, and colleagues, however, has shown that long-term weight management is possible and occurs more frequently than previous studies had supposed. Wing's decades of work have

helped to determine the most-effective lifestyle interventions for obesity and obesity-related disorders. Ultimately, the data collected by the registry serve to provide those who choose to lose weight with a set of guidelines developed from thousands of previous success stories.

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Research Issues

Research from the National Weight Control Registry has expanded into other areas, in addition to its examination of strategies for long-term weight-loss maintenance. Registry members report many significant improvements in physical and psychological health, including improvements in energy level, physical mobility, general mood, and self-confidence (Klem et al., 1997). Much of R. R. Wing's recent research concerns behaviors associated with the prevention and treatment of type 2 diabetes, a disorder commonly associated with obesity.

See Also: Obesity, treatment.

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Niacin

Niacin, also known as vitamin B3, is a nutrient belonging to the class of water-soluble B vitamins. The term "niacin" refers to two related organic compounds: nicotinamide (also known as "niacinamide") with a chemical formula of $C_6H_6N_2O$, and nicotinic acid with a chemical formula of $C_6H_5NO_2$. The B vitamins are characterized by their role in the chemical reactions associated with cellular metabolism; they are integral to the breakdown of proteins, fats, and carbohydrates for energy, and to the synthesis of important biomolecules including proteins, fatty acids, and cholesterol. The two components of niacin—nicotinic acid and nicotinamide—are precursors to two coenzymes, nicotinamide adenine dinucleotide (NADH) and nicotinamide adenine dinucleotide phosphate (NADPH). These coenzymes participate in more than 200 metabolic pathways.

Pellagra and the Discovery of Niacin

The discovery of niacin as an essential nutrient arose from the study of the disease called "pellagra." Pellagra is a disease that typically results from a chronic deficiency in niacin or tryptophan. It is characterized by symptoms referred to as "the four D's"—dermatitis, diarrhea, dementia, and (eventually) death, if left untreated. People suffering from pellagra also might experience vomiting, indigestion, sensitivity to sunlight, and swelling of the mouth and tongue.

Today, pellagra is a rare occurrence in industrialized civilizations, but it once was an epidemic disease. It first was described in Europe in the 18th century. In Italy, people suffering from pellagra were referred to as "pellagrins" and a special hospital was set up for them. It also was not uncommon to find people suffering from pellagra in mental hospitals due to the dementia resulting from the disease. During the Great Depression in the United States, a quarter of a million people were estimated as suffering from pellagra, particularly in the poor South. Pellagra was common among corn-eating people and it originally was thought to occur from consuming moldy corn. Other theories included the consumption of rancid vegetable oil (Brody, 1999).

American physician Joseph Goldberger sought to determine whether pellagra was an infectious disease (Brody, 1999). Goldberger observed that health workers caring for people with pellagra did not develop the disease. He also noted the monotonous diets associated with the impoverished conditions typical of people with pellagra. In 1916, to prove that pellagra was not infectious, Goldberger injected himself with the blood of infected patients and also consumed their urine, feces, and scaled skin. He did not become ill, and later found that people could be cured of pellagra by drinking milk.

At this time, scientists also noted that Mexican people who consumed corn-based diets did not become ill with pellagra. In Mexico, corn tortillas traditionally are prepared with mineral lime; thus it was assumed that the mineral lime was killing mold on the corn. Eventually, however, research determined that the alkali nature of mineral lime releases niacin from the protein to which it typically binds in

corn, and this was keeping pellagra from affecting this population. Ultimately it was discovered that a diet of inadequate protein can lead to pellagra; this was a common condition among the poor, who subsisted mainly on untreated corn. Niacin, however, is found directly in meats or is synthesized from tryptophan found in meats. It remains bio-unavailable in untreated grains. In the 1930s, scientists at the University of Wisconsin eventually determined that niacin specifically is the curative for pellagra (Brody, 1999). Pellagra began to decline in the United States after a government mandate that cereal grains be fortified with niacin, and as people increased meat consumption (Insel, Ross, McMahon, & Bernstein, 2014). Pellagra still develops in populations having diets low in protein and niacin.

Role of Niacin in Cellular Metabolism

In the body, chemical processes often are catalyzed by enzymes, typically of protein structure. Coenzymes are non-protein-structured organic molecules that bind with enzymes and are necessary for the enzyme's function. Niacin is a key structural component of coenzymes NADH and NADPH. Both nicotinic acid and nicotinamide are converted to NADH and NADPH; in these conversions nicotinic acid is converted to nicotinamide, and nicotinamide forms the active part of the structure of each coenzyme. Nicotinamide adenine dinucleotide and NADPH are of similar structure. Nicotinamide adenine dinucleotide phosphate is synthesized from NADH by the adding of a phosphorous-containing functional group. The roles of NADH and NADPH in the human body are extensive; they are required by more than 400 enzymes (Higdon, Delage, & Jacobson, 2013).

Oxidation and reduction (redox) chemical reactions are the mechanisms by which many metabolic processes occur. Redox reactions involve a transfer of electrons in which molecules either gain or lose electrons. A substance that accepts electrons in a chemical transfer is an oxidizing agent, and a substance that donates electrons is a reducing agent. In its oxidized form, NADH is NAD+ and is an oxidizing agent that primarily is involved in catabolism (breaking chemical bonds). In its reduced form, NADPH is a reducing agent primarily involved in anabolism (building bonds), although there are exceptions. NAD+ and NADPH cycle between their oxidized and reduced forms in redox reactions. NAD+ becomes NADH in these processes, and NADPH becomes NADP+. Additionally, NAD+ often serves in the production of energy, and NADPH frequently serves in the synthesis of molecules. For example, glyceraldehyde 3-phosphate dehydrogenase is an NAD+ dependent enzyme that is involved in the breakdown of glucose for energy; NAD+ becomes NADH in this process. Enoyl reductase is an NADPH-dependent enzyme that is involved in the synthesis of fatty acids; NADPH becomes NADP+ in this process (Stipanuk & Caudill, 2012).

Dietary Sources of Niacin

Dietary niacin is found primarily in meats, including poultry and fish, and fortified cereal grain products. Some other foods such as peanut butter, brewer's yeast, and

mushrooms also contain significant amounts niacin. Niacin obtained from meat products primarily is in the form of nicotinamide. The coenzymes NAD+ and NADPH also can be present in foods. Upon ingestion, they are hydrolyzed to nicotinic acid or nicotinamide so they can be absorbed by the small intestine. Niacin in unfortified grains is bound to macromolecules that make it largely bio-unavailable. This is due to the inability of intestinal enzymes to hydrolyze the bonds that would free the niacin. In this bound form, niacin is referred to as "niacytin." A small fraction of niacytin can by hydrolyzed by hydrochloric acid (HCl) present in the stomach, but this releases only about 10% of niacin (Bender, 2009). Treating grains with alkali compounds frees niacin from the macromolecule structure and making it bioavailable when consumed. Roasting corn also increases the bioavailability of niacin because roasting releases alkali ammonia compounds (Bender, 2009).

Niacin can also be synthesized by the body from the amino acid tryptophan, making meats especially good sources. Synthesis occurs in the liver via a metabolite of tryptophan called "quinolinic acid." Quinolinic acid is converted into NADH and NADPH. An excess of NADH typically is produced in the conversion, and NADH is broken down into nicotinic acid and nicotinamide. Nicotinic acid and nicotinamide then are distributed to other tissues and resynthesized into NADH and NADPH (Bender, 2009). Sixty milligrams of tryptophan yields approximately 1 mg of niacin, or what is referred to as 1 niacin equivalent (NE), where 1 NE is equal to 1 mg of niacin or 60 mg of tryptophan. Approximately half of niacin intake in North American diets comes from tryptophan. The recommended dietary allowance (RDA) for niacin is 16 mg NE for adult men, 14 mg for women, 18 mg during pregnancy, and 17 mg during breast-feeding; the upper limit is set at 35 mg NE per day (Insel et al., 2014).

Therapeutic Benefits of Niacin Dietary Supplements

Supplemental niacin is known for its ability to treat hyperlipidemia (elevated blood lipids). Therapeutic doses of 150 mg to 400 mg of niacin per day result in the lowering of low-density lipoprotein (LDL) cholesterol, and blood triglycerides, and the raising of high-density lipoprotein (HDL) cholesterol (Higdon, Delage, & Jacobson, 2013). It is nicotinic acid specifically that has these lipid-lowering effects, niacinamide does not. Nicotinic acid has been demonstrated to reduce LDL cholesterol levels by about 10% to 20%, reduce triglycerides by 20% to 50%, and raise HDL cholesterol by 15% to 35% (MedicineNet, 2004). The degree of the lowering and raising effects of LDL and HDL are dose dependent, which means higher doses of niacin have a greater effect. Unfortunately, supplementation with pharmacological doses of niacin often comes with certain side effects. The most commonly experienced side effect is flushing, reddening, and itching of the skin. Other side effects include nausea, vomiting, and diarrhea. Liver toxicity has been observed at doses of 750 mg per day or more, and hepatitis has been associated with long-term use of time-released niacin. Because of these effects, niacin often is prescribed at lower doses with other lipid-reducing drugs. Although nicotinic acid has shown these cardio-protective effects in most studies, one study by the

National Institutes of Health demonstrated that a therapy of high-dose timed-released niacin combined with other cholesterol-lowering drugs (statins) produced a small increase in the rates of stroke for reasons that presently are unexplained (Insel et al., 2014). People interested in using niacin to reduce an atherogenic lipid profile should work with their health care providers to be sure this therapy is safe for them.

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See Also: Vitamins.

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Nickel

Nickel is a metal that combines with other elements, such as iron and copper, to form alloyed metals. It also binds readily with chlorine and oxygen to create water-soluble compounds that are found in soil and plants. Environmental exposure to nickel predominantly comes from ingesting food, although it is also present in the air and in drinking water. Skin contact with the metal is common, as nickel-containing alloys often are used in coins and jewelry and can trigger an allergic reaction known as nickel dermatitis. The resulting itchy rash reflects heightened nickel sensitivity, which occurs in 10 % to 20% of the population and is exacerbated by prolonged contact and possibly high dietary intake of nickel (Agency for Toxic Substances & Disease Registry, 2005). Flares of hand eczema can be induced after consumption of nickel. Chronic exposure to unusually high levels of nickel is rare and typically occurs only in specialized industrial workplaces. It can lead to chronic bronchitis and contribute to lung and sinus cancers (Agency for Toxic Substances & Disease Registry, 2005). The tolerable upper intake level for nickel is 1 mg per day.

Most people in North America consume approximately 80 mcg to 170 mcg of nickel daily, especially in foods such as bran, sesame and sunflower seeds,

pineapple, raspberries, chocolate, and nuts (Pennsylvania State University Dermatology, 2011). Nickel content of food varies and can be affected by the region in which plants and vegetables are grown and the method by which food is processed and stored. Cooking acidic foods in stainless steel cookware can result in the addition of nickel to foods. Ingestion of vitamin C and iron serve to decrease the absorption of nickel in the body and can be helpful for people with nickel sensitivity (Zirwas, 2009). Nickel is present in DNA and RNA. A few enzymes containing nickel have been identified, and nickel is considered an essential nutrient. Nickel deficiency has been observed only in animals, however, and no daily intake recommendations have been made.

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See Also: Minerals.

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Nitrates and Nitrites, Dietary

Inorganic nitrates are an important component of nature's nitrogen cycle, in which atmospheric dinitrogen (N_2) is made available for incorporation into plants and animals. In spite of this important role, inorganic nitrates have been viewed by the public as being potentially harmful additives in food and water supplies. An explosion of new research on the presence of nitrates and nitrites in food now is questioning this long-held view and is bringing to light the potential for positive effects these molecules could have on the human body (Weitzberg & Lundberg, 2011).

Sodium nitrite is an antioxidant used to cure meats such as ham, bacon, and hot dogs to prevent spoilage, as well as to retard the growth of harmful botulism-causing bacteria and Listeria. The USDA allows 156 parts per million to be added to cured meats. After processing, the amount of nitrites remaining in the meat is about 10 parts per million or less (American Meat Institute, 2008). When nitrites are mentioned, it is commonly assumed that the majority is consumed through processed and cured meats. In reality, however, most of the nitrite found in the human body actually is converted from naturally occurring nitrates. Leafy vegetables

such as spinach, radishes, lettuce, and beets are especially high in nitrates. Spinach, for example, contains between 500 and 1900 ppm nitrates (AMI, 2008).

When nitrates are ingested in food, 25% of the nitrates present are absorbed by the salivary glands and excreted in the saliva as nitrites. Some of the remaining 75% is reduced to nitrite by bacteria in the mouth, and the rest is swallowed along with the nitrite in the saliva. It is rapidly absorbed by the stomach and small intestine (Powlson, 2008). After moving from the small intestine, 65% of the nitrates is excreted in the urine; however, scientists cannot yet determine where the "missing" 35% goes. When in the stomach, nitrates mix with stomach acid to produce a soup of nitrous acid, nitrogen dioxide, dinitrogen trioxide, and nitric oxide. Of the 65% sent to the kidneys to be excreted, 80% of that is reabsorbed in the renal tubes, indicating that nitrates play a definite role in normal human physiology and are not merely unwanted toxins (Gilchrist, Winyard, & Benjamin, 2010).

Concern regarding the consumption of nitrates arose in the 1940s when cases were reported of infants developing methemoglobinemia, or "blue baby syndrome." These incidents were believed to be due to well water that had high nitrate concentrations and which was being used to make the formula the infants were consuming, contaminating the formula in the process. When nitrate is converted to nitrite in the stomach (or swallowed when converted in the salivary glands), it reacts with hemoglobin to produce methemoglobin, which is incapable of binding oxygen. For this reason, the U.S. Environmental Protection Agency (EPA) set a Maximal Contaminant Level for nitrate at 44 mg/mL (equal to 10 ppm). Further research into the contaminated wells, however, revealed that the contamination was due to fecal matter present in the well water. It is now believed that the methemoglobin was brought on not due to high nitrate levels, but instead because of bacteria present in the fecal matter contaminating the water—which can elicit the same symptoms (Katan, 2009). Since then, there has been a considerable amount of disagreement regarding the role of nitrates in causing methemoglobinemia. Regardless, Western governments contribute sizeable amounts of money per year to treat water supplies in an effort to lower nitrate levels (Gilchrist, Winyard, & Benjamin, 2010).

In the 1970s, further concern on the topic of dietary nitrates emerged when research showed that nitrates theoretically could be converted to N-nitrosamines, which are known cancer-causing agents. These metabolites can be produced when nitrate is reduced to nitrite (either salivary nitrite that was swallowed or that is converted in the stomach) and then acidified via stomach acid and combined with secondary amines found in the diet (L'hirondel, Avery, & Addiscott, 2006). Subsequent decades of research have revealed that the processes responsible for the formation of N-nitrosamines also produce helpful biochemicals in the body, most notably nitric oxide (Bryan, Alexander, Coughlin, Milkowski, & Boffetta, 2012).

In free-living animals, the formation of harmful N-nitrosamines usually is blocked by nutrients, such as vitamins C and E, and other phytochemicals, especially polyphenols, which are abundant in foods containing high nitrate levels. Currently, researchers do not think that dietary nitrate contributes in any

meaningful way to increased cancer risk, not even for stomach and esophageal cancers, which previously were thought to increase with a high dietary nitrate and nitrite intake (Bryan, Alexander, Coughlin, Milkowski, & Boffetta, 2012; Keszei et al., 2014).

Although, in the past, dietary nitrates have been viewed as toxins present in water and cured meats, recent studies suggest that nitrate intake and supplementation could have many positive effects on humans. These beneficial effects probably are due to the conversion of nitrites to nitrous oxide (NO) in the stomach. One of the main targets of NO is the circulatory system; NO plays important roles in decreasing blood pressure, maintaining blood vessels in their rest state, enhancing platelet function, and protecting against ischemia and reperfusion injury. Dietary nitrates might be helpful in preventing or slowing the progression of artery disease, and could be one of the mechanisms by which a high intake of fruits and vegetables helps reduce the risk of cardiovascular disease.

Recently, athletes have begun eating and drinking foods, such as beetroot juice, that are high in nitrates to encourage the production of NO and enhance exercise performance. Short-term sodium nitrate supplementation has been shown to improve muscular efficiency and to reduce oxygen consumption during submaximal exercise in healthy individuals, and could increase exercise tolerance and performance (Jones, 2014).

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See Also: Cardiovascular disease and nutrition.

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Nutritional Genomics

Nutritional genomics is the study of how nutrition and diet interact with a person's genes. Nutritional genomics can be split into two subgroups of focus, "nutrigenomics," and "nutrigenetics." Nutrigenomics focuses on the effects that nutrients have on physiology by means of influencing genetic expression, and consequently altering transcription and expression. By examining the interactions between bioactive substances in the diet and the gene expression, nutrigenomics studies draw conclusions about the effects of foods on protein production and physiological functions. Nutrigenomics promises to lend insight into why the effects of certain drugs and nutrients vary so greatly from person to person, as well as how it might be possible to design specific dietary treatments for common diseases on an individual basis.

Nutrigenetics examines the ways that the genome dictates how nutrients interact with physiological systems. This field of study seeks to answer the question of what mechanisms underlie the idea that some genotypes are more equipped to digest and metabolize certain nutrients. Nutrigenetics explores, for example, the reasons that some groups are especially prone to obesity. Nutrigenetics someday might help nutritionists and health care providers offer dietary advice for disease treatment and prevention based on a person's genetic profile.

Nutrigenomics in History

Scientists have been intrigued by the observation that factors influencing genetic expression can be inherited from the experiences of a person's parents and grandparents. Environmental factors like stress, food shortage, and food abundance, can affect the genetic expression of an individual organism. The food options and choices of one generation can drastically alter the fate of many subsequent generations.

The comprehensive 19th-century birth and death records of Sweden's northern most county, Norrbotten, were major catalysts of epigenetics research in the 20th century. Citizens of Norrbotten, which lies within the Arctic Circle, lived in extreme isolation from the rest of the world and were highly dependent on their own resources, namely their local agricultural yields. These people were subject to extreme fluctuations in the availability of food—and so were their epigenetic structures.

Severe famine in Norrbotten occurred in the years 1800, 1812, 1821, 1836, and 1856, leading to scarcity of food and high death rates. In the years 1801, 1822, 1828, 1844, and 1863, Norrbotten experienced bountiful harvests and had excess food. It was found that the nourishment received by the parent generation during development and growth was strongly correlated to longevity and general health of the following generations. People who were children during times of abundance

were found to be more likely to have children who were healthy and physically larger (Mead, 2007). Third-generation offspring—the people who were two generations removed from the direct effects of feast and famine, were subject to the same correlation between the their ancestors' nourishment and inherited epigenetic and physiological traits. This research reinforced the importance of good nutrition in fetal development and early life.

Nutritional Genomics: Understanding Gene Expression

Understanding the physiological mechanisms that help to explain how diet and nutrition influence gene expression, and how gene expression in turn can influence nutrient metabolism, requires a basic knowledge of cell biology, especially the mechanisms for protein coding and production. These mechanisms include the many processes influencing gene activation.

Deoxyribonucleic Acid and Protein Coding

Every living cell contains the genetic information necessary to code for proteins that are essential to organisms. In humans cells, deoxyribonucleic acid (DNA) molecules contain the genetic blueprints for life, stored as specifically ordered sequences of three nucleic acids called "codons," each of which codes for a specific amino acid (the building blocks of proteins). During a process called "transcription," DNA—with the help of enzymes—transfers its genetic code to a compound called "ribonucleic acid" (RNA). The genetic code then is carried by messenger RNA (mRNA) from the cell's nucleus to the cytoplasm, where it is read by a complex called a "ribosome," in a process called "translation."

When a genetic sequence is translated, a protein is made using the information that was originally coded for by the DNA. Genes that code for proteins that are expressed determine an individual's phenotype. All of the genes that make up the DNA of an individual—including those that never are expressed—make up an individual's genotype.

Deoxyribonucleic acid is part of a larger structure called "chromatin," and this structure influences the operation of the DNA. Chromatin is a complex structure of DNA and proteins that makes up the chromosomes. Genetic expression is influenced by factors that affect chromatin.

Epigenetics: The Basic Mechanisms behind Nutrigenomics

"Epigenetics" is the study of changes in the genome that do not involve changes in nucleotide (genetic) sequences. The core concept in epigenetics is that certain alterations can occur in the apparatuses involved in translation and transcription, and can influence which genes become "active" and initiate the manufacture of proteins. These changes include several types of chromatin remodeling, one of them being histone modification. Another type of epigenetic alteration that is influential is the phenomenon of DNA methylation, a process by which nucleotides gain

methyl groups. The structure that protects DNA strands from deteriorating over time is the "telomere"—a critical component of epigenetics.

Histone Modification

Histones are protein components of chromatin around which strands of DNA are tightly wrapped. When the amino acid sequences of histones and histone tails are changed or compromised, the wrapping of DNA also is altered. Alteration makes some segments—and thus some nucleotide sequences—more or less available for transcription. This increase or decrease in the likelihood that specific genes will be transcribed means that certain genes will or will not be transcribed, and thus the phenotype (genetic expression) will be altered.

Deoxyribonucleic Acid Methylation

Methylation occurs when methyl groups attach to cytosine or adenine nucleotides (components of DNA). Deoxyribonucleic acid methylation is an important regulator of gene expression. In embryonic development, for example, methyl groups bind to nucleotides in certain segments of the DNA of stem cells to suppress certain genes. By making segments unavailable for transcription, the cell will differentiate. DNA methylation plays a critical role in carcinogenesis, the process by which cells become cancerous. Methylation can be influenced by methyl donors present in the diet. Most methyl groups are stripped from the DNA during meiosis (the creation of the cells that will become eggs and sperm), but new research suggests that some methyl groups remain attached to zygotic DNA, and some epigenetic traits and phenotypic traits are passed along hereditarily.

Telomeres

"Telomeres" are regions of repeated nucleotide sequences that cap off the ends of every chromosome. Telomeres act as disposable buffer zones protecting the ends of the significant genetic sequences. As chromosomes replicate for cell division, chromatin deteriorates, but the significant portions of DNA go untouched as the telomeres progressively shorten over the life span. Telomeres can be rebuilt by the enzyme telomerase reverse transcriptase, and consequently made to better protect chromosomes from losing any critical information. Telomeres are believed to be at least partly responsible for the biological process of aging. Telomere length, and the level of protection offered by the telomeres, can be affected by environmental factors including diet, physical activity, and stress (Choi & Friso, 2010).

Folate and Epigenetic Change

One of the most highly cited bioactive substances responsible for epigenetic changes is folate (a water-soluble B vitamin), which is naturally found in leafy greens and many other foods. Folate is a source of the one-carbon methyl groups

that can methylate DNA. Data suggest that increased levels of plasma folate can increase chromosomal stability.

Nutrigenetics and Ethnicity

People with ancestors from different regions of the world have coevolved with certain agricultural practices and have adapted to eating different foods. These adaptations could translate to varied food intolerances and allergies. Some ethnicities are known to be less tolerant of certain foods. Rates of lactose intolerance, for example, are particularly high in people of African or Asian descent. Caucasians have greater rates of allergies to animal dander and peanuts.

Challenges in Nutritional Genomics

The study of nutritional genomics inherently is limited by the complexity of the genome juxtaposed with the control of variables required by the scientific method. In vitro experimentation has been the main source of data in this field of study, in which interactions between individual nutrients and gene pairs are observed. Because nutrients are not usually ingested alone, however, but rather in combination with other nutrients that create foods, the application of these studies is limited. The field of nutritional genomics is complex because it must take into consideration trillions of base pairs of nucleotides having the potential to be methylated, and nearly endless combinations of chromatin modifications. In the field of nutritional genomics, direct causation can rarely be concluded, and many studies only can be confident of associations between nutrient ingestion and physiological consequences.

Applied Nutritional Genomics

The mapping of the human genome in conjunction with nutritional genomics research has expanded the reach of medicine. To understand the genome is to revolutionize the way that health and illness are thought about. Researchers can now target specific genes with specific molecules. When these molecular messengers are components of foods, nutritional genomics research becomes relevant. The future of nutritional genomics might allow diet and lifestyle changes to effectively replace drugs for the prevention and treatment of some diseases.

Gabriella J. Zutrau

Research Issues

Many companies offer genetic testing services directly to consumers; such testing has become very popular. Consumers send in a genetic sample—typically a cheek swab from the inside of the mouth—and the company provides information on disease susceptibility markers. Some of these companies offer dietary advice and even market dietary supplements based on genetic analysis. Many professionals question the ethics of such marketing. How

should direct-to-consumer genetic testing services be regulated? How should nutritional professionals be involved? Read a perspective from the Academy of Nutrition and Dietetics listed in the Further Reading section.

See Also: Folate and folic acid; Lactose intolerance.

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Nutritionists and Dietitians

Nutritionists and dietitians are trained health professionals who typically work in a hospital, clinic, or private setting. They provide nutrition advice and support people's efforts to change their eating behaviors. They also design menus and oversee food services for a variety of institutions. The field of dietetics and nutrition is integral to many public health and community-outreach programs. Nutrition professionals have a growing number of work opportunities such as corporate wellness, academic research, and sports nutrition.

There are two major certifying bodies in the United States, the Academy of Nutrition and Dietetics (AND) and the Certification Board for Nutrition Specialists (CBNS). The AND began as the American Dietetic Association (ADA), which was founded in 1917. The ADA created the first nutrition licensure program, and the licensed professionals are known as registered dietitians (RDs). The first registered dietitians were employed by the U.S. Public Health Service for the management and preparation of food in hospital settings, particularly during World War I. The ADA changed it's named to Academy of Nutrition and Dietetics (AND) in 2012.

Currently, federal regulation in the United States requires practicing registered dietitians to be state licensed. Obtaining a state license enables nutritionists and dietitians to bill through insurance companies as well as to work in various institutional settings that require state licensing. To qualify for state licensure, registered

dietitians are required to earn a four-year bachelor's of science degree through an education program approved by the Accreditation Council for Education in Nutrition and Dietetics (ACEND). Additionally, candidates must complete a supervised practice program followed by an examination administered by the Commission on Dietetic Registration (CDR). The AND also offers another licensed certification called the Dietetic Technician, Registered (DTR). Licensure requires completion of at least a two-year associate's degree at an accredited college or university, certain required classes, completion of at least 450 hours of supervised work experience, and passing a national DTR examination. Dietetic technicians usually work with registered dietitians.

The CBNS was founded in 1993 by the American College of Nutrition. The American College of Nutrition created two certifications for people who do not follow the standard dietitian educational path but who are very qualified to give nutrition guidance, having advanced degrees in nutrition and significant clinical or research experience. These certifications are the Clinical Nutrition Specialist (CNS) and the Certified Nutrition Specialist–Scholar (CNS-S). Clinical Nutrition Specialists must hold an advanced degree from an accredited college or university; complete required courses in nutrition, biochemistry, and other sciences; complete 1,000 hours of supervised clinical work; and pass the CBNS board examination. Certified Nutrition Specialist–Scholars must have a doctoral degree in nutrition or a clinical health care field (such as an M.D. or Doctor of Nursing) from an accredited college or university; complete required coursework in nutrition, biochemistry, and other sciences; and show evidence of significant scholarly contributions to the field, such as at least five papers published in scholarly journals.

Many U.S. states grant licensing eligibility to nutrition specialists with CBNS certification. The term "nutritionist," however, is not currently federally regulated. Although all registered dietitians are considered nutritionists, not all nutritionists are considered registered dieticians. In Canada, the term "registered dietitian" is a protected professional title. Dietitians of Canada is the organization responsible for accrediting education programs for dietetic students and serves as the regulatory body for practicing registered dietitians.

Ana Maria Moise

See Also: Academy of Nutrition and Dietetics.

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O

Obesity, Causes

Obesity is defined as a condition of having excess body fat. Obesity prevalence is increasing around the world and is thought to be the fifth leading cause of death worldwide. Obesity prevalence has doubled since 1980 in both the United States and Canada, and the rate of obesity in children has tripled.

Causes of the Rapid Rise in Obesity Prevalence

The rapid rise in obesity rates around the world suggests that this increase is due primarily to changes in lifestyle. The worldwide gene pool has not changed substantially in the past few decades, so although genetics can explain body composition variance from person to person, it cannot explain a doubling of obesity rates for the United States and Canada in 30 years. Experts think that a number of lifestyle changes have created an "obesogenic" environment, an environment in which a majority of people naturally gain weight. An obesogenic environment pushes people into a positive energy balance, which means people are consuming more calories (as food) than they are burning through normal metabolic processes and physical activity. Some of the lifestyle changes that could be contributing to increasing rates of obesity include the following.



Approximately 35% of adults in the United States are obese and another 34% are overweight. Teens and children over 6 years old have an obesity rate of about 18%. (iStockPhoto .com)

Less Physical Activity

For a majority of North Americans, daily life requires fairly low levels of physical activity. Fewer than half of U.S. adults meet basic physical activity guidelines (at least

two and a half hours of exercise per week) (CDC, 2012). Although there are many exceptions, people expend less energy in manual labor and housekeeping than they did several decades ago. People tend to use transportation vehicles such as cars, buses, and trains rather than walking or bicycling. Recreational pursuits are likely to be watching media or playing electronic games rather than engaging in more active recreational activities and sports.

Many geographical locations have limited opportunities to engage in physical activity. In some locations it is difficult to walk or bicycle safely; residents could have little access to parks and other recreational facilities. Many schools do not offer enough high-quality physical education programs.

More Food

Eating habits have changed for a majority of North American families over the past 30 years. People now eat out more than they used to and cook less frequently at home. People also snack more often than they used to—frequently on fast food and snack foods available in vending machines and convenience stores. As a result, more processed foods higher in fats, sugar, and salt are consumed. Portion sizes have increased. The combination of all of these factors means that people are consuming more calories, more sugar, and more unhealthy fats.

Causes of Obesity in Individuals

People's genetic predisposition strongly influences how they respond to their environment. An individual's behaviors in turn interact with genetic predisposition to influence feelings of hunger, food choices, and engagement in physical activity.

Genetics

For centuries, scientists have observed enormous individual variation in body types, body composition, and the factors that contribute to energy balance. During the past three decades, studies of twins have led to the conclusion that genetic variation explains about 40% to 75% of the variation in BMI among people. Research in 5,092 twin pairs 8 to 11 years old found that genetics explained 77% of variation in waist circumference (Wardle, Carnell, Haworth, & Plomin, 2008). Researchers believe that a genetic predisposition to obesity allows an obesogenic environment to enable expression of obesity through long-term positive energy balance.

For some individuals and ethnic groups, genetic predisposition for obesity is especially strong. Their "thrifty" genes allow them to capture every calorie they consume and efficiently store energy—primarily as fat—against future lean times. Unfortunately, in an environment where food is plentiful, these thrifty genes translate almost automatically into obesity.

Obesity genes might work in different ways for different people. They could influence the amount of brown adipose tissue people develop and thus their ability

to "waste" extra calories as heat. Genes could influence resting metabolic rate and the rate at which certain energy-expending biochemical reactions occur in the body. People also vary in their tendencies to sit quietly for long periods of time, or inability to sit still for more than a few minutes, which influences daily energy expenditure. Genes also appear to influence individual experiences of hunger and satiety and preferences for certain foods.

Genes influence a person's size and shape. People usually look like others in their family. Everyone has noticed that some people are short and stocky—with a tendency to be both muscular and heavy—and others are tall and slender. Many more people are somewhere in between these types. The location of fat stores in the body also appears to be inherited. Some people might have lean upper bodies but heavy legs and thighs, or the other way around. Some women are busty and curvaceous, and others are not. Although some fat stores can be reduced with lifestyle-modification programs, it is not possible to direct which fat stores will be drawn from first. Similarly, strength training can increase muscle size in some people, but they inherit the basic shape of their muscles.

Interaction between Lifestyle and Genetics

It is likely that lifestyle and genetics interact during the development of obesity in any given individual. Research has demonstrated that dietary factors and excess body fat appear to be associated with damage to the hypothalamus, an area of the brain that helps to regulate hunger and thirst. Studies in mice have found epigenetic changes associated with both high-fat diets and with leptin deficiencies. In one study, both diet and leptin-deficient states altered the expression of genes and then, through these changes, changed neuron behavior in the hypothalamus (McNay et al., 2012). Mice receiving a high-fat diet showed suppressed neurogenesis. Leptin-deficient mice also generated fewer new neurons and lost hypothalamic neural stem cells.

Research on both mice and humans has found an association between obesity and inflammatory damage with significant structural and functional changes in the hypothalamus (Thaler et al., 2012). Researchers speculate that poor dietary choices could contribute to obesity not only by adding empty calories but also by damaging the hypothalamus. Damage to the hypothalamus can lead to feelings of hunger even when the individual has eaten enough. This conceivably could lead to a vicious cycle of increasing hunger driving poor eating behaviors, which in turn cause more damage to the hypothalamus and more hunger.

Digestive Tract Microorganisms

Intriguing research on the interaction of human cells with the bacteria living in the digestive tract suggest that these bacteria have wide-ranging effects, including energy balance. These collections of bacteria are called "microbiota." The bacterial cells inhabiting the body outnumber human cells 10 to 1. A majority of these bacteria—approximately 100 trillion organisms—inhabit the GI tract. These

bacteria interact with components from the food passing through and with the cells lining the GI tract. Dietary components influence the type and activity of these bacteria, which in turn influence several variables related to health, including immune response and inflammation.

Antibiotics exert strong effects on the composition of the microbiota, as these drugs kill indiscriminately. Interesting research has found that antibiotic administration might increase body-fat levels. Indeed, livestock farmers have used this observation to their advantage; adding antibiotics to animal feed increases weight and fat gain, along with profits. In one study, when antibiotics were given to human subjects to eliminate the stomach bacteria *H. pylori*, thought to contribute in some cases to stomach ulcers, levels of the hormone ghrelin failed to fall after a meal, remaining six times greater than the post-meal levels were before antibiotic administration (Francois et al., 2011). Ghrelin is a hormone that stimulates feelings of hunger. Normally, ghrelin levels fall after a meal, and hunger declines. Because higher ghrelin levels trigger hunger, this change could be one of the factors associated with increased obesity resulting from antibiotic administration. In fact, BMI increased in these subjects during the 18 months of the study.

Interesting studies in mice and humans suggest that certain types of bacteria are associated with obesity. In particular, a bacterial family known as *Firmicutes* appears to be good at extracting energy from the digestive mass in the gut and churning out small fatty-acid molecules that are easily absorbed by the human host (Kallus & Brandt, 2012). Conversely, more bacteria from the family *Bacteroidetes* are associated with leanness. Obese mice and humans tend to have higher *Firmicutes*: *Bacteroidetes* ratios. This ratio could help explain why lean mice gain weight in the laboratory when researchers cause the intestines of the mice to become colonized by the bacteria from the obese mice (Turnbaugh et al., 2006). In addition to generating more energy substrates for human absorption, the microbiota also might contribute to obesity by influencing levels of inflammation or by promoting fat deposition.

A few studies have found that specific probiotic supplements can change body fat level (Kadooka et al., 2010). It is probably too early to begin recommending treatments based on these studies, although including yogurt with a variety of cultures and probiotic supplements in the diet appears to be helpful for some people. These data reinforce the fact that scientists still have a long way to go in understanding the role of the microbiota, however, and the many physiological factors that influence energy balance and body composition. These studies also underscore the complexity of body composition and energy balance in any given individual. They help to explain why some people remain overweight even when restricting food intake and increasing physical activity levels.

Social Network

Studies suggest that when friends and family gain weight, obesity can become more acceptable to an individual. An interesting study examining weight changes in 12,067 participants in the Framingham Study found that risk of weight gain

increases when a person's close friends and family members gain weight (Christakis & Fowler, 2007). Subjects in this study experienced a 57% increase in risk of gaining weight (more than what normally would be predicted to occur over time) if a close friend gained weight. Risk increased by 40% if a sibling gained weight and by 37% if one's spouse gained weight. Although researchers could not pinpoint any particular causes for these associations they ruled out shared environment, as the strongest influence—the effect of close friends—did not vary with proximity to the subject. In other words, whether best friends lived thousands of miles apart or in the same town, the effect was the same. Instead, the researchers proposed that friends and family affect each other's perception of fatness and change each other's ideas of what kind of body size is acceptable.

Barbara A. Brehm

Research Issues

The United States regularly collects information about physical activity levels and obesity rates in each state. The maps presented here are interesting to explore, and are available online (http://www.cdc.gov/diabetes/statistics/slides/maps_diabetesobesity_trends.pdf). These maps also illustrate the dramatic increase in both obesity and diabetes since the 1990s. Additionally, it is interesting to note the significant regional differences that exist among the states.

See Also: Energy balance; Microbiota and microbiome; Obesity, definition and health effects; Obesity, treatment.

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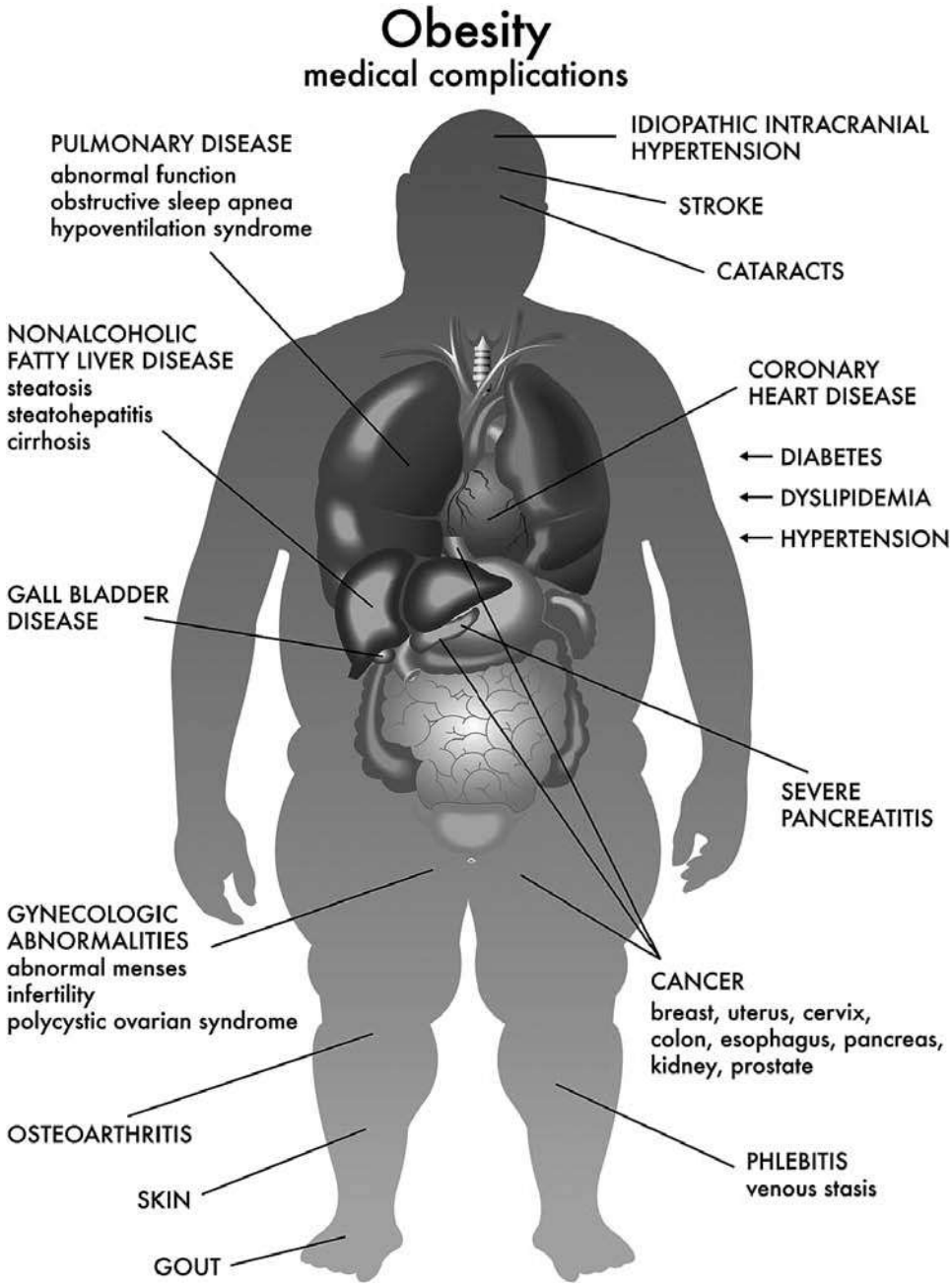
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Obesity, Definition and Health Effects

Obesity refers to a condition of having excess body fat. Obesity generally is defined worldwide by a weight (expressed in kg) for height (meters squared) standard known as body mass index (BMI). People with BMIs of 25 kg/m^2 to 29.9 kg/m^2 are classified as overweight, and BMIs of 30 kg/m^2 and greater are said to be obese. Because BMI is not a measure of body composition and is not reliably related to health for a particular individual, especially at lower BMIs, many clinicians combine BMI with other measures such as waist circumference and an assessment of other risk factors to determine whether a person's size could be increasing their health risks. Obesity is statistically associated with a number of health problems, especially at higher BMIs.

Obesity prevalence is increasing around the world, and is thought to be the fifth leading cause of death worldwide (WHO, 2012). Obesity prevalence has doubled since 1980 in both the United States and Canada, and rates of obesity in children have tripled. As obesity prevalence increases around the world, it is not just the high-income countries that are facing high health care costs associated with obesity. According to the World Health Organization, many low- and middle-income countries must now deal with a "double burden" of disease (WHO, 2012). Not only do these countries still have high rates of infectious diseases, but rising obesity rates are bringing increased rates of type 2 diabetes, hypertension, heart disease, and stroke. The World Health Organization also points out that people living in urban areas in low- and middle-income countries, just like low-income people in North America, often consume high-fat, high-sugar, and high-salt processed foods, which tend to be lower in both cost and nutrition.



Health issues related to obesity. Because obesity is a metabolic disorder, extra adipose tissue influences many physiological systems and organs. (Rob3000/Dreamstime.com)

Defining Obesity

Although BMI provides some information about a person's size, it does not tell the whole story about the health or quality of that size. Large, muscular people, especially athletes, for example, could have a high BMI but actually not be overweight in terms of being too fat. Similarly, people whose BMI is less than 25 actually might be obese because they have very little muscle mass and too much body fat. Nevertheless, BMI is the most commonly used indicator of overweight and obesity, primarily because weight and height are easy to measure. BMI is used by most physicians when evaluating patients and usually provides a good starting point for conversations about lifestyle and weight management.

The World Health Organization categorizes obesity into three classes, a system that most countries, including the United States and Canada, have adopted. Class I obesity refers to having a BMI of 30 kg/m^2 to 34.9 kg/m^2. Class II obesity indicates BMIs in the range of 35 kg/m^2 to 39.9 kg/m^2, and Class III obesity includes BMIs of 40 kg/m^2 and greater. The higher the classification number and the BMI, the greater the risk of obesity-related health problems.

Many health professionals now use waist circumference in addition to BMI to assess body fatness, especially for people with BMIs in the overweight or Class I obesity groups. Although waist circumference does not provide an estimate of body composition, it does provide information about torso mass. Excess fat stored in the abdominal region, especially inside the torso around body organs such as the liver and pancreas, exerts the greatest negative impact on health. This fat is referred to as visceral adipose tissue. The National Institutes of Health advises measuring the waist just above the iliac crests of the pelvis (the hipbones). Waist circumferences of more than 35 inches (88 cm) in women and 40 inches (102 cm) in men are associated with increased health risks.

Health professionals assessing the health risks of any individual obese patient should also check indicators such as blood pressure and blood glucose levels. Other risk factors that might indicate higher risk of obesity-related health problems include cigarette smoking; family history of premature heart disease; sedentary lifestyle; and a risky blood lipid profile, including high levels of LDL cholesterol and triglycerides and low levels of HDL cholesterol.

Health Risks Associated with Obesity

Obesity increases risk for several health problems. When people eat more calories than they burn, the body converts extra calories into fats called triglycerides and packs the triglycerides into fat cells. Fat cells can grow larger as more fat is stored, but they cannot expand indefinitely. Weight gain and too much body fat interfere with normal metabolic processes in many ways that contribute to the chronic health problems that are more likely to arise with obesity.

Researchers believe that when people are gaining weight and their bodies are making extra triglycerides, expanding fat cells can become damaged, manufacture faulty proteins, or simply reach the end of their life expectancies when they

get too full of fat (Iyer et al., 2010). It is possible that, with obesity, adipocytes (fat cells) cannot keep up with the body's demand to store triglycerides. When this happens, immune cells called macrophages come in to help dispose of damaged and dead fat cells. The job of macrophages is to disarm potential attackers, such as bacteria and viruses, by engulfing and digesting them. They try to attack triglycerides and dead fat cells in this manner but often are overwhelmed by the challenge. Macrophages, in turn, release chemical messengers called cytokines, such as interleukins, that summon more white blood cells and lead to more inflammation.

Another messenger affected by adipose stores is adiponectin. Greater levels of body fat have been associated with lower levels of adiponectin (Liu et al., 2012). Adiponectin helps insulin do its job of getting sugar from the bloodstream into cells, where it can be stored or burned for energy. This observation might help explain the blood sugar regulation problems that begin with insulin resistance that often develop with obesity (Liu et al., 2012). Adiponectin also helps regulate the metabolism of lipids. Adiponectin appears to have an anti-inflammatory effect on the cells that line the artery walls.

Although inflammation is helpful for healing a wound, chronic inflammation can interfere with a number of important biochemical processes in the body. Several of obesity's negative health effects are thought to be the result of inflammation in the fat tissue. Other negative health effects can result from the extra weight imposed upon the musculoskeletal system. The most common negative health effects of obesity include the following.

- Type 2 diabetes: Diabetes can result when some of the chemicals produced by the macrophages interfere with blood sugar regulation. These chemical messengers prevent the body's cells from responding appropriately to the hormone insulin, which signals cells to take up sugar (glucose) from the blood. High blood sugar levels in turn cause more damage, including accelerated aging of the arteries, thus contributing to artery disease, the leading cause of heart disease and stroke. High blood sugar also causes damage to the eyes, kidneys, and nerves.
- Hypertension: High insulin levels create a stress response in the body, raising levels of stress hormones and activating the fight-or-flight response. This can contribute to hypertension, which in turn increases risk for heart disease and stroke.
- Risky blood lipid levels: Excess triglyceride production (from excess calories) raises levels of blood fats, including blood triglycerides and low-density lipoprotein (LDL) cholesterol levels. These lipids contribute to the formation of arterial plaque and more inflammation, as macrophages attempt to deal with damaged arteries.
- Other inflammatory disorders: The inflammation caused by obesity can contribute to other disorders associated with inflammation, such as liver disease, pancreatitis, asthma, and rheumatoid arthritis. Obesity also increases risk for Alzheimer's disease (Juhasz, Foldi, & Penke, 2011).

- Cancer: Obesity is associated with increased risk for many types of cancers. Researchers have suggested that fat tissue might secrete chemicals that make people more susceptible to cancer. The inflammation associated with visceral adipose tissue could promote the transformation of precancerous cells into cancer cells, so that the immune system is aiding in cancer promotion rather than destroying dangerous cells (Balkwill, 2009). Adipose tissue also could promote existing cancers in other ways. Higher levels of adipose tissue increase estrogen levels, for example, and estrogen promotes the growth of certain types of cancers, such as ovarian and breast cancer. Additionally, excess subcutaneous fat could decrease the efficacy of cancer screenings, hiding cancer tumors. Health professionals emphasize, however, that this research is preliminary. Cancer patients are advised not to lose weight, because extra weight can be protective once cancer has already developed.
- Nonalcoholic fatty liver disease: Excess fat can be deposited in the liver. Excessive alcohol intake also can cause excess fat deposits, thus nonalcoholic fatty liver disease is diagnosed when fatty liver develops in people who drink little or no alcohol. In severe cases, the fat that accumulates in the liver can cause inflammation and scarring.
- Physical strain: The physical strain of excess weight can overload weight-bearing joints such as the hips, knees, and feet and accelerate development of the joint degeneration and pain associated with osteoarthritis. Excess weight in the belly can alter posture and cause back problems.
- Decreased quality of life: Obesity is associated with a reduced quality of life. Obesity increases risk for depression, social isolation, and discrimination in a multitude of settings. Obesity also increases risk of physical disability and discomfort, which contribute to a lower quality of life.

Barbara A. Brehm

Research Issues

Some research suggests that it is possible to be overweight or obese yet also healthy. This is most likely at the lower levels of obesity. Overweight people with healthy lifestyles, including good eating habits and regular physical activity, have lower health risks and rates of premature mortality than their normal-weight but sedentary friends (McAuley & Blair, 2011). A study conducted at the University of South Carolina, for example, followed 14,345 middle-aged men for 11 years (Lee et al., 2011). The researchers examined changes in weight and fitness over that time, as well as causes of death for subjects who died during the study period. Subjects whose fitness improved during the study had a 44% lower rate of all-cause mortality than subjects whose fitness declined. Interestingly, this observation held regardless of whether the subjects' weight changed or not, and it held for both normal-weight and overweight subjects. (The study included subjects who were overweight but not obese, as defined by BMI.) Similarly, subjects whose fitness stayed the same over the 11 years experienced a 30% lesser rate of all-cause mortality than subjects whose fitness declined independent of changes in body weight. The study did find that men who experienced an increase in BMI had a greater

rate of cardiovascular events—such as heart attacks—than men who did not show an increase in weight.

It is likely that the process of manufacturing and storing extra triglycerides explains part of the negative health effects associated with obesity. People actively gaining body fat could experience more obesity-related health problems than overweight and obese people who are in energy balance or actively losing body fat.

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See Also: Body composition; Body mass index; Obesity, causes; Obesity, treatment.

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Obesity, Treatment

Obesity refers to a condition of excess body fat. Obesity can be diagnosed by body mass index (BMI) (more than 30 kg/m2), waist size (more than 35

inches for women, more than 40 inches for men), and the presence of risk factors related to obesity, such as high blood pressure or blood sugar levels. Health professionals recommend a variety of strategies for the treatment of obesity. Weight loss need not be significant to have a positive effect on important health variables, such as blood pressure and blood sugar regulation. Losing just 5% to 7% of body weight can have desirable effects. For a person weighing 200 pounds, this would consist of a 10- to 14-pound weight loss. Even if weight loss does not occur, a healthful lifestyle that includes a nutritious diet and enough physical activity still can help prevent additional weight gain and can reduce the health risks associated with obesity.

Although the big picture of weight control and obesity is complex and filled with many interacting variables, the bottom line is very simple. To reduce body fat stores and prevent obesity, people must create a negative energy balance that stimulates the body to draw on its fat stores for energy. A negative energy balance can be created by eating less and becoming more active. Medications and surgeries can help efforts to reduce food intake, although these must be accompanied by appropriate lifestyle changes to be effective. Possible treatment strategies for obesity include the following.

Ascertain and Address Causes of Obesity

Obesity can be caused by many different factors. Often the cause never is discovered. Sometimes, however, people know why they are gaining weight. The cause could be overeating in response to emotional drives, eating the wrong kinds of food, or having limited access to healthful food. Some medications contribute to obesity. If this is the case, then people should consult their health care providers and adjust medications, if possible. Some health problems—such as depression or polycystic ovary syndrome—increase the risk of obesity. In some cases, addressing the health problem can reduce obesity.

Reduce Food Intake

No particular eating plan has been found to result in permanent weight loss. Eating plans that provide meals or meal substitutes tend to be a little more successful than plans that require people to make numerous food choices throughout the day. Unless dieters also develop new eating behaviors, however, the weight lost often is regained once the dieting period is over.

In a quest for rapid weight loss, many obese people turn to very low-calorie diets, which supply approximately 400 to 800 kcals per day. These diets only should be implemented with close medical supervision, as complications can result. Such diets can lead to rapid initial weight loss, which is a motivational factor. Unfortunately, people on these diets rarely succeed in maintaining the weight loss for even a year. Researchers have found that severely restricting calories leads to a drop in resting metabolic rate as the body shifts into a "starvation response."

The body puts all nonessential biological functions on hold. This can include reproductive function, immune response, and growth and repair. Very low-calorie diets can be harmful for adolescents and older adults, because bone density and muscle strength can be compromised.

Most diets will result in weight loss if followed. Only permanent lifestyle change, however, results in long-term weight-loss maintenance. In general, following healthful dietary guidelines combined with reducing intake of foods lower in nutrient density (e.g., soft drinks, desserts, white breads) is a sound approach to reducing food intake.

Increase Physical Activity

Physical activity not only burns calories; it also reduces risk of obesity-related disorders for those already overweight and obese. Exercise helps to normalize blood pressure, blood glucose, and blood lipid levels. Physical activity need not be vigorous and must be adapted so as to not cause injury. People with extreme obesity might require weight-supported exercise—such as water exercise—to avoid injury. People with low fitness levels should begin slowly and build exercise effort gradually. Building to 60 minutes or more per day is recommended for lifelong weight control. Minutes can be accumulated in several sessions and need not occur in one stretch of time.

Medication

To date, weight-loss medications have been plagued with risky side effects and low rates of long-term efficacy. An over-the-counter medication called "Alli" blocks some fat absorption. Success rates using this medication alone, however, without changes in eating behavior, are low. Similarly, a number of prescription medications are available, but all have serious side effects and must be combined with healthful eating and exercise behaviors (Mayo Clinic Staff, 2012). Diethylpropion ("Tenuate") and phentermine ("Adipex") decrease appetite and promote feelings of fullness, but only can be used for 12 weeks. Orlistat ("Xenical") is a stronger version of Alli, acting to block fat absorption. Locaserin ("Belviq") decreases appetite and increases sense of fullness. "Qsymia" contains phentermine and topiramate and is approved for long-term use.

Bariatric Surgery

Numerous surgeries have been developed to treat obesity. Most involve making the stomach smaller, thus causing discomfort if the patient overeats. Some surgeries bypass part of the small intestine, thus reducing nutrient and calorie absorption. Although surgeries usually lead to weight loss for several months following the surgery, many people regain the lost weight if they are unable to change the eating habits that caused the initial obesity.

Psychological Support

Private counselors, self-help groups, and commercial weight-loss programs all offer psychological and social support for individuals trying to lose weight. Some programs now are available online.

Best Evidence-Based Recommendations

Over the past two decades, scientists have studied the minority of people who manage to lose a significant amount of weight and keep it off. The following list describes what helps people maintain their weight.

- Limit empty calorie foods, and consume reasonable portions of healthful food.
- Consume plenty of vegetables.
- Exercise for at least an hour a day.
- Cultivate healthy habits that can be sustained, rather than severely restricting calories or cutting out entire food groups.

Barbara A. Brehm

Research Issues

Some health professionals question the value of treatments for obesity that impose health risks, because success rates for these treatments are fairly low. Medications, surgeries, and restrictive diets all carry risks of significant side effects. In some cases, obesity treatment appears to actually worsen obesity over time. Many people lose weight with obesity treatment, only to regain that weight—and more—once they stop their diet or other treatment; this phenomenon is known as weight cycling. Psychological damage can result from weight cycling experiences, as people initially feel proud of their self-control and weight loss, but over time eventually give in to hunger, food cravings, and strong drives to overeat, which can lead to feelings of guilt, shame, low self-esteem, and even to eating disorders. Some groups, such as Health at Every Size, oppose prescribing weight loss for obese patients, and instead propose making healthful lifestyle changes. More about Health at Every Size can be found on the organization's website (http://www.haescommunity.org/).

See Also: Bariatric surgery; Fad diets; National Weight Control Registry; Obesity, causes; Obesity, definitions and health risks; Weight Watchers.

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Older Adults, Nutrition Needs

Older adults—generally defined as people who are 65 years of age or older—comprise the fastest-growing segment of the U.S. population. This group grew from comprising about 4% of the population in 1900 to 13% of the total population, or more than 40 million people, in 2010 (Administration on Aging, 2011) and is expected to represent approximately 20% of the population, or 72 million people, by the year 2030 (CDC, 2013). Physiological and psychological changes that



Doug Lilly, left, of the Modesto Salvation Army meals on wheels delivers a meal to Ted Jenson, 73, in Modesto, California. Programs such as Meals on Wheels help to address the nutrition needs of older adults. (AP/Wide World Photos)

accompany the aging process often require adjustments in eating behavior and nutrient intake. Although general dietary guidelines apply to healthy older adults, reduced calorie needs because of declining energy output and reduced muscle mass mean that more nutrition must come from fewer calories, emphasizing the importance for older adults to make nutrient-dense food choices as much as possible.

The nutrition needs of older adults can be influenced by a number of factors, including the following.

- Changes in chewing and swallowing: Dental problems limit people's ability to chew some foods. Swallowing problems increase with age, making eating more difficult. Good dental care and swallowing therapies often can help address these issues.
- Less effective digestion and absorption of nutrients: With aging, the production of saliva and digestive secretions declines, as does gastrointestinal motility. Nutrients, especially vitamin B12, folic acid, calcium, iron, and zinc, can be more poorly absorbed, and the risk of constipation increases.
- Senses of smell and taste could change: The sense of smell and sense of taste tend to become less acute with age and could reduce the pleasure experienced during eating.
- Decreased vitamin D production in the skin: The skin becomes less effective at making vitamin D, therefore many older adults benefit from vitamin D supplementation.
- Reduced muscle and bone mass: Along with regular physical activity, a healthful diet can help slow these losses. Older adults usually need more calcium, vitamin D, protein, and adequate potassium.
- Obesity: Many older adults have unhealthy levels of excess body fat. Although some excess fat can help older adults fight illness, too much body fat is associated with all of the health risks seen in other adults: heart disease, hypertension, stroke, and type 2 diabetes. Excess fat also can worsen joint pain, especially in the back, hips, and legs.
- Health problems: Two out of three older adults suffer from one or more chronic conditions such as heart diseases, cancer, chronic lower respiratory diseases, stroke, Alzheimer's disease, and diabetes, which influence dietary recommendations. Limited vision and hearing, as well as arthritis and other musculoskeletal problems, can limit a person's ability to shop, cook, and eat.
- Medication side effects: Some nutrients interact with medications. People on blood thinners, for example, must limit foods high in vitamin K, such as kale, spinach, and collards. Some medications negatively influence hunger and appetite.
- Psychosocial factors: Living alone, losing friends and family members to illness or death, limited transportation options, financial difficulties, and other situations can influence people's eating behaviors.

The most common nutrition concerns for older adults include those listed below.

Nutrient-Dense Calories

Although older adults generally need fewer calories, their nutrient needs are greater. Older adults should strive to eat plenty of fruits and vegetables; lean sources of proteins, including eggs, nuts, legumes, seafood, poultry, and other meats; and healthful dairy products, if they are not lactose intolerant. Older adults might benefit from a multivitamin-mineral supplement. Additionally, to avoid obesity, older adults should limit intake of empty calorie foods such as salty snacks and dessert foods.

In addition to a healthful diet, older adults should engage in at least 30 minutes of physical activity every day. Examples of moderate physical activities include brisk walking, dancing, and swimming. Strength training is especially important for older adults, to reduce the age-related loss of muscle mass and functional decline. Older individuals who are inactive or have health problems should consult a health care provider before substantially increasing physical activity level.

Water

Water has many important roles in the body. It helps with digesting food, absorbing nutrients, and getting rid of waste. With age, a person's sense of thirst declines and might not reliably serve as an indicator of water needs. Thus, to avoid dehydration, it is important for people to drink water even if they are not feeling thirsty. Staying hydrated is especially important when engaging in physical activity and on warm days. Drinking plenty of water can help those adults that have insufficient saliva to better swallow food.

Calcium and Vitamin D

To maintain bone health, older adults benefit from consuming more calcium through food or supplements. The calcium recommendation for women ages 51 and older, and for men ages 71 and older is 1,200 mg per day. The recommendation for men who are ages 51 to 70 is 1,000 mg of calcium per day.

Adults between ages 50 and 70 years old need at least 600 international units (IUs) per day; individuals age 70 years or older need at least 800 IU of vitamin D per day. Vitamin D plays an important role in promoting calcium absorption and utilization. Vitamin D is available from direct sunlight, foods fortified with vitamin D, supplements, and multivitamins. Yogurt is a good source of calcium, and some brands are fortified with vitamin D. Fortified cereals, fortified fruit juices, dark green leafy vegetables, and canned fish with soft bones also are good calcium-rich food options. Be sure to check the food label to make sure that vitamin D is added to the food items.

Vitamin B12

Some individuals older than age 50 might have a difficulty absorbing vitamin B12. This group of individuals requires 2.4 microgram (mcg) of B12 each day. Foods

that are good sources of B12 are fortified cereals, lean meat, certain fish, and seafood.

Fiber

Fiber plays an important role in reducing the risk of heart disease, controlling weight, preventing type 2 diabetes, and reducing constipation. Examples of good sources of fiber are legumes (beans and peas); whole-grain breads and cereals; and nuts, seeds, fruits, and vegetables.

Potassium

Potassium plays an important role in reducing the risk of high blood pressure and reducing loss of lean body mass. Foods that are good sources of potassium include fruits, vegetables, milk, and yogurt.

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See Also: Cardiovascular disease and nutrition; Diabetes, type 2; Eye health; Hypertension and nutrition; Water needs, water balance.

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Organic Food and Farming

Organic foods are grown at farms that must meet certain standards of agricultural practice. In the United States, these standards are created and enforced by the USDA National Organic Program. These standards include no use of synthetic pesticides; foods are not processed using chemical food additives, irradiation, or industrial solvents; and foods contain no genetically modified organisms. Organic



Organic fruit and vegetables are commonly available at farmers' markets and many grocery stores. Sold alongside conventionally grown produce, consumers often have to choose between the additional cost of organic produce or possible health concerns due to the use of pesticides in conventionally grown produce. (morgueFile)

farming uses specific agricultural methods to produce crops that meet the definition for organic food. Organic farming is a growing industry now worth $26.7 billion in the United States (Walsh, 2012).

Many leading health experts believe that organic food is healthier but others argue that there is no difference in nutrient value between organic and conventional produce. People in favor of organic food believe it contains fewer harmful pesticides and is less harmful to agricultural workers and the environment. Those who favor conventional produce tend to argue that organic farming is not always eco-friendly and in some instances actually can be less sustainable than conventional farming.

Pesticides: Content and Risks

Conventional produce is grown at farms that use pesticides and fertilizers to make the crops grow faster and more abundantly. Although this type of agriculture hopes to supply the world with more produce, chemical pesticides have side effects

Labels for Organic and Other Foods from the U.S. Department of Agriculture

The term "organic" is regulated on food labels by the U.S. Department of Agriculture, Agricultural Marketing Service's National Organic Program. Its website provides the following information on the oversight and labeling of organic food products.

How Are Organic Products Overseen?

The National Organic Program regulates all organic crops, livestock, and agricultural products certified to the U.S. Department of Agriculture (USDA) organic standards. Organic certification agencies inspect and verify that organic farmers, ranchers, distributors, processors, and traders are complying with the USDA organic regulations. To sell, label, or represent products as organic, operations must follow all of the specifications set out by the USDA organic regulations.

How to Tell if Your Food Is Organic

Look at the label. If it has the USDA organic seal, then the product is certified organic and has organic content of 95% or more.

Other Labels

There are other voluntary labels for livestock products, such as meat and eggs. Animal-raising claims must be truthful and cannot be misleading. The USDA Food Safety Inspection Service verifies the truthfulness of these claims.

- Free-range. This label indicates that the flock was provided shelter in a building, room, or area with unlimited access to food, fresh water, and continuous access to the outdoors during their production cycle. The outdoor area might or might not be fenced and covered with netting-like material. This label is regulated by the USDA.
- Cage-free. This label indicates that the flock was able to freely roam a building, room, or enclosed area with unlimited access to food and fresh water during their production cycle.
- Natural. As required by USDA, meat, poultry, and egg products labeled as "natural" must be minimally processed and contain no artificial ingredients.
- Grass-fed. Grass-fed animals receive a majority of their nutrients from grass throughout their life, and organic animals' pasture diet can be supplemented with grain. Also USDA regulated, the grass-fed label does not limit the use of antibiotics, hormones, or pesticides. Meat products can be labeled "grass-fed organic."

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on people's health. Farmworkers who are exposed to pesticides on a daily basis and in large quantities face the great risk of developing short-term and long-term diseases. Laboratory studies have shown that pesticides can cause cancer, nerve damage, and birth defects, and especially have serious risks for growing children (EPA 2012). The federal government closely regulates pesticide use, trying to ensure that the residue leftover is not enough to pose any major risk to human health or the environment. Many health experts think that these levels are too high, however, and state that the pesticide residue left on produce can lead to serious health complications. Many consumers favor organic farming because it does not use synthetic fertilizers or chemical pesticides. This does not mean that organic food is completely free of pesticides, however. Pesticides migrating from neighboring farms or coming into contact with organic food during transportation can slightly contaminate organic produce. A meta-analysis performed by researchers at Stanford University concluded that organic produce has much lower levels of pesticide residue than does conventional produce, 7% compared to 38% (Smith-Spangler et al., 2012). There is no clear evidence that pesticides are completely harmless, even if the residue on conventional produce is below a certain level that the federal government declares to be acceptable. For this reason, many health experts recommend reducing intake of pesticides by buying organic.

Nutrition

The Stanford study concluded that organic labeled produce was, on average, no more nutritious than conventional produce. There were no consistent differences in the vitamins found between the two types of produce except for phosphorus, which can easily be attained in large quantities from one's diet and therefore, getting extra amounts from organic produce does not provide any major health benefits. The Stanford study did find that compounds called phenols were more plentiful in organic produce. Phenols are believed to help prevent cancer. Researchers found that the amounts of phenols varied significantly in each study of produce, however, and therefore interpret their findings with caution (Smith-Spangler et al., 2012). Conversely, several other well-designed studies have found organic produce to have greater levels of certain nutrients and antioxidants than their conventional counterparts. Because it is unclear at this point in time whether organic produce is more nutritious than conventionally produced fruits and vegetables, most nutritionists agree that consumers should not buy organic food solely because it might be more nutritious.

Environmental Impact

Whether the process of organic farming is more eco-friendly and sustainable than conventional farming causes some speculation. Conventional farms use pesticides and fertilizers to maximize the growth of produce. Proponents of conventional agriculture argue that these methods supply the world with more produce using

less land. Using less land means that less wilderness must be destroyed and converted into farmland. Because one-third of the planet's land already is used for farming, anything that limits the destruction of more wildernesses is beneficial for the environment (Walsh, 2012). The conclusion drawn in a meta-analysis published in the scientific journal *Nature* is that organic farming produces 5% to 34% lesser crop yields than does conventional farming, depending upon site and crop characteristics (Seufert, Ramankutty, & Foley, 2012). Studies such as these suggest that organic farming might not be as sustainable and eco-friendly as hoped.

Some experts argue with the notion that organic farming is necessarily less efficient than conventional agriculture, especially when organic methods are tailored to location and type of crop. Cornell University did a 22-year study that reviewed the study of the Rodale Institute Farming Systems Trial, the longest running comparison of organic versus conventional farming performed in the United States. The Cornell study found that the number of crops produced by organic farming was the same as conventional farming (Weil, 2008). According to this analysis, not only was organic farming just as productive as conventional farming methods; it was also more eco-friendly—using 30% less energy and water than conventional farming, and with no use of chemical pesticides (Weil, 2008). Another study reported in the March/April 2008 issue of *Agronomy Journal* stated that organic farming produced as much wheat, alfalfa, corn, soybeans, and winter wheat as conventional methods and the techniques used by organic farmers built up soil instead of depleting it (Weil, 2008).

Conventional agricultural methods can have harmful effects on the environment. Nitrogen, for example, is the key chemical ingredient in synthetic fertilizer. A large quantity of nitrogen-containing synthetic fertilizer is used each year by conventional farmers to promote rapid growth of crops. This growth is much faster and greater than the growth produced by releasing nitrogen from compost—a system used by organic farmers. Unfortunately, not all of the nitrogen from the fertilizer used by conventional producers ends up in the crops. A significant proportion of it runs off and pollutes water and soil. It should be noted that the manure used in organic farming—if not monitored and managed correctly—also can run off and pollute nearby water sources.

Organic farming might have a negative impact on the environment if the food produced must be transported long distances to markets. The term "organic" does not mean "local." The organic produce seen in the supermarket can come from outside of the United States. This means there is a significant carbon footprint in terms of transportation. Transporting produce requires significant carbon dioxide emissions for the food to reach the specific destination (the consumer). These gases emitted have negative effects on the environment, such as impacting climate change.

Theresa E. Lane

Research Issues

People concerned with pesticide residues on fruits and vegetables often turn to the Environmental Working Group's (EWG) *Shopper's Guide to Pesticides in Produce*. The EWG each year rates fruits and vegetables based on pesticide residue measures. The results are summarized in two food lists—the "Dirty Dozen Plus" lists foods that were raised conventionally and had the greatest levels of pesticide contamination, and the "Clean Fifteen," lists the conventionally raised fruits and vegetables with least pesticide residues. Many scientists argue that conventionally farmed produce sold in the United States has safe levels of pesticide residues. Many consumers, however, still believe that lower levels of pesticides probably are better for reducing certain health risks, such as cancer.

Environmental Working Group. (2013). *Executive summary: EWG's 2013 shopper's guide to pesticides in produce*. Retrieved from http://www.ewg.org/foodnews/summary.php

See Also: Sustainable agriculture.

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Orthorexia

Orthorexia, also known as "orthorexia nervosa," refers to an obsession with following a perfect, healthy diet, as defined by the person with orthorexia. Although orthorexia has not gained official recognition by the American Psychiatric Association as a clinical disorder, in its extreme form it shares traits with eating disorders, anxiety disorders, and obsessive-compulsive disorders. The term

"orthorexia" has been widely adopted, as it describes beliefs and behaviors that have become common in many groups, namely a concern for healthy eating and food quality. People who are orthorexic, however, should not be confused with people who are just conscious about their health. Orthorexics have an extreme preoccupation with the quality, purity, and quantity of what they consume. They refuse to eat anything that they consider incorrect. They might for example, refuse to eat foods that contain preservatives, artificial colors or flavors, unhealthy fats, genetically modified ingredients, pesticide residues, or foods that are high in salt, sugar, or other such ingredients. People with orthorexia also might be concerned with how their food is prepared and what materials and kitchenware were used to make it. Extreme forms of orthorexia can result in excessive weight loss, malnutrition, and in severe cases even death.

Steven Bratman, M.D., first coined the term "orthorexia" in 1997 to describe "an unhealthy obsession with healthy eating." The term describes a disorder parallel to the eating disorder anorexia. The term "anorexia" is derived from Greek words meaning "no appetite," and "orthorexia" is derived from root words meaning "correct appetite." People with anorexia struggle to eat less food, and people described as having orthorexia struggle to eat correctly. Although it initially was meant to be "tease therapy" for those of Dr. Bratman's patients who were anxiously absorbed in their diet selections, it has become a descriptive term for people with an unusually extreme preoccupancy.

Some people with orthorexia could begin changing their eating habits to conform to healthy eating guidelines. Following these guidelines then becomes increasingly important in their lives. People developing orthorexia could become more obsessive about following extreme food rules because they are consciously or unconsciously trying to become healthy, manage anxiety, lose weight, increase self-esteem, create meaning in life, or gain a sense of control. If orthorexics begin to meet any of these personal goals through obsessively selective eating habits, then they often begin to judge other people by their diets, and believe that those people who do not share the same diet are inferior. Withdrawal and isolation from society follow, and people with orthorexia could begin to neglect other aspects of their lives. If for any reason, people with orthorexia do not adhere to their food rules, then they might experience intense guilt that is punished by implementing stricter rules, and beginning behaviors such as fasting or extreme exercise. Thus, rather than just consuming healthful food, people with orthorexia are consumed by their rigid diet.

Some of the food rules developed by orthorexics are fairly common in North America. Many people designate foods and eating behaviors as "good" and "bad." This is unfortunate, because they then also label themselves as "good" or "bad," depending upon how they have eaten that day. When should people be worried that their concern for a healthy diet is becoming an obsession? If it seems that concerns about nutrition and eating behaviors are interfering with daily life or are causing feelings of distress, then the person should seek the advice of a mental-health professional who can help put food into perspective.

The first step toward recovery is for the orthorexic to admit he or she has a problem and then work to understand its cause. In the process, a diet with more flexibility must be adopted. Seeing a team of dieticians, physicians, and psychotherapists or a practitioner who is qualified to treat people affected by eating disorders might be necessary for recovery. Medications for underlying emotional health disorders also can be helpful.

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See Also: Eating disorders.

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Osteoporosis

Osteoporosis, which means "porous bones," is a bone disease characterized by gradually declining bone mass. As the mineral and protein content of bones is lost, the bones become less dense and have larger open spaces within them. As the bones become more porous they also become more fragile. This weakening of the bones can lead to fractures, most commonly in the spine, hip, and wrist. Fractures are debilitating injuries, especially in older adults. About half of all women and a quarter of all men older than age 50 experience a fracture at some time. Generally, women who are 50 years of age and older (postmenopausal) and men 70 years of age and older are most susceptible to significant decreases in bone mineral content, also known as bone mineral density (BMD). Osteoporosis is a silent disease and often remains undetected until a person suffers a fracture or notices a loss of height because of bone loss in the spinal column. Several lifestyle factors help to slow the age-related loss of bone tissue and prevent osteoporosis, including physical activity and good nutrition.

Bone Physiology

Bones are composed of several types of tissue, including bone marrow, nerves, blood vessels, and bone tissue. Bone tissue consists of a matrix of mineral salts (primarily calcium and phosphorus) that give bone its hardness, and a network of collagen fibers that give bone its strength. Special cells in the bone tissue, called "osteoblasts," are responsible for bone formation. The number of osteoblasts in the body decreases as a person ages, and this loss can contribute to the development of osteoporosis. "Osteoclasts," conversely, are involved in bone resorption (bone loss). Osteoblasts and osteoclasts work together in a process called remodeling, as bone tissue is continuously broken down and rebuilt in response to a number of factors, including diet, physical activity, and a variety of hormones and other signaling molecules.

Peak bone mass is achieved in young adulthood, and begins to decline at about age 40, at which time both men and women lose bone mass at a rate of about 0.5% per year (Knoke & Barrett-Connor, 2003). In the five years following menopause, women lose bone mass at a faster rate, even with a good diet and plenty of physical activity. After these five years, bone loss returns to a slower pace.

Osteoporosis is diagnosed when bone mineral density reaches a critically low level. Although many medications are available to help slow bone loss, all have side effects and result in only minor gains in bone mineral density. Several lifestyle factors—including regular physical activity and good nutrition—can help slow the rate of bone loss in midlife and possibly in old age as well. It therefore makes sense for women and men at risk for osteoporosis to be physically active and consume a healthful diet.

Diagnosing Osteoporosis

Unfortunately, researchers do not yet have a good way to measure bone strength. The most common measurement of bone health is bone mineral density (BMD), which is measured using a type of x-ray. Bone mineral density usually is measured in the spine, hip, and wrist, important areas to know about in terms of fracture risk. Although BMD is correlated with fracture risk, the amount of mineral deposited in bone is only partly responsible for a person's bone strength. Bone strength also depends on the structure of the mineral deposits—how they are arranged in the bone tissue. Bone quality is as important as BMD, for it determines how well a bone behaves in terms of responding to stress. Unfortunately, there presently are no simple tests for bone quality.

Osteoporosis Risk Factors

A variety of risk factors are associated with osteoporosis. Women are more likely than men to develop osteoporosis. Caucasian and Asian women are at greater risk than are other groups. People who are underweight also generally are more at risk than those at normal weight, especially at an older age. A family history of

osteoporosis is a strong risk factor. The sex hormones estrogen and testosterone protect against osteoporosis; thus, low levels of these hormones—such as that which occurs with aging, menopause, or disruption of the menstrual cycle in women—increase the rate of bone mineral loss. Poor digestive function can reduce the absorption of nutrients such as calcium that are important for bone health. A poor diet also can increase risk for osteoporosis. Physical activity that applies force to the bones, such as walking and strength training, increases bone density. Because peak bone mass is attained in young adulthood, osteoporosis prevention ideally begins in childhood and adolescence with a healthful diet and adequate vigorous physical activity.

Osteoporosis and Nutrition

Nutrition can affect rates of bone mineral deposition and loss throughout the lifespan. Although genetics, age, and hormonal status are much greater risk factors than diet is, a variety of dietary issues including calcium and vitamin D intake, net endogenous acid production (NEAP), protein intake, and the intake of other nutrients and dietary components affects bone metabolism.

Calcium and Vitamin D

Calcium is especially relevant to osteoporosis prevention. As a major component of bones, it is important to consume and absorb enough calcium. Calcium can be found in dairy products (i.e., milk, yogurt); in fish that are consumed without removing their bones, such as sardines and salmon; in greens such as spinach, bok choy, and broccoli; and in fortified foods and supplements. Calcium from food sources is more effective and more readily absorbed than is calcium from supplements. It is important to consume calcium supplements with vitamin D to avoid the negative health effects of too much elemental calcium, which has been associated with slightly increased risk of cardiovascular disease (Bolland et al., 2011). Calcium intake should be about 1,000 mg per day for adults, and 1,200 mg/day for adults 50 years old and older.

Cholecalciferol (vitamin D3) is essential for the absorption of calcium in the body. Calbindin, which is the protein that helps transport calcium into the bloodstream, relies on vitamin D3. Without vitamin D3, calcium is not well absorbed and is excreted, sometimes contributing to the formation of kidney stones.

Net Endogenous Acid Production

The Western diet, with its rich supply of meat and grain, could increase the risk of osteoporosis through a variable known as "net endogenous acid production" (NEAP). Net endogenous acid production does not reflect the acidity of foods eaten but rather how digestion of these foods affects the body's acid-base balance. In general, protein foods and grains cause a relatively high production of acid, and fruits and vegetables reduce NEAP. Therefore even lemon juice—which is quite

acidic—actually has an alkalizing effect on the body after digestion. Fruits and vegetables contain potassium and magnesium, which have an alkalizing effect on the body. Increased levels of NEAP have been associated with reduced bone density in several studies (Dawson-Hughes, 2010). NEAP levels are especially of concern as people age and kidney function declines. How does NEAP affect bone health? When the body becomes too acidic, bone tissue releases minerals to buffer the excess acids. Over time, a slow-but-steady loss of bone mineral can result in low bone density. Years of low-grade metabolic acidosis may help to explain why osteoporosis rates are so high in cultures consuming a lot of meat and grains and low levels of fruits and vegetables. Researchers have shown that an adequate intake of protein in the later years is important for the maintenance of muscle and bone, and they suggest that, rather than decreasing protein, it is more important for people to increase intake of vegetables and fruits (Dawson-Hughes, 2010).

Protein

Protein is an important nutrient and studies suggest an adequate protein intake is helpful in preventing osteoporosis in older adults. Older adults with low protein intakes tend to have an increased risk of fragility—with loss of both bone and muscle mass. Although protein foods such as meat and dairy products increase NEAP, studies on the long-term effects of high-protein diets on bone density in young and middle-aged adults over time are lacking. Available evidence reinforces the importance of a balanced diet, with adequate but not excessive amounts of protein.

Magnesium, Potassium, and Sodium

Magnesium is another mineral component of bone that contributes to bone density and strength. Both magnesium and potassium are electrolytes that maintain an alkaline environment in the body, and thereby are very important in preventing calcium excretion from the body. Conversely, greater sodium levels have been associated with increased risk for osteoporosis. High sodium levels in the blood lead to increased calcium excretion in the urine, as the kidneys reduce their rate of calcium reabsorption.

Vitamin K

Vitamin K is required for the manufacture of the calcium-binding proteins that help transport calcium from the digestive tract into the bloodstream and throughout the body. Vitamin K is important for osteocalcin formation. Osteocalcin is an important protein in bones and is required for bone mineralization. Vitamin K is obtained from both food, especially plant foods, and from bacteria residing in the large intestine. Foods high in vitamin K include green leafy vegetables such as broccoli, brussels sprouts, and spinach.

Vitamin C

Vitamin C is an important antioxidant; it reduces oxidative stress in the body and inhibits bone resorption. Oxidative stress (free radicals) causes bone resorption by affecting the production and survival of osteoclasts, osteoblasts, and osteocytes (cells in the bone), which maintain bone balance and health (Manolagas, 2010). Oxidative stress appears to play an important role in the development of osteoporosis in midlife and older adults, as bone-balancing hormones decline. Vitamin C also is associated with bone health as a cofactor in collagen formation; collagen is an important connective tissue protein found in bones. Vitamin C is found in many fruits and vegetables, including citrus fruit and potatoes.

Vitamin B12

Vitamin B12 is known for its participation in DNA synthesis. As it is an important cofactor in DNA synthesis, vitamin B12 is important for bone synthesis as it likely helps osteoblast activity and bone formation. Vitamin B12 is found in meat, seafood, eggs, and dairy products. A Framingham offspring study found that those with lower bone densities had lower B12 serum concentrations, suggesting the vitamin is important in bone density (Tucker, 2009).

Vitamin A

Adequate vitamin A is required for normal bone growth and development. High intakes of vitamin A, however, have been associated with increased risk of osteoporosis. This association is for retinol only, and has not been seen with the vitamin A precursors such as beta carotene and the other carotenoids. Vitamin A as retinol is added to many dietary supplements, therefore people should be sure that they do not consume too much vitamin A. The safe upper limit for vitamin A is about 3,000 mcg per day for adults.

Other Dietary Components

Food components and supplements that, like vitamin C, exert antioxidant effects in the body might help to reduce inflammation levels, and potentially could help to maintain bone health. Soy isoflavones and other phytoestrogens exert estrogen-like effects on bone, and might help to prevent bone mineral loss in older adults. Boron—a trace mineral—appears to contribute to bone health. Boron is found in fruits, vegetables, nuts, and legumes.

Alcohol and Cola

Alcoholism has been linked to osteoporosis; however, moderate alcohol use (1 to 2 drinks a day) has been shown to be associated with higher bone density in

women. The exact mechanism is not known, but the effect likely is due to an increase of estrogen in response to the alcohol.

Consumption of cola beverages and a high consumption of soft drinks in general have been linked to osteoporosis. Researchers speculate that people who drink several soft drinks per day might drink less milk or other more healthful beverages. Cola beverages appear to be most harmful, perhaps because they contain phosphoric acid. Ingesting too much phosphorus and too little calcium interferes with calcium absorption, as phosphorus binds to calcium making it unavailable.

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Research Issues

Some osteoporosis experts have called for the Institutes of Medicine to increase the Daily Recommended Intake (DRI) for vitamin D (Dawson-Hughes, 2010). The U.S. Preventive Services Task Force, however, in 2012 determined that calcium and vitamin D supplements have not been proven to be beneficial for everyone, and suggests that people should discuss their lifestyle with their doctors to determine whether taking a supplement is the recommended route to attaining bone health (U.S. Preventative Services Task Services). The U.S. Preventive Services Task Force does not deny that calcium and vitamin D are important for bone health; rather, it suggests that supplementation is not as helpful as anticipated and could lead to kidney stones, therefore supplements should not be recommended to everyone.

See Also: Antioxidants; Calcium; Female athlete triad; Phytoestrogens; Protein, Vitamin D.

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The Paleolithic Diet

The Paleolithic diet or "Paleo diet," also known as the "caveman diet," "Stone Age diet," and "hunter-gatherer diet," mimics the presumed diets of Paleolithic humans. Claiming that human DNA has changed little in the 10,000 to 40,000 years since the end of the Paleolithic era, the Paleo guidelines strive to simulate eating patterns and types of foods that were eaten prior to the development of agriculture and domestication of livestock to provide the body with the nutrients and types of foods that people evolved to consume. Anthropologists have studied and interpreted archaeological evidence as well as the diets of modern-day hunter-gatherer populations to describe the probable diets of early hominids. The term "Paleolithic diet" refers both to the anthropological perspective on hominid nutrition as well as popular interpretations of this evidence that have been built into prescriptions for healthful eating. Most people, however, use the term to refer to modern-day dietary regimens that are based on anthropological research.

Paleo diets prescribe only foods that would have been available to the hunter-gatherers such as grass-fed meats, wild seafood, eggs, fruits, vegetables, roots, nuts, seeds, mushrooms, insects, and herbs. Organic and non-genetically modified foods are recommended. The diets limit or prohibit consumption of grains, most legumes, milk, dairy foods, vegetable oils, refined salts, and processed sugars (some honey is allowed in some versions). Few processed foods are allowed, although some versions of the diet permit convenience foods such as almond milk and nut butters. Paleo diets generally are high in soluble fiber, antioxidants, vitamins, phytochemicals, omega-3 fatty acids, monounsaturated fats, and low glycemic carbohydrates. People often decide to try the Paleo diet as a tool for weight loss and weight maintenance. Another reason for following such diets is prevention and mitigation of the "diseases of civilization"—health problems typically associated with a poor diet and low levels of physical activity, such as cardiovascular disease, hypertension, type 2 diabetes, osteoporosis, and many gastrointestinal disorders. Studies have shown that the amount of highly processed foods present in the Western diet and the eating habits intrinsic to the Western diet are major factors in these chronic health problems. Archaeological evidence suggests that the people who survived the acute health problems that severely limited the life span during Paleolithic times (such as injury and infection) had little artery disease and strong bones.

Gastroenterologist Walter L. Voegtlin, who published *The Stone Age Diet: Based on In-Depth Studies of Human Ecology and the Diet of Man* in 1975, first

coined the term "Paleo diet." The dietary changes he asked his patients to follow resulted in positive outcomes for common GI health problems. Since then, the Paleo diet has evolved and has been adapted by many authors and journalists.

Paleo Diet Characteristics

Paleo diets have several characteristics that are meant to optimize a person's health, minimize risk of chronic disease, and promote weight loss in people who are overweight.

- Protein intake: Paleo diets have a greater protein intake than the typical Western diet. Protein comprises about 15% of the calories in the Western diet, whereas some Paleo diets recommend that protein comprise up to a third of caloric intake. Research on other high-protein diets supports the idea that a high-protein intake reduces feelings of hunger.
- Carbohydrate intake: Paleo diets advise that carbohydrates be consumed in the form of fruits and non-starchy vegetables. Because the intake of sugars, grains, and most processed foods usually is eliminated or reduced, the glycemic load (which reflects the effect of diet on blood sugar level) of Paleo diets is usually lower than that of the typical Western diet. A great deal of research suggests that low glycemic load diets are associated with reduced risk of cardiovascular disease, type 2 diabetes, and the cardiometabolic syndrome. Conversely, athletes and other very active people sometimes find that Paleo diets lead to suboptimal glycogen levels and poorer sport performance. (Glycogen is a storage carbohydrate found in the liver and skeletal muscles which helps supply energy for physical activity.)
- Fiber: Paleo diets supply high levels of dietary fiber from the large volumes of plant foods consumed. High fiber intakes are associated with reduced risk of gastrointestinal problems, and help support healthy microbe populations in the digestive tract.
- Fats: Paleo diets aim for a high intake of healthful fats, including omega-3 fatty acids, from plants, seafood, meats, and eggs. A hallmark of Paleo diets is the effort to achieve a better balance of omega-3 and omega-6 fatty acids in the diet. Western diets typically have a much greater intake of omega-6 fatty acids than omega-3 fatty acids. This imbalance is thought to be associated with a pro-inflammatory state and faster blood-clotting rates, both of which are associated with a great risk of cardiovascular disease and other health problems associated with excess inflammation. Paleo diets also promote the consumption of grass-fed animals, which have lesser body fat levels and more omega-3 fatty acids than livestock that are raised eating grains.
- Sodium and potassium: Paleo diets are high in potassium, plentiful in fruits and vegetables, and low in sodium. The average American consumes twice as much sodium as potassium. High levels of sodium and low levels of potassium have been associated with increased risk of high blood pressure, stroke, heart disease, and osteoporosis.

- Alkalinity and acidity: All foods present a load to the kidneys that is either net alkaline or net acidic. Foods such as meat, eggs, and grains present an acidic load, and fruits and vegetables present an alkaline load. Because of the relatively high intake of plant foods and low intake of grains, Paleo diets result in a more alkaline profile. A greater alkaline level is associated with better bone and muscle health, especially in older adults, whose kidneys become less efficient at regulating body pH.
- Micronutrients: Paleo diets are high in many vitamins, minerals, antioxidants, and phytochemicals.

Criticisms

When experimenting with the elimination of entire food groups, risk of malnutrition increases. In Paleo diets, the elimination of dairy, grains, and legumes can be problematic. Dairy is an affordable and widely available source of calcium and protein. Although calcium can be obtained from greens and other foods in the diet, it is more challenging to consume it in adequate amounts without dairy products. The elimination of whole grains and legumes, as prescribed by the Paleo diet, also has been criticized, though it is argued that the vitamins, minerals, and fibers found in these foods can also be found in fresh fruits and vegetables, and the protein these foods supply can be found in meats, seafood, and eggs.

Paleo diets can be very expensive due to the large amounts of fresh organic produce, grass-fed meat, and wild-caught seafood that are recommended. Some nutritionists advise that the high protein intakes found in some versions of the Paleo diet could be hard on people who have compromised kidney function. People who are not overweight might have difficulty obtaining enough calories to maintain body mass on a Paleo diet. Environmentalists state that livestock—grass fed or otherwise—contribute to greater atmospheric carbon levels, and cannot be produced at levels great enough to feed the global population. Grains and legumes require fewer planetary resources. Additionally, increased demand for seafood can lead to overfishing and alarming reductions in marine populations. Environmentalists have expressed concern at the significant environmental impacts of a diet high in animal products, and the resource demand of certain products—such as almond milk—for the people following the Paleolithic diet.

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See Also: Cardiometabolic syndrome; Cardiovascular disease and nutrition; Fatty acids; Glycemic index and glycemic load; Inflammation; Osteoporosis; Phytochemicals; Sustainable agriculture.

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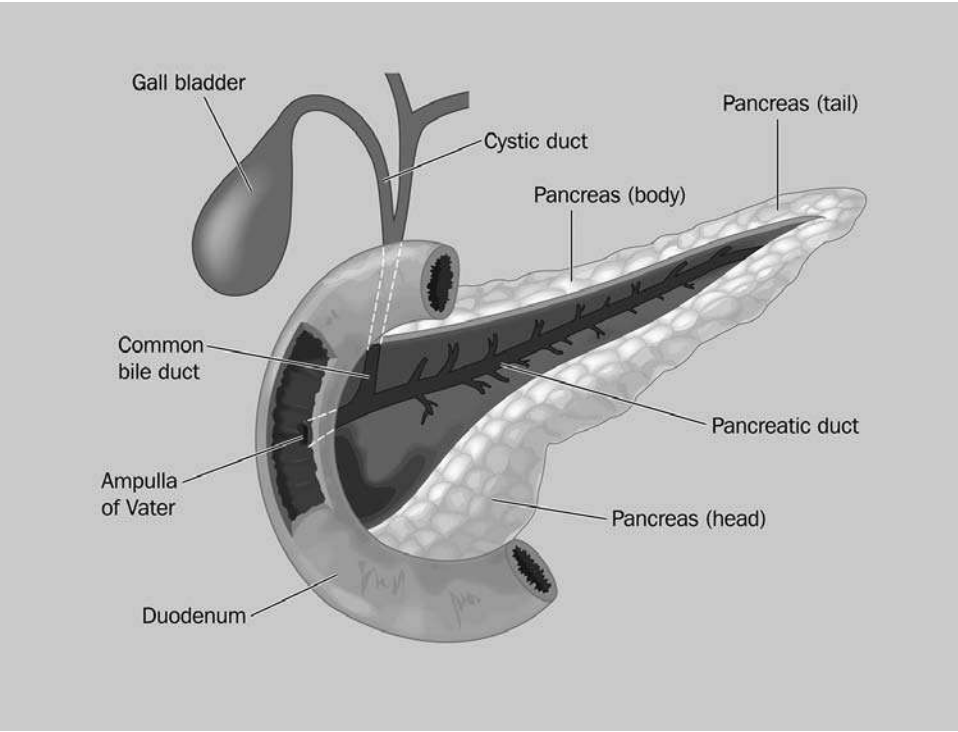
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Pancreas

The pancreas is a spongy J-shaped gland located behind the stomach on the posterior abdominal wall. Its main functions are to assist with digestive processes and to regulate blood glucose. Depending on a person's age, height, and weight, the pancreas can range anywhere between 12 cm to 15 cm in length. It is composed of five parts: the head, neck, body, tail, and uncinate process. The head is the widest part of the gland and lies in the curve of the duodenum (a portion of the small intestine). The head accounts for about 50% of the gland's total mass, making it the largest portion of the pancreas. The pancreas then narrows at the pancreatic neck, which connects the pancreatic head to the body. The pancreas body continues to narrow as it extends to the left laterally, finally forming the tail, which is the thinnest part of the gland. The narrow shape of the tail allows for it to be cupped by the spleen. The uncinate process curves behind the head and rests beneath the pancreatic body.

The pancreas is both an exocrine and endocrine gland, which means that it excretes both digestive enzymes and hormones. The exocrine tissue, which comprises 99% of the pancreas's weight, is clustered into groups of cells known as "acini" which produce digestive enzymes. These groups of cells are organized into masses that join to form ducts until they reach the main pancreatic duct. The main duct runs along the length of the pancreas and eventually merges with the bile duct before connecting to the small intestine. Endocrine tissue accounts for only 1% of the pancreas. It is found between the acinar cells in what are called "islets of Langerhans." These specific cells are involved in hormone production and distribution.

The pancreas assists in digestion by secreting pancreatic liquid into the small intestine. Pancreatic liquid is produced at a rate of about 1,500 mL per day. Water, bicarbonate, and digestive enzymes make up the majority of this liquid. The bicarbonate (a base) portion of the secretion is vital to the small intestine's ability to digest, because it mixes with acidic chyme from the stomach to create an environment with a more balanced pH level—which is necessary for proper function of small intestine enzymes.



The exocrine cells of the pancreas produce digestive enzymes that are secreted with a fluid that moves through the pancreatic duct and then into the small intestine. The endocrine cells produce insulin and glucagon, which do not travel in the pancreatic duct, but are released directly into the bloodstream. (Legger/Dreamstime.com)

Additionally, the enzyme portion of the pancreas's secretion aids in digestion by breaking down carbohydrates, fats, and proteins so that they can be absorbed and utilized by the body. Specifically, the enzymes secreted by the pancreas are: trypsin and chymotrypsin, to digest proteins; amylase, to aid in breaking down carbohydrates; and lipase, which breaks down fats into fatty acids and cholesterol.

The hormones secreted by the pancreas—insulin and glucagon—work in tandem to maintain proper blood sugar (glucose) levels. In response to an increase in blood glucose to above normal levels (usually following food consumption), the pancreas's beta cells increase their secretion of insulin into the bloodstream signaling for muscle cells, red blood cells, and fat cells to increase their rate of absorption of glucose from the blood. As these cells take in more glucose, the blood glucose level returns to the normal range, and the pancreas reduces its secretion of insulin. Conversely, if blood glucose falls below the normal range (usually due to exercise, or due to length of time between meals), the alpha cells of the pancreas secrete glucagon. The body's primary reaction to increased glucagon levels is for the liver to release stored glucose into the bloodstream. After the release of glucose restores glucose levels to within the normal range, the pancreas ceases to release glucagon.

Disruptions of Function

The main issues associated with disruption of pancreatic function are diarrhea and weight loss, and an increased risk of diabetes. Diarrhea and weight loss result from poor food absorption due to a decrease in the amount of enzymes secreted by the pancreas. Similarly, an increased risk of diabetes occurs when the pancreas does not secrete enough insulin. There are several possible ways for the function of the pancreas to be disrupted; the main two are pancreatitis and pancreatic cancer (Crosta, 2012).

Pancreatitis is the name given to inflammation of the pancreas. Inflammation generally is caused either by a tumor or a gallstone obstructing the pancreatic duct. When the pancreatic duct is blocked, pancreatic juices build up and cause damage to the pancreas. If left untreated, this can result in the pancreas digesting itself. Other possible causes of inflammation include complications associated with mumps, alcohol use, steroids, trauma, and drugs.

Pancreatitis is classified as either "acute" or "chronic." Acute pancreatitis involves a sudden onset of symptoms, including severe stomach pain, swelling and tenderness in the abdomen, nausea and vomiting, fever, and muscle aches. If pancreatitis permanently damages the organ, the condition is called "chronic pancreatitis." In addition to pain in the upper abdomen and back, chronic pancreatitis can present with diarrhea, diabetes, weight loss, and mild jaundice. Cases of chronic pancreatitis are most common in middle-aged men, and the cause of chronic pancreatitis most commonly is alcohol abuse.

Pancreatic cancer is a very serious cancer; it has a very high mortality rate—in the United States the rate is estimated to be about 32,000 people per year, a number almost equal to the number of people diagnosed with this cancer each year. Due to the pancreas's deep location in the abdomen, tumors are particularly difficult to feel during a physical exam. This makes pancreatic cancer especially difficult to diagnose. Its placement often masks symptoms until tumors are large enough to cause pain or affect the functioning of nearby organs. Pancreatic cancer can be metastatic, meaning that cancer can begin elsewhere in the body and eventually spread to the pancreas. Typically, however, the term "pancreatic cancer" refers to cancer originating in the pancreas itself (also known as "primary cancer"). The top three risk factors for developing pancreatic cancer are (1) smoking, (2) aging, and (3) ethnic background (African-Americans are at greater risk than are people of other ethnicities). Dietary factors also could influence the risk of pancreatic cancer. Diets high in meats are associated with increased risk and diets high in fruits and vegetables might reduce the risk of pancreatic cancer. Much like the symptoms of pancreatitis, the most common symptoms for cancer of the pancreas are abdominal pain, back pain, jaundice, lack of appetite, weight loss, as well as urine and stool discoloration, and swelling near injection sites during vaccine therapy (Johns Hopkins Medicine, 2012).

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See Also: Blood sugar regulation; Diabetes, type 1; Diabetes, type 2; Digestion and the digestive system; Insulin.

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Pantothenic Acid

Pantothenic acid is another name for vitamin B5. This water-soluble vitamin plays an important role in helping the human body obtain energy from the carbohydrates, proteins, and fats that it consumes. Pantothenic acid also assists with the synthesis of fatty acids necessary for cell membranes and nerves. Pantothenic acid deficiencies are rare, thanks to its presence in a wide variety of foods. Preliminary research suggests that dietary supplements derived from this vitamin might help improve blood lipid levels in some people. Risk of toxicity for pantothenic acid appears to be quite low.

Pantothenic acid derives its name from the Greek word "pantothen," meaning "everywhere" or "from every side." Dr. Roger J. Williams, a biochemist and nutrition scientist, discovered pantothenic acid while he was working at the University of Chicago. The scientific community officially acknowledged that pantothenic acid was a part of the vitamin B group in 1940 (Insel, Roth, McMahon, & Bernstein, 2013).

Physiological Functions and Deficiency Symptoms

Pantothenic acid is a component of coenzyme A (CoA), a critical compound that facilitates reactions that extract energy from carbohydrates, proteins, and fats. Additionally, coenzyme A assists with reactions that construct important fatty acids. These fatty acids help to form cell membranes, and the myelin (fatty sheath) that surrounds nerve cells. Pantothenic acid also aids in the synthesis of acetylcholine—an important neurotransmitter—and the hormone melatonin, which the pineal gland secretes to help regulate the sleep-wake cycle. Pantothenic acid is essential for the formation of heme, a component of hemoglobin, which is the compound in red blood cells that binds oxygen.

Pantothenic acid deficiencies are extremely rare, except in people who are severely malnourished. During World War II, prisoners of war were observed to have numbness, burning, and tingling in their feet, which was relieved by the administration of pantothenic acid. Subsequent studies—in which pantothenic acid deficiency was induced in humans by blocking its uptake from the digestive system—also demonstrated numbness and tingling in the hands and feet of participants. Additional symptoms associated with pantothenic acid deficiency include headache, fatigue, insomnia, and gastrointestinal problems. Animal studies have found pantothenic acid to be associated with the development of anemia.

Dietary Intake Recommendations

Pantothenic acid deficiencies are so rare that the Food and Nutrition Board of the Institute of Medicine does not have enough information to establish a Recommended Dietary Allowance (RDA) for this nutrient. Instead, the organization has set an adequate intake (AI) level for pantothenic acid at 5 mg per day for adults. The AI is based on estimated intakes of pantothenic acid in healthy people. Pantothenic acid can be found in many different food sources, including organ meats (such as liver), red meat, fish, eggs, milk and milk products, lentils, avocados, and sweet potatoes. Whole grains also contain a substantial amount of pantothenic acid, but the refining process destroys up to 75% of the pantothenic acid found in such sources. Freezing and canning processes similarly remove much of the pantothenic acid from foods, but ordinary cooking practices do not seem to have the same effect.

Health Benefits and Risks

The human body converts pantothenic acid to a similar compound called "pantethine." Studies have examined the effect of both pantothenic acid and pantethine supplements. Few health benefits or risks have been found for either compound. A few small studies have suggested that pantethine supplements might help improve blood lipid levels in some people, lowering blood triglyceride levels and improving cholesterol levels (EBSCO CAM Review Board, 2013). In one small study volunteers with rheumatoid arthritis taking pantothenic acid supplements experienced less morning stiffness and pain than subjects taking a placebo (EBSCO CAM Review Board, 2013). Because pantothenic acid and pantethine supplements appear to have few negative side effects, some researchers are interested in studying their potential as therapeutic agents, after more research has been conducted to establish whether they truly are effective. High levels of pantothenic acid do not appear to be toxic or have any additional adverse effects, therefore the Institute of Medicine has not set a tolerable upper intake level (UL) for the vitamin.

Hannah Green

See Also: Vitamins.

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Parenteral Nutrition

Parenteral nutrition (PN) refers to intravenous feeding that is designed for individuals who are unable or unwilling to receive adequate nutrition by mouth. Feeds are prepared and then placed into a solution bag that can hang for a maximum of 24 hours. Patients can either receive total parenteral nutrition (TPN), in which they rely entirely on parenteral feedings, or partial parenteral nutrition (PPN). Due to its potential risks and complications, parenteral feeding only should be considered when patients are unable to receive nutrition enterally. There are several types of parental nutrition methods (*see* Table 1).

History

Parenteral nutrition has been a successful mode of treatment since the 1960s. Published studies, however, can be traced back to Sir Christopher Wren, who in 1665 designed an experiment studying the effects of intravenous infusions in dogs. He found that solutions consisting of wine, ale, and opiates had the same inebriating effect on the animals as when taken orally by humans.

During the cholera epidemic of 1831 to 1832, Scottish physician Thomas Latta was the first to successfully treat a patient intravenously with water and saline. His discovery proved that dehydration and salt deficiencies associated with cholera could be eliminated by parenteral solutions. This was a significant contribution in the development of parenteral feeding.

Potential Reasons for Parenteral Feeding

Parental nutrition is considered only when patients are unable to consume food by mouth and when enteral feeding (the use of a feeding tube) is not an option. Some

Table 1. Types of Parenteral Nutrition

Type of Vascular Access	Route of Administration	Indications for Use	Short Term	Long Term
Non-Tunneled Central Venous Catheter	Subclavian, internal jugular, or femoral vein	Intended for short-term use, but has a high rate of infection.	✓	
Tunneled Central Venous Catheter (Broviac, Hickman)	Jugular vein or other vein in the neck	It is the most common type of long-term parenteral feeding and has the lowest rate of infection.		✓
Peripherally Inserted Central Catheter (PICC)	Basilic vein, cephalic vein, or brachial vein	Usually used in hospitalized patients or for mid-term therapy.	✓	✓
Midline Catheter	Cephalic vein	Partial parenteral nutrition only.	✓	
Peripheral Intravenous Catheter	Basilic vein	Partial parenteral nutrition only.		✓
Implanted Port Catheter ("Port" or "Port-a-Cath")	Subclavian or internal jugular vein, entirely beneath the skin	Typically used for intermittent access.		✓

Source: Data compiled by author.

conditions that might lead to a decision to employ parental feeding include the following.

- Abdominal surgery
- Dehydration
- Eating disorders
- Enteral or oral feeding cannot be tolerated or administered after a five-day period
- Inability to tolerate enteral feeding due to gastrointestinal obstruction, leakage, ileus, fistulae, or dysmotility
- Malabsorption issues
- Malnutrition
- Psychiatric disorders
- Sepsis

Parenteral Solutions

Parenteral nutrition solutions are composed of macronutrients, electrolytes, micronutrients, and water. A typical parenteral solution bag for adults contains 2 liters to

2.5 liters. The most commonly used solutions are known as "3 in 1" solutions (glucose, amino acids, and lipids). Each liter of solution contains the following.

- 900 to 1,200 calories
- Glucose (100 g to 175 g)
- Protein (35 g to 50 g)
- Lipid (25 g to 50 g)
- Potassium (25 mmol to 35 mmol)
- Sodium (30 mmol to 40 mmol)
- Magnesium (2.5 mmol to 5 mmol)
- Phosphate (7.5 mmol to 20 mmol)

Micronutrients are included as part of a PN regimen to avoid trace-element deficiencies, especially zinc, selenium, and copper deficiencies. These deficiencies are most common in patients who have diarrhea, those in intensive care, and previously malnourished individuals. It is vital that accurate calculations be made when determining the individual's nutrition requirements. Severe complications can arise, such as liver dysfunction, respiratory failure, hyperlipidemia, and acidosis (in the case of overfeeding).

Complications

Parental nutrition feedings could lead to several complications, including the following.

- Blood clots
- Breakage
- Clogging (which can be prevented by flushing the catheter regularly)
- Contamination of PN solutions, which can result in micronutrient toxicity
- Electrolyte disturbances
- Gall bladder and biliary complications (especially in pediatric patients, adults on long-term parenteral feeding, or people who have short bowel syndrome)
- Hepatic steatosis
- Hyperglycemia and hypoglycemia
- Infection
- Liver complications
- Micronutrient deficiency
- Refeeding syndrome
- Sepsis

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See Also: Enteral nutrition.

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Peptic Ulcers

Ulcers are sores that typically are located on the skin or in the lining of an organ. Peptic ulcers refer to sores that can occur within the mucosal lining of the esophagus, stomach, or upper portion of the small intestine. Ulcers in the lining of the stomach are called "gastric ulcers." Duodenal and gastric ulcers are worsened by exposure to hydrochloric acid and the enzyme pepsin, both of which are produced by the stomach during digestion. Pepsin is a digestive enzyme that breaks down dietary proteins. The gastrointestinal tract itself also is composed of proteins that become vulnerable to the damaging effects of pepsin once the protective mucosal lining is compromised. Ulcers also can form in the esophagus, although these are less common than duodenal and gastric ulcers.

For many years, researchers believed ulcers were caused mainly by stress, lifestyle factors, excess stomach acid, or genetic predispositions. Early animal studies—including those performed by Hans Selye—found stomach ulcers to be a common stress response, especially when the animals had no control over stressors (Selye, 1956). Stress and other lifestyle factors still are believed to contribute to the formation of ulcers. In 1982, research suggested that that the bacterial strain *Helicobacter pylori* (*H. pylori*) also might contribute to ulcer formation.

Evidence suggests that *H. pylori* is associated with as much as 80% of gastric ulcers and more than 90% of duodenal ulcers (Karriem-Norwood, 2014). *H. pylori* is thought to inflame the stomach lining or stimulate excess acid production, or do both. Because *H. pylori* bacteria infect approximately half of the human population, however—in most cases causing no symptoms—scientists are not yet sure exactly why some people develop ulcers in the presence of *H. pylori* and others do not. It could be that other microorganisms in the stomach help maintain the population of *H. pylori* at a reasonable level. In vitro research has demonstrated that norepinephrine—a hormone whose levels increase with chronic stress—encourages the growth of *H. pylori* and thus might precipitate ulcers in vulnerable people (Doherty, Tobias, Watson, & Atherton, 2009). It is possible that when the body is stressed norepinephrine causes blood vessels in the stomach lining to constrict,

decreasing mucus production and leaving the stomach wall vulnerable to the destructive action of hydrochloric acid.

In 1996, the Food and Drug Administration approved the first antibiotic for treatment of peptic ulcer disease. The following year, the Centers for Disease Control and Prevention (CDC) together with other government agencies launched a national education campaign that publicized the treatment of ulcers through eradication of *H. pylori*. In the past, treatment of ulcers often consisted of hospitalization and consumption of bland foods. Currently, uncomplicated ulcers are often treated with a regimen of several medications, including antibiotics. Gastric acid often plays a major role in ulcer disease. Antacids and proton-pump inhibitors are used to neutralize and decrease acid production, increasing the pH level within the stomach. One predisposing risk factor to ulcers is gastritis, which occurs when the protective lining becomes inflamed, which allows acids in the stomach to break down the stomach lining. Other causes are excessive alcohol intake, smoking, radiation, genetics, and immune abnormalities. Nonsteroidal anti-inflammatory (NSAID) drugs inhibit the production of an enzyme that protects the stomach from gastric acid. Continuous use of NSAIDS increases the risk peptic ulcers.

The most common symptom of ulcers is abdominal pain that often is worse when the stomach is empty. Other symptoms of ulcer development are bloating, nausea, fatigue, bloody stools, and weight loss. Ulcer complications consist of bleeding, gastric outlet obstruction, and tearing of the stomach and intestines. Perforated ulcers can lead to peritonitis, an inflammation of the thin membrane that lines the abdominal wall and covers the organs inside. An untreated stomach ulcer can cause anemia, and in severe cases blood transfusion might be necessary.

Ulcer prevention includes limiting aspirin, ibuprofen, and naproxen. Preventative lifestyle changes include the elimination of smoking and limiting alcohol consumption to no more than two drinks per day. Good stress management practices and a generally healthful diet with a high intake of fruits and vegetables are recommended for peptic ulcer prevention.

Jennifer Najera and Ana Maria Moise

See Also: Digestion and the digestive system; Stomach.

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Phenylketonuria

Phenylketonuria (PKU) is an inherited genetic disorder that results in a lack of the ability to break down the amino acid phenylalanine. The disorder is caused by mutations in the PAH gene and it is an autosomal recessive trait, which means that the person with the disorder must receive a copy of the mutated gene from both parents. The PAH gene is responsible for coding an enzyme called "phenylalanine hydroxylase" that breaks down the amino acid phenylalanine. Mutations in the gene either reduce the activity of the enzyme or stop the production of that enzyme. Both situations lead to a buildup of phenylalanine in the body, which causes harm to the central nervous system and damage to the brain. Phenylketonuria is a rare disorder, occurring in approximately 1 in 10,000 to 1 in 15,000 people in the United States (National Institutes of Health, 2012). This disorder can be treated with a careful diet that has extremely low phenylalanine content. Common foods that contain phenylalanine are dairy products, soy products, eggs, nuts, and all meats, including poultry and seafood. To eliminate any chances of damage to the nervous system and the brain, the diet should be maintained for life. If the disorder is left untreated, severe metal retardation occurs.

Phenylketonuria was first discovered in Norway in 1934 by Dr. Asbjörn Fölling, who was among the first physicians to use chemistry to solve medical problems. He named the disorder "imbecillitas phenylpyruvica" based on the severe mental retardation associated with it and the phenylpyruvic acid excreted in the urine of the patient. Later, Dr. Fölling found the cause for the acid in the urine to be the patient's inability to break down phenylalanine, and he proposed the disorder to be autosomal recessive. In 1935, the disorder was renamed "phenylketonuria" by the British medical geneticist, Dr. Lionel Penrose.

The first PKU formula that provided essential amino acids other than phenylalanine was developed in 1951 by a German professor, Horst Bickel. In 1958, Robert Guthrie, an American microbiologist, developed a simple and inexpensive blood test for high levels of phenylalanine in the blood, which hospitals eventually began to use to screen all newborns for the disorder. The Guthrie test made early diet treatment possible, which effectively avoided the development of intellectual disabilities in infants who had the disorder. Newborns in the United States and other countries are tested for PKU soon after birth. Although the disorder is rare, the consequences are serious, and treatment must begin at birth.

Because PKU is a genetic disorder, developmental impairment begins at birth, which is why early diagnosis is so critical. Symptoms of PKU in untreated

individuals range from mild to severe. Classic PKU is the most severe form. Infants with classic PKU seem normal for the first few months after birth, at which time seizures might begin to occur, and developmental disorders become increasingly apparent. Without treatment, permanent psychological deficits develop, and by the end of the baby's first year, mental retardation is permanent. Less severe forms of PKU, known as "variant PKU" and "non-PKU hyperphenylalaninemia," have a lesser risk of health problems. People with very mild forms of the disorder even might not require a special diet.

The development of protein supplement formulas was very beneficial for people with PKU. Babies with PKU are unable to consume breast milk or infant formula, as both contain phenylalanine. Babies with PKU are given a special infant formula that enables them to develop normally. Children and adults with PKU continue to consume special protein supplements to acquire the amino acids they need without ingesting phenylalanine. Children and adults with PKU receive periodic blood tests to monitor phenylalanine levels, and their diets are adjusted accordingly.

In 2007, the pharmaceutical company BioMarin developed a drug called "sapropterin" ("Kuvan"), which was approved by the FDA as a treatment for some PKU patients. Sapropterin is a cofactor for the enzyme phenylalanine hydroxylase, and when it is given to the patient in large doses, it can cause the patient's existing enzyme to work harder, which then reduces the level of phenylalanine. Because of the mechanism of the drug, it is only effective for a PKU patient who has at least a small amount of phenylalanine hydroxylase in his or her body. Other drugs to treat the disorder are in development.

Fei Peng

Research Issues

The genetic disorder Phenylketonuria (PKU) is treated via a diet that has extremely low phenylalanine content. In the past, however, doctors thought that children with PKU could follow a regular diet sometime after they were grown. This no longer is thought to be the case, and professionals think that the diet should be followed for a lifetime. Following this diet can be difficult for children and teens, especially if they dislike the protein supplements. Pregnant women with PKU must exert caution to prevent high blood levels of phenylalanine, because high phenylalanine levels have harmful effects on fetal development.

See Also: Amino acids.

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Phospholipids

Phospholipids are a class of chemicals found both in the diet and in living organisms, including plants and animals. Phospholipids are categorized as lipids because much of their structure consists of fatty acids. Phospholipids are similar in structure to triglycerides, but with a phosphate group in place of one of the fatty acid chains. In other words, triglycerides consist of a glycerol group connected to three fatty acid chains, and phospholipids consist of a glycerol group connected to two fatty acid chains and one phosphate group. Unlike other lipids, phospholipids are soluble in both fat and water. Phospholipids play several important roles in the human body. Phospholipids are found in several foods common to the human diet, but they are not essential nutrients because the body can manufacture them, given adequate precursor nutrients.

Physiological Functions

Phospholipids' behavior in aqueous (watery) environments, such as the human body, enables them to perform several useful biological functions. Due to its polar nature, the phospholipid's phosphate group is hydrophilic (attracted to water molecules), which allows it to mix with water and other polar liquids. Although the glycerol portion of triglycerides and phospholipids is also hydrophilic, in triglycerides this behavior is overwhelmed by the hydrophobic nature of the fatty acids. The fatty acids of the phospholipid structure are hydrophobic (do not bind with water), however; therefore they are drawn toward each other and other hydrophobic substances. This special property of phospholipids—having both hydrophilic and hydrophobic portions—is used by living organisms in several important ways.

Phospholipids are a major component of cell membranes, forming the basic phospholipid bilayer structure. The cell membrane is formed from two layers of phospholipid molecules. The polar regions face away from the cell membrane's interior, allowing the cell to operate in the body's aqueous environment, but they form a barrier that contains the cell contents. The glycerol and phosphate groups face both away from the cell membrane, toward the outside of the cell, and into the cell's aqueous environment. The inner lipid portion of the cell membrane allows important lipid substances to move into and out of the cell. Cell membranes also store fatty acids for the cell's use, as needed.

In an aqueous environment, phospholipids form structures called "micelles," a ball of molecules with the polar, hydrophilic groups on the surface and the

hydrophobic portion on the interior. This behavior is essential for the action of bile, a fluid produced by the liver and stored in the gall bladder. Bile is composed of phospholipids and bile salts. Bile is released into the small intestine during digestion. Bile mixes with the digestive mass and helps to break up larger groups of lipid molecules into smaller groups, increasing the surface area available to the action of digestive enzymes. This type of behavior, when phospholipids break up larger groups of lipids into smaller groups in an aqueous environment, is called "emulsification."

Phospholipids coat the exterior surface of the lipoprotein molecules that carry fats and cholesterol in the bloodstream. The fats and cholesterol are found inside the large lipoprotein structures. Lipoproteins include chylomicrons, very low-density lipoproteins (VLDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL).

Dietary Phospholipids

Phospholipids comprise about 2% of the lipids in the human diet (Insel, Ross, McMahon, & Bernstein, 2013). Lecithin is the most common phospholipid in the diet. Phospholipids are found naturally in egg yolk, soybeans and other legumes, seafood, liver, wheat germ, broccoli, and brussels sprouts. Phospholipids frequently are added to high-fat powdered products such as dry milk and coffee creamers; baked goods; salad dressings, sauces, and soups; and even chewing gum, to prevent the gum from sticking to the teeth. Phospholipids also can be found in dietary lecithin supplements, which usually are composed of a mixture of phospholipids mainly from soybeans. Phospholipids are not essential nutrients, although one form of lecithin, phosphatidylcholine, is a source of choline, an essential vitamin-like compound.

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See Also: Lecithin; Lipids; Triglycerides.

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Phosphorus

Phosphorus is a nonmetallic mineral listed on the periodic table as "P" with the atomic number 15. This element is abundant and essential to all life forms, including all plants and animals. For humans, phosphorus is vital as a component of

phospholipids, important in cellular membrane structures. Phosphorus is critical for the energy-transfer systems utilizing phosphates in high-energy chemical bonds (adenosine triphosphate and creatine phosphate). Phosphorus helps to activate and deactivate enzymes through a process known as "phosphorylation." Phosphorus is a crucial component of bone, and occurs in the structures of DNA (deoxyribonucleic acid), RNA (ribonucleic acid), and ATP (adenosine triphosphate). Phosphorus, because it is highly reactive elementally, most commonly takes the form of inorganic phosphate (PO_4^{3-}) in living systems.

Upon its discovery in 1669, phosphorus was the first element with a named discoverer; all other elements identified previously were known of since ancient times. Hennig Brand, the alchemist credited with discovering phosphorus, was renowned for attempting to create the illusive "philosopher's stone" (a substance that would give the user eternal life) from phosphorus extracted from urine. Although he did not distill the "philosopher's stone," Brand did extract a brilliant white powder that glowed in the dark and burned radiantly. The ability of phosphorus to burn easily earned it the nickname "the Devil's element" for its later use in explosives, nerve agents, and poisons (Stewart, 2012). Today, phosphorus also is used commercially in fertilizers, food preservatives, plasticizers, pesticides, flame-retardants, and matches.

In a human adult, approximately 700 g of phosphorus exist in tissue. Eighty-five percent is found as calcium phosphate ($Ca_2PO_4^{3-}$) in bone and teeth and the remaining 15% is split among the body's extra and intracellular fluid compartments. Serum phosphorus takes the form of $H_2PO_4^-$ and $H_2PO_4^{2-}$, acting as a buffer for H+. The remaining phosphorus is bound to proteins in the plasma or is incorporated into other substances. Inside cells, phosphorus is pulled from metabolically active pools and is integrated into nucleotides for DNA and RNA synthesis, high-energy molecules such as ATP, components of cell membranes, and various metabolic intermediates.

In the human diet, phosphorus-containing compounds are found naturally in some foods and added to others. Natural sources of phosphorus can be found in protein rich foods such as meat, poultry, fish, eggs, dairy products, legumes, cereals, and grains. Once a person consumes these foods, phosphate compounds are absorbed in a region of the small intestine known as the "duodenum." The body absorbs approximately 60% of the phosphate consumed, much more than its calcium counterpart, only 30% of which is absorbed after ingestion. If too much phosphorus is absorbed, then a hormone known as parathyroid hormone (PTH) initiates excretion of phosphorus by the kidneys. If too much phosphorus is absorbed by the small intestines, then the body does not absorb as much calcium—which is an essential component for ossification of the bones and other important cellular processes.

Although phosphorus is absolutely critical for life, it is overly abundant in the North American diet, especially in the preservatives added to processed foods and soft drinks. Inorganic phosphorus is added to many food products to preserve flavor, retain moisture, and maintain smoothness. Because so much phosphorus is added to food products, people's daily phosphorus intake often is double the recommended daily amount of 700 mg per day for adults. Many researchers are concerned that high intakes of phosphorus might compromise bone mineral density

and cause endocrine disruptions that could lead to calcium deposits in the blood vessels and kidney disease (Tufts University, 2014).

The abundance of phosphorus in the diet indicates that not much supplementation from external sources, such as supplements, is warranted. In certain conditions when a person is severely deficient in phosphorus, however, as in a condition known as "hypophosphatemia," sodium phosphate and potassium phosphate are prescribed as treatment used under medical supervision. Too much phosphorus in a person's system can cause a condition known as "hyperphosphatemia," in which various tissues in the body become calcified—especially the kidneys. Naturally very efficient, the kidneys normally only are overloaded with phosphorus in patients diagnosed with kidney failure. To avoid phosphorus toxicity, the upper intake levels of phosphorus have been set by the Food and Nutrition Board. The upper limit for adults is 4,000 mg per day, but for adults age 70 years and older, the upper limit is 3,000 mg per day, because the kidneys become less efficient in old age.

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See Also: Minerals; Osteoporosis.

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Phytochemicals

Phytochemicals, literally "plant chemicals," come from compounds made by plants such as fruits, vegetables, beans, and grains. Phytochemicals include both nutrients—without which people develop deficiency symptoms and diseases—and

other compounds that exert beneficial health effects. Current scientific knowledge of phytochemicals is limited because only a small percentage of the thousands of phytochemicals that have been identified have been studied. Scientists have estimated that there could be as many as 4,000 phytochemicals. Common groups of phytochemicals include the following: antioxidants, flavonoids, phytonutrients, flavanones, isoflavones, catechins, anthocyanidins, isothiocyanates, carotenoids, allyl sulfides, and polyphenols (Produce for Better Health Foundation, 2014b).

Phytochemicals work in the human body in a variety of ways. Some serve as antioxidants, working to prevent damage from oxidation by neutralizing reactive compounds. Antioxidants help to prevent cardiovascular disease by reducing inflammation along the walls of arteries (Produce for Better Health Foundation, 2014a). Other phytochemicals perform nutrient functions. Several of the carotenoids, such as beta- and alpha-carotenoid, for example, can be transformed into vitamin A. Some phytochemicals function as hormones. The phytoestrogens, such as the isoflavones found in soybeans, can have estrogenic effects in the body, possibly influencing hormone-related processes such as bone metabolism and the menstrual cycle. Some dietary fibers serve as prebiotics, providing nutrients for helpful bacteria in the gastrointestinal tract.

Common Phytochemicals

Carotenoids, lycopene, lutein, resveratrol, anthocyanidins, and isoflavones are six of the most studied groups of phytochemicals (Produce for Better Health Foundation, 2014b).

Carotenoids

Carotenoids benefit the immune system, vision, skin health, and bone health. Good food sources of the carotenoids include orange and dark leafy green vegetables, including pumpkin, sweet potato, carrots, winter squash, cantaloupe, apricots, spinach, collard greens, kale, and broccoli. When people see orange and dark leafy green vegetables they should think of beta-carotene.

Lycopene

Lycopene benefits prostate cancer and heart health. Good food sources with lycopene are tomatoes, pink grapefruit, red peppers, watermelon, and tomatoes. Lycopene can be easier for the body to absorb if the food product goes through the heating process.

Lutein

Lutein benefits eye health, cancer prevention, and heart health. Good food sources with lutein are collard greens, kale, spinach, broccoli, brussels sprouts, lettuces, and artichokes.

Resveratrol

Resveratrol contributes to heart health, cancer prevention, lung health, and prevention of inflammation. Good food sources of resveratrol are red wine, peanuts, and grapes.

Anthocyanidins

Anthocyanidins benefit blood vessel health. Good food sources with anthocyanidins are blueberries, blackberries, plums, cranberries, raspberries, red onions, red potatoes, red radishes, and strawberries.

Isoflavones

Isoflavones appear to influence breast cancer risk, bone health, joint inflammation, and cholesterol. They are found in soybeans.

Supplements

Phytochemicals that are consumed as part the diet are likely to be beneficial to health. Phytochemicals as dietary supplements have been growing in the market. Consuming large amounts of phytochemicals in the form of supplements, however, might not be helpful or safe. It is unclear, for example, whether isoflavones might promote cancers in certain individuals. Therefore, although soy foods are associated with health benefits, isoflavone supplements sometimes are associated with health problems.

Susana Leong

Research Issues

Helpful phytochemicals are best obtained through plant foods. How can people be convinced to increase their consumption of these foods? The "Fruits and Veggies More Matters" health initiative has partnered with the Centers for Disease Control and Prevention with the goal of helping people add more fruits and vegetables to their diet. More specifically, the slogan is to "fill half your plate with fruits and veggies" (Produce for Better Health Foundation, 2014b). More information on public health approaches to increasing phytochemical intake can be found on the organization's website (www.fruitsandveggiesmorematters.org/what-are-phytochemicals).

See Also: Anthocyanins; Antioxidants; Cancer and nutrition; Cardiovascular disease, and nutrition; Carotenoids; Dietary supplements; Lutein; Lycopene; Polyphenols; Resveratrol.

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Phytoestrogens

Phytoestrogens are chemicals that have estrogen-like properties and are produced by plants. Isoflavones, lignans, and coumestans represent the three major categories of phytoestrogens. Isoflavones are found primarily in soybeans, and flax seed contains the highest concentration of lignans. Dietary sources of coumestans include alfalfa sprouts and various legumes. Phytoestrogens also can be consumed in the form of supplements, such as red clover isoflavone extracts. Although they are nonsteroidal rather than steroidal compounds, the structural features phytoestrogens share with endogenous estrogens—particularly 17-beta-estradiol—allow them to bind to estrogen receptors (Vitale, Piazza, Meilli, Drago, & Salomone, 2012). Phytoestrogens appear to have a greater affinity for estrogen receptor beta than for estrogen receptor alpha and can act as either estrogen agonists or antagonists in different tissues, leading researchers to characterize them as natural selective estrogen receptor modulators (SERMs).

Health Benefits

Numerous beneficial effects of phytoestrogen consumption in humans have been proposed, including improved blood lipid profile; reduced risk of cardiovascular disease; osteoporosis prevention; alleviation of menopausal symptoms; and decreased risk of breast, endometrial, and prostate cancer. The isoflavones genistein and daidzein are among the best studied in terms of health outcomes. Studies in which participants replace a portion of their animal protein intake with soy generally have found reduced LDL cholesterol levels, but this effect remains even if isoflavones are removed from soy protein, implying that another component of soy protein or the decreased animal protein intake is responsible for the change (Patisaul & Jefferson, 2010).

Significant effects on HDL cholesterol, triglycerides, lipoprotein, and blood pressure have not been found consistently, indicating that the role of isoflavones in preventing heart disease might be limited. Yet, in vitro studies suggest that genistein could inhibit the proliferation and migration of vascular smooth muscle cells, thereby protecting against atherosclerosis (Pilšáková, Riečanský, & Jagla, 2010).

Phytoestrogens also have been investigated as a safer alternative to conventional hormone replacement therapy, which addresses symptoms of menopause such as hot flashes but could increase the risk of developing breast cancer. Additionally, isoflavones are thought to lower the risk of osteoporosis in postmenopausal women by stimulating bone formation and inhibiting bone resorption, decreasing bone mineral density losses overall. Most clinical trials have shown little or no improvement in menopausal symptoms, however, and have yielded mixed results regarding bone density (Higdon & Drake, 2009). The ability (or lack thereof) to metabolize daidzein into equol, however, which has stronger estrogenic activity, could explain why soy isoflavones are helpful for some people and not for others. Only about one-third of people in Western populations have the intestinal bacteria required to produce equol (Higdon & Drake, 2009).

Citing the lower rates of breast, endometrial, and prostate cancer in Asian countries—where isoflavone consumption averages 11 mg to 47 mg per day as opposed to 1 mg to 2 mg per day in Western countries—some researchers have hypothesized that increasing phytoestrogen intake reduces the risk of these cancers (Xiao, 2008). The proposed mechanism for preventing the development of breast or endometrial cancer is the competitive inhibition of endogenous estrogen by phytoestrogens, which stimulate estrogen receptors more weakly and therefore are less likely to promote the growth of estrogen-sensitive breast or uterine cancer cells. Phytoestrogens also can exert inhibitory effects on enzymes that play a role in estradiol synthesis, such as aromatase. Research results again are conflicting, but cell studies have revealed that phytoestrogens can either inhibit or promote—typically at low and high doses, respectively—the proliferation of breast cancer cells, and that they do not seem to significantly stimulate uterine cells (Rice & Whitehead, 2006). Epidemiological studies sometimes have shown an inverse relationship between phytoestrogen consumption and the risk of developing breast cancer or experiencing a recurrence, and others have found no relationship (Duffy, Perez, & Partridge, 2007). The effect of phytoestrogen intake on prostate cancer risk also is unclear, but there is some evidence that soy isoflavones can limit cancer progression, as indicated by decreased levels of prostate-specific antigen (PSA) in men who already have the disease (Xiao, 2008).

Adverse Effects

Although the existing literature suggests that a phytoestrogen-rich diet does not increase cancer risk, several other health concerns have been raised. Many relate to endocrine disruption impacting development or reproductive health. Given that the effects of prenatal exposure to phytoestrogens are not well understood, pregnant women are generally advised against taking supplements such as red clover or licorice extract, which often contain much greater concentrations of isoflavones than do food sources (Thompson, Boucher, Cotterchio, Krieger, & Liu, 2007).

Early life exposure to soy is common, however, with approximately 25% of infants in the United States now being raised on soy formula. In a 2010 report, the National Toxicology Program Center for the Evaluation of Risks to Human

Reproduction (NTP-CERHR) recognized that infants fed soy formula have very high blood levels of genistein—roughly 160 times greater than that of the average omnivorous adult in the United States—and reviewed studies demonstrating accelerated puberty, decreased fertility, and other issues in female rats and mice exposed to genistein. The NTP-CERHR, however, concluded that there is minimal concern for adverse effects in humans on the basis of evidence from both retrospective and prospective studies that the growth, development, and general health of soy formula–fed and cow milk formula–fed infants do not differ significantly.

With respect to adult reproductive health, case reports indicate that an extremely high intake of isoflavones can have adverse effects. In women, these can include dysmenorrhea, abnormal uterine bleeding, endometriosis, uterine fibroids, and secondary infertility (Chandrareddy, Muneyyirci-Delale, McFarlane, & Murad, 2008). In men consuming 12 or more servings of soy per day, low testosterone levels, erectile dysfunction, gynecomastia, and hot flashes have been reported. These effects are not observed in people eating normal dietary amounts of soy, or about 1 to 3 servings per day. Moreover, sperm count and quality do not appear to be affected by phytoestrogen intake (Messina, 2012).

Additional concerns include decreased thyroid function and possible drug interactions. Soy isoflavones might cause hypothyroidism and goiter, but these effects can be counteracted with elevated iodine intake (Patisaul & Jefferson, 2010). Taking isoflavone supplements or consuming large amounts of soy also is contraindicated for individuals on thyroid medications or the breast cancer drug tamoxifen, because high doses of isoflavones can reduce their efficacy. Claims that soy isoflavones reduce the effectiveness of oral contraceptives and compound the effects of blood thinners have been contradicted by recent research (EBSCO CAM Review Board, 2013). Further study is required to clarify the molecular mechanisms underlying phytoestrogen activity and determine the influence of factors such as dosage, duration, age, gender, ethnicity, and individual differences in hormonal status and metabolism.

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See Also: Cancer and nutrition; Phytochemicals; Premenstrual syndrome.

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Polyphenols

Polyphenols are compounds found in plant tissues. These compounds are responsible for plant pigmentation and also play a role in plant growth, reproduction, and resistance to pathogens and predators. Although polyphenols are "nonnutrients," meaning that they are not essential to life, they generally are credited with the benefits associated with a healthy diet that includes plant-derived foods (Martin & Appel, 2009; Thomás-Barberán & Andrés-Lacueva, 2012). With respect to humans, polyphenols have been shown in some studies to protect against dyslipidemia and cardiovascular disease, as well as the underlying mechanisms of other disease processes. Specifically, polyphenols have been linked to antioxidant activity in humans by which they can reduce oxidative stress-induced tissue damage caused by chronic diseases (Martin & Appel, 2009).

More recently, scientific research has been investigating the role of polyphenols in the gut. In terms of antioxidant effects, polyphenols in the gastrointestinal tract prevent the oxidation of vitamins and nutrients such as lipids, proteins, and cholesterol. The prevention of oxidation improves the quality of the nutrients being absorbed by the body. Additionally, polyphenols affect the activity of several gastrointestinal enzymes, including amylases, lipases, and proteases, and reduce the absorption of glucose and fatty acids. Reduced absorption of glucose and fatty acids combats obesity, diabetes, and metabolic syndrome. Furthermore,

polyphenols have been shown to have an interesting effect on gastrointestinal microbiota. They aid in the development of good bacteria such as lactobacilli and bifidobacteria, but simultaneously deter the growth of harmful bacteria, for instance, coliform (Thomás-Barberán & Andrés-Lacueva, 2012).

There are two main classifications of polyphenols, flavonoid and nonflavonoid. The flavonoid group shares a distinct basic chemical structure. The nonflavonoid group is composed of a wider variety of chemical structures. The following are the major classes of polyphenols, and their main dietary sources.

- Flavonols—onions, apples, broccoli, tea, and red wine
- Flavanones—citrus fruits
- Flavan-3-ols—fruits, tea, and wine
- Anthocyanins—plant pigments responsible for the colors of fruits and flowers
- Isoflavones—soy, in particular; significant amounts are found in soy, nuts, and tempeh; these have a chemical structure similar to that of estrogen
- Hydrolyzable tannins—berries and some nuts
- Lignans—fruits and vegetables; they are also found in tea, cereal products, coffee, and alcoholic drinks; lignans are phytoestrogens
- Hydroxycinnamates—coffee, spinach, and cereal bran
- Stillbenes—found in the woody parts of plants
- Benzoic acids—fruit; cranberries in particular

Despite the large array of different polyphenols, research has shown that most are metabolized by several species of intestinal bacteria into very similar metabolites; thus they all have similar effects on the body despite their variety. Observed variances in health effects of polyphenols on humans are attributed to differences in gut microbiota among individuals. It has been found that some individuals' microbiota lack the specific bacteria that produce polyphenol metabolites; hence these individuals do not experience the health benefits associated with polyphenols (Selma, 2009).

As far as polyphenol dietary supplements are concerned, research has shown that supplementation might be beneficial for people whose fruit and vegetable consumption is low. Research also suggests, however, that at high doses polyphenols can exhibit pro-oxidant activity and cause adverse effects. Nutrition experts generally recommend that people consume a variety of foods to obtain a healthful intake of polyphenols.

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See Also: Anthocyanins; Antioxidants; Phytochemicals; Phytoestrogens.

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Portion Size

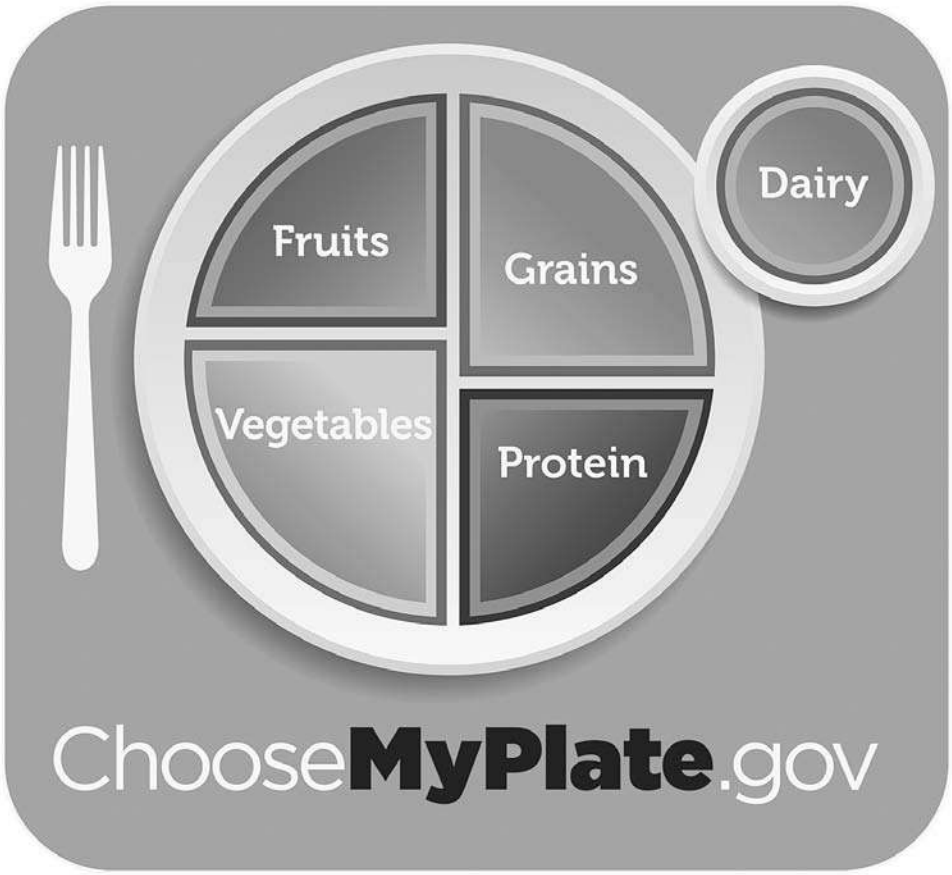
Portion size refers to the amount of food that is served to consumers or that an individual chooses to eat at any one time. Over the past several decades, typical portion sizes have increased. Individual items such as bagels, muffins, candy bars, and beverages are larger than they were 30 or 40 years ago. The average size of restaurant meals also has grown.

As the prevalence of obesity increases around the world, researchers and consumers alike have been considering how growing portion sizes might influence a person's propensity to become overweight or obese. Many experts believe that the increasing availability of food in greater portions has contributed to a phenomenon referred to as "portion distortion," in which case larger portion sizes appear "normal," and adults and children alike are encouraged to overeat. Oversized portions and the related intake of excess calories are believed to contribute to the increasing obesity rates in North America.

Increasing Portion Sizes

Although portion sizes began expanding in the 1970s, they continued increasing at a far faster rate in the 1980s, both in restaurants and in grocery stores. Most food sold on the market today exceeds the portion sizes served in the past, as well as the serving sizes suggested by standard public health guidelines such as the U.S. Department of Agriculture MyPlate guidelines and Health Canada's Food Guide—with the single exception being the standard slice of bread. ("Servings" means the amount of foods from each food group recommended for daily consumption as defined by consumer education materials, such as *Dietary Guidelines for Americans*, MyPlate, or *Eating Well with Canada's Food Guide*.)

Average portion sizes for salty snacks—foods such as pretzels, potato chips, crackers, and puffed rice cakes—increased from 1 oz to 1.6 oz from 1977 to 1996 (Young & Nestle, 2002). In the 1950s, the standard soft drink size was 7 oz, it is now sold in sizes up to 42 oz. An average bagel weighed 2 to 3 oz and contained 230 calories in the 1970s. Today, the average bagel is twice as large and has about 550 calories. Twenty years ago, a large popcorn sold at the movie theater contained five cups of popcorn and 270 calories. Today, a large popcorn contains 11 cups of popcorn and 630 calories—more than 25% of most adults' daily calorie needs (NHLBI, 2013).



The MyPlate icon illustrates the five food groups that are the building blocks for a healthy diet using a familiar image—a place setting for a meal. The MyPlate website spells out recommendations for portion sizes for the food groups for given daily calorie intake levels. (USDA/ChooseMyPlate.gov)

In the 1970s, a serving of french fries contained about 30 fries and 450 calories. Today, the "large" orders that many establishments serve contain 50 fries and 790 calories. To put this into perspective, back in the 1950s, McDonald's served only one portion size of fries, which today is equivalent in weight to the "small" serving size. The 2002 "large" size of french fries served at McDonald's was the same weight as the 1998 "supersize" serving of french fries (Young & Nestle, 2002). Interestingly, a serving of french fries, according to the USDA MyPlate guide, is only 10 fries, at 160 calories. Additionally, the standard 3.9 oz hamburger of the 1950s had grown to 12 oz by 2012 (Klein, 2012).



Dietary guidelines for a 2,000-calorie daily food plan. The top half of the image offers suggestions on food choices within each food group. The lower half explains portion sizes for each group. (choosemyplate.gov)

Impact of Portion Size on Amount of Food Eaten

As the amount of food served to people increases, so does the amount that people consume. In one study, 96 women were given either a 350 g or a 600 g serving of pasta. Before being asked to eat, the women were informed about the societal

What's the Difference between a Portion and a Serving?

A "portion" is the amount of a specific food you choose to eat for dinner, snack, or other eating occasion. Portions, of course, can be bigger or smaller than the recommended food servings.

A "serving" is a unit of measure used to describe the amount of food recommended from each food group. It is the amount of food listed on the Nutrition Facts panel on packaged food or the amount of food recommended in the "MyPlate" guidelines and the *Dietary Guidelines for Americans*.

For example, 6 to 11 servings of whole grains are recommended daily. A recommended serving of whole grains would be 1 slice of bread or one-half cup of rice or pasta. People often confuse the recommendation to mean 6 to 11 portions with no regard to size. It is not 6 to 11 portions meaning that one portion could is a large bowl of pasta rather than one-half cup. Keep an eye on portion size to see how your portions compare with the recommended servings.

Serving Sizes and Portions. (2013). National Heart, Lung, and Blood Institute (NHLBI). http://www.nhlbi.nih.gov/health/educational/wecan/eat-right/distortion.htm

influences encouraging people to overeat, and how portion sizes influence how much people eat. It was suggested to all subjects that they slow the speed of eating, appreciate the tastes of the food, and pay attention to how full they were. Researchers had hypothesized that making people more aware of their eating behaviors might counteract the tendency to overeat when faced with large portions. Despite the educational process, the women served a larger portion size ate, on average, about a third more than women served the smaller portion (Cavanagh, Vartanian, Herman & Polivy, 2013). This study supports the conclusion that if people are served larger portions, then they are more likely to eat more than if they are served smaller portions.

Table 1. Table Portion Size

Serving Sizes and Portions **Comparison of Portions and Calories 20 Years Ago to Present Day**				
20 Years Ago			**Today**	
Food Item	**Portion**	**Calories**	**Portion**	**Calories**
Bagel	3" diameter	140	6" diameter	350
Cheeseburger	1	333	1	590
Spaghetti w/ Meatballs	1 cup sauce 3 small meatballs	500	2 cups sauce 3 large meatballs	1,020
Soft Drink	6.5 ounces	82	20 ounces	250
Blueberry Muffin	1.5 ounces	210	5 ounces	500

Source: National Heart, Lung, and Blood Institute. (2013). *Serving sizes and portions*. Retrieved from http://www.nhlbi.nih.gov/health/educational/wecan/eat-right/distortion.htm

Impact of Dish Size on Food Consumption

Not only is more food being served, it also is being served on larger plates and in larger containers. Cupholders in cars even have expanded to accompany larger cup sizes (Young & Nestle, 2002). An interesting study on the effect of dish size reported that, in a subject group of 85 graduate students and nutrition professors, those who were given smaller dishes served themselves smaller portions of food and consumed fewer calories in a sitting (Wansink, Van Ittersum, & Painter, 2006). The participants of the study were given either a 17-oz or 34-oz bowl and either a 2-oz or 3-oz scoop of ice cream. Participants then were allowed to serve themselves ice cream. Those given the 34-oz bowl, on average, served themselves 31% more ice cream than those given a small bowl. Those participants given the combination of the 34-oz bowl and the 3-oz ice cream scoop served themselves, on average, 53% more ice cream than those given the combination of the 17-oz bowl and the 2-oz scoop of ice cream (Wansink, Van Ittersum, & Painter, 2006).

The Influence of Perceived Serving Size on Food Portions

Although nutrition labels can help consumers make informed decisions about the amount of food they would consume, many people fail to accurately estimate the size of the portions and the amount of calories being consumed. In one study on serving size versus actual consumption, for example, 46 college students were provided with 20-oz bowls and were then asked to fill the bowls with the amount of breakfast cereal they typically would consume. After doing so, they were shown the nutrition facts panel of the cereal and asked to pour into another 20-oz bowl what they estimated to be one serving. On average, the amount of cereal poured in the one-serving estimate was less than half the amount that the students predicted they would serve themselves on the average day. Additionally, the one-serving estimate typically was erroneous itself. Only one-third of the study group, when asked to serve themselves one serving, poured out an amount within 90% to 110% of the actual serving size. In the study's discussion, the researchers note the tendency of companies to list serving sizes on nutritional labels that are unrealistically small. This might create the illusion that there is more food in each container and lead people to believe that they are consuming fewer calories and grams of fat and sugar than they actually consume. The typical 20–fl oz soft drink bottle, for example, contains two and a half servings. For products such as soft drinks that are in containers labeled as two or more servings, but which people probably will consume entirely in one sitting, the label information might give consumers a false impression of what they actually are consuming if they do not take time to calculate the actual nutrition contents of the products (Bryant & Dundes, 2005).

Large Portion Sizes Lead to Sustained Overeating

Most experiments examining the effect of portion size on food consumption observe eating behaviors at one snack or meal. In the face of large portion sizes, is such eating behavior maintained meal after meal, and day after day? Or

do consumers, after eating an excess of calories for a period of days, naturally compensate by eating fewer calories on subsequent days? Barbara Rolls and colleagues (2007) conducted a study to answer these questions. The researchers provided a group of 23 normal and overweight men and women with food in standard portions for 11 days, and recorded the amount of food each subject consumed. The researchers then provided subjects with large portions of food for 11 days to see whether the subjects would begin to decrease calorie intake after overeating for the first few days. During the period when participants were given larger portions, participants increased their calorie intake on average by 423 calories per day. This increase in calorie intake was sustained in all participants regardless of their body mass index throughout the 11 days of large portions served for all meals and snacks except for those snacks that were fruits and vegetables (Rolls, Roe, & Meengs, 2007). This study suggests that as long as people are presented with larger portions, they tend to consistently overeat and do not spontaneously curb their calorie intake to regain energy balance.

Coping with Large Portions and Avoiding Overeating

People can develop new eating habits if they become aware of how large portions push overeating. When eating out, especially at fast-food restaurants, people can avoid bargains that promise better value. When restaurant portions are too large, consumers can split a meal with a friend or take the leftovers home for a meal the next day. People who can't resist cleaning their plates can order soup and salad. At home, people can serve small portions and eat them slowly.

Individuals often can reduce calorie consumption at a meal by using smaller dishware. When using smaller plates, one is forced to serve oneself less food due to space constraints of the dish. A small dish also creates the illusion that there is more food on the dish than actually is being served. Consumers can learn what amounts of food are recommended on an average basis and what portion constitutes a serving. People should eat more slowly, rather than hurrying to consume all of the food in front of them. It takes time for the body to register the fact that food is being consumed and to respond with the sensation of fullness.

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See Also: *Dietary Guidelines for Americans*; Obesity causes.

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Potassium

Potassium is an electrolyte critical to many cellular and electrical functions in the human body. In general, potassium plays important roles in helping to regulate the body's acid-base balance, build muscles, synthesize proteins, manage fluid balance, metabolize carbohydrates, and regulate electrical activity of the heart and nerves. Potassium is found in a wide variety of food sources. Fruits with significant amounts of potassium include: bananas, kiwis, prunes, dried apricots, and citrus fruits. Vegetables such as potatoes with their skins, broccoli, peas, lima beans, and squashes all contain potassium. All meats have potassium as do several fish sources including salmon, cod, flounder, and sardines. Potassium also is found in yogurt, milk, nuts, and soy products.

The adequate intake (AI) level of potassium for adults is 4,700 mg per day. Dietitians advocate individuals reach their AI by consuming dietary sources of potassium rather than taking supplements, unless prescribed by a doctor. Potassium intake levels have fallen by 10% in the United States since 1945. On average, most North Americans fall a full 1 g of potassium short of their AI. Recently, experts in the United States raised potassium's AI levels, based on research findings showing additional preventative health benefits of higher potassium consumption.

A relatively high potassium dietary intake level has been found to provide cardioprotective effects. An evaluation of 10 studies described in the USDA's Nutrition Evidence Library examined potassium and its effects on blood pressure. All but one study found a relationship between dietary potassium intake and significant reductions in systolic or diastolic blood pressure (USDA, 2012). In populations that consume significant amounts of fruits and vegetables the rate of hypertension is as low as 1% as compared to that of people in industrialized countries who have high intakes of processed foods and hypertension rates of 33% (Houston & Harper, 2008). Researchers have suggested that if people in industrialized countries increased their potassium levels to reach their AIs, then rates of hypertension would decrease by 10% (Houston & Harper, 2008).

Potassium's alkalinity might help combat age-related muscle mass loss. One study found that higher levels of potassium were associated with a greater percentage of lean body mass in healthy older men and women (Dawson-Hughes, Harris, & Ceglia, 2008). The acidosis that occurs gradually with age and contributes to several health problems in later adulthood could be neutralized by potassium-rich alkaline foods, such as fruits and vegetables. Potassium's alkalinity also could help maintain bone mineral density. One study compared subjects' dietary intakes of potassium to bone mineral density measures (Tucker et al., 1999). Results revealed positive associations between potassium intake and bone mineral density measures. High levels of acidity can result in excessive calcium excretion leading to more fragile and less healthy bones. Reducing calcium excretion through increased potassium intake might also reduce risk of kidney stones. Researchers performed a large study including more than 45,000 male subjects and tracked their development of kidney stones (Curhan, Willet, Rimm, & Stampfer, 1993). All subjects had no history of kidney stones. At the end of the study, dietary potassium levels were inversely related to kidney stone development. It has been suggested that potassium's ability to reduce calcium excretion caused this result.

Low blood level of potassium is called "hypokalemia." Typically, hypokalemia results from excessive potassium loss in urine and not from low levels in the diet. The most common causes include use of diuretics, kidney diseases, and prolonged vomiting or diarrhea. The symptoms of hypokalemia are weakness, constipation, fatigue, muscle cramps, and arrhythmias.

There is no set upper limit (UL) for potassium. "Hyperkalemia," high blood potassium level, can be a life-threatening condition. Most cases are caused by kidney disease, therefore treatment targets managing the underlying medical condition. Doctors recommend that individuals with some types of kidney problems do not consume excessive amounts of potassium-rich foods and also suggest eating a low-potassium diet. Hyperkalemia also can be caused pharmacologically by medications such as ACE-inhibitors and blood thinners. Symptoms of hyperkalemia include weakness, muscle fatigue, nausea, and arrhythmias.

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See Also: Electrolytes; The kidneys; Minerals.

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The Poverty-Obesity Paradox

One of the most pressing health issues around the world is the rapid rise of obesity and obesity-related illnesses. In resource-rich countries, rates of obesity tend to be highest among the most disadvantaged groups. Although one might expect that people with the fewest resources would have less to eat, the conditions created by poverty in the richer countries encourage obesity, a phenomenon called the "poverty-obesity paradox." The poverty-obesity paradox is probably attributable to a number of interacting factors.

Higher Intake of Energy-Dense Foods

Low-income families consume more energy-dense foods and fewer fruits and vegetables. Some researchers have found there is an inverse relationship between a food's energy density (calories per unit weight) and cost; that is, cheaper foods tend to have more calories per unit of volume. For example, 200 kcals of uncooked pasta costs about $0.21, and 200 kcals of peppers costs about $3.23. Potato chips are about $0.33 for 200 kcals, and carrots cost $2.50 for 200 kcals (Ping, 2013). One of the best buys is donuts, which provide 836 kcals per dollar (Kadet, 2012). If dollars are in short supply and a person has a family to feed, then it makes sense that economic pressures affect shopping choices. The cost of food has risen sharply over the past decade, in part due to increased demand for food from developing countries and the diversion of crops for the manufacture of biofuels. If food prices push consumers to choose filling but less-nutritious foods, then the rising costs of food might mean that more people than ever before will find it difficult to avoid obesity.

Some researchers suggest that overconsumption of calories might be partially driven by the need to consume adequate protein. Protein is the most expensive fuel, as compared with fats and carbohydrates. Meat, for example, tends to be more expensive than carbohydrate foods such as rice, pasta, and breads. People with inadequate resources might tend to choose cheaper foods with low protein levels and thus must consume more food—and more calories—to ingest enough protein.

Obesogenic Environments

Resource-poor neighborhoods offer less access to good food and fewer opportunities for physical activity. Such environments have been called "obesogenic," meaning

that they promote obesity. Poor neighborhoods tend to have fewer supermarkets and more convenience stores, liquor stores, and fast-food establishments. Food costs more when purchased at convenience stores rather than at large supermarkets, and the selection is poor. Convenience stores rarely offer fresh fruits and vegetables or high-quality meat and seafood. Most food choices are processed and high in salt, sugar, and fat.

Although people in poor areas might walk for transportation more frequently, other options for physical activity generally are more limited. Their neighborhoods typically offer less access to parks, recreation centers, and swimming pools. People who fear neighborhood crime restrict outdoor time for themselves and for family members. Children in resource-poor areas tend to have poorer schools, with fewer physical education and sports opportunities. They might have fewer after-school sports, dance, and other physical activity and recreation options.

More Stress and Less Self-Regulation

Poverty is stressful, and feelings of deprivation decrease people's drive to exert the energy required for self-regulation. Self-regulation refers to people's self-control or ability to control their behaviors. Psychologists believe that, in general, people have limited self-control and operate most effectively with the force of habit. It takes energy to change behaviors, and stress depletes the energy available for self-regulation and behavior change. Stress is a leading cause of behavior change relapse, for example, beginning to smoke or drink again after quitting, or resuming unhealthy eating habits after a period of good eating habits. People who feel stressed have less energy for other things, such as organizing meals, cooking, and cleaning the kitchen.

Reduced levels of self-control are associated with the downward spiral of poverty. Some research has looked at a concept called "trait self-control." Trait self-control reflects an individual's general level of self-control. Research suggests that individuals who have low levels of trait self-control are less likely to do well in school or in the workplace and are more likely to overeat (Moffit et al., 2011). Low levels of success in school and work could partly explain lower socioeconomic status (SES) and, thus, the link between poverty and obesity.

Self-control can be improved through training and practice. Children in better schools practice self-control in their educational systems. Children also gain self-control ability through family child-rearing practices, recreational sports programs, after-school activities, and in a variety of other ways. A scarcity of opportunity for the acquisition of self-control could contribute to both obesity and poverty in adulthood.

Discrimination, Poor Health, and Fewer Employment Opportunities

Anti-fat bias could push obese people into lower-status positions. People who are obese might have access to fewer educational, employment, and social opportunities than others. If people experience health problems along with obesity, they have

even fewer opportunities for employment. People with obesity are more likely to develop health disorders such as heart disease, hypertension, type 2 diabetes, arthritis, back problems, and other mobility problems. Once disorders such as diabetes and heart disease are added to the poverty mix, household organization and finances are further stressed. Such discrimination could exert pressure over time that causes obese people to be less successful and to move into the lower social classes. Because body size has strong genetic links, children of obese parents are more likely to be obese and, like their parents, face limited opportunities to improve their SES.

Pressure to Conform

People of higher SES value thinness and behaviors promoting healthy body weight. People of higher SES are exposed to more pressure to maintain a healthy body weight. They monitor their weight more frequently and hear more messages promoting the associations between weight and health (McLaren, 2007). They experience more workplace and societal norms that exert pressure to control body weight and are likely to perceive healthy eating and regular physical activity as normal and positive behaviors.

Disorganized Households

People often respond to chronic stress and poor health with fatigue and disorganization. People who have disorganized households have less energy to put toward long-term planning and shopping. For many people, eating reduces feelings of stress. Such people might eat more comfort foods to cope with stress. Preparing nutritious meals at home requires grocery shopping, planning meals ahead of time so the necessary ingredients are on hand, time to prepare the meal, and then time and energy for cleaning up after the meal has been eaten. When people do not have enough time and energy, they could choose to buy prepared foods or to eat at a restaurant.

Food for Pleasure

Food is an affordable pleasure, and people like the taste of fat and sugar. People enjoy food, and parents providing meals want to please their families. When access to food is limited, people preparing meals want to be sure no one feels hungry at the end of a meal. Filling bellies and satisfying those at the table comes ahead of nutrition recommendations. Food is used as a reward in many families. Feelings of deprivation are associated with overconsumption of calories when food is available (Crescioni et al., 2011).

Most people—especially children—enjoy the taste of foods that are high in fat and sugar. Food product manufacturers have invested time and money to devise products that please the palate and can be sold at an affordable price. About half the calories in the U.S. diet come from added sugars and fat. Although people's

tastes for fatty and sweet foods might have provided an evolutionary advantage, driving humans to eat enough to avoid starvation, in an environment with abundant food choices people consume too many calories. People purchasing food generally value taste more than they value health and nutrition.

Poverty and Obesity: A Complex Problem

The exact contribution made by each of the above factors is unclear and often confusing. Addressing the poverty-obesity paradox will require interventions at all levels, from public policy and legislative action, to neighborhood interventions increasing access to good food and physical activity, and, finally, to support for individual behavior change.

Barbara A. Brehm

Research Issues

Children are especially vulnerable to the poverty-obesity paradox. Younger children do not always have a lot of control over what they can eat, and when choices are offered, children might not make the most nutritious choices. It is interesting to explore the factors related to childhood obesity in the context of the poverty-obesity paradox.

See Also: Food security and food insecurity; Obesity, treatment; Public policy on nutrition.

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Prebiotics

Prebiotics are partially or nondigestible food components that stimulate the growth and activity of beneficial bacteria (gastrointestinal microflora) in the digestive system. Any food component that reaches the colon has the potential to serve as a food source for resident bacteria and other microorganisms, and thus serve as a prebiotic. Research on prebiotics is attempting to identify components that nurture beneficial rather than potentially harmful bacteria, thus influencing the composition of the gastrointestinal microflora in a positive fashion. Most of the prebiotic components under investigation are short-chain carbohydrates, known as "oligosaccharides." These are found in many foods, such as yogurt, soybeans, oats, chicory root, jicama, barley, wheat, asparagus, bananas, and fibrous vegetables. It is likely that many other food components, however, especially types of water-soluble fibers, also serve as prebiotics. Prebiotic supplements and food additives also are available. The most common prebiotic supplements and additives contain fructooligosaccharides, including inulin, and galactooligosaccharides.

Although found in many foods that humans have been consuming for hundreds of years, the term "prebiotics" was coined in 1995 by researchers Glenn Gibson and Marcel Roberfroid (Walker, 2005). Previous to that, some products that stimulated the growth of helpful bifidobacteria in the gut were called "bifidogenic."

Prebiotics are not to be confused with probiotics. Probiotics are live microorganisms that remain intact during the digestive process. Probiotics directly deliver healthy bacteria to the large intestine. Prebiotics serve as food for the probiotics, thus helping to support these bacterial colonies. Symbiotic supplements contain a combination of pro- and prebiotics. Prebiotics and probiotics thus work together to support the beneficial effects of helpful flora. Helpful microorganisms could improve gastrointestinal function, reduce risk of infection by harmful microbes, and improve symptoms associated with disorders such as irritable bowel syndrome and inflammatory bowel diseases. Interesting research on human milk has found that it contains many prebiotic oligosaccharides that can help to foster healthy microflora in infants. These oligosaccharides also can influence the development of an infant's immune system and immune response, either indirectly by influencing microflora composition or directly through interaction with immune cells (Jeurink, van Esch, Rijnierse, Garssen, & Knippels, 2013).

Most people can obtain adequate amounts of prebiotic food components by consuming 5 to 8 servings of fruits and vegetables per day. Although achieving an adequate intake of prebiotic components probably is helpful, consuming more prebiotics than necessary provides no additional benefits. Taking too high a dosage of prebiotic supplements can have the same side effects as consuming too much fiber, including bloating, gas, and diarrhea.

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See Also: Large intestine; Microbiota and microbiome; Probiotics.

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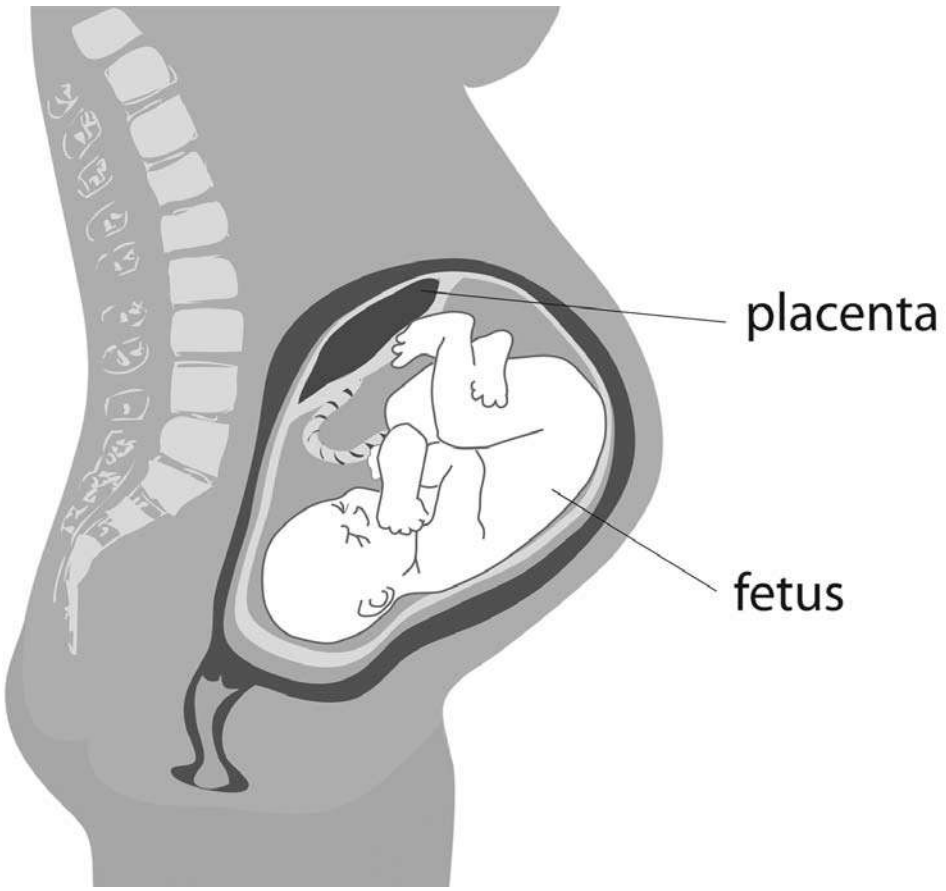
Pregnancy and Nutrition

During pregnancy, many of the habits a woman has taken for granted must be re-evaluated as she realizes that she has become responsible for shaping a new life. Some of the most important habits that deserve special consideration are those affecting the nutritional status of the mother-to-be and her developing offspring. Many studies have shown that a woman's diet during pregnancy has important effects on both the mental and physical development of the fetus and her own health as well. Needs for many nutrients, especially iron, folate, and protein increase during pregnancy, but caloric needs increase only by about 300 kcals per day. Additionally, certain foods—such as some types of seafood—present health risks because of possible contamination with heavy metals or bacteria. Many pregnant women find that the physiological changes experienced during pregnancy can make eating well a challenge.

People used to believe that the developing fetus was akin to a parasite that could take whatever nutrients it needed from its host, the mother. Scientists today no longer believe this to be true. Although the placenta—the organ supporting the baby's growth and development—can manufacture some nutrients, such as glycogen and cholesterol, most nutrients are brought to the fetus through the placenta's communication with the mother's bloodstream. Nutrients cross from the mother's circulation to the blood that supplies the fetus. If a nutrient is missing from the mother's bloodstream, fetal development can be compromised. If the amino acids needed for brain development are absent, for example, brain growth could be compromised.

Preconception Nutrition and Health Behaviors

Good nutrition and health behaviors are vital to the health of both mother and baby. Controlling or correcting health habits prior to pregnancy can improve the chances



Pregnancy places many extra nutritional demands upon the mother. The growing uterus, the fetus, the placenta, and the larger blood supply require nutritional support. (Shutterstock.com)

for having a healthy baby and successful childbirth. Women should change personal habits such as smoking and alcohol and drug use if they are planning to become pregnant, to prevent complications affecting fetal development in the early weeks of pregnancy. Pregnancy is divided into three trimester periods of prenatal development. The first trimester is the most vulnerable stage, when major structural embryonic development takes place.

Maternal Malnutrition

Inadequate nutrient intake during pregnancy can cause low birth weight in an infant. "Low birth weight" mean weighing less than 5.5 lbs (2.5 kg) at the time of birth. Low birth weight is associated with poorer health outcomes throughout the baby's life. Poor maternal nutritional status during pregnancy can lead to

long-term impairments in offspring body size and development. Undernutrition poses a risk for structural damage to a baby's brain, impairing cognitive development and infant motor development. Ironically, maternal malnutrition and low infant birth weight are associated with increased risk for obesity for the offspring later in life (Yang & Huffman, 2013).

Protein Requirements

Amino acids are the material from which life is made. Extra protein is required for the growth of the uterus, the placenta, the mother's increased blood volume, and the development of the baby. The recommended daily intake of protein increases by an additional 25 g per day during pregnancy. Many women already consume protein in excess of their need, however pregnant women should check to be sure they do not need to increase daily intake.

Folate Requirements

Folate facilitates DNA synthesis, and therefore cell division, which is essential for adequate maternal health and fetal growth during pregnancy. As cells grow rapidly during pregnancy, the daily requirement for folate increases from 400 mcg per day to 600 mcg per day. Increasing folate intake to meet this requirement can be achieved by choosing dietary sources rich in folate, ingesting a supplemental source of folic acid, or both. Research has shown that a woman who receives extra folate a month before conception and for the first few months of fetal development has a much lower risk of giving birth to a baby with neural-tube defects, such as spina bifida. For this reason, folate usually is added to prenatal dietary supplements. Many foods are fortified with folate. Folate is also plentiful in leafy greens, citrus fruits, lentils, other dried peas, beans, and egg yolks.

Iron Requirements

The DRI for iron increases from 18 mg per day to 27 mg per day for pregnant women. During pregnancy, blood volume increases dramatically. Both the fetus and the mother need iron to make red blood cells. Adequate amounts of iron are necessary for hemoglobin production. Food sources of iron include lean red meat, poultry, fish, spinach, and legumes. Iron also is added to enriched grains and breakfast cereals.

Iron supplements often are prescribed during pregnancy to prevent iron-deficiency anemia, and iron is included in prenatal supplements. Iron-deficiency anemia during pregnancy has negative health consequences for both pregnant women and their offspring. For the mother, iron-deficiency anemia is associated with increased risk of infections, preterm labor, heart failure, postpartum hemorrhage, and cesarean delivery (Gangopadhyay, Karoshi, & Keith, 2011). Anemia also can be physically debilitating, negatively affecting the quality of life during the stresses of pregnancy. For the offspring, iron deficiency increases risk of low birth weight and the development of cognitive and behavioral problems during

Table 1. Nutritional Recommendations for Pregnancy (19 to 30 Years of Age)

	Pregnant	Non-Pregnant
Biotin (µg) (microgram)	30	30
Calcium (mg) (milligram)	1,000	1,000
Chloride (g) (gram)	2.3	2.3
Choline (mg)	450	425
Chromium (µg)	30	25
Copper (µg)	1,000	900
Fluoride (mg)	3	3
Folate (µg)	600	400[6]
Iodine (µg)	220	150
Iron (mg)	27	18
Magnesium (mg)	350	310
Manganese (mg)	2.0	1.8
Molybdenum (µg)	50	45
Niacin (mg)	18	14
Pantothenic Acid (mg)	6	5
Phosphorus (mg)	700	700
Potassium (g)	4.7	4.7
Riboflavin (mg)	1.4	1.1
Selenium (µg)	60	55
Sodium (g)	1.5	1.5
Thiamin (mg)	1.4	1.1
Vitamin A (µg)	770	700
Vitamin B6 (mg)	1.9	1.3
Vitamin B12 (µg)	2.6	2.4
Vitamin C (mg)	85	75
Vitamin D (µg)	15	15
Vitamin E (mg)	15	15
Vitamin K (µg)	90	90
Water (L) (liter)	3.0	2.7
Zinc (mg)	11	8

Source: Compiled by author from data drawn from *Dietary Reference Intakes Reports* (1997–2011). Food and Nutrition Board. Washington, DC: National Academies Press. Retrieved from http://nap.edu

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Calcium Requirements

Calcium facilitates proper maintenance of muscle function, blood vessel dynamics, nerve impulse transmission, secretion of hormones, blood coagulation, cell

membrane functions, and skeletal development. Adequate calcium intake is necessary for the baby to build strong bones and teeth. Consumption of 1,000 mg of calcium per day during gestation reduces bone turnover markers in late stages of pregnancy. Although the dietary reference intake (DRI) for calcium is 1,000 mg per day for women who are both pregnant and adult women who are not pregnant, many women fail to achieve this intake. Calcium is actively transported across the placenta, with the transfer from mother to fetus, beginning by week 12 of gestation and peaking at week 36.

Fiber and Fluids

Although dietary fiber is not considered a nutrient, an adequate intake of fiber is important during pregnancy to prevent constipation. Constipation typically increases during pregnancy because of the action of progesterone, which relaxes smooth muscle, and compression of the colon by the growing uterus. Iron supplements, often prescribed during pregnancy, frequently contribute to constipation.

As metabolic rate and blood volume increase during pregnancy, so does a woman's need for fluids. Six to eight glasses daily are recommended. Fluid intake should be even greater in hot environments and if the pregnant woman is exercising.

Vitamin Overdose Risks

Some pregnant women become overzealous in their efforts to achieve optimal nutrition status and take extra dietary supplements. Overconsumption of multivitamin and mineral supplements poses risks to the mother and baby's health. Excess consumption of preformed vitamin A causes major malformations in one-fifth of fetuses exposed during the first trimester. The suggested upper limit of vitamin A intake is between 2,800 mcg and 3,000 mcg per day. Vitamin A from fruit and vegetable sources does not lead to toxicity, as the body simply stops converting the vitamin A precursors to active vitamin A.

Healthy Weight Gain

Weight gain recommendations vary with prepregnancy weight. For women with normal prepregnancy weight the recommended weight gain is approximately 25 to 35 lbs, or about 2 to 4 pounds during the first trimester and 0.75 to 1 pound weekly during the second and third trimesters. Prenatal nutritional counseling can help women maintain a healthy body mass index (BMI) and gestational weight gain. Inadequate weight maintenance can cause adverse pregnancy complications, particularly for overweight and underweight mothers. Women with a history of eating disorders should be monitored to facilitate adequate weight gain. Being overweight or obese during pregnancy increases the risk of maternal morbidity and fatality attributed to pregnancy complications, and poses risks to the baby's health (Brown & Avery, 2012).

Mild to moderate physical activity during pregnancy promotes maternal and child well-being. Advantages for the mother include appropriate weight control, increased cardiovascular function, positive and calm mood stability, decreased muscle cramps, and maintained blood pressure. To ensure good health, pregnant women who exercise require extra water intake and kilocalories. Although light exercise during pregnancy produces positive effects on newborns, nutrition and weight of expecting mothers should be monitored throughout each trimester to ensure a baby's optimum health.

Foods to Avoid

Alcohol is considered a teratogen, and increases risk of fetal alcohol spectrum disorders. Pregnant women are advised to avoid consuming alcohol during pregnancy. Caffeine appears to be safe in small amounts, under 200 mg per day, or the equivalent of about two cups of coffee.

Health authorities recommend that pregnant women limit intake of some foods because of heavy metal, such as mercury, content (FoodSafety.gov). Large predatory fish such as shark, swordfish, king mackerel, and tile fish appear to be most risky. Better choices are light (not albacore) canned tuna, shrimp, salmon, pollock, and catfish. Food safety recommendations should be followed during pregnancy to avoid foodborne illnesses, which are dangerous to both maternal and fetal health.

Challenges to Good Nutrition

A woman's typical eating practices often are disrupted by pregnancy. Hormonal changes can cause nausea and vomiting ("morning sickness"), especially during the first trimester. Because little weight gain occurs during the first trimester, many women don't realize how much the embryo is growing and assume that good nutrition is not yet a concern. Even though the embryo still is very tiny, good nutrition is as important as ever. Many women find that eating several small snacks works better than eating big meals, and they manage to get good nutrition that way.

During the second half of the pregnancy, the stomach becomes compressed as the uterus pushes up against the diaphragm, and big meals become impossible. Five or six small but nutritious meals usually work best during this time.

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Research Issues

Recommendations for pregnancy weight gain undergo frequent revision. Health care providers must balance the risk of maternal malnutrition against the difficulty many women have losing extra weight once the baby is born. Postpartum weight loss success varies widely from woman to woman, and many factors are related to postpartum weight. Globally, good maternal nutrition is a high priority goal for most countries. Many countries have enacted public policy measures to improve nutrition for women and children.

See Also: Calcium; Folate and folic acid; Foodborne illness and food safety; Iron; Iron-deficiency anemia.

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Premenstrual Syndrome

Premenstrual syndrome (PMS) refers to a group of symptoms that are linked to the menstrual cycle. Premenstrual syndrome is a common syndrome that presents with physical and emotional symptoms of variable degrees of severity which occur one to two weeks prior to the onset of menstruation. The symptoms usually cease soon after bleeding begins. Premenstrual syndrome is thought to be related to the monthly hormonal changes that are part of the menstrual cycle. Researchers think that PMS severity is influenced by biological, social, cultural, and psychological factors. Lifestyle changes and medications can reduce symptom severity. Several dietary factors, nutrients, and dietary supplements show promise for reducing PMS symptoms.

Premenstrual syndrome is most common among women who are 20 to 40 years old; however, it can occur any time during a woman's childbearing years. Approximately 75% of American women experience PMS sometime in their life, with 5% of those women becoming disabled by the severity of the symptoms (Vorvick, 2012). Premenstrual syndrome occurs most often in women who have

had at least one child; have a history of postpartum depression, mood disorder, or personal or family history of severe depression. Symptoms have been observed to worsen as women get older and approach menopause.

History

The first record of PMS dates back to the ancient Greeks when Hippocrates attributed the disorder to hysteria, also known as the "wandering uterus." Hippocrates stated that the uterus moved in response to the lunar phases, because the phases of the moon and the menstrual cycle mirror each other in duration. Hippocrates thought that the blood surrounding the uterus put pressure on the vital passages and heart, which caused the onset of mental illnesses. Later the Catholic Church thought that the mood changes associated with PMS were due to demonic possession as a punishment for acting immorally. This theory suggested that women deserved to experience these mood changes; the symptoms of PMS were thought to indicate that women experiencing these symptoms had acted against God. This idea persisted throughout medieval times. After the Renaissance, science began to dismiss the prior theories of hysteria of Hippocrates and demonic possession of the church. In the 19th century and early 20th century, scientists thought that it was the mind and not the body that was not functioning properly, due to pathological trauma. Freud added that the symptoms of PMS were caused by unresolved psychodynamic conflicts from childhood (Rodin, 1992).

It was not until 1931 that Dr. Robert T. Frank provided a more accurate description of the symptoms associated with PMS; he called the syndrome "premenstrual tension." About 20 years later, Dr. Katharina Dalton changed the name to "premenstrual syndrome." Dr. Dalton was able to help explain the occurrence of the symptoms by observing the hormonal changes associated with the menstrual cycle (Rodin, 1992).

Symptoms

Premenstrual syndrome is characterized by a large number of symptoms, including physical, behavioral, and emotional symptoms. The most commonly reported symptoms are listed below.

- Physical symptoms: Swelling, breast tenderness, aches, headache, bloating, weight gain, acne, upset stomach, constipation, and diarrhea.
- Behavioral symptoms: Sleep disturbance, tiredness, poor concentration, memory troubles, changes in appetite, decreased interest and motivation, and social withdrawal.
- Mood symptoms: Irritability, depression, anxiety, mood swings, crying spells, tension, and feeling out of control.

Although symptoms must occur in the luteal phase of the cycle to be considered premenstrual symptoms, the duration of symptoms has considerable variability.

Causes

The exact cause of PMS symptoms is unknown, however the relationship between PMS and the menstrual cycle suggest that the primary causes are related to hormonal changes. Some women might be more sensitive to the hormone drop in estrogen and increase in progesterone that occur during the premenstrual phase than are other women. Physical and neurochemical changes that accompany shifting hormone levels probably play a role in the generation of PMS symptoms. Lifestyle factors such as sleep deprivation, poor diet, and low levels of physical activity also could contribute to PMS.

As with many disorders, stress is a major component in influencing how disabling PMS can become. Stress depletes the neurotransmitters dopamine and serotonin, which are mood enhancers. Research conducted by Gollenberg and colleagues (2010) found that women who had higher stress levels tended to report having moderate to severe PMS symptoms, and the lower-stress group of women experienced milder PMS symptoms.

Many women experience food cravings during the premenstrual period. Some typically crave foods appear to increase PMS symptom severity, including sugar-sweetened beverages, salty foods, caffeinated beverages, and alcohol. Overeating can contribute to feelings of abdominal heaviness and bloating.

Premenstrual Syndrome and Obesity

Women who have a higher BMI have been found to be more likely to have PMS as compared to women having a lower BMI (Bertone-Johnson, Harkinson, Willett, Johnson, & Manson, 2010). A subset of subjects from the Nurses' Health Study 2, including 1,057 women who developed PMS and 1,968 controls, were followed for 10 years. A significant weight increase after age 18 years was associated with increased risk for PMS. It is not known exactly how obesity is related to the risk for PMS. Researchers have hypothesized that obese women might have many of the risk factors for PMS, such as decreased sleep, depression, and greater stress levels. The hormonal and neurochemical effects of obesity and accompanying inflammation might influence PMS. Although these data suggest that losing excess fat might reduce PMS symptoms, researchers have not yet demonstrated a reduction in PMS symptoms with weight loss in well-controlled studies.

Treatments

Women with mild PMS often find that lifestyle changes lead to a significant decrease in symptom severity. Women with more severe PMS would have a more serious diagnosis, "premenstrual dysphoric disorder" (PMDD), and should seek medical advice. Although PMDD often responds to lifestyle changes, many women with PMDD require additional support, such as psychotherapy and medication. Lifestyle changes most helpful for PMS include the following.

- Follow public health guidelines for engaging in adequate physical activity. People in general good health should try to exercise for at least 30 minutes, 5 or more days per week.
- Get adequate sleep. Most people need at least 7 to 8 hours of sleep per night.
- Manage stress. Some people find that lifestyle change itself reduces feelings of stress. Simple techniques such as breathing exercises, meditation, and counseling also can be effective.
- Avoid caffeine. Many women experience PMS symptom reduction when they reduce caffeine intake.
- Avoid alcohol. Alcohol might exacerbate PMS symptoms through a variety of pathways and could contribute to mood disorders.
- Follow guidelines for a healthful diet. Diets high in unprocessed foods and low in added sugars, salts, and fats might reduce PMS symptoms.

Dietary Factors

In addition to following general public health guidelines for a healthful diet, several dietary factors might especially influence PMS symptoms. These include the following.

Salt

Intake of foods high in salt content can lead to water retention—one of the most problematic symptoms of PMS. Women who suffer from PMS-related water retention should reduce their intake of salt. Many processed foods are high in added salt, including soups, tomato sauces, processed meats such as salami, and soy sauce. Pizza and most restaurant foods also tend to be high in salt.

Calcium and Vitamin D

Several studies have found that increasing calcium intake reduces physical and psychological symptoms caused by PMS. Increasing calcium intake has been shown to help relieve cramping, stress, breast tenderness, swelling, headaches, and backaches when consumed over an extended period (EBSCO CAM Review Board, 2013). In one study, women receiving an extra 500 mg of calcium per day reported reduced levels of depression, craving, and fatigue after three months, as compared to groups not receiving the supplement (Ghanbari, Haghollahi, Shariat, Foroshani, & Ashrafi, 2009).

Nutritionists generally recommend that people try to achieve adequate calcium from dietary sources when possible. Good calcium sources include dairy products such as milk, yogurt, and cheeses, some nuts such as almonds and Brazil nuts, some greens such as broccoli, mustard, kale, and Swiss chard, as well as sardines and salmon. If supplements are used, calcium should be paired with vitamin D.

Magnesium

Magnesium has been shown to relieve some of the symptoms of PMS, including reduced fluid retention, breast tenderness, and bloating. Research suggests that magnesium consumption before menses onset improves premenstrual mood changes, and reduces migraines, insomnia, and leg swelling (EBSCO CAM Review Board, 2013). Good dietary sources of magnesium include legumes, nuts, whole grains, and leafy vegetables.

Iron

In a 10-year study, researchers found that women who were in the top 10% for iron consumption were 40% less likely to experience PMS symptoms as compared to women in the bottom 20% (Chocano-Bedoya et al., 2013). Iron is essential to good health, as it is involved in oxygen and energy transport between cells. Iron deficiency can lead to anemia, and common symptoms include fatigue and weakness. The iron recommended amount for women ages 19 to 50 years is 18 mg per day. Iron should be obtained from foods as much as possible.

The B Vitamins and Vitamin B6

The B vitamins are a group of water-soluble vitamins that are involved in the process of energy production and usage as well as the formation of red blood cells. The B vitamins are found in a variety of foods, including fish, poultry, meat, eggs, dairy foods, leafy green vegetables, and peas.

Vitamin B6 aids in the production of neurotransmitters and hormones that influence mood—including serotonin and norepinephrine. Contrary to popular belief, not all studies have supported vitamin B6 as providing benefits in the relief or treatment of PMS symptoms (EBSCO CAM Review Board, 2013). Nutritionists often recommend a daily multivitamin and mineral supplement for women experiencing PMS. Obtaining adequate vitamin B6 probably is helpful for people who might be deficient.

Dietary Supplements

Several dietary supplements have been studied for possible effectiveness in reducing PMS symptoms, including the following.

- Chasteberry. Chasteberry is an herb widely used in Europe for treatment of PMS. A few studies support its helpfulness for reducing irritability, breast tenderness, depression, and headache (EBSCO CAM Review Board).
- Phytoestrogens. Phytoestrogens are found in foods (e.g., soy foods) and in supplements (e.g., black cohosh, dong quai, soy isoflavones). Although some studies report benefits from supplements, many nutritionists caution against overuse of phytoestrogen supplements, because research on the long-term health effects of these supplements is lacking. Increasing intake of soy foods appears to be safe.

- St. John's wort. St. John's wort is an herb that has shown some promise for the treatment of mild depression and could be helpful for the mood changes associated with PMS.
- Ginkgo biloba. Two small double-blind studies found that ginkgo biloba supplements helped reduce PMS symptoms, especially breast pain and mood disturbances (EBSCO CAM Review Board, 2012).

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See Also: Gingko biloba; Phytoestrogens; Sodium and salt; Soybeans and soy foods; St. John's wort.

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Probiotics

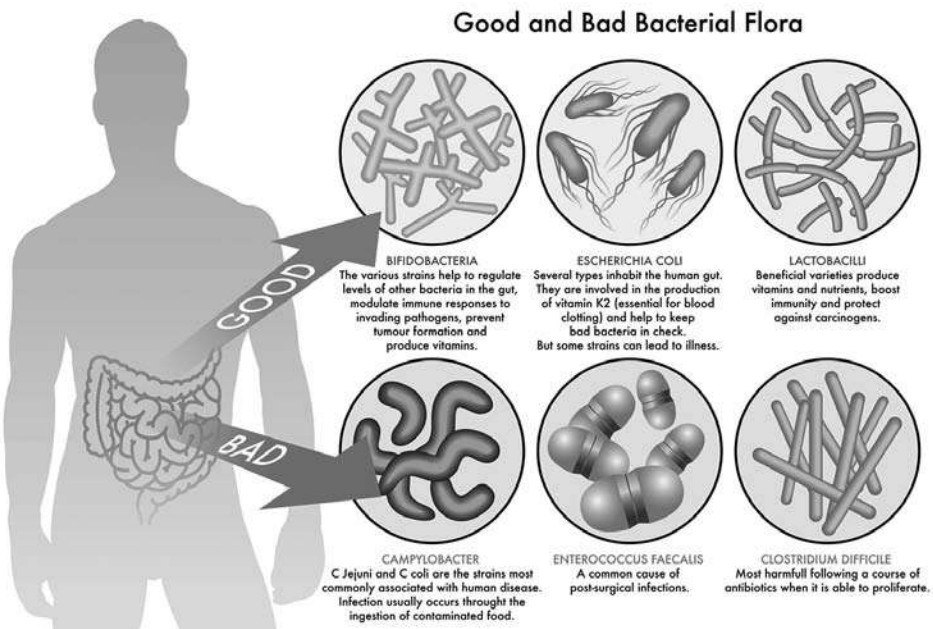
Probiotics are live microorganisms that increase the number of "good" or health-promoting bacteria in the body. Helpful bacteria appear to heighten the body's

resistance to microbes that cause various problems within the digestive system and in other physiological systems. Probiotic foods and supplements also could be useful in the treatment of digestive disorders, especially disorders involving colon function. Probiotics can be taken in the form of supplements or as food, such as yogurt and fermented foods which contain these live bacteria cultures. *Lactobacillus* and *Bifidobacterium* are two common strains of bacteria that humans consume to improve their bodies' balance of microorganisms.

Scientists are just beginning to understand the many activities of the microorganisms that inhabit the human body and the effects of these activities on health and disease. This collection of microorganisms is collectively referred to as the "microbiome." "Normal flora" is the term used to describe the harmless and helpful microorganisms, including bacteria, found in the gastrointestinal (GI) tract. They contribute to many biological processes, such as digestion. Normal flora not only aid digestion but also work to produce and release helpful compounds—such as vitamin K—and fight against the invasion and growth of harmful bacteria. More than 1,000 species of bacteria have been found to reside in the human GI tract, although most people have fewer than 500 species. Maintaining optimal GI health involves having the right number of bacteria and a healthful mix of health-promoting bacteria in the gut.

Probiotic products claim to promote various health benefits by contributing to a better microbiome in the GI tract. Evidence is strongest for the reduction of infectious diarrhea and antibiotic-associated diarrhea. Several studies have found that a variety of probiotic supplements help to reduce the severity of infectious diarrhea, especially in infants and children. Supplements containing *Lactobacillus GG* have been most widely tested, although many other bacterial strains also have been found to be helpful. One of the most dangerous side effects of antibiotic administration is overgrowth of the bacterium *Clostridium difficile*, or *C. diff* a normal resident of the GI tract in healthy people, but during antibiotic therapy—which kills off most GI bacteria as well as killing the target organism—*C. diff* can thrive and cause severe diarrhea, a condition particularly dangerous in sick people who are receiving antibiotic therapy. Probiotic therapies might reduce the likelihood of *C. diff* overgrowth during antibiotic treatments, although not all studies support this idea.

Probiotics have shown some promise for the treatment of irritable bowel syndrome (IBS). Irritable bowel syndrome symptoms, such as abdominal cramping, constipation, and diarrhea are exacerbated by feelings of stress. One study found that probiotics might lessen the effect of stress on the GI tract in laboratory mice (Sun et al., 2013). In this study, the bacteria introduced in the probiotic treatment appeared to inhibit the inflammation that worsens GI symptoms. Results for probiotic treatment of IBS in people have been mixed, with most health providers suggesting that patients try probiotics, but discontinue use if symptoms worsen. The probiotics used most frequently for people with IBS contain *Lactobacillus* or *Bifidobacterium* strains. Because of their potential ability to modulate inflammation and other immune-system activity, researchers are exploring the use of probiotics for the treatment of inflammatory bowel diseases such as ulcerative colitis and Crohn's disease, with some success.



Maintaining healthful colonies of bacterial flora can help to prevent the overgrowth of potentially harmful bacteria. Probiotic foods and supplements may help with this balance. (Rob3000/Dreamstime.com)

Probiotics could have the potential to treat other autoimmune disorders, such as eczema (an inflammatory skin condition). Babies with a family history of eczema have shown a reduced risk of developing eczema if their mothers consumed foods or supplements with probiotics during pregnancy, and if babies received probiotic supplements early in life.

Probiotics are found in many foods, including dairy products such as yogurt and kefir. Fermented vegetable products such as pickles, sauerkraut, and kimchi (a Korean dish) also have active bacterial cultures. Probiotic drinks are popular in Japan. Foods containing helpful bacterial cultures have been consumed in many cultures for thousands of years and are considered generally safe. Probiotic supplements must deliver live bacteria to be helpful. Labels measure probiotic dosage in "colony-forming units" (CFUs). Supplements usually contain millions or billions of CFUs. Although probiotic supplements appear to be safe for most people, those with compromised immune systems should seek the guidance of a health care provider before taking probiotic supplements.

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See Also: Fermentation and fermented foods; Large intestine; Microbiota and microbiome; Prebiotics.

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Protein

Proteins are nitrogen-containing organic compounds found in all plants and animals. Protein is found throughout the human body, in structures such as muscle and bone; the immune cells that fight infection; the red blood cells that carry oxygen to all parts of the body; neurochemicals and hormones, such as serotonin and epinephrine; and the enzymes that regulate biochemical processes such as digestion and energy production. Proteins are composed of smaller units called "amino acids." The body uses amino acids to build its own proteins. The body also can break down some amino acids to produce energy—especially during long or heavy bouts of physical activity or when glycogen stores are depleted. People obtain protein from food, and protein is plentiful in many foods, especially meat, poultry, seafood, dairy products, nuts, and legumes.

Experts often liken amino acids to letters and proteins to words spelled with those letters. To spell a given word, one must have all of the letters available. The human body needs about 20 different amino acids to make all of the proteins required for life. If humans have an adequate intake of protein in general, they can make 11 of these in sufficient quantities. The other 9 must be obtained from the diet on a daily basis. Amino acids that people must obtain from the diet are called "essential amino acids." Amino acids that the body can manufacture are called "nonessential amino acids." (Of course, both types of amino acids still are "essential" to life, but they are not an essential part of the diet.)

The human body can store only a limited amount of amino acids, which is why people must consume foods containing proteins every day. Foods that contain all nine essential amino acids are called "complete proteins." These foods include eggs, dairy products, animal flesh (i.e., chicken, fish, beef), animal organs (i.e., liver, kidneys), soybeans, and a few other plant foods. Animal foods more closely match the amino acid profile needed by humans, which is logical because humans

How Much Food from the Protein Foods Group Is Needed Daily?

The following recommendations for protein intake come from the MyPlate guidelines. The amount of food from the "Protein Foods Group" a person should eat depends on age, gender, and level of physical activity. Most Americans eat enough food from this group, but need to make leaner and more varied selections of these foods. Recommended daily amounts are shown in the chart below, from the MyPlate website (http://www.choosemyplate.gov/printpages/MyPlateFoodGroups/ProteinFoods/food-groups.protein-foods-amount.pdf).

Protein Recommended Daily Intake

	Age	Amount
Children	2–3 years old	2-ounce equivalents
	4–8 years old	4-ounce equivalents
Girls	9–13 years old	5-ounce equivalents
	14–18 years old	5-ounce equivalents
Boys	9–13 years old	5-ounce equivalents
	14–18 years old	6.5-ounce equivalents
Women	19–30 years old	5.5-ounce equivalents
	31–50 years old	5-ounce equivalents
	51+ years old	5-ounce equivalents
Men	19–30 years old	6.5-ounce equivalents
	31–50 years old	6-ounce equivalents
	51+ years old	5.5-ounce equivalents

The amounts given are appropriate for individuals who get less than 30 minutes per day of moderate physical activity, beyond normal daily activities. Those who are more physically active could consume more and stay within calorie needs.

U.S. Department of Agriculture. (n.d.) How much food from the protein foods group is needed daily? Retrieved from http://www.choosemyplate.gov/printpages/MyPlateFoodGroups/ProteinFoods/food-groups.protein-foods-amount.pdf

are animals, so human composition is similar. It is not difficult, however, to consume adequate amino acids if one eats a variety of plant sources, because the amino acids that generally are low in grains, for example, are more plentiful in legumes, and vice versa. Combining incomplete proteins (proteins lacking one or more essential amino acids) usually results in an adequate intake of protein. The U.S. Department of Agriculture recommends 0.8 g of protein per kilogram of body weight (or 0.36 g per lb). People who are significantly overweight (in the form of excess body fat) should base their protein intake calculations on a weight that is healthier for them.

Conditions Requiring Extra Dietary Protein

Several conditions call for extra protein in the diet. Whenever more tissue is being built, more protein is required. Pregnancy, bodybuilding, strength training, and adolescent growth spurts place high demands for amino acids on the body. Lactating mothers produce a quart or more of milk per day and thus need a greater-than-normal protein intake. People who are restricting calories—especially athletes—force the body to consume protein for fuel, thus depleting valuable amino acid stores. These people must consume more protein to make up for the loss of other food groups in their diets. (Such athletes also should add some carbohydrate to their diets.) Endurance athletes usually burn a certain amount of protein for fuel and require greater protein intakes than do sedentary people. Vegetarians—especially vegans (who consume no animal products)—require somewhat greater protein intakes than do people who are omnivores (eating all kinds of foods of both plant and animal sources), because much of their protein is incomplete. Any combination of the factors discussed above (such as pregnant vegans) requires more dietary protein, up to 1.2 g to 2 g per kilogram of body weight.

Protein Foods

Foods that are relatively high in protein often are called "protein foods." Protein foods, however, also include many other nutrients. Protein food choices therefore include overall diet quality. Some protein foods—especially meats—are very high in fat. Processed meats often contain excess fat and salt. Other protein foods, such as cold-water fish, are high in healthful omega-3 fatty acids. Plants high in protein often are high in vitamins, minerals, fiber, and helpful phytochemicals.

Suggestions for choosing healthful sources of protein foods can be found at the MyPlate website, which offers the suggestions listed below (U.S. Department of Agriculture, 2014).

Protein Food Ounce Equivalents: What Counts as an Ounce Equivalent in the Protein Foods Group?

MyPlate guidelines offer recommendations for protein food intake in terms of ounce equivalents. The MyPlate website contains a table for calculating ounce equivalents for a variety of protein foods.

In general, one ounce of meat, poultry, or fish; one-quarter cup cooked beans; one egg; one tablespoon of peanut butter; or one-half ounce of nuts or seeds can be considered as a one-ounce equivalent from the protein foods group.

U.S. Department of Agriculture. (n.d.) *What counts as an ounce equivalent in the protein foods group?* Retrieved from http://www.choosemyplate.gov/printpages/MyPlateFoodGroups/ProteinFoods/food-groups.protein-foods-counts.pdf

Choose Lean Meat

- The leanest beef cuts include round steaks and roasts (eye of round, top round, bottom round, round tip), top loin, top sirloin, and chuck shoulder and arm roasts.
- The leanest pork includes pork loin, tenderloin, center loin, and ham.
- Lean ground beef is at least "90% lean."
- Boneless skinless chicken breasts and turkey cutlets are the leanest poultry choices. Remove skin from of other poultry parts.
- Choose lean turkey, roast beef, ham, or low-fat lunch meats for sandwiches instead of deli meats containing more fat, such as bologna and salami.

Remove Fat

- Trim away all of the visible fat from meats and poultry before cooking.
- Broil, grill, roast, poach, or boil meat, poultry, or fish instead of frying it.
- Drain off any fat that appears during cooking.
- Skip or limit the breading on meat, poultry, and fish. Breading adds calories. It also causes the food to soak up more fat during frying.
- Fix beans and peas without added fats.
- Choose and prepare foods without high-fat sauces or gravies.

Other Good Protein Choices

Eat seafood at least twice a week as the main protein food. Seafood rich in omega-3 fatty acids include such fish as salmon, trout, and herring. Eat beans, peas, or soy products as a main dish or part of a meal often. Some healthy options are listed below.

- Chili with kidney or pinto beans
- Stir-fried tofu
- Split pea, lentil, minestrone, or white bean soups
- Baked beans
- Black bean enchiladas
- Garbanzo or kidney beans on a chef's salad
- Rice and beans
- Veggie burgers

Choose unsalted nuts as a snack, and use them in salads and in main dishes. Use nuts to replace meat or poultry (not in addition to) with pasta, vegetables, and in stir fry, as ice cream or yogurt toppings, and on salads.

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See Also: Amino acids; Legumes; MyPlate guidelines; Vegetarian and vegan diets; Whey protein.

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Public Policy on Nutrition

Public policy refers to principles and plans that guide governments in their actions. Public policy helps all levels of government formulate laws, establish funding priorities, develop regulatory measures, and take other actions to address the needs of constituents. Public policies are created in response to particular issues. Some public policies are designed to influence people's eating behavior in ways that might improve health. Public policies and consequent government regulation influence food production, animal husbandry and slaughtering practices, and the manufacture and marketing of food products. Public health is protected by regulations that influence how restaurants and other food vendors prepare and handle food, to prevent foodborne illnesses. Public policy sometimes aims to influence the choices people make in their daily lives.

Most people take for granted the variety of ways in which the U.S. government attempts to influence the health and nutrition of citizens. The Department of Agriculture (USDA) and the Department of Health and Human Services (HHS), for example, issue dietary guidelines advising people on the balance of foods and beverages that can help them to reduce risk of disease and promote good health. The USDA also sets the nutritional standards for the food served for lunch in all of the country's public schools (Child nutrition reauthorization, 2010). Many privately owned chain restaurants even post calorie counts on their menus as the result of planned federal guidelines. As health care costs continue to escalate in the United States—costs that the government itself often covers through Medicare, Medicaid, and other similar programs—public policies that address issues of health and nutrition are likely to multiply, and not just at the federal level. Federal, state, and city governments increasingly are adopting different policies to incentivize people to make healthier and more nutritious choices in their daily lives.

One of the major nutrition issues that the government has tried to address during the past decade involves trans fats in food. Trans fatty acids are created when unsaturated fats have extra hydrogen atoms added to them to make them more saturated, a process known as "hydrogenation." Research has found that the consumption of trans fatty acids increases the level of "bad" LDL cholesterol and lowers the level of "good" HDL cholesterol, thus increasing the risk for heart disease. Although those in favor of government regulation of trans fats have focused on these health

risks, those against regulation believe that removing these fats would increase costs for food manufacturers, restaurants, and other similar entities.

In 2003, the U.S. Food and Drug Administration (FDA) issued a regulation that required all food labels to list trans fat content by 2006 (CDC, 2012). Mayor Michael Bloomberg chose to take a different approach in 2006, preventing New York City restaurants from serving any food that contained more than 0.5 grams of trans fat per serving (National Council of State Legislatures, 2013). Other major cities, such as Philadelphia and Boston, subsequently enacted similar legislation. At the state level, California passed a law in 2008 that prevented foods containing trans fats from being served at any food facility. Oregon required restaurants to post trans fat content on their menus in 2009, and Colorado banned foods containing trans fats from being served in public schools in 2012 (National Council of State Legislatures, 2013). According to the National Conference of State Legislatures, at least 30 states had considered some sort of regulation of trans fats as of January 2013 (National Council of State Legislatures, 2013). At this time, the federal government has yet to enact any legislation modeled after these state- and city-level proposals.

Initiatives to place calorie counts or other nutritional information on restaurant menus, particularly at fast-food establishments, also have become increasingly prevalent during the past few years. According to the Rudd Center for Food Policy and Obesity at Yale University, Americans now receive about a third of their calories from restaurants or other food-service vendors, and individuals underestimate the number of calories in restaurant food by as much as 600 calories (Yale Rudd Center, 2008). Proponents of this sort of legislation hope that more transparency about calorie counts and other similar information will empower consumers to make more healthful choices and prompt restaurants to offer more nutritious options. Critics, on the other hand, fear that legislation will impose added costs to businesses and doubt that such information will be effective in changing people's decisions (Yale Rudd Center, 2008).

Under Mayor Bloomberg's leadership, New York City pioneered other regulations involving menu labeling. In 2006, the city approved a plan to require restaurants with more than 15 locations to post calorie counts on menus and menu boards (Kliff, 2012). A lawsuit filed by the New York State Restaurant Association—arguing that the rules violated the First Amendment rights of local businesses—delayed the proposal, but a district court judge upheld a slightly revised version of the plan in April 2008 (Barron, 2008). California also required chains with more than 20 restaurants to provide information about calories, carbohydrate, saturated and trans fat, and sodium content in a "clear and conspicuous manner" in 2008, and at least five states enacted similar policies over the next two years (National Council of State Legislatures, 2013). The federal government gave the FDA the authority to create national regulations on menu labeling in the Patient Protection and Affordable Care Act of 2010. These rules require restaurant chains with more than 20 locations—as well as operators of more than 20 vending machines—to post calorie counts for menu items and make additional nutrition information available upon request (Yale Rudd Center, 2013).

One of the most controversial sets of policy initiatives regarding nutrition has focused on soft drinks and other sugar-sweetened beverages. These drinks typically are high in calories but have little to no nutritional value. American adults' consumption of these beverages has more than doubled since the 1970s, and research has linked frequent consumption of these drinks to increased risks of obesity, dental problems, cardiovascular disease, and type 2 diabetes (Friedman & Brownell, 2012). Those who favor regulating sugar-sweetened beverages often cite the need to address these health problems, but critics claim that the government should not regulate personal behavior and argue that such policies unfairly target low-income and minority populations who frequently consume these drinks.

Legislation in this policy area is still in the very early stages and frequently has met obstacles. Mayor Bloomberg requested a waiver from the federal government to allow New York City to ban the use of food stamps to purchase sugar-sweetened beverages, but the request was denied in 2011 (Kliff, 2012). Mayor Bloomberg then attempted to ban the purchase of sugar-sweetened beverages larger than 16 oz at restaurants, movie theaters, and food carts, but a New York State Supreme Court judge found these regulations to be "arbitrary and capricious" and blocked the initiative (Grynbaum, 2013). Imposing an additional tax on sugar-sweetened beverages has been a popular policy proposal in other settings. According to a report from the Rudd Center for Food Policy and Obesity, 24 states and 6 cities introduced legislation to impose taxes on sugar-sweetened beverages between 2009 and 2012, but no laws on this issue have yet been enacted (Friedman & Brownell, 2012). The federal government also has not implemented any new policies in this area.

Researchers have tried to evaluate the effectiveness of these public policy initiatives. Because Mayor Bloomberg pioneered many of these laws, studies often focus on programs and policies in New York City. Regarding New York City's trans fat legislation, a 2009 study found that the percentage of restaurants using trans fats in the city decreased from 50% before the ban was enacted to less than 2% after the policy went into effect in 2008 (Kliff, 2012). Other researchers, however, are hesitant to praise the policy until more detailed studies about changes in the cholesterol levels of New York City residents are available (Kliff, 2012).

Evaluations of New York City's menu labeling regulations are similarly mixed. In a study of adults eating at fast-food restaurants in New York City, 27.7% of those surveyed claimed that calorie information influenced their choices (Elbel, Kersh, Brescoll, & Dixon, 2009). Yet researchers did not find a major difference in the number of calories consumed by these New York City residents and by individuals eating at fast-food restaurants in Newark, New Jersey—a city that does not require restaurants to post calorie counts (Elbel, Kersh, Brescoll, & Dixon, 2009).

Finally, although there are not policies in place in New York City to evaluate taxes on sugar-sweetened beverages, economic models in one study suggested that increasing the price of soft drinks by 10% would decrease consumption by 8% (Kliff, 2012). Thus, although New York City health officials frequently point to increases in the life expectancy of New Yorker City residents during the past decade as a sign that the mayor's nutritional initiatives have had a positive impact on

the health of city residents, more data on specific policies undoubtedly are needed to evaluate these claims.

Federal, state, and city governments have clearly attempted to improve the health and nutrition of the American people through a variety of different programs and policies. Officials and other advocates likely will continue to address all three policy areas in the future, as well tackling other issues such as sodium reduction and the marketing of food to children. New approaches to promoting health and nutrition also are likely to be considered, such as the public-private partnerships that First Lady Michelle Obama promoted by working with the Walt Disney Company to voluntarily limit advertising for unhealthy foods on its cable television channels (White House Office of the First Lady, 2012). It will be interesting to see what other innovative ideas arise in the days, months, and years ahead.

Hannah Green

Research Issues

Public policy efforts to influence people's food choices can take the form of passive education. Passive education refers to the dissemination of information. Public health messages on billboards, television, and in print media, for example, sometimes urge people to adopt more healthful eating behaviors, such as consuming more fruits and vegetables. Monitor local public-policy efforts to educate consumers about food choices, and record your findings. Include the bulletin boards of local schools, libraries, health centers, and other resource centers in the area, as well as local newspapers.

See Also: Food gardens; Sugar-sweetened beverages; Trans fatty acids.

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Pyruvate and Pyruvic Acid

Pyruvic acid is a versatile molecule which serves as an intermediate in several metabolic pathways. Due to its acidity, pyruvic acid is prone to losing one hydrogen atom, which turns it into a pyruvate molecule. In glycolysis, glucose is cleaved into two pyruvic acid molecules and adenosine triphosphate (ATP), the body's energy-storage molecule, is released. When oxygen is not available, pyruvic acid accumulates and is converted into lactic acid. A buildup of lactic acid in the blood suggests limited oxygen is available to metabolize pyruvate. In plants, this process is called "fermentation" and results in ethanol rather than lactic acid. When oxygen is present, pyruvate is converted to acetyl CoA for use in the citric acid (Kreb's) cycle which supplies the electron transport chain and yields more ATP. Besides its pivotal role in energy production, pyruvic acid also is utilized in the creation of glucose in periods of stress through gluconeogenesis as well as formation of the amino acid alanine, which is a part of many proteins.

Direct sources of pyruvate in the diet include apples as well as beer and wine. Pyruvate is available as a supplement and sometimes is used by bodybuilders. A few small studies have suggested that high doses of pyruvate supplements might enhance weight loss and fat burning (EBSCO, 2012); large-scale studies are lacking, however. Nevertheless, pyruvate has been a popular ingredient in herbal weight-loss products. Pyruvic acid has proved effective as a topical peel in treatment of facial acne and could help in treatment of other dermatological issues—from wrinkles to acne scars (Cotellessa, Manunta, Ghersetich, Brazzini, & Peris, 2004). It is unique in its ability to reduce seborrhea, leading to some relief from oily skin but maintaining hydration of outer skin layers.

Patricia M. Cipicchio

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Q

Quercetin

Quercetin is a flavonoid, a type of plant compound that has antioxidant qualities beneficial to both plants and the animals that eat them. Quercetin is found in many fruits and vegetables, including citrus fruits, apples, blueberries, blackberries, grapes, and onions; it also is plentiful in green tea and red wine. Quercetin is available as a dietary supplement and has been marketed as a treatment for several medical conditions. Quercetin supplements have been recommended to increase aerobic capacity in endurance athletes, although evidence for this benefit is not strong.

Early studies on quercetin, conducted with animals and cell cultures, pointed to quercetin's potential health benefits. In the laboratory, quercetin exerts antioxidant and anti-inflammatory effects. In cell cultures, quercetin also exerts antihistamine effects on immune cells, suggesting that quercetin might help to dampen allergic responses.

The strongest evidence for use of supplemental quercetin is for prostatitis, acute inflammation of the prostate gland. Quercetin appears to help reduce the pain and swelling associated with this condition. Interesting research also suggests that quercetin might help reduce blood pressure somewhat in people with hypertension.

As an antioxidant, quercetin could reduce the damage to LDL cholesterol that contributes to artery disease, the most common form of heart disease. Foods high in quercetin and other helpful phytochemicals have been observed to protect against cancer, heart attack, and stroke. More studies are necessary, however, for scientists to understand the ways in which certain phytochemicals like quercetin interact with other substances in foods to determine whether the supplement form of quercetin will provide the same benefits that it does when it is included as a part of a healthy diet. Consuming a diet with plenty of fruits and vegetables appears to yield more health benefits than taking handfuls of individual supplements, such as quercetin, each day.

Quercetin also has been promoted as an aid to athletic performance. A study in mice suggested that the supplement enhanced aerobic capacity in muscles through increased mitochondrial biogenesis (Davis, Murphy, Carmichael, & Davis, 2009). Subsequent studies in animals and humans, however, have not shown strong results (Casuso, Martinez-Amat, Martinez-Lopez, Camiletti-Moiron, Porres, & Aranda, 2013). The effect of quercetin supplementation on athletic performance was

described in one meta-analysis as being "between trivial and small" (Kressler, Millard-Stafford, & Warren, 2011). Athletes remain interested in quercetin, as two studies have suggested that quercetin supplements might reduce risk of upper respiratory tract infections following high amounts of exercise, a common problem.

Supplement dosage ranges from 50 mg to 500 mg to treat various conditions. Quercetin supplements seem to be safe for healthy adults at doses of 500 mg, twice a day, for 12 weeks (Ehrlich, 2011). The effects of the supplement have not been studied on women who are pregnant. Quercetin might interact with other medications by interfering with the liver's ability to break down these medicines. It also could decrease the effectiveness of antibiotics by preventing the antibiotics from killing bacteria. Doses greater than 1 g per day could lead to side effects including nausea, headache, and tingling in the limbs. A few cases of kidney damage from very high doses of quercetin have been observed. It is unlikely, however, that quercetin will cause any major problems when taken in small doses.

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See Also: Dietary supplements.

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Quorn

Quorn is a food brand that offers a wide range of meat-alternative products, which was born 50-plus years ago in a research center out of an effort to provide

protein-rich alternatives to predicted food shortages. Quorn is manufactured from a fungus known as *Fusarium venenatum*, a type of mold. The fungus is grown in a glucose solution and allowed to ferment, a process similar to that which produces other fermented foods, such as tempeh (from soybeans). As the mold grows and ferments, it produces tiny fibers called "hyphae," which are harvested and made into cooking ingredients and ready-to-eat food products. The food material harvested from the fungus is referred to as "mycoprotein." "Myco" is from the Greek word for fungus. Ingredients such as egg whites and vegetable compounds typically are mixed in with the mycoprotein to create food products. Mycoprotein meat-alternative products are popular in Europe, but less so in North America, as several organizations have challenged the marketing and safety of Quorn products.

The idea to develop mycoprotein food products originated in England in the 1960s. In the 1950s, a number of scientists predicted a worldwide shortage of protein-rich foods, a shortage forecast to arise as early as the 1980s. Investigators increased efforts to develop protein-rich products from widely available substances such as algae, fungus, and various plants. Quorn products were created by the Rank Hovis McDougall Research Centre, and named after Quorn, a village in Leicestershire. Quorn reached the marketplace in 1985, produced by the newly created company Marlow Foods. The products spread to other European countries and Australia. In 2002, Quorn was launched in the United States, but the products encountered resistance, led primarily by the consumer advocacy organization, Center for Science in the Public Interest (CSPI). The CSPI objected to the labeling of Quorn (originally marketed as a mushroom product; mycoprotein is not made from a mushroom) and expressed safety concerns, when a number of consumers reported adverse reactions after consuming Quorn products (CSPI, 2012). Spokespersons for Quorn products have noted that people also have allergic and other negative responses to many other foods, such as soy, wheat, and nuts, yet products with these ingredients remain on the market.

The patent on Quorn products expired in 2010, so anyone can now produce mycoprotein products (but cannot use the Quorn brand name). These meat-alternative products remain popular in Europe.

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See Also: Protein; Vegetarian and vegan diets.

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R

Raw Food Diets

Adherents to a raw food diet—an extreme lifestyle and diet trend—eat only uncooked foods. Although there are different versions of raw food diets, they generally require that all food consumed must be in the most untouched natural form possible. The less extreme versions allow for the inclusion of raw fish, other raw meats, raw milk, and eggs. Some versions suggest that people consume 75% or more of their food raw, thus allowing for some cooked food. The most extreme raw food diets eliminate all animal products and substances such as coffee, tea, alcohol, and even dietary supplements. The most commonly followed version is a vegan raw food diet, which does not include any animal products.

Like many other fad diets, raw food diets often require a complete lifestyle overhaul. The claimed benefits of following these extreme diets are increased energy, reduced body weight and BMI, prevention of chronic illnesses related to obesity, and overall spiritual and mental clarity. Scientific research supporting these claims, however, is lacking. Raw food diets do have some healthful aspects, such as including more fruits and vegetables and limiting red meat and processed foods having added sugars and fats. Eating entirely raw foods all the time is not recommended, however, as cooking food allows for a greater intake of calories and certain nutrients, and kills some foodborne pathogens.

A raw food diet is not a lifestyle choice that should be made lightly; followers must do extensive research and preparation to ensure that they are covering all their nutrient and calorie requirements to maintain good health. Raw food enthusiasts note that it is best to transition to an entirely raw diet by slowly eliminating non-raw and processed foods and incorporating more uncooked fruits and vegetables. The goal is to eventually eliminate all foods derived from animals and all foods that are heated to more than 92 to 118 degrees Fahrenheit. Generally, the diet guidelines state the food items (or categories) that should be eliminated from the diet rather than those included. The standard guidelines which most people on raw food diets follow, is to eliminate meat and all animal flesh, eggs, all processed foods, all fast foods, all soft drinks and processed drinks, cigarettes and nicotine, alcohol, fried oils, all processed sugars and artificial sweeteners, all flours, and gluten grains. Most eat seasonally, which sometimes entails eating the same thing every day for months. Even tofu is not allowed, because the soybeans it is made from are cooked.



The raw food diet has become increasingly popular. Many restaurants specialize in producing interesting and tasty raw food options. Raw food dishes, such as the rolls pictured here, often mimic their cooked counterparts (in this case, sushi). (Bratova/Dreamstime.com)

Raw food enthusiasts claim that heat depletes food's vitamin content and concentrates any pesticides already present, and destroys the beneficial enzymes and "life force" already present in the food—which followers say aids in digestion of that particular food item. Proponents of the diet emphasize the importance of food being consumed in its most "natural state," although food processors, blenders, and dehydrators are used by many on such diets to allow for a wider range of recipes and meals. Less extreme versions of the diet seem more accessible due to the inclusion of dairy and animal products. These dairy and animal products must still be consumed in their most raw state, however, such as raw milk, for example.

The large number of recipe books available for raw food diets attests to the fact that these diets have become a significant part of the commercial diet industry. The recipe titles usually use familiar names, such as "raw Mexican tacos" or "Portobello sushi rolls," to give some reference for what the food will taste like. An example recipe for "seed cheese" includes sunflower seeds, almonds, basil, lemon juice, and white onion. The seeds and almonds are soaked for 12 hours, rinsed and allowed to sprout for 3 hours. All ingredients are then emulsified in a food processor. This is a fairly simple recipe, but it requires quite a bit of time to prepare. Raw vegan recipes often require time and various culinary tools that are not standard in most kitchens or stores. Many restaurants in the United States cater to people following

raw food diets, but the most of them are located on the East or West coasts, predominantly in New York or California.

Raw food enthusiasts often argue that it is more "natural" for people to consume raw food, because this is what other animals—including primates—eat. Anthropologists, however, think that the ability to use fire to cook foods furthered human evolution by enabling people to consume more calories per day with less time spent gathering and eating food, enabling the growth and support of larger brains (Gibbons, 2012).

Although nutrition professionals support the idea that most people would benefit from increasing their consumption of raw fruits and vegetables, they are generally critical of raw food diets. Some of the criticisms of raw food diets include the following.

- The plant enzymes destroyed by cooking also are destroyed by the acidic environment of the stomach. Hence, the benefits of consuming raw foods are probably due to factors other than these enzymes.
- Raw vegan diets tend to be low in the same nutrients as other vegan diets. Such diets lack vitamin B12 and tend to be low in iron, calcium, and zinc. Unless people on raw food diets receive adequate sun exposure, their serum vitamin D levels also can be low.
- Cooking can destroy pathogenic bacteria, like salmonella and *E. coli*.
- Some nutrients become more available when cooked. The bioavailability of lycopene, an antioxidant in tomatoes or carrots, for example, increases significantly when foods containing it are cooked.
- Cooking breaks and softens the tough fibers in foods making many plants, such as potatoes and legumes, more available for consumption.
- Raw food diets might not provide sufficient calories for some people. Although people wishing to lose weight can do so on this diet, people at a healthful weight might have difficulty maintaining this weight. Too few calories can lead to decreased muscle mass, bone loss, and, in young women, menstrual disturbances and reduced fertility.
- Many people enjoy hot and warm cooked foods as part of their diet, especially in colder weather. They feel less satisfied consuming only raw foods.

Raw food diets do offer some beneficial features. They encourage people to increase daily intake of fruits and vegetables, eliminate processed foods and sugars, and limit many sources of saturated fat such as red meat. People on raw food diets tend to consume a wide range of healthful plant foods. Sprouted grains and seeds have high levels of many nutrients. Raw food diets tend to be high in fiber along with many vitamins and minerals, and low in calories, trans fats, added sugars, and sodium. Experimenting with raw food diets could prompt some people to make better food choices, even though they might not follow a raw food diet all of the time.

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See Also: Vegetarian and vegan diets.

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Raw Milk

Raw milk is milk that has not been pasteurized or homogenized. Pasteurization—invented by Louis Pasteur in the 1860s—is the process of heating milk to a high temperature very rapidly. Homogenization is the process of pumping milk through a fine mesh at high pressure to break up the cream and make the milk more uniform. Consumer demand for raw milk has increased significantly over the past decade, often as part of an interest in consuming foods that are less processed



A woman buys milk at a milk vending machine, installed at vegetable market in Ljubljana, Slovenia. Fresh raw milk is available 24 hours a day. (Maljalen/Dreamstime.com)

and locally produced. Although pasteurization and homogenization do alter the content and character of milk, pasteurization reduces risk of foodborne illness.

Pasteurization became required by law after unsanitary urban dairies spread diseases, such as tuberculosis, in the late 19th century and the early 20th century. Pasteurization kills salmonella, *E. coli*, campylobacter, and other bacteria dangerous to humans. Pasteurization is also popular in the U.S. industrial dairy system because it increases the shelf life of milk.

Proponents of raw milk claim that raw milk is a healthier food than pasteurized milk. They profess that pasteurization destroys many nutrients and other components of raw milk, such as digestive enzymes. Scientific analyses of raw versus pasteurized milk, however, show little difference in nutrient content. The nutrient most affected by heat, vitamin C, is present only in small quantities in raw milk, therefore milk is not a great source of this nutrient, whether raw or pasteurized (Claeys et al., 2013). Researchers currently do not know whether the enzymes that are destroyed by pasteurization contribute to human health. Some people who are lactose intolerant but drink raw milk claim that their bodies better tolerate raw milk.

Proponents of raw milk also argue that pasteurization denatures some proteins and kills beneficial bacteria (probiotics). In actuality, the protein content of raw and pasteurized milk is very similar (Marler Clark, 2014). The issue of probiotics in raw milk is an interesting one. Milk is a sterile substance until it leaves the mammal's body. The bacteria present in milk come from places such as the teat ducts, the milking equipment, and the mammal's skin and hair. The number of beneficial bacteria in raw milk from clean sources is quite small, far fewer than those found in products such as yogurt and kefir into which bacteria are added and cultured, which makes these cultured products better choices for consumers desiring to increase their intake of probiotics.

Many of the benefits of raw milk are associated with milk from pastured, or grass-fed, cattle. Grass-fed dairy products contain somewhat greater amounts of omega-3 fats, vitamin A, beta-carotene, and antioxidants than found in milk that comes from grain-fed cows. Milk from grass-fed cows (whether the milk is raw or pasteurized) contains a greater amount of conjugated linoleic acid—a form of the essential fatty acid, linoleic acid—associated with several health benefits. Dairy farmers milking grass-fed cattle are less likely to use or need antibiotics than farmers whose animals do not leave the barn to graze. Therefore, people concerned about the overuse of antibiotics and other drugs in agriculture often wish to support farmers using fewer of these chemicals. Dairy products are not allowed to have detectable levels of antibiotics, so the antibiotic concern centers on the risk of developing antibiotic-resistant pathogens because of excessive use of antibiotics in farming practices.

Consumption of raw milk is considered risky by many people and agencies. The FDA's position stance points out that raw milk can carry foodborne illnesses, such as salmonella, *E. coli*, and campylobacter, and has not been shown to have meaningful nutritional advantages over industrial, pasteurized, homogenized milk.

The U.S. Centers of Disease Control received 56 reports of foodborne illness related to fluid milk products between 1993 and 2006 (David, 2012). Of these reports, 82% involved the consumption of raw milk, resulting in 930 reported illnesses and 71 hospitalizations. Groups at the highest risk for foodborne illnesses from raw milk include infants, children, the elderly, and people who are immune compromised.

In the United States, the sale of raw milk is subject to different laws in each state. Dairy farmers who choose to sell raw milk may sell it directly to consumers, if the milk and dairy farm meet state regulations. Dairy farms may not sell raw milk in other states. Canada prohibits the sale of raw milk to consumers, although the sale of raw milk cheeses is permitted, if the products meet certain regulations. Australia also prohibits the sale of raw milk. New Zealand allows sale of raw milk, but its production is strictly regulated. Raw milk is available widely in most European countries and in parts of Asian and African countries.

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Research Issues

Researchers are exploring ways to achieve the safety benefits of milk pasteurization without the loss of fragile nutrients and raw milk flavor. One method under investigation is called "sonication" (Smith, 2010). Sonication exposes milk to sound waves that produce a lower temperature than that required for pasteurization. The process kills harmful pathogens but is less damaging to healthful milk components.

See Also: Dairy foods; Sustainable agriculture.

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Resveratrol

Resveratrol is a phytochemical found in several plants, including grapes, peanuts, cranberries, raspberries, and mulberries. It belongs chemically to a group of plant compounds called "polyphenols" that seems to promote health in a variety of ways. Resveratrol is produced by plants as part of their defense system against pathogens such as bacteria and fungi. Resveratrol's mildly toxic effect appears to stimulate helpful defense mechanisms in humans and other animals. Because it is present in grape skins and seeds, resveratrol is found in wine—especially red wine, which is fermented with the grape skins; the skins are removed for the fermentation of white wine. Some people often claim that resveratrol is responsible for the beneficial health effects that are associated with red wine, the Mediterranean Diet, and the "French Paradox." The clinical effects that have been observed with resveratrol, however, occur at far greater doses than people actually obtain with wine or other food sources. It has been estimated that to receive the clinical benefits of resveratrol observed in animal studies, a person would have to drink 80 liters of red wine per day (Mayo Clinic Staff, 2011).

In vitro, animal, and a small number of well-designed studies in human subjects suggest that high doses of resveratrol might offer beneficial effects, especially for the prevention and treatment of artery disease. Resveratrol is best known as an antioxidant. An interesting yearlong trial of resveratrol supplementation in humans found that the group of subjects that received the supplement showed lower markers of systemic inflammation and slower blood-clotting rates as compared to those of the control group participants (people who were given plain grape juice or a placebo) (Tome-Caneiro et al., 2012). Other studies have found that resveratrol supplements inhibit oxidation of LDL cholesterol, thus potentially slowing the progression of artery disease. Resveratrol appears to increase the production of nitric oxide in the arteries, which helps the arteries relax and accommodate blood flow, thus reducing resting blood pressure (Gresele et al., 2011).

The positive effect of resveratrol on blood flow is hoped to one day be harnessed to prevent the progression of Alzheimer's disease, although increased blood flow to the brain has been demonstrated in humans receiving a high dose of resveratrol, improvement in cognitive function has not. Small studies have suggested that resveratrol supplements might improve the body's responsiveness to insulin in people with type 2 diabetes.

Resveratrol behaves as a phytoestrogen in the human body. Its influence on hormonal cancers has been mixed. Resveratrol appears to reduce risk of prostate cancer in men. Some research on the effect of resveratrol on breast tissue estrogen receptors suggests that resveratrol might stimulate cell proliferation (thus possibly promoting breast cancer), but other research suggests that resveratrol might exert more helpful effects such as triggering apoptosis, which limits tumor growth.

Resveratrol is found in foods in very small amounts, and safety is not an issue. One cup of grapes, for example, contains about 0.25 mg to 1.25 mg of resveratrol. A liter of red wine contains about 2 mg to 13 mg. Resveratrol doses of about 500 mg per day from supplements appear to be safe, although long-term studies on

resveratrol's safety as a dietary supplement have not been conducted. Resveratrol's bioavailability is fairly low, as it is quickly broken down by the liver after it is absorbed into the bloodstream. High doses (2.5 g to 5 g) have been associated with gastrointestinal distress and diarrhea. Because resveratrol could slow down the development of blood vessels, which suppresses tumors, it also might slow healing. People on anticoagulant medications should speak with their health care providers before taking resveratrol supplements.

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See Also: Antioxidants; Phytoestrogens.

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Riboflavin

Riboflavin—or vitamin B2—is a water-soluble micronutrient that is essential to enzyme function, antioxidant activity, and—together with other B vitamins—energy production. It also appears to support body growth, red blood cell production, and eye health. Therapeutic and medicinal uses such as preventing cataracts, migraines, preeclampsia, and some types of cancer have some support, but require further research.

A thiamin-riboflavin complex was isolated by scientists in the late 1800s. They later found that the complex was composed of two different compounds, eventually called "vitamin B1" (which became "thiamin") and "vitamin B2" (which became "riboflavin"). Riboflavin also was named "lactochrome" and "vitamin G" by various research groups (Baker, 2013). It is named for the two primary structures in its molecular formation: a 5-carbon sugar alcohol, "D-ribitol," and a flavin group

that is characterized by a yellow hue ("flavin" is derived from the Latin word, "flavus," for "yellow").

Functions in the Body

As a component of the coenzymes "flavin adenine dinucleotide" (FAD) and "flavin mononucleotide" (FMN), riboflavin participates in many oxidation-reduction reactions that are vital for carbohydrate, lipid, and protein metabolism. Flavin adenine dinucleotide is involved in the electron transport chain, making riboflavin important for cellular respiration. Further, FAD supports antioxidant function through its role in the glutathione redox cycle, which protects against oxidative stress. Flavin adenine dinucleotide enables the enzyme glutathione reductase to regenerate reduced glutathione from oxidized glutathione (Higdon, Delage, & McNulty, 2013). Riboflavin, again in the form of the flavocoenzymes FAD and FMN, also facilitates the metabolism of other B vitamins, such as vitamin B6, niacin, and folate. Additionally, riboflavin is thought to contribute to the efficient absorption and utilization of iron, along with healthy red blood cell production.

Dietary Requirements and Sources

The Recommended Dietary Allowance (RDA) for riboflavin is 1.3 mg per day for adult men and 1.1 milligrams per day for adult women. Slightly greater intakes are

Table 1. Foods and Riboflavin Content

Food	Serving	Riboflavin (mg)
Almonds	1 oz	0.29
Asparagus (boiled)	6 spears	0.13
Beef (ground, cooked)	3 oz	0.15
Bread, white (enriched)	1 slice	0.09
Bread, whole wheat	1 slice	0.06
Broccoli (boiled)	1/2 cup chopped	0.10
Cereal, fortified, wheat, puffed	1 cup	0.22
Cheddar cheese	1 oz	0.11
Chicken, dark meat (roasted)	3 oz	0.16
Chicken, light meat (roasted)	3 oz	0.08
Egg (cooked, hard-boiled)	1 large	0.26
Halibut (Greenland, cooked, dry heat)	3 oz	0.09
Milk (nonfat)	1 cup (8 oz)	0.45
Salmon (cooked)	3 oz	0.13
Spinach (boiled)	1/2 cup	0.21

Compiled from Food and Nutrition Board, Institute of Medicine. (1998). *Dietary reference intakes: Thiamin, riboflavin, niacin, vitamin B6, vitamin B12, pantothenic acid, biotin, and choline.* Washington, DC: National Academy Press;:87–122. (National Academy Press); Food and Nutrition Information Center, *U.S.D.A. riboflavin (vitamin B2)*. Retrieved from http://fnic.nal.usda.gov/food-composition/vitamins-and-minerals/riboflavin-vitamin-b2

advised for pregnant and breast-feeding women—1.4 mg and 1.6 mg per day, respectively (Insel, Ross, McMahon, & Bernstein, 2012). Food sources of vitamin B2 include the following.

- Milk
- Dairy products
- Fortified cereals and grain products
- Eggs
- Meats (especially organ meats)
- Fatty fish
- Almonds
- Dark green vegetables

Exposure to ultraviolet light leads to riboflavin degradation, therefore opaque packaging or storage away from sunlight helps preserve the vitamin B2 content of these foods (Medline Plus, 2013). Riboflavin also is available as an ingredient in daily multivitamins or vitamin B–complex supplements, and as an individual supplement.

Deficiency

Riboflavin deficiency, "ariboflavinosis," is thought to be uncommon in the United States. Inadequate intakes of vitamin B2, however, do occur among the elderly and among low-income individuals—who often consume nutrient-poor diets—as well as in pregnant or breast-feeding women, whose riboflavin requirements are elevated. Moreover, conditions such as alcoholism, celiac disease, and some cancers can interfere with the absorption of riboflavin, leading to a deficiency (Baker, 2013). People deficient in riboflavin usually also are deficient in other nutrients. Symptoms of ariboflavinosis tend to manifest when a person's daily intake falls below 0.5 mg to 0.6 mg, and can include fatigue, a sore throat, a swollen tongue, cracked skin at the corners of the lips, rashes, anemia, and neuropathy (tingling, burning, or prickling sensations). Riboflavin deficiency also has been reported to slow growth in children and adolescents and to negatively impact eye health, sometimes resulting in blurred vision; red, watery, or itchy eyes; and excessive light sensitivity (Weil, 2014). Riboflavin deficiency might increase the risk of preeclampsia in pregnant women (Higdon, Delage, & McNulty, 2013). Preeclampsia is a dangerous condition that can occur during pregnancy and is marked by high blood pressure, protein in the urine, and swelling. Preeclampsia can progress to eclampsia, which is characterized by a worsening of preeclampsia symptoms that can lead to seizures and increased risk of hemorrhage.

Health Benefits

Some evidence suggests that riboflavin can have beneficial effects on health beyond preventing ariboflavinosis and its symptoms. At least one study suggests that migraine frequency—but not pain or duration—can be reduced by taking

400 mg of riboflavin per day (National Institutes of Health, 2012). A dose of around 3 mg per day of riboflavin may reduce the risk of cataracts, but participants in the major study relating to this hypothesis also took 40 mg of niacin per day. Epidemiological research suggests that riboflavin intakes of somewhat more than the RDA are associated with reduced risk of eye cataracts (Higdon, Delage, & McNulty, 2013). Evidence that riboflavin—along with other B vitamins—can prevent cervical dysplasia or cancer is preliminary.

Toxicity

Despite the fact that riboflavin supplementation often means consuming amounts of the vitamin which substantially exceed the RDA, no serious adverse effects have been observed. Excess riboflavin is readily excreted in urine. As a result, a Tolerable Upper Intake Level (UL) for riboflavin has not been established. High doses, however, can cause urine discoloration, itching, and—as is the case for low levels of riboflavin—neuropathy and light sensitivity. Taking riboflavin alone for a long duration also could cause an imbalance of other B vitamins (Ehrlich, 2011).

Laura C. Keenan

See Also: Vitamins.

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S-Adenosylmethionine

S-adenosylmethionine (SAMe) is a compound made naturally by the human body. Because the body makes SAMe, it is not considered an essential nutrient. In fact, SAMe is only found in very small amounts in food, so all research on SAMe's effects involves use of SAMe as a dietary supplement. S-adenosylmethionine, taken as a dietary supplement, appears to be somewhat effective for the treatment of several disorders, including mild to moderate depression and osteoarthritis.

S-adenosylmethionine was discovered in Italy in 1952. It has been used as a supplement in Italy since the late 1970s and used in other European countries since the mid to late 1980s. It was not used as a supplement in the United States, however, until the late 1990s. The body makes SAMe from two precursor molecules—methione and adenosine triphosphate. Methionine is a sulfur-containing essential amino acid found in food. Adenosine triphosphate is the body's primary energy-containing molecule that stores and delivers energy for almost all energy-requiring metabolic processes in the body. In the human body, methionine and adenosine triphosphate come together in a reaction that is catalyzed by an enzyme called methionine adenosyltransferase to form SAMe. S-adenosylmethionine is found in every living cell and plays an important role as a donor of methyl groups in biochemical reactions. Deficiencies in methionine, folate, and vitamin B12 can cause low SAMe levels in the body.

S-adenosylmethionine first was used clinically for its potentially beneficial effects in the treatment of depression. Several small studies suggest that SAMe has an effectiveness level similar to that of antidepressants, and might even work synergistically with some antidepressant medications (Carpenter, 2011). But, like other drugs that have antidepressant effects, SAMe can trigger mania in people who have bipolar disorder, thus it might not be an appropriate treatment for this condition. People considering the use of SAMe for depressive disorders should use the supplement with the advice of their health care providers, especially if they are already taking other medications for this condition.

S-adenosylmethionine also appears to be somewhat effective in relieving the pain of osteoarthritis, the most common form of arthritis, which involves the degeneration of the cartilage coating the ends of the bones that form a joint. Interestingly, researchers accidentally discovered SAMe's helpful effects on osteoarthritis when investigating its benefits for treating depression. Several studies have shown that SAMe is as effective as standard anti-inflammatory drugs such as

ibuprofen at reducing the inflammation and pain associated with osteoarthritis (De Silva, El-Metwally, Ernst, Lewith, & Macfarlane, 2011). Animal studies have demonstrated that SAMe even might help to protect cartilage from damage, although this action has not yet been studied extensively in humans.

S-adenosylmethionine has been explored as a possible treatment for a liver condition known as "cholestasis," in which bile flow in the liver slows or stops. This condition sometimes is associated with pregnancy; SAMe appears to be potentially helpful for this condition, and does not appear to cause harm to the developing fetus, although experts recommend using SAMe or any other medications during pregnancy only under medical supervision. Preliminary evidence also indicates that SAMe might be helpful for fibromyalgia and possibly depression associated with Parkinson's disease, although more research is needed to confirm SAMe's benefits for these conditions.

When SAMe is taken as a supplement it usually is prescribed at a dosage of 400 mg taken three to four times per day. S-adenosylmethionine is expensive to manufacture, and therefore the supplement itself also is quite expensive. S-adenosylmethionine appears to be fairly safe, although it could cause nausea or digestive problems in some people. S-adenosylmethionine might increase risk of pneumonia in immunocompromised patients.

Samantha Blanchett and Barbara A. Brehm

See Also: Arthritis and nutrition; Depression and nutrition.

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Salivary Glands and Saliva

Salivary glands are accessory organs of the digestive system that manufacture and secrete a watery digestive fluid called "saliva." The human body has three pairs of salivary glands—the parotid, sublingual, and submandibular—which all play a role in the digestive system. The most important function of the glands is to secrete saliva, which begins the process of digestion. The salivary glands, teeth, and tongue work together to break down the food into small wet lumps to be ingested through esophagus into the stomach. The three major pairs of glands are located outside of the oral cavity. The largest glands—the parotid glands—are located slightly below and in front of each ear, the submandibular glands are under the mandible (lower jaw bone), and the sublingual glands lie between the tongue and mandible on the floor of the mouth. The salivary glands are responsible for secreting the saliva directly into the mouth. There also are a few minor glands located under the mucosal lining of the mouth, lips, throat, nose, sinuses, and voice box.

The parotid salivary glands each have a duct called a "Stenson's duct" that leaves the gland and penetrates through muscle and fat and opens into the mouth. The two submandibular glands each contain a duct called a "Wharton's duct." The sublingual salivary glands each have a duct called a "duct of Rivinus" that opens directly into the mouth to secrete saliva.

The saliva is composed of about 97% to 99.5% water and an enzyme called "ptyalin," or "salivary amylase." The saliva also contains trace amounts of mucin and calcium salts. Some of these other chemicals help to buffer against acidic foods. The salivary amylase starts the breakdown of starches—which account for most of the carbohydrates consumed. The stomach and small intestine also are responsible for secreting other enzymes to help with this breakdown.

The sight and smell of food is enough to trigger the production of saliva. Receptors in the mouth send messages through the nervous system to the salivary nuclei in the brain, which then proceed to send chemical impulses to the salivary glands to create saliva. The body is conditioned to produce saliva with the anticipation of food, alone. The body produces 1 to 1.5 liters of saliva a day.

Saliva is responsible for moistening the mouth and lubricating the food enough for the food to become a "bolus" (soft mass) that then can be swallowed. The tongue is responsible for moving the food around in the mouth to become mixed with the saliva and form a bolus. The salivary glands work with the teeth in the mechanical breakdown of food into smaller pieces. In the process of chemical digestion, the breakdown of large molecules of carbohydrates, fats, and proteins into smaller compounds is called "hydrolysis." Hydrolysis is the splitting of bonds by adding the hydrogen and oxygen atoms in water. The saliva also functions as a mouth cleaner. Even with no food, the mouth contains saliva to keep the mouth wet and the teeth clean. When the mouth is dry, it accelerates dental decay.

Infection is a common problem that can occur in the salivary glands, and often is due to dehydration. Bacteria in the mouth can cause an infection when there is a decrease in saliva flow. A decrease in saliva flow also can be caused by stones, which can collect in the ducts of the glands. Stones develop from deposits of

minerals, such as calcium, within the saliva. Tumors can develop in the parotid glands; however, 80% of tumors found in this area are benign. Signs of salivary gland cancer include lumps, swelling, numbness, muscle weakness, persistent pain, difficulty swallowing, and difficulty opening the mouth in the areas near the neck, jaw, or mouth. Mumps is a virus that can attack the parotid glands. This virus can cause fever, malaise, sore throat, and swelling of the cheeks.

Lydia T. Carron

See Also: Digestion and the digestive system; The mouth.

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Saponins

Saponins are compounds named for their characteristic ability to form foam in an aqueous environment. The word "saponin" comes from the Latin word "sapo" which means "soap." There are many kinds of saponins; all of them are glycosides. A glycoside is a molecule that contains both a carbohydrate group and another functional group. Some saponins are very large, containing many carbohydrate and many other groups. Saponins contain both hydrophobic and hydrophilic components, which give saponins their foaming property.

Saponins are found in desert plants such as yucca, soapwart, and quillaia, as well as common foods such as garlic, soybeans, and peas, and in many herbs. Saponins are produced by plants as a defense against herbivores, pathogens, and fungal infections. Saponins have many wide-ranging industrial applications, and several applications are thought to be beneficial to human health. Saponins most commonly are known for their soap-like foaming properties which manifest when the compound is mixed with water. For this reason, they are used in toothpastes to promote dental health, are components of many cleaning supplies, and frequently are used in cosmetics and shampoos. Saponins also are added to beverages such as beer and root beer to help stabilize the foam produced when pouring the beverages. Industrial uses include additive to cat litter to reduce fecal odor. Saponins also play a variety of roles in animal husbandry.

The most significant nutrition application of saponins involves their ability to lower LDL cholesterol. Saponins bind with bile acids and other cholesterol-containing compounds in the small intestine. Once the bile and cholesterol have bound to the saponins they cannot be reabsorbed by the body, and eventually are excreted. This pathway of reducing LDL cholesterol, or "bad cholesterol," does not appear to influence HDL cholesterol, the "good cholesterol." This action of saponins could be one of the mechanisms whereby garlic, soybeans, and a high intake of other plant foods help prevent artery disease.

Preliminary studies suggest that some saponins might have anti-tumor and anticancer properties. Some saponins could have an inhibitory effect on human carcinoma cells and potentially could be used to prevent colon cancer (Man, Gao, Zhang, Huang, & Liu, 2010). These compounds bind with bile acid, preventing the production of secondary bile acids which are known promoters of colon cancer. Certain saponins also could prove to be helpful in preventing foodborne viral illnesses. Saponins appear to alter the host cell membranes in ways that prevent viral binding, thus reducing risk of infection (Li, Baert, & Uyttendaele, 2013).

Alison Hogeboom

See Also: Phytochemicals.

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School Lunch Program

In the United States, the National School Lunch Program is a federal program that provides nutritionally balanced, low-cost or free lunches to children in participating public and nonprofit private schools and residential child-care institutions. The program is one of many child-nutrition programs run by the U.S. Department of Agriculture (USDA), Food and Nutrition Service. Other programs include the School Breakfast Program, which helps states operate



Student at Fairmeadow Elementary School pays for fruits and vegetables during a school lunch program in Palo Alto, California. Many school lunch programs have tried to increase student intake of fruits and vegetables. (AP/Wide World Photos)

nonprofit breakfast programs; the Fresh Fruit and Vegetable Program, the goal of which is to support schools in introducing students to a variety of produce; the Special Milk Program, which provides milk to schools and child-care institutions who do not participate in other federal meal programs; the Summer Food Service Program, which provides food to eligible children during summer break; and the Child and Adult Care Food Program, which helps child- and adult-care institutions and family or group day-care homes provide nutritious meals.

Canada has no similar federally operated programs, although many provinces offer programs run by local governments or nonprofit organizations that provide free or low-cost meals to schoolchildren.

History

The National School Lunch Program was signed into law by President Harry Truman in 1946, but its origins extend further back. As early as 1853, the Children's Aid Society of New York began serving meals to students at its vocational school. By the early 1900s, school lunch programs run by charitable organizations were becoming more common around the country. In 1912, the Philadelphia School

Board created a Department of High School Lunches and began food services in all city high schools. Similar programs were initiated in New York, Boston, Cleveland, St. Louis, Chicago, Milwaukee, and Los Angeles. Through support from philanthropic organizations, school boards, and generous individuals, school lunch programs continued to expand throughout the 1920s in both urban and rural areas (Gunderson, 2013).

When the Great Depression began, more widespread unemployment and limited family resources meant thousands of students were unable to pay for school lunches or provide their own, and children's malnutrition became a national concern. At the same time, crop surpluses were mounting and spoiling in local markets despite the multitudes of hungry people who had no resources to purchase food. In 1936, Congress passed Public Law 320 in an attempt to aid both hungry children and needy farmers. Through this law, the government purchased surplus foods from farmers and donated them to consumers. School lunch programs provided the ideal outlet for the surplus food. By the 1941–1942 school year, school lunch programs were operating in all states as well as in Washington, DC, and Puerto Rico (Gunderson, 2013).

World War II changed the economy dramatically; farm surpluses were now directed to the military, and commodities available for the school lunch program dwindled. Federal support for the school lunch program continued, but on a year-to-year basis. Because future funding of the program was uncertain, many school boards were wary of initiating or expanding school lunch programs.

In 1946, President Harry Truman signed into law the National School Lunch Act, which guaranteed federal support for the school lunch program. To participate in the National School Lunch program, schools were required serve lunches that met the minimum nutritional guidelines prescribed by the Secretary of Agriculture. Participating schools were required to serve low-cost and no-cost meals to children who were unable to pay the full price and could not discriminate against those children in any way; operate as a nonprofit program, using commodities donated by the USDA; maintain proper records; and submit reports as required.

Child Nutrition Act of 1966

In October 1966, President Lyndon B. Johnson signed into law the Child Nutrition Act of 1966. The act was designed to close gaps in the National School Lunch Act. The act accomplished several tasks, including the following.

- Offered financial support to schools to purchase equipment needed for food service
- Provided administrative funds to help states run their programs
- Added a pilot school-breakfast program, which was so successful that it became permanent in 1975
- Extended the act to include preschools that were part of a school system

- Incorporated the existing but separate special milk program into the school lunch program

Further Expansion

In 1998, the school lunch program was expanded to reimburse schools for snacks served during after-school educational and enrichment programs for children through 18 years of age. Most recently, the National School Lunch Program was updated and expanded through the 2010 Healthy, Hunger-Free Kids Act, also called the Child Nutrition Reauthorization Bill. The purpose of the bill is to increase the nutrition value in school food in an effort to reduce childhood obesity. It calls for the following changes to take place over the next several years.

- All foods sold in schools (including in vending machines and school stores) must meet nutritional standards set by the USDA.
- Provide additional funding to schools that meet updated nutrition standards
- Assist schools in establishing local farm-to-school networks and creating and maintaining school gardens
- Expand access to drinking water in schools
- Improve the nutritional quality of commodity foods that schools receive from the USDA
- Increase the number of children eligible to enroll in school meal programs
- Improve recall procedures for foods used in school meals
- Require schools to make nutrition information more available to parents
- Audit school districts every three years to ensure that they are complying with nutritional standards
- Provide training and technical assistance for school food-service workers

How Does the National School Lunch Program Work?

At the federal level, the Food and Nutrition Service agency administers the National School Lunch Program. At the state level, the program is operated by state education agencies and school food authorities. Public and nonprofit private schools through twelfth grade can participate, as well as public and nonprofit private residential child care institutions.

Participating schools and school districts receive cash subsidies and foods from the U.S. Department of Agriculture (USDA) for each meal they serve. Schools must offer free or reduced-priced lunches to eligible students, and meals must meet federal nutritional requirements.

Any student at a participating school may purchase a meal, and programs should be operated in a way so that students do not know who qualifies for free and reduced-price meals and who does not. Free meals and after-school snacks are offered to families with incomes at or below 130% of the poverty level. Reduced-priced meals and after-school snacks are offered to children from families with incomes that are between 130% and 185% of the poverty level. Full-paid meal

prices are set by local school food authorities, but meal service programs must be nonprofit. If at least 50% of the students in an after-school program qualify for free or reduced-price meals, all snacks can be served for free (USDA Food and Nutrition Service, 2013).

Nutrition Guidelines

The Child Nutrition Reauthorization Bill requires meal programs to follow updated nutrition standards based on 2009 recommendations of the Institute of Medicine and the latest *Dietary Guidelines for Americans*. These changes went into effect at the beginning of school year 2012–2013. The changes require meals to increase fruits, vegetables, and whole grains, offer fat-free or low-fat milk, and have decreased amounts of saturated fat, trans fat, and sodium. Meals also must fall between age-appropriate calorie limits (Institute of Medicine of the National Academies, 2009a). The following table shows the new requirements.

Lisa P. Ritchie

Table 1. Updated School Lunch Nutrition Requirements Beginning July 2012

Vegetables	3/4 cup to 1 cup of vegetables per day
	Weekly requirements for dark green and orange vegetables and legumes
	Limits on starchy vegetables
Fruit	1/2 cup to 1 cup per day
Meat/Meat Alternatives	1.6 oz to 2.4 oz daily (on average over a 5-day week)
Grains	1.8 oz to 2.6 oz daily (on average over a 5-day week)
	At least 50% of the grains must be whole-grain rich
Milk	Fat content should be 1% or skim
Maximum Calories per Lunch	650 calories for kindergarten through fifth grade students
	700 calories for sixth through eighth grade students
	850 calories for ninth through twelfth grade students
Percent of Calories from Saturated Fat	Less than 10%
Sodium	Major reductions in sodium to be implemented over 10 years
Trans Fat	Zero grams of trans fat allowed

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Research Issues

Should Canada establish a national school food program? Canada is one of the few developed nations without a federally funded school food program. Instead, the country relies on a variety of school food programs, which are run, funded, and supported by a changing combination of nonprofit organizations, municipal, and provincial governments; local fundraising; charities; and individual businesses. The federal government says it is not planning to take on school food as a national project. "We see education very clearly as a provincial/territorial jurisdiction, so it's nothing that's being considered by our government at this point in time," said Steve Outhouse, a spokesman for Canada's Health Minister (Leeder, 2012). The increasing focus on childhood obesity and other nutritional concerns, however, is expanding the debate over school food. Many organizations and politicians are urging the federal government to take action. Is it the job of the federal government to support a national school food program? If so, what should the main goals of the program be, and how should they be implemented?

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See Also: The poverty-obesity paradox; Public policy on nutrition.

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Seafood

Seafood is a popular food in many regions throughout the world. It plays a significant part in the diets of people living in coastal regions, for example around the Mediterranean Sea. There are many different kinds of seafood to choose from—each with a different nutritional profile. Fish in general is a good source of protein, and oily fish in particular is lauded as a good source of omega-3 fatty acids. The American Heart Association recommends two servings of fish per week, including choices with high omega-3 content. Seafood consumption, however, also is associated with negative health concerns—such as mercury consumption—especially regarding eating larger fishes. Unsustainable fishing methods and unhealthful farming practices also have produced ethical and additional health concerns regarding seafood.

Seafood can be categorized in several ways, an example of which is fish, roe, shellfish, and echinoderms. There are many other types of fish, such as skate, stingray, and eel. Fish can further be categorized according to color, oil content, and firmness. Examples of dark and oily fish are bluefin tuna and salmon, and examples of medium and oily fish are mahi-mahi, sockeye salmon, and yellowfin tuna. White and lean fish can be firm—like pollock and swordfish—or flaky—like black sea bass and tilapia. White fish also can be oil rich, such as albacore tuna and Chilean sea bass. Oil from fish is beneficial, as it contains omega-3 fatty acids. Three ounces of fish can provide 80 to 200 calories, depending on oil content, 20 mg to 80 mg of cholesterol and 16 g to 26 g of protein. The basic nutritional profile of fish is similar to that of other animal protein such as beef and pork, but fish contains considerably less cholesterol.

"Roe" refers to fish eggs and is a good source of omega-3 fatty acids. In particular, roe of the Atlantic bonito, mackerel, squid, cuttlefish, lumpsucker, hake, and salmon contain a high concentration of omega-3—upwards of 30% of the fatty acids in the roe. As such, minimal consumption of lumpsucker, hake, or salmon roe can satisfy the body's omega-3 requirements (Rincón-Cervera, Suárez-Medina, & Guil-Guerrero, 2009).

Shellfish can be further broken down into the categories of mollusks and crustaceans. Mollusks are a group of soft-bodied invertebrates, some of which have a shell. Examples include abalone, clam, oyster, as well as octopus and squid. Although similar to mollusks in that it has a shell, a crustacean actually is completely different because it has a segmented body. Popular crustaceans include crab, lobster, and shrimp. Shellfish have a lower fat content compared to oily fish, and are high in protein as well. Although the cholesterol levels in shellfish are somewhat high—more than 100 mg per 3 ounces of shrimp, for example—dietary cholesterol content is not believed to be as harmful as overall diet quality in terms of heart disease risk. It is important to note that shellfish allergy is common, with a prevalence rate of 1.9% for the U.S. population (FARRP, 2013). Allergic reactions can occur from exposure to the fish itself or to parasites, bacterium, viruses, and toxins found on the shellfish. Reactions also can be caused by inhaling vapors when cooking or by handling seafood. Reactions typically are immediate or occur

within two hours of ingesting the shellfish, with the most common reaction being respiratory distress.

Lastly is the category of seafood called "echinoderms." Echinoderms are not as commonly consumed as fish or shellfish, and include sea cucumber—commonly consumed in East Asian cuisine—as well as "uni," a common ingredient in Japanese sushi. "Uni" is the gonads of a sea urchin, and is low in fat with a considerable amount of protein. Sea cucumbers also are low fat and high in protein.

Health Benefits of Seafood

Many people eat seafood for the benefits of the omega-3 fatty acids. The omega-3s found in seafood are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Eicosapentaenoic acid and DHA can be found in all seafood and other marine products such as algae, although oily fish have higher concentrations. Recommended intake of EPA and DHA are 250 mg per day, and the American Heart Association recommends 1,000 mg per day for people with cardiovascular disease. The *2010 Dietary Guidelines for Americans* recommend consumption of more than 8 oz of seafood per week to have adequate EPA and DHA intake. An omega-3 fatty acid intake of 2 g, equivalent to 1 to 2 servings of fatty fish per week, reduces the chances of dying from heart diseases by more than a third. It can also reduce the risks of stroke, depression, and other chronic conditions (HSPH, 2014) and also might decrease the risk of dementia and Alzheimer's disease (HSPH, 2014).

Having a sufficient omega-3 intake is especially important in fetal development and early childhood. The fetal brain is 70% the size of an adult brain, and brain growth is completed by 5 to 6 years of age. The brain is fattiest organ of the body, with DHA being a predominant structural fatty acid in the brain. The Food and Agriculture Organization (FAO) of the World Health Organization therefore recommends regular intake of omega-3 fatty acids during pregnancy (FAO, 2010). Research suggests that gestation period and birth weight are increased when omega-3–rich foods or DHA supplements are taken in the last trimester of pregnancy, and there is a linear correlation between dietary intake of DHA and the DHA content of breast milk. Babies with more DHA intake have higher IQ—as much as 8 points more as compared to formula-fed babies, and also have better psychomotor development, eye-hand coordination, and visual acuity at 2.5 years of age (FAO, 2010).

In addition to omega-3 fatty acids, seafood also is a rich source of niacin. A 100 g portion of canned tuna supplies 13.28 mg of niacin, which is comparable to chicken which contains 13.71 mg per 100 g. Vitamin B12 content is also high, with sport-caught fish having higher B-12 concentrations than beef, pork, chicken, or eggs. Fish also is high in vitamin D—essential for the body's absorption of calcium and thus bone health. A 100 g portion of herring and tuna can provide 22 mg and 6 mg of vitamin D, respectively (Murkin & Sheeshka, 1999).

Health Risks of Seafood

Most of the health concerns about consuming seafood come from the elevated mercury levels in some types of seafood. Mercury accumulates in a fish's body through bioaccumulation. Absorption of mercury is easy, but comparatively it takes a much longer time for it to be flushed out of a fish's system. Larger fish, such as swordfish, for example, are higher up the food chain and have a higher concentration of mercury.

The main form of mercury found in seafood is methylmercury, which is a neurotoxin. The effect is especially profound in fetuses, infants, and children, and causes impaired neurological development at high enough concentrations. Exposure to methylmercury in utero from the mother's ingestion of at-risk seafood can adversely affect the fetus's growing brain, nervous system, cognitive thinking, memory, attention, language, fine motor skills, and visual spatial skills. Symptoms of mercury poisoning in adults include impairment of peripheral vision; disturbances in sensations (a "pins and needles" feeling, usually in the hands, feet, and around the mouth); lack of coordination of movements; impairment of speech, hearing, walking; and muscle weakness (U.S. EPA, 2013).

Additional potential health complications arise from the consumption of some farmed fish. Overcrowding in fish farming leads to high rates of diseases and infestations, necessitating the use of antibiotics. Eating farmed salmon high in antibiotics can increase the risk of antibiotic resistance to the drugs used in humans. Farmed seafood also can contain other natural and man-made toxic substances such as pesticides, polybrominated diphenyl ethers (PBDE), polychlorinated biphenols (PCB), and dioxins. Exposure to PBDE is associated with cognitive and endocrine risks, PCB is associated with cancer and cognitive risks, and dioxin is associated with cancer, hormonal, and immune cardiovascular system risks (Cole et al., 2009).

Adding to the potential dangers of farmed seafood is the very low inspection rates for seafood imports. Europe inspects 20% to 50%; Japan about 20%; Canada, 2% to 18%; and the United States, just 2%. There are only 24 violations found per year on average by U.S. inspectors, and seafood is not tested for many drugs commonly used in aquaculture. Inspectors have found the cancer-causing nitrofuran, banned since 2002, and the suspected carcinogen dye "malachite green," banned since 1983 (Shute, 2011).

Sustainability Issues

Environmental concerns should also factor into the decision of which type of seafood to consume. Many of the popular fishes consumed today come from unsustainable production methods. Big predator fishes such as bluefin tuna, Chilean sea bass, and beluga sturgeon take 20 to 50 years to grow to maturity, and rapid harvesting is driving down their population. It is thus more sustainable to eat smaller fishes lower down on the food chain, such as herrings and squid. Even among farmed fish, more sustainable choices can be made. Carnivorous fishes eat protein,

for example 20 kg of fish protein is needed to create 1 kg of farmed tuna and the ratio is 5:1 for farmed salmon (Steir, 2007). It is thus more efficient to eat herbivorous fishes such as carp, catfish, and tilapia that feed on a diet of plant matter.

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Research Issues

Do the health benefits of seafood consumption outweigh the risks? The Food and Agriculture Organization of the World Health Organization has compiled an extensive analysis to answer this question (Food and Agricultural Organization, 2010).

See Also: Marine omega-3 fatty acids; Mercury.

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Selenium

Selenium is an essential mineral that people need in small amounts, and which must be obtained from the diet. Selenium is a component of numerous selenium-containing proteins (selenoproteins), which serve multiple physiological functions, including protection from oxidative damage, thyroid hormone metabolism, and immune response. Adequate or therapeutic levels of selenium could help to protect against certain types of cancer.

Selenium was identified as a toxic chemical in 1817, when it was found to cause illness in workers at a sulfuric acid plant (Oldfield, 2002). North American researchers first became interested in selenium in the food supply when animals grazing in areas with high selenium content in the soil developed selenium poisoning, which resulted in the loss of mane and tail hair and severely damaged hooves. Research on livestock nutrition in the 1950s, however, began to reveal the deficiency symptoms associated with diets too low in selenium. Epidemiological studies of humans with very low selenium intakes supported the idea that small amounts of the trace element are essential for good health. The Recommended Dietary Allowance for selenium was not established until 1989.

Selenium Deficiency

Selenium deficiency is rare in North America. It is most common in parts of China, Tibet, and Siberia, where soil levels of selenium are low. People who consume few animal products in these areas are at a greater risk of deficiency, because selenium levels generally are low in fruits and vegetables. Selenium deficiency is associated with Keshan disease, named for the Chinese province of Keshan where this heart disorder was found to develop in some children. Keshan disease actually is not caused by selenium deficiency. Rather, a deficiency in this nutrient appears to make the heart more vulnerable to damage from some other agent, possibly a virus (Insel, Ross, McMahon, & Bernstein, 2014). People with low selenium intakes also might be more vulnerable to other viral infections. This is especially a concern for people living with HIV, as this population already is vulnerable to infection because of a weakened immune system and reduced gastrointestinal function. Selenium deficiency also is associated with male infertility, and Kashin-Beck disease, a type of osteoarthritis that usually affects children who are between 5 and 13 years old. Selenium deficiency appears to worsen the effects of iodine deficiency, increasing risk of cretinism in infants (National Institutes of Health ODS, 2013).

Roles of Selenium in the Body

Selenium is necessary for the function of selenoproteins. Research has identified at least 25 selenoproteins, but has only discovered the function of about half. Selenium is a component of an important antioxidant called "glutathione peroxidase." This antioxidant aids in protecting cell membranes and the artery lining from free radicals. Selenoproteins help regulate the activation and inactivation of the thyroid

hormones; participate in spermatogenesis; and could help regulate certain immune responses (Higdon, Drake, & Whanger, 2009).

The dietary reference intake for adult men and women is 55 mcg. Selenium is most highly concentrated in Brazil nuts, which have 544 mcg per 6- to 8-nut serving. The next richest source, yellowfin tuna, has 92 mcg per 3 oz serving (National Institutes of Health ODS, 2013). Good sources of selenium include other seafood, shellfish, and meats. Selenium also is found in enriched breads, dairy products, poultry, eggs, grains, and garlic. The amount of selenium in all foods varies with the soil content of selenium for plants, and the dietary selenium content of animals.

Health Benefits

Research supports the importance of an adequate selenium intake for prevention of selenium deficiency disorders and for optimal immune function. Low selenium intake has been associated with increased risk for several types of cancer, and adequate intake is associated with reduced cancer risk, especially for prostate, colorectal, and lung cancers (National Institutes of Health ODS, 2013). Animal studies support selenium's cancer-prevention benefits. Benefits of selenium supplementation for people who already have adequate dietary intakes of this mineral are not well established in humans, but appear promising (Higdon, Drake, & Whanger, 2009).

Supplemental selenium also is being studied for possible roles in preventing cardiovascular disease, thyroid disease, and cognitive decline, but evidence does not currently support significant benefits in these areas (National Institutes of Health ODS, 2013). The potential health benefits of many antioxidant nutrients and phytochemicals have tantalized researchers in the past, but once well-designed studies were conducted, results indicated no benefits and even showed some harms. Nutrients and phytochemicals interact with one another during digestion and absorption, and in thousands of metabolic pathways in the body; elevating levels of one could interfere with the behavior of the system as a whole. Consuming a healthful diet and including selenium foods and supplements to achieve the current DRI is likely to be safe.

Selenium Toxicity

A condition called "selenosis" can develop if too much selenium enters the bloodstream. Symptoms of selenosis include hair loss, nausea, fatigue, brittle nails, irritability, mild nerve damage, skin rashes, and a metallic taste in the mouth. More severe selenium toxicity can cause kidney failure, heart failure, heart attacks, tremors, and difficulty breathing (National Institutes of Health ODS, 2013). The Tolerable Upper Intake Level (UL) for selenium is 400 mcg for adults.

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See Also: Antioxidants; Cancer and nutrition; Minerals.

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Slow Food Movement

The "Slow Food movement" was initiated by Carlo Petrini in 1986 when the U.S. fast-food giant, McDonald's, decided to open a restaurant in the Piazza di Spagna, in the heart of Rome, Italy. The movement was created in response to the fast-food culture that many people held responsible for the industrialization of food and the homogenization of flavor. It was influenced by the countercultural and anti-consumerist ideals of Italy in the 1970s. The goal of the Slow Food movement is "to counteract fast food and fast life, the disappearance of local food traditions and people's dwindling interest in the food they eat, where it comes from, how it tastes and how food choices affect the rest of the world" (Slow Food USA, 2014).

The Slow Food movement was built upon earlier efforts by an organization known as Arcigola, which was part of the Italian Communist Party's Recreational and Cultural Association in 1983. Arcigola translates as "The Ark of Taste," in reference to Noah's Ark. Instead of saving animals, Arcigola was dedicated to preserving the traditional regional foods that were fast disappearing with the spread of urbanization. As the English name "Slow Food" caught on, Arcigola became "Arcigola Slow Food," and eventually, "Slow Food." The Slow Food movement grew rapidly. In 1989, Slow Food founders held the International Slow Food meeting in Paris and the Slow Food Manifesto was signed (Slow Food, 2014a). The name itself serves as a direct reminder of its mission to literally slow down, enjoy food, and promote a new food system that supports local farms and food producers, and seasonal foods.

Today, Slow Food has grown to more than 100,000 members in more than 150 countries around the world. Local chapters are forums for supporters to practice the Slow Food philosophy "that everyone has a fundamental right to the pleasure of good food and consequently the responsibility to protect the heritage of food, tradition and culture that make this pleasure possible" (Slow Food, 2014b). Members organize conferences and discussions, film screenings, and education



The creators of the Slow Food movement chose a snail to symbolize the movement. Snails move slowly and are also a culinary specialty in northern Italy where the Slow Food movement began. (Ksya/Dreamstime.com)

courses, and support local and international campaigns. The Slow Food movement encourages people to choose food that is good, clean, and fair: good food, which is seasonal and flavorful; clean food, in which the production and consumption of food does not harm the environment; and fair food, in which food is accessible to consumers as well as fair to small-scale producers in terms of compensation and working conditions. In the Slow Food philosophy, consumers are called "coproducers," to emphasize the fact that consumer choice drives food production systems, and that small farmers and food and beverage artisans will stay in business only with consumer support.

Questions have been raised concerning how the changes proposed by the Slow Food movement can be implemented. Many agricultural organizations have argued that industrial farming is the only way to economically feed a rapidly growing global population. Others have argued that fast-food establishments serve a useful purpose in certain settings, and that their menus have expanded to accommodate a wider range of tastes. Family members responsible for preparing meals

have expressed feeling overwhelmed by the dictates of Slow Food ideals. Yet the concepts promoted by the Slow Food movement remain appealing to many, who long to live more slowly and more mindfully, savoring life's pleasures. People searching for healthful eating recommendations often appreciate Slow Food's advice to eat slowly and enjoy one's meals.

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See Also: Fast food; Food gardens; The locavore movement; Sustainable agriculture.

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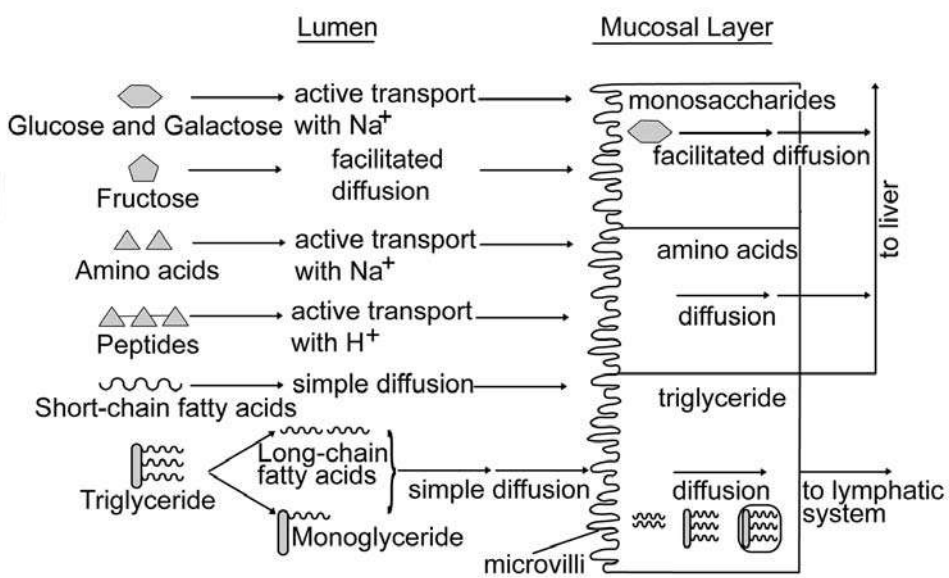
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Small Intestine

The small intestine is a digestive organ that comprises a major portion of the gastrointestinal tract, a series of organs that begins with the mouth and continues to the anal sphincter. After food is ingested, it is swallowed from the mouth into the esophagus, and then reaches the stomach. The food mass, which at this point is called "chyme," is partially degraded by digestive enzymes in the mouth and stomach before it enters the small intestine from the stomach. Approximately 90% of nutrients and water are digested and absorbed in the small intestine. The small intestine's length and inner projections (circular folds, villi, microvilli) provide a large surface area for digestion and absorption to occur. Food mass remaining in the gastrointestinal tract at the end of the small intestine passes into the large intestine and then exits the body.

The small intestine has four distinct tissue layers. The innermost layer that lines the small intestine is the "mucosa." The mucosal layer contains a variety of cells, including specialized cells called "absorptive cells" that take up, digest, and absorb nutrients from the food mass moving through the lumen (interior portion) of the digestive tract. The next layer out is the "submucosa," which contains loose connective tissue, blood vessels, and nerves. Two layers of muscle fibers surround the submucosa. The fibers of the innermost layer circle the small intestine, and the fibers of the next layer run longitudinally, along the length of the small intestine.



Nutrient absorption in the small intestine. Monosaccharides and most amino acids proceed directly to the liver, while the triglycerides enter in the lymphatic system. Triglycerides are first disassembled in the lumen and then reassembled into chylomicrons for transport in the lymphatic system. (Sandy Windelspecht)

The outer layer, "serosa," forms the surface of the small intestine. The serosa secretes serous fluid, which reduces friction between the small intestine as it moves against itself and other organs.

The structure of the lining of the small intestine optimizes efficiency in absorption of nutrients. In addition to the significant length of the small intestine, ranging from 3 to 10 meters and averaging about 6.5 meters, miniscule finger-like projections on the intestinal wall, called "villi," increase the surface area of the small intestine lining. Additionally, each surface on the villi has additional projections called "microvilli," which further increase interior surface area.

The human small intestine consists of three parts, the duodenum, jejunum, and ileum. The first section of the small intestine is called the "duodenum," and is connected to the stomach. The duodenum receives broken-down food, called chyme, from the stomach. The bile and pancreatic duct is connected to the duodenum via the "Ampulla of Vater," and through this channel bile (from the liver, via the gallbladder) and pancreatic juice enter the duodenum. These substances are mixed with chyme so that further digestion of food can occur.

The second and third sections of the small intestine are the jejunum and the ileum. The ileum connects directly to the large intestine at an area known

as the "cecum." At the junction of this connection is a structure called the "ileocecal valve," which prevents the reflux of cecal contents into the terminal ileum.

The main function of the duodenum jejunum and ileum—aided by the villi—is the absorption of nutrients. There is a slight distinction between jejunal and ileal villi in that jejunal villi are longer, broader, and more leaf-shaped and ileal villi are shorter, rounder and more blunted. Both types of villi, however, serve the same purpose of nutrient absorption.

Villi speed up the absorption of food by virtue of their structure. The surface of the villi is only about one cell thick; this speeds up the diffusion process by which nutrients enter the bloodstream. Each villus also is served by a network of capillaries, so that blood flow is constantly drawing nutrients into the bloodstream. The constant flow of blood helps to maintain a diffusion gradient so that nutrients can effectively enter the bloodstream. Additionally, the microvilli contain small lymphatic vessels, known as "lacteals," which receive fats and lipids.

The muscular layers of the small intestine move the food mass along through coordinated contractions called "peristalsis." The circular muscles squeeze the food mass, breaking it into smaller sections, in a process called "segmentation."

Several different cell types comprise the lining of the small intestine. Simple columnar epithelium lines the small intestine; it contains absorptive cells, goblet cells, enteroendocrine cells, and paneth cells. The absorptive cells are responsible for the digestion and absorption of nutrients in the small intestinal chyme. The goblet cells secrete mucous that adds to the general makeup of the intestinal juice and acts as a lubricant for the chyme. Enteroendocrine cells discharge secretin (in response to acidification of the duodenum), cholecystokinin (a hormone which causes the release of bile and secretion of pancreatic digestive enzymes), and glucose-dependent insulinotropic peptide (a hormone that regulates glucose-induced insulin secretion). Lastly, paneth cells secrete lysozyme, a bacterial enzyme involved in antimicrobial activities into the lumen, and which also can perform "phagocytosis"; this cell type can contribute to the regulation of the microbial population in the small intestine.

Chemical digestion of the chyme occurs from the mixing of the pancreatic juice, bile, and intestinal juice in the small intestine by segmentation. Segmentation enhances the mixing of chyme with the digestive juices during localized circular muscle fiber contractions. Segmentation also brings the food particles to the surface mucosa for absorption. Enzymatic digestion occurs in both the lumen and epithelial cell surface, where digestive enzymes are released from the microvilli, or brush border, that will break down the carbohydrates, proteins, and lipids of the chyme. Carbohydrate digestion is facilitated in the small intestine by pancreatic amylase. Brush border enzymes—enzymes expelled from the microvilli and intestinal epithelium cells—also help break down disaccharides into their respective monosaccharides. The small intestine can absorb monosaccharides from the lumen via facilitated diffusion or active transport.

Finally, the monosaccharides enter the capillaries of the villus by traveling across the basolateral membrane of the absorptive cells.

Protein digestion begins in the stomach, where they are further broken down into peptides (small protein units) by enzymes—such as trypsin, chymotrypsin, and elastase—in the pancreatic juice. Each enzyme acts to cleave the peptide bond of a specific amino acid and its neighbor. Two digestive peptidases from the small intestine's brush border complete protein digestion. The majority of chyme proteins are absorbed as amino acids via active transport where they enter absorptive cells through specific protein transporters. Amino acids, like monosaccharides, enter the capillaries of the villus and continue to the liver or enter general circulation.

Triglycerides are the most prevalent lipid found in chyme. Large lipid globules containing triglycerides must be broken down by the process of emulsification, in which the amphipathic (dual hydrophilic and hydrophobic) nature of the bile salts in the small intestine emulsifies the large lipid globules. The enzyme pancreatic lipase then splits triglycerides and phospholipids in the small intestine. Triglycerides are cleaved to their monomers: fatty acids and monoglycerides. Dietary lipids are absorbed into the small intestine's mucous membrane via simple diffusion. Short-chain fatty acids follow similar pathways of the monosaccharides and amino acids into the capillary of the villus. Long-chain fatty acids and monoglycerides are bulky and hydrophobic, but bile salts help make these lipid components more soluble. The hydrophobic regions of the bile salts interact with the long-chain fatty acids and monoglycerides and direct them away from the hydrophilic intestinal chyme to the brush border of the absorptive cells. Other hydrophobic molecules such as fat-soluble vitamins and cholesterol also follow this absorption pathway. Upon being absorbed, the monoglycerides and fatty acids recombine to form triglycerides that aggregate with phospholipids and cholesterol in a mass called "chylomicrons." Chylomicrons exit the absorptive cells through exocytosis through which they enter the lacteals. The lymphatic system eventually carries the chylomicrons to the bloodstream.

Bile salts are reabsorbed via active transport in the small intestine's ileum region and returned to the liver by the blood. Electrolytes found in the small intestine, such as iron and potassium, are absorbed via active transport mechanisms. As for water, the small intestine absorbs approximately 8.3 liters of water per day and the remainder passes into the large intestine. All water absorption occurs by osmosis across the lumen to the absorptive cells and into the blood capillaries. A concentration gradient produced from the movement of electrolytes, monosaccharides, and amino acids affects the direction that the water moves. The small intestine functions by coupling the mechanical forces of segmentation and peristalsis with the chemical reactions of digestive enzymes to achieve the absorption of most nutrients from the digestive mass.

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See Also: Celiac disease; Digestion and the digestive system; Inflammatory bowel disease; Large intestine.

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Sodium and Salt

Sodium in an essential nutrient, a mineral found primarily in salts. Salts are ionic compounds that result from the combining of an acid and a base. Table salt is a combination of the positively and negatively charged ions sodium and chloride. In an aqueous environment, such as in the human body, sodium chloride dissolves to produce the positively charged ion, or electrolyte, sodium, and the negatively charged chloride. Table salt is the primary source of sodium in the diet, and the terms "salt" and "sodium" often are used interchangeably when discussing dietary recommendations.

Sodium performs many essential functions in the body, including the generation of nerve impulses and muscle contraction; nutrient absorption in the gastrointestinal tract and transport in the bloodstream; and the regulation of blood volume and blood pressure. Sodium is plentiful in people's diets around the world, and most people enjoy the flavor salt adds to food. Too much salt in the diet contributes to hypertension (high blood pressure). A high sodium intake also can contribute to stomach cancer, osteoporosis, and kidney stones.

People around the world have used salt for thousands of years to flavor and preserve foods. Historical references to salt abound (Brief history, 1982). Although today salt is obtained from underground deposits, long ago, people obtained salt from surface deposits left by evaporated saltwater. These rare deposits made salt a highly valued commodity. In Sub-Saharan Africa, salt and gold had equal value by weight. Salt was used as money in many parts of the world. The expression "not worth his salt," comes from ancient Greece and Rome, where slaves were bought with salt as the currency. In ancient Rome, the world for salt ("sal") derived from the word for health, as salt baths were used for their healthful effects. A Roman soldier's pay included a portion of salt, from which English gets its word "salary."

Roles of Sodium in the Body

Sodium is an important electrolyte in fluids found outside of body cells. It is found in the fluid that surrounds body cells (interstitial fluid) and in blood plasma (the

Table Salt, Kosher Salt, and Sea Salt

Table salt is mined from underground deposits. After it is removed from the earth, it is refined to remove impurities—a process that also removes any other minerals that might be present. Some table salt products have iodine added, to combat iodine deficiency. Table salt also has small amounts of additives to prevent clumping.

Kosher salt usually comes from mined salt, but is less refined than table salt, with fewer or no additives and larger salt crystals. The term "kosher salt" comes from "koshering salt," as this salt was used traditionally as part of the process of making meat kosher, in the removal of surface blood. Kosher salt usually does not have iodine added.

Sea salt is made from evaporated seawater. It contains other minerals and fewer if any additives. The many varieties of sea salt, including French gray salt and Himalayan salt, come in a variety of colors and textures, and have become popular in recipes and for use at the table. Sea salts taste different from standard table salts and are preferred by many people.

Is sea salt better for you? Nutritionists believe that the extra minerals in sea salt do not add significant nutritional value because they are consumed in such small amounts. For a given serving size—such as a teaspoon—salt with larger crystals contains more air in the serving (the space between the crystals), and thus has less salt. But sea salt still is salt, and contributes to a person's sodium intake, so it must be used sparingly.

What about iodine? Iodine deficiency has become relatively rare in North America. Iodine intake has declined over the years in the United States, however, from about 250 mcg per day several decades ago to 157 mcg per day. Recommended iodine intake level for adults is 150 mcg per day. Processed and restaurant foods do not contain iodized salt. Experts believe less cooking at home explains the drop in iodine intake. People in the United States rarely experience iodine deficiency, because iodine also is found in seafood, plants grown in soils containing iodine, and animals consuming plants and commercial animal feeds that contain iodine. Pregnant and breast-feeding women have greater iodine needs, however, and should be sure to prevent iodine deficiency by ingesting the recommended daily amount.

liquid portion of blood in which blood cells are suspended). It works with other major electrolytes—including chloride and potassium—to regulate the distribution of water throughout the body. Sodium is essential for nerve conduction and muscle contraction, processes that rely on the electrochemical gradient maintained on either side of cell membranes. Special ion pumps embedded in cell membranes maintain this electrochemical difference by regulating the concentration of ions in these two regions. The concentration of sodium is about 10 times greater outside of the cell than inside the cell; the concentration of potassium is about 30 times greater inside cells (Higdon, Drake, & Obarzanek, 2008). The activity of these ion pumps accounts for about 20% to 40% of the energy expended as part of a person's resting metabolic rate.

Sodium absorption in the gastrointestinal tract enhances the absorption of other nutrients, including amino acids and glucose. Sodium concentration in the plasma influences the activity of the hormones that affect the kidney's regulation of water balance and blood pressure.

Sodium deficiency is diagnosed by low blood sodium levels and is called "hyponatremia." Hyponatremia rarely is caused by a low sodium intake; it usually is caused by dehydration accompanying illness, use of diuretics, and kidney disease. It also can be caused by excessive intake of water, perhaps combined with impaired fluid excretion, occurring most commonly in people engaged in prolonged exercise events. Symptoms of hyponatremia include nausea, vomiting, muscle cramps, headaches, fatigue, and disorientation. Without intervention hyponatremia can lead to brain damage, seizures, coma, and death (Higdon, Drake, & Obarzanek, 2008).

The recommended maximal intake of sodium for people ages 9 to 50 years old is 2,300 mg per day. The kidney's ability to regulate blood sodium level declines with age, and excess sodium levels are associated with increased risk for high blood pressure, therefore the recommended intake drops to 1,500 mg per day for people who are 51 years of age and older. The Tolerable Upper Intake Level (UL) for adults is 2,300 mg per day, which also is the recommended intake target for daily consumption. Most people's daily sodium consumption is well above this level.

Health Problems Associated with Excess Dietary Sodium

Unlike most other minerals needed in the diet, sodium is associated with health problems rather than with health benefits. People enjoy the taste of salt, and salt is used as a flavor enhancer and preservative in many foods. Salt is widely available and consumed at levels significantly greater than the recommended minimum in countries around the world.

The most common health problem associated with excess dietary sodium is hypertension. Hypertension contributes to both heart disease and stroke—leading causes of death in many countries. Experts generally agree that, in the long run, on the average sodium intake does influence blood pressure (IOM, 2013). Scientists, however, continue to argue about the extent of this relationship. Reducing dietary salt intake can lead to modest but meaningful decreases in resting blood pressure for people with elevated blood pressure. In one well-controlled study, for example, subjects reducing sodium intake from high to low with no other dietary changes experienced an average decrease in systolic blood pressure of more than 6 mm Hg (Sacks et al., 2001). Subjects who adopted a diet rich in plant foods, the DASH diet (Dietary Approaches to Stop Hypertension) and low in salt reduced resting blood pressure by 7.1 mm Hg (in subjects who began the study without hypertension) and 11.5 mm Hg (in subjects with existing hypertension). Critics point out that a high intake of other important electrolytes, such as potassium, magnesium, and calcium—which can be achieved on the DASH diet—might blunt the negative effect of sodium.

The goal of hypertension control is to reduce risk of cardiovascular and other serious health problems. One well-designed study found that reducing sodium intake was associated with 25% lower rates of cardiovascular events (such as heart attack and stroke) in adults with prehypertension (Cook et al., 2007). This study has

prompted some public health organizations to press for reductions in the sodium content in food products—the primary source of sodium in most people's diets.

Excess dietary sodium influences the absorption, utilization, and excretion of other electrolytes, and through these metabolic pathways influences additional health conditions. Sodium intake is associated with greater levels of calcium excretion. Preliminary research concerning the impact of high sodium intakes on osteoporosis has yielded mixed results, and longitudinal studies examining fracture rates are lacking, therefore it is too early to draw conclusions regarding the relationship between sodium intake and osteoporosis (Higdon, Drake, & Obarzanek, 2008).

Higher urinary calcium levels can increase risk for kidney stones. A few studies have suggested that reducing sodium intake could be helpful for people prone to the development of calcium stones (Higdon, Drake, & Obarzanek, 2008).

Stomach cancers are more prevalent in countries where people consume high levels of sodium, such as many Asian countries (Higdon, Drake, & Obarzanek, 2008). Salt itself, however, does not appear to act as a carcinogen. Diets high in salt often also are high in smoked and pickled foods, which might contribute to cancer risk. It is possible that high-salt diets injure the stomach lining, making it more susceptible to carcinogens.

Reducing Sodium Intake

Public health organizations generally agree that reducing daily sodium intake is a good idea for most people, and especially for people at highest risk for hypertension—people with a family history of hypertension, older adults, and African-Americans. A target daily intake of 2,300 mg for most people has fairly strong support. The current USDA recommendation to limit daily sodium intake to 1,500 mg per day for high-risk groups has less support (IOM, 2013). The USDA *Dietary Guidelines for Americans* recommends the lower intake for about half of the U.S. population: people age 51 and older; all African-Americans; and everyone who has hypertension, diabetes, or chronic kidney disease (USDA, 2010).

Sodium is found naturally in some foods, including dairy products such as milk and cheese. Salt is added to many food products, including tomato sauce, pickles, processed meats, soups, sauces, salad dressings, and prepared meals such as frozen dinners. Many snack foods, such as potato chips and pretzels, are high in sodium. Soy sauce has about 1,000 mg of sodium per tablespoon. The Nutrition Facts Panel on food labels includes sodium content. The USDA MyPlate website has good advice on reducing sodium intake (USDA, 2011). Reducing intake of processed foods and restaurant meals; preparing meals at home and limiting salt in recipes; and consuming a plant-based whole-foods diet or a DASH diet can help to reduce dietary sodium levels.

Barbara A. Brehm

See Also: Cardiovascular disease and nutrition; Electrolytes; Hypertension and nutrition; Minerals.

Reducing Salt Intake

The U.S. Food and Drug Administration urges consumers to make healthful food choices. Here are the FDA's ten suggestions for reducing intake of sodium and salt. If you follow these tips for reducing the amount of sodium you are consuming, the "taste" for salt gradually will decrease over time—eventually, you might not even miss it.

- Read the Nutrition Facts Label to see how much sodium is contained in the foods you are considering. People should consume less than 100% of the Daily Value or less than 2,300 mg of sodium each day.
- Prepare your own food when possible.
- Add flavor without adding sodium. Use herbs and spices instead of salt to add flavor to foods.
- Get fresh food when you can. Buy fresh or frozen (not processed) poultry, pork, and lean meat rather than canned, smoked, or processed meats such as lunch meats, sausages, and corned beef. Fresh foods generally contain less sodium. Also check the package on fresh meat and poultry to determine whether saltwater or saline has been added.
- Watch your veggies. Buy fresh, frozen (without sauce), and low-sodium or no-salt-added canned vegetables.
- Give sodium the "rinse." Rinse sodium-containing canned foods, such as tuna, vegetables, and beans before using. This removes some of the sodium.
- Examine dairy products. Fat-free or low-fat milk and milk products, such as milk, yogurt, cheese, and fortified soy beverages (often called soymilk) have less sodium than do processed cheese products and spreads.
- "Unsalt" your snacks. Choose unsalted nuts and seeds, and snack products such as chips and pretzels that are marked "low sodium" or "no-salt-added." Better yet, eat a carrot or celery stick instead.
- Consider your condiments. Sodium in soy sauce, ketchup, salad dressings, and seasoning packets can add up.
- Speak up at restaurants. Ask to see the nutrition information for the food served in restaurants and choose a lower-sodium option.

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Soybeans and Soy Foods

The soybean plant, or *Glycine max*, is a member of the pea family. The soybean is one of the few plant foods whose protein is complete, in that it supplies all of the essential amino acids that the human body requires. Soybeans also are high in fiber, low in fat, and contain no cholesterol. Soybeans are consumed as "edamame,"—fresh green soybeans in the pod that are steamed or boiled—and are made into many other foods, including tofu, tempeh, natto, and miso. Soybeans are made into a wide variety of meat analogues—food products flavored to resemble meats. Soy beverages and soy flours also are produced from this legume, as are some types of infant formulas. Soybeans contain phytochemicals that act as antioxidants and can exert hormonal effects in the body. These effects appear to be beneficial in some cases, although negative effects could occur as well.

Soybeans have been used in Asian cuisine for more than 5,000 years. Europe has been using soybeans for more than 300 years, and the United States has been using soybeans for more than 200 years. Today, the United States grows more than half of the world's soybeans (Natural Standard Research Collaboration, 2012).

Soy Foods

Soybeans are made into a wide variety of foods and food products. Tofu is a fermented form of soybeans that was invented during the 2nd century in China, and comes in a variety of different textures ranging from soft to firm. Tofu is not



Soy is available to consumers in a variety of food products. Soy foods are especially popular as substitutes for other more common foods. For example people avoiding meat or dairy foods can enjoy soy burgers, soy milk, soy yogurt, and soy cheese. (U.S. Department of Agriculture)

flavorful on its own, but it can absorb the flavor of spices and marinades. Tempeh is made from cooked soybeans that have been slightly fermented and formed into a patty, and has a nutty flavor. Natto is a soy food that comes from Japan. Natto is made by soaking soybeans overnight and then steaming them. Special natto bacteria are added, and the mixture is fermented for several days. Natto has a nutty, salty, pungent taste, that some have compared to ripe cheese. Miso is a form of fermented soybeans that has been formed into a thick paste. Miso has a tangy, salty taste, and often is used to flavor soups and sauces.

Soy beverages, also known as "soymilk," are made by soaking dried soybeans in water, then grinding and heating them. The mixture then is pressed to extract the liquid. Flavorings, sweeteners, and other ingredients are added to make the beverage palatable and more nutritious. People use soy beverages as a substitute for milk, either consumed as a beverage or as a replacement for milk in recipes. People allergic to milk proteins or lactose might better tolerate soy beverages. Soy beverages generally are fortified with calcium and vitamin D, because many people consume the product as a milk substitute. Some soy beverages also are fortified with vitamin B12 and other nutrients which are most likely to be deficient in a vegan diet. Soy-based infant formulas are manufactured in a similar fashion to soy beverages, except that more nutrients are added in an effort to meet the dietary

requirements of human infants. Soybeans also are made into products resembling cheese, yogurt, and ice cream.

Soy-based meat analogues include a wide range of products whose appearance, texture, and taste resembles meat products, most commonly ground-meat patties and hot dogs. Textured soy protein is a product that resembles dried flakes; these flakes can be added to recipes for soups and sauces. The flakes absorb liquid and flavors, and resemble ground meat once the dish is prepared.

Soy Food Health Benefits and Risks

Interest in the link between soy consumption and health began at the end of the 20th century, when epidemiologists observed that people who consumed greater amounts of soy foods tended to have a reduced risk of developing several health problems, including heart disease and breast cancer. Researchers still are exploring the biological mechanisms that explain these positive associations. Beneficial effects of soy foods have been attributed—at least partly—to the high-fiber, low-fat diet of which it is generally a part. Many people who consume soy foods also follow an Asian-type diet, for example—lower in meat and higher in plant foods than the typical Western diet. This could indicate that some of the health benefits observed with soy foods simply might be due to including more fiber and less fat in the diet, rather than to soybeans, per se.

Studies also suggest that soybeans can reduce levels of low-density lipoprotein cholesterol (LDL) (NIH, 2012). High levels of LDL cholesterol are associated with increased risk of heart disease. The evidence linking soy intake to reduced LDL levels is strong enough that the U.S. Food and Drug Administration has stated that a daily intake of 25 g of soy protein added to a low-cholesterol and low–saturated fat diet might reduce the risk of heart disease (Evert, 2011).

Some of the health effects of soy might be attributable to natural chemicals in soybeans called "isoflavones." Isoflavones are similar to estrogen, which is why they often are referred to as "phytoestrogens." Because of their estrogen-like qualities, isoflavones inherently have both health benefits and risks. Soybeans could provide a variety of hormonal benefits such as easing the symptoms of menopause; reducing the risk of osteoporosis; and preventing breast cancer, endometrial cancer, prostate cancer, and other hormone-related cancers (Evert, 2011). Soybeans, however, also might cause endometrial hyperplasia (a thickening of the lining of the uterus that can lead to cancer) or even increase the risk of hormone-related cancers in some people (NIH, 2012). The scientific community still is uncertain about the impact of isoflavones on overall health.

Soy dietary supplements are available. Some soy supplements contain soy isoflavones, some contain soy protein, and some contain both. It has been hypothesized that soy supplements produce the same health benefits as soybeans, but evidence to date does not strongly support this idea.

Soybeans contain chemicals called "purines." Purines can worsen gout, a form of arthritis; therefore, people with gout should eat soybeans in moderation. Soybeans occasionally can cause nausea, bloating, constipation, or diarrhea in

some people. Some individuals are allergic to soybeans. For this reason, food labels must alert consumers if products contain soy-derived ingredients. A large percentage of the soybeans grown in the United States are genetically modified, a fact that concerns some consumer groups.

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See Also: Genetically modified organisms; Lecithin; Organic food and farming; Phytochemicals; Sustainable agriculture.

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Spirulina

Spirulina is a type of cyanobacteria that flourishes in salty, alkaline lakes in subtropical and tropical regions. Of the approximately 15 species of this microscopic, corkscrew-shaped microorganism, *Arthrospira platensis* historically has been used for food by people in Africa and Asia, and *Arthrospira maxima* has served as a food source in Central America. Spirulina contains relatively large amounts of protein, B vitamins, and beta-carotene, and other carotenoids. Additionally, it contains relatively high concentrations of the minerals iron, selenium, manganese, and zinc. Spirulina is a good source of gamma-linolenic acid (GLA), an omega-6 fatty acid. Spirulina however, also can contain heavy metals—such as arsenic, cadmium, lead, and mercury—depending upon the environment in which it is grown. As a dietary supplement, spirulina can be consumed as a capsule, tablet, powder, in a food product, or as a fresh plant. Many health claims have been made for spirulina; however, good evidence to support these claims is lacking.

Cyanobacteria are aquatic, prokaryotic (single-celled) organisms that photosynthesize. They are one of the largest taxonomic groups of eubacteria. These bacteria contain two types of pigments, phycocyanin and chlorophyll, which together give it its blue-green color. Cyanobacteria derive their name from the phycocyanin (blue) pigment. The other pigment, chlorophyll—which is located in the cytoplasm

of the cell—has a greenish color. The organism uses this pigment during photosynthesis to capture light. This photosynthesizing characteristic is how the bacterium produces its energy.

Spanish explorers first documented the use of spirulina for food (Wolters Kluwer Health, 2009). The explorers observed the Aztecs harvesting a blue-colored sludge from Lake Texcoco, near what is today Mexico City. The Aztecs dried the mixture to form flakes or loaves. Similar procedures later were observed in the Sahara Desert in areas near Lake Chad.

Spirulina is especially important in areas where it is easy to cultivate and where food security is an issue. Its high protein, vitamin, and mineral content make it a useful food source for people living in areas that lack nutritional foods, or lack access to such foods. In 2013, for example, the United Nations supported a program in east and central Africa with the goal being to increase local access to spirulina as a food source, by sharing knowledge of spirulina growing, harvesting, and production (UN, n.d.).

Spirulina is high in protein. By weight, spirulina contains protein in an amount comparable to that of milk and eggs—about 6.5 g of protein per 10 g of food. This makes spirulina a good food choice in places where it can be locally grown. (In supplement form in North America, however, spirulina is a very expensive protein source.) Spirulina contains many vitamins, including beta-carotene, a phytochemical that the body can convert to vitamin A.

Spirulina's presence in the specialized health food market has increased over the years. Its effectiveness as a supplement, however, has yet to receive strong scientific support. Small, preliminary studies of spirulina and its components suggest possible antioxidant, antibacterial, antiviral, and anticancer activity (Wolters Kluwer Health, 2009). Intriguing studies suggest that people living in African regions where spirulina is consumed have lower than expected rates of HIV infection. Spirulina might reduce the risk of oral cancer in consumers. A few studies have demonstrated a reduction in symptoms of asthma and allergic rhinitis in subjects given spirulina. It is hoped that further research will clarify these potential applications.

Spirulina often is confused with blue-green algae supplements. Some species of blue-green algae produce neurotoxins, but spirulina supplements appear to be safe at normal doses.

Lydia T. Carron

Research Issues

In 1974 experts from the United Nations Food Conference called spirulina "the best food for the future" (UN, n.d.). Does spirulina cultivation have the potential to help to address issues of food insecurity and malnutrition? Read a review by the Food and Agriculture Organization of the United Nations on the potential use of spirulina as food.

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See Also: Chlorella; Dietary supplements.

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Sports Beverages

Sports beverages originally were created as a dietary supplement for endurance athletes who lose excessive amounts of carbohydrates, electrolytes, and water during prolonged physical activity, especially in hot environmental conditions. Many people do not consume as much water as they lose during prolonged physical activity, and consequently become substantially dehydrated. Dehydration decreases athletic performance and causes heat illnesses. If a person is dehydrated, then sports beverages can improve rehydration status more quickly than plain water or other beverages can.

Sports beverages vary in composition depending upon their purpose. Some are designed to prevent or treat dehydration, and others contain a greater carbohydrate and (sometimes) protein content to enhance recovery from prolonged or high-intensity physical activity. When used correctly, sports beverages can be useful for people who engage in frequent physical activity—especially high-intensity exercise that is sustained for more than an hour. Sports beverages, however, often are overconsumed by people who do not need them. Health care professionals especially discourage the consumption of sports beverages by children and teens, as these drinks provide unnecessary empty calories and contribute to obesity. Some beverages are enhanced with drugs such as caffeine, which can contribute to undesirable side effects, especially in children. Additionally, dental-care professionals have expressed concern about the acidity of these beverages and the contribution to the erosion of tooth enamel.

History of Sports Beverages

Athletes throughout recorded history have used various substances with the goal of achieving a performance advantage. Modern sports beverages date back to 1965, when coaches for the University of Florida football team, the Gators, sought help

from the team's physicians to determine why so many players were suffering from heat illness (Sports, 2008). Team physician Dr. J. Robert Cade and his colleagues studied the athletes and determined that the players often lost up to 4.5 kg in just one practice session due to sweating, thus losing significant amounts of electrolytes and water. Cade developed a drink that enabled water and sodium to be absorbed quickly to help prevent and treat dehydration—and "Gatorade" was born. The Gators' athletic performance improved considerably after the team began using the beverage, and the University of Florida's first Orange Bowl win in 1966 was attributed to the new drink. Other teams quickly adopted the beverage as well.

In 1967, the rights to Gatorade were bought by Stokely-Van Camp which put the drink in supermarkets a year later. In 1983, the rights were bought by Quaker Oats which began to market Gatorade nationally. In 2001, the rights were acquired by PepsiCo. Similar products were created by many other manufacturers, and by 2006 sports drinks had become the third-fastest growing beverage category in the United States (Story & Klein, 2012).

Potential Benefits of Sports Beverages

During prolonged exercise—especially in a hot environment—the human body loses water and electrolytes, especially sodium, in sweat. Strenuous exercise in hot weather can cause the loss of more than two liters of water per hour. With dehydration, water is lost from all body compartments. Water levels decline inside the cells and in the fluid between the cells. Blood volume decreases. The body slows its production of fluids, such as urine, digestive juices, and sweat. When a dehydrated person drinks plain water, the water is quickly absorbed from the digestive system into the bloodstream. As blood volume increases, the kidneys sense a drop in electrolyte levels in the blood and begin excreting water in an attempt to restore normal blood chemistry. The kidneys begin excreting water before intracellular and various tissue fluid levels are restored.

When sodium is taken along with water, dehydrated subjects rehydrate to a greater level than that of subjects ingesting only water. Sodium helps to restore blood volume without inhibiting thirst. Adding sodium to sports drinks also helps to prevent a condition called "hyponatremia," or low blood sodium levels, a condition which can develop in people who drink too much water.

Along with water and sodium, sports beverages designed to prevent and treat dehydration usually contain other minerals that can be lost in sweat, including potassium, calcium, and magnesium. Carbohydrates are included to make the drinks taste good, and to support optimal blood glucose levels to prevent fatigue during exercise. After more than an hour of exercise, blood glucose becomes an important energy source because it is used to supply energy for muscle contraction. Muscle glycogen stores decline, causing a need for an ongoing supply of carbohydrates to avoid fatigue and maintain performance. The carbohydrates commonly found in sports drinks include glucose and fructose, as well as special glucose polymers that allow glucose to be digested and absorbed more slowly. Many endurance athletes rely on sports drinks to provide fuel for hardworking muscles and

to keep blood sugar levels stable, which allows for longer, more intense periods of workout without the need to eat.

Why not drink fruit juice or other sweetened beverages? The concentration of sugars in these drinks makes the fluid difficult to absorb, which slows rehydration and can cause stomach cramps. Researchers recommend that the sports drinks used before and during exercise contain enough carbohydrate to contribute approximately 50 kilocalories per 8 fluid ounces. This allows the fluid and its contents to be rapidly digested and absorbed, and reduces risk of gastric distress. Athletes are urged to use any sports beverage regularly during practices to be sure the drink works for them, however, and are cautioned to never try new beverages immediately before or during contests.

Some sports beverages are designed to speed recovery from high-intensity, prolonged physical activity. These drinks contain extra carbohydrate to help replenish muscle and liver glycogen stores. Some drinks also contain amino acids to replenish protein stores and speed muscle repair.

Sports beverages can encourage people to adequately rehydrate after prolonged physical activity. Most people fail to drink the amount of water needed after exercising and overestimate the amount they already have ingested. The pleasant taste of sports beverages encourages people to drink more fluids than they normally would consume if only water was available.

Some of the performance benefit derived from use of sports beverages could be psychological. Research suggests that the presence of a sugar-containing sports drink in the mouth alone is enough to improve physical endurance, even if the drink is not swallowed. An interesting study compared groups of exercisers who swished a mouthful of a drink around in their mouths, and then spit it out. One group swished a beverage containing an artificial, noncaloric sweetener, and other groups swished preparations made with caloric sweeteners such as glucose. The groups swishing the caloric drinks showed significantly better endurance on cycling tests. Brain-imaging tests suggested that receptors in the mouth activate regions of the brain involved with reward and motor control (Chambers, Bridge, & Jones, 2009). This activation could reduce feelings of fatigue and enable athletes to increase work output.

Negative Health Effects

Sports drinks can be helpful for endurance athletes; however, during a short exercise period the electrolytes, minerals, and sugar found in sports drinks are not needed. For the average person, water and a healthy diet should be sufficient to replenish any losses due to exercise. Sports drinks, however, often are seen as a healthy alternative to soda and fruit juice, therefore some parents allow their children to drink sports beverages even when children are not engaging in prolonged exercise. The products also are heavily advertised to children and teens. Consumption of sports drinks adds unnecessary sugar and salt to the diet, and has been linked to weight gain, and to an increased risk of obesity and diabetes. In the diets of many children, these drinks have replaced healthier beverages such as

water and milk. The number of American children consuming sports beverages has increased dramatically over the past two decades (Story & Klein, 2012).

Another problem with sports beverage consumption is that the line between sport beverages and energy drinks often is unclear. Children and teens especially might not realize the difference between the two, and inadvertently could consume caffeinated sports beverages. In adults, studies have shown that caffeine increases strength, alertness, endurance, and impedes fatigue, although these effects vary from person to person. Caffeine, however, also has been linked to sleep disturbances, anxiety, and irregular heart beat. Caffeine can become addictive, and thus can lead to withdrawal symptoms such as fatigue, headaches, decreased alertness, irritability, depressed mood, and nausea when caffeine is not consumed.

Sports drinks have been linked to the weakening of tooth enamel. Most of these beverages have a pH level in the acidic range, which is associated with enamel demineralization. After exposure to sports beverages, tooth enamel begins to soften. Brushing teeth immediately after consuming a sports drink, without letting saliva re-mineralize the teeth, can cause more damage by removing enamel.

Easy-to-Make Sports Beverage Recipe

Many people prefer to avoid the artificial colors, flavors, and other additives found in sports beverages, and instead make their own sport beverages. Nancy Clark, a well-known sports nutritionist, recommends the following recipe in her sports nutrition book (Clark, 2008).

Mix together the following ingredients until solids are dissolved.

- ¼ cup sugar
- ¼ teaspoon salt
- ¼ cup hot water

Add the following ingredients to the mixture.

- ¼ cup orange juice
- 2 tablespoons lemon juice
- 3 ½ cups cold water

Diluting fruit juice with water to achieve 50 kilocalories per cup, and adding ¼ teaspoon of salt per quart of beverage, also creates a good sports drink.

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Research Issues

A staggering variety of sports beverages is available in most supermarkets. It is interesting to compare ingredients and labels and try to determine which drink is most appropriate. Many sports beverages also contain herbs, vitamins, and other dietary supplement ingredients to make the product seem special. The "Dietary Supplements" entry in this encyclopedia includes guidelines for researching supplement ingredients to learn more about them.

See Also: Dietary supplements; Electrolytes; Sports nutrition.

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Sports Nutrition

Sports nutrition is a field that applies the science of nutrition to sport and exercise training and competition. Good nutrition supports a person's ability to participate in and respond to demanding exercise training programs. Sports nutrition works closely with the exercise sciences, applying theoretical knowledge in exercise physiology, and sport and exercise psychology, to help athletes develop to their full potential. The application of sports nutrition includes the design of individualized daily eating plans to facilitate repair, recovery, and physiological adaptation to training, and to provide fuel for physical training and competition. These plans help athletes and active individuals optimize their athletic performance, health, and wellness.

History of Sports Nutrition

Sports nutrition evolved as an academic discipline in exercise physiology laboratories beginning in Sweden during the 1930s. Early studies examined carbohydrate and fat metabolism, and explored the production of energy from these fuel substrates. In the 1960s, Scandinavian scientists began studying muscle glycogen storage, use, and resynthesis and how these factors relate to extensive exercise activities. Glycogen is a primary source of fuel for exercising muscle, therefore an

understanding of glycogen pathways is a cornerstone of sports nutrition to this day. This area of study also was supported in the United States in the 1960s by scientist David Costill at Ball State University, in Illinois.

Dehydration can lead to heat illness and even death in athletes who train in the heat. In 1965, University of Florida scientist Robert Cade and his research team developed Gatorade, a scientifically formulated sports drink to help the university's football team with late-game hydration. The beverage was engineered to replenish carbohydrates and electrolytes lost during physical activity, to help athletes perform well even as they began to fatigue. Preventing and coping with dehydration continues to be a major focus of sports nutrition research and practice.

The field of sports nutrition continued to expand in the 1970s, as exercise physiologists created exercise laboratories at universities to study athletes. In addition to continuing research on optimizing glycogen stores and hydration status, researchers studied foods, diets, and food components (such as caffeine, creatine, etc.) that might enhance athletic performance. By the 1980s, good nutrition was considered essential for improving athletic performance.

Licensing

Exercise and sports professionals can provide athletes and clients with general nutrition information found in the "public domain." Although team coaches, health coaches, athletic trainers, strength and conditioning coaches, and physicians cannot provide medical nutrition therapy, many are qualified and able to work with clients and athletes on setting general nutrition goals for health and performance, and designing strategies for improving eating behaviors.

Sports professionals and licensed dieticians can work together to create nutrition plans for athletes. Athletes diagnosed with iron-deficiency anemia, for example, can meet with a dietician to develop daily eating plans. An athletic trainer then might follow up with these athletes to monitor iron status and progress in implementing meal plans, and then work with the coach in determining the athletes' ability to participate in training and contests.

Students and professionals interested in sports nutrition must have the appropriate educational background and practical experience to give sports nutrition–related advice. Teaching and graduate assistantships, classes, research, hospitals, health clubs, and internships can provide vital opportunities to gain practical experience in the field.

People interested in developing a career as a sports nutritionist might choose to obtain a license in dietetics. Obtaining licensure gives individuals the ability to practice broadly. Licensed professionals can design daily meal plans for athletes with a variety of health issues. Athletes consulting licensed professionals for health reasons often can be reimbursed by their health care plans for the expenses. The requirements for becoming a registered dietician (RD) in the United States include the following.

Registered Dietician Requirements

- Obtain a four-year degree with a nutrition major
- Perform undergraduate coursework that meets Didactic Program in Dietetics (DPD) requirements
- Complete a six- to twelve-month dietetic internship—postbaccalaureate and with 900 hours of experience, supervised by an RD
- Pass the national board exam for dieticians
- Acquire significant knowledge of general nutrition, exercise physiology, body composition, and eating disorders
- Optional graduate degrees can be obtained in several areas, including human nutrition, sports nutrition, exercise science, kinesiology, sports management, athletic training, and sports medicine

Board Certification as Specialist in Sports Dietetics Credential

Registered dieticians who wish to specialize in sports nutrition often consider becoming board certified in this area. Sports dietetic professionals are registered dieticians with experience in applying evidence-based nutrition knowledge in exercise and sports. Continuing education is offered by the Commission on Dietetic Registration (CDR) of the American Academy of Nutrition and Dietetics (AND) for those who choose to obtain Certified Specialist in Sports Dietetics (CSSD) credentials. Applicants must provide documented practice experience in sports nutrition and successfully complete a computerized exam. Some of the benefits of certification can include the following.

- Individuals with CSSD credentials can assess, educate, and counsel athletes and active individuals.
- Individuals with CSSD credentials can design, implement, and manage nutrition plans to encourage health, fitness, and optimal athletic performance.
- The CSSD credential is valid for five years before specialists must apply for recertification.

Career Opportunities

Sports nutrition professionals work in a variety of settings. Some of the most popular career opportunities include the following.

- Clinical Settings: Sports dieticians can counsel athletes on sports injury treatment, prevention, and ways to improve performance using good nutrition practices. Professionals can work as dieticians with hospitalized patients and with outpatients in a sports-medicine facility.
- Sport Performance Companies: These companies often are associated with sports-medicine practices to help educate teams and individuals regarding how to improve their athletic performances.

- Fitness/Wellness Facilities: Sports nutritionists can instruct group nutrition classes and provide individualized sports nutrition counseling, wellness education, and clinical nutrition management.
- Academics: Professionals can instruct sports nutrition classes in dietetics or exercise science, and possibly conduct applicable research.
- Professional Teams: Limited positions (typically as a part-time consultant) are available in this area. These positions usually are filled by well-seasoned dieticians.
- Corporations/Food Industry: Companies producing or marketing sports nutrition products often seek dieticians to help with research, development, marketing, and sales.
- Private Consulting: Some sports nutrition professionals open private consulting practices for athletes or for active people of all ages.

Application of Sports Nutrition in Sports Performance

Sports nutrition professionals perform a variety of tasks as they work with athletes and teams. Some of these tasks are discussed below.

Individual Nutrition Counseling

Sports nutritionists often work with individual athletes to help athletes maximize their ability to train at optimal levels and perform well in their sports. Some of the activities a professional might engage in include the following.

- Assess and analyze dietary habits, body composition, and energy balance for athletes to help their athletic performance and overall health.
- Provide athletes with nutrition recommendations to help with practices, performance goals, competition, recovery, weight management, hydration, eating disorders, and travel.
- Help educate athletes on how to achieve and maintain appropriate levels of body mass, body fat, and muscle mass to promote good health and athletic performance.
- Create personalized meal and snack plans for pre-competition, post-competition, and training meals to help athletes achieve both short-term and long-term goals.
- Develop appropriate hydration recommendations for use during training, pre-competition, competition, and post-competition.
- Address nutritional challenges hindering performance, such as food allergies, bone mineral disturbances, gastrointestinal issues, and iron-deficiency anemia.
- Provide medical nutrition therapy to help athletes manage or treat medical conditions.
- Help athletes optimize nutrition for recovery after illness or injury.
- Assist with programs helping athletes with eating disorders.

- Evaluate and monitor use of dietary supplements and herbal supplements. Monitor legality, safety, and quality of approved supplements that athletes utilize.

Menu Development for Athletes

Sports dieticians often coordinate and oversee quality food production and distribution for the development and management of training table (meals shared by team athletes) and catering for athletic functions. They might organize nutrition for domestic or international travel, working with catering groups, hotels, and airlines. Professionals often supervise the team's budget for purchasing and distributing nutritional supplements.

Nutritional Education for Teams

Sports nutrition professionals often conduct nutrition education presentations, demonstrations, or events for teams, coaches, and athletic departments about various topics relative to nutrition and athletic performance. As they work with teams, sports nutritionists can provide individual nutrition counseling as needed. Professionals often act as a nutrition resource for coaches, teachers, trainers, and parents. They can provide education in food selection: grocery store tours, food storage, and food preparation (cooking courses).

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See Also: Blood sugar regulation; Carbohydrate loading; Creatine.

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Sports Supplements

Sport supplements or "ergogenic aids" are substances that enhance an individual's athletic performance. Sports supplements claim to improve an individual's fitness level by assisting in the recovery and adaptation of the body's systems after exercise or by improving stamina, strength, and speed during exercise or performance. Dietary supplements are available over the counter; many promise enhanced

athletic performance, but few live up to the promises made on their labels. Dietary supplements differ from pharmacological aids such as anabolic androgenic steroids, which are only legally available by prescription. The FDA regulates dietary supplements as foods rather than as drugs, which means that manufacturers do not need to adhere to the stricter manufacturing standards required for drugs. Sometimes unethical producers add ingredients to supplements without listing them on the label; for this reason, taking sports supplements can be risky for athletes because some supplement ingredients are banned in athletic competitions. Some athletes have claimed that their positive drug tests were caused by unlisted ingredients in sports supplements.

Historically, warriors and athletes consumed herbs and body parts of animals in an effort to transfer the traits of bravery, strength, speed, and endurance from that plant or animal to themselves. Before a battle, gladiators often ate meals containing dill because it was thought to give them courage. After a battle, the meat of muscular animals (e.g., ram) was fed to the victors (Reed, 1977). Ancient Olympians ate garlic, mushrooms, and raw animal testicles to enhance performance (Kelland, 2012); ancient Chinese warriors consumed deer antlers to strengthen their heart; and Cree warriors ate raw bison liver to gain the power of the bison (Hastings, Selbie, & Gray, 1919). Early competitors in the Tour de France used strychnine, ether, nitroglycerine, and alcohol to dull the pain and combat fatigue (Holt, Ioulietta, & Sönksen, 2009).

Some of the most commonly used performance-enhancing supplements include the following.

Sports Drinks and Gels

Sports drinks, gels, and similar preparations deliver carbohydrates, electrolytes, and other nutrients in an easily processed form. Consuming these products can be helpful for competitors in long-distance sports such as marathon running or cycling, or for athletes at risk of dehydration because of prolonged physical activity or hot environmental conditions.

Protein and Amino Acid Products

Protein drinks and powders are used to support muscle repair and building. They often are consumed before and after workouts. Amino acid supplements also are popular, because amino acids are the building blocks of protein. Three commonly used ingredients are glutamine, branched chain amino acids (BCAA), and arginine. Low levels of glutamine are found in muscle when the muscle is being broken down. Supplementation with glutamine restores muscular force that was decreased due to inflammation (Meador & Huey, 2009). The BCAAs are used for energy during exercise, and supplementation could reduce muscle soreness, minimize damage, and improve muscle performance when taken prophylactically (Howatson et al., 2012). Arginine is involved in the production of nitric oxide (NO), a gas that improves dilation of blood vessels. It is thought that improved

circulation via nitric oxide improves performance by extending the time it takes to reach exhaustion.

Anabolic-Androgenic Steroid Precursors

Steroid precursors such as androstenedione and dehydroepiandrosterone (DHEA) commonly are taken because athletes believe these hormones will increase their testosterone levels and provide the same ergogenic aid as an anabolic steroid. The amounts of testosterone actually produced in response to these supplements is unknown, and users might test positive for banned substances on a drug test.

Caffeine

Caffeine is a stimulant that affects the central nervous system. It can make exercise seem easier and thus enable an increase in the volume or intensity of exercise. Caffeine also can raise the level of free fatty acids in the blood, encouraging the body to use fat for fuel and spare glycogen, the body's limited but preferred energy source. Caffeine is an effective ergogenic aid, and its use in high doses is banned by many sports governing bodies.

Creatine

Creatine is a nitrogenous organic acid manufactured from nonessential amino acids. Used as a supplement to the body's own production of creatine, it generally is taken in pill or powder form. The human body uses creatine to produce the molecule phosphocreatine, which helps to replenish adenosine triphosphate (ATP), the body's primary energy molecule. Phosphocreatine is especially important for energy production during the first few seconds of exercise. Creatine also works by supporting the synthesis of protein in the muscles, which works to enhance muscle growth. Many athletes find creatine to be an effective aid that supports training at greater intensities and improved performance in power-related athletic events.

L-carnitine

L-carnitine is biosynthesized from the amino acids lysine and methionine. L-carnitine has been reported to increase the level of androgen receptors on skeletal muscle, and spare muscle glycogen during exercise by making fat more readily available for fuel (Kraemer et al., 2009; Wall et al., 2011). These effects can promote muscle growth and improve performance, but research generally has not yet found a performance benefit associated with carnitine supplementation.

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Research Issues

The U.S. Food and Drug Administration regulates what claims are permitted on dietary supplement labels and advertisements. Health claims are strictly regulated. Supplements containing calcium, for example, may say, "Adequate calcium may reduce risk of osteoporosis." But so-called structure or "function" claims do not require FDA authorization, as long as manufacturers also add the following statement to their labels: "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease." An examination of sports supplement labels and advertisements illustrates the fact that outrageous and dubious photos and claims about enhanced athletic and bodybuilding performance can be made within these contexts.

See Also: Arginine; Carnitine; Dietary supplements; Glutamine; Sports beverages; Sports nutrition; Whey protein.

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St. John's Wort

St. John's wort, *Hypericum perforatum*, is a shrubby looking plant that grows to one- to three-feet high with bright yellow flowers that blossom from the top. It is also known as Klamath weed and goatweed. St. John's wort can be found in meadows and woods in Europe, Canada, and the United States, and 20% of the world's supply is found in Australia. Supplements are made from the plant's flowers and leaves. It has been suggested that compounds found in St. John's wort, including hypericin, hyperforin, and flavonoids, can interact with nerve receptors involved in depression. Although the exact nature of its antidepressant effects remains unknown, evidence has shown St. John's wort to have a positive effect in the treatment of mild to moderate depression.

History

Some of the earliest medical records of St. John's wort date back to ancient Greece, where it was used to protect against evil spirits and witches. It was later used as a folk remedy to treat wounds, headaches, kidney diseases, and gout. The plant did not become popular in the United States until the first study in 1959. Its name is derived from the date when it reaches full bloom, around June 24, which is the birthday of John the Baptist.

The herb has become controversial around the world. Although it commonly is prescribed in Germany as an antidepressant, both France and Ireland have banned over-the-counter sales of St. John's wort because of its interactions with other medications.



St John's wort is widely known as a herbal treatment for depression. The plant is native to southern Europe and southwestern Asia but is now grown in gardens in North America as well. (iStockPhoto.com)

How It Works

St. John's wort is sold in liquid, capsule, pill, or topical form. Its leaves also can be used to prepare teas. The form in which it is distributed is dependent on what it is being used to treat. Its oil can be applied directly to the skin, and is used to treat bruises, wounds, burns, bug bites, muscle or

nerve pain, and hemorrhoids. Individuals targeting symptoms of depression take St. John's wort by mouth in pill or capsule form. There are three neurotransmitters that are most often linked with depression—serotonin, dopamine, and norepinephrine. St. John's wort might inhibit the neuronal uptake of all three of these at potencies similar to that of antidepressants.

Effectiveness

St. John's wort has been effective in treating mild-to-moderate depression. One analysis of short-term 18 placebo-controlled and 17 antidepressant comparison studies showed that those assigned to *hypericum* reported fewer side effects than found with antidepressants (Linde, Berner, & Kriston, 2008). Furthermore, *hypericum* preparations were more effective than placebo, and were just as effective as standard antidepressants. Similarly, another meta-analysis showed that *hypericum* had a 1.5-fold greater success rate in treating mild-to-moderate depression than the placebo, and had effects similar to those of tricyclic antidepressants (Kim, Streltzer, & Goebert 1999). Other studies, however, have shown either the same or no difference between a placebo and antidepressants.

Hypericin and hyperforin are known for their antioxidant, anti-inflammatory, anticancer, and antimicrobial properties. Recent research has shown some support for St. John's wort and medical skin care. Some in vitro and in vivo studies also have found evidence of its ability to treat inflammatory conditions such as fibromyalgia, but these studies are preliminary. More research is needed to confirm the efficacy of these findings.

Side Effects

Side effects associated with St. John's wort usually are mild and include gastrointestinal symptoms, sensitivity to sunlight after topical application, skin rashes, headache, anxiety and fatigue. Its use can worsen symptoms of attention deficit disorder and, in rare cases, cause symptoms of mania or psychosis for people with preexisting mental illness.

Interactions

Several pharmacokinetic and pharmacodynamic interactions exist when combining St. John's wort with other medications. Mixing St. John's wort with selective serotonin re-uptake inhibitors (SSRIs) in some individuals has been shown to mimic symptoms of serotonin syndrome, a life-threatening illness characterized by a dangerous buildup of serotonin in the blood (Henderson et al., 2002). There is an increased risk for adverse reactions of prescribed drugs for individuals taking St. John's wort, as well as a decrease in the effectiveness of some medications including the following.

- Oral contraceptives
- HIV protease inhibitors
- HIV non-nucleoside reverse transcriptase inhibitors
- Warfarin and other blood thinners
- Digoxin and other heart medications
- Anticonvulsants
- Triptans

Criticisms

St. John's wort is not regulated by the Food and Drug Administration (FDA). Dietary supplements thus are subject to a range in potency, can have contaminants, and have the potential to interfere with standard medicines.

Individuals considering taking St. John's wort should consult with a doctor before beginning a new regimen. Although it has been found to be effective for treating mild-to-moderate depression, St. John's wort should not be used to treat major depression. Furthermore, long-term follow-up studies are needed to test the validity of the claims for St. John's wort.

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See Also: Depression and nutrition; Dietary supplements.

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Stevia

The alternative sweetener commonly known as "stevia" comes from the *Stevia rebaudiana* plant, a perennial shrub from the same family as the chrysanthemum (*Asteraceae*). Stevia is 200 to 300 times sweeter than sugar, provides no calories, and does not promote tooth decay. The plant is indigenous to northern South America and has been used for centuries in Brazil and Paraguay as both a sweetener and an herbal remedy. It has been used medicinally to fight infection and bacteria, decrease inflammation, alleviate fatigue and depression, regulate blood sugar levels, and lower blood pressure. Its side effects can include mild nausea and a feeling of fullness.

The stevia leaf can be used whole, but commercial products use highly purified extracts from the leaf that act as a nonnutritive sweeteners. These sweet-tasting compounds are called "steviol glycosides"; the two sweetest are stevioside and rebaudioside (which comes in various forms, such as rebaudioside A and rebaudioside B). In many countries, including Canada, purified extracts of both stevioside and rebaudioside can be used in products. In the United States, however, only highly purified extracts of rebaudioside A are allowed, and go by the trade name of "rebiana." Rebiana then is marketed by different companies under various brand names, such as SweetLeaf, Truvia, and PureVia.

Commercially, whole leaf and extracted forms of stevia have been used in Japan since 1970, in China since 1984, and in Brazil since 1986. Stevia's introduction to the United States was delayed, however, because of studies that raised concerns about its effect on the liver, kidneys, and reproductive system, as well as its possible role in cell mutation when consumed in large quantities. In 1995, the U.S. Food and Drug Administration (FDA) approved stevia's use as a dietary supplement. In 2008, several big companies, including Cargill, Merisant, and Wisdom Natural Foods, supplied the FDA with updated research and urged the FDA to declare rebiana (not stevia) as "generally recognized as safe" (GRAS). The FDA agreed, opening the door to rebiana's use as a food additive. Canada followed suit in 2012, allowing highly purified extractions of steviol glycosides to be used as food additives. Whole leaf and unrefined stevia, however, continue to be available only as dietary supplements in the United States and Canada.

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See Also: Alternative sweeteners (sugar substitutes); Artificial sweeteners; Food additives.

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Stomach

The stomach is an organ of the digestive system. It is located in the upper-left abdominal cavity, below the diaphragm and between the esophagus and small intestine. When a person eats, food is swallowed from the mouth and travels down the esophagus and into the stomach. The stomach performs multiple functions, including temporary storage of ingested matter, mechanical digestion, chemical digestion, and some absorption.

Structure

The stomach wall is made up of four different layers. Starting from the inside of the gastrointestinal tract these layers are the mucosa, the submucosa, the muscularis externa, and the serosa. The innermost layer is the mucosa. The mucosa is a mucus membrane made up of a layer of epithelial cells that line the interior of the stomach and loose connective tissue. Further in this layer is a thin layer of smooth muscle called the "muscularis mucosae," allowing the stomach to form folds, known as "rugae." Depending on the size of the meal that enters the stomach, the stomach can extend or contract its muscular walls through the longitudinal folds of the rugae. When the stomach expands the rugae unfold, and when the stomach empties the rugae contract. Next is the submucosa layer which contains blood vessels to provide transport of nutrients and other substances, and nerves that communicate with other parts of the body to facilitate stomach contractions. Outward from the submucosa is the "muscularis externa" layer, which is the largest layer of the stomach. It contains three sublayers of smooth muscle, the oblique muscle layer, the circular muscle layer, and the longitudinal muscle layer. These layers allow for the strong stomach contractions that enable mechanical digestion. The final, most peripheral layer is the serosa, which secretes serous fluid that allows for lubrication that protects the stomach from friction against adjacent tissues and organs as the stomach expands and mixes.

The stomach lining contains small pits, known as "gastric glands," that open into the mucosa. The gastric glands contain a number of specialized cells that produce a variety of secretions. Parietal cells secrete hydrochloric acid, which causes the strong acidity of the stomach contents. The parietal cells also secrete intrinsic factor, a compound essential for the body's absorption of vitamin B12. Mucus cells secrete mucus that clings to and protects the stomach lining, and helps lubricate the food mass. The peptic or chief cells secrete a digestive enzyme precursor called "pepsinogen." Enteroendocrine cells secrete a hormone called "gastrin." Gastrin stimulates the production of the other secretions of the gastric glands, increases stomach muscle contractions, contracts the esophageal sphincter, and relaxes the pyloric sphincter. All of the fluids produced by the stomach are referred to collectively as "gastric juice."

The regions of the stomach are called the "fundus," the "body," the "antrum," and the "pylorus." The fundus is the extended section of the stomach that curves up above the cardia, or opening of the stomach (where the stomach connects to the

esophagus). The body is located in the center of the stomach. It is the largest area of the stomach, and is used to store the digested food. The antrum is the funnel-shaped lower part of the stomach. Its wide end is a continuation of the body, and its narrow end connects with the most posterior area of the stomach, the pylorus. The pylorus is the smallest section of the stomach and serves as the connection between the stomach and the first segment of the small intestine, the duodenum. In this section there is a thickening of muscle that forms the pyloric sphincter. For the partially digested food mass to pass into the small intestine this valve must open.

Food Storage and Gastric Emptying

Softened by chewing and saliva but still largely undigested, food travels from mouth down the esophagus, and enters the stomach through the lower esophageal sphincter. The stomach stretches to accommodate the food and liquids ingested. Stomach size varies between individuals, but most can readily accommodate 1 to 2 liters of food. Four liters of food is a rough estimate of the maximum volume the average stomach can hold at a given time. This amount generally is considered to be excessive, in part due to the fact that it impedes mechanical digestion.

A meal typically remains in the stomach for one to four hours before being gradually released into the small intestine through the pyloric sphincter as chyme—a mixture of partially digested food and digestive secretions. Gastric emptying rate is influenced by a variety of factors. Non-nutritive liquids such as water leave the stomach the fastest. Carbohydrate-based foods also empty quickly; those high in protein and fat empty more slowly. The size of a meal also plays a role—very small quantities of food barely stretch the stomach, and the lack of distension can fail to stimulate gastric motility, delaying emptying. Large meals take longer to empty than do medium-sized meals, because stomach contents are released fairly slowly through the pyloric sphincter.

Mechanical and Chemical Digestion

In the stomach the process of mechanical digestion relies largely on muscle contractions. Strong peristaltic contractions in the distal (lower) stomach in particular work to break down solid food into smaller units and to mix it with liquids. Chemical digestion, however, is facilitated by gastric acid as well as numerous enzymes and hormones. The hydrochloric acid secreted by the gastric glands lowers the stomach's pH to around 2 and denatures proteins, unfolding their three-dimensional structures into linear chains. It also converts the enzyme precursor pepsinogen into the active enzyme "pepsin," which furthers protein digestion by catalyzing the hydrolysis of peptide bonds. Additionally, as a nondigestive function, stomach acid kills some potentially pathogenic microorganisms ingested along with food and liquid. Some fat digestion also occurs in the stomach, with the enzyme gastric lipase enabling the removal of one fatty acid from certain triglycerides, such as those found in butterfat. No significant carbohydrate chemical digestion occurs in the stomach.

Absorption

The vast majority of nutrient absorption occurs farther down in the gastrointestinal tract, in the small intestine, particularly. Some lipid-soluble drugs, however, such as aspirin can be absorbed in the stomach. Some alcohol and water also can enter the bloodstream through the stomach lining.

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See Also: Bariatric surgery; Digestion and the digestive system; Gastroesophageal reflux disease; Peptic ulcers.

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Sugar Alcohols

Sugar alcohols, which also are called "polyols" because of their chemical makeup, are a group of sweeteners frequently used in processed foods as a lower-calorie substitute for sugar. Sugar alcohols are carbohydrates that exist naturally in plant products, including some fruits, vegetables, mushrooms, trees, corncobs, and plant stalks. Despite their name they are not sugars, nor are they alcohols; "sugar alcohol" alludes to the chemical structure. They are commercially produced through the hydrogenation (addition of hydrogen) of different types of saccharides (sugars). The sugar alcohol lactitol, for example, is produced from the sugar lactose. The hydrogenation process creates a class of polyols that taste sweet but have fewer calories per gram than sugar and do not promote tooth decay. These characteristics make them common sugar substitutes in a variety of products, from toothpaste and chewing gum to sugar-free ice cream and cookies. Because sugar alcohols are not absorbed fully by the body, however, they can cause gastrointestinal distress, particularly when eaten in large quantities. Both the United States and Canada allow eight sugar alcohols (listed below) to be used in products.

- Erythritol
- Isomalt
- Lactitol
- Maltitol
- Mannitol
- Sorbitol

- Xylitol
- Hydrogenated starch hydrolysates (HSH)

The regulation and product labeling of sugar alcohols varies by country. In the United States, some sugar alcohols are regulated by the Food and Drug Administration (FDA) as food additives, and others are considered "Generally Recognized As Safe" (GRAS). A GRAS status means that enough research has been conducted on the additive to deem it safe without regulation when used for its intended purpose.

Sugar alcohols vary in their sweetness levels and in the specific characteristics they bring to products. Xylitol is 100% as sweet as sucrose, for example, and it creates a cooling sensation in the mouth. Xylitol also has been found to actively fight tooth decay (American Academy of Pediatric Dentistry, 2010), so it is frequently used in gum and toothpaste. Consumers should be aware, however, that xylitol is toxic to dogs. Isomalt is 45% to 65% as sweet as sucrose and is less sticky, so it is often used in hard candies. It also withstands heat well, and can be used in baked goods. Maltitol is 75% as sweet as sucrose and creates a creamy consistency. It often is used in ice creams (International Food Information Council Foundation, 2009).

Sugar alcohols should not be confused with non-nutritive sweeteners. Non-nutritive sweeteners provide zero calories, and sugar alcohols average 2 calories per gram as compared to sugar's 4 calories per gram. Erythritol contains the fewest calories with 0.2 per gram, and HSH contains the most calories with 3.0 per gram (International Food Information Council Foundation, 2009). Sugar alcohols often are used in conjunction with non-nutritive sweeteners such as aspartame or sucralose to combine the bulking properties of the sugar alcohols with the sweeter taste of non-nutritive sweeteners.

Sugar alcohols are not digested and metabolized like sugar. They are only partially absorbed into the blood from the small intestine. The portion that is absorbed is converted to glucose slowly, thus triggering little or no insulin response. The portion that is not absorbed passes into the large intestine, where it is fermented by bacteria. Because of the fermentation, overconsumption of sugar alcohols can lead to gas, abdominal discomfort, and diarrhea. Products that contain significant amounts of sugar alcohols are required to state "Excess consumption may have a laxative effect" on their packaging. Children are particularly susceptible to the laxative effects of sugar alcohols.

Foods that contain sugar alcohol but no added sugars can be labeled as "no sugar added" or "sugar-free" foods. Many people mistakenly believe this means they are low calorie and therefore eat them in large quantities. Not only can this lead to gastrointestinal distress, but many of these foods are highly caloric and contain few beneficial nutrients. Individuals with diabetes must be particularly careful because although normal portions of foods with sugar alcohols do not raise blood glucose levels significantly, levels can rise if large quantities are eaten.

Sugar alcohols are relatively new to the food industry (for example, isomalt has had GRAS status in the United States only since 1990 [Walters, 2013]), therefore

further research is needed to determine long-term benefits and consequences (if any) of eating sugar alcohols.

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See Also: Alternative sweeteners (sugar substitutes); Artificial sweeteners; Blood sugar regulation; Dental caries (cavities); Food additives.

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Sugar-Sweetened Beverages

Sugar-sweetened beverages (SSBs) are beverages that contain added caloric sweeteners such as high fructose corn syrup or sucrose. Although the definition used by researchers varies, all sources list soft drinks, or sodas (excluding diet sodas), as SSBs. Most researchers define SSBs to include not only sodas, but also fruit drinks, sports drinks, energy drinks, and other beverages that contain added caloric sweeteners, such as sweetened coffee and tea, rice drinks, bean beverages, sugar cane beverages, horchata, and nonalcoholic wines and malt beverages (Gortmaker, Long, & Wang, 2009; Centers for Disease Control and Prevention, 2010). Sugar-sweetened beverages tend to have few nutrients and are thought to be the largest source of added sugar in the U.S. diet (Centers for Disease Control and Prevention, 2010).

As early as the 1st century, ancient Greeks and Romans added sugar to water, believing the mixture to be medicinal; they drank sugar water to improve intestinal health and to alleviate pain in the bladder and kidneys. In combination with sugar water, carbonation led to the creation of the modern day "soft drink." The

discovery of carbonation dates back to 1767, when English chemist Joseph Priestley figured out how to infuse water with carbon dioxide. Like sugar water, carbonated water ("soda water") also was thought to have healing qualities and was consumed to relieve a variety of ailments, including gout, indigestion, and arthritis. In 1832, inventor John Mathews created a soda carbonation machine, an invention that later would earn him the title "Soda Fountain King." Because of this machine, soda water became widely available to the public. Soon after, flavored syrups were created by crushing up fruits or nuts, and soda fountains were set up along main streets and in local pharmacies. Customers then could choose from dozens of flavors of this new beverage that was being sold by pharmacists as medicine. In 1885, a pharmacist in Waco, Texas, named Charles Alderton noticed that many of his customers could not decide which flavor to order, so he combined 23 of the flavorings available in his shop. The taste of a "Waco" (as customers dubbed it) was difficult to describe, although a hint of cherry could be detected. The mysterious blend became wildly popular and eventually was given its medicinal name, "Dr. Pepper." Other pharmacists followed suit and began developing name-brand sodas. Another soft drink was invented in Atlanta in 1886, when pharmacist John Pemberton combined caffeine-rich kola nuts, extracts from the coca leaf, sugar, and other secret ingredients to create what would become Coca-Cola (Vegesna, & Turlington, 2014).

By 2010, the average American was drinking about a gallon of soda per week, and the worldwide soda business was worth $290 billion (Vegesna, & Turlington, 2014). The bottling industry played an important role in the evolution of sugar-sweetened beverages, as new packaging methods continually were developed to meet consumer demands. Before the 1950s, the standard soft drink bottle was 6.5 ounces. In the 1950s, manufacturers introduced larger sizes, including the 12-ounce can, and by the early 1990s, the norm had shifted to 20-ounce contoured plastic bottles. Larger plastic bottles now are widely available; the 1.25-liter (42-oz) bottle was introduced in 2011 (Harvard School of Public Health Nutrition Source, 2012). These growing portion sizes for SSBs have changed what people think of as a "normal" portion, which can lead to increased caloric intake (Gortmaker, Long, & Wang, 2009).

Consistent with sugary drinks' medicinal roots, some types of SSBs still are believed to have certain health benefits. The carbonation in some types of soda, for example, could help relieve problems such as indigestion and nausea. Some fruit drinks contain vitamins and nutrients from real fruits; others are fortified with vitamins and minerals. Additionally, the caffeine present in many SSBs might be beneficial. There is evidence to suggest that long-term consumption of caffeine could reduce cardiovascular disease and diabetes, and short-term consumption can increase the metabolic rate. Caffeinated drinks that have not been sweetened with sugar, however, are likely to provide the same health benefits.

Gatorade—which most sources cite as the first sports drink—was invented by researchers who sought to formulate a beverage that would adequately replenish carbohydrates and electrolytes that athletes lost during performance (Yale Rudd Center for Food Policy and Obesity, 2012). Still, today, science does support the

notion that sports drinks rich in sodium and potassium can help to deliver carbohydrates to muscles, prevent dehydration, replenish mineral stores, and inhibit muscle cramping. The American College of Sports Medicine recommends consuming sports drinks when exercising strenuously for more than one hour. Sports drinks are not recommended for moderate or recreational activities, however; nor are they recommended for shorter bouts of activity (Passing the Sugar, 2007; Yale Rudd Center for Food Policy and Obesity, 2012). As sports drinks have become more popular and readily available, research shows that many people are consuming sports drinks when they do not need them; consequently, the extra sugar in these drinks contributes to health problems associated with excess caloric intake (Passing the Sugar, 2007; Yale Rudd Center for Food Policy and Obesity, 2012).

A large body of epidemiologic evidence and experimental research shows that consumption of SSBs is causally related to obesity; that is, a greater consumption of SSBs results in increased body weight in adults and higher adiposity in children. The USDA's recommended daily maximum of added sugars is 10 teaspoons per day for a 2,000-calorie diet. A typical 20-ounce soda contains 15 to 18 teaspoons of sugar, usually around 240 calories (Harvard School of Public Health Nutrition Source, 2012). It is hypothesized by many researchers that consumption of SSBs is linked not only with obesity, but other adverse health conditions, such as type 2 diabetes, dental caries, gout, cardiovascular disease, bone loss, and low nutrient levels.

In recent years, much controversy has arisen about the regulation of SSBs, especially regarding their availability to youth. As a response to the rising incidence of obesity in New York City, Mayor Michael Bloomberg led the effort in 2012 to amend Article 81 of the New York City Health Code. The amendment proposed to ban the sale of SSBs larger than 16 oz in many retail outlets, but was invalidated by the New York State Supreme Court just before it was about to go into effect in 2013. Another debate is whether vending machines selling SSBs should be present in schools. Vending machine proponents assert that SSBs are not the sole factor in the obesity epidemic, and also note that soft drink companies bring a large amount of funding to schools. Opponents of school vending machines maintain that schools have a responsibility to oversee the health of their students, and research has shown that children are consuming more SSBs than ever before. In 2004, SSBs amounted for an average of 124 calories per day (7% of their daily total) for children ages 2 to 5 years, 184 calories (9%) for children ages 6 to 11 years, and 300 calories (13%) for adolescents (Gortmaker, Long, & Wang, 2009); these figures are believed to be on the rise. Opponents of school vending machines also note that children need help making healthy choices because they are not always informed consumers and can be swayed by the companies selling sugar-sweetened beverages, which spend a half billion dollars annually on targeted marketing to children ages 2 to 17 years (Harvard School of Public Health Nutrition Source, 2012). Recently, however, the two largest soft drink businesses, Coca-Cola Co. and PepsiCo, have funded research to experiment with removing sugar from their drinks and replacing it with sweeteners made from plant extracts. The companies also have made the business decisions

to sell bottled water and juices with less sugar content than the non-diet versions of their soft drinks.

The Center for Science in the Public Interest—a nonprofit consumer advocacy group that focuses on nutritional education and awareness—has published reports emphasizing the harms of sugar-sweetened beverage consumption, criticizing soft drink companies' marketing strategies, petitioning the FDA to determine a safe level of added sugars for beverages, and urging lawmakers to pass SSB regulations (Center for Science in the Public Interest, 2012). In the United States and some other countries, legislators are considering increasing the taxes on SSBs. Opponents of taxation assert that taxing SSBs is a "slippery slope" that could lead to the taxation of other foods or drinks thought to be unhealthy. Those who support taxation refer to the scientific studies that have predicted how increased prices would reduce SSB consumption. Another key argument made by many supporters is that revenue could be used to fund health education programs and other projects to increase consumer awareness.

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See Also: Adolescence and nutrition; Carbohydrates; Childhood nutrition; Energy drinks; High-fructose corn syrup; Obesity, causes; Public policy on nutrition; Sports beverages.

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Supplemental Nutrition Assistance Program

The Supplemental Nutrition Assistance Program (SNAP) is an assistance program administered by the U.S. Department of Agriculture (USDA) to help low-income families pay for food. This program formerly was called the Food Stamp Program (FSP). Moving away from the idea of paper food stamps, SNAP now offers an Electronic Benefit Transfer (EBT) Card–a plastic card that can be used at stores for credit. Every family participating in the SNAP program receives a specific SNAP amount based on household size, expenses, and income (FNS, 2013a).

The Food Stamp Program was first started in May of 1939 by Henry Wallace, the Secretary of Agriculture. The Early Food Stamp Program (EFSP) allowed citizens to purchase orange food stamps at a reduced cost. For every orange food stamp that was purchased, the customer was given additional blue food stamps. Every $1 in orange stamps purchased would provide $0.50 in blue stamps. Blue stamps could only be used to buy foods that the USDA determined to be surplus. The purpose of EFSP was to reduce the surplus of food that was seasonally supplied by farms and to supply food to unemployed people. The EFSP program ended in 1943 when there no longer was a large food surplus (FNS, 2013b).

No program took the place of the EFSP until the Pilot Food Stamp Program was introduced in 1961. This program eliminated the surplus stamps and prioritized getting perishable foods to low-income families. Congresswoman Leonor Sullivan worked with Isabelle Kelley on a committee to pass this legislation. Isabelle Kelley went on to be the FSP director and first woman director in the USDA to head an action program. The pilot program ended in 1964 when President Johnson asked Congress to make FSP a permanent program.

The Food Stamp Program that is today known as SNAP was created by legislation passed in August of 1964. The purpose of FSP was to strengthen the agricultural economy and provide improved levels of nutrition to low-income households. The FSP grew to reach 15 million people by 1975 (FNS, 2013b). The Food Stamp Program changed its name to SNAP in 2008 to show the support of healthy nutrition. When the program changed to SNAP a new slogan was crafted, "Putting Healthy Food Within Reach" (FNS, 2013).

The USDA oversees SNAP, but each state receives funding from the USDA and is responsible for implementing this program. To be eligible for the SNAP program a person must have limited resources and meet certain income requirements. The monthly benefit received from SNAP is based on income and a variety of expenses. The allotment increases as the number of eligible family members increases. Benefits also increase if a person has high shelter expenses, medical expenses, expenses related to work, or tax expenses. Some adults only are eligible for SNAP benefits if they meet certain work requirements.

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See Also: U.S. Department of Agriculture; Women, Infants, and Children, Special Supplemental Nutrition Program for.

Supplemental Nutrition Assistance Program: Eligible Food Items

What are people allowed to purchase with their Supplemental Nutrition Assistance Program (SNAP) funds? The following are excerpts from the Food and Nutrition Service of the USDA website (http://www.fns.usda.gov/snap/eligible-food-items).

Households are permitted to use SNAP benefits to buy foods for members of the household to eat, such as the following.

- Breads and cereals
- Fruits and vegetables
- Meats, fish, and poultry
- Dairy products
- Seeds and plants which produce food for the household to eat

In some areas, restaurants can be authorized to accept SNAP benefits from qualified homeless, elderly, or disabled people in exchange for low-cost meals. Households may NOT use SNAP benefits to buy beer, wine, liquor, cigarettes, or tobacco, or any nonfood items including those listed below.

- Pet foods
- Soaps, paper products
- Household supplies
- Vitamins and medicines
- Food that will be eaten in the store
- Hot foods
- "Junk food" and luxury items

Soft drinks, candy, cookies, snack crackers, and ice cream are food items and therefore are eligible. Seafood, steak, and bakery cakes also are food items and therefore are eligible items.

Because the current definition of food is a specific part of the Act, any change to this definition requires action by Congress. Several times in the history of SNAP Congress had considered placing limits on the types of food that could be purchased with program benefits. Congress concluded, however, that designating foods as luxury or non-nutritious would be administratively costly and burdensome.

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Sustainable Agriculture

"Sustainable agriculture" is a fairly new term and is attributed to Australian agricultural scientist Gordon McClymont (Rural Science Graduates Association, 2002). Sustainable agriculture refers to an integrated system of agricultural practices that seeks to satisfy agricultural needs, limit environmental degradation, efficiently use natural resources, and economically sustain the farming community. The goal of sustainable agriculture is to produce profitable yields for farmers that minimize detrimental environmental and social effects, with the long-term hope that future generations will be able to continue farming and have sustained productivity.

History of Agriculture in the United States

Agriculture long has been a factor in human civilizations. Three main revolutions have occurred within the last 12,000 years that have changed farming practices (Muneeruddin, 2010). The first revolution was approximately 12,000 years ago, when humans began to rely on farming for sustenance. During this time, humans shifted from living mainly as nomadic groups of hunter-gatherers to settled farming populations. One benefit of farming was the ability to produce surplus crops, which supported larger communities and economic expansion. The second agricultural revolution occurred shortly after the Industrial Revolution, and was largely due to improved technology and demand to feed the world's growing population. The third agricultural revolution occurred in the mid 20th century, when new agricultural techniques were used to improve agriculture in developing countries.

Farms became an integral part of the North American landscape as colonists began to settle in the 17th century. Many of these were small family farms, which produced food for the family and local community. Larger plantation-style farms were common in the southern U.S. colonies. These farms had high yields and profits, but most of their crops were exported. Of the 4 million people living in the colonies during the late 18th century, nearly 90% were farmers (National Institute of Food and Agriculture, 2013).

The late 19th century and early 20th century saw significant improvements for farmers in North America. Many of these improvements were driven by the U.S. federal government, which wanted the country to expand westward and grow as a nation. In 1862, the federal government passed the Homestead Act, which granted federal land to citizens to promote farming and expansion. In

Clean Energy Farming

The Sustainable Agriculture Research and Energy (SARE) grants and education program promotes sustainable agriculture practices in a variety of areas. Some of the projects it sponsors support clean-energy practices on farms. The following information is from the bulletin, *Clean Energy Farming*.

A Missouri farmer found a solution for the waste fruit that remained after harvest—he distills it into clean-burning, high-octane fuel to power his farm equipment. A New Mexico farmer uses recycled solar panels to heat a new greenhouse, extending his season and nearly eliminating sky-high fossil-fuel energy bills that were threatening his family's 400-year-old farm. Using high-efficiency irrigation, a Texas rancher avoids expensive and energy-intensive pumping from Texas' ever-shrinking Ogallala Aquifer.

Across the country, as energy prices climb, farmers and ranchers are turning more and more frequently to clean-energy practices. From energy-saving lightbulbs to solar panels to fuel grown and processed on the farm, farmers are making their operations more profitable, efficient, and cleaner. In the process they are helping the nation. Generating renewable energy and using fossil fuels more efficiently reduces dependence on foreign oil, providing greater local and national energy security. It also curbs global warming and pollution and offers new economic opportunities for communities.

Clean Energy Farming explores this emerging trend in agriculture and explains how farmers can:

- Improve energy efficiency and save money;
- Implement farming practices that both save energy and protect natural resources; and
- Produce and use renewable energy.

A New Mexico farmer's solar-heated greenhouse, for example, can eliminate most fossil-fuel costs. Energy audits—such as those recently performed on 25 farms on Maryland's Eastern Shore—revealed potential total savings of almost $115,000 annually for the participating farmers.

USDA Sustainable Agriculture Research & Energy (SARE). (2012). *Clean energy farming*. Retrieved from http://www.sare.org/Learning-Center/Bulletins/Clean-Energy-Farming/Text-Version

the late 1800s, the U.S. Congress passed the Morrill Act and the Hatch Act, which established a land-grant university and experimental agriculture stations in each state. The mission of the universities was to teach and study agriculture, and the experimental stations conducted scientific investigations dealing with agricultural issues. During this time frame, the number of farms increased from 2 million in 1860 to 6 million in 1905 (U.S. Bureau of the Census, 1975).

The most significant change to farming in the United States occurred after World War II. The two major factors that initiated these changes were mechanization on farms and government subsidies. The combination of these two factors encouraged farmers to increase the size and efficiency of their farming operations. The rapid mechanization of farms put strain on small farming operations that did not have the necessary funds to buy machinery or increase their labor forces. As a

result, successful farming operations increased in size and often specialized in fewer crops, and many small farms ceased production or were bought out by large farms. This trend has continued to the present, but is under increasing scrutiny as the ramifications of large-scale agriculture are becoming known. As of 1990, only 1.7% of the U.S. labor force was employed on farms, down from 38.8% in 1900 (NASS, 2009).

Why Sustainable Agriculture?

Understanding the history of agriculture is vital to understanding why some groups are trying to promote sustainable practices. Many of the challenges that farmers currently face are due to the two most recent agricultural revolutions. Although mechanization of farming and government subsidies have helped to improve agricultural yields and feed growing populations, these improvements also have had negative environmental and societal effects. Implementing more sustainable practices into farming could lessen these effects, ideally without reducing yields or profits.

Environmental Health

Modern agricultural techniques are harmful to the environment in a variety of ways. Common problems faced by farmers include soil erosion, limited water availability, greenhouse gas emissions, fertilizer usage, and pesticide usage. Soil erosion has become one of the greatest problems for farmers worldwide. Tillage of soil is the main contributor to soil erosion, and monocropping and fertilizer usage also exacerbate the problem. Water availability has become an issue due to the increased demand from large-scale farms. These farms require great amounts of water that are not often readily available. Farmers tend to rely on irrigation systems, which are typically unsustainable and can cause pollution of natural waterways. The EPA estimates that 70% of the pollution in the nation's rivers and streams is due to farming (Horrigan, Lawrence, & Walker, 2002). Greenhouse gas emissions from farming operations—both small and large—have been shown to be significant contributors to the levels of greenhouse gasses in the atmosphere.

Industrial agriculture relies on energy for mechanical operations, food processing, storage, and transportation (Sims, 2011). Large-scale farms have become reliant on chemical fertilizers to offset nutrient imbalances in soils due to overfarming. These fertilizers have been linked to eutrophication, water pollution, and elevated greenhouse gas emissions. Eutrophication—the enrichment of water with dissolved nutrients—has been one of the biggest problems associated with fertilizers due to the effects on fish and wildlife. A problem similar to fertilizer usage is pesticide usage. Pesticides have been linked to numerous environmental hazards. Their harms first gained public attention with the publication of Rachel Carson's *Silent Spring* (Carson, 1962). The book brought attention to the effects that DDT and other pesticides had on ecosystems. Most notably, Carson highlighted the significant declines in bird and fish populations in New England. Many of these environmental issues with modern agriculture have been largely ignored because

of the consistently high yields from farms. Remarkable strides have been made in sustainable agriculture, however, to address many of these issues.

Human Health

Since the first agricultural revolution 12,000 years ago, farming has been the main source of nutrients in the human diet. The types of food produced and the methods by which they are produced have greatly changed since then, but agriculture always has been a vital factor to the well-being of populations. One of the biggest challenges in human health today is providing adequate nutrients to the world's population. Economic inequality is the main reason behind the nutritional imbalance faced around the world. An estimated 2 billion people in the world are undernourished (lacking vital macro- and micronutrients) and another 1 billion are overnourished (consuming excess nutrients) (Foresight, 2011). Global nutritional imbalance is a concern for sustainable agriculture, because it indicates that resources are being wasted or improperly managed. Better management of agricultural yields would improve nutrition, and also would enable farming operations to be more efficient.

Aside from nutritional imbalances, human health also becomes a factor in agriculture with regard to chemical, antibiotic, and hormone usage on farms. As noted, chemical pesticides have had detrimental effects on wildlife populations. Equally important, however, are the effects on human health. Pesticides have been shown to affect the nervous and endocrine systems, in addition to being potential carcinogens (U.S. EPA, 2012). Industrial agriculture also has become reliant on antibiotics and hormones for beef and dairy production. Overuse of antibiotics in livestock is dangerous due to the potential for bacteria to become resistant to the antibiotics. Overuse also weakens the ability of the immune system to deal with dangerous bacteria. Lastly, hormone usage in livestock has been controversial due to the potential carcinogenic effects in humans.

Local Economies

A concern that has been echoed for the past century is the decline in farm employment. The transition from small family farms to large industrial farms and the increased use of machinery over the past century has caused a significant decline in the number of people working on farms. Another trend that has affected local economies is the buyout of small farms by large corporations. When these small farms are bought out, they begin to contribute to the monopolization of farming. Local economies are affected as fewer people are required for agricultural work. The exception is seasonal labor, often performed by migrant workers who do not reside in the local communities. Many small towns in agricultural areas have experienced a declining population over the past several decades.

The connection between communities and local farms is drastically different than it was when farming began in North America more than 300 years ago. Even just since 1900, changes in farming practices have caused a division between food

sources and food markets. It has been estimated that fresh produce in the United States travels nearly 1,500 miles before being purchased by the consumer (Hendrickson, 1994). Much of the money consumers spend on food goes to companies outside of their local communities.

Strategies for Implementing Sustainable Practices

Scientists and farmers have begun to work together in many communities to implement more sustainable techniques to limit the harmful effects of large-scale agriculture. With the help of funding from the government and nongovernmental organizations, scientists are researching ways in which agriculture can become more sustainable and continue to produce high yields and profit for the farmers. Scientists and farmers have found that reverting to preindustrial farming techniques can cause significant environmental improvements and also can reduce costs.

Environmental Health

The issue of soil erosion has been dealt with in a variety of ways. Many of the more sustainable techniques are simple and date back to preindustrial farming. Farmers are encouraged to minimize tillage, maintain permanent soil cover, and rotate crops regularly. To deal with the issue of water availability, farmers are encouraged to limit or eliminate irrigation. Although this might be difficult for larger farming operations, farmers are encouraged to utilize natural water reservoirs and raise crops that are able to grow with the available water supply. Limiting irrigation not only will better manage water usage, but it also will help to protect nearby rivers and water bodies from pollution. The issue of greenhouse gas emissions is more difficult to solve, because emissions come from a range of sources. Incorporating more fuel-efficient machinery, reducing transportation distance to food distributors, and reducing the use of chemical fertilizers all help to reduce greenhouse gas emissions (Sims, 2011). The issue of chemical fertilizers and pesticides has been one of the most controversial issues of large-scale agriculture. Many different techniques have been used to replace or limit the use of these substances, including integrated pest management, diversification of crops and livestock, and use of crop and livestock breeds that are well adapted to certain environmental conditions and pests.

In general, farmers are encouraged to consider reverting to older farming techniques to reduce the impact of intensive agriculture. Realistic and often overlooked techniques include selecting crops that are adapted to local conditions, diversifying crops and livestock, implementing long-term crop rotations, and taking advantage of natural climate cycles.

Human Health

Worldwide malnutrition often is blamed on a lack of good nutrient sources, but a greater problem actually is the distribution of food throughout the world. Developed

countries are plagued with overnutrition, which often leads to high rates of obesity, cardiovascular diseases, and diabetes. Developing countries face the problem of undernutrition, which leads to stunted growth, anemia, vitamin deficiency, kwashiorkor, and marasmus. Kwashiorkor and marasmus are two of the most serious nutritional problems that developing countries face. Kwashiorkor results from a diet deficient in protein but adequate in total energy intake, whereas marasmus results from inadequate energy intake. These problems can be remedied through better management of agricultural yields, which would also help to reduce food waste and costs due to transportation and storage.

Even though farms in North America produce a surplus of nutritious fruits, vegetables, and meats, many of these foods do not make it to American dinner plates. Much of the yield from American farming goes toward livestock feed or into processing plants to be made into less nutritious food products. Nutrition education programs often attempt to encourage consumers to choose fresh, local fruits and vegetables rather than processed foods high in added sugars and fats. One way to mitigate this problem is through farmers markets and farm-to-school programs. Farmers markets work with local farmers to bring fresh fruits and vegetables to local communities. These markets often have fresh meats and dairy products as well. In addition to promoting small-scale farming, these markets reduce food transportation and storage costs. Farm-to-school programs use local farms as food suppliers for school meals, which helps to bring more nutritious foods to children. Demand for these types of programs has increased as the fight against obesity has strengthened. The number of farm-to-school programs increased to 2,571 in 2013 from 400 in 2004 (Martinez, 2010).

Local farming also has contributed to the availability of pesticide-free and hormone-free foods. Consumer demand for organic foods has increased as the potential dangers of pesticide use have become evident. Because small farmers are more in touch with their local communities and are able to listen to consumer demands, many have opted to incorporate organic farming techniques into their farms. Due to their lower transportation and storage costs, local farmers can offer organic products for reasonable prices to their consumers, Additionally, the reduction in transportation and storage decreases greenhouse gas emissions.

Local Economies

The push for sustainable agriculture in the United States has led to an economic boom for some local economies. As more small farms are created and larger farms revert to using less machinery, more workers are hired as farmhands. The reduction in processing, transportation, and storage costs also reduces the cost of food for consumers. Farmers markets also have had a significant impact on local economics. A state study released in 2010 estimates that more than $59 million was added to the Iowa economy as a result of local farmers markets (Otto, 2010). The farmers markets also added an estimated 574 jobs to the Iowa economy.

Challenges and Future Outlook

One of the biggest challenges in sustainable agriculture is persuading large-scale farms to change how they operate and ensure that sustainable practices are profitable. Large-scale farms have been consistently increasing yields and profits, so it is difficult to convey to these businesses why sustainable techniques are important. The transition to sustainable agriculture requires investment and management changes, which many industrial farmers are not willing to adopt. Additionally, skepticism about greenhouse gas emissions and their effects on the environment prevents many people from understanding the environmental concern.

Another challenge is government regulation of agriculture. Since the first Farm Bill was passed in the United States in 1933, the federal government has provided aid to farmers in the form of subsidies. Although these subsidies have helped farmers to make a living, they also have pushed farmers to grow certain types of crops. This pressure has caused many farmers to transition to "monocropping"—designating their farm to grow one specific crop. Monocropping is bad for agriculture because it worsens soil erosion and makes crops more susceptible to pests and disease. Fortunately, policymakers are becoming more aware of the flaws in the regulations on agriculture, and are attempting to resolve some of the issues. An updated Farm Bill is passed every five years to follow current trends and economic cycles.

The outlook for sustainable agriculture is positive. Since the environmental movement in the 1960s and 1970s, the general public has become more aware of environmental issues. Education and outreach programs have worked in communities to reinforce the importance of supporting local farmers and farm programs. Even though there is still a long way to go before sustainability goals are achieved, the movement has begun and efforts to expand sustainable practices are increasing around the world. Cooperation between farmers, communities, governments, and scientists is crucial for these goals to be met.

Riley A. Gage

See Also: Climate change, and food supply; Locavore movement; Organic food and farming; Public policy on nutrition.

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T

Taurine

Taurine is an amino acid that has an array of functions in the body and is a common component of energy drinks. It is present in nearly all animal cells, although it is particularly concentrated in the brain, retina, and heart. It can be synthesized by the body with the amino acids methionine and cysteine, and usually exists as a free molecule instead of binding to form proteins. The body uses taurine in multiple ways, especially in the development and proper function of the nervous system, in which it might play a role in modulating the inhibitory actions of neurons. It also is a component of bile, and helps to regulate the volume of cells, which could have implications for proper T-cell response in the immune system. Taurine also can act as an antioxidant. Taurine can be found in protein-rich foods such as beef, fish, and dairy products. It is found in breast milk and is a necessary additive in baby formula, as infants are not able to synthesize the molecule independently.

Research has led to the use of taurine supplements to help treat several cardiovascular issues including high blood pressure, high cholesterol, and congestive heart failure. Although studies have been small, the beneficial effects for congestive heart failure presently seem to be supported, as taurine appears to reduce congestive heart failure symptoms, such as breathlessness and fluid retention. Its protective role is thought to be related to preventing adverse effects caused by extreme fluctuations in calcium levels. Unlike caffeine, taurine in energy drinks has not been found to contribute positively to cognitive function. Further, taurine also appears to act more as a sedative than a stimulant, making its application in energy drinks tenuous. Taurine also has been suggested as a muscle-building supplement due to its cell-volumizing properties, but no conclusive evidence supports its use as an exercise aid.

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See Also: Amino acids; Electrolytes.

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Tea

Tea is an aromatic drink made from the infusion of *Camellia sinensis* leaves and boiling water. Tea has been consumed for more than 4,000 years and currently is the second most widely consumed beverage in the world (after water). Its history is complex, beginning in China and spreading to many cultures, each of which has adopted its own tea-drinking traditions. It comes in six main varieties—white, yellow, green, oolong, black, and pu-erh—depending on the amount of fermentation of the *Camellia sinensis* leaves. Green (unfermented) and black (completely fermented) are the most commonly consumed and studied. People have long believed in tea's medicinal qualities, and research suggests that drinking tea could reduce the risk of heart disease and cancer, in addition to boosting health in a broad range of other ways.

History

Legend traces the origin of tea drinking to Emperor Shen Nong. Legend says that in 2737 BCE, leaves fell from a *Camellia sinensis* shrub into the emperor's cup of boiling water. Upon drinking it, he declared that "tea gives vigour to the body, contentment to the mind and determination of purpose" (Saberi, 2010). In traditional Chinese medicine, green tea was used as a stimulant, diuretic, and astringent. In the 8th century, tea began leaving China via the Silk Road to Central Asia and the "Tea Horse Road" to Japan. The Japanese developed a religious tea ceremony and linked tea drinking to Buddhism, as it was thought to help monks focus during long hours of meditation.

As tea traveled, it evolved. During the Ming Dynasty (1368–1644), black tea was developed. By completely fermenting the leaves, black tea retained its qualities better than did green tea during the long caravan journeys. This variety became popular in Europe, after Dutch traders first imported it in the 7th century. Due to its bitter taste, Europeans viewed tea as medicinal and drank it to alleviate fever, headache, stomach ache, and joint pain. It spread from the Netherlands to France, Germany, and eventually to England, where for many years it was an aristocratic drink because it was more expensive than coffee. Colonists brought tea drinking to the United States, where it played a pivotal role in the American Revolution—the Tea Tax prompted the Sons of Liberty to dump vast quantities of



Leaves on a tea plant on the Gatoonga Tea Estate, 1 of more than 800 in Jorhat in Assam, India, where the plant was introduced during the first half of the 19th century by the British colonials. (AP Photo/Denis Gray)

tea into the Boston Harbor. After independence was won, tea drinking in America decreased dramatically because it was considered a British (i.e., unpatriotic) habit. Americans have since contributed to tea's ever-evolving nature, however, by serving it iced and sweetened.

Tea and Health

Both green and black tea consumption have been associated with a number of health benefits. Most of these health benefits are thought to come from organic chemicals known as "polyphenols." Certain polyphenols, called "flavonoids," are known for their antioxidant activity and ability to neutralize harmful free radicals. Green tea polyphenols include a variety of chemicals called "catechins." One of these, *epigallocatechin gallate* (EGCG), has received a great deal of research attention and has been used in dietary supplements of green tea extract. When tea undergoes fermentation, this oxidation process transforms green tea polyphenols into more complex polyphenols such as "theaflavins" and "thearubigins." The more the leaves are fermented, the less the polyphenol content and the greater

the caffeine content of the tea. Green tea, therefore, has the highest polyphenol content, and black tea has more caffeine than green tea has.

Some of the health benefits associated with all types of tea appear to be due its caffeine content. A cup of black tea contains about 15mg to 80 mg of caffeine. Additionally, a chemical in black tea, "L-theanine," enhances caffeine's effects. Caffeine improves alertness, increases metabolic rate, and promotes the use of fat as an energy source. Caffeine also might influence the function of neurotransmitters in the brain. Several studies have found that a higher consumption of green or black tea is associated with a reduced risk of developing Parkinson's disease.

Research suggests that components in green tea have a therapeutic effect on skin cells. The U.S. Food and Drug Administration (FDA) has approved a green tea extract ointment to treat genital warts, and preliminary studies are exploring its effectiveness in the treatment of cervical dysplasia, cellular changes that can lead to cervical cancer.

The EGCG studies have found that this compound might slightly enhance weight-loss efforts of overweight adults. The effect is small, however, and does not appear to result in long-term weight-loss maintenance. Nevertheless, researchers are interested in the observation that EGCG could exert its metabolic effects not only through increasing metabolic rate, but by also increasing the use of fatty acids for fuel.

Consumption of both green and black tea has been associated with cardiovascular benefits. The polyphenols in tea might lower the risk of coronary artery disease by improving endothelial function, combating atherosclerosis, and lowering cholesterol. A study conducted by the U.S. Agricultural Research Service found that blood lipid and lipoprotein concentrations decreased by 6% to 10% in adults with mildly high cholesterol, when served black tea and a healthy diet for three weeks (U.S. Department of Agriculture, 2014). "Good" cholesterol was unaffected. Despite analyses suggesting that 3 cups of tea per day can reduce the rate of heart attack by 11% (Ehrlich, 2010), the FDA has yet to allow manufacturers to declare that tea reduces heart disease risk due to a lack of credible evidence (some studies lack statistical significance or are weakened by confounding variables). A few small studies have found a reduced risk of stroke in tea drinkers as well.

Tea flavonoids also are being researched as potential anticancer agents. As antioxidants, flavonoids protect DNA and cell membranes from oxidation. Numerous studies have examined the relationship between green and black tea consumption and several kinds of cancer. These studies suggest that tea drinkers might receive some protection from cancers of the ovary, bladder, esophagus, lung, and pancreas. In many cases, researchers believe tea's antiangiogenic properties help "starve" tumors by inhibiting the growth of tumor-feeding blood vessels.

Risks of Consumption

Very few adverse effects have been found when tea is consumed in moderation. Excessive caffeine (more than five cups of tea or other caffeinated beverage per day, or less in people who are sensitive to caffeine) can lead to headache, nervousness,

insomnia, irregular heartbeat, nausea, tremor, and dizziness. Several reports of liver damage have been associated with consumption of green tea extracts, although it is not known whether the extracts directly caused the liver damage. Until the safety of these extracts is established, consumers should drink tea rather than use supplements to attain tea's health benefits. Tea could decrease the absorption of iron, so those with iron deficiency should consume tea between meals instead of with meals. Pregnant and nursing women should be cautious and people on medications should check with a doctor before adding tea to the diet, because interactions might exist.

Colleen Irby and Honor Hisame Hawkins

See Also: Caffeine; Polyphenols.

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Thiamin

Thiamin is one of the eight B vitamins, a family of compounds that also includes riboflavin, niacin, pantothenic acid, biotin, vitamin B6, folate, and vitamin B12. Thiamin also is known as vitamin B1, and can be spelled, "thiamine." Like other B vitamins, thiamin is water soluble and enables the body to convert carbohydrates into energy. It is essential for the metabolism of carbohydrates, branched-chain amino acids, and fatty acids, and for neurological functioning. Too little thiamin in the diet produces the deficiency disorders "beriberi," and a form of dementia known as "Wernicke-Korsakoff syndrome." Because thiamin is plentiful in the

food supply, deficiency is unusual except in people experiencing alcohol-induced or other forms of malnutrition.

History

In the late 19th century, a Dutch medical researcher Christiaan Eijkman noticed that prisoners in the Dutch colony of Java (now Indonesia) receiving primarily white polished rice as their food had higher rates of the disease called "beriberi" than the rates of the prisoners receiving brown rice. Early researchers sought for an infectious agent that might explain beriberi. Eijkman's experiments, however, confirmed a link between polished rice and health problems in young chickens. His research demonstrated that polished white rice lacked an important nutrient, a substance that could be found in the outer layer of the rice grain that was removed to create white rice.

Later research isolated the compound that prevented the development of beriberi, and the compound was named "aneurin," as it prevented the neurological effects that develop with the deficiency disorder. It later was renamed "thiamin." The thiamin molecule includes both a sulfur-containing and a nitrogen-containing ring. The vitamin is named for these structures, "thio" for the sulfur group and "amine" for the nitrogen group.

Deficiency

A lack of thiamin in the diet can lead to thiamin-deficiency disease, also known as beriberi. Its name originates from the Sinhalese phrase for "I can't, I can't." Beriberi is characterized by muscle weakness, poor arm and leg coordination, muscle pain in the calves, poor appetite, irritability, and nerve degeneration. Individuals can develop severe edema, trouble breathing, and, in some cases, an enlarged heart. Significant thiamin deficiency can cause brain damage, resulting in Wernicke-Korsakoff syndrome (WKS). Wernicke-Korsakoff syndrome is the combined presence of two disorders: Wernicke's disease, which is characterized by confusion, loss of muscle coordination, and vision changes; and Korsakoff syndrome, a condition resulting in memory loss. Most symptoms routinely are treated with high doses of thiamin, but chances of reversing the memory loss are slim.

Thiamin deficiencies can exist in individuals who suffer from malnutrition, Crohn's disease, or alcoholism (excess alcohol inhibits the body's ability to absorb thiamin). Thiamin deficiency also can occur among people with congestive heart failure, cancer, inflammatory bowel disease, and liver disease. Symptoms of thiamin deficiency include fatigue, irritability, depression, and abdominal pain.

Roles in the Body

Thiamin is found in the human body in several forms—free thiamin, and several phosphorylated forms including thiamin monophosphate, thiamin pyrophosphate (also known as "thiamin diphosphate"), and thiamin triphosphate. Like other

B vitamins, thiamin acts as a coenzyme in several biochemical pathways. A coenzyme enables an enzyme complex to function.

Thiamin pyrophosphate (TPP) participates in the conversion of pyruvate to acetyl CoA, an essential step in the metabolism of carbohydrates to produce energy. In this process, TPP assists in the process of decarboxylation, in which a carboxyl group (COOH) is removed from pyruvate. Thiamin pyrophosphate also assists with decarboxylation in a step of the citric acid cycle, a chain of biochemical steps that produces energy from carbohydrates, fats, and proteins. (TPP helps decarboxylate alpha-ketoglutarate to produce succinyl-CoA.) Thiamin pyrophosphate participates in the biochemical conversion of amino acids to certain neurotransmitters, including glutamate and gamma-aminobutyric acid (GABA). Thiamin assists in metabolic pathways for fatty acid synthesis, plays an important part in muscle contraction, and helps transmit nerve signals.

About half of the body's thiamin is stored in the skeletal muscles; the remainder is found in the liver, heart, kidneys, and brain. Dietary sources of thiamin include whole grains, legumes, pork, egg, green beans, squash, orange juice, and soymilk. The Dietary Reference Intake is 1.1 mg per day for women and 1.2 mg per day for men. If supplementation is needed, thiamin is available in tablets, softgels, and lozenges; however, 50% to 90% of dietary B vitamins are absorbed by the body.

Health Benefits

Thiamin is used medically to control symptoms of WKS, alcohol withdrawal, and certain genetic diseases such as Leigh's disease (a rare neurometabolic disorder) and maple syrup urine disease (marked by errors of branched-chain amino acid metabolism). Given the relationship between thiamin and dementia seen in WKS, some research has suggested that large doses of thiamin could be beneficial in the treatment of Alzheimer's disease, but research in this area thus far has failed to support evidence of improvement in Alzheimer's symptoms with thiamin supplementation.

Toxicity

A tolerable Upper Intake Level has not been set for thiamin. Because it is water soluble, toxicity is rare because any excess thiamin is excreted rapidly in the urine. Adverse effects associated with thiamin due to dietary or supplemental intake have not been reported.

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See Also: Vitamins.

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Trans Fatty Acids

Trans fatty acids (also called "trans fats" and TFAs) are a type of fatty acid that occurs both naturally and as a result of the hydrogenation of vegetable oils. Most of the TFAs in the human diet come from food products containing hydrogenated or partially hydrogenated oils. Hydrogenation is a process used by food product manufacturers to make fatty acids in foods more saturated, and thus more stable at room temperature. This stability gives food products a longer shelf life. Foods with



French fries have long been a source of trans fats in the North American diet because of the partially hydrogenated oils often used in the frying process. These oils are fairly stable and can be reused in the frying process. (Edward J Bock/Dreamstime.com)

unsaturated oils as ingredients can develop a rancid smell and taste because the carbon-carbon double bonds in these fats are vulnerable to oxidation. Research suggests that people whose diets are high in TFAs have a greater risk of cardiovascular disease.

Most carbon-carbon double bonds in plant oils are found in what is called a "cis formation." A cis formation means that the hydrogens attached to the carbons forming the double bond are on the same side of that double bond, which causes a bend in the hydrocarbon chain. During the process of hydrogenation, hydrogen is added to vegetable oils and most of the carbon-carbon double bonds in the unsaturated fats are transformed to single bonds, because the carbons pick up additional hydrogen atoms. Sometimes the process is incomplete, however, and the carbon-carbon double bonds remain. Trans fatty acids result when the hydrogen atoms of this carbon-carbon bond undergo rearrangement and end up on opposite sides of the double bond. This is known as a "trans" formation. The goal of hydrogenation is not to produce TFAs, they simply are a by-product of the process. The trans formation removes the bend typically produced by the cis formation, which makes the fatty acid hydrocarbon chain straighter, and

Hydrogenation

Hydrogenation is the process of adding hydrogen to a molecule, which rearranges its chemical structure. Most often this occurs in organic molecules with a double bond between two carbons. The double bond becomes a single bond, leaving each carbon the opportunity to bind with an additional hydrogen atom. Although this phenomenon happens in nature, it also occurs as part of a synthetic process in the food industry using vegetable oils. Hydrogenated fats are desirable to the food industry because their bonds are not as easily broken by oxygen; therefore shelf life is extended and taste is preserved longer.

To initiate hydrogenation, oil must typically be heated to more than 150°C in the presence of hydrogen and a catalyst like nickel, copper, or platinum. The level of hydrogenation can be carefully controlled through manipulation of temperature, pressure, agitation, and concentration of the catalyst. A by-product of hydrogenation is the creation of a fatty acid structure called a "trans fatty acid," or "trans fat," in which a carbon-carbon double bond is not broken, but one of the hydrogens shifts position thus altering the shape of the fatty acid.

Due to the possible negative health effects of trans fat, the Food and Drug Administration now requires manufacturers to include all partially hydrogenated oils on the product ingredient label, as well as including the amount (in grams) of trans fats contained in a serving of the product. Some products claim to be free of trans fat but still list partially hydrogenated oils on the labels. Although misleading, this practice is legal because the FDA considers foods with less than 0.5g of trans fat per serving to be trans-fat free.

Brown, J. L. (2006). *Hydrogenated vegetable oils and trans fatty acids*. Penn State College of Agricultural Sciences Publications. Retrieved from http://pubs.cas.psu.edu/freepubs/pdfs/uk093.pdf

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structurally similar to a saturated fatty acid. (A saturated fatty acid has no carbon-carbon double bonds.)

Researchers do not know why a greater intake of TFAs is associated with increased risk of artery disease. The TFAs appear to increase blood levels of low-density lipoprotein (LDL) cholesterol, which is associated with increased development of arterial plaque. Because the relationship between TFA consumption and cardiovascular

Decreasing Trans Fat Intake

Public health and government organizations advise consumers to minimize their intake of trans fatty acids. Following is advice excerpted from the U.S. Centers for Disease Control and Prevention website (http://www.cdc.gov/nutrition/everyone/basics/fat/transfat.html).

Although trans fat intake has significantly decreased in the United States as a result of efforts to increase awareness of its health effects, "Nutrition Facts" label changes, industry efforts to voluntarily reformulate foods, and some state and local governments' restriction of its use in restaurants and other food-service outlets, Americans still consume on average 1.3 grams of artificial trans fat each day. Major contributors to artificial trans fat intake include fried items, snacks (such as microwave popcorn), frozen pizzas, cake, cookies, pie, margarines and spreads, ready-to-use frosting, and coffee creamers. The amount of trans fat can vary among similar food categories.

Trans fats also are found in restaurant and cafeteria foods that contain—or are prepared with—partially hydrogenated oil. Currently, only about 1 in 5 Americans (20%) lives where there are policies that limit the use or sale of foods that contain more than 0.5 grams of artificial trans fat per serving.

Reducing Artificial Trans Fat

- Read the Nutrition Facts label and ingredient list to compare foods.
- Choose products that contain 0 grams of trans fat.
- Check the ingredient list to determine whether there is any partially hydrogenated oil in the product.
- Products containing less than 0.5 gram of trans fat per serving can be labeled as having 0 grams of trans fat, therefore checking the ingredient list is important if trying to avoid all artificial trans fat.
- Make sure that low–trans fat foods are also low in saturated fat; look for foods containing 5% or less of the Daily Value. Foods that contain 20% or more of the Daily Value of these two components are high in fat.
- Use monounsaturated fat (canola and olive oil) and polyunsaturated fat (soybean, corn, sunflower oil) in recipes that call for fat.
- Eat a balanced diet that is rich in fruits, vegetables, whole grains, lean sources of protein, and low-fat or fat-free dairy products.

Centers for Disease Control and Prevention. (2014). *Trans fat*. Retrieved from http://www.cdc.gov/nutrition/everyone/basics/fat/transfat.html

disease has been documented in a number of studies, the U.S. Food and Drug Administration requires food products to include TFA amounts on their nutrition labels. As a result of this labeling and the public concern, many large food companies no longer use trans fats. Restaurants, too, often advertise that their food contains "no trans fats."

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See Also: Cardiovascular disease and nutrition; Fatty acids; Lipids.

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Triglycerides

Triglycerides are a type of fat found in the diet and in the body. Triglycerides are the primary molecule of fat storage in adipose cells. Triglycerides are composed of one molecule of triglyceride bound to three fatty acid chains. The human body naturally produces triglycerides from carbohydrates, fats, and proteins in the diet, especially when excess calories are consumed. Triglyceride levels in the blood often are tested to predict an individual's risk for developing artery disease. Coronary artery disease is the most common type of heart disease. In the United States, CAD is the leading cause of death for both men and women.

Triglyceride Levels

A normal blood triglyceride level is considered to be less than 150 mg/dL; borderline high is 150 to 199 mg/dL; high is 200 to 499 mg/dL; and very high is 500 mg/dL or greater (NIH, 2014a). A high triglyceride level can be caused by cirrhosis or liver damage, a diet low in protein and high in carbohydrates, hypothyroidism, nephrotic syndrome, and diabetes that is poorly controlled. Low triglyceride levels can be the result of a low-fat diet, hyperthyroidism, malabsorption syndrome, and malnutrition.

Blood Sample

A blood sample is needed to determine a person's serum triglyceride level. It is important to not consume any food 8 to 12 hours before the test, as food intake alters blood triglyceride levels. Certain types of medications can increase or decrease triglyceride measurements. Thus, it is important for the patient's primary

care provider to be informed about any medications that are taken. This also includes drugs and supplements that are available over the counter, as well. For the blood test to be as accurate as possible, a patient's primary care provider might ask the individual to refrain from taking certain medications before the blood test.

Never stop taking any prescribed medication without consulting with a doctor. The following drugs can increase triglyceride measurements: Beta blockers, cholestyramine, colestipol, estrogens, protease inhibitors, retinoids, thiazide diuretics, certain antipsychotics, and birth control pills. The following drugs can decrease triglyceride measurements: Ascorbic acid, asparaginase, clofibrate, fish oil, and statin medications (NIH, 2014a). Test results might not be accurate if the patient is pregnant. Talking to a primary care provider is an important step in understanding triglyceride levels. In addition to triglyceride blood level measurement, a primary care provider usually wants a complete fasting lipoprotein profile to learn more about the patient's cholesterol level.

Diet

The combination of diet and exercise can reduce a person's weight, triglyceride level, and cholesterol, which in turn reduces the person's chance of developing heart diseases. If people have high triglyceride levels, then it is important that they follow recommendations for a heart-healthy diet. A heart-healthy diet means consuming a plant-based diet with plenty of vegetables and fruits; reducing intake of red meat by replacing some servings of meat with plant sources of protein such as soy, whole grains, legumes, nuts, and seeds; limiting salt intake; avoiding food products with added sugars and fats; and consuming two or more servings of seafood per week, especially oily fish high in omega-3 fatty acids. Excess consumption of food products made from refined grains and sugars are especially likely to lead to high blood triglyceride levels, because the liver converts excess calories to triglycerides.

Exercise

Maintaining a regular exercise routine is important to a person's triglyceride levels and overall health. Adults should participate in moderate-intensity exercise every week for 2 hours and 30 minutes (CDC, 2014). A good strategy is to aim for 30 minutes of physical activity 5 to 7 days per week. For individuals who are overweight, losing 5 to 10 pounds is a great start toward reducing triglycerides (Mayo Clinic, 2012). Losing even a small amount of weight can lead to more healthful blood triglyceride levels.

Medications and Supplements

If healthful lifestyle changes are not sufficient to reduce triglycerides, then medications such as fibrates and statins can reduce triglycerides by lowering a person's low-density lipoprotein (bad) cholesterol (Mayo Clinic, 2012). As for supplementation, omega-3 fatty acid supplements are sold over the counter and might reduce

triglycerides. It is important to consult with a health care provider before taking any omega-3 fatty acid supplements because they could interact with other medications.

Susana Leong

See Also: Cardiometabolic syndrome; Cardiovascular disease and nutrition; Cholesterol; Fatty acids; Lipids; Lipoproteins; The liver; Marine omega-3 fatty acids; Obesity, definition and health effects.

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Underweight

People typically are considered to be underweight if their body mass index (BMI) is less than 18.5 kg/m^2, according to the World Health Association (WHO). The United States and Canada use the same categories for defining "underweight" as the WHO uses. Research shows that, statistically, a BMI in the underweight range is associated with poorer health than are BMIs in the healthy weight range (18.5 kg/m^2 to 24.9 kg/m^2), with lower BMIs considered more risky than those closer to 18.5 kg/m^2. In the United States, approximately 1% of adult men and 2.4% of adult women fall into the underweight category (Fryar & Ogden, 2012a). For children, determining whether a child is underweight also takes into account the child's age; children in the lowest 5% of BMI for their age group are considered underweight. About 3.5% of children and adolescents in the United States are underweight (Fryar & Ogden, 2012b).

Causes of Underweight

Many people have a somewhat low BMI simply because this is their inherited body type. Unless the underweight condition is accompanied by markers of poor health, it is usually not a medical concern. In children and adolescents, underweight is a cause for concern if it is an indicator of underlying health problems or eating disorders. In both children and adults, when underweight is the result of recent unexplained weight loss or is accompanied by undernutrition and health problems, then treatment should be considered. Underweight that is caused by undernutrition usually indicates inadequate intake of calories, protein, vitamins, and minerals. This condition puts an individual at risk for a number of health problems, including a compromised immune system, loss of muscle and bone tissue, and electrolyte imbalances. When underweight is characterized by a loss of lean body mass—as often occurs with aging and illness—frailty can be the result. Becoming frail predisposes a person to injury from falls, which can lead to fractures and other disabilities. Frailty is associated with a reduced quality of life, as the activities of daily living become more difficult. Sometimes underweight is caused by underlying psychological problems, such as eating disorders, orthorexia, or obsessive -compulsive disorders. Depression also can cause a loss of appetite and loss of interest in eating, and consequent weight loss.

Treatment

The first step to treating people concerned about underweight is to determine the causes of the underweight condition. If the weight is indicative of underlying health problems, these must be addressed along with appropriate nutrition therapy. Underweight people with medical disorders should meet with a dietician or other licensed nutrition professional to receive advice on improving nutrient intake using meal planning and possibly nutritional drinks and supplements. When underweight is associated with health problems that interfere with normal food consumption, underweight people might need to receive nutrition either through tube feeding (enteral nutrition) or intravenous administration (parenteral nutrition). People who are underweight because of psychological problems—such as depression or eating disorders—require psychological therapy in addition to nutrition therapy.

Dental and oral health problems can limit chewing ability. People who are missing teeth, have poorly fitting dentures, or have other chewing difficulties might need to choose foods that require less chewing. Swallowing difficulties are common in older adults, and make eating difficult or less pleasurable. People with swallowing difficulties could benefit from special therapy to improve their ability to chew and swallow food safely.

Otherwise healthy but underweight and frail adults should strive to increase their intake of nutrient-dense food and drinks, and exercise appropriately to conserve or build lean body mass. Exercise programs for underweight adults can improve muscle strength and flexibility, along with balance. Appropriate exercise programs reduce a person's risk of falling and make it easier for frail people to perform the activities of daily life. When underweight (or even normal weight) healthy people desire weight gain for aesthetic or athletic reasons, treatment usually consists of a combination of nutrition therapy accompanied by an exercise program to increase lean body mass.

Some underweight people have low levels of hunger and small appetites and have trouble eating a lot at meals. Presuming that the person is healthy, he or she might find that greater amounts of exercise can increase appetite and make eating more enjoyable. They also should eat more frequently throughout the day to increase calorie consumption.

Most people seeking weight gain desire to preserve or build muscle mass, so they should participate in a strength-training exercise program appropriate to their health and fitness levels. The foundation of weight gain is good strength training combined with increasing intake of high-quality calories. Some suggestions for people trying to increase energy and nutrient intake include the following.

- Assess current lifestyle and solve any problems that prevent adequate food intake. If a person is skipping meals or consuming meals that are too small, then a little organization and planning can help improve access to the desired foods and make more time for eating. Some people might require assistance with shopping and food preparation.
- Reduce feelings of stress, if stress interferes with appetite. People can learn to eat more mindfully and in a relaxing environment.

- Eat a good snack after exercise. Strength training stimulates muscle repair and growth. During recovery, the body replenishes muscle glycogen stores and rebuilds muscle fibers to make them bigger and stronger. Consuming some protein within 30 minutes of exercising allows recovery metabolism to work in high gear. Most people are not very hungry immediately after they exercise, therefore cool beverages such as smoothies and shakes could be the best options.
- Allow muscles at least 48 hours of recovery time to optimize muscle building. If people strength train nearly every day, then they must structure workouts to alternate muscle groups and include at least one rest day each week.
- Eat more food throughout the day. Individuals trying to gain weight should add more meals and snacks to their day, thinking of snacks as small meals. Clients probably must plan ahead to be sure good food choices are available when they need to eat.
- Choose energy-dense foods. People trying to gain weight should choose healthy calorie-dense foods as often as possible. They should choose chili or split pea soup, for example, rather than broth-based soups. Granola has more calories per bowl than puffy cereal. Beverages such as smoothies also are a great way to add calories.
- Add meal replacement beverages. People who are having trouble eating enough food can add meal replacement beverages to their diets. These beverages are high in calories and nutrition—and it usually is easier to drink calories than to eat them. Calories from meal replacement beverages are more expensive than the protein in food, and usually are unnecessary for young, healthy people with a good appetite.
- Read the labels on weight-gain supplements. These supplements often have unnecessary and even harmful ingredients added, such as hormones and caffeine.
- Consume some protein foods with each meal or snack. This recommendation is especially important for frail elders, who build muscle much more slowly.

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Research Issues

Adolescent athletes who want to gain weight—particularly for reasons associated with a particular sport—can follow the weight-gain recommendations described in this entry. A teenage boy, for example, might be told by a football coach to gain weight if he wants to join the team. Sometimes people achieve weight gain by adding too much adipose tissue, however, and end up with a lifelong weight problem. This is especially likely when overeating occurs at the time when adolescents stop growing. It is interesting to explore when weight gain is beneficial for sport participation, and the ways that weight gain can be best accomplished without resulting in an undesirable body composition.

See Also: Body mass index; Eating disorders; Energy balance; Enteral nutrition; Parenteral nutrition.

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Upper Respiratory Tract Infections

Upper respiratory tract infection (URI) is a general term used to describe an acute infection of the upper airway, and usually is referred to as the "common cold." The upper respiratory tract directs outside air to the trachea and the bronchi of the lungs for respiration to take place, and includes the sinuses, nasal passages, pharynx (throat), and larynx (voicebox). Transmission of organisms causing URIs occurs by aerosol, droplet, or direct contact with infected secretions and subsequent passage to the nostrils or the eyes. Spreading of URIs, therefore, occurs more commonly in crowded conditions. Upper respiratory tract infections can occur in specific areas of the respiratory tract by direct invasion of the respiratory epithelium and can result in a variety of symptoms and disease states. Diseases often accompanying URIs include sinusitis, a swelling of the tissues of the sinuses causing a stuffy nose; pharyngitis, when swelling occurs in the back of the throat (pharynx) between the tonsils and the larynx (the voice box); and bronchitis, which is a respiratory disease in which the mucous lining of the bronchial passages becomes inflamed causing coughing, difficulty breathing, and breathlessness.

The upper respiratory tract is the most common site of infection by pathogens because it comes in direct contact with the outside environment and is exposed to airborne microorganisms. Viruses cause most URIs, with the most common being the rhinovirus and influenza virus, but some can be caused by bacteria, such as group A beta-hemolytic streptococci and Streptococcus pneumonia, which cause bacterial forms of pharyngitis and sinusitis, respectively (Mossad, 2014).

Epidemiology

Acute respiratory infections account for 20% to 40% of outpatient treatment and 15% to 35% of inpatient attendance in general hospitals, and the common cold causes the most physician visits in the United States (Mossad, 2014). Adults develop an average of two to four colds annually, which can be complicated by acute otitis media (ear infections), tonsillitis, sinusitis, and lower respiratory tract infections (Mossad, 2014).

Linus Pauling and Vitamin C

Linus Pauling was a chemist who received the Langmuir Prize and the Nobel Prize in Chemistry for his work published in 1930 in the *Journal of the American Chemical Society*, titled "The Nature of the Chemical Bond." Pauling was only 30 years old (Offit, 2013). Pauling's publication introduced the idea of electron sharing, a novel concept that made even Albert Einstein say, "It was too complicated for me" (Offit, 2013). In 1941, Pauling published another paper in *Science* that single-handedly proved that sickle-cell anemia is caused by diseased hemoglobin that has a different electrical charge, impinging on the hemoglobin's oxygen-binding capability, and establishing the field of molecular biology. In addition to these and other groundbreaking scientific discoveries, Pauling was a peace activist beginning in the 1950s and continuing throughout World War II and the Vietnam War. He was awarded the Nobel Peace Prize in 1962 (Offit, 2013).

In 1966, Pauling's attention turned to the use of vitamin C to cure the common cold after he was encouraged by a friend to use the supplement (Offit, 2013). The chemist believed that the common cold would be a illness of the past, publishing the paper *Vitamin C and the Common Cold* in 1970, urging the public to take 3,000 milligrams of vitamin C daily (about 50 times the recommended dietary allowance). Sales of vitamin C to the public skyrocketed, but scientists failed to validate Pauling's claims in a laboratory setting. The "Linus Pauling Effect" has created a booming vitamin industry that continues to grow. In 2010, the vitamin industry grossed $28 billion, an increase of 4.4% from the year before (Offit, 2013).

Linus Pauling was persistent in his beliefs and went on to claim that high doses of vitamin C and other supplements could cure cancer and a myriad of other diseases including heart disease, mental illness, hepatitis, polio, cold sores, pneumonia, and burns (Offit, 2013). Researchers who have followed up on these claims do see Pauling's logic: If fruits and vegetables contain antioxidants, and people who consume more of them are healthier, then people who take supplemental antioxidants should be healthier. The research results obtained, however, generally found supplements to be ineffective at preventing the common cold and other diseases. The judgment and claims of the once exalted scientist became heavily scrutinized. Pauling's wife died of stomach cancer in 1981, and the chemist died of prostate cancer in 1994, at age 93 (Offit, 2013).

Nutrition and Upper Respiratory Tract Infections

Upper respiratory tract infections are caused not only by invading pathogens, but also by the failure of the body's immune system to eliminate the invaders. Dietary factors are significant modulators of immune function, with approximately 70% of the body's immune cells coming in contact with foods in the digestive tract (Forster et al., 2012). Many people in the United States—approximately 50%—get less than half the Dietary Reference Intake for many micronutrients, and deficiencies are known to impair immune function (Gibson et al., 2012). Although some micronutrient intake changes have been found to stimulate immune function, these improvements mainly have been observed in clinical laboratory settings, using nutritional supplements rather than nutrient-containing whole foods. The results of these studies often are mixed, and the scientific community often questions the validity of such research.

Vitamins

Vitamins are crucial to overall health and immunity, but the effectiveness of supplements in reducing URI incidence and symptoms is varied. Vitamins C and D are most often linked with immune function by the public and these vitamins are marketed as ways to stave off catching a cold or flu. Another marketed supplement is vitamin E, a lipid-soluble antioxidant also important for immune function, but so far there is no substantial research backing its efficacy for reducing cold incidence or symptoms (NCAAM, 2013). Vitamin A has also been linked to better immune function and vaccination responses, but these observations primarily have occurred in developing countries, where vitamin A deficiencies can be common (Schardt, 2014). In vitamin A supplemental trials that occurred in developed countries where vitamin A deficiencies are rare, no differences in cold incidence or severity were observed (Schardt, 2014).

The popular "cold-fighter" vitamin C is a water-soluble vitamin that affects several components of the human immune system, including the stimulation of both the production and function of leukocytes (white blood cells) (Higdon, Angelo, Frei, & Alexander, 2013). Leukocytes collect vitamin C, which can protect these cells from the oxidative damage that occurs during regular cellular metabolism and during the invasion of microorganisms. Total absorption of vitamin C occurs at doses of up to 200 mg at a time, and once plasma levels reach saturation excess vitamin C largely is excreted into urine (Higdon, Angelo, Frei, & Alexander, 2013). Supplemental vitamin C also increases urinary oxalate levels, a normal by-product of metabolism that can combine with vitamin C to form kidney stones. Whether an increase in urinary oxalate elevates the risk for kidney stones is not yet known, but those predisposed to kidney stone formation might want to avoid doses of more than 1,000mg per day (Higdon, Angelo, Frei, & Alexander, 2013). Vitamin C generally is considered safe, but high doses can lead to digestive disturbances such as diarrhea, nausea, and abdominal cramps.

It is widely thought by the general public that vitamin C boosts immune function, yet the human research performed to date has had conflicting results. A

review done in 2010 took the results from 29 clinical trials, involving more than 11,000 people, and found that taking vitamin C regularly in doses of at least 0.2 g per day did not reduce the likelihood of the subject catching a cold, but was associated with modest reductions in the length and severity of cold symptoms (NCCAM, 2013). In five trials that looked at people who were exposed to extreme physical stress (i.e., marathon runners, skiers, soldiers training in subarctic conditions), however, taking vitamin C led to half the number of colds experienced in the other trials (NCCAM, 2013). In trials performed on otherwise healthy adults, those who only took vitamin C when cold symptoms already had begun generally saw no decrease in the length or severity of URIs (NCCAM, 2013).

Basic research concerning the protective role of vitamin D in the immune system has shown that the vitamin acts on the innate immune system by increasing the production of cathelicidin antimicrobial peptide, which works within neutrophils and other cells of the body to clear away bacteria and strengthen epithelial barriers to infection (Linder, 2012). Observational studies have shown that there might be an association between rates of URIs and vitamin D deficiency, with the seasonal variation in vitamin D levels mirroring the seasonality of URIs (Linder, 2012). That being said, well-performed clinical trials using randomization and double-blind tactics that have been published by the American Medical Association found no significant link between vitamin D levels and the rates of URIs (Linder, 2012).

Minerals

Several nutritionally essential minerals—including zinc, selenium, iron, and copper—play important roles in the development and expression of immune responses. Zinc is required for both innate and adaptive immunity and, as is the case for many minerals, much of the knowledge of its immune functions comes about by studying nutritional deficiencies (Drake, 2010). Zinc deficiency, for example, impairs the system that functions to kill invading pathogens by direct cell rupture and promote phagocytosis of invading microorganisms or foreign particles by immune cells. Zinc deficiency also impairs components of innate immunity, including the ability of immune cells to generate oxidants and toxins that kill invading pathogens (Drake, 2010).

A systematic review performed in 2011 of 15 clinical trials using oral zinc medications that involved more than 1,300 people concluded that zinc helps to reduce the length and severity of the common cold in healthy people when taken within 24 hours after symptoms start (NCAAM, 2013). A general recommendation for using zinc has not been made, however, because the trials differed greatly in the amounts and forms of zinc used (lozenges, tablets, or syrup). The side effects of oral zinc usage can be nausea and adverse gastrointestinal symptoms, and long-term use can cause copper deficiency or even reduce immune function (NCAAM, 2013). Also, the use of intranasal zinc is not recommended after the FDA ruled in 2009 that its use is linked to anosmia (loss of the sense of smell) (NCAAM, 2013).

Selenium is another mineral that is required for the normal function of several enzymes within the immune system, including glutathione peroxidases that are key redox regulators and cellular antioxidants (Drake, 2010). Selenium deficiency can

impair numerous immune responses, including cytokine (cell-signaling molecules) expression, and antibody production, and even might enhance the progression of some viral infections such as URIs (Drake, 2010).

The last two prevalent minerals in immune function are copper and iron. Iron deficiency is the most prevalent micronutrient deficiency in the world, and it can result in impaired immune function due to the necessity of the mineral in the differentiation and proliferation of lymphocytes (a type of white blood cell) and in the generation of reactive oxygen species that kill pathogens. Unlike iron, the exact mechanism of copper action in immune function is not yet known. Studies have shown, however, that copper deficiency results in an abnormally low number of neutrophils (neutropenia) and white blood cells that are pivotal in mounting an immune response (Drake, 2010).

Other Alternative Approaches

Few alternative approaches besides vitamin and mineral supplementation for cold reduction have proven to be beneficial (NCAAM, 2013). Widely used complementary health approaches are the use of probiotics and of the herb echinacea (NCAAM, 2013). Probiotics are live microorganisms that aid in digestive and immune health by interacting with the GI tract and host microbiota. Despite a 2011 systematic review of 10 clinical trials involving more than 3,000 people that indicated probiotics might aid in the prevention of URIs, evidence that probiotics can help to prevent colds is weak and the experimental results have limitations (NCAAM, 2013). Also, little is known about the safety of long-term use of probiotics, as pointed out by the Agency for Healthcare Research and Quality assessment in 2011, although research is ongoing (NCAAM, 2013).

Echinacea refers to a group of flowering plants in the daisy family; the leaves, flowers, and roots of many of these species are used to make herbal medicines. This flower species is native to North America and was used in traditional herbal remedies by the Great Plains Indian tribes and early settlers (NCAAM, 2013). Echinacea is used to fight infections, especially the common cold and other URIs, as it is thought that it can help stimulate the production of chemicals that decrease inflammation and alleviate symptoms. Commercially available echinacea products come in many forms including tablets, juice, and tea.

Current scientific research on echinacea for colds is inconclusive due to the wide variance in products, preparations, and research methods (NCAAM, 2013). Overall, there is limited evidence that echinacea products might reduce the length or severity of colds (NCAAM, 2013). Four government-funded clinical trials indicated that echinacea did not reduce the length of severity of cold symptoms and did not reduce the incidence of URIs (NCAAM, 2013).

Whole-Food Therapy

Two studies concerning the consumption of whole foods were published in late 2012, linking healthy eating and immune function. Gibson and colleagues (2012) focused

on how fruit and vegetable intake impacts antibody production in response to the pneumonia vaccine (a mechanism to test immune function and disease prevention) in older populations. Older populations were focused upon because aging has been associated with changes in physiologic, social, and economic status, resulting in low fruit and vegetable intakes, disregulation of the immune system, and an elevated risk of infection. Participants were free to choose any fruits or vegetables to add to their diets, but were encouraged to eat a wide variety of produce. Results indicated that the group that ate at least five servings a day of fruits and vegetables (one serving was defined as 80 grams of fruit—about one apple, orange, or banana—or three-quarter cup of fruit juice, or three heaping tablespoons of vegetables) responded significantly better to the vaccine (Gibson et al., 2012). This was the first study to show an immunity-enhancing effect from a "free-choice" mixture of fruits and vegetables, rather from than dietary supplements. Although the mechanism of how fruits and vegetables might boost immunity is not clear (although it possibly could be due to an increased bioavailability of nutrients), this research highlights the possibility that a food-based approach could be more beneficial than using a supplement.

The second randomized study also examined an older population using both supplements and dietary intervention. Forster and colleagues (2012) instructed the dietary group to eat at least five servings of fruits and vegetables daily, fish twice a week, nuts at least once a week, and only whole-grain bread. The study included whole grains in the dietary group program because whole-grain bread and other whole-grain foods might improve gut health by promoting "good bacteria" and could have a beneficial impact on the immune system (Forster et al., 2012). The supplement group was given a capsule containing the same approximated nutrients as the dietary group received: 1,500 mcg beta-carotene, 2 mg vitamin E, 80 mg vitamin C, 2 mg zinc, and 25 mcg selenium. There also was a placebo capsule containing only cellulose that was given to a third group. Results indicated that the number of weeks in which URI symptoms lasted was significantly fewer in the dietary group than in the micronutrient or placebo groups during the six-month period of the study. The number of hospital visits, however, was significantly fewer for both the food and micronutrient groups than for the placebo group.

Supplements and Marketing

As the preceding evidence has documented, people who take vitamin or mineral supplements in well-conducted clinical trials do not become sick less often than do people in the control groups. Hundreds of products that contain these ingredients, however, claim to "support" immunity or "help with immune function" without having evidence to suggest that people who ingest them are less likely to get a URI. Such claims can be misleading for the public and are overused by many companies. Multivitamin brands, for example, make such claims (Schardt, 2014). In fact, since 2002, the three studies conducted on the use of these multivitamins which included a total of 2,150 middle-aged men and women found no difference in cold incidence or severity between the multivitamin-taking group and the placebo group (Schardt, 2014).

Products that contain high doses of vitamin C and other nutrients, such as "Airborne" and "Emergen-C," market themselves as a way to prevent and treat colds. Airborne toned down such claims after settling a false-advertising lawsuit in 2008 (Gordon, 2011), although the manufacturer denied any wrongdoing. The class action lawsuit originated after a clinical trial used by Airborne as proof that its product works was questioned in 2006 by individuals and the Center for Science in the Public Interest, which conducts periodic review of dietary supplements (Gordon, 2011). Airborne is now marketed as an "immune booster." Emergen-C also settled a class-action suit in 2014.

Companies can make such statements about immune function without proof because the Food and Drug Administration announced in 2000 that "supports," "maintains," and "enhances immunity" are claims that don't promise to help "prevent or lessen disease" and do not need to be backed by strong evidence (Schardt, 2014). Consumers interpret such claims, however, to mean enhanced protection against colds and other diseases, even if such promises are false.

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See Also: Echinacea; Iron-deficiency anemia; Selenium; Vitamin C; Vitamin D; Vitamin E; Zinc.

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U.S. Department of Agriculture

The U.S. Department of Agriculture (USDA) was established by President Abraham Lincoln on May 15, 1862. The mid-1860s marked a time when approximately 50% of Americans lived on farms, and farmers comprised 58% of the labor force. (Today, only 2% of Americans live on farms.) Lincoln's vision was to create a department to positively affect the lives of all Americans, by supporting farmers and agriculture. The USDA has grown and developed over the years. Today it has several mission areas, including the following (USDA, 2013a).

- Farm and Foreign Agricultural Services: The Farm Service Agency, Foreign Agricultural Service, and Risk Management Agency administer programs that strive to support American farmers and ranchers. Programs provide assistance for enhancing domestic production of agricultural products; marketing U.S. agricultural products to other countries; and credit, disaster, and emergency assistance.
- Food, Nutrition, and Consumer Services: The USDA provides nutrition aid programs and nutrition policy and education materials.
- Food Safety: The USDA administers food safety and inspection programs, as well as labeling and packaging regulations.
- Marketing and Regulatory Programs: The USDA helps set national and international standards for agricultural marketing. This agency also oversees animal and plant health inspection, and regulates meatpacking and stockyards.
- Natural Resources and Environment: The Forest Service and Natural Resources Conservation Service work to promote good land management and conservation practices.
- Research, Education, and Economics: The USDA generates research and reports that help guide policy, strategy, and regulation.
- Rural Development: Support for rural development includes economic support for water and sewage systems, housing, health clinics, and utilities in rural areas.

Food, Nutrition, and Consumer Services

The Center for Nutrition Policy and Promotion (CNPP) was established by the USDA in 1994 to improve the nutrition and well-being of Americans. Food and nutrition is one of USDA's programs and services. The Child Nutrition Programs; Expanded Food and Nutrition Education Program (EFNEP); Organic Program; Supplemental Nutrition Assistance Program (SNAP); and the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) represent different efforts of the USDA to foster a nutritious diet for all Americans (USDA, 2014).

- Child Nutrition Programs: These programs aim to increase healthy food options in school meals by increasing the availability of fruits, vegetables, whole grains, and fat-free and low-fat milk. The programs also strive to reduce sodium and saturated fat.
- Expanded Food and Nutrition Education Program (EFNEP): The goal of EFNEP is to improve food choices and physical activity behaviors among children and adults with limited resources in all 50 states, the District of Columbia, and six U.S. territories by using evidence-based research and practices.
- Organic Program: All farms, wild crop harvesting, and handling operations that are interested in having the USDA organic label on their agricultural products must meet the USDA's National Organic Program standards.
- Special Supplemental Nutrition Program for Women, Infants, and Children (WIC): WIC provides low-income pregnant, breast-feeding, non-breast-feeding postpartum women, infants, and nutritional-risk children up to age five with supplemental foods, health care referrals, and nutrition education.
- Supplemental Nutrition Assistance Program (SNAP): SNAP provides low-income households with debit cards to be used to purchase groceries.

Dietary Guidelines

Every five years, the USDA and the Department of Health and Human Services (HHS) update the *Dietary Guidelines for Americans*. The *Guidelines* target Americans ages two years old and older for education on five main issues (USDA, 2013b).

- Consuming fewer calories
- Making informed food choices
- Being physically active
- Reducing the risk of chronic disease
- Promoting overall health by maintaining a healthy weight

The most recent *Dietary Guidelines for Americans* is available for download at no cost directly from the USDA website, and will be released shortly after publication of this book.

The official 95-page *Guidelines* prove very informative. Chapter one introduces the *Dietary Guidelines for Americans, 2010*. Chapter two focuses on balancing calories to manage weight. Chapter three recommends foods and food components

to reduce. Chapter four recommends which foods and nutrients to increase. Chapter five includes information on how to build healthy eating patterns. Chapter six is a call to action chapter on helping Americans make healthy choices. There is a list of appendices of information on topics ranging from using food labels to track calories to recommendations for vegetarians.

MyPlate

The USDA's website ChooseMyPlate.gov (referred to as "MyPlate") is dedicated to helping Americans choose healthy options from the five food groups—fruits, vegetables, grains, protein, and dairy. MyPlate replaced the Food Guide Pyramid that was introduced in 1992, revamped in 2005, and discontinued in 2010. MyPlate shows a plate with a visual colorful indication of how much a person should consume from each food group arranged on a standard plate.

The ChooseMyPlate.gov website also includes information on physical activity, healthy eating tips, and other tools that encourage individuals to lead healthful lifestyles. It is a very interactive website, providing videos along with applications such as the "SuperTracker "to help individuals to plan, analyze, and track their diet and physical activity. The SuperTracker is available at http://www.choosemyplate.gov/supertracker-tools.html.

Controversies

Some critics have charged the USDA with conflicts between promoting and supporting American agriculture and also providing food guidelines, such as MyPlate. Concerns exist, for example, that (especially in the past) the USDA has promoted the dairy and meat industries by recommending milk, cheese, butter, and meat as healthful and nutritious for all. It has been recommended that food guidelines be moved to the purview of another agency, such as the Centers for Disease Control or National Institutes of Health.

Susana Leong and Barbara A. Brehm

Research Issues

Critics have charged that an agency whose mission includes the promotion of agricultural products could be influenced by special interests as it designs dietary guidelines. Some critics have suggested moving the design of dietary guidelines to a science-based department, such as the Centers for Disease Control and Prevention or the Institute of Medicine (Willett & Ludwig, 2011).

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See Also: *Dietary Guidelines for Americans*; Supplemental Nutrition Assistance Program; Women, Infants, and Children, Special Supplemental Nutrition Program.

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U.S. Food and Drug Administration

The U.S. Food and Drug Administration (FDA) is a federal agency within the Department of Health and Human Services. It monitors the manufacture, transport, sale, storage, import, safety, and efficacy of a variety of products in the United States, Puerto Rico, Guam, the Virgin Islands, American Samoa, and other U.S. territories. Its annual budget is more than $4 billion, and it has nearly 15,000 employees, including chemists, pharmacologists, physicians, microbiologists, veterinarians, pharmacists, lawyers, analysts, administrators, and other professionals.

In the 19th century—before the creation of the FDA—there was no federal agency overseeing the safety and quality of food, drugs, and related products. Instead, states exercised regulatory control over domestic foods and drugs, and imported foods were regulated at the federal level. The inconsistency of this system led to frequent adulteration, contamination, and false advertising of a wide variety of goods. Medications containing opium and cocaine were sold over the counter without warning labels or ingredient lists; and completely innocuous substances were marketed as the cure for various diseases and symptoms. Foods frequently were contaminated with toxic chemicals and colors. In 1862, the newly established Department of Agriculture created a Chemistry Division whose purpose was to analyze agricultural products, including food, soil, and fertilizer. Consumer protection was not the focus, however, until Harvey Washington Wiley became the chief chemist in 1883. In response to Wiley's efforts and the mounting public concern over the safety and quality of goods, Congress passed the Pure Food and Drugs Act in 1906, which prohibited interstate commerce in contaminated and misbranded food and drugs. In 1930, the agency's name was changed to the Food and Drug Administration, and its authority was extended through the

1938 Federal Food, Drug, and Cosmetic Act to cover a wider range of products and manufacturing standards.

Today the FDA is responsible for regulating products including the following.

- Food (excludes non-game meat and poultry, which are regulated by the U.S. Department of Agriculture)
- Beverages (excludes alcohol)
- Tobacco
- Cosmetics (although they do not require FDA approval before entering the market, the FDA researches products and acts when they are found to be harmful)
- Human and veterinary drugs (both prescription and nonprescription)
- Medical devices (from tongue depressors to pacemakers)
- Biological products (e.g., vaccines, blood, and tissue)
- Products that emit radiation, such as ultraviolet lights for tanning and medical imaging devices

The FDA plays a role in regulating the following items.

- Pesticides: The Environmental Protection Agency (EPA) regulates pesticides, but the FDA regularly tests food for elevated levels of pesticides.
- Water: The FDA regulates bottled water, and the EPA sets standards for local drinking water.
- Dietary supplements: Until 1994, dietary supplements were regulated similarly to foods. The Dietary Supplement Health and Education Act (DSHEA), however, gave the manufacturer the responsibility for assuring the safety, efficacy, and truthful labeling of dietary supplements. Once the product is available to consumers, the FDA is responsible for proving a dietary supplement unsafe if concerns arise.

The FDA regulates product labeling, but it does not regulate advertising, with the exception of tobacco, prescription drugs, and medical devices. The FDA also is responsible for inspecting manufacturing facilities of FDA-regulated items. If a product is found to be unfit for consumers, then three types of recalls can take place—products can be recalled by the company voluntarily; the FDA can request a recall; or the goods can be seized by the FDA.

Many critics have charged that the FDA should be more effective in its regulation of dietary supplements and food additives. Current regulations allow food and supplement manufacturers to collect data on ingredient safety; however, such studies often lack scientific rigor and are cursory, as manufacturers are more interested in getting products into the marketplace.

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See Also: Dietary supplements; Food additives; Health Canada; U.S. Department of Agriculture.

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U.S. Pharmacopeial Convention and USP-Verified Mark

The "USP-verified" insignia is issued by a nonprofit organization known as the United States Pharmacopeial Convention. The USP verification mark is meant to be a certification that assures consumers that a particular supplement or medication is safe for human use. The USP is not a government agency but an independent nonprofit organization composed of more than 450 practitioner, academic, government, industrial, science, and consumer organizations from around the world (USP, 2013a). The mission of the USP is to promote high standards of quality for medicine, food, and dietary-supplement products available to consumers. The USP's independent voluntary testing program has been especially valuable to people purchasing dietary supplements, as these are more loosely regulated by governmental agencies than are prescription medicines. The USP-verified mark on the label of dietary supplements indicates that the product contains the ingredients in the amounts listed on the label; does not contain harmful levels of certain contaminants; will dissolve in the body within a standard time; and was manufactured in accordance with FDA Good Manufacturing Practices with sanitary procedures (USP Verified Dietary Supplements, 2013).

The USP was founded in 1820, when a group of 11 delegates from state medical societies joined together to establish a national system of standards and quality control for medication as well as to compile a formulary of 217 widely known medications (USP, 2013b). A formulary is an official list describing medicines that can be prescribed. As time progressed, numerous revisions have been made to the original formulary, and the USP has established connections with government organizations such as the American Medical Association and the National Formulary

(NF) to compile all drug and therapeutic information into a single publication. Since 2002, the USP National Formulary publication has been issued annually.

Currently, through voluntary testing procedures, dietary supplement or pharmaceutical companies can opt to have their products tested by the USP so that the company may include the "USP-verified" statement on their product labels. It is important to note that merely seeing the word "USP" on a product label is not confirmation that the product's company has opted for voluntary testing. Only when the product label indicates that a product is "USP-verified" does it mean that the product has been extensively tested by the USP. During testing, USP scientists evaluate whether a medication or supplement contains the amount of dietary ingredients indicated on package labels. They also test for the presence of contaminants such as lead, caffeine, and other substances. Scientists examine the rate at which a particular supplement dissolves in the digestive tract to ensure that the product is available for absorption. USP scientists also verify that the product is manufactured according to good manufacturing practices.

Various sources have confirmed that there can be great discrepancies between the concentration of ingredients listed on dietary supplements and the amount of ingredients in the actual product. A recent study, for example, found that of 55 different vitamin D supplements, the levels of vitamin D could differ by 9% to 146% from the values that were stated on the supplement labels (LeBlanc, Perrin, Johnson, Ballatore, & Hillier, 2013). Additionally, these discrepancies not only occurred between different brands or bottles of supplements, but great variation was found in the vitamin D levels of individual pills within the same bottle of supplements (Mann, 2013). These results underscore the importance of the USP's work.

Consumers should note, however, that the USP verification mark on a dietary supplement label is only the first step in ensuring the safe use of supplements. Any dietary supplement potentially could interact with other supplements or medications a person is taking. Supplements might not actually be effective for their labeled health claims, and side effects could occur. Consumers must research the dietary supplements they are taking, and speak with a knowledgeable health care provider, especially if supplement-medication interactions might be a problem.

Mia Copeland-Brock

See Also: Dietary supplements.

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V

Valerian

Valerian is an herb most commonly used to help treat sleep disorders, as an alternative to prescribed medications. It comes from a perennial plant (*Valeriana officinalis*) native to Europe. The valerian supplement is made from the plant's roots, which can be dried and prepared as teas, made into extracts and put into capsules, or incorporated into tablets. Valerian also can be pressed into a fresh juice, or freeze-dried to form a powder. Although best known for its use as a sleep aid, valerian sometimes can be helpful in treating anxiety and restlessness.

Valerian has been used since the time of ancient Greece and Rome, when Hippocrates described its usefulness. Galen, a famous physician from the 2nd century, recommended valerian to treat insomnia. In the 16th century, valerian was used to treat nervousness, trembling, headaches, and heart palpitations. During World War II, its calming properties were found to be beneficial in England to reduce the stress caused by air raids.

Valerian seems to be a gentle and fairly safe sleep aid. Although scientists are unsure of the exact mechanisms exerted by valerian in the human body, the herb appears to increase the amount of a chemical called "gamma aminobutyric acid" (GABA) in the brain. Gamma aminobutyric acid helps regulate nerve cells and has been shown to promote feelings of relaxation and to reduce anxiety. Evidence suggests that valerian generally helps people fall asleep faster, and their quality of sleep is improved. The sedating effects of valerian are milder than those of prescription medications for insomnia, and people taking valerian report fewer side effects (such as morning drowsiness) than they report with prescribed sleep aids. People trying to decrease their reliance on prescription sleep aids sometimes use valerian to cope with increased insomnia during the withdrawal process.

Valerian seems to be most effective for people with insomnia if it is taken 1 to 2 hours before bed. If taken in tea, it is recommended that one teaspoon of valerian be mixed with one cup of water and allowed to steep for five to ten minutes before drinking. For the dried powder product, 250mg to 600 mg is recommended to help treat insomnia. For anxiety, 200 mg is recommended to be taken three or four times a day (UMMC, 2011).

Because of its sedating effects, valerian should not be taken with alcohol or other sedative preparations, including supplements such as melatonin, SAMe, and St. John's wort. People should not operate machinery or drive after taking valerian.

Although taking valerian seems to be generally safe, experts advise that children and nursing or pregnant women should not take valerian. Valerian has not been known to cause dependency or withdrawal problems. It is best to stop taking valerian over a gradual period, however, rather than eliminating its use all at once. Valerian could have side effects in some people, including (ironically) causing restlessness and insomnia. Long-term studies of valerian's safety are lacking, so only short-term use (4 to 8 weeks) currently is recommended.

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See Also: Dietary supplements.

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Vanadium

Vanadium is a toxic transition metal that is used to strengthen metal alloys such as steel. Due to the array of colors present in vanadium compounds, Nils Gabriel Sefstrom named the element after the Norse goddess of beauty, "Vanadis," in 1930. It is present in 65 minerals as well as fossil fuels and occurs most commonly as a part of the compound "vanadium pentoxide." Vanadium-containing compounds also are used to purify uranium for its use in nuclear power. Vanadium is present in trace amounts in food, particularly mushrooms, shellfish, and grain products. In North America, its daily intake is estimated to be from 10 μg to 60 μg per day. After ingestion, vanadium primarily is drawn to the kidneys and, to a lesser extent, the spleen, liver, and bones of humans. Vanadium is an essential nutrient for some species such as rats and chickens, but its precise roles in human metabolism and health have not been firmly established, and no deficiency disorders have been observed in humans. Vanadium is considered an ultratrace mineral, and probably is essential for human health, but needed only in very small amounts.

Vanadium appears to reduce blood sugar levels in animal models, and has been investigated for use as a therapeutic agent for treatment of diabetes. Although there have been a few somewhat promising results in human trials, however, overall the evidence for a beneficial effect is weak. Vanadium doses effective in animal models could be toxic to humans.

Because of its purported insulin-like action, vanadium has been added to body-building supplements, because insulin also enhances protein anabolism. One small study examining this effect in people found no muscle-building effects. Like other metals, vanadium is toxic at high doses, and could cause liver and kidney damage. Some researchers have expressed alarm at the addition of vanadium to supplements (Nielsen, 2006). Similarly, vanadium has shown anti-tumor effects in vitro for human cancer cells, but also could act as a carcinogen. Vanadium might act on cellular pathways that initiate inflammation, and is an acknowledged producer of reactive oxygen species, although its long-term biochemical effects remain largely unknown. The upper limit for vanadium intake is 1.8 mg per day.

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See Also: Minerals.

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Vegetarian and Vegan Diets

People who avoid consuming certain groups of animal products are known as "vegetarians." Different types of vegetarianism include the following.

- Lactoovovegetarianism, diet includes dairy products and eggs, but excludes all meat and fish products.
- Lactovegetarianism, diet excludes all meat, fish, and egg products, but permits dairy products.
- Ovovegetarianism, diet excludes all meat, fish, and dairy products, but allows eggs.
- Veganism, diet excludes all meat, fish, and products of animal origin.

Vegetarian-based diets allow some meat and include "pescetarianism," which excludes only meat products but permits seafood; and "flexitarianism" or "semi-vegetarianism," which sometimes excludes meat. "Omnivores" tend not to exclude any food groups.

Vegetarianism in recorded history dates back at least to ancient Egypt near 3200 BCE. Most world religions have a sect that advocates a vegetarian diet, and between 2% and 5% of the population in Western cultures is vegetarian. Women are twice as likely as men to be vegetarians. Motivations for a vegetarian diet include health and nutrition, ethical, environmental, and religious reasons. Many people believe that a plant-based diet is more nutritious and can result in weight loss. Ethical reasons to abstain from eating meat products include avoiding cruel treatment and the killing of animals used as food. Additionally, raising meat is environmentally expensive, as animal foods require more resources to produce than are required to grow plants, and produces more atmospheric carbon gas. Certain religions encourage abstinence from meat, including some groups of Seventh-day Adventists and Buddhists. Many vegetarians cite a mixture of motivations as well as individualized reasons for their diets, such as economic and philosophical. Some vegetarians state that they simply do not care for the taste of animal products.

Nutrition Issues

A vegetarian diet is rich in many nutrients as compared to an omnivorous diet. A diet rich in vegetables and fruits usually results in a higher intake of fiber, nonheme iron (Fe^{3+}), magnesium, vitamin C, vitamin E and other antioxidants, and omega-6 polyunsaturated fatty acids (PUFAs). The absence of meat generally results in a diet lower in total fat, saturated fat, and cholesterol, and these consequences likely are beneficial. The vegetarian diet, however, tends to be deficient in some nutrients. The more restrictive the diet, the more careful people must be about food choices to avoid nutrient deficiencies. Depending upon which food groups are excluded, the vegetarian diet can result in a lower intake of heme iron (Fe^{2+}), zinc, calcium, vitamins D and B12, and omega-3 PUFAs (omega-3 polyunsaturated fatty acids).

Iron

Iron is an extremely important micronutrient for the transportation of oxygen through the blood. Heme and nonheme iron are the two types of bioavailable iron. Heme iron comes from animal sources and is readily absorbed by the human body. Nonheme iron comes from plant sources, is less bioavailable, and therefore is more difficult for the body to absorb than is heme iron. To improve the absorption of nonheme iron, vitamin C (ascorbic acid) should be eaten at the same time; vitamin C chelates with iron and aids in absorption. In addition to vitamin C, amino acids (proteins), citric acid, and hydrochloric acid chelate with nonheme iron. Conversely, phosphates, phytates (sources of phosphate), tannins, and oxalates (which are common in vegetarian diet) chelate with nonheme iron in ways that inhibit

absorption because the complexes formed are insoluble in the body. Phytates are found in whole grains, legumes, and soy products. Tannins are found in tea, coffee, and wine. Oxalates are found in spinach, rhubarb, and chocolate. The food additive EDTA (ethylenediamine tetraacetic acid) also binds to nonheme iron and inhibits its absorption. Dairy products and calcium in other foods and supplements also can inhibit nonheme iron absorption.

Vegetarians should increase their intake of nonheme iron, or ensure intake is adequate, because without it they could develop anemia, which means that the levels of healthy erythrocytes (red blood cells) are too low. Without iron, the blood cells cannot carry adequate oxygen. If anemia is left untreated it can lead to hypoxia (lack of oxygen) in the organs. To increase the intake of iron and decrease risk for anemia, vegetarians should consume foods rich in vitamin C and consider introducing an iron supplement. Although their diet puts them at a greater risk for iron deficiency in general, vegetarians have not been found to be more iron deficient than omnivores. Women of childbearing age are most at risk for iron deficiency, and should take extra care to maintain adequate iron stores.

Zinc

Zinc is a component of more than 50 enzymes in the body, and most are involved in metabolic pathways. Without enough zinc, these enzymes do not function properly. Similar to iron, zinc from animal sources is more bioavailable than is zinc from non-animal sources, and phytates and proteins inhibit absorption of zinc. Additionally, fiber—which tends to be higher in a vegetarian diet—inhibits absorption of zinc. Vegetarians tend to have less zinc than omnivores. Non-animal sources of zinc mostly are cereal products; therefore vegetarians should be sure to consume such products to ensure that the body has sufficient zinc levels.

Calcium and Vitamin D

Vegans in particular tend to have lower levels of calcium and vitamin D. Calcium is important in bone synthesis, and for maintaining high bone density. As with iron and zinc, absorption of calcium is reduced when consumed with oxalates and phytates, because they form insoluble forms of calcium. Calcium intake usually is sufficient in lacto-ovo vegetarians. Many dark green vegetables such as bok choy, broccoli, and kale contain calcium. Vegans with reduced calcium intakes can choose foods that are fortified with calcium, such as soy beverages, orange juice, and tofu.

Vitamin D is extremely important for supporting calcium metabolism. Without vitamin D, very little calcium is absorbed. In some locations, sunlight exposure provides a fully adequate source of vitamin D because the sun causes the body to convert cholesterol to vitamin D. People living in northern climates, however, might need to obtain additional vitamin D from foods or supplements. Vitamin D is found naturally in only a few foods, including oily fish and fish oils such as cod liver oil. Egg yolk, liver, and butter can contain some vitamin D, depending upon

the diet of the animals from which the foods originate. Vitamin D is added to milk and many dairy products, therefore lacto-vegetarians can obtain vitamin D from these sources.

Vitamin B12

Vitamin B12 is especially important for proper neurological function. It is involved in myelin synthesis, which protects the axon in nerve cells. Without myelin protecting the axon, the nerve cell and the nerve synapses die—this damage is irreversible. Although the body does not require much vitamin B12 to function (1 mg per day), it only is available from animal sources, and usually comes from bacteria in the intestine of the animal (although seaweed might be an analogue). Lacto-ovo vegetarians can receive vitamin B12 from eggs and dairy products. Vegans can obtain vitamin B12 from seaweed and some fungi (mushrooms). The body also conserves vitamin B12 in the intestines, thus serious deficiency usually is avoided in healthy, young vegans for a few years after the initiation of a vegan diet. Older adults could have more difficulty absorbing this vitamin, therefore older adults and long-term vegans should consider adding supplement or fortified foods to ensure adequate intake of vitamin B12.

Protein

Because meat is a concentrated source of protein, protein is often the new vegetarian's first concern. Fortunately, an adequate mix of essential amino acids (the building blocks of protein) can be obtained by consuming a wide variety of non-animal foods. Vegetarians who consume eggs or dairy products also obtain protein from these foods. Vegans can ingest sufficient protein by consuming a variety of grains, legumes, and seeds. Although certain amino acids are lacking or are low in each plant group, protein consumption typically will meet physiological need if foods from different groups are selected. For example, the amino acids lacking in grains are found abundantly in legumes.

Long-Chain Polyunsaturated Fatty Acids

Theoretically, another concern for vegetarians is their relatively low intake of the long-chain omega-3-polyunsaturated fatty acids "eicosapentaenoic acid" (EPA) and "docosahexaenoic acid" (DHA). Higher intakes of EPA and DHA are associated with reduced levels of systemic inflammation in the body and slower rates of blood clotting, thus reducing the risk of heart attack and stroke. These PUFAs commonly come from fish in an omnivore's diet, although they sometimes are found in eggs, depending upon the chicken's diet. Vegans might have no long-chain omega-3 PUFAs in their diet. Although vegans and other vegetarians have low tissue levels of these PUFAs, they do not show signs of deficiency. Researchers have suggested, however, that their levels might not be optimal for good health (Saunders, Davis, & Garg, 2012). People do convert alpha-linolenic

acid (ALA) to long-chain omega-3 PUFAs, although it is unclear whether conversion rates result in optimal EPA and DHA supplies. Alpha-linolenic acid is plentiful nuts, canola oil, ground flaxseed, and chia seeds. The ratio between the intake of omega-3 to omega-6 PUFAs appears to contribute to the health benefits associated with higher levels of long-chain PUFAs. The most common PUFA in the Western diet is linoleic acid, found in vegetable oil, which is an omega-6 PUFA. A vegetarian diet generally is high in omega-6 PUFAs, which provides a less-than-optimal ratio of omega-3 to omega-6 PUFAs. Some experts have recommended that vegetarians consider supplements derived from algae to provide EPA and EPA. As noted, the concern about PUFA ratio mostly is theoretical, as vegetarians do not appear to suffer from higher levels of inflammation or thrombosis than that of omnivores. This might be because many helpful phytochemicals found in plant foods have anti-inflammatory and antithrombotic effects.

Health Effects

Simply eliminating animal foods from a diet does not automatically make it a healthful one. Exchanging servings of meat for french fries and milkshakes, for example, does not reduce calorie or fat content, and adds excessive carbohydrates. When diets are well planned, however, vegetarianism has been associated with decreased risk for several chronic illnesses and disease markers.

Vegetarians tend to have better cardiovascular health, including lower blood pressure and lower rates of coronary artery disease. These benefits could be attributed to the high-fiber and high-phytochemical content of a well-planned vegetarian diet, as well as to the diet's reduced saturated fat and cholesterol content. People consuming vegetarian diets tend to show a lower risk of type 2 diabetes, probably associated with their lesser rates of obesity.

Observational studies have linked a diet rich in fruits and vegetables and whole grains to a lower risk of developing cancer. A study comparing Seventh-day Adventist subjects who consumed a variety of vegetarian and omnivorous diets concluded that vegetarian diets are associated with reduced cancer risk (Tantamango-Bartley, Jaceldo-Siegl, Fan, & Fraser, 2013). Vegan diets were associated with lower overall cancer risk, and lower risk for female-specific cancers. A lacto-ovo vegetarian diet was associated with a decreased risk for cancers of the gastrointestinal tract.

Although vegetarianism generally is associated with better physical health, it presently is not possible to conclude that it improves mental health. Some researchers have suggested that vegetarians could have a greater risk for depression, possibly because of lower levels of B12 and long-chain omega-3 PUFAs (Michalak, Zhang, & Jacobi, 2012). Research in this area is preliminary, however, and although some studies have found higher rates of depression in vegetarians, other research has found the opposite (Beezhold & Johnston, 2012).

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Research Issues

One of the possible problems with vegetarianism is that it can serve as a mask for restrained or disordered eating. Younger female vegetarians sometimes are motivated to adopt a vegetarian diet to lose weight. Some adolescents use a vegetarian diet to justify eating less at meals and to explain weight loss. An eating disorder should be suspected when vegetarianism occurs in conjunction with a preoccupation with appearance, food, and weight.

See Also: Amino acids; Cancer and nutrition; Cardiovascular disease and nutrition; Depression and nutrition; Fatty acids; Iron; Iron-deficiency anemia.

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Vitamin A

Vitamin A is a fat-soluble vitamin composed of unsaturated hydrocarbons. Like all vitamins, vitamin A is an organic compound that is necessary in small amounts for normal growth, development, and maintenance of basic functions in the human body. Unlike water-soluble vitamins, which are excreted from the body when not

used, fat-soluble vitamins are stored in the liver and the fatty tissues. Vitamin A comes in two different forms, "preformed vitamin A" and "provitamin A." Preformed vitamin A is found in animal products in the form of retinoids. Retinoids are a group of chemical compounds that include retinol, retinal, and retinoic acid. Provitamin A is found in plant products in the form of carotenoids, which are a group of more than 600 plant pigments found in red, orange, and deep-yellow fruits and vegetables, as well as many dark, leafy greens (Higdon & Drake, 2009a).

Several forms of carotenoids can be converted into vitamin A in the human body, including beta-carotene, alpha-carotene, and beta-cryptoxanthin. Once ingested, both preformed vitamin A and provitamin A are metabolized into retinal and retinoic acid, which are the active forms of vitamin A. They are stored in the form of retinyl esters, mainly in the liver. Vitamin A is important for many bodily functions, including vision, immune function, growth and development, disease prevention, and skin and bone health. Both vitamin A deficiency and vitamin A toxicity can lead to health problems.

Background and History

For centuries, liver has been prescribed for those suffering from night blindness. References to this treatment are found in texts from around the world, including ancient Egypt, Greece, and China, as well as medieval Europe (Wolf, 1996). By the second half of the 18th century, researchers had determined that night blindness was caused by a nutritional deficiency, but vitamin A had not yet been identified.

The discovery of vitamin A began with research on the diets of mice by scientist G. Lunin in 1881. Lunin's mice had a much greater rate of survival when certain foods—such as whole dried milk—were added to their diet. In the early 20th century, researcher E. V. McCollum performed similar experiments that produced sickly, visually impaired animals. McCollum ultimately determined that the nutrient lacking from their diet was "fat-soluble factor A," now known as "vitamin A" (Wolf, 1996, p.1104). The role of vitamin A in vision, especially night vision, was discovered 1925 by observing the ability of rats to visually adapt when moving from light to dark areas. Research in the late 20th century began to uncover the effects of vitamin A on molecular function and gene expression (Wolf, 1996).

Physiological Functions and Deficiency Symptoms

Vitamin A plays many important roles in the body, some of which are well understood, and others less so. The most clearly understood is vitamin A's role in vision. In fact, the term "retinoids" comes from their importance to the retina. Vitamin A helps the eye see images, distinguish colors, and adjust to dim light. When light enters the eye, it enters through the cornea, travels to the lens, and then hits the retina. The light combines with retinal located in the retina, and this reaction sends a signal to the brain that is interpreted as an image.

Without vitamin A, vision deteriorates. Night blindness—the inability to see in dim light—is a common symptom of vitamin A deficiency. If vitamin A deficiency continues, then the cells along the cornea lose their ability to produce tears and mucus, which causes the eye to become dry. Dry eyes can be scratched by dirt and other particles, and the scratches can become infected. This condition is called "xerophthalmia," and the eye can develop a clouding of the cornea, ultimately causing blindness.

Vitamin A also plays an important role in the reproduction and growth of cells. Cell differentiation, the process through which immature cells develop into specialized cells, requires vitamin A. It is particularly important for epithelial cells, which line the lungs, digestive tract, eyes, and skin, and for immune cells called "T lymphocytes." Vitamin A deficiency, therefore, decreases the body's immune response. Vitamin A also plays a role in breaking down and building bone tissue, in reproduction, and in skin health.

Retinoids have been studied at length for their potential benefits relating to aging and skin problems such as acne. Skin creams and acne medication often contain vitamin A derivatives (vitamin A itself has no effect on acne). Some, such as "tretinoin" (better known by its brand name, "Retin-A"), are applied topically; others, such as "isotretinoin" (commonly known as "Accutane"), are taken orally. Because vitamin A can be toxic, these substances should be used only with the supervision of a physician. Accutane can cause severe birth defects if taken by the mother while pregnant.

Vitamin A supplements are not required for adults who maintain a balanced diet, although vitamin A can be helpful for the elderly and chronically ill individuals. Vitamin A deficiency (VAD) most commonly is found in people living in resource-poor countries where poor nutrition is a major health concern. Children and pregnant and lactating women are particularly at risk for VAD. The symptoms of VAD include night blindness, xerophthalmia, dry skin and hair, and a decreased ability to fight infection. Treatment for less serious cases of VAD involves a diet containing foods rich in vitamin A. More serious cases require high levels of vitamin A supplementation.

Dietary Intake Recommendations

The recommended daily intake of vitamin A is 900 mcg for adult men and 700 mcg for adult women (Evert, 2013). The majority of vitamin A ingested is absorbed in the intestine and travels with fats into cells; thus it is absorbed best when eaten with fat. Vitamin A is stored in the liver and fatty tissue until specific carriers transport it to where it is needed throughout the body.

The best sources of preformed vitamin A are animal liver and fish oils, and the best sources of provitamin A are leafy greens, orange and yellow fruits and vegetables, and tomato products. Whole milk is another good source of vitamin A. The process of creating reduced-fat milk removes much of the vitamin A; however, low-fat and skim milk often are fortified with vitamin A. Unlike water-soluble vitamins, fat-soluble vitamins are not lost through cooking. In fact, chopping

Table 1. Selected Food Sources of Vitamin A

Food	mcg RAE per serving	IU per serving	Percent DV*
Sweet potato, baked in skin, 1 whole	1,403	28,058	561
Beef liver, pan fried, 3 oz	6,582	22,175	444
Spinach, frozen, boiled, ½ cup	573	11,458	229
Carrots, raw, ½ cup	459	9,189	184
Pumpkin pie, commercially prepared, 1 piece	488	3,743	249
Cantaloupe, raw, ½ cup	135	2,706	54
Peppers, sweet, red, raw, ½ cup	117	2,332	47
Mangos, raw, 1 whole	112	2,240	45
Black-eyed peas (cowpeas), boiled, 1 cup	66	1,305	26
Apricots, dried, sulfured, 10 halves	63	1,261	25
Broccoli, boiled, ½ cup	60	1,208	24
Ice cream, French vanilla, soft serve, 1 cup	278	1,014	20
Cheese, ricotta, part skim, 1 cup	263	945	19
Tomato juice, canned, ¾ cup	42	821	16
Herring, Atlantic, pickled, 3 oz	219	731	15
Ready-to-eat cereal, fortified with 10% of the DV for vitamin A, ¾–1 cup (more heavily fortified cereals might provide more of the DV)	127–149	500	10
Milk, fat-free or skim, with added vitamin A and vitamin D, 1 cup	149	500	10
Baked beans, canned, plain or vegetarian, 1 cup	13	274	5
Egg, hard boiled, 1 large	75	260	5
Summer squash, all varieties, boiled, ½ cup	10	191	4
Salmon, sockeye, cooked, 3 oz	59	176	4
Yogurt, plain, low fat, 1 cup	32	116	2
Pistachio nuts, dry-roasted, 1 ounce	4	73	1
Tuna, light, canned in oil, drained solids, 3 oz	20	65	1
Chicken, breast meat and skin, roasted, ½ breast	5	18	0

Source: Originally "Table 2: Selected Food Sources of Vitamin A." U.S. Department of Agriculture, Agricultural Research Service. *USDA National Nutrient Database for Standard Reference, Release 24.* Nutrient Data Laboratory Home Page, 2011. National Institutes of Health. Office of Dietary Supplements (2013). *Vitamin A. fact sheet for health professionals.* Retrieved from http://ods.od.nih.gov/factsheets/VitaminA-HealthProfessional/

Notes

*DV = Daily Value. Developed by the U.S. Food and Drug Administration (FDA) to help consumers compare the nutrient contents of products within the context of a total diet. The DV for vitamin A is 5,000 IU for adults and children age 4 years and older. Foods providing 20% or more of the DV are considered to be high sources of a nutrient. The U.S. Department of Agriculture's (USDA) Nutrient Database website (http://www.ars.usda.gov/main/site_main.htm?modecode=12-35-45-00) lists the nutrient content of many foods and provides a comprehensive list of foods containing vitamin A in IUs and foods containing beta-carotene in micrograms.

RAE: Recommended dietary allowances for vitamin A are given as micrograms of retinol activity equivalents (RAE) to account for the different bioactivities of retinol and provitamin A carotenoids. Because the body

(*continued*)

Table 1. Continued

converts all dietary sources of vitamin A into retinol, 1 mcg of physiologically available retinol is equivalent to the following amounts from dietary sources: 1 mcg of retinol, 12 mcg of beta-carotene, and 24 mcg of alpha-carotene or beta-cryptoxanthin. From dietary supplements, the body converts 2 mcg of beta-carotene to 1 mcg of retinol.

Currently, vitamin A is listed on food and supplement labels in international units (IUs) even though nutrition scientists rarely use this measure. Conversion rates between micrograms RAE and IU are as follows.

1 IU retinol = 0.3 mcg RAE
1 IU beta-carotene from dietary supplements = 0.15 mcg RAE
1 IU beta-carotene from food = 0.05 mcg RAE
1 IU alpha-carotene or beta-cryptoxanthin = 0.025 mcg RAE

(From Otten, J. J., Hellwig, J. P., & Meyers, L. D. (eds.) [2006]. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*. Washington, DC: The National Academies Press)

An RAE cannot be directly converted into an IU without knowing the source of the vitamin A. For example, the RDA of 900 mcg RAE for adolescent and adult men is equivalent to 3,000 IU if the food or supplement source is preformed vitamin A (retinol). This RDA, however, also is equivalent to 6,000 IU of beta-carotene from supplements, 18,000 IU of beta-carotene from food, or 36,000 IU of alpha-carotene or beta-cryptoxanthin from food. Therefore a mixed diet containing 900 mcg RAE provides between 3,000 and 36,000 IU of vitamin A, depending on the foods consumed.

carotenoid-containing foods and cooking them in oil generally increases their bioavailability (Higdon & Drake 2009a).

Because vitamin A is important for cell growth and differentiation, research has focused on its potential role in cancer reduction or prevention. Studies, however, have yielded mixed results. In some cases, beta-carotene and retinyl palmitate supplements appear to correlate with lower levels of cancer, but other studies have not replicated these findings (NIH ODS, 2013). Vitamin A also can reduce mortality due to measles and pneumonia in children, as well as help prevent macular degeneration in aging populations (NIH ODS, 2013). The use of retinyl palmitate in sunscreen generated some concern when one study using mice showed that this vitamin A derivative could accelerate the growth of skin cancer; however, further research has not replicated this finding (Morison & Wang, 2014).

Excess intake of vitamin A, called "hypervitaminosis A," can result in a myriad of negative effects, including blurred vision, headache, irritability, nausea, loss of appetite, hair and skin changes, and mild fever. Excess alcohol consumption in conjunction with excess vitamin A supplementation can result in liver damage. The tolerable upper intake levels (UL) of vitamin A in adult men and women is 3,000 mcg per day (NIH ODS, 2013). Hypervitaminosis A can be caused by excess short-term or long-term consumption of vitamin A, generally in supplement form. Symptoms usually can be reversed without lasting effects by stopping the excess intake of vitamin A. The body converts beta-carotene into vitamin A as needed, therefore beta-carotene is a safe source of vitamin A.

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See Also: Beta-carotene.

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Vitamin B6

Vitamin B6, also known as "pyridoxine," is a water-soluble vitamin that primarily functions in metabolism and the nervous system. Because it is a water-soluble, vitamin B6 cannot be stored in the body and therefore must be consumed regularly. Natural food sources include fish, organ meat, non-citrus fruits, potatoes, and other starchy vegetables. Fortified cereal grains also are a common source.

Vitamin B6 works with the other vitamins of the B complex in many enzymatic reactions. It plays a major role in protein metabolism and aids in gluconeogenesis and glyconeogenesis (the production of blood glucose from amino acids and glycogen). Vitamin B6 functions in the biosynthesis of the neurotransmitters serotonin and norepinephrine. Its other uses include formation of the myelin of the nervous system, maintenance of homocysteine blood levels, support of adrenal function, and promotion of immune cell production. Vitamin B6 is a group of six compounds, three containing a phosphate group and three without. During digestion, the phosphate group is stripped and the remaining compounds are sent to the liver where they are converted to the primary active coenzyme form, pyridoxal phosphate (PLP).

Recommended Intake

The recommended dietary allowance (RDA) of vitamin B6 for adult men and women 19 to 50 years old is 1.3 mg. Values increase to 1.9 mg to 2.0 mg for pregnant and lactating women due to evidence demonstrating the importance of vitamin B6 in infancy. Symptoms of a vitamin B6 deficiency include nerve damage in the feet and hands, microcytic anemia, dermatitis, inflamed tongue and mouth,

Table 1. Selected Food Sources of Vitamin B6

Food	Milligrams (mg) per serving	Percent DV*
Chickpeas, canned, 1 cup	1.1	55
Beef liver, pan fried, 3 oz	0.9	45
Tuna, yellowfin, fresh, cooked, 3 oz	0.9	45
Salmon, sockeye, cooked, 3 oz	0.6	30
Chicken breast, roasted, 3 oz	0.5	25
Breakfast cereals, fortified with 25% of the DV for vitamin B6	0.5	25
Potatoes, boiled, 1 cup	0.4	20
Turkey, meat only, roasted, 3 oz	0.4	20
Banana, 1 medium	0.4	20
Marinara (spaghetti) sauce, ready to serve, 1 cup	0.4	20
Ground beef, patty, 85% lean, broiled, 3 oz	0.3	15
Waffles, plain, ready to heat, toasted, 1 waffle	0.3	15
Bulgur, cooked, 1 cup	0.2	10
Cottage cheese, 1% low-fat, 1 cup	0.2	10
Squash, winter, baked, ½ cup	0.2	10
Rice, white, long-grain, enriched, cooked, 1 cup	0.1	5
Nuts, mixed, dry-roasted, 1 oz	0.1	5
Raisins, seedless, ½ cup	0.1	5
Onions, chopped, ½ cup	0.1	5
Spinach, frozen, chopped, boiled, ½ cup	0.1	5
Tofu, raw, firm, prepared with calcium sulfate, ½ cup	0.1	5
Watermelon, raw, 1 cup	0.1	5

*DV = Daily Value. Daily Values were developed by the U.S. Food and Drug Administration (FDA) to help consumers compare the nutrient contents of products within the context of a total diet. The DV for vitamin B6 is 2 mg for adults and children age 4 years and older. The FDA, however, does not require food labels to list vitamin B6 content unless a food has been fortified with this nutrient. Foods providing 20% or more of the DV are considered to be high sources of a nutrient.

Source: *Vitamin B6*. (2011). Table 2, (From U.S. Department of Agriculture, Agricultural Research Service. 2011. USDA National Nutrient Database for Standard Reference, Release 24. Nutrient Data Laboratory Home Page (http://www.ars.usda.gov/ba/bhnrc/ndlexternal link icon). Office of Dietary Supplements. Retrieved from http://ods.od.nih.gov/factsheets/VitaminB6-HealthProfessional/

confusion, depression, and insomnia. A mild deficiency is relatively common, especially in children and the elderly, but often presents no symptoms. Kidney or heart failure, hyperthyroidism, liver scarring, and certain medications usually cause more extreme deficiencies along with the less severe effects. Pyridoxine-dependent epilepsy is a seizure condition that starts prenatally or in infancy. The cause of this epilepsy is thought to be a genetic mutation that interferes with vitamin B6 functioning, leading to a deficiency and severe neurological effects. The treatment involves high daily doses of vitamin B6.

The upper level of vitamin B6 (UL) is established at 100 mg per day for adults, which is likely only a concern for those using supplements. High intake of vitamin B6 through foods does not appear to cause negative health effects. Chronically high levels of B6 supplementation, however, can lead to serious neuropathy, painful skin lesions, photosensitivity, and gastrointestinal issues.

Health Applications

Research into potential positive health effects could support appropriate B6 supplementation with other B vitamins, folic acid, and B12. Researchers have identified vitamin B6 as a crucial ingredient to one of the metabolic pathways of homocysteine. Without vitamin B6 and several other B vitamins, dangerous levels of homocysteine would accumulate in the body.

The important role played by vitamin B6 in homocysteine blood level regulation has led to research on its effect on heart disease and other conditions with a possible homocysteine component, such as Alzheimer's disease and macular degeneration. One study used more than 80,000 female subjects from the Nurses' Health Study who had no history of cardiovascular disease. With data collected over the course of 14 years, the results showed that women who regularly consumed amounts of vitamin B6 and folate above the RDAs might be less likely to suffer from heart disease (Rimm et al., 1998). The researchers saw the decreased risk when vitamin B6 came from both food and supplementation sources, and the strongest effects were seen when both vitamin B6 and folate RDAs were regularly achieved, suggesting the combination of nutrients is of the most importance.

Vitamin B6 also is a candidate for depression research and treatment. The homocysteine hypothesis of depression suggests that high levels of homocysteine cause cerebral vascular disease and neurotransmitter deficiency, which in turn leads to a depressed mood state (Folstein, 2007). Vitamin B6 is among other vitamins suggested to reduce these high homocysteine levels. Also, vitamin B6's role in serotonin synthesis presents a strong case for its connection to depression. Serotonin is a neurotransmitter with its deficiencies implicated in some models of depression. One study did find an association with vitamin B6 deficiency and high depression scores (Hvas, Juul, Bech, & Nexo, 2004). The research hypothesized serotonin's production dependency on the PLP component of vitamin B6 led to vitamin B6's effect on the subjects' depression scores.

A large amount of research on vitamin B6 has targeted premenstrual syndrome (PMS) and carpal tunnel syndrome (CTS). Unfortunately, the research to date on these conditions consists of too few well-designed studies, making any strong conclusions premature. A double-blind randomized control trial with a small subject pool did find statistically significant improvements in reported PMS symptoms after three months of vitamin B6 supplementation (Kashanian, Mazinani, & Jalalmanesh, 2007). Researchers hypothesize that vitamin B6's effects on PMS symptoms could be due to its role in neurotransmitter synthesis. Despite inconclusive results, medical professionals frequently recommend vitamin B6 along with anti-inflammatory drugs and other therapies as a method to postpone hand surgery

in CTS sufferers. The studies to date suggest that vitamin B6 does not have a direct result on CTS, but rather might improve a separate neural condition that intensifies the CTS symptoms or increases the pain threshold of the CTS patients.

Vitamin B6 supplementation frequently is used as a treatment for nausea and vomiting during pregnancy. Supplementation appears to be helpful for mild to moderate nausea; however it remains unclear whether severe nausea responds as effectively. The American Congress of Obstetrics and Gynecology recommends vitamin B6 supplementation as a "first-line" treatment, but cautions that supplementation must supervised by a physician to avoid reaching the upper limit.

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See Also: Cardiovascular disease and nutrition; Depression and nutrition; Premenstrual syndrome; Vitamins.

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Vitamin B12

Vitamin B12 is an essential water-soluble vitamin that exists in many forms. All forms are known collectively as "cobalamins," because they contain the mineral cobalt. Cyanocobalamin most commonly is used in dietary supplements and in food fortification. Methylcobalamin and 5-deoxyadenosylcobalamin are the most common forms in human metabolic pathways. Vitamin B12's functions include aiding DNA synthesis, maintaining red blood cells, supporting adrenal gland

Table 1. Selected Food Sources of Vitamin B12

Food	Micrograms (mcg) per serving	Percent DV*
Clams, cooked, 3 oz	84.1	1,402
Liver, beef, cooked, 3 oz	70.7	1,178
Breakfast cereals, fortified with 100% of the DV for vitamin B12, 1 serving	6.0	100
Trout, rainbow, wild, cooked, 3 oz	5.4	90
Salmon, sockeye, cooked, 3 oz	4.8	80
Trout, rainbow, farmed, cooked, 3 oz	3.5	58
Tuna fish, light, canned in water, 3 oz	2.5	42
Cheeseburger, double patty and bun, 1 sandwich	2.1	35
Haddock, cooked, 3 oz	1.8	30
Breakfast cereal, fortified with 25% of the DV for vitamin B12, 1 serving	1.5	25
Beef, top sirloin, broiled, 3 oz	1.4	23
Milk, low-fat, 1 cup	1.2	18
Yogurt, fruit, low-fat, 8 oz	1.1	18
Cheese, Swiss, 1 oz	0.9	15
Beef taco, 1 soft taco	0.9	15
Ham, cured, roasted, 3 oz	0.6	10
Egg, whole, hard boiled, 1 large	0.6	10
Chicken, breast meat, roasted, 3 oz	0.3	5

*DV = Daily Value. Daily Values were developed by the U.S. Food and Drug Administration (FDA) to help consumers determine the level of various nutrients in a standard serving of food in relation to the approximate requirement for it. The DV for vitamin B12 is 6.0 mcg. The FDA, however, does not require food labels to list vitamin B12 content unless a food has been fortified with this nutrient. Foods providing 20% or more of the DV are considered to be high sources of a nutrient, but foods providing lesser percentages of the DV also contribute to a healthful diet. (U.S. Department of Agriculture's (USDA) Nutrient Database)

Source: Data from U.S. Department of Agriculture, Agricultural Research Service. 2011. USDA National Nutrient Database for Standard Reference, Release 24. Nutrient Data Laboratory Home Page (http://www.ars.usda.gov/ba/bhnrc/ndl). Reprinted in *Vitamin B12* (2011). Office of Dietary Supplements. Retrieved from http://ods.od.nih.gov/factsheets/VitaminB12-HealthProfessional/

function, and participating in production of neurotransmitters. Vitamin B12 helps to maintain the myelin sheath of nerve cells, and works closely with folate and vitamin B6 in a number of cellular pathways.

Animal products are the only dietary source of vitamin B12; good food sources are meat, eggs, fish, shellfish, poultry, and dairy products. Individuals with no or inadequate animal-derived food sources can get their dietary vitamin B12 from fortified foods. Foods such as breakfast cereals, meat substitutes, soy milk, and non-dairy margarines are often fortified with vitamin B12.

Recommended Intake

The recommended dietary allowance (RDA) of vitamin B12 for men and women age 19 years and older is 2.4 mcg. Up to a third of adults age 50 years and older have difficulty absorbing vitamin B12, however, therefore many experts recommend a higher intake for this group. On average, most North Americans exceed their RDA and consume 3.4 mcg each day. No upper limit (UL) has been established as there do not appear to be adverse effects associated with high intakes of vitamin B12. The human body only can absorb a fixed amount of B12, therefore ingesting more does not result directly in greater health benefits.

Deficiency Symptoms and Causes

The extensive symptom list of a vitamin B12 deficiency includes ataxia, muscle weakness, spasticity, fatigue, shortness of breath, heart palpitations, bleeding gums, mouth sores, poor appetite, nausea, diarrhea, incontinence, hypotension, vision problems, mood disturbances, and—in severe cases—dementia. These symptoms present slowly and often can be mistaken for other medical conditions. Vitamin B12 deficiency is one cause of megaloblastic anemia.

Groups most at risk for insufficient dietary intake of vitamin B12 are vegans (who consume no animal products), although the human liver stores several years' worth of vitamin B12. Vitamin B12 deficiency usually is a result of problems involving absorption of the vitamin. Adequate absorption depends upon a number of factors. The salivary glands produce a protein known as "R-protein" which binds with vitamin B12 in the stomach. This protein is thought to help protect vitamin B12 as it travels through the stomach to the small intestine. In the small intestine, pancreatic enzymes partially degrade R-protein, releasing vitamin B12 to bind with a compound called "intrinsic factor," which is produced by the parietal cells of the stomach. Vitamin B12, attached to intrinsic factor, travels to the distal portion of the small intestine, where it attaches to special receptors that absorb vitamin B12 into the absorptive cells. Once inside these cells, vitamin B12 becomes attached to a special transporter protein called transcobalamin II, which carries vitamin B12 into the bloodstream, delivering the vitamin to target cells and tissues.

Several issues can limit the absorption of vitamin B12. Groups at risk for vitamin B12 deficiency due to malabsorption include diabetics taking prescribed "metformin" (a hypoglycemic agent), patients taking stomach acid–reducing medications, individuals with excessive alcohol use, and patients with disorders of the gastrointestinal tract, such as celiac disease or Crohn's disease. Vitamin B12 deficiency occurs frequently in older adults. With age, production of hydrochloric acid and intrinsic factor decrease, making absorption less effective. Pernicious anemia is a condition caused by autoimmune destruction of the cells that line the stomach, resulting in an inability to produce stomach acid or intrinsic factor and, consequently, a vitamin B12 deficiency. The anemia results from nutrient malabsorption.

To treat a vitamin B12 deficiency, individuals should either take a supplement or increase consumption of vitamin B12–fortified foods. Fortified foods

contain vitamin B12 in its free form, which makes absorption easier. People with gastrointestinal disorders might need to supplement with either a sublingual tablet or an oral spray, because absorption will occur via the blood vessels of the mouth rather than the small intestine. In some cases, injections of vitamin B12 are required.

Health Applications

Vitamin B12 plays an essential role in folate metabolism. Vitamin B12 transfers methyl groups from folate to important cell compounds. This reaction is critical for DNA synthesis, for example. This reaction also occurs in the transformation of homocysteine to methionine. Homocysteine is an amino acid that, at high levels, has been associated with cardiovascular disease and stroke, as well as Alzheimer's disease and other forms of dementia. Low levels of vitamin B12 are associated with increased levels of homocysteine.

The important role of vitamin B12 in homocysteine metabolism has led to interesting research on the effect of the vitamin's impacts on cardiovascular disease and dementia. Although increasing dietary intake of vitamin B12 has been shown to reduce homocysteine levels, research has not found sufficient evidence that vitamin B12 levels influence the risk of cardiovascular disease. Vitamin B12 could play some role in cognition. One study tested elderly subjects on cognitive measures and evaluated brain MRIs in relation to four different markers of vitamin B12 plus vitamin B12 serum levels (Tangney, 2011). Deficiencies in vitamin B12 markers indicated greater risk for poor performance on cognitive tests. Deficiencies in these markers also were associated with a decrease in total brain volume. Other studies have found that low vitamin B12 levels are associated with cognitive decline. Experts suggest that vitamin B12 status should be assessed in people with cognitive impairment and symptoms of dementia. Restoring healthy vitamin B12 levels demonstrates some effectiveness for ameliorating symptoms in people with mild cognitive impairment, and mild to moderate dementia (Werder, 2010). Some research suggests that elderly people with vitamin B12 deficiency could have an increased risk for presenting symptoms of depression.

Because of its role in energy metabolism, some athletes use vitamin B12 as an energy enhancer based on the belief that it will boost their performance. Research shows, however, that additional vitamin B12 beyond an individual's RDA does not result in any advantageous effect on performance.

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See Also: Alzheimer's disease and nutrition; Folate and folic acid; Megaloblastic anemia; S-adenosylmethionine.

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Vitamin C

Vitamin C, also known as "ascorbic acid," is a water-soluble antioxidant. As an antioxidant, vitamin C helps eliminate free radicals from the body. Free radicals are substances that cause damage to DNA through oxidation. A buildup of these free radicals can contribute to the development of diseases such as cancer, arthritis, and heart disease. Vitamin C's other functions include assisting in collagen production, intensifying the body's absorption of iron, aiding in wound healing, and maintaining healthy bones and teeth.

Lack of dietary vitamin C causes a deficiency disease known as "scurvy." Documented descriptions of scurvy date back to the days of Hippocrates and extend throughout the early 20th century. Symptoms were described as purple spots all over the body, swollen gums, inability to close teeth, and extensive pain throughout the body. When opening and closing the mouth to eat became impossible, death soon followed. Throughout history, scurvy was known as "sailor's disease," as they were the most at-risk group. Ships could not carry aboard adequate supplies of fresh fruits and vegetables for its sailors because hot weather and long expeditions quickly lead to perished goods. Accordingly, sailors frequently acquired vitamin C deficiencies leading to scurvy symptoms. In 1753, Scottish naval surgeon, James Lind, discovered citrus fruits and leafy greens prevented scurvy development. Although Lind did not know exactly how these foods prevented scurvy, future research would show vitamin C's role in the disease prevention. As a result, ships began carrying large amounts of "antiscorbutic" foods, foods known to prevent scurvy, such as lemons, limes, oranges, sauerkraut, cabbage, malt, and portable soup. Scurvy rates declined. Today scurvy is rare, and almost entirely restricted to elderly adults, infants, and people on restrictive diets. Treatment is simple vitamin C intake and the recovery occurs quickly.

Diets rich in vitamin C have been associated with reduced risk of heart disease in some studies, although it is unclear whether vitamin C is the causative agent, or simply a marker for diets rich in fruits and vegetables. Vitamin C is known to help the body's immune system by supporting the function of immune cells. The human body needs vitamin C to help produce other essential compounds such as the neurotransmitter serotonin, bile salts, thyroid hormone, steroid hormones, and parts of the DNA molecule.

Vitamin C is found in many fruits and vegetables such as apples, asparagus, berries, broccoli, cabbage, melons, cauliflower, citrus fruits, kiwi, dark leafy greens, peppers, potatoes, and tomatoes (*see* Table 1). Breads, grains, cereals, and juices often are fortified with vitamin C. Fresh, raw fruits and vegetables supply

Table 1. Dietary Sources of Vitamin C

Food, Standard Amount	Vitamin C (mg)	Calories
Guava, raw, ½ cup	188	56
Bell pepper, red, raw, ½ cup	142	20
Bell pepper, red, cooked, ½ cup	116	19
Kiwi fruit, 1 medium	70	46
Orange, raw, 1 medium	70	62
Orange juice, ¾ cup	61–93	79–84
Bell pepper, green, raw, ½ cup	60	15
Bell pepper, green, cooked, ½ cup	51	19
Grapefruit juice, ¾ cup	50–70	71–86
Vegetable juice cocktail, ¾ cup	50	34
Strawberries, raw, ½ cup	49	27
Brussels sprouts, cooked, ½ cup	48	28
Cantaloupe, ¼ medium	47	51
Papaya, raw, ¼ medium	47	30
Kohlrabi, cooked, ½ cup	45	24
Broccoli, raw, ½ cup	39	15
Pod peas (edible), cooked, ½ cup	38	34
Broccoli, cooked, ½ cup	37	26
Sweet potato, canned, ½ cup	34	116
Tomato juice, ¾ cup	33	31
Cauliflower, cooked, ½ cup	28	17
Pineapple, raw, ½ cup	28	37
Kale, cooked, ½ cup	27	18
Mango, raw, ½ cup	23	54

Food sources of vitamin C are ranked by milligrams (mg) of vitamin C per standard amount, and also calories in the standard amount. (All amounts listed provide 20% or more of the Recommended Dietary Allowance [RDA] of 90 mg per day for adult men.)

Source: USDA/HHS *Dietary Guidelines for Americans, 2005*. Nutrient values from Agricultural Research Service (ARS), *Nutrient Database for Standard Reference*, Release 17. Foods are from ARS single nutrient reports, sorted in descending order by nutrient content in terms of common household measures. Food items and weights in the single nutrient reports are adapted from those in the 2002 revision of USDA *Home and Garden Bulletin No. 72, Nutritive Value of Foods*. Mixed dishes and multiple preparations of the same food item have been omitted from this table.

Reprinted in Centers for Disease Control. (2011). *Iron and Iron Deficiency.* http://www.cdc.gov/nutrition/everyone/basics/vitamins/iron.html

the greatest amounts of vitamin C. Because vitamin C is water soluble, cooking foods in water decreases the vitamin content. To preserve this vitamin content, best practices suggest decreasing cooking time as much as possible, using minimal amounts of water, and draining the water immediately after cooking.

As food is digested, its vitamin C content is released and absorbed through the intestinal cells. The intestinal cells bring vitamin C directly into the bloodstream where it is transported to necessary areas in the body. Vitamin C is an essential micronutrient, meaning the body does not synthesize vitamin C on its own and therefore must receive its required intake from food consumption.

Following the appropriate vitamin C recommended dietary allowance (RDA) helps to ensure individual needs are met. The RDA for adult men ages 19 years and older is 90 mg, and is 75 mg for adult women ages 19 years and older. Smokers are at a higher risk for vitamin C deficiency, therefore their RDA is 35 mg higher than the RDA for nonsmokers. Food sources are more ideal than supplementation for achieving the RDA. Once daily consumption reaches 2,000 mg, through any combination of foods or supplements, vitamin C has reached its maximum absorption capacity and additional intake will result in loss via the urine. Megadosing—taking too much vitamin C—can cause headaches, diarrhea, nausea, insomnia, bloating, abdominal cramping, heartburn, vomiting, and frequent urination. Individuals at an increased risk for kidney stones should not consume high levels of vitamin C. Excess vitamin C is converted into oxalate, which is a component of a very common type of kidney stone, calcium oxalate. A Swedish study of more than 23,000 men supported this correlation and found a 92% greater risk of developing kidney stones in men who consumed excess vitamin C supplementation.

Companies often market their vitamin C supplementation products as prevention or treatment methods against the common cold. Several scientific studies dispel these claims, including a meta-analysis of 29 individual studies with a total of more than 11,000 participants. This meta-analysis found no decreased incidence in cold development when vitamin C was routinely administered. Although no significant effect was noted on the general population, some evidence suggested individuals living in a cold temperature environment or athletes undergoing daily strenuous physical activity could benefit from occasional megadosing.

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See Also: Antioxidants; Dietary supplements; Upper respiratory tract infections; Vitamins.

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Vitamin D

Vitamin D is a fat-soluble vitamin that is converted to a chemical that functions as a hormone in the body. Vitamin D actually is a group of approximately 10 related chemicals. The 2 most commonly found in the diet are vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). Vitamin D is often referred to as the "sunshine vitamin" as the body can make vitamin D from a precursor in the skin when the skin is exposed to ultraviolet B (UVB) radiation from the sun. Vitamin D helps to maintain optimal levels of calcium and phosphorus in the blood, and helps the body absorb calcium and phosphorus in the small intestine. It encourages normal bone development in children and helps prevent loss of bone mineral in adults. Adequate levels of vitamin D are associated with better muscle function and a reduced risk of falls in older adults. Adequate vitamin D levels might reduce the risk of some cancers, autoimmune disorders, and heart disease. Vitamin D is found naturally in very few foods, but has been added to foods and also can be taken as a dietary supplement. Too much vitamin D poses a risk, as it leads to high amounts of calcium in the blood and calcium deposits in soft tissues such as the blood vessels, heart, and kidneys.



Vitamin D tablets. (Boomfeed/Dreamstime.com)

The discovery of vitamin D followed a long search for a cure to a bone disorder known as "rickets." Rickets is marked by soft bones that lack adequate mineral deposition, and typically appears in childhood. As children begin to walk, their soft bones have difficulty bearing their body weight, and legs often become bowed. Cod liver oil, which contains vitamin D along with other important nutrients, was used to treat and

prevent rickets for many decades before the actual isolation of vitamin D in the laboratory. Additionally, many groups had observed that exposure to outdoor air and sunlight appeared to prevent the development of rickets. Several research groups in the 1920s eventually isolated and named vitamin D, and discovered its metabolic pathways (Wolf, 2004).

Physiological Pathways, Actions, and Health

In the skin, provitamin D3 (7-dehydrocholesterol) is converted to vitamin D3 (cholecalciferol). Dietary forms of vitamin D as well as vitamin D3 from the skin are taken up by the liver, and converted to calcidiol (25-dihydroxyvitamin D). In the kidneys, calcidiol is converted to calcitriol (1,25-dihydroxyvitamin D), the active hormone form.

Because vitamin D status is influenced by both diet and UVB exposure, studies on dietary intake alone can fail to capture the relationship between vitamin D and health. Measures of serum vitamin D have been assessed in some studies, but sometimes these measurements have been inaccurate. Research on vitamin D and health continues to refine both dietary and serum measures, and to explore the physiological activity of vitamin D.

Many cells in the body have receptors for vitamin D, suggesting that the hormone has a number of regulatory functions and health effects. Vitamin D is best known for its role in helping the body absorb calcium. Calcium is a nutrient that is essential in the formation and proper growth of the bones in the skeletal system. Without adequate amounts of vitamin D, osteoporosis can result in adults, and rickets can occur in children. Vitamin D works with other hormones to regulate blood calcium level by influencing movement of calcium from the gastrointestinal tract into the bloodstream. If blood calcium levels fall too low and dietary calcium is not adequate, vitamin D also helps to mobilize calcium from bone tissue. This is why vitamin D alone is not sufficient to ensure healthy bones; dietary calcium is required as well.

Emerging evidence suggests that vitamin D also has an impact on skeletal muscle strength and function. Research has found that optimal vitamin D levels are associated with stronger muscles and decreased risk of falling in older adults. Vitamin D could help keep the heart muscle healthy.

Vitamin D receptors are found in the cell membranes of immune cells, and are believed to help modulate the activity of a family of immune cells known as "T cells." Optimal vitamin D levels are associated with a reduced risk of developing autoimmune diseases such as insulin-dependent diabetes mellitus (type 1 diabetes), multiple sclerosis, and rheumatoid arthritis. Vitamin D might help reduce the frequency of winter upper respiratory tract infections, perhaps by improving immune function.

It appears that vitamin D influences the activity of dividing cells, encouraging cells to differentiate and inhibiting cell proliferation. These influences help to reduce the risk of cancer, a process in which cells proliferate too rapidly and fail to behave normally. Research suggests that greater intakes of vitamin D and optimal

serum vitamin D levels are associated with reduced risk of several types of cancers, although research in this area still is preliminary.

Vitamin D influences insulin metabolism and blood pressure. Adequate vitamin D levels might be helpful for preventing cardiometabolic syndrome and type 2 diabetes, although other factors play important roles in these disorders as well.

Dietary Recommendations and Food Sources

People who manufacture adequate amounts of vitamin D via UVB radiation exposure do not require dietary sources of vitamin D. Populations in northern latitudes, people with darker skin, older adults, and people who rarely get outdoors, however, often have suboptimal vitamin D levels. People whose skin is always covered by

Table 1. Selected Food Sources of Vitamin D

Food	IUs per serving*	Percent DV**
Cod liver oil, 1 tablespoon	1,360	340
Swordfish, cooked, 3 oz	566	142
Salmon (sockeye), cooked, 3 oz	447	112
Tuna fish, canned in water, drained, 3 oz	154	39
Orange juice fortified with vitamin D, 1 cup (check product labels, as amount of added vitamin D varies)	137	34
Milk, nonfat, reduced fat, and whole, vitamin D-fortified, 1 cup	115–124	29–31
Yogurt, fortified with 20% of the DV for vitamin D, 6 oz (more heavily fortified yogurts provide more of the DV)	80	20
Margarine, fortified, 1 tablespoon	60	15
Sardines, canned in oil, drained, 2 sardines	46	12
Liver, beef, cooked, 3 oz	42	11
Egg, 1 large (vitamin D is found in yolk)	41	10
Ready-to-eat cereal, fortified with 10% of the DV for vitamin D, 0.75 to 1 cup (more fortified cereals might provide more of the DV)	40	10
Cheese, Swiss, 1 oz	6	2

* IUs = International Units.

** DV = Daily Value. Daily Values were developed by the U.S. Food and Drug Administration to help consumers compare the nutrient contents among products within the context of a total daily diet. The DV for vitamin D is currently set at 400 IU for adults and children ages 4 years old and older. Food labels, however, are not required to list vitamin D content unless a food has been fortified with this nutrient. Foods providing 20% or more of the DV are considered to be high sources of a nutrient, but foods providing lesser percentages of the DV also contribute to a healthful diet.

Source: U.S. Department of Agriculture, Agricultural Research Service. 2011. *USDA National Nutrient Database for Standard Reference, Release 24*. Nutrient Data Laboratory Home Page, http://www.ars.usda.gov/ba/bhnrc/ndl

Reprinted in *Vitamin D*. (2011). Office of Dietary Supplements. Retrieved from http://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional/

clothing or sunscreens also are at greater risk of vitamin D deficiency. It is important to note that dermatologists caution that sun exposure can increase risk for skin cancer, especially in people with fair skin or genetic predispositions. Dermatologists encourage people to obtain vitamin D from foods rather than from sun exposure. The Dietary Reference Intake for vitamin D is 600 International Units (IU) per day for people ages 9 to 70 years old, and 800 IU per day for people ages 70 years and older.

Vitamin D rarely is found naturally in food. The largest natural supply of vitamin D is fish. Vitamin D can be found in oily fish and cod liver oil. (Cod liver oil is not considered a safe daily supplement, however, because its high levels of vitamin A can cause toxicity.) Egg yolk, butter, and liver also contain some vitamin D, although amounts in these foods vary with the diet of the source animal. Some mushrooms contain the plant form of vitamin D. Because there are few food sources of vitamin D, and because many people are unable to make enough vitamin given limitations such as limited winter sun exposure, several food sources have been fortified with vitamin D. Milk is fortified with vitamin D in several countries including the United States and Canada. Most milk in the United States is fortified with 400 IU of vitamin D per quart. Milk was chosen as the vehicle for fortification because vitamin D enhances calcium absorption, and milk contains this mineral. Most products made with milk (e.g., cheese, ice cream) have not been fortified with vitamin D. Breakfast cereal also commonly is fortified with vitamin D. Vitamin D is added to some brands of soy beverages, orange juice, yogurt, and margarine. Because not all of these food products have added vitamin D it is important to read food labels. Vitamin D3 is believed to be more effective as a supplement than vitamin D2.

Presently, experts are unclear as to what levels of serum vitamin D are optimal for good health, although recommendations generally range from 20 to 30 ng/mL (nanograms per milliliter). Some health providers recommend vitamin D supplementation based on blood tests, and others simply recommend that individuals consume the DRI daily. Understanding the effect of vitamin D on various health outcomes is complicated because it works in conjunction with other nutrients, such as calcium, magnesium, vitamin A, and vitamin K. Individuals working to maintain optimal vitamin D status should be sure to achieve an adequate dietary intake of these other nutrients as well.

Vitamin D Toxicity

Sun exposure does not cause vitamin D toxicity, but toxicity can result from a greater-than-recommended intake of dietary supplements. Too much vitamin D in the body can lead to an abnormally high level of calcium in the blood; over time, this can lead to calcium deposits in soft tissues such as the heart, lungs, blood vessels, and kidneys. Although vitamin D toxicity is unlikely at intakes up to 10,000 IU per day, because of the severity of toxicity effects, the Tolerable Upper Intake Level (UL) has been set fairly low, at 4,000 IU per day.

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See Also: Enrichment and fortification; Osteoporosis; Vitamins.

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Vitamin E

Vitamin E is an essential nutrient necessary for optimal human health and tissue function. Vitamin E occurs as eight different isomers: alpha-, beta-, gamma-, and delta-tocopherol; and alpha-, beta-, gamma-, and delta-tocotrienol; the alpha and gamma forms are predominant in nature. Synthetic vitamin E, and the form found in most supplements, is alpha-tocopherol. Alpha-tocopherol is the form that has been most extensively studied and the form used in most scientific trials. Vitamin E is a fat-soluble antioxidant that stops the formation of reactive oxidative species—free radicals—during oxidation of fat. It might confer some protection against certain eye diseases, cancers, and heart disease, although the evidence is mixed. A healthy diet can provide adequate amounts of natural vitamin E. Supplementing with high doses has not been clearly shown to be of great benefit and could increase risks of certain cancers and bleeding disorders.

Scientists Herbert Evans and Katharine Scott Bishop first discovered vitamin E in 1922 when they noticed that rats fed a diet that contained lard became infertile. This was reversed when an extract from cereals was added to the diet that was subsequently called "anti-sterility factor." In 1925 it was officially recognized as the fifth vitamin (hence the name vitamin E), and in 1969 the FDA officially declared it a nutrient essential to normal development. The name "tocopherol" comes from the Greek word "toc" meaning "child," and "phero" meaning "to bring forth," recognizing its importance in fertility and normal development (Pazirandeh & Bums, 2013).

Vitamin E acts as a scavenger of free radicals. Free radicals are molecules containing an unshared electron, and are thought to be damaging to various body

systems and might contribute to diseases such as atherosclerotic heart disease and cancer. After vitamin E is ingested, it is absorbed by the small intestine and then taken up by the liver, which is the rate-limiting step in vitamin E distribution. The liver then metabolizes and excretes most forms of vitamin E, but redistributes primarily alpha-tocopherol back into the circulation. For this reason it long has been believed that the alpha-tocopherol form is the preferred form for use by the body. There is emerging evidence, however, that suggests that other tocopherols—particularly gamma-tocopherol—could be equally, if not more, important and that high doses of alpha-tocopherol actually could deplete body tissues of the gamma form (Ju et al., 2010). Furthermore, absorption of the different forms of vitamin E could have different benefits to the body, and the amount of each form that is absorbed can vary from person to person depending on the individual's genetic makeup (Kroner, 2011).

True vitamin E deficiency is rare in healthy individuals, although it can be seen in premature babies and in people suffering from any disease that impairs fat absorption such as pancreatic enzyme insufficiency. These include diseases such as cystic fibrosis, Crohn's disease, and other diseases affecting the liver and gallbladder. For these patients, water-soluble forms of vitamin E are available to prevent deficiency. Vitamin E deficiency can lead to shortened red blood cell life span, hemolysis, peripheral neuropathies, ataxia, and balance problems that can progress over time and ultimately lead to death if not corrected (Kroner, 2011; Pazirandeh & Bums, 2013).

Vitamin E can be found naturally in a variety of foods including wheat germ, vegetable oils, meats, eggs, seeds, nuts, and leafy green vegetables (*see* Table 1). Dietary vitamin E contains all eight forms. The synthetic form of alpha (or DL) isomer is only half as active as the vitamin E found in its natural form, therefore people need to ingest about 50% more of the synthetic vitamin E to obtain the same amount of the nutrient (NIH, 2013). The Recommended Dietary Allowance for adult men and women is 15 mg per day.

Several observational studies have supported the theory that a higher intake of vitamin E confers cancer protection; however, as scientists have done more rigorous controlled studies, the results have been mixed. The SELECT Trial, (Selenium and Vitamin E Cancer Prevention Trial) and data from the Women's Health Study did not show any benefit of taking vitamin E in preventing certain cancers (Kroner, 2011). Additionally, follow-up data from the SELECT trial found that men taking vitamin E actually showed slightly elevated risk for prostate cancer (NIH, 2013).

The studies mentioned above were done using alpha-tocopherol; however, recent attention has been turned toward its lesser-known cousin, gamma-tocopherol as a potentially potent health protector. Gamma-tocopherol accounts for about 70% of the vitamin E found in the North American diet, and is a potent defender against damaging reactive nitrogen oxides. Gamma-tocopherol has unique chemical properties that distinguish it from its alpha counterpart and some of these lead to its ability to trap nitrogen dioxide (found in car exhaust and cigarette smoke) and peroxynitrite (a by-product of inflammation), both of which can be damaging to body tissues and can lead to degenerative processes. Another unique feature of

Table 1. Selected Food Sources of Vitamin E (Alpha-Tocopherol)

Food	Milligrams (mg) per serving	Percent DV*
Wheat germ oil, 1 tablespoon	20.3	100
Sunflower seeds, dry roasted, 1 oz	7.4	37
Almonds, dry roasted, 1 oz	6.8	34
Sunflower oil, 1 tablespoon	5.6	28
Safflower oil, 1 tablespoon	4.6	25
Hazelnuts, dry roasted, 1 oz	4.3	22
Peanut butter, 2 tablespoons	2.9	15
Peanuts, dry roasted, 1 oz	2.2	11
Corn oil, 1 tablespoon	1.9	10
Spinach, boiled, ½ cup	1.9	10
Broccoli, chopped, boiled, ½ cup	1.2	6
Soybean oil, 1 tablespoon	1.1	6
Kiwifruit, 1 medium	1.1	6
Mango, sliced, ½ cup	0.7	4
Tomato, raw, 1 medium	0.7	4
Spinach, raw, 1 cup	0.6	3

*DV = Daily Value. The U.S. Department of Agriculture's (USDA) Nutrient Database website lists the nutrient content of many foods, in some cases including the amounts of alpha-, beta-, gamma-, and delta-tocopherol. The USDA also provides a comprehensive list of foods containing vitamin E.

At present, the vitamin E content of foods and dietary supplements is listed on labels in international units (IUs), a measure of biological activity rather than quantity. Naturally sourced vitamin E is called d-alpha-tocopherol; the synthetically produced form is dl-alpha-tocopherol. Conversion rules are as follows.

- To convert from mg to IU: 1 mg of alpha-tocopherol is equivalent to 1.49 IU of the natural form or 2.22 IU of the synthetic form.
- To convert from IU to mg: 1 IU of alpha-tocopherol is equivalent to 0.67 mg of the natural form or 0.45 mg of the synthetic form.

For the natural form of alpha-tocopheral, for example, the conversion is 15 mg x 1.49 IU/mg = 22.4 IU. The corresponding value for synthetic alpha-tocopherol is 33.3 IU (15 mg x 2.22 IU/mg).

Source: U.S. Department of Agriculture, Agricultural Research Service (2011). *USDA National Nutrient Database for Standard Reference, Release 24*. Nutrient Data Laboratory Home Page (http://www.ars.usda.gov/ba/bhnrc/ndl). Reprinted in *Vitamin E*. (2013). Office of Dietary Supplements. Retrieved from http://ods.od.nih.gov/factsheets/VitaminE-HealthProfessional/

gamma-tocopherol is its ability to block cyclooxygenase-2, an enzyme central to the inflammatory cascade and a contributor to several diseases, such as cardiovascular disease and certain cancers (Jiang, 2014). Early research suggests that a gamma-tocopherol–rich mixture of tocopherols and tocotrienols might help prevent colon, prostate, mammary, and lung cancers (Ju et al., 2010).

Meta-analyses looking at all-cause mortality have found slightly increased risk for people who ingest high doses of vitamin E (alpha-tocopherol) (400 IU or more per day). The Heart Outcomes Prevention Evaluation (HOPE) studies, for

example, found no decrease in cancer or major cardiac events, but found slightly greater rates of heart failure in 10,000 people who were at increased risk of heart attack or stroke (Kroner, 2011; NIH 2013). Interestingly, several studies have shown that people with advanced cardiovascular disease have normal levels of alpha-tocopherol, but very low levels of gamma-tocopherol, and because alpha-tocopherol depletes gamma-tocopherol, the benefits of supplementing with alpha-tocopherol could be overshadowed by the low levels of its gamma counterpart, and the ratio in fact could be the more important factor for optimal antioxidant protection (Jiang, 2001).

Some research suggests that dietary vitamin E (compared to alpha-tocopherol supplements) affects the expression of genes involved in clearing amyloid beta proteins, which are involved in the development of Alzheimer's disease. Studies looking at alpha-tocopherol and Alzheimer's disease, however, have found no clear benefit to supplementation (Kroner, 2011). Trials of vitamin E along with other antioxidants suggest that this mix could help to prevent two common eye diseases, cataracts and macular degeneration.

Vitamin E inhibits protein kinase C, which is an enzyme involved in the proliferation of platelets, smooth muscle cells, and monocytes. It also can affect endothelial cells within blood vessels leading to decreased adherence of blood components to the vessel wall (NIH, 2013). At high doses, this can increase the risk of bleeding or hemorrhage and the upper limit of intake, 1,000 mg per day, is based on increased bleeding risk associated high doses of vitamin E.

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See Also: Antioxidants; Cancer and nutrition; Cardiovascular disease and nutrition; Eye health.

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Vitamin K

Vitamin K is a family of fat-soluble vitamins that includes vitamin K1 (phylloquinone), from plant sources, and the basic form of vitamin K in the diet; vitamin K2 (menaquinones [MKs]), from animal sources and synthesized by bacteria in the large intestine; and synthetic forms, collectively known as vitamin K3 (menadione and others). The vitamin K2 group includes a number of compounds, all containing at least one five-carbon configuration in the side chain; the designations for the specific compounds reflect the number of these five-carbon units; for example, MK-4 has four of these units. Vitamin K is essential for the activation of several calcium-binding proteins, including a number of blood-clotting components, as well as the activation of proteins necessary for bone metabolism. Vitamin K is found in many foods, especially vegetables. People on blood-thinning medications must limit intake of foods high in vitamin K, as this vitamin interferes with medication effects.

History

Danish scientist Henrik Dam is credited with the discovery of vitamin K in the late 1920s, receiving the Nobel Prize in Chemistry in 1946 for this work. He conducted experiments studying the effects of a cholesterol-depleted diet on young chickens. After a period of several weeks on the diet, the chicks displayed symptoms of delayed blood clotting and suffered major hemorrhages in their muscles and organs. Dam discovered that a second compound, then known as "koagulationsvitamin," in addition to cholesterol, was missing from the chicks' diet. The vitamin-K deficient chick model sparked further studies in the research of vitamin K and its coagulative properties.

Roles in the Body

Vitamin K functions as a cofactor for an enzyme that facilitates activation of several important proteins. Vitamin K is essential for blood coagulation, in which the blood transitions from a liquid to a gel-like form. This allows for blood-loss cessation following an injury to the vessel. Vitamin K also is necessary for the activation of proteins that bind calcium in the bones, cartilage, blood vessels, and other soft tissues, playing a vital role in the formation of strong bones and the prevention of bone fractures, and in regulating calcium deposition. Preliminary evidence suggests that activation of calcium-binding proteins in soft tissues could help prevent calcium deposits where they might be harmful, such as in the blood vessels (Higdon, Drake, Booth, & Costakos, 2011).

Vitamin K1 can be found in leafy green and other vegetables, such as kale, turnip greens, spinach, lettuce, brussels sprouts, asparagus, broccoli, and red cabbage. Soybean, canola, cottonseed, and olive oils also contain vitamin K1. Vitamin K2 can be obtained from animal products such as eggs, meats, poultry, milk, and cheese. It is also found in high amounts in the Japanese fermented soy product

"natto." The Adequate Intake (AI) is 90 mcg per day for women, and 120 mcg per day for men. The majority of vitamin K1 is absorbed by the liver and used by the liver for clotting-factor synthesis; K2-vitamins are integrated into low-density lipoproteins (LDL) and released into the bloodstream.

Deficiency

Vitamin K routinely is administered to newborn babies, who are at risk of deficiency due to their immature intestinal tracts and the low levels of vitamin K contained in breast milk. Infants who are vitamin K deficient are at significant risk of experiencing intracranial hemorrhage.

Deficiencies can exist in adults who abuse alcohol or suffer from malnutrition, Crohn's disease, celiac disease, or cirrhosis. Antacids, blood thinners, as well as certain medications for cancer, seizures, and high cholesterol can pose a significant risk for developing vitamin K deficiency. Long-term use of antibiotics also can interfere with the production of vitamin K within intestinal bacteria. In the case of deficiency, symptoms such as bruising and bleeding can occur. Other deficiency symptoms include hemorrhage, fractures, tarry or bloody stools, heavy menstrual periods, nosebleeds, gum bleeding, and blood in the urine.

Health Benefits

Epidemiological evidence has found that people with higher dietary intakes of vitamin K have a reduced risk of osteoporosis. Researchers have pointed out, however, that because a high dietary vitamin K intake generally reflects a greater intake of vegetables rich in other nutrients and phytochemicals, a high vitamin K intake simply might be a marker for a healthful diet. Several well-controlled studies have found that vitamin K supplementation, along with vitamin D, calcium, and (sometimes) magnesium, reduce the risk of fracture in older women who have bone loss (Higdon, Drake, Booth, & Costakos, 2011).

Vitamin K and Anticoagulant Medications

People at risk for the formation of blood clots within the cardiovascular system often are prescribed medications such as "warfarin" ("Coumadin"). Clots formed within the cardiovascular system can cause life-threatening events such as heart attack and stroke. Because vitamin K activates proteins that promote blood clotting, people on anticoagulant medication usually are instructed to reduce vitamin K intake.

Toxicity

Fat-soluble vitamins are absorbed with dietary fat and travel through the lymph system via lipoproteins into the bloodstream. They ultimately are stored in the liver and adipose tissue, where they remain for longer periods than do water-soluble

vitamins. Unlike other fat-soluble vitamins, however, vitamin K is not stored in large quantities in the body. Vitamin K is metabolized by the liver relatively quickly and excreted through urine and bile; thus, vitamin K toxicity is rare. Although a Tolerable Upper Intake Level (UL) for vitamin K has yet to be established, large doses of vitamin K supplements are not advised and consultation with a physician regarding supplementation is recommended, due to the theoretical increased risk of blood clotting and stroke.

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See Also: Osteoporosis; Vitamins.

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Vitamins

Vitamins are organic compounds that are required by organisms for normal growth, development, and the maintenance of basic physiological functions. Vitamins almost always must be obtained from foods (or supplements), although a few vitamins can be obtained in additional ways. In addition to being available in certain foods, for example, vitamin K is manufactured by microorganisms that live in the colon; the vitamin then is absorbed by the human host. Vitamin D can be made by the skin in the presence of ultraviolet light (UVB). Vitamins differ from other organic nutrients, such as carbohydrates, fats, and proteins, in that the body does not break down the chemical bonds between atoms to produce energy. Instead, vitamins work with other molecules to enable a variety of chemical pathways.

Vitamins are classified as micronutrients, which means that they are needed in relatively small amounts as compared to the other organic nutrients. Vitamins are required in amounts such as a few milligrams or micrograms per day, for example,



Multivitamin and mineral (MVM) supplements have been available to consumers since the 1940s. While nutritionists agree that people should get most of their vitamins from foods, about a third of adults in North America take an MVM supplement. (Kornwa/Dreamstime.com)

and daily carbohydrate intake typically is more than 100 g per day. Vitamin needs vary widely among organisms. A given compound might be a vitamin to one organism but not another. Most animals, for example, can manufacture the compound ascorbic acid—also known as vitamin C—but humans must obtain this chemical from the diet or supplements.

Scientists throughout history have observed relationships between food and health. It was widely known in the 18th century and 19th century, for instance, that sailors consuming only dried foods on long voyages would develop scurvy—a disease marked by joint pain, weakness, and even death. Yet, if sailors made it back to land and began consuming fresh fruits and vegetables, they would quickly recover. In the 1890s, Dutch physician Christiaan Eijkman observed that prisoners being held in the Dutch colony of Java (now Indonesia) often developed a disease called "beriberi." Those who were in prisons that served white rice showed much greater rates of beriberi, however, than did the people in the prisons which served brown rice. Eijkman and other scientists began searching for the substance in rice polishings (the outer layer of brown rice that is removed to produce white rice) that would cure beriberi. The concept of "vitamins" evolved from this search. Polish chemist Casimir Funk proposed that substances belonging to the chemical class of "amines" (such as the amino acids from which the body builds

proteins) are needed by the body. He called these substances "vitamines" from "vital amines." Years later, when it became apparent that vitamins were not amines, the word was changed to vitamins (Carpenter, 2013).

Vitamins are named and categorized based on their structure and function. Vitamins A, D, E, and K are classified as fat soluble, and the B vitamins and vitamin C are water soluble. Fat-soluble vitamins are more easily stored in the body, and water-soluble vitamins tend to be readily excreted in the urine. Some vitamins include groups of similar compounds. Vitamin A, for example, includes carotenoids such as beta-carotene that come from plants that the body readily converts to vitamin A when needed. Humans are known to need 13 vitamins. The word "vitamin" is also used colloquially to refer to dietary supplements, typically multivitamin supplements.

Barbara A. Brehm

See Also: Biotin; Dietary supplements; Folate and folic acid; Niacin; Pantothenic acid; Riboflavin; Thiamin; Vitamin A; Vitamin B6; Vitamin B12; Vitamin C; Vitamin D; Vitamin E; Vitamin K.

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W

Water Needs; Water Balance

A water molecule (H_2O) is made up of two hydrogen atoms and one oxygen atom. Water is an essential element for life. Humans can survive only for a few days without water, because all cells, tissues, and organs need water to function. The human body is about 45% to 75% water by weight. Lean people have relatively greater water content, as muscle tissue is about 75% water, and adipose tissue is only about 10% water.

Water is an important constituent of all body fluids, from the cytoplasm in every cell to the blood that flows throughout the cardiovascular system. The lymphatic fluid, the digestive juices, the synovial fluid in joints, and the cerebrospinal fluid all are aqueous solutions. Fluid also is found in the minute spaces between cells. Water is lost daily through the production of the urine and feces, during exhalation as inhaled air is hydrated by the lungs, and in the sweat released from the skin. Daily water needs are met by the ingestion of food and beverages, with a little water produced by a variety of metabolic processes.

Water Needs

The U.S. Food and Nutrition Board (as well as Health Canada) recommend an Adequate Intake (AI) of water that is based on the average intakes of people in good health. The AI for adult men is 3.7 liters per day, and for adult women is 2.7 liters per day. Recommendations are higher for conditions that increase water needs, such as pregnancy and lactation, and for higher levels of physical activity or environmental conditions that increase sweating rate. About 80% of water needs are met with the intake of beverages, with the rest supplied by foods. Many foods, especially fruits and vegetables, contain quite a bit of water. Thirst is not always an adequate indication of water needs. Most people, especially children and older adults, should drink more than they actually thirst for. Even mild dehydration can lead to feelings of fatigue.

Plain water offers many advantages over other beverages. Sweetened beverages and fruit juices and drinks are high in calories and sugars, therefore daily consumption of these should be limited. Caffeinated beverages exert a mildly diuretic effect, although research suggests that they still contribute substantially to people's daily water needs. Conversely, alcoholic beverages can cause dehydration—not to mention other health problems—when people consume more than one

or two alcoholic drinks per day. Many people find that filling a reusable water bottle each day helps them to consume an optimal amount of water.

Signs of adequate hydration include the regular production of pale-colored urine. Dark, scant urine production is a sign of dehydration. (It should be noted that supplements containing riboflavin and foods such as beets with abundant plant pigments can alter urine color; such alteration is not a sign of dehydration.) Water loss due to heavy sweating often results in dehydration that is marked by temporary weight loss. People should consume 1.5 liters of fluids for every kilogram of weight lost due to sweating (about 2.5 cups per pound of weight loss). Sports beverages can be helpful for recovering from dehydration.

Fluid Restrictions

It is important to follow the recommendations of a primary care provider when it comes to water restrictions. Individuals with kidney disease, for example, might have fluid restrictions. Anyone who has been told by a health care provider to restrict fluid due to a health problem should follow the provider's advice.

Susana Leong

See Also: Bottled water; Sports beverages; Sugar-sweetened beverages.

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Weight Watchers

Weight Watchers International, Inc. has come to be a leading provider of weight-management services, operating through a combination of company-owned and franchise locations. Every week 45,000 Weight Watchers meetings are held worldwide, attended by 1.3 million members and 12,000 leaders who have successfully lost weight on Weight Watchers programs (Weight Watchers, 2012). The program, contrary to many weight-loss diet plans, focuses on the attractive focal point that no foods are prohibited. The lack of restriction theoretically is meant to assist members in making better food choices that can be implemented in a long-term



Weight Watchers' Smart Ones were created to make good tasting low-calorie food that is nutritious and fits into the Weight Watchers dietary plans. The brand has created a variety of flavors that contain no more that 350 calories and 10 grams of fat or less. (Photo by Edouard H. R. Gluck/Bloomberg via Getty Images)

lifestyle alteration. This coupled with group support and self-monitoring is argued by Weight Watchers to be most successful for both weight loss and weight management.

Weight Watchers was founded in the early 1960s by Jean Nidetch. According to Nidetch, the organization was born when she began to invite friends into her home for weekly meetings to discuss best ways to lose weight. Fifty years after its founding, Weight Watchers has become one of the most recognizable and trusted brand names in the diet arena. Weight Watchers consistently is highly regarded by experts in nutrition, diet, diabetes, heart disease, and obesity, ranking #1 Best Weight-Loss Diet, Best Commercial Program, and Easiest Diet to Follow by *U.S. News & World Report* for four consecutive years (Haupt, 2015).

The essence of Weight Watchers is the points system, called "Points Plus." Every food, drink, and Weight Watchers–developed recipe is assigned a point value based on its fat, carbohydrate, protein, and fiber content, a revision of the previous "Points" program that calculated values by calories, fat, and fiber. The goal is to eat nutrient-dense and less-processed foods. Every member is assigned a daily Points Plus target based on gender, age, height, and weight. The newest program, "Weight

Watchers 360," built on the Points Plus system, lets members choose between attending in-person meetings and using an online support system.

The encouragement to use the in-person support group resource is what sets Weight Watchers apart from self-help methods and other commercial weight-loss programs. Participation in support groups for habitual overconsumption has been common since the 1930s for overcoming problems such as alcohol and overspending. A two-year study focused on the weekly meetings described the program as a quest for well-being organized around a three-core practice—the therapeutic confession, the therapeutic oversight, and the autotherapeutic testimonial. (The autotherapeutic testimonial refers to the therapeutic benefits members receive from telling their success stories.) Put most simply, the Weight Watchers model provides shared support, acts as disciplinary guardian, and allows the celebration of success among members (Moisio & Beruchashvili 2010).

Several research groups have studied the effectiveness of Weight Watchers in comparison to self-help methods and other well-established commercial weight-loss programs. In general, participants in Weight Watchers programs appear to be as successful in their weight-loss efforts as participants in other types of weight-loss programs. An observational study was conducted in 2007 in which primary care physicians referred patients to Weight Watchers and funded a 12-week session. A third of participants lost more than 5% of their initial body weight, which typically is the marker associated with health benefits for overweight and obese individuals. The study concluded that the effectiveness of Weight Watchers is comparable to other primary care weight loss programs. The study, however, did not examine long-term impact; did not look at why patients with a BMI of greater than 40 lost the least amount of weight; and did not evaluate the impact of providing the patients with funding for the Weight Watchers program. (Ahern, Olson, Louise, & Jebb, 2011).

A commercial-program comparison study was conducted between 2000 and 2002 comparing the Atkins, Ornish, Weight Watchers, and Zone diets in terms of weight loss and reduction of cardiac risk factors. At the one year mark, statistical analysis revealed that all the diets resulted in a modest weight loss, with approximately 25% of participants experiencing a 5% reduction in weight. No significant difference was found among commercial programs ($p = 0.40$), however. All of the programs also caused a modest improvement in cardiac risk factors, although triglycerides, blood pressure, and fasting glucose showed no statistically significant change (Dansinger, Gleason, Griffith, Selker, & Schaefer, 2005).

Although such research suggests that weight-loss methods do not differ drastically in terms of subjects' weight-loss success rates, more important is whether the weight loss is maintained. Weight Watchers promotes behaviors that have been shown to promote long-term weight maintenance. A randomized trial conducted between 1998 and 2001 compared the effectiveness of self-help methods of weight loss to Weight Watchers over a two-year period. After two years, the self-help group's median weight had increased to baseline, whereas the Weight Watchers group concluded the study weighing between 2.7 kg and 3.0 kg less than the baseline. The results showed that Weight Watchers provided a modest—yet more effec-

tive—method of weight loss in comparison to self-help methods (Heshka et al., 2003).

Critics of Weight Watchers argue that the focus lies too heavily on weight and numerical values of success to measure or define health and well-being. The critics have pointed out that weight is not a stand-in for health, that weight loss does not automatically solve health problems, and weight gain does not automatically create them. It is possible for a person to be active, healthy, and still overweight. The Weight Watchers corporation admits to a consistent reenrollment of members for years, illustrating the strong likelihood that participants in a diet program—even one that focuses on long-term lifestyle changes—continue to experience obstacles to successful weight control throughout life.

Allison R. Ferreira

Research Issues

Group support is a central feature of Weight Watchers programs. Social support might benefit behavior-change efforts for many reasons, including building confidence in one's ability to change, modeling social norms for weight-control behaviors, and creating positive emotions associated with experiencing connection to others.

See Also: National Weight Control Registry; Obesity, treatment.

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Wheatgrass

Wheatgrass, *Triticum aestivum*, is a member of the Poaceae grass family. The grass is found in temperate climates in the United States and Europe, and its roots, rhizomes, and aboveground parts are used in herbal remedies and as a concentrated nutrient source. Wheatgrass is produced from wheat seeds soaked in water; it takes about a week for the seeds to produce harvestable grass. Promoted as a "superfood," wheatgrass generally has not lived up to the marketing promises made. For apparently healthy people, wheatgrass does not appear to be more nutritious or health promoting than many other better-tasting vegetables. A few small studies, however, suggest wheatgrass might be helpful for reducing symptoms of ulcerative colitis and the genetic disorder thalassemia major, and for reducing the toxic side effects of chemotherapy in breast cancer patients.

The nutritional and healing benefits of wheatgrass first were publicized by Ann Wigmore, a holistic health practitioner, in the 1940s. Wigmore observed that cats and dogs often ate grass when they were sick. She also was inspired by the biblical story of King Nebuchadnezzar who went crazy and lived like a wild animal, eating grass for seven years. Wigmore might have assumed that the king overcame his insanity by ingesting grass, although this does not appear to be the intent of the story (Weil, 2006). Wheatgrass originally was employed as a detoxification agent, blended into a juice for easier digestion. The juice was ingested orally or through an enema, a choice still available for wheatgrass enthusiasts today. Wigmore, however, also fallaciously claimed that wheatgrass could cure diabetes and AIDS—a claim which was met with legal action from the Massachusetts attorney general (ACS, 2008).

Wheatgrass might contain antioxidant and anti-inflammatory agents—a reason why it could help treat ulcerative colitis. In one study, subjects with this disorder who drank approximately three ounces of wheatgrass juice per day for one month had less pain, diarrhea, and rectal bleeding than subjects drinking the placebo (ACS, 2008). Another small study suggested that wheatgrass juice could reduce the myelotoxicity (toxicity to bone marrow) of chemotherapy treatments in breast cancer patients (MSKCC, 2011). Research on patients with a genetic blood disorder called "thalassemia major," in which red blood cells are misshapen, noted that patients taking wheatgrass juice needed fewer transfusions than during periods when they received no juice (MSKCC, 2011). These studies indicate that further research on wheatgrass benefits, especially in these populations, might be warranted.

Although wheatgrass is considered relatively safe, there are some potential side effects of ingesting the grass. Some individuals have complained of nausea, headaches, hives, and throat swelling after drinking the juice, and those with wheat or gluten allergies are advised to use caution when trying wheatgrass. Because it is consumed raw, bacteria and mold contamination also are concerns. Because not much is known about the effects of wheatgrass, it is not recommended that women who are breast-feeding or pregnant ingest it. Although wheatgrass can be used as a



Wheatgrass is available in many stores and at juice bars. Some people grow wheatgrass in their homes. Wheatgrass is also available as a liquid herbal supplement, in capsules, as frozen juice, and as a powder. (Daniaphoto/Dreamstime.com)

part of holistic medicine, it is not recommended that one rely on wheatgrass in place of traditional medical care.

Hannah E. Underwood

See Also: Dietary supplements; Phytochemicals.

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Whey Protein

Whey is one of two protein classes found in milk and makes up about 20% of the total proteins in cow's milk, and about 80% of the proteins in human breast milk. Whey is the liquid portion of milk that remains when the curd—the solid component, composed of the casein protein group—is removed in the cheese-making process. Whey contains very digestible proteins and appears to have a number of health-promoting properties. Whey is used in many food products, such as ice cream and other dessert foods, as it contributes to food texture and quality. Whey protein powders and other products often are consumed by people interested in increasing protein intake, managing body weight, and improving physical fitness.

Whey is comprised of several different types of protein, many of which have been extensively studied in vitro, in laboratory animals, and in humans. One of the proteins in whey is alpha-lactalbumin, for example, which contains significant amounts of the amino acid tryptophan. Tryptophan is a precursor to serotonin, a neurochemical thought to influence mood and brain activity. Alpha-lactalbumin consumed by a person in the evening could improve morning alertness the next day, perhaps by improving sleep quality, and it appears to reduce anxiety in animals (Krissansen, 2007). Whey protein also contains beta-lactoglobulin, which might inhibit allergic response and carcinogenesis in animals. Other proteins in whey have been found to inhibit inflammation in the gastrointestinal tract, improve cholesterol metabolism, and inhibit hormones associated with high blood pressure. Whey protein might help people who are trying to eat less as it could help reduce hunger and increase satiety hormones. Whey protein also could help reduce some symptoms of diabetes (Sousa et al., 2012).

Whey contains high levels of the amino acid cysteine. The body uses cysteine to produce an important antioxidant, glutathione. Glutathione appears to protect many body tissues from the harmful effects of oxidation. Theoretically, increasing glutathione might help slow the process of certain diseases which lower glutathione levels such as cataracts, HIV, some types of cancer, and liver disease, although such results have not yet been demonstrated with whey protein supplementation in humans.

Whey protein is a component of milk-based infant formulas. Some infant formulas contain whey protein that has been chemically broken down ("predigested" or "hydrolyzed"). This formula appears to be less likely than regular infant formula to lead to the development of allergies in infants at high risk for this health problem.

Protein intake combined with strength training has been shown to increase muscle strength and mass. People often use whey protein as their protein source, consuming whey protein shakes and other supplements immediately before or

after training to ensure an adequate supply of amino acids for muscle building. There is no strong evidence that whey is more beneficial than casein—the other protein in milk—however, therefore simply drinking milk might produce a good result.

Whey protein appears to be safe even at fairly high doses (up to 50 g per day) when taken for several weeks. Long-term effects of high doses have not been studied, therefore taking lower doses (15 g to 20 g per day) could be more prudent. People who are lactose-intolerant might be able to tolerate whey isolate, which is only 1% lactose (whey concentrate contains 4% lactose). Because whey protein can lower blood pressure or alter blood sugar regulation, people taking medications should check with their health care providers before taking whey protein supplements. Long-term consumption of whey protein supplements could lead to kidney damage or bone loss because of the high protein content of whey.

Thea J. Dennis

See Also: Amino acids; Dairy foods.

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Women, Infants, and Children, Special Supplemental Nutrition Program for

The Special Supplemental Nutrition Program for Women, Infants and Children (WIC) carries out the mission "to safeguard the health of low-income women, infants, and children up to age 5 who are at nutrition risk by providing nutritious foods to supplement diets, information on healthy eating, and referrals to health care" (Food and Nutrition Service, 2012a). WIC provides federal grants to states for nutrition programs aimed at improving the health of low-income women and their young children. Established in 1972, WIC continues to serve families in communities across the United States. Many evaluative studies have supported the

efficacy of the program, though some have argued there is room for the program to adapt to the changing nutritional environment of the United States.

The WIC program originated in the 1960s to address a growing public concern that the health of low-income Americans was at risk due to malnutrition. The Food, Nutrition and Health Conference held at the White House concluded with recommendations to address malnutrition, such as implementing a program to address the nutritional needs of low-income pregnant women and young children (Oliveira & Frazão, 2009). In 1968, a meeting between clinicians and public health officials led to a plan for pregnant or breast-feeding women to be given prescriptions for certain foods. Soon after, in 1972, WIC began as a pilot program and on October 7, 1975, after three years of positive program feedback, WIC was permanently established (Oliveira & Frazão, 2009). Originally, WIC was named the "Special Supplemental Food Program for Women, Infants, and Children" but that was changed to the "Special Supplemental Nutrition Program for Women, Infants and Children" in 1994. The name was changed to emphasize WIC as a nutrition-focused health program (Food and Nutrition Service, 2012a).

Today, WIC is available in all 50 U.S. states; 34 Indian Tribal Organizations; the District of Columbia; and in the U.S. territories of American Samoa, Guam, Commonwealth of the Northern Mariana Islands, Puerto Rico, and the Virgin Islands. Among these 90 state agencies, there are 1,836 local agencies and 9,000 clinic sites (Food and Nutrition Service, 2012c). When it began in 1972, WIC started with 88,000 participants and received $20.6 million in government funding. In 2012, WIC served nearly 9 million participants and was appropriated a total of $6.618 billion (Oliviera & Frazão, 2009).

Eligible participants for WIC programs include pregnant, postpartum, and breast-feeding women as well as infants and children 5 years of age and younger who are low-income and at risk nutritionally. To meet the income requirement, applicants must be below the 185% of the federal poverty income level. In 2013, an income of $42,643 or less for a family of four made people eligible for the WIC program. The specific guidelines can vary by state, but income eligibility limits can be no greater than 185% of the federal poverty income level. Participants in other supplemental programs (such as Supplemental Nutrition Assistance Program, Medicaid, Temporary Assistance for Needy Families, and many state-administered programs) automatically meet the income-eligibility requirement (Food and Nutrition Service, 2012b).

In addition to the income requirement, participants also must meet the criteria for nutrition risk. Eligibility due to nutrition risk is determined through an evaluation by a health professional such as a physician, nurse, or nutritionist. The evaluation usually is performed at no cost to the applicants at the WIC clinic (Food and Nutrition Service, 2012b). Participants must meet one of two categories for nutrition risk. The two types recognized by WIC are medically based risks (such as anemia, under or overweight, or history of pregnancy complication) and dietary risks (such as inappropriate feeding practices or failure to meet the current *Dietary Guidelines for Americans*) (Food and Nutrition Service, 2012c). In 2011, WIC released a Prescreening Tool, which was accessible online to help applicants determine if they are likely to be eligible to receive benefits. The Prescreening Tool is

now available in English, Spanish, and Chinese, with plans for more languages to be added (Food and Nutrition Service, 2012d).

Once granted eligibility to participate in the WIC program, participants can access supplemental food packages, nutritional education programs, and referrals to health care and social services. The food packages are put together to meet the needs of each individual participant. Food packages do not vary according to income but are rather tailored to the nutritional needs and personal preferences of the participant. Nutritional education is made available to help participants improve their health by making dietary and lifestyle changes. Lessons emphasize the relationships between food, exercise, and health and are adapted to the needs of specific populations. Participants also are advised on how to obtain health care and services such as immunizations, food stamps, and Medicaid. Women who are breast-feeding receive enhanced benefits, including food packages with greater quantities of food and one-on-one counseling (Oliviera & Frazão, 2009). In most states, WIC participants receive checks or vouchers to purchase foods from vendors. Many states are implementing electronic cards, similar to debit cards, with which participants purchase food. A few states distribute food to participants at warehouses or even deliver food to people's homes.

Numerous studies and committees have evaluated the efficacy of WIC programs. One research study, for instance, compared the infant mortality rates of WIC participants to non-WIC participants. The researchers found that the infant mortality was lower for WIC participants overall and that the WIC program dramatically reduced the racial disparity of infant mortality rates (Khanani, Elam, Hearn, Jones, & Maseru, 2010). Another study evaluated the nutrition-education programs and found the education programs to be effective—people who had received nutrition education had a greater recognition for nutritional messages and made greater efforts to consume nutritious foods (Ritchie, Whaley, Spector, Gomez, & Crawford, 2010). Additionally, participation in WIC led to increased birth weight and gestational age and reduced prevalence of iron-deficiency anemia (Owen & Owen, 1997). When participating in WIC, Medicaid costs also are significantly lower for women and their babies (Food and Nutrition Service, 2012a).

Despite the efficacy that various evaluative studies have reported, some suggest that there is room for improvement. In a 2005 report by the Committee to Review the WIC Food Packages, the committee suggested that the WIC program must adapt to the changing food environment in the United States. Although the program originally was established to reduce food insufficiency and combat undernutrition, the committee argues that WIC must balance its original goal with the current need for accessible nutritious food options to reduce chronic disease (Committee to Review the WIC Food Packages, 2005). Further, many have argued that—following the Institute of Medicine's recommendation that everyone consume more fruits and vegetables—WIC must offer a wider variety of foods and should direct food vouchers toward fresh produce. The U.S. food environment is continually changing and WIC must continue to adapt. Further evaluative studies should be performed to continue assessing the efficacy of WIC programs for the population it seeks to serve, and to determine directions for program development.

Eliza N. Cooley

Research Issues

The Food and Nutrition Program has created a special program called the "WIC Farmers' Market Nutrition Program," which allows program participants to shop at local farmers' markets. Only a minority of states in the United States, however, currently allows farmers to accept WIC cash-value vouchers. If increasing people's consumption of fresh fruits and vegetables is a program goal, however, then allowing voucher use at farmers' markets could help attain this goal. The Food and Nutrition Program website (provided below) provides more information about this program.

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See Also: Public policy on nutrition.

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Y

Yerba Mate

The yerba mate plant is a small tree (*Ilex paraguariensis*) native to southern South America, whose leaves are used to make a type of tea known as "mate." This tea traditionally is used as both a medicinal and social beverage, and often is passed around a group in a dried gourd and consumed through a filtered metal straw. When sold commercially, yerba mate is dried and aged to achieve the desired flavor. The drink can be prepared by steeping leaves and twigs from the plant in hot water, which yields a caffeinated tea with high antioxidant content. A typical cup of yerba mate tea contains more caffeine than black tea, but less than that found in a cup of coffee. Its beneficial ingredients also include vitamins B and C, manganese, zinc, and potassium in addition to plant-specific phytochemicals such as xanthines and polyphenols (Heck & de Mejia, 2007).

Scientific literature on yerba mate has shown it to have possible cholesterol-reducing effects as well as the ability to protect the liver. A few small studies suggest that yerba mate could increase fat metabolism but, in general, the results of studies regarding the relationship between yerba mate and weight loss are ambivalent. Although still not definitive, epidemiological evidence suggests that consumption of yerba mate beverages increases the risk of esophageal, larynx, and oral-cavity cancer, perhaps because hot yerba mate drinks can damage the mucosa that forms a protective lining of these areas (Loria, Barrios, & Zanetti, 2009). The carcinogenic effects of yerba mate appear to increase with tobacco use. These negative effects could present a risk for long-term heavy use by consumers, although occasional use by adults probably is safe.

Patricia M. Cipicchio

See Also: Phytochemicals.

Further Reading

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Z

Zeaxanthin

Zeaxanthin is a type of carotenoid produced by plants that is thought to play a protective role in the retina of the eye. It is a member of the xanthophyll class of carotenoids, which are yellow oxygen-containing pigment molecules. In the human diet, this antioxidant is found is corn, spinach, oranges, kale, Swiss chard, and other leafy greens. Zeaxanthin is one of only two carotenoids that accumulate in the human retina. Along with lutein, their concentration is especially high in the macular region of the retina, the area which absorbs short-wavelength blue and ultraviolet light and is responsible for visual acuity. Over time, light damage to the retina can result in "ghosts" where photoreceptor cells have died, resulting in a noticeable loss of central vision. Enduring atrophy of photoreceptors in this area is known as age-related macular degeneration (AMD).

Though there is no daily intake recommendation for zeaxanthin, its positive benefits are becoming increasingly apparent. Studies have shown that high macular-pigment density is associated with a reduced risk of AMD. Additionally, research has demonstrated that individuals with high dietary carotenoid intake have a significantly lower risk of AMD than do subjects consuming the lowest levels of dietary carotenoids. Some research also suggests that zeaxanthin supplements could improve night vision. Although many experts still are reluctant to recommend zeaxanthin supplements, all agree that increasing intake of foods high in this carotenoid is likely to be beneficial to eye health. Due to the demonstrated positive effects of this molecule after the onset of AMD, the National Eye Institute suggests special supplement formulations that include zeaxanthin for those with intermediate or advanced AMD (AREDS2 Research Group et al., 2014).

Patricia M. Cipicchio

See Also: Eye health; Phytochemicals.

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Zinc

Zinc is an essential metal that is important to human health. In terms of human nutrition, it is classified as a trace element or mineral. Individuals who are deficient in zinc can experience wounds healing more slowly. Children can experience stunted growth and acute diarrhea. Zinc plays many important roles in the body. It appears to participate in more than 100 different enzyme pathways, and is an important structural component of many proteins. Zinc proteins help to regulate gene expression and also participate in cell signaling pathways. Zinc supplements and cold remedies are used to boost the immune system to treat upper respiratory and ear infections. Zinc also is a component of dietary supplements that have been shown to be helpful for slowing the progression of age-related macular degeneration.

The importance of dietary zinc was not discovered until 1961, when scientists observed certain male population groups in Iran and Egypt who suffered from severe growth retardation, anemia, and hypogonadism (underdeveloped sexual organs) (Insel, Ross, McMahon, & Bernstein, 2014). The diets of the affected men primarily consisted of wheat bread and included few animal products. The best dietary sources of zinc are animal products, thus the zinc intake in the groups of affected men was very low. Additionally, the phytic acid found in wheat products inhibited the absorption of the little dietary zinc that was ingested. (Phytic acid binds with minerals in the digestive tract, making these minerals unavailable for absorption.)

Dietary Zinc

Zinc has many important functions in the body. It is a component of the important enzyme "superoxide dismutase," which enhances antioxidant activity and protects cells from free-radical damage. Zinc also is a component of the enzyme that assists the work of vitamin A in the eye's retina. Zinc interacts with several hormones, including insulin, and thus is integral to metabolism of carbohydrates. This important mineral plays a role in apoptosis—programmed cell death—which can limit the replication of damaged cells. Zinc influences taste perception and the regulation of appetite.

The daily recommended intake of zinc is 11 mg per day for adult men and 8 mg per day for adult women (NIH, 2014). Oysters are exceptionally good sources of zinc. Foods with high amounts of animal proteins such as beef, pork, dark-meat chicken, and lamb also are good sources of zinc. Plant foods such as grains, legumes, fruits, and vegetables supply some zinc, but the human body is less able to effectively use the zinc from plant sources. Thus, vegetarians who consume a low protein diet are at risk for being low in zinc. In the long term, however, the body adapts and becomes more efficient when it comes to absorbing zinc (NIH, 2014).

Table 1. Selected Food Sources of Zinc

Food	Milligrams (mg) per Serving	Percent DV*
Oysters, cooked, breaded, and fried, 3 oz	74	493
Beef chuck roast, braised, 3 oz	7	47
Crab, Alaska king, cooked, 3 oz	6.5	43
Beef patty, broiled, 3 oz	5.3	35
Breakfast cereal, fortified with 25% of the DV for zinc, ¾ cup serving	3.8	25
Lobster, cooked, 3 oz	3.4	23
Pork chop, loin, cooked, 3 oz	2.9	19
Baked beans, canned, plain or vegetarian, ½ cup	2.9	19
Chicken, dark meat, cooked, 3 oz	2.4	16
Yogurt, fruit, low fat, 8 oz	1.7	11
Cashews, dry roasted, 1 oz	1.6	11
Chickpeas, cooked, ½ cup	1.3	9
Cheese, Swiss, 1 oz	1.2	8
Oatmeal, instant, plain, prepared with water, 1 packet	1.1	7
Milk, low-fat or non-fat, 1 cup	1	7
Almonds, dry roasted, 1 oz	0.9	6
Kidney beans, cooked, ½ cup	0.9	6
Chicken breast, roasted, skin removed, ½ breast	0.9	6
Cheese, cheddar or mozzarella, 1 oz	0.9	6
Peas, green, frozen, cooked, ½ cup	0.5	3
Flounder or sole, cooked, 3 oz	0.3	2

* DV = Daily Value. Daily Values were developed by the U.S. Food and Drug Administration to help consumers compare the nutrient contents of products within the context of a total diet. The DV for zinc is 15 mg for adults and for children 4 years of age and older. Food labels, however, are not required to list zinc content unless a food has been fortified with this nutrient. Foods providing 20% or more of the DV are considered to be high sources of a nutrient. The U.S. Department of Agriculture's Nutrient Database website lists the nutrient content of many foods and provides a comprehensive list of foods containing zinc.

Source: U.S. Department of Agriculture, Agricultural Research Service. (2011). *USDA National Nutrient Database for Standard Reference, Release 24*. Nutrient Data Laboratory Home Page (http://www.ars.usda.gov/ba/bhnrc/ndl). Reprinted in *Zinc*. (2013). Office of Dietary Supplements. http://ods.od.nih.gov/factsheets/Zinc-HealthProfessional/

The digestive tract absorbs about 10% to 30% of the zinc supplied by the diet, which is comparable to iron absorption rates (Insel et al., 2014). Coffee, dairy products, calcium, calcium-fortified foods, and fiber can reduce zinc absorption (NIH, 2014). The following supplements can reduce the rate of absorption for zinc—bromelain, calcium, chromium, copper, EDTA, IP-6 (phytic acid), and iron. There is conflicting evidence on the absorption rate of zinc when it comes to interaction with folic acid, magnesium, and vitamin D. Conversely, manganese and riboflavin (vitamin B2) might improve the absorption rate of zinc.

Zinc Dietary Supplements

Zinc is available in multivitamin and mineral supplements, and as a single-nutrient dietary supplement. There are three different forms of zinc—zinc gluconate, zinc sulfate, and zinc acetate. More research is needed to determine whether one form of zinc has a better absorption rate than another. Many over-the-counter medications such as cold lozenges, nasal sprays, and nasal gels contain zinc (NIH, 2014). It is important to note that that nasal sprays with zinc possibly are unsafe because the zinc potentially can cause the loss of the ability to smell (NIH, 2014).

Because of the many roles zinc plays in the body, zinc supplements have been investigated as potential agents for the prevention and treatment of a variety of disorders. Zinc supplements appear to offer some promise for reducing the length and severity of upper respiratory tract infections. Zinc enhances wound healing and is found in a variety of skin-care products. Zinc supplements are recommended by the World Health Organization for treatment of childhood diarrhea (ODS, 2013). The Age-Related Eye Disease Study (AREDS) found that antioxidant supplements (composed of vitamins C, E, and beta-carotene) alone failed to slow the progression of age-related macular degeneration (AMD) in older subjects. Supplements containing both antioxidants and zinc, however, did significantly reduce the risk of advanced AMD and vision loss (ODS, 2013). Zinc supplements sometimes are given as treatment for Wilson's disease—a disorder that causes excessive copper absorption and storage in the body—because a high intake of zinc reduces copper absorption by the digestive tract.

Upper Limits, Toxicity, and Warning

Zinc should be avoided as a routine high-dose supplement unless recommended by a health care professional. When zinc is taken by mouth or applied to the skin, it is recommended that the amount used be no greater than 40 mg per day. Long-term consumption of zinc supplements at this level can cause a copper deficiency. Zinc can be fatal if a single dose of 10g to 30 g (1,000 to 3,000 mg) is consumed (NIH, 2014). Problems with blood iron can arise when 450 mg or more of zinc is consumed daily. Research suggests that men who have been taking 100 mg of supplemental zinc daily for 10 years or more could have increased risk of developing prostate cancer (NIH, 2014).

Susana Leong

See Also: Eye health; Minerals; Upper respiratory tract infections.

Further Reading

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Recommended Resources

Agency for Healthcare Research and Quality (www.ahrq.gov/research/findings/evidence-based-reports).
The Agency for Healthcare Research and Quality (AHRQ) is administered by the U.S. Department of Health and Human Services. Through its Evidence-Based Practice Centers Program, it sponsors reports that summarize and evaluate the research on a variety of health-related topics.

Academy of Nutrition and Dietetics (www.eatright.org).
The Academy of Nutrition and Dietetics website offers a plethora of science-based information, including position papers on a variety of nutrition and health topics. Research summaries also can be accessed on this site via a link to the Evidence Analysis Library.

Blake, J. S., Munoz, K. D., & Volpe, S. (2013). *Nutrition: From Science to You*. San Francisco: Benjamin Cummings.

Centers for Disease Control and Prevention (CDC) (www.cdc.gov).
The Centers for Disease Control and Prevention (CDC) conduct scientific research, compiles morbidity and mortality data for the United States, and provides extensive health information on its website.

Cochrane Collaboration (www.cochrane.org/reviews/).
The Cochrane Collaboration is an independent network of researchers from more than 120 countries that produces extensive high-quality literature reviews on a variety of health topics.

ConsumerLab.com (requires subscription) (https://www.consumerlab.com/).
ConsumerLab.com independently tests health and nutrition products. Its website also features reports on the health efficacy of supplement ingredients.

EBSCO Complementary and Alternative Medicine Review Board (http://www.ebscohost.com/nursing/products/patient-education-reference-center/patient-education-reference-center-editorial-policies).

The EBSCO Complementary and Alternative Medicine (CAM) Review Board publishes summaries on the research evaluating the efficacy of a variety of nutrients and supplements. EBSCO Information Services publishes research databases, e-books, and e-journals, and requires a subscription. Much of the material from the CAM Review Board, however, is purchased by hospitals and other health care organizations and posted on their websites.

Food and Drug Administration (www.fda.gov/food).
The Food and Drug Administration (FDA) oversees food and drug safety in the United States. Its website includes extensive information about foodborne illness, food recalls, food ingredients and labeling, dietary supplements, and other popular food- and drug-related topics.

Harvard School of Public Health (http://www.hsph.harvard.edu/nutritionsource/).
The Harvard website offers many interesting perspectives on nutrition and health.

Health Canada (www.hc-sc.gc.ca/index-eng.php).
Health Canada's website offers a wide variety of resources on nutrition and health.

Insel, P., Ross, D., McMahon, K., & Bernstein. (2014). *Nutrition*. Burlington, MA: Jones & Bartlett.

Institute of Medicine (www.iom.edu).
The Institute of Medicine (IOM) website offers a range of research reports on a variety of health issues. The Food and Nutrition Board of the IOM website provides reports on a variety of activities and nutrition topics (http://www.iom.edu/About-IOM/Leadership-Staff/Boards/Food-and-Nutrition-Board.aspx). The Board also compiles reports and tables for the Dietary Reference Intake (DRI) and Tolerable Upper Intake Level (UL) values for nutrients.

Linus Pauling Institute, Micronutrient Information Center, Oregon State University (http://lpi.oregonstate.edu/infocenter/).
The Linus Pauling Institute sponsors research and compiles scientific reports on vitamins, minerals, other nutrients, phytochemicals, and some foods and beverages.

Mayo Clinic (www.mayoclinic.com).
The Patient Care and Health Information section of the Mayo Clinic website offers sound information on a broad range of health problems and about dietary supplements.

McGuire, M., & Beerman, K. A. (2013). *Nutritional Sciences: From Fundamentals to Food*. Belmont, CA: Wadsworth, Cengage Learning.

MedlinePlus (http://www.nlm.nih.gov/medlineplus/).
The MedlinePlus website is provided by the National Institutes of Health and is produced by the National Library of Medicine. This site provides good information on many nutrition and health topics and about dietary supplements.

Memorial Sloan Kettering Cancer Center. Integrative Medicine (search About Herbs, http://www.mskcc.org/cancer-care/integrative-medicine/about-herbs).
The Integrative Medicine section of the Memorial Sloan Kettering Cancer Center provides solid information about a great number of herbs, botanicals, and dietary supplements.

National Agricultural Library (www.nal.usda.gov).
The National Agricultural Library (NAL) website provides sound information on agriculture, farmers markets, animal welfare, and meal planning. The NAL also offers a list of helpful links on the Nutrition.gov website (http://www.nutrition.gov).

National Center for Complementary and Alternative Medicine, National Institutes of Health (http://nccam.nih.gov).
The National Center for Complementary and Alternative Medicine (NCCAM) is part of the National Institutes of Health and sponsors research on a variety of complementary and alternative medical practices, including nutrition therapies. Its website offers good information on a variety of health topics, herbs, and dietary supplements.

National Institute of Diabetes and Digestive and Kidney Diseases (http://www.niddk.nih.gov/health-information/health-information-clearinghouses/Pages/default.aspx).
The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) website links to several lists of helpful websites. The National Digestive Diseases Information Clearinghouse page is especially useful for information on digestive diseases (http://digestive.niddk.nih.gov).

National Institutes of Health, Office of Dietary Supplements (ods.od.nih.gov).
The National Institutes of Health, Office of Dietary Supplements (ODS) evaluates scientific information, supports research, and offers a wide range of educational materials about dietary supplements.

Nutrition Action (http://www.nutritionaction.com).
The Nutrition Action website and health letter provide valuable overviews of the latest research on health and nutrition. Nutrition Action materials are produced by the nonprofit Center for Science in the Public Interest (CSPI), which receives no funding from advertising, government, or industry. The website offers free materials, and the health letter can be obtained through libraries or by subscription.

Pennington, J. A. T., & Spungen, J. (2010). *Bowes & Church's Food Values of Portions Commonly Used*. Philadelphia: Lippincott Williams & Wilkins.

Smolin, L. A., & Grosvenor, M. B. (2013). *Nutrition: Science and Applications*. Hoboken, NJ: John Wiley & Sons.

Thompson, J. J., Manore, M., & Vaughan, L. (2013). *The Science of Nutrition*. San Francisco: Pearson Benjamin Cummings.

Tufts University, Health & Nutrition Letter (http://www.nutritionletter.tufts.edu).
The information on the Tufts University Health & Nutrition Letter website and newsletters come from Tufts University's Friedman School of Nutrition Science and Policy, and focuses on nutrition and health.

United States Department of Agriculture, Food Composition (http://fnic.nal.usda.gov/food-composition).
The Food Composition website provides a searchable database of foods and nutrients, plus other valuable information.

University of Maryland Medical Center, Complementary and Alternative Medicine Guide (https://umm.edu/health/medical/altmed).
The University of Maryland Medical Center Complementary and Alternative Medicine Guide website offers in-depth reports on a variety of health conditions, nutrients, herbal treatments, and dietary supplements.

Whitney, E. N., & Rolfes, S. R. (2013). *Understanding Nutrition*. Belmont, CA: Wadsworth, Cengage Learning.

Willett, W. (2013). *Nutritional Epidemiology*. New York: Oxford University Press.

World Health Organization (http://www.who.int/topics/en/).
The World Health Organization (WHO) website includes a topic list which provides links to a broad range of health and nutrition information from around the world.

Sources to Avoid

When searching for information on nutrition—especially dietary supplements—it's imperative to beware of sites that masquerade as news articles or authoritative discussions but include links to purchase the product being discussed. In 2012, for example, the Federal Trade Commission fined several organizations that were promoting acai berry products for weight loss. Consumers would click on an attention-grabbing ad that appeared when they used popular search engines and websites. Ads used wording such as "Acai Berry EXPOSED—Health Reporter Discovers the Shocking Truth." The ads then took readers to fake "news" sites with

opportunities to order the product. (Federal Trade Commission. [2012, January 25]. *FTC permanently stops six operators from using fake news sites that allegedly deceived consumers about acai berry weight-loss products*. Retrieved November 12, 2014, from http://www.ftc.gov/news-events/press-releases/2012/01/ftc-permanently-stops-six-operators-using-fake-news-sites.

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