DIETARY MINERALS
GOALS AND OBJECTIVES

Course Description
"Dietary Minerals" is a home study continuing education course for rehabilitation professionals. This course presents current information about essential dietary minerals including sections on recommended dietary guidelines, food sources, effects of deficiencies, supplementation, up-to-date published research findings, and toxicity.

Course Rationale
The purpose of this course is to present rehabilitation professionals with current information about many of the essential dietary minerals and the roles they play in disease, health maintenance, and prophylaxis. Both therapists and therapy assistants will find this information pertinent and useful when providing care for individuals who have, or are at risk for having, a compromised nutritional status.

Course Goals and Objectives
Upon completion of this course, the therapist or assistant will be able to

1. recognize the specific physiologic function of each of the common dietary minerals
2. identify several food sources that provide high levels of each of the discussed dietary minerals
3. recognize the health risks, conditions, and symptomology associated with mineral deficiencies
4. differentiate the various supplemental forms of each of the dietary minerals
5. recognize the role dietary minerals play in human disease process, health maintenance, and prophylaxis.
6. identify and review current research data and information about essential dietary minerals.
7. identify health risks, conditions, and symptomology associated with mineral toxicity

Course Instructor
Michael Niss PT

Target Audience
Occupational Therapists, occupational therapist assistants, physical therapists, physical therapist assistants

Course Educational Level
This course is applicable for introductory learners.

Course Prerequisites
None

Criteria for issuance of Continuing Education Credits
A documented score of 70% or greater on the written post-test.

Continuing Education Credits
Five (5 hours of continuing education credit (5 NBCOT PDUs/5 contact hours)
AOTA - .5 AOTA CEU, Category 1: Domain of OT – Client Factors, Context

Determination of Continuing Education Contact Hours
"Dietary Minerals" has been established to be a 5 hour continuing education program. This determination is based on an accepted standard for home-based self-study courses of 12 pages of text (12 pt font) per hour. The complete instructional text for this course is 63 pages (excluding Post-Test).

DIETARY MINERALS

OUTLINE

DIETARY MINERALS

Calcium

Overview

Calcium, the most abundant mineral in the human body, has several important functions. More than 99% of total body calcium is stored in the bones and teeth where it functions to support their structure [1]. The remaining 1% is found throughout the body in blood, muscle, and the fluid between cells. Calcium is needed for muscle contraction, vaso-constriction and dilation, the secretion of hormones and enzymes, and neuro-conduction [2]. A constant level of calcium is maintained in body fluid and tissues so that these vital body processes function efficiently.

Bone undergoes continuous remodeling, with constant resorption and deposition of calcium into newly deposited bone. The balance between bone resorption and deposition changes as people age. During childhood there is a higher amount of bone formation and less breakdown. In early and middle adulthood, these processes are relatively equal. In aging adults, particularly among postmenopausal women, bone breakdown exceeds its formation, resulting in bone loss, which increases the risk for osteoporosis.

Recommended Calcium Intake

Recommendations for calcium are provided in the Dietary Reference Intakes (DRIs) developed by the Institute of Medicine (IOM) of the National Academy of Sciences. Dietary Reference Intake (DRI) is the general term for a set of reference values used for planning and assessing nutrient intakes of healthy people. Three important types of reference values included in the DRIs are Recommended Dietary Allowances (RDA), Adequate Intakes (AI), and Tolerable Upper Intake Levels (UL). The RDA recommends the average daily intake that is sufficient to meet the nutrient requirements of nearly all (97-98%) healthy individuals in each age and gender group. An AI is set when there is insufficient scientific data available to establish a RDA. AIs meet or exceed the amount needed to maintain a nutritional state of adequacy in nearly all members of a specific age and gender group. The UL, on the other hand, is the maximum daily intake unlikely to result in adverse effects.

For calcium, the recommended intake is listed as an Adequate Intake (AI), which is a recommended average intake level based on observed or experimentally determined levels. Table 1 contains the current recommendations for calcium for infants, children and adults.

Table 1: Recommended Adequate Intake by the IOM for Calcium [2]

Male and Female Age	Calcium (mg/day)	Pregnancy & Lactation
0 to 6 months	210	N/A
7 to 12 months	270	N/A
1 to 3 years	500	N/A
4 to 8 years	800	N/A
9 to 13 years	1300	N/A
14 to 18 years	1300	1300
19 to 50 years	1000	1000
51+ years	1200	N/A

*mg=milligrams

There is a widespread concern that Americans are not meeting the recommended intake for calcium. According to the Continuing Survey of Food Intakes of Individuals (CSFII 1994-96), the following percentage of Americans are not meeting their recommended intake for calcium [3]:

- 44% boys and 58% girls ages 6-11
- 64% boys and 87% girls ages 12-19
- 55% men and 78% of women ages 20+

Calcium in Foods

In the United States (U.S.), milk, yogurt and cheese are the major contributors of calcium in the typical diet [4]. The inadequate intake of dairy foods may explain why some Americans are deficient in calcium since dairy foods are the major source of calcium in the diet. The U.S. Department of Agriculture's Food Guide Pyramid recommends that individuals two years and older eat 2-3 servings of dairy products per day. A serving is equal to:

- 1 cup (8 fl oz) of milk
- 8 oz of yogurt
- 1.5 oz of natural cheese (such as Cheddar)
- 2.0 oz of processed cheese (such as American)

A variety of non-fat and reduced fat dairy products that contain the same amount of calcium as regular dairy products are available in the U.S. today for individuals concerned about saturated fat content from regular dairy products.

Although dairy products are the main source of calcium in the U.S. diet, other foods also contribute to overall calcium intake. Individuals with lactose intolerance and those who are vegan tend to avoid or completely eliminate dairy products from their diets. Thus, it is important for these individuals to meet their

calcium needs with alternative calcium sources if they choose to avoid or eliminate dairy products from their diet. Foods such as Chinese cabbage, kale and broccoli are other alternative calcium sources. Although most grains are not high in calcium (unless fortified), they do contribute calcium to the diet because they are consumed frequently. Additionally, there are several calcium-fortified food sources presently available, including fruit juices, fruit drinks, tofu and cereals.

Table 2: Selected Food Sources of Calcium [6-8]

Food	Calcium (mg)	% DV*
Yogurt, plain, low fat, 8 oz.	415	42%
Yogurt, fruit, low fat, 8 oz.	245-384	25%-38%
Sardines, canned in oil, with bones, 3 oz.	324	32%
Cheddar cheese, 1 ½ oz shredded	306	31%
Milk, non-fat, 8 fl oz.	302	30%
Milk, reduced fat (2% milk fat), no solids, 8 fl oz.	297	30%
Milk, whole (3.25% milk fat), 8 fl oz	291	29%
Milk, buttermilk, 8 fl oz.	285	29%
Milk, lactose reduced, 8 fl oz.**	285-302	29-30%
Mozzarella, part skim 1 ½ oz.	275	28%
Tofu, firm, made w/calcium sulfate, ½ cup***	204	20%
Orange juice, calcium fortified, 6 fl oz.	200-260	20-26%
Salmon, pink, canned, solids with bone, 3 oz.	181	18%
Pudding, chocolate, instant, made w/ 2% milk, ½ cup	153	15%
Cottage cheese, 1% milk fat, 1 cup unpacked	138	14%
Tofu, soft, made w/calcium sulfate, ½ cup***	138	14%
Spinach, cooked, ½ cup	120	12%
Instant breakfast drink, various flavors and brands, powder prepared with water, 8 fl oz.	105-250	10-25%
Frozen yogurt, vanilla, soft serve, ½ cup	103	10%
Ready to eat cereal, calcium fortified, 1 cup	100-1000	10%-100%
Turnip greens, boiled, ½ cup	99	10%
Kale, cooked, 1 cup	94	9%
Kale, raw, 1 cup	90	9%
Ice cream, vanilla, ½ cup	85	8.5%
Soy beverage, calcium fortified, 8 fl oz.	80-500	8-50%
Chinese cabbage, raw, 1 cup	74	7%
Tortilla, corn, ready to bake/fry, 1 medium	42	4%
Tortilla, flour, ready to bake/fry, one 6" diameter	37	4%
Sour cream, reduced fat, cultured, 2 Tbsp	32	3%
Bread, white, 1 oz	31	3%
Broccoli, raw, ½ cup	21	2%
Bread, whole wheat, 1 slice	20	2%
Cheese, cream, regular, 1 Tbsp	12	1%

*DV=Daily Value
**Content varies slightly according to fat content; average =300 mg calcium
*** Calcium values are only for tofu processed with a calcium salt. Tofu processed with a non-calcium salt will not contain significant amounts of calcium.

Calcium Absorption

Calcium absorption refers to the amount of calcium that is absorbed from the digestive tract into our body's circulation. Calcium absorption can be affected by the calcium status of the body, vitamin D status, age, pregnancy and plant substances in the diet. The amount of calcium consumed at one time such as in a meal can also affect absorption. For example, the efficiency of calcium absorption decreases as the amount of calcium consumed at a meal increases.

Age

Net calcium absorption can be as high as 60% in infants and young children, when the body needs calcium to build strong bones [11]. Absorption slowly decreases to 15-20% in adulthood and even more as one ages [12]. Because calcium absorption declines with age, recommendations for dietary intake of calcium are higher for adults ages 51 and over.

Vitamin D

Vitamin D helps improve calcium absorption. Your body can obtain vitamin D from food and it can also make vitamin D when your skin is exposed to sunlight. Thus, adequate vitamin D intake from food and sun exposure is essential to bone health.

Pregnancy

Current calcium recommendations for non-pregnant women are also sufficient for pregnant women because intestinal calcium absorption increases during pregnancy. For this reason, the calcium recommendations established for pregnant women are not different than the recommendations for women who are not pregnant.

Plant Substances

Phytic acid and oxalic acid, which are found naturally in some plants, may bind to calcium and prevent it from being absorbed optimally. These substances affect the absorption of calcium from the plant itself not the calcium found in other calcium-containing foods eaten at the same time. Examples of foods high in oxalic acid are spinach, collard greens, sweet potatoes, rhubarb, and beans. Foods high in phytic acid include whole grain bread, beans, seeds, nuts, grains, and soy isolates. Although soybeans are high in phytic acid, the calcium present in soybeans is still partially absorbed [13]. Fiber, particularly from wheat bran, could also prevent calcium absorption because of its content of phytate.

However, the effect of fiber on calcium absorption is more of a concern for individuals with low calcium intakes. The average American tends to consume much less fiber per day than the level that would be needed to affect calcium absorption.

Calcium Excretion

Calcium excretion refers to the amount of calcium eliminated from the body in urine, feces and sweat. Calcium excretion can be affected by many factors including dietary sodium, protein, caffeine and potassium.

Sodium and Protein

Typically, dietary sodium and protein increase calcium excretion as the amount of their intake is increased [14]. However, if a high protein, high sodium food also contains calcium, this may help counteract the loss of calcium.

Potassium

Increasing dietary potassium intake (such as from 7-8 servings of fruits and vegetables per day) in the presence of a high sodium diet (>5100 mg/day, which is more than twice the Tolerable Upper Intake Level of 2300 mg for sodium per day) may help decrease calcium excretion particularly in postmenopausal women [15,16].

Caffeine

Caffeine has a small effect on calcium absorption. It can temporarily increase calcium excretion and may modestly decrease calcium absorption, an effect easily offset by increasing calcium consumption in the diet [17]. One cup of regular brewed coffee causes a loss of only 2-3 mg of calcium easily offset by adding a tablespoon of milk. Moderate caffeine consumption, (1 cup of coffee or 2 cups of tea per day), in young women who have adequate calcium intakes has little to no negative effects on their bones [18].

Phosphorus

The effect of dietary phosphorus on calcium is minimal. Some researchers speculate that the detrimental effects of consuming foods high in phosphate such as carbonated soft drinks is due to the replacement of milk with soda rather than the phosphate level itself [19,20].

Alcohol

Alcohol can affect calcium status by reducing the intestinal absorption of calcium [21]. It can also inhibit enzymes in the liver that help convert vitamin D to its active form which in turn reduces calcium absorption. However, the amount of alcohol required to affect calcium absorption is unknown. Evidence is currently conflicting whether moderate alcohol consumption is helpful or harmful to bone. In summary, a variety of factors that may cause a decrease in calcium absorption and/or increase in calcium excretion may negatively affect bone health.

Research and Current Health Issues

Calcium and Bone Health

Bones are living tissues and continue to change throughout life. During childhood and adolescence, bones increase in size and mass. Bones continue to add more mass until around age 30, when peak bone mass is reached. Peak bone mass is the point when the maximum amount of bone is achieved. Because bone loss, like bone growth, is a gradual process, the stronger your bones are at age 30, the more your bone loss will be delayed as you age. Therefore, it is particularly important to consume adequate calcium and vitamin D throughout infancy, childhood, and adolescence. It is also important to engage in weight-bearing exercise to maximize bone strength and bone density to help prevent osteoporosis later in life.

Osteoporosis is a disorder characterized by porous, fragile bones. It is a serious public health problem for more than 10 million Americans, 80% of whom are women. Another 34 million Americans have osteopenia, or low bone mass, which precedes osteoporosis. Osteoporosis is a concern because of its association with fractures of the hip, vertebrae, wrist, pelvis, ribs, and other bones [22]. Each year, Americans suffer from 1.5 million fractures because of osteoporosis [23].

Osteoporosis and osteopenia can result from dietary factors such as [24,25]:

- chronically low calcium intake
- low vitamin D intake
- poor calcium absorption
- excess calcium excretion

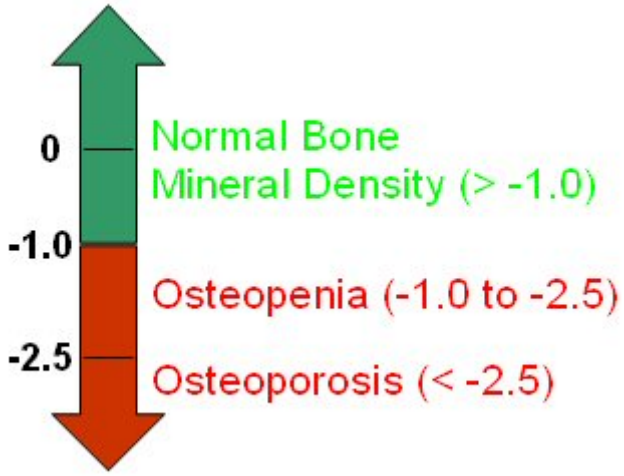
When calcium intake is low or calcium is poorly absorbed, bone breakdown occurs because the body must use the calcium stored in bones to maintain normal biological functions such as nerve and muscle function. Bone loss also occurs as a part of the aging process. A prime example is the loss of bone mass observed in post-menopausal women because of decreased amounts of the hormone estrogen. Researchers have identified many factors that increase the risk for developing osteoporosis. These factors include being female, thin, inactive, of advanced age, cigarette smoking, excessive intake of alcohol, and having a family history of osteoporosis [26].

In 1993 the FDA authorized a health claim for food labels on calcium and osteoporosis in response to scientific evidence that an inadequate calcium intake is one factor that can lead to low peak bone mass and is considered a risk factor for osteoporosis [27]. The claim states that "adequate calcium intake throughout life is linked to reduced risk of osteoporosis through the mechanism of optimizing peak bone mass during adolescence and early adulthood and decreasing bone loss later in life".

Various bone mineral density (BMD) tests, including those that measure your hip,

spine, wrist, finger, shin bone, and heel, can help determine bone mass. These tests provide a T-score which is a measure of bone mineral density that compares an individual's BMD to an optimal BMD of a 30 year old healthy adult. See Figure 2 below. A T-Score of -1.0 and above indicates normal bone density. A T-score of -1.0 to -2.5 indicates that a person is considered to have low bone mass (osteopenia). A score below -2.5 indicates osteoporosis [28].

Figure 2: Interpreting Bone Mineral Density Scores



Although osteoporosis affects people of different races, genders and ethnicities, women are at highest risk because their skeletons are smaller to start with and because of the accelerated bone loss that accompanies menopause. Adequate calcium and vitamin D intakes, as well as weight bearing exercise are critical to the development and maintenance of healthy bone throughout the lifecycle. Older adults should strive to maintain recommended daily calcium intakes as well as an adequate vitamin D intake.

Calcium and high blood pressure

Some observational studies and experimental studies indicate that individuals who eat a vegetarian diet high in minerals (including calcium, magnesium and potassium) and fiber, and low in fat, tend to have reduced blood pressure [29-31].

Findings from some clinical trials indicate that an increased calcium intake lowers blood pressure and the risk of hypertension [32,33]. However, the results of some studies produced small and inconsistent reductions in blood pressure.

To help test the combined effect of nutrients including calcium from food on blood pressure, a study was conducted to investigate the impact of various dietary eating patterns on blood pressure. This study titled "Dietary Approaches to Stop Hypertension (DASH)" was reported in 1997 by the National, Heart, Lung and Blood Institute of the National Institutes of Health. It investigated the effect of various eating patterns on lowering blood pressure. The DASH study was a

multi-center research trial where food was provided to over 450 adults. It examined the effects of three different diets on high blood pressure: a control, "typical American" diet and two modified diets (high fruits-and-vegetables and a combination "DASH" diet - high in fruits, vegetables, and low fat dairy). See Table 3 for a comparison of some of the components of the three diets.

Table 3: Comparison of the Three Diets Tested in the "DASH" Study

Diet Components	Fruit & Vegetable Servings	Lowfat Dairy Servings	Calcium (mg)	Fat (% of total calories)	Sodium (mg)	Cholesterol (mg)	Fiber (g)
Control "Typical American" diet	3.5	0.1	**450**	37	3000	300	9
Fruits-and-Vegetables diet	8.5	0.0	**450**	37	3000	300	31
Combination "DASH" diet	9.5	2.0	**1240**	27	3000	150	31

Of the three diets tested, the combination "DASH" diet resulted in the greatest decrease in blood pressure [34]. Thus, this finding from a large and carefully executed clinical trial helped demonstrate that the combination "DASH" diet, with increased calcium, decreased blood pressure [35]. A number of further studies have been done, all showing a similar relationship between increasing calcium intakes and decreased blood pressure [36]. A study conducted after the original "DASH" study, referred to as the "DASH-Sodium" study showed that the DASH diet without sodium restriction provided as much blood pressure reduction as did severe sodium restriction on the control diet (1500 mg sodium/day) [37]. Overall it appears that consuming an adequate intake of fruits and vegetables as well as calcium from low fat dairy products plays a significant role in controlling blood pressure.

Calcium and Cancer

Colorectal cancer - The relationship between calcium intake and the risk of colon cancer has not been conclusively determined. Observational and experimental research studies investigating the role calcium plays in the prevention of colon cancer show mixed results. Some studies suggest that increased intakes of dietary (low fat dairy sources) and supplemental calcium are associated with a decreased risk of colon cancer [38-41]. Supplementation with calcium carbonate is reported to lead to reduced risk of adenomas (nonmalignant tumors) in the colon, a precursor to colon cancer, but it is not known if this will ultimately translate into reduced cancer risk [42]. Another study reported on the

association between diet and colon cancer history in 135,000 men and women participating in two large health surveys, the Nurses' Health Study and the Physicians' Health Study. The authors found that those who consumed 700 to 800 mg calcium per day had a 40 to 50% lower risk of developing left side colon cancer [43]. However, a few other observational studies found inconclusive evidence regarding any association of calcium intake with colon cancer [44-46]. Although some research findings indicate a protective effect of calcium or low fat dairy foods against colon cancer, further studies are necessary to confirm this role for calcium.

Prostate cancer - There is some evidence to suggest that higher calcium (ranging from 600 mg to >2000 mg of calcium) and/or dairy intakes (>2.5 servings) may be associated with the development of prostate cancer [47-50]. However, these studies are observational in nature rather than clinical trials and cannot establish a definite causal relationship between calcium and prostate cancer. Other findings only show a weak relationship, no relationship at all or the opposite relationship between calcium and prostate cancer [51-54]. Thus, the relationship between calcium intake, dairy intake and prostate cancer risk remains unclear. At the present time, it is recommended that men ages 19 and over consume a "modest" intake of calcium ranging from 1000-1200 mg per day and maintain an intake below the upper tolerable limit (2500 mg).

Calcium and Kidney Stones

Kidney stones are crystallized deposits of calcium and other minerals in the urinary tract. Calcium oxalate stones are the most common form of kidney stones in the US. High calcium intakes or high calcium absorption were previously thought to contribute to the development of kidney stones. However, more recent studies show that high dietary calcium intakes actually decrease the risk for kidney stones [55-57]. Other factors such as high oxalate intake and reduced fluid consumption appear to be more of a risk factor in the formation of kidney stones than calcium in most individuals [58].

Calcium and Weight Management

Research suggests that calcium, especially calcium derived from dairy products, may help to regulate body fat. Laboratory and animal studies provide initial evidence of calcium's role in decreasing body fat while other studies confirm this potential benefit for humans. At this time, lowfat dairy products seem more beneficial than calcium supplements alone in helping to reduce body fat and reduce weight [59-63]. However, larger studies in humans need to be conducted to help confirm the benefit of calcium for weight loss.

Calcium Deficiency

Inadequate calcium intake, decreased calcium absorption, and increased calcium loss in urine can decrease total calcium in the body, with the potential of producing osteoporosis and the other consequences of chronically low calcium intake. If an individual does not consume enough dietary calcium or experiences rapid losses of calcium from the body, calcium is withdrawn from their bones in order to maintain calcium levels in the blood.

Because circulating blood calcium levels are tightly regulated in the bloodstream, hypocalcemia (low blood calcium) does not usually occur due to low calcium intake, but rather results from a medical problem or treatment such as renal failure, surgical removal of the stomach (which significantly decreases calcium absorption), and use of certain types of diuretics (which result in increased loss of calcium and fluid through urine). Simple dietary calcium deficiency produces no signs at all. Hypocalcemia can cause numbness and tingling in fingers, muscle cramps, convulsions, lethargy, poor appetite, and mental confusion. It can also result in abnormal heart rhythms and even death. Individuals with medical problems that result in hypocalcemia should be under a medical doctor's care and receive specific treatment aimed at normalizing calcium levels in the blood.

Calcium Deficiency High Risk Groups
There are four distinct groups of individuals that are considered to be at high risk for calcium deficiency:

- Post-Menopausal Women
- Amenorrheic Women
- Lactose-Intolerant Individuals
- Vegetarians

Post-Menopausal Women - Menopause often leads to increases in bone loss with the most rapid rates of bone loss occurring during the first five years after menopause [64]. Drops in estrogen production after menopause result in increased bone resorption, and decreased calcium absorption [65,66]. Annual decreases in bone mass of 3-5% per year are often seen during the years immediately following menopause, with decreases less than 1% per year seen after age 65 [67]. Two studies are in agreement that increased calcium intakes during menopause will not completely offset menopause bone loss [68,69].

Hormone therapy (HT), previously known as hormone replacement therapy (HRT), with sex hormones such as estrogen and progesterone, helps to prevent osteoporosis and fractures. However, some medical groups and professional societies such as the American College of Obstetricians and Gynecologists, The North American Menopause Society and The American Society for Bone and Mineral Research recommend that postmenopausal women consider using other agents such as bisphosphonates because of potential health risks of HT if combination HT (estrogen and progestin) is solely being administered to prevent or treat osteoporosis [70-72]. Postmenopausal women using combination HT to

reduce bone loss should consult with their physician about the risks and benefits of estrogen therapy for their health.

Estrogen therapy works to restore postmenopausal bone remodeling levels back to those of premenopause, leading to a lower rate of bone loss. Estrogen appears to interact with supplemental calcium by increasing calcium absorption in the gut. However, including adequate amounts of calcium in the diet may help slow the rate of bone loss for all women.

Amenorrheic Women and the Female Athlete Triad - Amenorrhea is the condition when menstrual periods stop or fail to initiate in women who are of childbearing age. Secondary amenorrhea is the absence of three or more consecutive menstrual cycles after menarche occurs (first menstrual period). The secondary type of amenorrhea can be induced by exercise in athletes and is referred to as "athletic amenorrhea". Potential causes of athletic amenorrhea include low body weight and low percent body fat, rapid weight loss, sudden onset of vigorous exercise, disordered eating and stress [73]. Amenorrhea results from decreases in circulating estrogen, which then negatively affect calcium balance. Studies comparing healthy women with normal menstrual cycles to amenorrheic women with anorexia nervosa (a type of disordered eating) found decreased levels of calcium absorption, a higher urinary calcium excretion, and a lower rate of bone formation in women with anorexia [74].

The condition "female athlete triad" refers to the combination of disordered eating, amenorrhea, and osteoporosis. Exercise-induced amenorrhea has been shown to result in decreases in bone mass [75,76]. In female athletes, low bone mineral density, menstrual irregularities, dietary factors, and a history of prior stress fractures are associated with an increased risk of future stress fractures [77]. Stress fractures can severely impact health and cause financial burden, especially in physically active females such women in the military [78]. Thus, it is important for amenorrheic women to maintain the recommended Adequate Intake for calcium.

Lactose Intolerant Individuals - Lactose maldigestion (or "lactase non-persistence") describes the inability of an individual to completely digest lactose, the naturally occurring sugar in milk. Lactose intolerance refers to the symptoms that occur when the amount of lactose exceeds the ability of an individual's digestive tract to break down lactose. In the US, approximately 25% of all adults have a limited ability to digest lactose. Lactose maldigestion varies by ethnicity, with a prevalence of 85% in Asians, 50% in African Americans, and 10% in Caucasians [79-81].

Symptoms of lactose intolerance include bloating, flatulence, and diarrhea after consuming large amounts of lactose (such as the amount in 1 quart of milk) [82]. Lactose maldigesters may be at risk for calcium deficiency, not due to an inability to absorb calcium, but rather from the avoidance of dairy products [83,84].

Although some lactose maldigesters avoid dairy products, others are able to consume moderate amounts of lactose, such as the amount in an 8-oz glass of milk. Some individuals may be able to consume two 8-oz glasses of milk a day if they do so at different meals [85-87].

Symptoms of lactose intolerance vary from individual to individual depending on the amount of lactose consumed, history of previous consumption of foods with lactose and the type of meal with which the lactose is consumed [88-91]. Drinking milk with a meal helps reduce symptoms of lactose intolerance substantially. In addition, regularly eating foods (e.g. daily for 2-3 weeks) with lactose (such as milk) can help the body adapt to the lactose and thus reduce symptoms of lactose intolerance [88,90,92]. Other dietary options for lactose maldigesters include choosing aged cheeses (such as Cheddar and Swiss) which contain little lactose, yogurt which contains live active cultures that aid in lactose digestion, or lactose reduced and lactose free milk.

If an individual is a lactose maldigester and chooses to avoid dairy products, it is important for them to include non-dairy sources of calcium in their daily diet.

Vegetarians - There are several types of vegetarian eating practices. Individuals may choose to include some animal products (ovo-vegetarian, lacto-vegetarian, lacto-ovo vegetarian, pesco-vegetarian) or no animal products (vegan) in their diet. Calcium intakes between lacto-ovo-vegetarians (those who consume eggs and dairy products) and non-vegetarians have been shown to be similar [93,94]. Calcium absorption may be reduced in vegetarians because they eat more plant foods containing oxalic and phytic acids, compounds which interfere with calcium absorption. However, vegetarian diets that contain less protein may reduce calcium excretion. Yet, vegans may be at increased risk for inadequate intake of calcium because of their lack of consumption of dairy products [95]. Therefore, it is important for vegans to include adequate amounts of non-dairy sources of calcium in their daily diet or consider taking a calcium supplement to meet their recommended calcium intake. Furthermore, while early studies found vegetarian diets to be beneficial for bone health, more recent studies have found no benefits or even the opposite effect [96].

Calcium Toxicity

The Tolerable Upper Limit (UL) is the highest level of daily intake of calcium from food, water and supplements that is likely to pose no risks of adverse health effects to almost all individuals in the general population. The UL for children and adults ages 1 year and older (including pregnant and lactating women) is 2500 mg/day. It was not possible to establish a UL for infants under the age of 1 year.

While low intakes of calcium can result in deficiency and undesirable health conditions, excessively high intakes of calcium can also have adverse effects. Adverse conditions associated with high calcium intakes are hypercalcemia,

impaired kidney function and decreased absorption of other minerals. Hypercalcemia can also result from excess intake of vitamin D, such as from supplement overuse at levels of 50,000 IU or higher. However, hypercalcemia from diet and supplements is very rare. Most cases of hypercalcemia occur as a result of malignancy - especially in the advanced stages.

Another concern with high calcium intakes is the potential for calcium to interfere with the absorption of other minerals, iron, zinc, magnesium, and phosphorus [97-100].

Most Americans should consider their intake of calcium from all foods including fortified ones before adding supplements to their diet to help avoid the risk of reaching levels at or near the UL for calcium (2500 mg).

Calcium and Medication Interactions

Calcium supplements have the potential to interact with several prescription and over the counter medications. Some examples of medications that may interact with calcium include:

- digoxin
- fluroquinolones
- levothyroxine
- antibiotics in tetracycline family
- tiludronate disodium
- anticonvulsants such as phenytoin
- thiazide, type of diuretic
- glucocorticoids
- mineral oil or stimulant laxatives
- aluminum or magnesium containing antacids

Calcium supplements may decrease levels of the drug digoxin, a medication given to heart patients [101]. The interaction between calcium and vitamin D supplements and digoxin may also increase the risk of hypercalcemia. Calcium supplements also interact with fluoroquinolones (a class of antibiotics including ciprofloxacin), levothyroxine (thyroid hormone) used to treat thyroid deficiency, antibiotics in the tetracycline family, tiludronate disodium (a drug used to treat Paget's disease), and phenytoin (an anti-convulsant drug). In all of these cases, calcium supplements decrease the absorption of these drugs when the two are taken at the same time [102].

Thiazide, and diuretics similar to thiazide, can interact with calcium carbonate and vitamin D supplements to increase the chances of developing hypercalcemia and hypercalciuria (elevated levels of calcium in urine). Aluminum and magnesium antacids can both increase urinary calcium excretion. Mineral oil and stimulant laxatives can both decrease dietary calcium absorption. Furthermore,

glucocorticoids (for example: prednisone) can cause calcium depletion and eventually osteoporosis, when used for more than a few weeks.

Supplemental Sources of Calcium

The 2000 Dietary Guidelines for Americans recommend that individuals consume a variety of foods to meet their nutrient needs since no single food can supply all the nutrients in the amounts needed by an individual [103]. However, for some people it may be necessary to take supplements in order to meet the recommended intakes for calcium. In 2002, calcium supplements were the number one selling mineral supplement and the 3rd highest selling supplement overall in the U.S. nutrition industry totaling approximately $877 million in sales [104].

The two main forms of calcium found in supplements are carbonate and citrate. Calcium carbonate is the most common because it is inexpensive and convenient. The absorption of calcium citrate is similar to calcium carbonate. For instance, a calcium carbonate supplement contains 40% calcium while a calcium citrate supplement only contains 21% calcium. However, you have to take more pills of calcium citrate to get the same amount of calcium as you would get from a calcium carbonate pill since citrate is a larger molecule than carbonate. One advantage of calcium citrate over calcium carbonate is better absorption in those individuals who have decreased stomach acid. Calcium citrate malate is a form of calcium used in the fortification of certain juices and is also well absorbed [105]. Other forms of calcium in supplements or fortified foods include calcium gluconate, lactate, and phosphate.

The amount of calcium your body obtains from various supplements depends on the amount of elemental calcium in the tablet. The amount of elemental calcium is the amount of calcium that actually is in the supplement. Calcium absorption also depends on the total amount of calcium consumed at one time and whether the calcium is taken with food or on an empty stomach. Absorption from supplements is best in doses 500 mg or less because the percent of calcium absorbed decreases as the amount of calcium in the supplement increases [106,107]. Therefore, someone taking 1000 mg of calcium in a supplement should take 500 mg twice a day instead of 1000 mg calcium at one time.

Calcium References

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Iron

DIETARY MINERALS

Overview

Iron, one of the most abundant metals on Earth, is essential to most life forms and to normal human physiology. Iron is an integral part of many proteins and enzymes that maintain good health. In humans, iron is an essential component of proteins involved in oxygen transport [1,2]. It is also essential for the regulation of cell growth and differentiation [3,4]. A deficiency of iron limits oxygen delivery to cells, resulting in fatigue, poor work performance, and decreased immunity [5-6]. On the other hand, excess amounts of iron can result in toxicity and even death [7].

Almost two-thirds of iron in the body is found in hemoglobin, the protein in red blood cells that carries oxygen to tissues. Smaller amounts of iron are found in myoglobin, a protein that helps supply oxygen to muscle, and in enzymes that assist biochemical reactions. Iron is also found in proteins that store iron for future needs and that transport iron in blood. Iron stores are regulated by intestinal iron absorption [8].

Iron in Foods

There are two forms of dietary iron: heme and nonheme. Heme iron is derived from hemoglobin, the protein in red blood cells that delivers oxygen to cells. Heme iron is found in animal foods that originally contained hemoglobin, such as red meats, fish, and poultry. Iron in plant foods such as lentils and beans is arranged in a chemical structure called nonheme iron [9]. This is the form of iron added to iron-enriched and iron-fortified foods. Heme iron is absorbed better than nonheme iron, but most dietary iron is nonheme iron. A variety of heme and nonheme sources of iron are listed in Tables 1 and 2.

Table 1: Selected Food Sources of Heme Iron [10]

Food	Milligrams per serving	% DV*
Chicken liver, cooked, 3½ ounces	12.8	70
Oysters, breaded and fried, 6 pieces	4.5	25
Beef, chuck, lean only, braised, 3 ounces	3.2	20
Clams, breaded, fried, ¾ cup	3.0	15
Beef, tenderloin, roasted, 3 ounces	3.0	15
Turkey, dark meat, roasted, 3½ ounces	2.3	10
Beef, eye of round, roasted, 3 ounces	2.2	10
Turkey, light meat, roasted, 3½ ounces	1.6	8
Chicken, leg, meat only, roasted, 3½ ounces	1.3	6
Tuna, fresh bluefin, cooked, dry heat, 3 ounces	1.1	6

Chicken, breast, roasted, 3 ounces	1.1	6
Halibut, cooked, dry heat, 3 ounces	0.9	6
Crab, blue crab, cooked, moist heat, 3 ounces	0.8	4
Pork, loin, broiled, 3 ounces	0.8	4
Tuna, white, canned in water, 3 ounces	0.8	4
Shrimp, mixed species, cooked, moist heat, 4 large	0.7	4

Table 2: Selected Food Sources of Nonheme Iron [10]

Food	Milligrams per serving	% DV*
Ready-to-eat cereal, 100% iron fortified, ¾ cup	18.0	100
Oatmeal, instant, fortified, prepared with water, 1 cup	10.0	60
Soybeans, mature, boiled, 1 cup	8.8	50
Lentils, boiled, 1 cup	6.6	35
Beans, kidney, mature, boiled, 1 cup	5.2	25
Beans, lima, large, mature, boiled, 1 cup	4.5	25
Beans, navy, mature, boiled, 1 cup	4.5	25
Ready-to-eat cereal, 25% iron fortified, ¾ cup	4.5	25
Beans, black, mature, boiled, 1 cup	3.6	20
Beans, pinto, mature, boiled, 1 cup	3.6	20
Molasses, blackstrap, 1 tablespoon	3.5	20
Tofu, raw, firm, ½ cup	3.4	20
Spinach, boiled, drained, ½ cup	3.2	20
Spinach, canned, drained solids ½ cup	2.5	10
Black-eyed peas (cowpeas), boiled, 1 cup	1.8	10
Spinach, frozen, chopped, boiled ½ cup	1.9	10
Grits, white, enriched, quick, prepared with water, 1 cup	1.5	8
Raisins, seedless, packed, ½ cup	1.5	8
Whole wheat bread, 1 slice	0.9	6
White bread, enriched, 1 slice	0.9	6

*DV = Daily Value. DVs are reference numbers developed by the Food and Drug Administration (FDA) to help consumers determine if a food contains a lot or a little of a specific nutrient. The FDA requires all food labels to include the percent DV (%DV) for iron. The percent DV tells you what percent of the DV is provided in one serving. The DV for iron is 18 milligrams (mg). A food providing 5% of the

DV or less is a low source while a food that provides 10-19% of the DV is a good source. A food that provides 20% or more of the DV is high in that nutrient.

Iron Absorbtion

Iron absorption refers to the amount of dietary iron that the body obtains and uses from food. Healthy adults absorb about 10% to 15% of dietary iron, but individual absorption is influenced by several factors [11-15].

Storage levels of iron have the greatest influence on iron absorption. Iron absorption increases when body stores are low. When iron stores are high, absorption decreases to help protect against toxic effects of iron overload. Iron absorption is also influenced by the type of dietary iron consumed. Absorption of heme iron from meat proteins is efficient. Absorption of heme iron ranges from 15% to 35%, and is not significantly affected by diet [15]. In contrast, 2% to 20% of nonheme iron in plant foods such as rice, maize, black beans, soybeans and wheat is absorbed [16]. Nonheme iron absorption is significantly influenced by various food components.

Meat proteins and vitamin C will improve the absorption of nonheme iron [17-18]. Tannins (found in tea), calcium, polyphenols, and phytates (found in legumes and whole grains) can decrease absorption of nonheme iron [19-24]. Some proteins found in soybeans also inhibit nonheme iron absorption [25]. It is most important to include foods that enhance nonheme iron absorption when daily iron intake is less than recommended, when iron losses are high (which may occur with heavy menstrual losses), when iron requirements are high (as in pregnancy), and when only vegetarian nonheme sources of iron are consumed.

Recommended Iron Intake

Recommendations for iron are provided in the Dietary Reference Intakes (DRIs) developed by the Institute of Medicine of the National Academy of Sciences [1]. *Dietary Reference Intakes* is the general term for a set of reference values used for planning and assessing nutrient intake for healthy people. Three important types of reference values included in the DRIs are *Recommended Dietary Allowances* (RDA), *Adequate Intakes* (AI), and *Tolerable Upper Intake Levels* (UL). The RDA recommends the average daily intake that is sufficient to meet the nutrient requirements of nearly all (97-98%) healthy individuals in each age and gender group. An AI is set when there is insufficient scientific data available to establish a RDA. AIs meet or exceed the amount needed to maintain a nutritional state of adequacy in nearly all members of a specific age and gender group. The UL, on the other hand, is the maximum daily intake unlikely to result in adverse health effects. Table 3 lists the RDAs for iron, in milligrams, for infants, children and adults.

Table 3: Recommended Dietary Allowances for Iron for Infants (7 to 12 months), Children, and Adults [1]

Age	Males (mg/day)	Females (mg/day)	Pregnancy (mg/day)	Lactation (mg/day)
7 to 12 months	11	11	N/A	N/A
1 to 3 years	7	7	N/A	N/A
4 to 8 years	10	10	N/A	N/A
9 to 13 years	8	8	N/A	N/A
14 to 18 years	11	15	27	10
19 to 50 years	8	18	27	9
51+ years	8	8	N/A	N/A

Healthy full term infants are born with a supply of iron that lasts for 4 to 6 months. There is not enough evidence available to establish a RDA for iron for infants from birth through 6 months of age. Recommended iron intake for this age group is based on an Adequate Intake (AI) that reflects the average iron intake of healthy infants fed breast milk. Table 4 lists the AI for iron, in milligrams, for infants up to 6 months of age.

Table 4: Adequate Intake for Iron for Infants (0 to 6 months) [1]

Age (months)	Males and Females (mg/day)
0 to 6	0.27

Iron in human breast milk is well absorbed by infants. It is estimated that infants can use greater than 50% of the iron in breast milk as compared to less than 12% of the iron in infant formula. The amount of iron in cow's milk is low, and infants poorly absorb it. Feeding cow's milk to infants also may result in gastrointestinal bleeding. For these reasons, cow's milk should not be fed to infants until they are at least 1 year old. The American Academy of Pediatrics (AAP) recommends that infants be exclusively breast fed for the first six months of life. Gradual introduction of iron-enriched solid foods should complement breast milk from 7 to 12 months of age [26]. Infants weaned from breast milk before 12 months of age should receive iron-fortified infant formula. Infant formulas that contain from 4 to 12 milligrams of iron per liter are considered iron-fortified [27].

Data from the National Health and Nutrition Examination Survey (NHANES) describe dietary intake of Americans 2 months of age and older. NHANES (1988-

94) data suggest that males of all racial and ethnic groups consume recommended amounts of iron. However, iron intakes are generally low in females of childbearing age and young children [28-29].

Researchers also examine specific groups within the NHANES population. For example, researchers have compared dietary intakes of adults who consider themselves to be food insufficient to those who are food sufficient. Older adults from food insufficient families had significantly lower intakes of iron than older adults who are food sufficient. In one survey, twenty percent of adults age 20 to 59 and 13.6% of adults age 60 and older from food insufficient families consumed less than 50% of the RDA for iron, as compared to 13% of adults age 20 to 50 and 2.5% of adults age 60 and older from food sufficient families [30].

Iron intake is negatively influenced by low nutrient density foods, which are high in calories but low in vitamins and minerals. Sugar sweetened sodas and most desserts are examples of low nutrient density foods, as are snack foods such as potato chips. Among almost 5,000 children and adolescents between the ages of 8 and 18 who were surveyed, low nutrient density foods contributed almost 30% of daily caloric intake, with sweeteners and desserts jointly accounting for almost 25% of caloric intake. Those children and adolescents who consumed fewer "low nutrient density" foods were more likely to consume recommended amounts of iron [31].

Data from The Continuing Survey of Food Intakes by Individuals (CSFII1994-6 and 1998) was used to examine the effect of major food and beverage sources of added sugars on micronutrient intake of U.S. children aged 6 to 17 years. Researchers found that consumption of presweetened cereals, which are fortified with iron, increased the likelihood of meeting recommendations for iron intake. On the other hand, as intake of sugar-sweetened beverages, sugars, sweets, and sweetened grains increased, children were less likely to consume recommended amounts of iron [32].

Iron Deficiency

The World Health Organization considers iron deficiency the number one nutritional disorder in the world [33]. As many as 80% of the world's population may be iron deficient, while 30% may have iron deficiency anemia [34].

Iron deficiency develops gradually and usually begins with a negative iron balance, when iron intake does not meet the daily need for dietary iron. This negative balance initially depletes the storage form of iron while the blood hemoglobin level, a marker of iron status, remains normal. Iron deficiency anemia is an advanced stage of iron depletion. It occurs when storage sites of iron are deficient and blood levels of iron cannot meet daily needs. Blood hemoglobin levels are below normal with iron deficiency anemia.

Iron deficiency anemia can be associated with low dietary intake of iron, inadequate absorption of iron, or excessive blood loss [35]. Women of childbearing age, pregnant women, preterm and low birth weight infants, older infants and toddlers, and teenage girls are at greatest risk of developing iron deficiency anemia because they have the greatest need for iron. Women with heavy menstrual losses can lose a significant amount of iron and are at considerable risk for iron deficiency. Adult men and post-menopausal women lose very little iron, and have a low risk of iron deficiency.

Individuals with kidney failure, especially those being treated with dialysis, are at high risk for developing iron deficiency anemia. This is because their kidneys cannot create enough erythropoietin, a hormone needed to make red blood cells. Both iron and erythropoietin can be lost during kidney dialysis. Individuals who receive routine dialysis treatments usually need extra iron and synthetic erythropoietin to prevent iron deficiency [36-38].

Vitamin A helps mobilize iron from its storage sites, so a deficiency of vitamin A limits the body's ability to use stored iron. This results in an "apparent" iron deficiency because hemoglobin levels are low even though the body can maintain normal amounts of stored iron [39-40]. While uncommon in the U.S., this problem is seen in developing countries where vitamin A deficiency often occurs.

Chronic malabsorption can contribute to iron depletion and deficiency by limiting dietary iron absorption or by contributing to intestinal blood loss. Most iron is absorbed in the small intestines. Gastrointestinal disorders that result in inflammation of the small intestine may result in diarrhea, poor absorption of dietary iron, and iron depletion [41].

Signs of iron deficiency anemia include [42]:

- feeling tired and weak
- decreased work and school performance
- slow cognitive and social development during childhood
- difficulty maintaining body temperature
- decreased immune function, which increases susceptibility to infection
- glossitis (an inflamed tongue)

Eating nonnutritive substances such as dirt and clay, often referred to as pica or geophagia, is sometimes seen in persons with iron deficiency. There is disagreement about the cause of this association. Some researchers believe that these eating abnormalities may result in an iron deficiency. Other researchers believe that iron deficiency may somehow increase the likelihood of these eating problems [43-44].

People with chronic infectious, inflammatory, or malignant disorders such as arthritis and cancer may become anemic. However, the anemia that occurs with

inflammatory disorders differs from iron deficiency anemia and may not respond to iron supplements [45-47]. Research suggests that inflammation may over-activate a protein involved in iron metabolism. This protein may inhibit iron absorption and reduce the amount of iron circulating in blood, resulting in anemia [48].

Iron Supplementation

Three groups of people are most likely to benefit from iron supplements: people with a greater need for iron, individuals who tend to lose more iron, and people who do not absorb iron normally. These individuals include [49-57]:

- pregnant women
- preterm and low birth weight infants
- older infants and toddlers
- teenage girls
- women of childbearing age, especially those with heavy menstrual losses
- people with renal failure, especially those undergoing routine dialysis
- people with gastrointestinal disorders who do not absorb iron normally

Celiac Disease and Crohn's Syndrome are associated with gastrointestinal malabsorption and may impair iron absorption. Iron supplementation may be needed if these conditions result in iron deficiency anemia.

Women taking oral contraceptives may experience less bleeding during their periods and have a lower risk of developing an iron deficiency. Women who use an intrauterine device (IUD) to prevent pregnancy may experience more bleeding and have a greater risk of developing an iron deficiency. If laboratory tests indicate iron deficiency anemia, iron supplements may be recommended.

Total dietary iron intake in vegetarian diets may meet recommended levels; however that iron is less available for absorption than in diets that include meat [58]. Vegetarians who exclude all animal products from their diet may need almost twice as much dietary iron each day as non-vegetarians because of the lower intestinal absorption of nonheme iron in plant foods. Vegetarians should consider consuming nonheme iron sources together with a good source of vitamin C, such as citrus fruits, to improve the absorption of nonheme iron.

Iron Requirements During Pregnancy

Nutrient requirements increase during pregnancy to support fetal growth and maternal health. Iron requirements of pregnant women are approximately double that of non-pregnant women because of increased blood volume during pregnancy, increased needs of the fetus, and blood losses that occur during delivery. If iron intake does not meet increased requirements, iron deficiency anemia can occur. Iron deficiency anemia of pregnancy is responsible for significant morbidity, such as premature deliveries and giving birth to infants with

low birth weight [59-62].

Low levels of hemoglobin and hematocrit may indicate iron deficiency. Hemoglobin is the protein in red blood cells that carries oxygen to tissues. Hematocrit is the proportion of whole blood that is made up of red blood cells. Nutritionists estimate that over half of pregnant women in the world may have hemoglobin levels consistent with iron deficiency. In the U.S., the Centers for Disease Control (CDC) estimated that 12% of all women age 12 to 49 years were iron deficient in 1999-2000. When broken down by groups, 10% of non-Hispanic white women, 22% of Mexican-American women, and 19% of non-Hispanic black women were iron deficient. Prevalence of iron deficiency anemia among lower income pregnant women has remained the same, at about 30%, since the 1980s [63].

The RDA for iron for pregnant women increases to 27 mg per day. Unfortunately, data from the 1988-94 NHANES survey suggested that the median iron intake among pregnant women was approximately 15 mg per day [1]. When median iron intake is less than the RDA, more than half of the group consumes less iron than is recommended each day.

Several major health organizations recommend iron supplementation during pregnancy to help pregnant women meet their iron requirements. The CDC recommends routine low-dose iron supplementation (30 mg/day) for all pregnant women, beginning at the first prenatal visit [33]. When a low hemoglobin or hematocrit is confirmed by repeat testing, the CDC recommends larger doses of supplemental iron. The Institute of Medicine of the National Academy of Sciences also supports iron supplementation during pregnancy [1].

Facts about Iron Supplements

Iron supplementation is indicated when diet alone cannot restore deficient iron levels to normal within an acceptable timeframe. Supplements are especially important when an individual is experiencing clinical symptoms of iron deficiency anemia. The goals of providing oral iron supplements are to supply sufficient iron to restore normal storage levels of iron and to replenish hemoglobin deficits. When hemoglobin levels are below normal, physicians often measure serum ferritin, the storage form of iron. A serum ferritin level less than or equal to 15 micrograms per liter confirms iron deficiency anemia in women, and suggests a possible need for iron supplementation.

Supplemental iron is available in two forms: ferrous and ferric. Ferrous iron salts (ferrous fumarate, ferrous sulfate, and ferrous gluconate) are the best absorbed forms of iron supplements [64]. Elemental iron is the amount of iron in a supplement that is available for absorption. Figure 1 lists the percent elemental iron in these supplements.

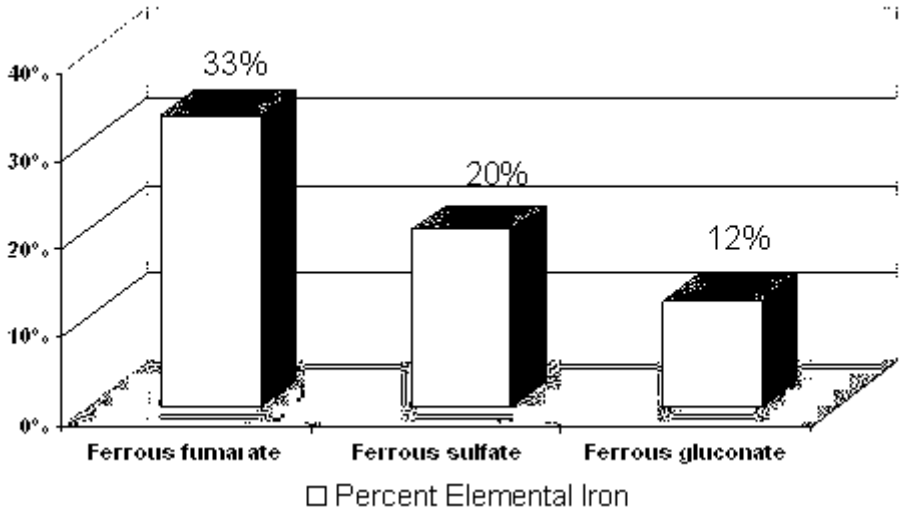

Figure 1: Percent Elemental Iron in Iron Supplements [65]

The amount of iron absorbed decreases with increasing doses. For this reason, it is recommended that most people take their prescribed daily iron supplement in two or three equally spaced doses. For adults who are not pregnant, the CDC recommends taking 50 mg to 60 mg of oral elemental iron (the approximate amount of elemental iron in one 300 mg tablet of ferrous sulfate) twice daily for three months for the therapeutic treatment of iron deficiency anemia.

Therapeutic doses of iron supplements, which are prescribed for iron deficiency anemia, may cause gastrointestinal side effects such as nausea, vomiting, constipation, diarrhea, dark colored stools, and/or abdominal distress. Starting with half the recommended dose and gradually increasing to the full dose will help minimize these side effects. Taking the supplement in divided doses and with food also may help limit these symptoms. Iron from enteric coated or delayed-release preparations may have fewer side effects, but is not as well absorbed and not usually recommended [64].

Physicians monitor the effectiveness of iron supplements by measuring laboratory indices, including reticulocyte count (levels of newly formed red blood cells), hemoglobin levels, and ferritin levels. In the presence of anemia, reticulocyte counts will begin to rise after a few days of supplementation. Hemoglobin usually increases within 2 to 3 weeks of starting iron supplementation.

In rare situations parenteral iron (provided by injection or I.V.) is required. Doctors will carefully manage the administration of parenteral iron [66].

Iron Supplement Precautions

Iron deficiency is uncommon among adult men and postmenopausal women. These individuals should only take iron supplements when prescribed by a physician because of their greater risk of iron overload.

Iron overload is a condition in which excess iron is found in the blood and stored in organs such as the liver and heart. Iron overload is associated with several genetic diseases including hemochromatosis, which affects approximately 1 in 250 individuals of northern European descent [67]. Individuals with hemochromatosis absorb iron very efficiently, which can result in a build up of excess iron and can cause organ damage such as cirrhosis of the liver and heart failure [67-69]. Hemochromatosis is often not diagnosed until excess iron stores have damaged an organ. Iron supplementation may accelerate the effects of hemochromatosis, an important reason why adult men and postmenopausal women who are not iron deficient should avoid iron supplements. Individuals with blood disorders that require frequent blood transfusions are also at risk of iron overload and are usually advised to avoid iron supplements.

Research and Current Health Issues

Iron and heart disease

Because known risk factors cannot explain all cases of heart disease, researchers continue to look for new causes. Some evidence suggests that iron can stimulate the activity of free radicals. Free radicals are natural by-products of oxygen metabolism that are associated with chronic diseases, including cardiovascular disease. Free radicals may inflame and damage coronary arteries, the blood vessels that supply the heart muscle. This inflammation may contribute to the development of atherosclerosis, a condition characterized by partial or complete blockage of one or more coronary arteries. Other researchers suggest that iron may contribute to the oxidation of LDL ("bad") cholesterol, changing it to a form that is more damaging to coronary arteries.

As far back as the 1980s, some researchers suggested that the regular menstrual loss of iron, rather than a protective effect from estrogen, could better explain the lower incidence of heart disease seen in pre-menopausal women [70]. After menopause, a woman's risk of developing coronary heart disease increases along with her iron stores. Researchers have also observed lower rates of heart disease in populations with lower iron stores, such as those in developing countries [71-74]. In those geographic areas, lower iron stores are attributed to low meat (and iron) intake, high fiber diets that inhibit iron absorption, and gastrointestinal (GI) blood (and iron) loss due to parasitic infections.

In the 1980s, researchers linked high iron stores with increased risk of heart attacks in Finnish men [75]. However, more recent studies have not supported

such an association [76-77].

One way of testing an association between iron stores and coronary heart disease is to compare levels of ferritin, the storage form of iron, to the degree of atherosclerosis in coronary arteries. In one study, researchers examined the relationship between ferritin levels and atherosclerosis in 100 men and women referred for cardiac examination. In this population, higher ferritin levels were not associated with an increased degree of atherosclerosis, as measured by angiography [78]. In a different study, researchers found that ferritin levels were higher in male patients diagnosed with coronary artery disease. They did not find any association between ferritin levels and risk of coronary disease in women [79].

A second way to test this association is to examine rates of coronary disease in people who frequently donate blood. If excess iron stores contribute to heart disease, frequent blood donation could potentially lower heart disease rates because of the iron loss associated with blood donation. Over 2,000 men over age 39 and women over age 50 who donated blood between 1988 and 1990 were surveyed 10 years later to compare rates of cardiac events to frequency of blood donation. Cardiac events were defined as (1) occurrence of an acute myocardial infarction (heart attack), (2) undergoing angioplasty, a medical procedure that opens a blocked coronary artery; or (3) undergoing bypass grafting, a surgical procedure that replaces blocked coronary arteries with healthy blood vessels. Researchers found that frequent donors, who donated more than 1 unit of whole blood each year between 1988 and 1990, were less likely to experience cardiac events than casual donors (those who only donated a single unit in that 3-year period). Researchers concluded that frequent and long-term blood donation may decrease the risk of cardiac events [80].

Conflicting results, and different methods to measure iron stores, make it difficult to reach a final conclusion on this issue. However, researchers know that it is feasible to decrease iron stores in healthy individual through phlebotomy (blood letting or donation).

Iron and intense exercise

Many men and women who engage in regular, intense exercise such as jogging, competitive swimming, and cycling have marginal or inadequate iron status [81-85]. Possible explanations include increased gastrointestinal blood loss after running and a greater turnover of red blood cells. Also, red blood cells within the foot can rupture while running. For these reasons, the need for iron may be 30% greater in those who engage in regular intense exercise.

Three groups of athletes may be at greatest risk of iron depletion and deficiency: female athletes, distance runners, and vegetarian athletes. It is particularly important for members of these groups to consume recommended amounts of iron and to pay attention to dietary factors that enhance iron absorption. If

appropriate nutrition intervention does not promote normal iron status, iron supplementation may be indicated. In one study of female swimmers, researchers found that supplementation with 125 milligrams (mg) of ferrous sulfate per day prevented iron depletion. These swimmers maintained adequate iron stores, and did not experience the gastrointestinal side effects often seen with higher doses of iron supplementation [86].

Iron and Mineral Interactions

Some researchers have raised concerns about interactions between iron, zinc, and calcium. When iron and zinc supplements are given together in a water solution and without food, greater doses of iron may decrease zinc absorption. However, the effect of supplemental iron on zinc absorption does not appear to be significant when supplements are consumed with food [87-88]. There is evidence that calcium from supplements and dairy foods may inhibit iron absorption, but it has been very difficult to distinguish between the effects of calcium on iron absorption versus other inhibitory factors such as phytate.

Toxicity

There is considerable potential for iron toxicity because very little iron is excreted from the body. Thus, iron can accumulate in body tissues and organs when normal storage sites are full. For example, people with hemachromatosis are at risk of developing iron toxicity because of their high iron stores.

In children, death has occurred from ingesting 200 mg of iron. It is important to keep iron supplements tightly capped and away from children's reach.

In 2001, the Institute of Medicine of the National Academy of Sciences set a tolerable upper intake level (UL) for iron for healthy people [1]. There may be times when a physician prescribes an intake higher than the upper limit, such as when individuals with iron deficiency anemia need higher doses to replenish their iron stores. Table 5 lists the ULs for healthy adults, children, and infants 7 to 12 months of age.

Table 5: Tolerable Upper Intake Levels for Iron for Infants 7 to 12 months, Children, and Adults [1]

Age	Males (mg/day)	Females (mg/day)	Pregnancy (mg/day)	Lactation (mg/day)
7 to 12 months	40	40	N/A	N/A
1 to 13 years	40	40	N/A	N/A
14 to 18 years	45	45	45	45
19 + years	45	45	45	45

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Magnesium

Overview

Magnesium is the fourth most abundant mineral in the body and is essential to good health. Approximately 50% of total body magnesium is found in bone. The other half is found predominantly inside cells of body tissues and organs. Only 1% of magnesium is found in blood, but the body works very hard to keep blood levels of magnesium constant [1].

Magnesium is needed for more than 300 biochemical reactions in the body. It helps maintain normal muscle and nerve function, keeps heart rhythm steady, supports a healthy immune system, and keeps bones strong. Magnesium also helps regulate blood sugar levels, promotes normal blood pressure, and is known to be involved in energy metabolism and protein synthesis [2-3]. There is an increased interest in the role of magnesium in preventing and managing disorders such as hypertension, cardiovascular disease, and diabetes. Dietary magnesium is absorbed in the small intestines. Magnesium is excreted through the kidneys [4].

Magnesium in Food

Green vegetables such as spinach are good sources of magnesium because the center of the chlorophyll molecule contains magnesium. Some legumes (beans and peas), nuts and seeds, and whole, unrefined grains are also good sources of magnesium [5]. Refined grains are generally low in magnesium. When white flour is refined and processed, the magnesium-rich germ and bran are removed. Bread made from whole grain wheat flour provides more magnesium than bread made from white refined flour. Tap water can be a source of magnesium, but the amount varies according to the water supply. Water that naturally contains more minerals is described as "hard". "Hard" water contains more magnesium than

"soft" water.

Selected food sources of magnesium are listed in Table 1.

Table 1: Selected food sources of magnesium [5]

FOOD	Milligrams (mg)	%DV*
Halibut, cooked, 3 ounces	90	20
Almonds, dry roasted, 1 ounce	80	20
Cashews, dry roasted, 1 ounce	75	20
Soybeans, mature, cooked, ½ cup	75	20
Spinach, frozen, cooked, ½ cup	75	20
Nuts, mixed, dry roasted, 1 ounce	65	15
Cereal, shredded wheat, 2 rectangular biscuits	55	15
Oatmeal, instant, fortified, prepared w/ water, 1 cup	55	15
Potato, baked w/ skin, 1 medium	50	15
Peanuts, dry roasted, 1 ounce	50	15
Peanut butter, smooth, 2 Tablespoons	50	15
Wheat Bran, crude, 2 Tablespoons	45	10
Blackeyed Peas, cooked, ½ cup	45	10
Yogurt, plain, skim milk, 8 fluid ounces	45	10
Bran Flakes, ¾ cup	40	10
Vegetarian Baked Beans, ½ cup	40	10
Rice, brown, long-grained, cooked, ½ cup	40	10
Lentils, mature seeds, cooked, ½ cup	35	8
Avocado, California, ½ cup pureed	35	8
Kidney Beans, canned, ½ cup	35	8
Pinto Beans, cooked, ½ cup	35	8
Wheat Germ, crude, 2 Tablespoons	35	8
Chocolate milk, 1 cup	33	8
Banana, raw, 1 medium	30	8
Milk Chocolate candy bar, 1.5 ounce bar	28	8
Milk, reduced fat (2%) or fat free, 1 cup	27	8
Bread, whole wheat, commercially prepared, 1 slice	25	6
Raisins, seedless, ¼ cup packed	25	6
Whole Milk, 1 cup	24	6

*DV = Daily Value. DVs are reference numbers developed by the Food and Drug Administration (FDA) to help consumers determine if a food contains a lot or a little of a specific nutrient. The DV for magnesium is 400 milligrams (mg). Most food labels do not list a food's magnesium content. The percent DV (%DV) listed on the table above indicates the percentage of the DV provided in one serving. A food providing 5% of the DV or less per serving is a low source while a food that provides 10-19% of the DV is a good source. A food that provides 20% or more of the DV is high in that nutrient.

Recommended Dietary Intake of Magnesium

Recommendations for magnesium are provided in the Dietary Reference Intakes (DRIs) developed by the Institute of Medicine of the National Academy of Sciences [4]. Dietary Reference Intakes is the general term for a set of reference values used for planning and assessing nutrient intake for healthy people. Three important types of reference values included in the DRIs are Recommended Dietary Allowances (RDA), Adequate Intakes (AI), and Tolerable Upper Intake Levels (UL). The RDA recommends the average daily intake that is sufficient to meet the nutrient requirements of nearly all (97-98%) healthy individuals in each age and gender group. An AI is set when there is insufficient scientific data available to establish a RDA for specific age/gender groups. AIs meet or exceed the amount needed to maintain a nutritional state of adequacy in nearly all members of a specific age and gender group. The UL, on the other hand, is the *maximum* daily intake unlikely to result in adverse health effects. Table 2 lists the RDAs for magnesium, in milligrams, for children and adults.

Table 2: RDA for magnesium for children and adults [4]

Age (years)	Male (mg/day)	Female (mg/day)	Pregnancy (mg/day)	Lactation (mg/day)
1-3	80	80	N/A	N/A
4-8	130	130	N/A	N/A
9-13	240	240	N/A	N/A
14-18	410	360	400	360
19-30	400	310	350	310
31+	420	320	360	320

There is insufficient information on magnesium to establish a RDA for infants. For infants 0 to 12 months, the DRI is in the form of an Adequate Intake (AI), which is the mean intake of magnesium in healthy, breastfed infants. Table 3 lists the AIs for infants in milligrams (mg).

Table 3: Recommended Adequate Intake for magnesium for infants [4]

Age (months)	Males and Females (mg/day)
0 to 6	30
7 to 12	75

Data from the 1999-2000 National Health and Nutrition Examination Survey suggest that substantial numbers of adults in the United States (US) fail to consume recommended amounts of magnesium. Among adult men and women, Caucasians consume significantly more magnesium than African-Americans. Magnesium intake is lower among older adults in every racial and ethnic group. African-American men and Caucasian men and women who take dietary supplements consume significantly more magnesium than those who do not [6].

Magnesium Deficiency

Even though dietary surveys suggest that many Americans do not consume recommended amounts of magnesium, symptoms of magnesium deficiency are rarely seen in the US. However, there is concern about the prevalence of sub-optimal magnesium stores in the body. For many people, dietary intake may not be high enough to promote an optimal magnesium status, which may be protective against disorders such as cardiovascular disease and immune dysfunction [7-8].

The health status of the digestive system and the kidneys significantly influence magnesium status. Magnesium is absorbed in the intestines and then transported through the blood to cells and tissues. Approximately one-third to one-half of dietary magnesium is absorbed into the body [9-10]. Gastrointestinal disorders that impair absorption such as Crohn's disease can limit the body's ability to absorb magnesium. These disorders can deplete the body's stores of magnesium and in extreme cases may result in magnesium deficiency. Chronic or excessive vomiting and diarrhea may also result in magnesium depletion [10].

Healthy kidneys are able to limit urinary excretion of magnesium to compensate for low dietary intake. However, excessive loss of magnesium in urine can be a side effect of some medications and can also occur in cases of poorly-controlled diabetes and alcohol abuse [11-18].

Early signs of magnesium deficiency include loss of appetite, nausea, vomiting,

fatigue, and weakness. As magnesium deficiency worsens, numbness, tingling, muscle contractions and cramps, seizures, personality changes, abnormal heart rhythms, and coronary spasms can occur. Severe magnesium deficiency can result in low levels of calcium in the blood (hypocalcemia). Magnesium deficiency is also associated with low levels of potassium in the blood (hypokalemia) [19-20].

Magnesium Supplementation

Magnesium supplementation may be indicated when a specific health problem or condition causes an excessive loss of magnesium or limits magnesium absorption.

- Some medicines may result in magnesium deficiency, including certain diuretics, antibiotics, and medications used to treat cancer (anti-neoplastic medication). Examples of these medications are:
  - Diuretics: Lasix, Bumex, Edecrin, and hydrochlorothiazide
  - Antibiotics: Gentamicin, Amphotericin, and Cyclosporin
  - Anti-neoplastic medication: Cisplatin
- Individuals with poorly-controlled diabetes may benefit from magnesium supplements because of increased magnesium loss in urine associated with hyperglycemia [21].
- Magnesium supplementation may be indicated for persons with alcoholism. Low blood levels of magnesium occur in 30% to 60% of alcoholics, and in nearly 90% of patients experiencing alcohol withdrawal [17-18]. Anyone who substitutes alcohol for food will usually have significantly lower magnesium intakes.
- Individuals with chronic malabsorptive problems such as Crohn's disease, gluten sensitive enteropathy, regional enteritis, and intestinal surgery may lose magnesium through diarrhea and fat malabsorption [22]. Individuals with these conditions may need supplemental magnesium.
- Individuals with chronically low blood levels of potassium and calcium may have an underlying problem with magnesium deficiency. Magnesium supplements may help correct the potassium and calcium deficiencies.
- Older adults are at increased risk for magnesium deficiency. The 1999-2000 and 1998-94 National Health and Nutrition Examination Surveys suggest that older adults have lower dietary intakes of magnesium than younger adults [23]. In addition, magnesium absorption decreases and renal excretion of magnesium increases in older adults. Seniors are also more likely to be taking drugs that interact with magnesium. This combination of factors places older adults at risk for magnesium deficiency. It is very important for older adults to consume recommended amounts of dietary magnesium.

Table 4 describes some important interactions between certain drugs and magnesium. These interactions may result in higher or lower levels of

magnesium, or may influence absorption of the medication.

Table 4: Common and important magnesium/drug interactions

Drug	Potential Interaction
Loop and thiazide diuretics (e.g. lasix, bumex, edecrin, and hydrochlorthiazide Anti-neoplastic drugs (e.g. cisplatin) Antibiotics (e.g. gentamicin, amphotericin, and cyclosporine)	These drugs may increase the loss of magnesium in urine. Thus, taking these medications for long periods of time may contribute to magnesium depletion [9-10,12].
Tetracycline antibiotics	Magnesium binds tetracycline in the gut and decreases the absorption of tetracycline [24].
Magnesium-containing antacids and laxatives	Many antacids and laxatives contain magnesium. When frequently taken in large doses, these drugs can inadvertently lead to excessive magnesium consumption [25-26] and hypermagnesemia, which refers to elevated levels of magnesium in blood.

Types of Magnesium Supplementation

When blood levels of magnesium are very low, intravenous (i.e. by IV) magnesium replacement is usually recommended. Magnesium tablets also may be prescribed, although some forms can cause diarrhea [27]. Because people with kidney disease may not be able to excrete excess amounts of magnesium, they should not consume magnesium supplements unless prescribed by a physician.

Oral magnesium supplements combine magnesium with another substance such as a salt. Examples of magnesium supplements include magnesium oxide, magnesium sulfate, and magnesium carbonate. Elemental magnesium refers to the amount of magnesium in each compound. Figure 1 compares the amount of elemental magnesium in different types of magnesium supplements [28]. The amount of elemental magnesium in a compound and its bioavailability influence the effectiveness of the magnesium supplement. Bioavailability refers to the amount of magnesium in food, medications, and supplements that is absorbed in the intestines and ultimately available for biological activity in your cells and tissues. Enteric coating of a magnesium compound can decrease bioavailability [29]. In a study that compared four forms of magnesium preparations, results suggested lower bioavailability of magnesium oxide, with significantly higher and equal absorption and bioavailability of magnesium chloride and magnesium

lactate [30]. This supports the belief that both the magnesium content of a dietary supplement and its bioavailability contribute to its ability to replete deficient levels of magnesium.

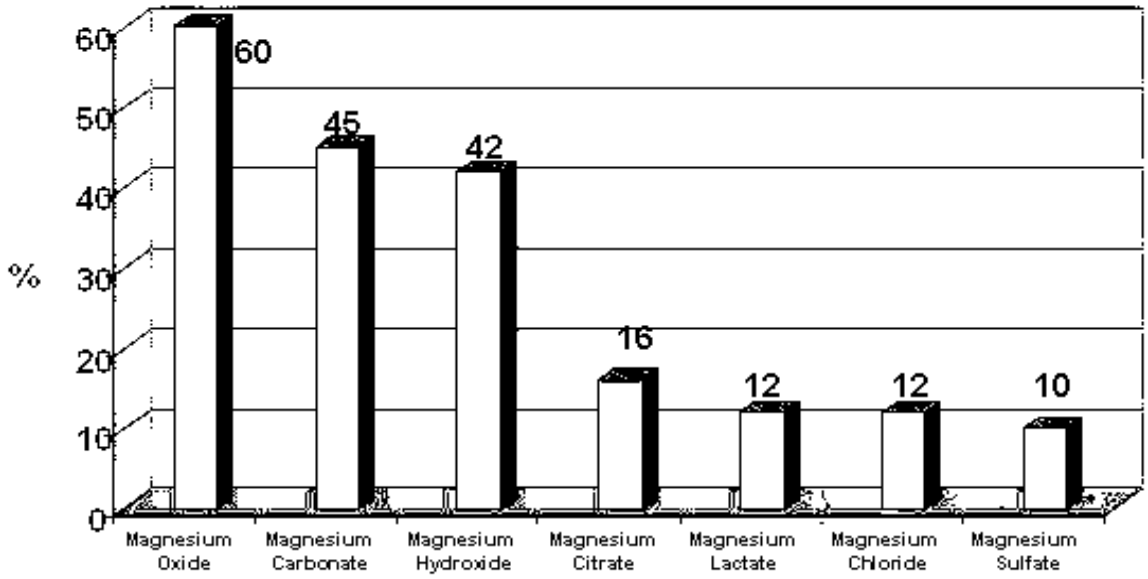

Figure 1: ☐ Percent Magnesium content of oral supplements

Research and Current Issues

Magnesium and Blood Pressure

Epidemiologic evidence suggests that magnesium may play an important role in regulating blood pressure [4]. Diets that provide plenty of fruits and vegetables, which are good sources of potassium and magnesium, are consistently associated with lower blood pressure [31-33]. The DASH study (Dietary Approaches to Stop Hypertension), a human clinical trial, suggested that high blood pressure could be significantly lowered by a diet that emphasizes fruits, vegetables, and low fat dairy foods. Such a diet will be high in magnesium, potassium, and calcium, and low in sodium and fat [34-36].

An observational study examined the effect of various nutritional factors on incidence of high blood pressure in over 30,000 US male health professionals. After four years of follow-up, it was found that a lower risk of hypertension was associated with dietary patterns that provided more magnesium, potassium, and dietary fiber [37]. For 6 years, the Atherosclerosis Risk in Communities (ARIC) Study followed approximately 8,000 men and women who were initially free of hypertension. In this study, the risk of developing hypertension decreased as dietary magnesium intake increased in women, but not in men [38].

Foods high in magnesium are frequently high in potassium and dietary fiber. This

makes it difficult to evaluate the independent effect of magnesium on blood pressure. However, newer scientific evidence from DASH clinical trials is strong enough that the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure states that diets that provide plenty of magnesium are positive lifestyle modifications for individuals with hypertension.

Magnesium and Diabetes

Magnesium plays an important role in carbohydrate metabolism. It may influence the release and activity of insulin [13]. Low blood levels of magnesium (hypomagnesemia) are frequently seen in individuals with type 2 diabetes. Hypomagnesemia may worsen insulin resistance, a condition that often precedes diabetes, or may be a consequence of insulin resistance. Individuals with insulin resistance do not use insulin efficiently and require greater amounts of insulin to maintain blood sugar within normal levels. The kidneys possibly lose their ability to retain magnesium during periods of severe hyperglycemia (significantly elevated blood glucose). The increased loss of magnesium in urine may then result in lower blood levels of magnesium. In older adults, correcting magnesium depletion may improve insulin response and action [42].

The Nurses' Health Study (NHS) and the Health Professionals' Follow-up Study (HFS) follow more than 170,000 health professionals through biennial questionnaires. Diet was first evaluated in 1980 in the NHS and in 1986 in the HFS, and dietary assessments have been completed every 2 to 4 years since. Information on the use of dietary supplements, including multivitamins, is also collected. As part of these studies, over 127,000 research subjects (85,060 women and 42,872 men) with no history of diabetes, cardiovascular disease, or cancer at baseline were followed to examine risk factors for developing type 2 diabetes. Women were followed for 18 years; men were followed for 12 years. Over time, the risk for developing type 2 diabetes was greater in men and women with a lower magnesium intake. This study supports the dietary recommendation to increase consumption of major food sources of magnesium, such as whole grains, nuts, and green leafy vegetables [43].

The Iowa Women's Health Study has followed a group of older women since 1986. Researchers from this study examined the association between women's risk of developing type 2 diabetes and intake of carbohydrates, dietary fiber, and dietary magnesium. Dietary intake was estimated by a food frequency questionnaire, and incidence of diabetes throughout 6 years of follow-up was determined by asking participants if they had been diagnosed by a doctor as having diabetes. Based on baseline dietary intake assessment only, researchers' findings suggested that a greater intake of whole grains, dietary fiber, and magnesium decreased the risk of developing diabetes in older women [44].

The Women's Health Study was originally designed to evaluate the benefits versus risks of low-dose aspirin and vitamin E supplementation in the primary prevention of cardiovascular disease and cancer in women 45 years of age and

older. In an examination of almost 40,000 women participating in this study, researchers also examined the association between magnesium intake and incidence of type 2 diabetes over an average of 6 years. Among women who were overweight, the risk of developing type 2 diabetes was significantly greater among those with lower magnesium intake [45].

On the other hand, the Atherosclerosis Risk in Communities (ARIC) study did not find any association between dietary magnesium intake and the risk for type 2 diabetes. During 6 years of follow-up, ARIC researchers examined the risk for type 2 diabetes in over 12,000 middle-aged adults without diabetes at baseline examination. In this study, there was no statistical association between dietary magnesium intake and incidence of type 2 diabetes in either black or white research subjects [46]..

Several clinical studies have examined the potential benefit of supplemental magnesium on metabolic control of type 2 diabetes. In one such study, 63 subjects with below normal serum magnesium levels received either 2.5 grams of oral magnesium chloride daily "in liquid form" (providing 300 mg elemental magnesium per day) or a placebo. At the end of the 16-week study period, those who received the magnesium supplement had higher blood levels of magnesium and improved metabolic control of diabetes, as suggested by lower Hemoglobin A1C levels, than those who received a placebo [47]. Hemoglobin A1C is a test that measures overall control of blood glucose over the previous 2 to 3 months, and is considered by many doctors to be the single most important blood test for diabetics.

In another study, 128 patients with poorly controlled type 2 diabetes were randomized to receive a placebo or a supplement with either 500 mg or 1000 mg of magnesium oxide (MgO) for 30 days. All patients were also treated with diet or diet plus oral medication to control blood glucose levels. Magnesium levels increased in the group receiving 1000 mg magnesium oxide per day (equal to 600 mg elemental magnesium per day) but did not significantly change in the placebo group or the group receiving 500 mg of magnesium oxide per day (equal to 300 mg elemental magnesium per day). However, neither level of magnesium supplementation significantly improved blood glucose control [48].

These studies provide intriguing results but also suggest that additional research is needed to better explain the association between blood magnesium levels, dietary magnesium intake, and type 2 diabetes. In 1999, the American Diabetes Association (ADA) issued nutrition recommendations for diabetics stating that "…routine evaluation of blood magnesium level is recommended only in patients at high risk for magnesium deficiency. Levels of magnesium should be repleted (replaced) only if hypomagnesemia can be demonstrated" [21].

Magnesium and Cardiovascular disease

Magnesium metabolism is very important to insulin sensitivity and blood pressure regulation, and magnesium deficiency is common in individuals with diabetes. The observed associations between magnesium metabolism, diabetes, and high blood pressure increase the likelihood that magnesium metabolism may influence cardiovascular disease [49].

Some observational surveys have associated higher blood levels of magnesium with lower risk of coronary heart disease [50-51]. In addition, some dietary surveys have suggested that a higher magnesium intake may reduce the risk of having a stroke [52]. There is also evidence that low body stores of magnesium increase the risk of abnormal heart rhythms, which may increase the risk of complications after a heart attack [4]. These studies suggest that consuming recommended amounts of magnesium may be beneficial to the cardiovascular system. They have also prompted interest in clinical trials to determine the effect of magnesium supplements on cardiovascular disease.

Several small studies suggest that magnesium supplementation may improve clinical outcomes in individuals with coronary disease. In one of these studies, the effect of magnesium supplementation on exercise tolerance, exercise-induced chest pain, and quality of life was examined in 187 patients. Patients received either a placebo or a supplement providing 365 milligrams of magnesium citrate twice daily for 6 months. At the end of the study period researchers found that magnesium therapy significantly increased magnesium levels. Patients receiving magnesium had a 14 percent improvement in exercise duration as compared to no change in the placebo group. Those receiving magnesium were also less likely to experience exercise-induced chest pain [53].

In another study, 50 men and women with stable coronary disease were randomized to receive either a placebo or a magnesium supplement that provided 342 mg magnesium oxide twice daily. After 6 months, those who received the oral magnesium supplement were found to have improved exercise tolerance [54].

In a third study, researchers examined whether magnesium supplementation would add to the anti-thrombotic (anti-clotting) effects of aspirin in 42 coronary patients [55]. For three months, each patient received either a placebo or a supplement with 400 mg of magnesium oxide two to three times daily. After a four-week break without any treatment, treatment groups were reversed so that each person in the study then received the alternate treatment for three months. Researchers found that supplemental magnesium did provide an additional anti-thrombotic effect.

These studies are encouraging, but involved small numbers. Additional studies are needed to better understand the complex relationships between magnesium intake, indicators of magnesium status, and heart disease.

Magnesium and Osteoporosis

Bone health is supported by many factors, most notably calcium and vitamin D. However, some evidence suggests that magnesium deficiency may be an additional risk factor for postmenopausal osteoporosis. This may be due to the fact that magnesium deficiency alters calcium metabolism and the hormones that regulate calcium. Several human studies have suggested that magnesium supplementation may improve bone mineral density [4]. In a study of older adults, a greater magnesium intake maintained bone mineral density to a greater degree than a lower magnesium intake [56]. Diets that provide recommended levels of magnesium are beneficial for bone health, but further investigation on the role of magnesium in bone metabolism and osteoporosis is needed.

Magnesium Toxicity

Dietary magnesium does not pose a health risk, however pharmacologic doses of magnesium in supplements can promote adverse effects such as diarrhea and abdominal cramping. Risk of magnesium toxicity increases with kidney failure, when the kidney loses the ability to remove excess magnesium. Very large doses of magnesium-containing laxatives and antacids also have been associated with magnesium toxicity [25]. For example, a case of hypermagnesemia after unsupervised intake of aluminum magnesia oral suspension occurred after a 16 year old girl decided to take the antacid every two hours rather than four times per day, as prescribed. Three days later, she became unresponsive and demonstrated loss of deep tendon reflex [57]. Doctors were unable to determine her exact magnesium intake, but the young lady presented with blood levels of magnesium five times higher than normal [25]. Therefore, it is important for medical professionals to be aware of the use of any magnesium-containing laxatives or antacids. Signs of excess magnesium can be similar to magnesium deficiency and include changes in mental status, nausea, diarrhea, appetite loss, muscle weakness, difficulty breathing, extremely low blood pressure, and irregular heartbeat [57-60].

Table 5 lists the ULs for supplemental magnesium for healthy infants, children, and adults in milligrams (mg) [4]. Physicians may prescribe magnesium in higher doses for specific medical problems. There is no UL for dietary intake of magnesium; only for magnesium supplements.

Table 5: Tolerable Upper Intake Levels for supplemental magnesium [4]

Age (years)	Male (mg/day)	Female (mg/day)	Pregnancy (mg/day)	Lactation (mg/day)
Infants	Undetermined	Undetermined	N/A	N/A
1-3	65	65	N/A	N/A
4 - 8	110	110	N/A	N/A
9 - 18	350	350	350	350
19+	350	350	350	350

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Selenium

Overview

Selenium is a trace mineral that is essential to good health but required only in small amounts [1]. Selenium is incorporated into proteins to make selenoproteins, which are important antioxidant enzymes. The antioxidant properties of selenoproteins help prevent cellular damage from free radicals. Free radicals are natural by-products of oxygen metabolism that may contribute to the development of chronic diseases such as cancer and heart disease [2,3]. Other selenoproteins help regulate thyroid function and play a role in the immune system [4-7].

Selenium in Food

Plant foods are the major dietary sources of selenium in most countries throughout the world. The content of selenium in food depends on the selenium content of the soil where plants are grown or animals are raised. For example, researchers know that soils in the high plains of northern Nebraska and the Dakotas have very high levels of selenium. People living in those regions generally have the highest selenium intakes in the United States [8]. In the U.S., food distribution patterns across the country help prevent people living in low-selenium geographic areas from having low dietary selenium intakes. Soils in some parts of China and Russia have very low amounts of selenium. Selenium deficiency is often reported in those regions because most food in those areas is grown and eaten locally.

Selenium also can be found in some meats and seafood. Animals that eat grains or plants that were grown in selenium-rich soil have higher levels of selenium in their muscle. In the U.S., meats and bread are common sources of dietary selenium [9,10]. Some nuts are also sources of selenium.

Selenium content of foods can vary. For example, Brazil nuts may contain as much as 544 micrograms of selenium per ounce. They also may contain far less selenium. It is wise to eat Brazil nuts only occasionally because of their unusually high intake of selenium. Selected food sources of selenium are provided in Table 1 [11].

Table 1: Selected food sources of selenium [11]

Food	Micrograms (µg)	Percent DV*
Brazil nuts, dried, unblanched, 1 ounce	544	780
Tuna, light, canned in oil, drained, 3 ounces	63	95
Beef, cooked, 3½ ounces	35	50

Spaghetti w/ meat sauce, frozen entrée, 1 serving	34	50
Cod, cooked, 3 ounces	32	45
Turkey, light meat, roasted, 3½ ounces	32	45
Beef chuck roast, lean only, roasted, 3 ounces	23	35
Chicken Breast, meat only, roasted, 3½ ounces	20	30
Noodles, enriched, boiled, 1/2 cup	17	25
Macaroni, elbow, enriched, boiled, 1/2 cup	15	20
Egg, whole, 1 medium	14	20
Cottage cheese, low fat 2%, 1/2 cup	12	15
Oatmeal, instant, fortified, cooked, 1 cup	12	15
Rice, white, enriched, long grain, cooked, 1/2 cup	12	15
Rice, brown, long-grained, cooked, 1/2 cup	10	15
Bread, enriched, whole wheat, commercially prepared, 1 slice	10	15
Walnuts, black, dried, 1 ounce	5	8
Bread, enriched, white, commercially prepared, 1 slice	4	6
Cheddar cheese, 1 ounce	4	6

*DV = Daily Value. DVs are reference numbers developed by the Food and Drug Administration (FDA) to help consumers determine if a food contains a lot or a little of a specific nutrient. The DV for selenium is 70 micrograms (ug). Most food labels do not list a food's selenium content. The percent DV (%DV) listed on the table indicates the percentage of the DV provided in one serving. A food providing 5% of the DV or less is a low source while a food that provides 10-19% of the DV is a good source. A food that provides 20% or more of the DV is high in that nutrient. It is important to remember that foods that provide lower percentages of the DV also contribute to a healthful diet.

Recommended Dietary Intake for Selenium

Recommendations for selenium are provided in the Dietary Reference Intakes developed by the Institute of Medicine [12]. Dietary Reference Intakes (DRIs) is the general term for a set of reference values used for planning and assessing nutrient intake for healthy people. Three important types of reference values included in the DRIs are Recommended Dietary Allowances (RDA), Adequate Intakes (AI), and Tolerable Upper Intake Levels (UL). The RDA recommends the average daily dietary intake level that is sufficient to meet the nutrient requirements of nearly all (97-98%) healthy individuals in each age and gender group [12]. An AI is set when there is insufficient scientific data available to establish a RDA. AIs meet or exceed the amount needed to maintain a nutritional state of adequacy in nearly all members of a specific age and gender group. The UL, on the other hand, is the maximum daily intake unlikely to result in adverse health effects. Table 2 lists the RDAs for selenium, in micrograms (µg) per day,

for children and adults.

Table 2: Recommended Dietary Allowances (RDA) for selenium for children and adults [12]

Age (years)	Males and Females (µg/day)	Pregnancy (µg/day)	Lactation (µg/day)
1-3 y	20	N/A	N/A
4-8 y	30	N/A	N/A
9-13 y	40	N/A	N/A
14-18 y	55	60	70
19 y +	55	60	70

There is insufficient information on selenium to establish a RDA for infants. An Adequate Intake (AI) has been established that is based on the amount of selenium consumed by healthy infants who are fed breast milk. Table 3 lists the AIs for selenium, in micrograms (µg) per day, for infants.

Table 2: Adequate Intake for selenium for infants [12]

Age (months)	Males and Females (µg/day)
0-6 months	15
7-12 months	20

Results of the National Health and Nutrition Examination Survey (NHANES III-1988-94) indicated that diets of most Americans provide recommended amounts of selenium [13]. The INTERMAP study examined nutrient intakes of almost 5,000 middle-aged men and women in four countries in the late 1990s, including the U.S. The primary aim of the study was to evaluate the effect of dietary micronutrients on blood pressure. Each study participant completed four, 24-hour dietary recalls, during which they were asked to record everything consumed (food, beverages, and dietary supplements) over the previous 24 hours. Selenium intake was lowest among residents of China, the country with the highest known rate of selenium deficiency. Mean dietary intake of selenium of U.S. participants was 153 µg for men and 109 µg for women. Both values exceed the recommended selenium intake for adults and are further evidence of adequate selenium intakes in the U.S. [14].

Selenium Deficiency

Human selenium deficiency is rare in the U.S. but is seen in other countries, most notably China, where soil concentration of selenium is low [15]. There is

evidence that selenium deficiency may contribute to development of a form of heart disease, hypothyroidism, and a weakened immune system [16,17]. There is also evidence that selenium deficiency does not usually cause illness by itself. Rather, it can make the body more susceptible to illnesses caused by other nutritional, biochemical or infectious stresses [18].

Three specific diseases have been associated with selenium deficiency:

- Keshan Disease, which results in an enlarged heart and poor heart function, occurs in selenium deficient children.
- Kashin-Beck Disease, which results in osteoarthropathy
- Myxedematous Endemic Cretinism, which results in mental retardation

Keshan disease was first described in the early 1930s in China, and is still seen in large areas of the Chinese countryside with selenium poor soil [18]. Dietary intake in these areas is less than 19 micrograms per day for men and less than 13 micrograms per day for women, significantly lower than the current RDA for selenium. Researchers believe that selenium deficient people infected with a specific virus are most likely to develop Keshan disease [18,19].

Selenium deficiency has also been seen in people who rely on total parenteral nutrition (TPN) as their sole source of nutrition [20,21]. TPN is a method of feeding nutrients through an intravenous (IV) line to people whose digestive systems do not function. Forms of nutrients that do not require digestion are dissolved in liquid and infused through the IV line. It is important for TPN solutions to provide selenium in order to prevent a deficiency [22].

Severe gastrointestinal disorders may decrease the absorption of selenium, resulting in selenium depletion or deficiency [23]. Gastrointestinal problems that impair selenium absorption usually affect absorption of other nutrients as well, and require routine monitoring of nutritional status so that appropriate medical and nutritional treatment can be provided.

Selenium Supplementation

In the U.S., most cases of selenium depletion or deficiency are associated with severe gastrointestinal problems, such as Crohn's disease, or with surgical removal of part of the stomach. These and other gastrointestinal disorders can impair selenium absorption [24-26]. People with acute severe illness who develop inflammation and widespread infection often have decreased levels of selenium in their blood [27].

People with iodine deficiency may also benefit from selenium supplementation. Iodine deficiency is rare in the U.S., but is still common in developing countries where access to iodine is limited [28]. Researchers believe that selenium deficiency may worsen the effects of iodine deficiency on thyroid function, and that adequate selenium nutritional status may help protect against some of the

neurological effects of iodine deficiency. Researchers involved in the Supplementation en Vitamines et Mineraux AntioXydants (SU.VI.MAX) study in France, which was designed to assess the effect of vitamin and mineral supplements on chronic disease risk, evaluated the relationship between goiter and selenium in a subset of this research population. Their findings suggest that selenium supplements may be protective against goiter [29].

As noted above, selenium supplementation during TPN administration is now routine. While specific medical problems such as those described above indicate a need for selenium supplementation, evidence is lacking for recommending selenium supplements for healthy children and adults.

Selenium supplements

Selenium occurs in staple foods such as corn, wheat, and soybean as selenomethionine, the organic selenium analogue of the amino acid methionine [30,31]. Selenomethionine can be incorporated into body proteins in place of methionine, and serves as a vehicle for selenium storage in organs and tissues. Selenium supplements may also contain sodium selenite and sodium selenate, two inorganic forms of selenium. Selenomethionine is generally considered to be the best absorbed and utilized form of selenium.

Selenium is also available in 'high selenium yeasts', which may contain as much as 1,000 to 2,000 micrograms of selenium per gram [30]. Most of the selenium in these yeasts is in the form of selenomethionine. This form of selenium was used in the large scale cancer prevention trial in 1983, which demonstrated that taking a daily supplement containing 200 micrograms of selenium per day could lower the risk of developing prostate, lung, and colorectal cancer [32]. However, some yeasts may contain inorganic forms of selenium, which are not utilized as well as selenomethionine.

A study conducted in 1995 suggested that the organic forms of selenium increased blood selenium concentration to a greater extent than inorganic forms. However, it did not significantly improve the activity of the selenium-dependent enzyme, glutathione peroxidase [33]. Researchers are continuing to examine the effects of different chemical forms of selenium, but the organic form currently appears to be the best choice.

Research and Current Health Issues

Selenium and cancer

Observational studies indicate that death from cancer, including lung, colorectal, and prostate cancers, is lower among people with higher blood levels or intake of selenium [34-40]. In addition, the incidence of nonmelanoma skin cancer is significantly higher in areas of the United States with low soil selenium content [37]. The effect of selenium supplementation on the recurrence of different types of skin cancers was studied in seven dermatology clinics in the U.S. from 1983

through the early 1990s. Taking a daily supplement containing 200 µg of selenium did not affect recurrence of skin cancer, but significantly reduced the occurrence and death from total cancers. The incidence of prostate cancer, colorectal cancer, and lung cancer was notably lower in the group given selenium supplements [41].

Research suggests that selenium affects cancer risk in two ways. As an anti-oxidant, selenium can help protect the body from damaging effects of free radicals. Selenium may also prevent or slow tumor growth. Certain breakdown products of selenium are believed to prevent tumor growth by enhancing immune cell activity and suppressing development of blood vessels to the tumor [42].

However, not all studies have shown a relationship between selenium status and cancer. In 1982, over 60,000 participants of the Nurse's Health Study with no history of cancer submitted toenail clippings for selenium analysis. Toenails are thought to reflect selenium status over the previous year. After three and a half years of data collection, researchers compared toenail selenium levels of nurses with and without cancer. Those nurses with higher levels of selenium in their toenails did not have a reduced risk of cancer [43].

Two important long-term studies, the SU.VI.MAX study in France and the Selenium and Vitamin E Cancer Prevention Trial (SELECT) study in the U.S., are now underway to further investigate the selenium/cancer prevention link.

The SU.VI.MAX Study is a prevention trial looking at the effects of antioxidant vitamins and minerals on chronic diseases such as cancer and cardiovascular disease. Doses of the nutrients provided in the study are one to three times higher than recommended intakes, including a daily supplement of 100 µg selenium. The SU.VI.MAX study, which began in 1994, has followed more than 12,000 adult men and women. This study was designed to continue for eight years, and the research community is eagerly awaiting the results of this study [44].

The SELECT study, a long-term study sponsored by the NIH, is investigating whether supplemental selenium and/or vitamin E can decrease the risk of prostate cancer in healthy men. Past evidence as well as pre-clinical trials for the SELECT study suggests that these two nutrients may be effective in preventing prostate cancer. A daily supplement containing 200 µg of selenium will be given to individuals in the selenium-only study group, while men in the combined-nutrients group will receive a daily supplement containing 200 µg selenium and 400 mg vitamin E. The study, which will span from 2001 to 2013, will include 32,400 healthy adult men [45].

Selenium and heart disease

Some population surveys have suggested an association between lower antioxidant intake and a greater incidence of heart disease [46]. Evidence also

suggests that oxidative stress from free radicals, which are natural by-products of oxygen metabolism, may promote heart disease [47-49]. For example, it is the oxidized form of low-density lipoproteins (LDL, often called "bad" cholesterol) that promotes plaque build-up in coronary arteries. Selenium is one of a group of antioxidants that may help limit the oxidation of LDL cholesterol and thereby help to prevent coronary artery disease. Currently there is insufficient evidence available to recommend selenium supplements for the prevention of coronary heart disease; however, the SU.VI.MAX study mentioned earlier is looking at the effects of antioxidant nutrients such as selenium on heart disease.

Selenium and arthritis

Surveys indicate that individuals with rheumatoid arthritis have reduced selenium levels in their blood [50-51]. In addition, some individuals with arthritis have a low selenium intake [52].

The body's immune system naturally makes free radicals that can help destroy invading organisms and damaged tissue, but that can also harm healthy tissue [53]. Selenium, as an antioxidant, may help to relieve symptoms of arthritis by controlling levels of free radicals [54]. Current findings are considered preliminary, and further research is needed before selenium supplements can be recommended for individuals with arthritis.

Selenium and HIV

HIV/AIDS malabsorption can deplete levels of many nutrients, including selenium. Selenium deficiency is associated with decreased immune cell counts, increased disease progression, and high risk of death in the HIV/AIDS population [55,56]. HIV/AIDS gradually destroys the immune system, and oxidative stress may contribute to further damage of immune cells. Antioxidant nutrients such as selenium help protect cells from oxidative stress, thus potentially slowing progression of the disease [57]. Selenium also may be needed for the replication of the HIV virus, which could further deplete levels of selenium [58].

An examination of 125 HIV-positive men and women linked selenium deficiency with a higher rate of death from HIV [59]. In a small study of 24 children with HIV who were observed for five years, those with low selenium levels died at a younger age, which may indicate faster disease progression [60]. Results of research studies have led experts to suggest that selenium status may be a significant predictor of survival for those infected with HIV [61].

Researchers continue to investigate the relationship between selenium and HIV/AIDS, including the effect of selenium levels on disease progression and mortality. There is insufficient evidence to routinely recommend selenium supplements for individuals with HIV/AIDS, but physicians may prescribe such supplements as part of an overall treatment plan. It is also important for HIV-positive individuals to consume recommended amounts of selenium in their diet.

Selenium Toxicity

High blood levels of selenium (greater than 100 µg/dL) can result in a condition called selenosis [62]. Symptoms of selenosis include gastrointestinal upsets, hair loss, white blotchy nails, garlic breath odor, fatigue, irritability, and mild nerve damage.

Selenium toxicity is rare in the U.S. The few reported cases have been associated with industrial accidents and a manufacturing error that led to an excessively high dose of selenium in a supplement [63,64]. The Institute of Medicine of the National Academy of Sciences has set a tolerable upper intake level (UL) for selenium at 400 micrograms per day for adults to prevent the risk of developing selenosis [12]. Table 4 lists ULs for selenium, in micrograms per day, for infants, children, and adults.

Table 4: Tolerable Upper Intake Levels for selenium for infants, children, and adults [12]

Age	Males and Females (µg/day)
0 - 6 months	45
7 - 12 months	60
1-3 y	90
4-8 y	150
9-13 y	280
14-18 y	400
19 y +	400

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Zinc

Overview

Zinc is an essential mineral that is found in almost every cell. It stimulates the activity of approximately 100 enzymes, which are substances that promote biochemical reactions in your body [1,2]. Zinc supports a healthy immune system [3,4], is needed for wound healing [5], helps maintain your sense of taste and smell [6], and is needed for DNA synthesis. Zinc also supports normal growth and development during pregnancy, childhood, and adolescence [7, 8].

Zinc in Food

Zinc is found in a wide variety of foods. Oysters contain more zinc per serving than any other food, but red meat and poultry provide the majority of zinc in the American diet. Other good food sources include beans, nuts, certain seafood, whole grains, fortified breakfast cereals, and dairy products [9]. Zinc absorption is

greater from a diet high in animal protein than a diet rich in plant proteins. Phytates, which are found in whole grain breads, cereals, legumes and other products, can decrease zinc absorption [10, 11].

The following table suggests a variety of dietary sources of zinc and lists the milligrams (mg) and percent Daily Value (%DV*) per portion. As the table indicates, red meat, poultry, fortified breakfast cereal, some seafood, whole grains, dry beans, and nuts provide zinc. Fortified foods including breakfast cereals make it easier to consume the RDA for zinc, however they also make it easier to consume too much zinc, especially if supplemental zinc is being taken. Anyone considering taking a zinc supplement should first consider whether their needs could be met by dietary zinc sources and from fortified foods.

Table 1: Selected Food Sources of Zinc (9)

Food	Milligrams	%DV*
Oysters, battered and fried, 6 medium	16.0	100
Ready-to-Eat (RTE) Breakfast cereal, fortified with 100% of the DV for zinc per serving, 3/4 c serving	15.0	100
Beef shank, lean only, cooked 3 oz	8.9	60
Beef chuck, arm pot roast, lean only, cooked, 3 oz	7.4	50
Beef tenderloin, lean only, cooked, 3 oz	4.8	30
Pork shoulder, arm picnic, lean only, cooked, 3 oz	4.2	30
Beef, eye of round, lean only, cooked, 3 oz	4.0	25
RTE Breakfast cereal, fortified with 25% of the DV for zinc per serving, 3/4 c	3.8	25
RTE Breakfast cereal, complete wheat bran flakes, 3/4 c serving	3.7	25
Chicken leg, meat only, roasted, 1 leg	2.7	20
Pork tenderloin, lean only, cooked, 3 oz	2.5	15
Pork loin, sirloin roast, lean only,	2.2	15

cooked, 3 oz		
Yogurt, plain, low fat, 1 c	2.2	15
Baked beans, canned, with pork, 1/2 c	1.8	10
Baked beans, canned, plain or vegetarian, 1/2 c	1.7	10
Cashews, dry roasted w/out salt, 1 oz	1.6	10
Yogurt, fruit, low fat, 1 c	1.6	10
Pecans, dry roasted w/out salt, 1 oz	1.4	10
Raisin bran, 3/4 c	1.3	8
Chickpeas, mature seeds, canned, 1/2 c	1.3	8
Mixed nuts, dry roasted w/peanuts, w/out salt, 1 oz	1.1	8
Cheese, Swiss, 1 oz	1.1	8
Almonds, dry roasted, w/out salt, 1 oz	1.0	6
Walnuts, black, dried, 1 oz	1.0	6
Milk, fluid, any kind, 1 c	.9	6
Chicken breast, meat only, roasted, 1/2 breast with bone and skin removed	0.9	6
Cheese, cheddar, 1 oz	0.9	6
Cheese, mozzarella, part skim, low moisture, 1 oz	0.9	6
Beans, kidney, California red, cooked, 1/2 c	0.8	6
Peas, green, frozen, boiled, 1/2 c	0.8	6
Oatmeal, instant, low sodium, 1 packet	0.8	6
Flounder/sole, cooked, 3 oz	0.5	4
* DV = Daily Value. DVs are reference numbers based on the Recommended Dietary Allowance (RDA). They were developed to help consumers determine if a food contains very much of a specific nutrient. The DV for zinc is 15 milligrams (mg). The percent DV (%DV) listed on the nutrition facts panel of food labels tells adults what percentage of the DV is provided in one serving. Percent DVs are based on a 2,000 calorie diet. Your Daily Values may be higher or lower depending on your calorie needs. Foods that provide lower percentages of the DV also contribute to		

a healthful diet.

Recommended Dietary Intake for Zinc

The latest recommendations for zinc intake are given in the new Dietary Reference Intakes developed by the Institute of Medicine. Dietary Reference Intakes (DRIs) is the umbrella term for a group of reference values used for planning and assessing nutrient intake for healthy people. The Recommended Dietary Allowance (RDA), one of the DRIs, is the average daily dietary intake level that is sufficient to meet the nutrient requirements of nearly all (97-98%) healthy individuals. For infants 0 to 6 months, the DRI is in the form of an Adequate Intake (AI), which is the mean intake of zinc in healthy, breastfed infants. The AI for zinc for infants from 0 through 6 months is 2.0 milligrams (mg) per day. The 2001 RDAs for zinc (2) for infants 7 through 12 months, children and adults in mg per day are:

Recommended Dietary Allowances for Zinc for Infants over 7 months, Children, and Adults

Age	Infants and Children	Males	Females	Pregnancy	Lactation
7 months to 3 years	3 mg				
4 to 8 years	5 mg				
9 to 13 years	8 mg				
14 to 18 years		11 mg	9 mg	13 mg	14 mg
19+		11 mg	8 mg	11 mg	12 mg

Results of two national surveys, the National Health and Nutrition Examination Survey (NHANES III 1988-91) (12) and the Continuing Survey of Food Intakes of Individuals (1994 CSFII) (13) indicated that most infants, children, and adults consume recommended amounts of zinc.

Zinc Deficiency

Zinc deficiency most often occurs when zinc intake is inadequate or poorly absorbed, when there are increased losses of zinc from the body, or when the

body's requirement for zinc increases [14-16]. Signs of zinc deficiency include growth retardation, hair loss, diarrhea, delayed sexual maturation and impotence, eye and skin lesions, and loss of appetite. There is also evidence that weight loss, delayed healing of wounds, taste abnormalities, and mental lethargy can occur [15-19].

Zinc Supplementation

There is no single laboratory test that adequately measures zinc nutritional status [20]. Medical doctors who suspect a zinc deficiency will consider risk factors such as inadequate caloric intake, alcoholism, digestive diseases, and symptoms such as impaired growth in infants and children when determining a need for zinc supplementation. Vegetarians may need as much as 50% more zinc than non-vegetarians because of the lower absorption of zinc from plant foods, so it is very important for vegetarians to include good sources of zinc in their diet [21].

Maternal zinc deficiency can slow fetal growth. Zinc supplementation has improved growth rate in some children who demonstrate mild to moderate growth failure and who also have a zinc deficiency [22]. Human milk does not provide recommended amounts of zinc for older infants between the ages of 7 months and 12 months, so breast-fed infants of this age should also consume age-appropriate foods containing zinc or be given formula containing zinc. Alternately, pediatricians may recommend supplemental zinc in this situation. Breastfeeding also may deplete maternal zinc stores because of the greater need for zinc during lactation [23]. It is important for mothers who breast-feed to include good sources of zinc in their daily diet and for pregnant women to follow their doctor's advice about taking vitamin and mineral supplements.

Low zinc status has been observed in 30% to 50% of alcoholics. Alcohol decreases the absorption of zinc and increases loss of zinc in urine. In addition, many alcoholics do not eat an acceptable variety or amount of food, so their dietary intake of zinc may be inadequate [24,25].

Diarrhea results in a loss of zinc. Individuals who have had gastrointestinal surgery or who have digestive disorders that result in malabsorption, including sprue, Crohn's disease and short bowel syndrome, are at greater risk of a zinc deficiency [26]. Individuals who experience chronic diarrhea should make sure they include sources of zinc in their daily diet and may benefit from zinc supplementation.

Research and Current Health Issues

Zinc, Infections, and Wound Healing

The immune system is adversely affected by even moderate degrees of zinc deficiency. Severe zinc deficiency depresses immune function [27]. Zinc is required for the development and activation of T-lymphocytes, a kind of white

blood cell that helps fight infection [28). When zinc supplements are given to individuals with low zinc levels, the numbers of T-cell lymphocytes circulating in the blood increase and the ability of lymphocytes to fight infection improves. Studies show that poor, malnourished children in India, Africa, South America, and Southeast Asia experience shorter courses of infectious diarrhea after taking zinc supplements [29]. Amounts of zinc provided in these studies ranged from 4 mg a day up to 40 mg per day and were provided in a variety of forms (zinc acetate, zinc gluconate, or zinc sulfate). Zinc supplements are often given to help heal skin ulcers or bed sores [30], but they do not increase rates of wound healing when zinc levels are normal.

Zinc and the Common Cold

The effect of zinc treatments on the severity or duration of cold symptoms is controversial. A study of over 100 employees of the Cleveland Clinic indicated that zinc lozenges decreased the duration of colds by one-half, although no differences were seen in how long fevers lasted or the level of muscle aches [31]. Other researchers examined the effect of zinc supplements on cold duration and severity in over 400 randomized subjects. In their first study, a virus was used to induce cold symptoms. The duration of illness was significantly lower in the group receiving zinc gluconate lozenges (providing 13.3 mg zinc) but not in the group receiving zinc acetate lozenges (providing 5 or 11.5 mg zinc). None of the zinc preparations affected the severity of cold symptoms in the first 3 days of treatment. In the second study, which examined the effects of zinc supplements on duration and severity of natural colds, no differences were seen between individuals receiving zinc and those receiving a placebo (sugar pill) [32]. Recent research suggests that the effect of zinc may be influenced by the ability of the specific supplement formula to deliver zinc ions to the oral mucosa [32]. Additional research is needed to determine whether zinc compounds have any effect on the common cold.

Zinc and Iron Absorption

Iron deficiency anemia is considered a serious public health problem in the world today. Iron fortification programs were developed to prevent this deficiency, and they have been credited with improving the iron status of millions of women, infants, and children. Some researchers have questioned the effect of iron fortification on absorption of other nutrients, including zinc. Fortification of foods with iron does not significantly affect zinc absorption. However, large amounts of iron in supplements (greater than 25 mg) may decrease zinc absorption, as can iron in solutions [33]. Taking iron supplements between meals will help decrease its effect on zinc absorption.

Zinc Toxicity

Zinc toxicity has been seen in both acute and chronic forms. Intakes of 150 to 450 mg of zinc per day have been associated with low copper status, altered iron function, reduced immune function, and reduced levels of high-density

lipoproteins [34]. One case report cited severe nausea and vomiting within 30 minutes after the person ingested four grams of zinc gluconate (570 mg elemental zinc) (35). In 2001 the National Academy of Sciences established tolerable upper levels (UL), the highest daily intake associated with no adverse health effects, for zinc for infants, children, and adults. The ULs do not apply to individuals who are receiving zinc for medical treatment, but it is important for such individuals to be under the care of a medical doctor who will monitor for adverse health effects. The 2001 Upper Levels for infants, children and adults are:

Table 2: Upper Levels for Zinc for Infants, Children, and Adults

Age	Infants and Children	Males and Females	Pregnancy and Lactation
0 to 6 months	4 mg		
7 to 12 months	5 mg		
1 to 3 years	7 mg		
4 to 8 years	12 mg		
9 to 13 years	23 mg		
14 to 18 years	34 mg		34 mg
Ages 19+		40 mg	40 mg

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POST-TEST

1. What percentage of American girls (ages 12-19) are not meeting their recommended intake of calcium?
    A. 58%
    B. 64%
    C. 78%
    D. 87%

2. Which of the following is NOT one of the high risk groups for calcium deficiency?
    A. Post-menopausal women
    B. Hemophiliacs
    C. Lactose intolerant individuals
    D. Vegetarians

3. The two main forms of calcium found in supplements are
    A. calcium carbonate and calcium gluconate
    B. calcium lactate and calcium phosphate
    C. calcium citrate and calcium lactate
    D. calcium carbonate and calcium citrate

4. Which of the following has the greatest amount of non heme iron?
    A. 3.5 ounces of chicken liver
    B. 3 ounces of broiled pork loin
    C. 1 cup of boiled lentils
    D. 1 slice of enriched white bread

5. A serum ferritin level of less than or equal to ___ micrograms per liter confirms iron deficiency in women.
    A. 15
    B. 21
    C. 60
    D. 112

6. Which of the following is a sign of advanced magnesium deficiency?
    A. Nausea
    B. Numbness
    C. Fatigue
    D. Weakness

7. What effect may occur when both tetracycline and magnesium are taken by an individual?
    A. Decreased absorption of tetracycline
    B. Increased absorption of tetracycline
    C. Decreased absorption of magnesium
    D. Increased absorption of magnesium

8. Which of the following is NOT associated with selenium deficiency?
    A. Keshan Disease
    B. Kashin-Beck disease
    C. Szakal Encephalopathy
    D. Myxedematous Endemic Cretinism

9. Which specific laboratory test is performed to conclusively determine an individual's zinc nutritional status?
    A. Fursetzer Screen
    B. Kirk Assay
    C. Kashdin Titer
    D. None of the above

10. What is the established Upper Level (UL) of zinc for a 7 year old child?
    A. 5 mg
    B. 7 mg
    C. 12 mg
    D. 23 mg