Vitamins and Minerals:

Does the Epidemiologic Evidence Justify General Supplementation?
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SECOND EDITION

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Millions of Americans take vitamin and mineral supplements because they hope or believe supplements will help prevent such diseases as cancer, heart disease, osteoporosis and age-related macular degeneration (a common form of blindness in the elderly). Recent scientific evidence that taking supplements of specific nutrients such as vitamin C, vitamin E, beta-carotene, selenium, and calcium may be protective is not uniformly strong. There is stronger evidence that a diet rich in fruits and vegetables containing these nutrients can lower the risk of disease. Furthermore, because foods are complex mixtures of many substances, it is not clear that the nutrients currently promoted as protective are really the most important or effective ones.

Supplementation can be prudent in a variety of situations; for example, during early pregnancy folate supplementation can help prevent some birth defects. Supplementation can, however, involve risks—toxicity from megadoses of certain nutrients, negative interactions between nutrients, and a false sense of security about the adequacy of a supplemented diet.

Guidelines are available to help consumers evaluate and alter their diets when it is advisable to do so. The Recommended Dietary Allowances (RDAs) of the National Research Council’s Food and Nutrition Board provide recommended levels of intake of many nutrients. These allowances are not minimums, but are set well above average requirements to allow for differences in individual needs and body storage, less than optimal absorption or low availability of nutrients from foods. Tolerable upper intake levels for some nutrients have also been established to increase consumers’ awareness of potential problems with high doses.

The Dietary Guidelines for Americans make general recommendations on overall diet, and the Food Guide Pyramid translates these into a graphic representation of groups of foods. Both the RDAs and the Dietary Guidelines are periodically reevaluated and updated.

As a national public health organization,
ACSH feels its recommendations should be based on the evidence, not on a “Well, it probably won’t hurt and might help” philosophy. ACSH therefore recommends that consumers carefully evaluate their own dietary intake in relation to personal risk factors and the current guidelines when considering whether or not to take vitamin and/or mineral supplements.

While it may look promising, the evidence supporting the effectiveness of supplementation in preventing chronic disease is not yet compelling. If it becomes compelling, our advice will change. Until such a time, the evidence does not warrant a broad recommendation that supplements be taken routinely by healthy individuals, especially when the evidence is far stronger that a balanced diet, especially when rich in fruits and vegetables, can reduce the risk of some chronic diseases.
INTRODUCTION

Vitamin and mineral supplements are among the most widely used nonprescription products in the United States today.\(^1,2\) The 1987 and 1992 National Health Interview Surveys\(^3\) found that about 24% of Americans between 18 and 75 years of age reported using a vitamin and/or mineral supplement of some type daily. In 1998, sales of vitamins and mineral supplements in the United States reached nearly five billion dollars (up from about three and one half billion in 1994).\(^4\)

Nutrient supplements—either vitamins alone, minerals alone, or combinations thereof—are used for a variety of reasons, traditionally for prevention and treatment of dietary deficiencies. Recently, both public and scientific attention has focused increasingly on certain chronic diseases and their relation to diet and nutrient intake. The possibility that so-called antioxidant nutrients can decrease the risk of heart disease, cancer and certain visual problems, the possibility that calcium supplements can protect against osteoporosis, and the potential for folate and other B vitamins to reduce the risk of cardiovascular disease, have generated both wide interest and controversy, as well as certain health claims for some foods. Experts disagree about whether vitamin and mineral supplements are appropriate for healthy individuals for preventing chronic diseases. Thus, this report focuses primarily on the epidemiologic evidence relating these nutrients to reduction of disease risk.

This report explores the general issues surrounding the use of vitamin and/or mineral supplements, reviews arguments for and against their use and evaluates the evidence for the efficacy of specific supplements. In it we suggest how consumers can rationally evaluate their own diets and decide—on an individual basis—whether or not to use supplements. Many other types of dietary supplements—herbs, hormones, and various metabolites, for example—are widely available in the American market today. Although the availability and use of such supplements makes them important subjects for investigation, their large number and variety precludes their inclusion in this report.
USES OF VITAMIN AND MINERAL SUPPLEMENTS

Traditional Approaches

The dictionary definition of a supplement is something added to complete a diet or to make up for a deficiency. The key here is the concept of deficiency: When an essential nutrient is absent from a diet for a prolonged period, or when an inadequate amount of it is present, a specific deficiency disease results. That disease can be diagnosed and then treated by providing the missing dietary element, as long as no irreversible damage has occurred.

Nutrition scientists agree that supplementation may be advisable to prevent deficiencies that result from an inadequate diet. A diet may be incomplete because of poverty, ignorance, adherence to particular dietary beliefs, a physical inability to obtain or eat certain foods or even a dislike of particular foods. Nutritional needs change, too, as we progress from infancy to old age: On a body-weight basis, an infant needs more protein, vitamins and minerals than an adult. Around the time of puberty, the accelerated growth of both boys and girls increases the need for a number of nutrients to provide for increases in bone, muscle and blood volume. Women’s requirements for iron are higher during the reproductive years than after menopause (when menstrual losses of blood and iron cease).

Most nutritionists agree that individuals may benefit from dietary supplements in the following situations:

- Infants and young children between the ages of 6 months and 3 years who live in an area where the drinking water supply is low in fluoride may need fluoride supplementation.
- Because of rapid growth, a child may need supplements from infancy until he or she begins eating a nutritionally balanced variety of foods (usually by age 2).
- During the reproductive years, women who consume an inadequate diet need folic acid (a B vitamin) supplementation. Folic acid is important for the prevention of some types of birth defects. Additionally, pregnancy and lactation may increase a woman's needs for iron, folic acid and calcium to a degree not easily satisfied by dietary intake.
- Strict vegetarians (vegans) need supplements to obtain adequate amounts of vitamin B₁₂, calcium, and zinc.
Nutrient supplements can also be efficacious in the treatment of some diseases not directly related to dietary deficiency. For example, individuals who have pernicious anemia (a disease in which a protein necessary for vitamin B$_{12}$ absorption is not produced by the stomach) are unable to absorb vitamin B$_{12}$ from their food. This inability to absorb B$_{12}$ results in vitamin B$_{12}$ deficiency, which leads to anemia and, if not treated, damage to the nervous system. Individuals with pernicious anemia can be treated with monthly injections of B$_{12}$, thereby bypassing the defective absorption process, or by oral administration of very large amounts of the vitamin.

The treatment of diseases with certain therapeutic drugs can also alter the absorption and/or metabolism of vitamins and minerals and produce a deficiency even when the diet of the person being treated is complete. Some types of diuretics,* for example, increase the excretion of potassium, magnesium, and zinc from the body. Similarly, some anticonvulsant medications increase the need for vitamin D, folic acid and biotin (another B vitamin). Physicians who routinely prescribe such medications are usually aware of these interactions and will prescribe appropriate vitamin and mineral supplements as needed.

With the exception of situations such as those described above, the prevailing scientific viewpoint is that the best way to prevent nutritional deficiencies is to eat a varied, balanced diet—one that includes foods from each of the five major food groups depicted in the Food Guide Pyramid (see page 31). Some groups and individuals advise consumers to take vitamin and/or mineral supplements as general “insurance” against nutrient deficiencies; and a wide variety of individual as well as combination vitamin/mineral preparations are available to insure people against such deficiencies. Many such supplements provide 100% or more of the recommended dietary intake.

**Newer Approaches**

**Prevention of Chronic Diseases**

A different perspective on vitamins and minerals has emerged recently—a perspective in which some nutrients are considered potentially effective prophylactics against chronic and debilitating diseases. These nutrients are sold both as individual supplements to prevent specific diseases and in combinations containing, for example, a single category of nutrients like antioxidant nutrients.

* See Glossary for definition

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Does the Epidemiologic Evidence Justify General Supplementation?
Avery popular belief is that so-called antioxidant nutrients (e.g., vitamins C and E, selenium, and the vitamin A precursor beta-carotene), as well as some B vitamins decrease morbidity* and mortality* from heart disease and cancer. Such nutrients also are claimed to decrease one form of blindness. Calcium supplementation is suggested by some to be necessary to prevent and/or treat osteoporosis. People are being urged to take extra doses of individual nutrients as preventive measures.

Some proponents of supplementation promote this practice as leading to a state of “optimal” nutrition. This nutritional state is not clearly defined and is implied to be unreachable without the use of supplements.

**Do Supplements Prevent Chronic Disease?**

*Epidemiologic Evidence*

Before describing observations of associations between supplement use and chronic disease in humans, it is important to understand epidemiology* and the nature of epidemiological studies which have provided the data. Epidemiological studies compare the occurrence of disease with characteristics of the individuals under study. These characteristics can include both genetic (race and gender, for example) and environmental differences (diet, geographical location, smoking and drinking habits, socio-economic status and religious affiliation).

There are two major types of epidemiological studies—observational and interventional studies.

In observational studies, scientists compare the occurrence of a characteristic in people who have a disease with its occurrence in those who are free of that disease. Nothing is done to the subjects that would not be done in the normal course of their lives.

There are two types of observational studies, prospective and retrospective.

In retrospective studies, investigators compare people with a disease (called “cases”) with those without it (called “controls”) and compare past exposure to a compound, treatment or drug of interest. For example, the past intake of vitamin C by people who currently have heart disease might be compared to the past vitamin C intake of similar people without the disease. The study is called “retrospective” because the behavior of interest (the intake or—lack of it—of vitamin C) thought to lead to the disease occurred in the past.

If cases and controls differ significantly with respect to any of the fac-
tors examined, a correlation is claimed to exist between that factor and the disease. In our example, if there is less heart disease among the people who took vitamin C supplements in the past than among those who did not, a negative correlation is claimed between vitamin C intake and heart disease risk.

Such differences do not necessarily mean that one factor causes the other. The disease and the dietary difference may occur together by chance or coincidentally, or because both are caused by an underlying unmeasured factor. It could be, for example, that people who do not develop heart disease and who also take vitamin C exercise more than those who do not take vitamin C.

A weakness of this type of study as a means for investigating diet-to-disease relationships is its retrospective nature. The knowledge of having a disease may cause people to alter their diets. Additionally, individuals may not accurately remember their past diet, or their recall may be selective or unreliable.

Another type of observational study, the prospective study, involves monitoring diets and health before the onset of a disease. This type of study provides more valuable data—because inaccurate reporting due to faulty memory is reduced and because establishing the onset of the disease can be more precise.

Importantly, observational studies, whether prospective or retrospective, cannot establish a cause-and-effect relationship—regardless of the differences between people with and people without the disease. Nevertheless, such studies and the relationships they detect can have significant value. By examining the differences between people with and without a disease, scientists generate hypotheses about disease causation. These hypotheses can then be tested in intervention studies.

Interventional studies (also called experimental or clinical trials) are always prospective. They involve giving some of the subjects a potentially beneficial compound to reduce the risk of the disease(s) under investigation. Well-designed intervention studies have subjects assigned at random to either a treatment group or a control group. In a recent study of the effects of beta-carotene and vitamin E on lung cancer in Finnish men, one group took beta-carotene; another took vitamin E; a third group received both; and the control group received an inactive substance—a placebo.5

Because neither the study subjects nor the people dealing directly with them knew who received which substance, this study is designated dou-
ble-blind. The benefit of a double-blind study is twofold: The subjects’ reports of their reactions are not influenced by knowledge of their assigned treatment, and the experimenters can not accidentally provide the identity of the compound.

The length of such studies is important. Dr. Charles Hennekens, a noted nutritional epidemiologist at Harvard Medical School, has estimated, for example, that to detect an effect of antioxidant nutrients on heart disease observations for three to five years are required. Detecting an effect on the incidence of cancer would require eight to ten years. The number of subjects needed in such studies is often very large—perhaps many thousands—in order to generate significant results. Study size depends on which nutrients and diseases are examined, and the size of the effect expected by the investigators. A small study would likely not be able to detect a weak effect of a nutrient on a disease.

**B Vitamins and Cardiovascular Disease: Homocysteine**

While ‘everyone knows’ that a high level of blood LDL (‘bad’) cholesterol is a significant risk factor for cardiovascular disease (CVD), there is another blood constituent that is currently being evaluated as a risk factor for this and for other chronic diseases. That compound is the amino acid homocysteine.

Unlike the essential amino acids, whose source is the diet, homocysteine is produced by the body and is not used to form body proteins. Homocysteine is what is called a ‘metabolic intermediate’. That is, it is produced in biochemical pathways that form and break down other biological compounds. The connection with vitamins is that in order for the body to handle homocysteine properly, three B vitamins are required — folate, vitamin B<sub>6</sub>, and vitamin B<sub>12</sub>. These vitamins act as cofactors or helpers for the enzymes* that are necessary for homocysteine metabolism. When any of these vitamins are not present in sufficient quantities, homocysteine levels in the blood rise.

The relationship between homocysteine and CVD was suggested by observations of individuals with genetic disorders involving a lack or impairment of one of the enzymes that convert homocysteine to other compounds. Persons with such deficiencies develop very high levels of blood homocysteine, are found to have advanced atherosclerosis early in life, and are at high risk of heart disease, heart attacks and strokes.

Several studies have shown that homocysteine levels were higher in people with increased incidence of heart attacks or stroke than in...
healthy controls. It has also been shown that in people with coronary artery disease, eating cereals fortified with folic acid did reduce plasma homocysteine levels significantly — by about 4 to 14 percentage points, depending on the amount of folic acid consumed. And a preliminary study in healthy young women also demonstrated that it is possible to lower blood homocysteine levels by taking supplements of folic acid. These studies do not show, however, that moderately elevated homocysteine levels cause CVD.

These data indicate that very high levels of homocysteine (as in genetic abnormalities) are associated with increased risk of cardiovascular disease, and that additional folic acid can lower plasma homocysteine levels. Further, recent data from observational studies indicate that moderately elevated levels of homocysteine are common in the general population, and are associated with an increased risk of CVD and deaths from CVD. No investigation has been completed, however, showing that lowering plasma homocysteine levels decreases the risk of CVD. Thus, the value of using supplements of folate and vitamins B and B to decrease the risk of CVD is unclear at present. A recent advisory from the American Heart Association (AHA) suggests that until intervention trials have demonstrated that lowering homocysteine also lowers CVD risk, "emphasis should be placed on meeting current RDAs for folate, as well as vitamins B and B, by intake of vegetables, fruits, legumes, meats, fish, and fortified grains and cereals." Until such data become available, the advisory also does not recommend widespread screening for elevated plasma homocysteine levels among healthy adults. The advisory does not preclude that individuals who have demonstrated CVD or indications of increased risk, might not benefit from increasing their intake of these B vitamins; it further suggests that they discuss with their physicians the advisability of measuring their homocysteine levels.

Antioxidants: What They Are and What They Do

Antioxidants are substances that prevent the oxidation of another substance. Antioxidants are found naturally in food as carotenes, vitamin E and vitamin C, and minerals such as copper, selenium, and zinc. There are also synthetic antioxidants, substances that may be added to foods during processing to preserve them from unwanted oxidation. Synthetic antioxidants include BHT (butylated hydroxytoluene), BHA (butylated hydroxyanisole) and isoascorbate.

A major reason for trying to prevent oxidation in foods and in our bod-
ies is to minimize the formation of substances known as free radicals. There are several different types of free radicals, but their common feature is their high chemical reactivity. They can affect the structure and function of many nearby molecules, either in food or in the body. The problem with free radicals is that they can start chain reactions—reactions that generate more free radicals.

Fatty acids, particularly unsaturated ones, are easily oxidized by free radicals. In foods, such oxidation leads to rancidity—‘off’ odors and objectionable tastes. In rubber, such as tires and erasers, oxidation brings about gradual hardening. In the body, there is evidence that the oxidation of lipids* in low-density lipoproteins (LDL)*—components in the blood that carry cholesterol and fatty acids—increases the likelihood that the oxidized LDL will be deposited as plaque in arteries, thus increasing the risk of heart disease. Free radicals can also attack and damage DNA,* leading to mutations and possibly to cancer.18 Antioxidants may help block this process.

Free radicals are continuously produced by normal body processes and by the actions of some external toxins, such as those present in tobacco smoke. Some white blood cells can produce their own free radicals and use them to destroy bacteria and other invaders.

Free radicals are always with us, and the body has defenses against excesses of them. Our cells have enzymes that stop the chain reaction of free-radical formation, for example. These enzymes include superoxide dismutase (SOD), catalases and glutathione peroxidase, an enzyme that requires the mineral selenium to function.18 Vitamins C and E and beta-carotene also can function as free-radical quenchers—at least in laboratory studies. Our cells also have enzymes that can cut out and replace pieces of DNA if they are damaged by free radicals.

Thus, it is well established that:

- Free radicals are highly reactive molecules that can damage body components;
- Free radicals are constantly produced in the human body;
- Several defenses against damage by free radicals involve antioxidant vitamins, some minerals, and other chemicals derived from food.

Important questions about antioxidant nutrients include: How strong is the evidence that such nutrients from food or supplements actually protect against free-radical damage; and to what extent do antioxidant nutri-
ents from food or supplements reduce the risk of chronic diseases, especially heart disease and cancer?

Antioxidants and Cancer

Observational studies

Fruits and vegetables are major sources of many antioxidant nutrients such as beta-carotene and related carotenoids like lycopene and lutein, and vitamin C; vitamin E is obtained more from seeds and grains (see Table 1, page 16). The main impetus for investigating the value of diet-derived antioxidants for cancer prevention was the observation that people with low intakes of fruits and vegetables have a higher risk of several kinds of cancer.\textsuperscript{19-21} In addition to this dietary information, some studies indicate that cancer patients have lower levels of these antioxidant nutrients in their blood than do people without cancer. Because there is evidence suggesting that oxidative damage is a cause of cancer, it is reasonable to ask whether these antioxidant nutrients are protective. Numerous studies suggest that this is true.

Eighty-three epidemiological studies examined the relationship between estimated dietary intake of vitamin C and the occurrence of several forms of cancer. A recent review of these studies concluded that 37 showed that a higher intake of vitamin C was associated with a range of protective effects.\textsuperscript{19,20} The evidence was most consistent for cancers of the stomach, the esophagus, the oral cavity and the pharynx.

Another observational study examined lung cancer and blood levels of beta-carotene, vitamins A, C, and E and the mineral selenium. The strongest association was between low blood levels of vitamin E and beta-carotene and an increased risk of lung cancer. There was no association between blood levels of selenium, vitamin A or vitamin C and risk of cancer.\textsuperscript{22} Thus, different antioxidant nutrients appear to be associated with different cancer sites.

As noted above, the best one can expect from such observational epidemiological studies is associations. This type of investigation does not prove cause and effect; only an intervention trial can do that. So what do intervention trials tell us about antioxidants and cancer? The results have been mixed.

Intervention trials

Beta-carotene has been used successfully to treat oral leukoplakia, a precancerous condition.\textsuperscript{23} However another compound, isotretinoin (a
Vitamins and minerals:

A large intervention trial examined the effects of supplemental beta-carotene and vitamins C and E on the recurrence of colorectal adenomas (also called polyps—a condition which may progress to bowel cancer). After four years, there was no evidence that these nutrients had reduced the risk of recurrences. (The four-year follow-up may have been too short
to detect an effect of these nutrients on this condition, however.)

Neither beta-carotene nor vitamin E reduced the risk of lung cancer in the recently reported Finnish trial described above. In fact, although it may be simply a chance occurrence, those individuals who received beta-carotene had an 18% higher incidence of lung cancer, as well as an 8% higher total mortality. Those who took vitamin E supplements had a non-significant decrease in prostate cancer, but also had a nonsignificant increased risk of hemorrhagic stroke (the type of stroke caused by bleeding in the brain).

Similarly, the Carotene and Retinol Efficacy Trial (CARET) examined the effects of retinol (vitamin A) and beta-carotene on the risk of lung cancer in people who worked with asbestos or were heavy smokers. This trial was terminated early when an interim evaluation showed an increased occurrence of lung cancer in subjects who took the supplements.

Both of the above trials, however, evaluated the effects of supplements on people whose risk of cancer was elevated by smoking or by occupational exposure. They thus could not clearly address the issue of the preventive value of beta-carotene supplements in people with healthier lifestyles. In the Physicians’ Health Study, in contrast, 22,000 healthy male doctors were studied in an intervention trial to examine the effect of beta-carotene on cancer. Only about 11 percent of these individuals were smokers, and thus there was no reason to expect an increased risk of lung cancer. Indeed, in this study, there was no increased risk in those who took the supplement compared to those who did not—but just as importantly, there was no decrease in risk either.

In addition to its putative effects on heart disease and cancer, data from observational studies suggested that beta-carotene might also protect against type 2 diabetes mellitus (the type that typically occurs in overweight adults). An analysis of the data on beta-carotene supplementation from the Physicians’ Health Study, however, indicates that beta-carotene had no effect on the occurrence of this disease in middle-aged men.

A more recent report extended these disappointing findings of no protective effect of beta-carotene to women. In the Women’s Health Study, nearly 40,000 women aged 45 or more, took either beta-carotene or a placebo for approximately two years, and their health status was monitored for an additional two years. There were no significant changes in the risk of CVD, stroke or total deaths from all causes in these initially healthy women (only 13% smoked).
Another double-blind, randomized trial of an antioxidant nutrient—the mineral selenium—had more promising results. In this study, 1,312 patients with a history of non-melanoma skin cancers took selenium supplements for an average of four and one half years. The subjects who took the selenium had no fewer skin cancers than those who took the placebo, but there were significantly fewer cases of all forms of cancer and significantly fewer cancer deaths in that group than in the placebo group.\(^{31}\) However, it is important to remember that the subjects of the study were chosen because of a previous skin cancer history. Whether the same results would be seen in people without earlier skin cancers has not yet been determined.

These studies do not support the theory that supplementation with antioxidant nutrients—specifically beta-carotene, vitamin E, and selenium—is a valuable strategy for the general public. Indeed, in some cases, they raise the possibility that such supplementation may be harmful, while healthy people may not benefit. Although numerous studies in laboratory rodents show beta-carotene to be useful in reducing the risk of cancer development, this has not been shown in humans with respect to either cancer or heart disease.

**Antioxidants and Heart Disease**

*Observational studies*

As with cancer, epidemiological data indicate that diets high in fruits and vegetables are correlated with lower risk of heart disease.\(^ {32,33}\) Some data from inter-country comparisons also correlate increased risk of ischemic heart disease\(^*\) with low plasma levels of vitamins C and E\(^ {34}\) and of beta-carotene.\(^ {35}\)

Recently, two prospective studies, one with women and one with men, have shed some light on the relationship between vitamin E intake and the occurrence of heart disease. The Nurses’Health Study followed over 80,000 middle-aged nurses for up to 8 years.\(^ {36}\) A significantly decreased risk of heart disease was correlated with high intake of vitamin E, mostly due to supplement use. Other antioxidants had no significant effect. The authors of the report noted that there were some lifestyle differences between women who took supplements and those who did not; for example, the women who took supplemental vitamin E (in multivitamins and/or single supplements) were also slightly more likely to take post-menopausal hormone supplements, to be vigorous exercisers and to be
nonsmokers—all factors that lower the risk of heart disease. The authors also noted that there appeared to be no additional benefit gained (in terms of reduced risk of heart disease) from taking more than 100 international units (IU)* per day of vitamin E.

The same group of investigators conducted a similar prospective study of male health professionals. As in the women’s study, there was also a significantly decreased risk of heart disease among men with higher levels of vitamin E intake. Unlike the women’s study, however, there was also a significant protective effect of high beta-carotene intake among men who smoked, but not among those men who had never smoked.

Again, as in the women’s study, there were lifestyle differences; the men with the highest vitamin E intake were more likely to exercise vigorously and to take aspirin (which has been shown to significantly decrease the risk of heart disease). The greatest reduction in heart disease occurred in those men taking between 100 and 250 IU per day of vitamin E; there was no further reduction with higher doses. It is possible that the effect of vitamin E on heart disease was due not to its antioxidant activity, but rather to the fact that it also acts as an anticoagulant; i.e., it can decrease the rate of blood clotting.

Do these two studies “prove” that vitamin E helps prevent heart attacks? Unfortunately, no. Observational studies such as these provide only correlational information; the groups of subjects are essentially self-selected, not randomly assigned to treatment groups. Differences between the studies’ supplement users and nonusers may have influenced the results.

This is not to imply that these are not important data. They are consistent with the hypothesis that antioxidant supplements reduce the risk of heart disease, but much remains to be learned. Intervention studies of the effect of vitamin E on disease are currently under way; they should shed more light on the efficacy of this nutrient for reducing the risk of disease.

Because the data are not conclusive, the American Heart Association suggests that “…the most prudent… recommendation for the general population is to consume a balanced diet with emphasis on antioxidant-rich fruits, vegetables, and whole grains.”

**Antioxidants and Age-Related Macular Degeneration (AMD)**

*Observational studies*

Age-related macular degeneration (AMD) is the leading cause of
vitamins and minerals: blindness in the elderly. The macula is the small central part of the retina where vision is sharpest. When the macula degenerates, only peripheral vision remains; the victim’s ability to read, write and drive are permanently impaired.

Because the retina is rich in polyunsaturated fatty acids, which are susceptible to oxidation, the possibility exists that high levels of antioxidants may prevent or retard the progression of this disease. This hypothesis was recently tested in a large case-control study. The investigation compared the diets of patients who had been diagnosed with AMD within the previous year with the diets of controls without AMD. Individuals with the highest intake of carotenoids (the chemical group to which beta-carotene belongs) had a significantly reduced risk of AMD.

Interestingly, the dietary records indicated that the foods most strongly associated with the reduced risk were spinach and collard greens, not carrots (a vegetable high in beta-carotene). The investigators concluded that other carotenoids found in these dark-green leafy vegetables—specifically the carotenoids lutein and zeaxanthin—were probably more important in reducing risk of AMD than was beta-carotene. This interpretation is biologically plausible because both lutein and zeaxanthin are found in the macula. Intake of vitamins C and E and preformed vitamin A (retinol*) was not associated with significant risk reduction.

Does this study “prove” that lutein and zeaxanthin reduce the risk of AMD? No, because the study design cannot exclude the possibility that people may alter their diets after learning they have a disease. Later studies of AMD have, however, not shown consistent benefits of increased serum levels or dietary intakes of the carotenoids lutein, zeaxanthin or beta-carotene. Furthermore, it is always possible that a significant interaction between these compounds and other food components led to positive results in the studies that found them. These data are consistent, however, with the hypothesis that diets rich in antioxidant-containing foods may reduce the risk of AMD, and helps explain why nutritionists so often stress the importance of obtaining nutrients from foods rather than from pills.

Calcium and Osteoporosis

Osteoporosis is a condition that results from the loss of minerals, especially calcium, from the bones. Decalcified bones become fragile and break easily. It has been estimated that by age 65, twenty percent of American women suffer one or more broken bones due to osteoporosis;
at older ages as many as 40 percent suffer such fractures.\textsuperscript{41,42} Because the fastest-growing age group in America is the one 65-and-over, osteoporosis is a public health issue of increasing importance. Over twenty million Americans are estimated to have the disease to date.

The strength of an adult’s bones (bone density) is related to the amount of minerals deposited in the bones during growth. Bones lengthen fastest around the time of puberty in both boys and girls, and density continues to increase until around ages 25 to 30. Bone density remains constant until ages 40 to 45; it then starts to decline in both men and women.\textsuperscript{42}

In women, the rate of bone loss substantially increases during the period around menopause when production of the hormone estrogen decreases. Postmenopausal women thus may have bones that are significantly less dense (more brittle) than bones of men of the same age. It is important to recognize that the denser a woman’s bones are at the beginning of menopause, the denser they will be later in life. Thus, the greater a woman’s peak bone density, the lower her risk of osteoporosis.

Adequate calcium intake is essential in order to develop the skeleton to its peak density, but American women consume only about one-half the recommended amount of calcium.\textsuperscript{42} Increasing calcium intake increases bone density in prepubertal children,\textsuperscript{43,44} and calcium intake must be maintained at a high level throughout the important bone-forming years for bone density to reach peak levels during adulthood.\textsuperscript{45}

The benefits of increased calcium intake by postmenopausal women or by those already showing indications of osteoporosis are not clear. Some investigators have found benefits in calcium supplementation in the elderly, others have not. Bone loss may be slowed by increased calcium intake, but bone density is not restored.\textsuperscript{46} The greatest benefits in postmenopausal women seem to result from the use of hormone (particularly estrogen) replacement therapy (HRT); but not all women are able, or willing, to use HRT.\textsuperscript{47}

The current Adequate Intake (see DRIs, page 27 for definition) for calcium (set in 1997) takes into account the changing requirements throughout life.\textsuperscript{48} Thus, 1300 milligrams (mg) per day is recommended for adolescents (9-18 years); 1,000 mg/day is recommended for those between 19 and 50 years, and 1,200 for those 51 and over. In recognition of the possible positive effects of increased calcium for older women, higher calcium intake up to 1500 mg/day has been recommended for postmenopausal women, especially those not on hormone replacement therapy.\textsuperscript{47} These higher recommendations (which are seldom attainable from

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diet alone) were not accepted by the committee that sets the levels of the RDAs, and thus 1,200 mg/day is the recommended dietary intake amount for post-menopausal women.

[Other nutrients are also crucial for bone health. Vitamin D, for example, allows the body to absorb calcium from foods and supplements. Vitamin D is produced in the skin when it is exposed to sunlight. Older individuals, however, may be less efficient at producing it, even when they have ample exposure to sunlight; they may therefore need increased amounts in the diet or through supplements.]

At present, the best advice is to consume at least the current recommended amount of calcium. But is it necessary to take supplements to do so?

The most widely and regularly consumed sources of calcium in the American diet are dairy products. One cup of milk provides about 300 mg of calcium—about one-fourth the recommended daily amount for a young woman. The calcium in milk is well absorbed; calcium from other sources (including some types of supplements) is not always as well absorbed (see Table 1 for other good sources of calcium).

It has been argued that milk and dairy products are not the best sources of calcium for the prevention of osteoporosis. The basis for this contention is data indicating that the risk of osteoporosis and bone fracture is much greater in Scandinavian women, who have a relatively high consumption of dairy products, than in other populations who do not. These data may be at least partially explained by the high consumption of pre-formed vitamin A (retinol) by these women from fish liver oils as well as from highly fortified milk. Very high vitamin A (but not beta-carotene) consumption is known to have a negative impact on bone.49

People who cannot or will not consume milk or dairy products will have difficulty getting enough calcium from food alone.42,50 By paying attention to diet and choosing a variety of foods rich in calcium, however, it should still be possible to obtain much of this essential mineral from foods (see Table 1, page 16). Persons who get much or most of their calcium from calcium-rich foods increase the probability of obtaining a variety of other important nutrients—such as high-quality protein, magnesium, riboflavin and vitamins A and D—from those foods as well.

Individuals who choose calcium supplements to increase intake should be aware that not all supplements are equal. More than a dozen different types of calcium supplements are now available. Bone meal-derived and and dolomite*-based calcium supplements may be contami-
nated with impurities, such as heavy metals, and are not generally rec-
ommended. Calcium carbonate, calcium citrate and calcium phosphate
are the most thoroughly studied supplements. All three are absorbed well
by normal, healthy people; but for those at high risk for kidney stones or
for those with impaired production of stomach acid (as may be the case
in many of the elderly), calcium citrate may be the best choice. Individuals
who are also at greater risk of iron deficiency should remem-
ber that high calcium intake can diminish the absorption of dietary iron.

Taking calcium supplements between meals is advised to avoid such an
interaction. In addition, calcium absorption is most efficient at doses of
500 mg or less; thus, a 1000-mg calcium supplement should be taken in
two separate doses of 500 mg each.

ARGUMENTS AGAINST SUPPLEMENTATION

Those who do not support the widespread use of dietary supplements
for either insurance or prevention are concerned about two aspects of the
use of such products: safety and effectiveness. If a pharmaceutical prod-
uct is to be sold in the United States, the vendor must show that it is both
safe and effective for its intended purpose, at the intended level of intake.
“Safe” does not mean completely safe for everyone under all possible cir-
cumstances, however. Many drugs have negative side effects which must
be disclosed by the manufacturer so that physicians can evaluate whether
a particular drug is appropriate for a particular patient. Much research and
testing is performed to define and establish such guidelines.

Such testing is not required for vitamins and minerals, even though
they are frequently used in pharmacological doses (doses much larger
than could be obtained from foods). Thus, these chemicals (vitamins and
minerals are chemicals) may be sold without prior certification that they
are either safe or effective for the purposes for which people buy them,
and without scientifically established dosage levels for particular purpos-
es. From a legal standpoint, dietary supplements are considered foods, not
drugs. Manufacturers thus do not have to prove either safety or efficacy;
and according to legislation passed in 1994, if any safety issue arises, it
will be up to the Food and Drug Administration (FDA) to prove that a
problem exists.

There is some cause for concern about some preparations. A recent
review of the prices and contents of various vitamin and mineral supple-
ments revealed that some were labeled inaccurately. In addition, there

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was a sixfold range in price for what were essentially the same items. A study of all types of dietary supplements (including vitamins and minerals) also found a wide variation in prices, and that prices varied predictably by source of purchase. Products purchased from Internet sites were, on average, twice as costly as those purchased from stores. A consumer can thus buy a product that is inaccurately labeled, which may be overpriced, and that may not be effective for its intended purpose.

Nutritionists have expressed concerns about safety and the possibility of negative effects from massive doses of some nutrients—particularly when they create an imbalance with other nutrients consumed at the same time, and with which they may interact. This concern primarily involves the use of supplements of individual nutrients.

The idea that “if a little is good, a lot is better” does not apply to a number of vitamins and minerals, just as it does not apply to over-the-counter medications such as aspirin, to prescription drugs—or even to table salt. But because vitamins and minerals are viewed as foods and as relatively “natural” products that are “good for you” and essential, consumers tend to be less wary about possible ill effects of overdoses.

High doses of several nutrients are known to cause toxic effects. For example, prolonged intake of high doses of vitamin A (retinol), when taken by pregnant women, may lead to liver damage and birth defects. Despite the fact that the water-soluble vitamins—among them vitamin C, vitamin B6 and niacin—are eliminated from the body relatively quickly, megadoses of such nutrients are not necessarily innocuous. Excess vitamin B6—which has been used to treat premenstrual syndrome—can impair nervous system function. Megadoses of vitamin C can cause diarrhea and changes in the way the body handles glucose—which may be important to diabetics. Large doses of niacin can also change the way the body handles glucose and can cause liver damage and unpleasant skin flushing.

There can also be negative interactions between nutrients, especially when some are taken in very large amounts. Excess zinc intake interferes with the body’s use of copper, another essential mineral. As noted earlier, large doses of calcium can diminish the absorption of dietary iron and zinc.

It is also important to consider possible problems with large doses of the antioxidant vitamins. Some recent data suggest that excesses of antioxidants may be harmful and should not be taken until long-term studies of tolerance or toxicity are completed. Indeed, because it would be unethical to ask subjects to consume levels of nutrients that might
cause adverse effects, in the long term, we may not be able to assess toxicity until those who “self-medicate” at high doses are identified and the results of such supplementation assessed. Antioxidant substances may not always act as antioxidants. Under some conditions, they may produce more oxidations instead of suppressing them. In the presence of excess iron vitamin C, rather than acting as an antioxidant, becomes just such a pro-oxidant. This could be undesirable for people with high levels of LDL (“bad”) cholesterol, because oxidation of LDL increases the risk that this cholesterol will form deposits in the arteries. In such cases, high levels of vitamin C taken to help protect against heart attack may increase the risk.

Approximately ten percent of Americans have an inherited genetic disorder that predisposes them to higher-than-usual levels of body iron. For these individuals, especially if they also have high levels of LDL cholesterol, megadose vitamin C supplementation could be counterproductive and possibly injurious.

Use of dietary supplements may provide a false sense of security. Individuals who rely too completely on supplements may ignore symptoms of illness or treat them with supplements rather than seeking medical care. This may allow a disease to progress and not be treated effectively. Persons who take vitamins and/or minerals may think they have fulfilled all dietary requirements and may ignore other important dietary advice. Someone eating a “meat-and-potatoes” diet, for example—which contains high levels of saturated fatty acids, few fruits and vegetables and few or no dairy products—may rely on supplements to supply “good nutrition.”

Reliance on supplements in this way assumes that the knowledge of important dietary constituents is complete, and that most important nutrients can be obtained from supplements. Foods are extraordinarily complex combinations of chemical compounds, however, and many of them have not yet been investigated for their health effects. Reliance on supplements may lead consumers to miss out on very important nutrients, as well as nonnutrient components (like fiber) that contribute to better health.

There are over 600 different carotenoids*, for example. Some, like lycopene (from tomatoes) and lutein and zeaxanthin (from spinach), may be better antioxidants than is beta-carotene. Other chemicals—like sulforaphane, found in broccoli—activate liver enzymes that inactivate some carcinogenic substances. Because the research on these compounds is
incomplete, information is lacking about effective dosage or possible adverse reactions. Indeed, the strongest epidemiological evidence supporting the possible beneficial effects of antioxidants for cancer prevention comes from studies involving fruit and vegetable consumption. Of 156 recent epidemiological studies, 128 found a decreased risk of certain cancers in persons with the highest consumption of fruits and vegetables. Similarly, an analysis of data from the Framingham Study indicated that increased consumption of fruits and vegetables is associated with a decreased risk of stroke.

Fruits and vegetables are important sources of antioxidant nutrients. And beta-carotene, vitamin C and vitamin E represent only three among many such compounds and may not necessarily be the most effective ones. The efficacy of these nutrients may also be increased when they are consumed with other compounds normally found with them in foods. Further, those who consume high levels of fruits and vegetables may also consume less of some dietary constituents, like saturated fats, that are considered detrimental to health.

Are supplements effective? A recent epidemiological study analyzed dietary and supplementation data from nearly 11,000 people, and examined death rates occurring 12 to 16 years after the initial survey. There was no difference in mortality rate, either from all causes or from cancer, between those who reported taking supplements on a regular basis and those who did not do so.

Although these data argue against the hypothesis that increased vitamin and mineral intake will prolong life, they don't speak directly to the issues raised above about the prevention of chronic diseases. Some authorities, while extolling the benefits of increased fruit and vegetable consumption, indicate that the evidence that isolated supplements of vitamins help to prevent cancer is not yet substantial.

**DIETARY GUIDES**

Substantial agreement among nutrition experts is yet to be reached about the use of vitamin and mineral supplements for prevention of chronic diseases. In contrast, there is strong evidence that a balanced diet high in fruits and vegetables can really help prevent chronic diseases. What are the responsible factors in such diets? Where should the consumer look for scientifically valid guidelines? There are three major sources for such information: the Dietary Reference Intakes (DRIs); the
Dietary Guidelines for Americans; and the Food Guide Pyramid. These are described below.

The Origins of the Dietary Reference Intakes

Since the early 1940s, the National Research Council (NRC) of the National Academy of Sciences\(^\text{§}\) has been charged with establishing a set of dietary standards to be used to ensure the adequacy of nutrient intake for various groups of people. These standards, the Recommended Dietary Allowances, or RDAs, are “the levels of intake of essential nutrients that, on the basis of scientific knowledge, are judged by the Food and Nutrition Board to be adequate to meet the known nutrient needs of practically all healthy persons”\(^{48}\). The RDAs were formulated primarily to help Americans avoid nutrient deficiencies by indicating the appropriate levels of intake of essential nutrients to provide for growth and development and health maintenance.

Since the RDAs were first promulgated, however, and particularly in the last decade, there has been an explosion of nutrition research, and the recognition that there have been changes in the American food supply—e.g., in the level of fortification of foods with various nutrients—as well as in the manner in which Americans obtain essential nutrients. It is estimated, for example, that 100 million Americans are now using some form of dietary supplement\(^{65}\). Further, it is now recognized that nutrition may be of significant value in preventing, ameliorating or treating chronic diseases such as Type 2 diabetes, heart disease, some types of cancer and hypertension. For these reasons, the nutritional guidelines produced by the National Research Council have been expanded. They now include four categories of recommendations under the rubric of “Dietary Reference Intakes”.

Dietary Reference Intakes (DRIs)

- *Estimated Average Requirement*: An average level of intake of a nutrient or food component that appears sufficient to maintain the desired biochemical and/or physiological function in a population.

- *Recommended Dietary Allowance*: A level of intake of a nutrient or food component considered adequate to meet the known nutritional needs of practically all healthy persons in a population. As with the

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\(^{\text{§}}\) The NAS is a nonprofit, private society of scholars chartered in 1863 by Congress to advise the federal government on scientific and technical matters.
current RDAs, this reference point is based on, but is higher than, the Estimated Average Requirement to allow for individual variability in needs, absorption, etc. Because the RDAs are set to meet the requirements of people whose needs are high, they actually will exceed the requirements of most people—they cover the needs of over 95 percent of the population. Also, since the RDAs are set high, it would be an error to assume that an individual’s intake is inadequate or that he or she is at risk of deficiency if his or her intake does not meet or exceed the RDAs. It would be an accurate interpretation to say that the farther the average intake falls below the RDAs, the greater the risk of deficiency. In practice, what is sometimes done is to use a particular cut-off below which the probability of deficiency is said to increase—e.g., two-thirds or 70 percent of the RDA for a given nutrient. Clinical or biochemical tests would be necessary to determine deficiency in a particular individual. The RDAs are divided into age and gender groups, and for the first time, they include values for people over 70, when appropriate scientific data are available.

• **Adequate Intake (AI)** If there are not sufficient scientific data to estimate an average requirement (and from that, an RDA), AIs will be set. In the absence of an RDA, individuals should use the AI as a goal for intake of a particular nutrient or food component.

• **Tolerable Upper Intake Level (TUL)** A level of intake of a nutrient or food component that appears to be safe for most healthy individuals and beyond which there is concern that symptoms of toxicity may occur. The TUL is not a recommended level of intake, and in general there is no benefit for individuals to consume nutrients at this level (or, indeed above the RDA or AI). See Table 2, page 29, for current TUL.

**Current status of the DRIs**

The Dietary Reference Intakes are being established in seven groups of related nutrients; thus there will be seven separate reports published. DRIs for each group of nutrients are being determined by a separate panel of scientists with expertise in the nutrients being examined. The seven groups of nutrients are:

• calcium, vitamin D, phosphorus, magnesium, and fluoride;
• folate and other B vitamins;
• antioxidants (e.g., vitamins C and E, selenium and beta-carotene);
• macronutrients (e.g., protein, fat, carbohydrate);
Table 2. **TOLERABLE UPPER INTAKE LEVEL FOR SELECTED NUTRIENTS**

<table>
<thead>
<tr>
<th>NUTRIENT</th>
<th>TOLERABLE UPPER INTAKE LEVEL (Daily Intake)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>2.5 grams</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>4 grams</td>
</tr>
<tr>
<td>Magnesium</td>
<td>350 mgm (does not include intake from food and water)</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>50 micrograms (2,000 IU)</td>
</tr>
<tr>
<td>Fluoride</td>
<td>10 mgm</td>
</tr>
<tr>
<td>Niacin</td>
<td>35 mgm</td>
</tr>
<tr>
<td>Vitamin B₆</td>
<td>100 mgm</td>
</tr>
<tr>
<td>Folate</td>
<td>1 mgm</td>
</tr>
<tr>
<td>Choline</td>
<td>3.5 gm</td>
</tr>
</tbody>
</table>

* Tolerable upper intake is that level above which no additional benefit is likely to occur, and negative effects may be encountered. There is no benefit to taking these levels of nutrients, and these are not recommended intake levels. (mgm = milligram)

**Values given are for adults between the ages of 19-70 years**

- trace elements (e.g., iron, zinc);
- electrolytes and water; and
- other food components (e.g., fiber, phytoestrogens).

The report of the first committee was released in August, 1997, and included calcium, phosphorus, magnesium, vitamin D and fluoride. In April, 1998 the second committee reported the DRIs for folate and other B vitamins. The next group of nutrients to be examined will be the antioxidants.

As each group of DRIs are released, they may be viewed on the website of the National Academy of Sciences (http://www2.nas.edu/fnb/).
**But What About Food?**

Important as the DRIs are, it is also important to realize that most government and professional nutrition groups emphasize that Americans should meet their nutritional needs through diet — from foods rather than from pills.

In 1995 the United States Departments of Agriculture (USDA) and Health and Human Services (HHS) updated their 1990 dietary guidelines to bring them into line with current scientific thinking. These guidelines emphasize the importance of variety in the diet, moderate use of some foods items and the maintenance of healthy body weight. The guidelines are reviewed every five years to keep them current with the latest scientific information; they are currently undergoing revision and the updated version will be published in 2000.

The USDA and HHS published the Food Guide Pyramid (Figure 1) in 1992 to help consumers translate recommendations into types and amounts of food. Consumers who follow the recommendations of the Pyramid should achieve a balanced diet containing at least the RDAs— the recommended levels of the known essential nutrients.

**CONCLUSIONS AND RECOMMENDATIONS**

While intriguing and encouraging, the scientific evidence to date does not provide a firm basis for advocating dietary supplementation in normal, healthy adults to prevent chronic diseases such as cancer and heart disease. Some studies support the idea that some nutrients, in particular the antioxidants, may be protective; but there are also some indications that those nutrients may be at best neutral or—at worst—harmful for some people with particular lifestyles or genetic profiles.

Most intriguing is the possibility that there are beneficial compounds in foods—phytochemicals—other than those we currently recognize. These compounds may be as important or even more important than those now recognized. Compounds such as resveratrol (grapes), sulforaphane (cruciferous vegetables), lutein (spinach) and zeaxanthin (collard greens), diallyl sulfides (garlic) are all thought to have health benefits, but the data supporting many of these are not yet strong, nor is there precise information on exactly which chemical form might be most beneficial or what a

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§ Dietary Guidelines for Americans (HG-232) and the USDA’s “Food Guide Pyramid” (HG-252) can be obtained from the Consumer Information Center, Department 159-Y, Pueblo, CO 81002
Figure 1: **THE FOOD GUIDE PYRAMID**  
A GUIDE TO DAILY FOOD CHOICES

<table>
<thead>
<tr>
<th>FOOD GROUP</th>
<th>ONE SERVING IS:</th>
</tr>
</thead>
<tbody>
<tr>
<td>BREAD, CEREALS, RICE, AND PASTA</td>
<td>1 slice bread; 1/2 cup cooked rice or pasta</td>
</tr>
<tr>
<td>VEGETABLES</td>
<td>1/2 cup chopped, raw or cooked; 1 cup of leafy raw vegetables</td>
</tr>
<tr>
<td>FRUITS</td>
<td>1 piece of fruit or melon wedge; 3/4 cup (6 oz) juice; 1/2 cup canned fruit; 1/4 cup dried fruit</td>
</tr>
<tr>
<td>MILK, YOGURT, AND CHEESE</td>
<td>1 cup (8 oz) milk or yogurt; 1 1/2–2 oz cheese or cereal; 1 oz ready-to-eat cereal</td>
</tr>
<tr>
<td>MEAT, POULTRY, FISH, DRY BEANS, EGGS, AND NUTS</td>
<td>2 1/2–3 oz cooked lean meat, poultry or fish; 1/2 cup cooked beans or 1 egg or 2 tbs peanut butter is equivalent to 1 oz lean meat (about 1/3 serving).</td>
</tr>
</tbody>
</table>

Source: U.S. Department of Agriculture

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safe and effective dose might be. What the data do confirm very strongly is the value of eating more fruits and vegetables. Only 10 percent of the U.S. population consumes the recommended five servings of fruit and vegetables per day.19

The case for calcium is somewhat different. As noted in the section above on osteoporosis, there is increasing evidence suggesting that high calcium intake helps young women reach peak bone density and decreases their risk of osteoporosis later in life. Menopausal or postmenopausal women should also be aware that a high calcium intake may be helpful in slowing bone loss due to diminishing hormone levels. This information is particularly important for those women who do not use hormone replacement therapy.

While it is likely that the best source for additional calcium remains dairy products, for those unable or unwilling to increase their consumption of dairy products, calcium—and perhaps vitamin D—supplementation is recommended.

ACSH recommends that individuals make dietary decisions in a rational and prudent manner—not as emotional responses to fears of possible deficiency or the lack of some elusive and undefined “optimal” nutrition, or in response to the latest “hot” media release.

The following are ACSH’s suggestions for the consumer:

• Evaluate current diet for adequacy in terms of official recommendations (the Food Guide Pyramid and the Dietary Guidelines for Americans) by:
  1. keeping a record, for at least 3 days, of the kinds and amounts of foods eaten;
  2. determining if the current daily diet includes (on average):
     - 6-11 servings of bread, cereals, rice or pasta;
     - 3-5 servings of vegetables;
     - 2-4 servings of fruits;
     - 2-3 servings of dairy products;
     - 2-3 servings of meat or a meat substitute.
(See sidebar for definition of serving size for each food group. Remember that the appropriate number of servings for an individual depends on total calorie intake, which in turn should depend on body weight and activity level.)

• Evaluate personal risk factors—such as family history of disease, lifestyle and personal health status—that may change nutrient needs. For example:
1. Thin white women who are current or former smokers may have an increased risk of osteoporosis. They may need to emphasize increasing their intake of calcium-rich foods or consider calcium supplementation.

2. Individuals with family history of early (occurring before age 60) heart disease should emphasize a diet low in saturated fats and high in fruits and vegetables—especially if they have a personal history of elevated blood cholesterol.

3. Women of reproductive age should emphasize foods that supply folate (see Table 1 for some examples) even before a pregnancy is planned (or if unable or unwilling to do so, should take supplements containing 400 mg of folic acid/day).

- If, based on such an evaluation, your diet is inappropriate, take steps to improve it by altering food choices and/or amounts of foods consumed whenever possible. For assistance with evaluations, consult a professional nutritionist such as a registered dietitian or a knowledgeable physician.

- If supplementation seems desirable to ensure adequacy, amounts of nutrients as specified in the RDAs are the most appropriate; avoid potentially toxic levels of supplementation (see Table 2 for estimated upper safe limits for a number of nutrients).

- Recognize that our understanding of human nutritional needs is constantly evolving; stay aware of the latest developments by reading the science-based literature. Be aware that sound nutritional policy is based on the consistent results of a variety of studies, not on individual experiments or investigations.

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GLOSSARY

Carotenes or carotenoids: Hundreds of chemical compounds (usually colored—e.g., carotene = yellow; lycopene = red) that are widely distributed in both plants and animals. Some, such as beta-carotene, can be converted into vitamin A by the body; some have antioxidant activity.

Diuretic: A chemical substance that increases the excretion of urine by the kidneys.

DNA: Deoxyribonucleic acid; the material found in chromosomes, which makes up the genes, or units of heredity.

Dolomite: Mineral deposits containing calcium magnesium carbonate.

Drug: A therapeutic agent; any substance, other than food, used in the prevention, diagnosis, alleviation, treatment or cure of disease.

Enzyme: A protein with catalytic activity—it enables and speeds up the rate of a specific chemical reaction in the body. All enzymes are made of protein, but not all proteins are enzymes. Enzymes consumed in foods (that is animal and plant enzymes) are generally denatured and inactivated by the acid in the human stomach.

Epidemiology: The study of the occurrence and spread of a disease in a population group.

International Unit (IU): A measure of the biological activity of a substance.

Ischemic heart disease: Heart disease due to inadequate blood supply to the heart, e.g., that caused by partial blockage of a coronary artery.

LDL: “Low-density lipoprotein”—the blood component that carries cholesterol and fatty acids. High levels of LDL in the blood are associated with increased incidence of atherosclerotic plaques in the arteries and with increased risk of heart disease.
**Lipids:** Chemicals, usually fats, that do not dissolve in water, but do dissolve in ether and similar fat solvents.

**Morbidity:** The ratio of sick to well individuals in a community or population.

**Mortality:** The ratio of the number of deaths to the total number of individuals in a population (usually expressed as deaths per 1000, 10,000 or 100,000 persons) per unit of time. Also known as the death rate.

**Phytochemicals:** Chemicals found in or derived from plants.

**Retinol:** Chemical name for preformed vitamin A. Retinol can be formed in the body from beta-carotene and other carotenes.
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