NATURAL CHOICES
INFORMED DECISIONS

BY HEALTHTRUST ALLIANCE

ANTIOXIDANTS

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The intelligent use of antioxidant nutrients enables individuals to exert a substantial degree of control over their own aging process. This issue of ***The Herbal Pharm*** newsletter will discuss the relationship between free radicals and antioxidants and explain how to maximize the benefits of antioxidant nutrients.

Americans spent 1.25 billion dollars on vitamins last year and antioxidant nutrients have become one of the largest selling categories of nutritional supplements. Enormous amounts of advertising dollars and media attention now promote antioxidants in supplements, foods and cosmetics as keys to anti-aging. However, many people only have a vague idea of what an antioxidant is, what they have to do with free radicals and what are the best dosage levels to be taking. Understanding this important concept can help you educate your customers about one of the most important ways they can improve overall health, enhance their immune system, reduce risk of chronic degenerative conditions such as **cancer, arthritis, cardiovascular disease and slow down the aging process**. Virtually everyone, from children to the elderly, can benefit from taking additional antioxidants as nutritional supplements. Let us begin by discussing free radicals. With that understanding, we can then discuss antioxidant nutrients and explain how and why they are able to help us control our own aging process.

In 1956, **Denham Harman, M.D., from the University of Nebraska published his "Free Radical Theory of Aging**."[1] Initially the scientific community was quite critical and skeptical of this "radical" new theory. However, Dr. Harman has now gained worldwide recognition and respect and free radicals are now understood and accepted as the principal cause of the aging process.

In order to understand free radicals, we need to discuss chemical bonds. Chemical bonds are pairs of electrons. Everything in the universe is held together by chemical bonds. The electrons in chemical bonds spin in opposite directions, and thus they balance each other. Their spin rate is incredibly fast, spinning at nearly the speed of light (186,000 miles/sec). This is a difficult concept to comprehend. In every stone, every leaf, the chrome on the bumper of your car, every fiber in your clothing and in every cell in our bodies, millions of these electron pairs are spinning at this incredible rate of speed.

A free radical is a molecule, or a molecular fragment that has a free, or unpaired electron. A free radical is created when one electron in an electron pair is somehow dislodged so that a single, unpaired electron remains. This single electron, with its incredibly high rate of spin, and without its mate for balance, is one of the most **violently unstable conditions in the universe**. At the cellular level, it goes on a rampage and violently grabs an electron away from somewhere else in order to regain its electron pair stability. However, by taking an electron away from somewhere else, it can damage a cell wall, an enzyme, or your DNA. This is the aging process.

Chemical Bond (electron pair) **Free Radical**

[1] Harman, Denham, "Aging: A theory based on free radicals and radiation chemistry." Journal of Gerontology, Vol. II (1956) pp. 298-300.

When a free radical steals an electron to regain its own stability, something else ends up missing an electron. Hence, another free radical has been created. What I have described thus far sounds like a one to one relationship; one free radical steals one electron, creating one new free radical. Actually, free radical reactions are much more complicated and much more dangerous than this.

In order to explain the true nature of a free radical reaction, I have created what I refer to as a "visualization experiment" called **Mousetraps and Ping-Pong Balls**. Visualize in your mind enough mousetraps lined up neatly, side by side, to completely cover the entire surface of a football field (it takes nearly a million mouse traps to fill a football field). Each of these mousetraps is cocked in its ready-to-spring position and a Ping-Pong ball rests on each springing arm. Now, you are standing on the sideline with a single Ping-Pong ball in your hand which represents a single free radical. When you throw this extra Ping-Pong ball out onto the field, within seconds you will have started a chain reaction that results in hundreds, thousands and then hundreds of thousands of Ping-Pong balls flying around. This demonstrates and represents the true nature of a free radical reaction. They are self-generating, self-perpetuating chain reactions. One unchecked free radical can create hundreds of thousands of damaging incidents at the cellular level.

MINIMIZING FREE RADICAL (FR) DAMAGE

Understanding free radicals opens up two ways individuals can improve their health and slow down their aging process. Minimizing one's exposure to free radicals is one important step, while the second aspect is taking specific nutritional supplements that neutralize free radicals, thus preventing their destructive damage.

Since free radicals are the "bad guys" we need to know how and where we are exposed to them in order to understand how to minimize our exposure. Events that generate free radicals include **nuclear radiation, X-rays and ultra-violet rays from the sun**. When any of these rays strike your body, they have sufficient energy to dislodge an electron, creating a free radical, which can start a chain reaction of destruction at the cellular level.

When we dropped atomic bombs on Hiroshima and Nagasaki in World War II, thousands of people who were not killed by the initial blast died in the following weeks and months. These people died from **free radical poisoning**. Exposure to nuclear radiation generated massive amounts of free radicals that destroyed their bodies.

The side effects from **radiation therapy experienced by cancer patients** is another example of radiation-induced free radical damage. Sunburn is also the result of free radical damage. The ultra-violet rays from the sun have sufficient energy so that when they strike your skin, they are able to "kick" electrons out of their orbits, which creates radicals. After noticing your skin has started to burn, if you then cover up or go inside to avoid more sun exposure, you skin continues to get redder and hurt more for several hours. This is an example of an ongoing free radical chain reaction doing more damage.

Cigarette smoking also generates enormous quantities of free radicals. The intense energy generated by the red-hot tip of a burning cigarette causes electrons to break loose and "fly off", creating millions of free radicals. This explains why smokers have a much higher incidence of health problems like emphysema and lung cancer. Every smoker should at least be taking antioxidants to fight free radical damage.

There are many other conditions that cause free radicals to be produced. For example, the hormones that the body produces during stress generate free radicals. This is why long-term stress is associated with faster aging. Burns and other types of injuries result in free radicals. Exercise will also create free radicals. This is not a problem for most people, but individuals who train hard and compete in events like **triathlons and other long-distance events definitely have a need for extra antioxidants**. Adding heat to unsaturated fats creates FRs. **Frying foods is like creating free radicals and then eating them**. Fried foods should be totally avoided. Arthritis and other inflammatory conditions generate FRs. Many drugs, both prescription and recreational, also result in the formation of free radicals as they are metabolized. Our exposure to these types of conditions overwhelms our body's protective mechanisms.

A very serious source of free radical generation comes from exposure to **pesticides, insecticides and herbicides**. Commercial agriculture puts millions of tons of these powerfully toxic chemicals into our environment each year. Trace amounts are now commonly found in our food and water supply. The best way to avoid these potent free radical generating poisons is to avoid or minimize ingestion of meat and dairy products and to buy organically grown food whenever possible. Information published in the ***Pesticide Monitoring Journal*** **shows the largest percentage of pesticide residues in the U.S. diet comes from the consumption of meat and dairy products.[2] This is because pesticides are fat-soluble substances**. They are stored and build up in the fatty tissues and the milk supply of animals. When humans eat these food products, the toxins are stored and accumulate in our fatty tissues. Many of these poisons can generate free radicals, even at very low levels of exposure.

Not all free radicals are bad. In fact, there are many free radicals reactions that occur naturally in our bodies all the time. For example, white blood cells called macrophages need to generate free radicals in order to kill bacteria. Also, tremendous amounts of FRs are continually being generated in the mitochondria in every cell in our bodies during the process of producing energy. Under normal conditions, antioxidant enzyme control systems minimize the amount of damage from the free radicals that are being generated within the body. However, unhealthy environments, diets and lifestyles cause an increase in free radicals that overwhelms the body's defense mechanisms, which results in illnesses and accelerated aging.

This concludes our discussion of free radicals. Now it is time to explore how we can prevent free radical damage and begin to exert a larger degree of control over our own aging process.

ANTIOXIDANTS: THE FREE RADICAL SCAVENGERS

Fortunately nature provides us with a way to protect ourselves from the destructive effects of free radicals. Antioxidant nutrients neutralize free radicals. The most important antioxidant nutrients are **vitamin C, vitamin E, vitamin A and its cousin beta-carotene and the trace mineral, selenium**. Although there are other nutrients with antioxidant activity, these are the four most important antioxidant nutrients. Studies are showing that "Structured Water" is exhibiting powerful antioxidant capability. Some experts in this field believe this may become one of the most powerful antioxidants known to man. Understanding how to utilize these antioxidant nutrients enables an individual to slow down and prevent much of the free radical damage that causes the aging process.

When an antioxidant nutrient reacts with a free radical, the antioxidant actually gives up one of its electrons to neutralize the free radical. In fact, compounds are antioxidants because their chemical structure enables them to give up one or more of their electrons. This neutralizes the destructive energy of the free radical. The antioxidant, having lost an electron, now has a different electrical charge and at this point, the antioxidant nutrient is dead. However, it saved your life, or it saved the life of one of your cells, but in doing so, it sacrificed itself. It is important to understand that **our body's supply of antioxidant nutrients is continually being depleted as they interact with free radicals**.

When an antioxidant nutrient gives up an electron to neutralize a free radical, the antioxidant itself becomes a free radical. However, an antioxidant that has given up one of its electrons is a much weaker free radical compared to the destructive power of the original free radical. This newly-generated free radical is then passed down through a chain of antioxidant nutrients, which continues to diffuse the power of the free radical. It is important to realize that all of the antioxidant nutrients function together like a symphony as they work to neutralize free radicals. Thus, it is **important to have adequate levels of all the primary antioxidant nutrients in the body**. This does not mean you actually have to take the antioxidants at the same time. It means you should not be taking one or two antioxidant nutrients while excluding the others from your supplement program.

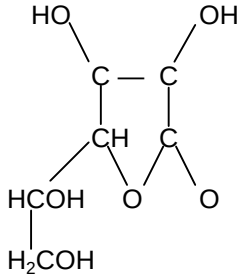
This information is important for the following reason. Several years ago a research study called The **Finnish Smokers Study was discontinued** because the men taking beta-carotene were getting more

[2] Robbins, John. Diet For A New America. Walpole, NH, Stillpoint Publishing, 1987.

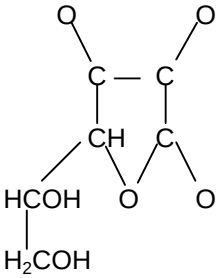
lung cancer than the control group. The media seemed to take great joy in announcing that beta-carotene was dangerous. A similar situation happened in April of this year (1998) when authors of a study announced that 500-mg dosages of vitamin C had been shown to cause genetic damage. The negative results produced in both of these studies are easy to explain. Problems are likely to occur when **elevated levels of a single antioxidant are given to a group of high-risk individuals while excluding all other antioxidants**. In the process of battling the free radicals, the antioxidant molecules are converted to free radicals themselves. Even though they are weaker than the original free radical, toxic levels can begin to accumulate if other antioxidants are not present to neutralize and diffuse the buildup.

Having made these general comments about antioxidant nutrients and how they work, it is now time to examine and review some of the important characteristics of the individual antioxidant nutrients. The four main antioxidant nutrients, vitamin C, vitamin E, vitamin A/beta-carotene and selenium will be discussed in depth. However, other important antioxidants will also be reviewed.

Vitamin C certainly leads the list as one of the most important antioxidant nutrients. Because it is water soluble, it can enter into and **protect every cell in the human body**. Structurally, ascorbic acid is a 5-sided ring (4 carbons and 1 oxygen) with two hydroxyl (OH) groups. It is its ability to donate the hydrogen atoms from these two hydroxyl groups that gives vitamin C its antioxidant properties.



Ascorbic acid



Dehydroascorbic acid

In 1753 the Scottish physician James Lind published his book titled ***A Treatise on Scurvy*** in which he discussed his now-famous experiment showing that oranges or lemons are able to treat and prevent scurvy. In 1928, Albert Szent-Gyorgyi isolated a small amount of vitamin C from pork adrenal glands and named it hexuronic acid. In 1933 the correct structural formula was established, it was successfully synthesized and the name was changed to ascorbic acid.

Most animals are able to synthesize their own vitamin C from the glucose in the foods they eat. The only **mammals that cannot synthesize vitamin C are primates (including man), guinea pigs, and the Indian fruit bat**. It is estimated that a mutation occurred about twenty-five million years ago which destroyed an enzyme in the liver that catalyzes the synthesis of ascorbic acid from glucose. It is interesting to note that many animals (the goat, cow, sheep, mouse, squirrel, gerbil, rabbit, cat and dog) manufacture ascorbic acid at a rate that equates to approximately **10,000 mg/day for a 70-kilogram (154-pound) human being**.[3] Knowing this, doesn't it seem a little ridiculous that the RDA for vitamin C for a 154 pound man is 60 mg/day? After reviewing a number of studies evaluating the amount of vitamin C that various species of animals make, Dr. Pauling concluded that the optimum daily intake of ascorbic acid for most adult humans should be in the range of 2.3 grams to 10 grams daily.[4]

In addition to functioning as an antioxidant, vitamin C participates in a multitude of other biological activities. In his 1972 book titled ***The Healing Factor: Vitamin C Against Disease***, Irwin Stone, M.D. discussed and reviewed over 500 published studies which reported the value of high doses of **vitamin C**

[3] Chatterjee IB, et al. Synthesis and some major functions of vitamin C in animals. Annals of the New York Academy of Sciences 1975; 258:24-47.
[4] Pauling Linus. How to Live Longer and Feel Better. W.H. Freeman and Company, New York, 1986, p. 78.

in preventing and treating about 100 diseases.[5] Some of vitamin C's important activities and functions will be reviewed.

Health Benefits of Vitamin C

- **Cancer:** Vitamin C is effective in the prevention and treatment of many forms of cancer. In a landmark study, Dr. Gladys Block reviewed over **90 epidemiological studies on the role of vitamin C and cancer**.[6] In her conclusion she states, "The overwhelming majority have shown statistically significant protective effects."

- **Immune Function:** Vitamin C substantially increases a) the mobility of leukocytes which enables them to migrate to the site of an infection quicker, b) the phagocytic activity which is a measure of the leukocytes' ability to surround and destroy bacteria and/or cancer cells, and c) blastogenesis, which is the production of new lymphocytes.[7]

- **Cardiovascular Health:** Low levels of vitamin C are associated with oxidation of LDL cholesterol (a), elevated blood pressure (b), increased platelet aggregation (c) and increased incidence of stroke (d).[8]

- **Collagen:** Vitamin C is required for the synthesis of the connective tissues called collagen and elastin. Collagen is the most abundant protein in the human body. A strand of collagen is stronger than a steel wire of the same weight. Collagen helps provide structural integrity for our bodies.[9]

- **Wound Healing:** Vitamin C is necessary for collagen formation in wound healing; high-dose vitamin C supplementation has been shown to reduce healing time and strengthen scar formation.[10]

- **Diabetes:** Ascorbic acid and glucose have very similar chemical structures and compete with each other in a common cellular transport mechanism. In individuals with elevated blood sugar, the competition between glucose and vitamin C for transport into cells may result in intracellular depletion of vitamin C. This increases the **risk of damage to the nerves, eyes, and the vascular system** that are so common in diabetics.[11]

- **Colds:** Studies show that vitamin C is helpful in treating the common cold. A meta-analysis of 16 studies revealed the following: In five studies where only 70 to 200 mg of vitamin C was used per day, the symptoms and severity of **colds was decreased an average of 31%**. In eleven studies in which 1,000 mg or more per day were used, the average **decrease in the amount of illness per person was 40%**.[12]

Vitamin C has also been shown to be helpful in treating and/or preventing many other conditions including **herpes, cervical dysplasia, cataracts, macular degeneration, asthma and AIDS**. For example, vitamin C's antioxidant properties help reduce the **inflammatory aspect of asthma attacks and it prevents the FR damage that causes cataracts and macular degeneration**.

Vitamin C supplements are available in several forms. Straight vitamin C is called ascorbic acid. Buffered vitamin C refers to the various mineral (sodium, calcium, magnesium or potassium) ascorbate salts. Individuals who are acid-sensitive usually do better taking the buffered (non-acidic) forms of vitamin C. A proprietary product called Ester C is actually a combination of vitamin C metabolites.

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[5] Stone Irwin. The Healing Factor: Vitamin C against Disease. Grossett and Dunlap, New York, 1972.
[6] Block, Gladys. Epidemiologic evidence regarding vitamin C and cancer. Am J Clin Nutr 1991; 54:1310S-1314S.
[7] Yonemoto RH, et al. Enhanced lymphocyte blastogenesis by oral ascorbic acid. Proceedings of the American Association for Cancer Research 1976;17:288.
[8] Simon JA. Vitamin C and cardiovascular disease: A review. J Am Coll Nutr 1992;11:107-125.
[9] Pauling Linus. How to Live Longer and Feel Better. W.H. Freeman and Company, New York, 1986, pp.67-73.
[10] Ringsdorf WM Jr., Cheraskin E. Vitamin C and human wound healing. Oral Surgery 1982;53(3):231-236.
[11] Pecoraro RE, Chen MS. Ascorbic acid metabolism in diabetes mellitus. In: Third Conference on Vitamin C. Ann N Y Acad Sci 1987;498:248-258.
[12] Pauling Linus. How to Live Longer and Feel Better. W.H. Freeman and Company, New York, 1986, p 120.

Claims that Ester C is more easily absorbed remain controversial. However, it is has been established that Ester C is absorbed differently than vitamin C. Whereas **high doses of vitamin C will cause diarrhea, high doses of Ester C will not**. Sometimes companies justify charging higher prices by using terms that have little significance, such as vitamin C with natural rose hips. Rose hips is a flower that naturally contains a high level of vitamin C. However, these products generally contain mostly synthetic ascorbic acid with a little vitamin C from rose hips added.

Since vitamin C is water soluble, it is best to take it in divided doses in order to maintain a more constant blood level and a more stable level of antioxidant protection throughout the day. Many health professionals suggest taking a **minimum of 1,000 mg of vitamin C three times daily**. The RDA for vitamin C is 60 mg daily.

Fresh fruits are the best dietary sources of vitamin C, especially citrus fruits. A number of vegetables also contain vitamin C including Brussels sprouts, collard greens, lettuce, cabbage, peas, strawberries and asparagus. However, vitamin C is destroyed rather rapidly after picking. A number of years ago the vitamin C content of oranges was analyzed. Oranges picked directly from the trees at their peak of ripeness had an average of 160 mg or vitamin C per orange, whereas **oranges taken from the bins at commercial grocery stores contained virtually zero vitamin C**.

Bowel Tolerance of Vitamin C: The titration of vitamin C to one's bowel tolerance is a therapeutic protocol that can be used to great advantage. The only side effect from taking too much vitamin C is diarrhea. When an individual approaches bowel tolerance, the consistency of the stools begins to loosen. This enables people to increase and adjust the frequency and size of vitamin C dosing so that they come close to bowel tolerance. When an individual is under high levels of stress, saturating the system with vitamin C provides powerful therapeutic benefits such as increased support of the immune system and additional detoxification capabilities. If a person is suffering from intestinal fungal conditions such as candidiasis or an intestinal bacterial condition, taking approximately **4 grams of vitamin C every 15 minutes to force a vitamin C intestinal purge can be helpful**. This is called a vitamin C flush and it quickly clears the pathogens out of the intestinal tract. **Reinoculation of the bowel with probiotics such as acidophilus is recommended after doing a vitamin C flush**.

In addition to its own antioxidant activity, vitamin C is capable of regenerating the antioxidant form of vitamin E.[13] Vitamin E actually gives up one of its electrons when it interacts with a free radical. Vitamin C gives up one of its electrons to restore vitamin E to its active antioxidant status. Thus, vitamin C and vitamin E are a powerful synergistic antioxidant team.

Vitamin E is the primary fat-soluble antioxidant nutrient. It was discovered in 1932 when scientists realized that something in vegetable oils was necessary for reproduction in rats. They named it vitamin E or the anti-sterility vitamin (an unfortunate designation since it was subsequently found to not have this activity in humans). The same researchers, Evans and Bishop, isolated the pure substance from wheat germ oil in 1936 and elucidated the structure in 1938, giving it the chemical name of tocopherol (after the Greek words ***tokos***, meaning offspring, and ***phero***, meaning to bring forth).

Vitamin E resides in fatty tissues, especially cell walls and membranes. It helps to protect the stability and integrity of **cellular tissues and membranes throughout the body by preventing free radical (lipid peroxidation) damage**. Lipid peroxidation is the process whereby oxygen reacts with unsaturated fatty acids in cellular membranes creating free radical damage.

When polyunsaturated fatty acids undergo oxidative breakdown (free radical damage), straight chain hydrocarbons are produced which are excreted in the breath. Ethane is produced from the oxidation of omega-3 fats and pentane is produced from the oxidation of omega-6 fats. The **Hydrocarbon Breath Test is a non-invasive, extremely sensitive laboratory test that can assess the level of oxidative stress in an individual**. Stated another way, the Hydrocarbon Breath Test is a way of measuring

[13] Beyer RE. The role of ascorbate in antioxidant protection of biomembranes: interaction with vitamin E and coenzyme Q. J Bioerg Biomembr 1994 Aug; 26(4):349-358.

whether or not an individual has enough vitamin E in the system to prevent free radical lipid peroxidation from occurring.

A study documenting vitamin E's protective antioxidant effects was conducted with mountain climbers who received either 400 mg of vitamin E/day or a placebo. The climbers receiving the vitamin E daily for four weeks did not show an increase in their pentane production while climbing, whereas the controls experienced more than a **100% increase in their pentane exhalation**.[14]

Vitamin E is actually a group of compounds that includes four tocopherols and four tocotrienols. Usually vitamin E refers to alpha tocopherol, which is the most biologically active form. Natural vitamin E (d-alpha tocopherol) has been found to be about **34% more bioavailable than synthetic vitamin E** which is a mixture of the d & l isomers. Although natural vitamin E products are more expensive, I feel it is a worthwhile expenditure to insure that you are getting optimal antioxidant protection.

Health Benefits of Vitamin E

- **Heart Disease:** One of vitamin E's major effects is the reduction of risk factors associated with cardiovascular disease. It effectively **decreases platelet stickiness, improves intermittent claudication, prevents atherosclerosis and protects against ischemic reperfusion injuries, especially during cardiac bypass surgery**.

  a) **Reduction in Heart Attacks**: Results of the CHAOS study (Cambridge Heart Antioxidant Study) revealed that patients taking 400 IU or 800 IU of vitamin E had a **47% reduction in heart attacks compared to placebo controls**.[15]
  b) **Prevents Atherosclerosis**: A study utilizing serial coronary angiography showed that individuals taking 100 IU or more of vitamin E per day had substantially less coronary artery lesion progression than placebo controls.[16]

- **Cancer:** Low levels of vitamin E are associated with greater risks of various forms of cancer including **lung, oral, colon, rectal, cervical, pancreatic and liver**. For example, in one large prospective epidemiological study, cancer risk was found to be 4.4 times higher in individuals in the lowest compared to the highest quintile of vitamin E.[17]

- **Immunity & Infection:** Vitamin E supplementation has been shown to enhance the immune system and increase resistance to infection. In a well-controlled double-blind study, healthy subjects 60 years of age and older who were given 800 IU of vitamin E per day showed significant improvement in the following clinical indicators of immune function: **improved delayed hypersensitivity skin test response, increased interleukin-II response and decreased plasma lipid peroxides**.[18] The important point to be made about this study is that the elderly participants were HEALTHY to begin with, yet supplementation with 800 IU of vitamin E daily provided substantial improvements in their immune system.

- **Cataracts & Macular Degeneration**: Few things terrify the elderly more than the possibility of losing their vision. Studies show that **vitamin E helps prevent both cataracts [19] and macular degeneration**.[20]

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[14] Simon-Schnass I, et al. Effect of vitamin E on exercise parameters in high altitude mountaineering. Deutsch Z. Sportmeti 1987;38:200-206.
[15] Stephens NG, et al. Randomized controlled trial of vitamin E in patients with coronary disease: Cambridge Heart Antioxidant Study (CHAOS). Lancet 1996;347:781-786.
[16] Hodis HN, et al. Serial coronary angiographic evidence that antioxidant vitamin intake reduces progression of coronary artery atherosclerosis. JAMA 1995 Jun 21;273(23):1849-1854.
[17] Kok FJ, et al. Micronutrients and the risk of lung cancer. N Engl J Med 1987;316:1416.
[18] Meydani SN, et al. Effect of vitamin E supplementation on immune responsiveness of healthy elderly subjects. FASEB 1989;3:A1057
[19] Robertson JM, et al. Vitamin E intake and risk of cataracts in humans. Ann N Y Acad Sci 1989;570:372-382.
[20] West S, et al. Are antioxidants or supplements protective for age-related macular degeneration? Arch Ophthalmol 1994 Feb;112(2):222-227.

Since vitamin E is a fat-soluble nutrient, taking too much could eventually produce toxic side effects. However, this hardly ever occurs, and the problems associated with not taking enough vitamin E are far greater than the theoretical possibility of toxicity from overdosing. Many health professionals suggest taking from 400 to 800 IU of natural vitamin E daily, compared to the RDA suggestion of 30 IU.

Vitamin A and Beta-carotene are structurally similar and they both function as antioxidant nutrients. All vitamin A comes from the fatty tissues of animals whereas beta-carotene is found exclusively in plant foods with brightly colored (red and yellow) fruits and vegetables being the best sources.

Vitamin A was the first fat-soluble vitamin to be recognized. It was discovered in 1913 as a result of its ability to prevent night blindness and xerophthalmia (a drying and hardening of the mucous membranes that line the eyelids). In 1932, beta-carotene (also called provitamin A) was discovered to be a precursor to vitamin A. Actually, beta-carotene is two molecules of vitamin A, linked head-to-head (A-A). Enzymes in the intestines cleave beta-carotene into two molecules of vitamin A when the body needs it.

Vitamin A's antioxidant effects are primarily in the prevention of LDL lipid peroxidation and in protecting the retina of the eye against free radical damage. Vitamin A is necessary in maintaining the health of epithelial tissues throughout the body and in the prevention of infection.

- **Cancer**: Numerous studies report an association between low serum retinol levels and the incidence of several types of cancer, yet some studies have produced conflicting results. However, it is well known that vitamin A plays a critical role in regulating the differentiation and proliferation of epithelial tissues which is where the majority of cancers develop.[21] Vitamin A has also been shown to increase the tumoricidal activity of human monocytes.

- **Immunity**: Vitamin A plays a critical role in maintaining immunity. One proposed explanation for this effect is that vitamin A deficiency causes abnormal growth of mucous-secreting epithelial cells. Mucous secretions create a natural barrier against pathogens and infection. Research has shown that levels of vitamin A decline dramatically during bacterial or viral infections.[22] This acute loss further weakens the immune system, making recovery even more difficult. Many health practitioners are now suggesting that substantially higher doses of **vitamin A (50,000 to 100,000 IU/day) be given for short periods of time (seven to ten days) during the acute phase of an infection**.

Since vitamin A is a fat-soluble nutrient, taking too much could result in toxic side effects. However, taking 5,000 IU daily is considered to be a safe level of supplementation for adults. The RDA for vitamin A is also 5,000 IU.

Beta-carotene, which is a member of the carotenoids, has some powerful antioxidant properties that vitamin A does not possess. For example, beta-carotene (in addition to superoxide dismutase) provides effective **protection against the superoxide radical (O2-) which, if not controlled, produces a significant amount of free radical damage to DNA**.[23] Since superoxide (O2-) is the most abundant reactive oxygen species that is generated in the body, it is important to have adequate amounts of antioxidants like beta-carotene which can neutralize the destructive effects of this free radical.

Beta-carotene plays another important protective role. It is an extremely effective quencher of singlet oxygen, which is another commonly generated form of reactive oxygen.[24] Singlet oxygen itself is not a free radical. However, it is an electrically excited, very unstable state of oxygen that possesses a high degree of chemical reactivity, which enables it to generate free radical reactions.

[21] Sankaranarayanan R, Mathew B. Retinoids as cancer-preventive agents. IARC Sci Publ 1996;139:47-59.
[22] Semgba RD, et al. Maternal vitamin A deficiency and mother-to-child transmission of HIV-1. Lancet 1994;343: 1593-1597.
[23] Sah NK, et al. Variation in the modulation of superoxide-induced single-strand breaks in plasmid pBR322 DNA by biological antioxidants. Biochem Mol Biol Int 1995 Feb;35(2):291-296.
[24] Sies H. Relationship between free radicals and vitamins: an overview. Int J Vitam Nutr Res Suppl 1989;30:215-223.

Beta-carotene is non-toxic. However, taking high doses can cause a side effect called keratinosis, which means you start to build up a noticeable **carrot-like color in your skin**. Beta-carotene helps enhance the immune system. It also helps **prevent cervical dysplasia as well as cancers of the mouth, throat, vagina and cervix**. For most people, supplementation with 25,000 IU of beta-carotene once or twice per day is adequate. There is no RDA for beta-carotene.

Selenium is another one of the major antioxidant nutrients. Selenium had always been known as a toxic substance but in the late 1940s it began to be recognized as an important essential nutrient, albeit in trace amounts. Selenium's antioxidant activity derives from its role as an indispensable co-factor in glutathione peroxidase, which is one of the most important antioxidant enzymes in our immune system. Each molecule of this enzyme contains four atoms of selenium.

Health Benefits of Selenium

- **Cancer:** In a double-blind, placebo-controlled four-year study, individuals were given 200 mcg/day of selenium in an effort to prevent skin cancer. Although it failed to decrease the incidence of skin cancer, selenium caused an overall **50% reduction in cancer (45% less lung cancer, 58% less colorectal cancer, 63% less prostate cancer**).[25]

- **Antiviral:** Because of its antiviral activity, some doctors are recognizing that selenium supplementation can provide important additional support for people infected with the HIV virus. The authors of one study report that many **individuals with AIDS are selenium-deficient** and suggest that selenium supplementation could influence the course of HIV and also potentiate the effectiveness of **AIDS vaccines and other therapies**.[26]

- **Heart Disease:** Nine types of cardiovascular deaths were compared in 17 matched U.S. cities located in areas with either high or low soil selenium. There was a **significantly lower death rate from heart disease for both men and women in the cities located in areas with higher levels of selenium in the soil**.[27]

Patients with other diseases such as **asthma and arthritis** often benefit from selenium supplementation. One other important function of selenium is its ability to **detoxify heavy metal toxins such as mercury and cadmium**.

Whole grains are one of the best dietary sources of selenium, however many areas of the country have low selenium content in the soil. Other selenium-rich foods are liver, eggs, dairy products, seafood, garlic, wheat germ, Brazil nuts and some vegetables such as cabbage, celery, cucumbers and radishes.

Selenium is a trace mineral and toxic effects can develop if too high a dose is taken for an extended period of time. The RDA for selenium is 70 micrograms/day for men and 55 micrograms/day for women. However, the scientific literature indicates that supplementing with 200 micrograms/day of selenium is safe.

Coenzyme Q-10 is a lipid soluble antioxidant that is structurally similar to vitamin E. In 1958 Professor Karl Folkers and his coworkers at **Merck, Inc**. elucidated the structure of coenzyme Q-10, synthesized it, and figured out a method of producing limited quantities by fermentation. Although early research showed that this newly discovered compound looked promising as a treatment for various forms of cardiovascular disease, Folkers was unable to convince Merck executives to pursue CoQ-10 research. Merck's reluctance may have been due to the fact that they had just recently marketed a **new drug in the cardiovascular disease arena named Diuril**. Subsequently, the rights to coenzyme Q-10 were sold to a Japanese company. The Japanese quickly developed new technology that enabled them to produce

[25] Clark LC, et al. Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin. A randomized controlled trial. JAMA 1966 Dec 25;276(24):1957-1963.
[26] Schrauzer GN, et al. Selenium in the maintenance and therapy of HIV-infected patients. Chem Biol Interact 1994 Jun;91(2-3):199-205.
[27] Shamberger RJ. Selenium and the antioxidant defense system. J Adv Med 1992 spring;5(1):7-19.

large quantities of pure CoQ-10. This stimulated research and consequently coenzyme **Q-10 became one of the most successful and frequently prescribed drugs for the treatment of cardiovascular disease in Japan**.

CoQ-10 is an extremely important antioxidant nutrient because it is able to cross mitochondrial membranes, providing protection inside the mitochondria where the vast majority of free radicals are generated. In fact, CoQ-10 has been shown to be more effective than vitamin E in preventing lipid peroxidation of LDL cholesterol and other lipid subfractions in mitochondrial membranes.[28] Another significant aspect of **CoQ-10 is its ability to regenerate or recycle vitamin E**.[29]

In addition to its role as an antioxidant, coenzyme Q-10 also plays a critical role in the production of **ATP (adenosine triphosphate), which is the fundamental energy molecule of all cells**. This is especially important for the cardiovascular system because the heart is the most metabolically active, energy-demanding muscle in the human body. Under normal conditions, the **heart contains more CoQ-10 than any other muscle and studies have shown that most patients with cardiovascular conditions have a significant deficiency of CoQ-10**.

The following studies exemplify how dramatically CoQ-10 can benefit individuals with cardiovascular problems. For example, in one study, CoQ-10 caused an **improvement in every measurement of cardiac function** after three months of treatment in 2,664 patients with heart disease.[30] In another study, **51% of people with high blood pressure were normalized to the point where they were able to stop taking their anti-hypertensive medications after three months**.[31]

Prescription medications such as tricyclic antidepressants (Elavil, Pamelor, Tofranil, Asendin, Norpramin, Etrafon, Sinequan), anti-diabetic drugs (Diabeta, Glynase, Tolinase, Micronase, Dymelor), beta blockers (Inderal, Lopressor, Tenormin, Visken), cholesterol lowering drugs (Lescol, Mevacor, Pravachol, Zocor) and tranquilizers (Thorazine, Navane, Mellaril, Prolixin) deplete the body of CoQ-10. Therefore, if you are taking any of these drugs, CoQ-10 should be a part of your supplementation regimen to prevent a deficiency.

The dosage range of CoQ-10 for people who are relatively healthy is from 30 to 60 mg/day. For individuals with some form of cardiovascular disease or other health problems, therapeutic dosages range from 200 to 400 mg/day.[32] To date there has not been a RDA set for coenzyme Q-10.

Superoxide dismutases (SOD) are an extremely important group of antioxidant enzymes. When superoxide (O2-) is produced (see paragraph on beta-carotene), it leads to the generation of oxidants such as hydrogen peroxide, peroxynitrite (ONOO-) and the extremely damaging hydroxyl free radical ($OH^{\cdot}$).[33] By scavenging superoxide, the superoxide dismutase enzymes minimize free radical damage and slow down the aging process,

SOD enzymes are not effective when taken orally. They will most likely be destroyed in the stomach by hydrochloric acid and digestive enzymes. Even if they are given in enteric-coated tablets, they are such large molecules that they probably cannot be absorbed across the gut mucosa.

Two forms of SOD are called metalloenzymes. One form contains the metals copper and zinc (Cu/ZnSOD) and the other contains manganese (MnSOD). Thus, the minerals **copper**, **zinc** and

[28] Stocker R, et al. Ubiquinol-10 protects human low-density lipoproteins more efficiently against lipid peroxidation than does alpha tocopherol. Proc Natl Acad Sci USA 1991;88:1646-1650.
[29] Maguire JJ, et al. Succinate-ubiquinone reductase linked recycling of alpha-tocopherol in reconstituted systems and mitochondria: requirement for reduced ubiquinone. Arch Biochem Biophys 1992;292:47-53.
[30] Baggio E, et al. Italian multicenter study of the safety and efficacy of coenzyme Q-10 as adjunctive therapy in heart failure. Molecular Aspects of Medicine 1994;15(Suppl):S287-S290.
[31] Langsjoen P, et al. Treatment of essential hypertension with coenzyme Q-10. Molecular Aspects of Medicine 1994;15(Suppl):S265-S272.
[32] Sinatra ST. Coenzyme Q10: a vital therapeutic nutrient for the heart with special application in congestive heart failure. Conn Med 1997 Nov;61(11):707-711.
[33] Fridovich I. Superoxide radical and superoxide dismutases. Annu Rev Biochem 1995;64:97-112.

manganese can be thought of as antioxidant nutrients because of the role they play in the synthesis of these important antioxidant enzymes. A deficiency of these enzymes can only be determined by utilizing laboratory tests that are relatively expensive. The best approach is to be optimally nourished so that the body has the fundamental nutrients it needs to synthesize the SOD enzymes.

Melatonin is a potent free radical scavenger and has multiple functions related to antioxidant activity. It functions as an antioxidant in the cell nucleus, in the aqueous cytosol within cells, and in lipid-rich cellular membranes. Melatonin is one of the **most effective scavengers of the highly toxic hydroxyl and peroxyl radicals**, it neutralizes the toxicity of singlet oxygen and it also enhances the production of the important antioxidant enzyme, glutathione peroxidase.[34] Studies have shown that melatonin effectively inhibits DNA damage, lipid peroxidation and cataract formation. The usual dosage for melatonin is from 1 to 2 mg nightly at bedtime. Melatonin only occurs in foods (such as bananas) in trace amounts.

Melatonin also functions as a hormone. It is produced by the pineal gland in the brain and functions as the regulator of our biological clock. Actually, melatonin is the chemical substance in our bodies that triggers sleep. As such, melatonin supplements are useful therapeutically to **treat insomnia and jet lag**.

Lipoic acid (also known as thioctic acid) is a sulfur-containing, vitamin-like antioxidant that has recently gained a considerable amount of attention. It possesses four types of antioxidant activity which include: its **heavy metal chelating capability, its ability to scavenge reactive oxygen species such as superoxide, hydroxyl and peroxyl radicals, hypochlorous acid and singlet oxygen, its ability to regenerate antioxidants like vitamin E, vitamin C, coenzyme Q-10 and glutathione and its ability to repair oxidative damage**.[35] Lipoic acid is both water-soluble and fat-soluble, which enables it to provide a wider range of antioxidant activity than most other antioxidants.

In Germany, lipoic acid is approved for the treatment of **diabetic neuropathy** and it will probably help in other conditions (such as AIDS) where antioxidant defenses are weakened. Famed free radical scientist Lester Packer said, "The antioxidant alpha-lipoic acid may protect against a variety of brain and nervous system diseases." Part of lipoic acid's unique power is due to the fact that it can **cross mitochondrial membranes and the blood-brain barrier**.[36] The dosage range for prevention is 20 to 50 mg/day. The therapeutic dosage range for people with conditions such as **diabetes or AIDS is from 300 to 600 mg/day**. The best food sources of lipoic acid are liver and yeast.

Phytochemical Antioxidants: For hundreds of thousands of years of evolutionary history, humans ate primarily a plant-based natural food diet which contained ample quantities of plant-based antioxidants. These compounds are part of the immune system of plants. Although these phytochemical antioxidants are not really nutrients for the human body, they support and enhance the immune system of humans (or animals) when they are ingested. It is beyond the scope of this newsletter to attempt to cover phytochemicals in depth. However, two of the largest and best-known categories, carotenoids and flavonoids, will be briefly summarized.

Carotenoids are plant pigment compounds with antioxidant activity that are found throughout nature. Over **500 carotenoids have been discovered**. Provitamin A carotenoids are compounds that the human body can convert into vitamin A. In addition to beta-carotene, other members of this group include alpha-carotene, gamma-carotene, beta-zeacarotene and cryptoxanthin. Non-provitamin A carotenoids include lycopene, zeaxanthin, lutein, canthaxanthin, crocetin and capsanthin. Carotenoids exert a wide variety of antioxidant, anticancer and anti-aging effects in the human body.

Flavonoids are one of the largest classes of naturally occurring phytochemicals. **Over 5,000 flavonoids have been discovered** and the major subcategories of flavonoids include the following: a) quercetin: structural backbone of many other flavonoids, b) citrus bioflavonoids: rutin, hesperidin, quercitrin and

[34] Reiter RJ, et al. Oxygen radical detoxification processes during aging: The functional importance of melatonin. Aging Clinical and Experimental Research 1995;7(5):340-351.
[35] Biewenga GP, et al. The pharmacology of the antioxidant lipoic acid. Gen Pharmacol 1997 Sep;29(3):315-331.
[36] Packer, L. Neuroprotection by the metabolic antioxidant alpha-lipoic acid. Free Radical Biology & Medicine 1997;22(1-2):359-378.

naringin, c) **proanthocyanidins: grape seed extract and European pine bark extract (pycnogenol)**, d) isoflavones: genistein, diadzein.

Proanthocyanidins have been in the news a lot lately. They are sometimes referred to as "OPCs" which stands for oligomeric proanthocyanidins. In addition to their powerful antioxidant activity, proanthocyanidins also help in the stabilization of collagen and maintenance of elastin—two critical proteins in **connective tissue, blood vessels and muscle**.

Proanthocyanidins occur in many plants, most notably pine bark and grape seeds. However, bilberry, cranberry, blackcurrant, green tea and black tea are also good sources. Nutritional supplements containing extracts of proanthocyanidins from various plant sources are available, alone or in combination with other nutrients, in herbal extracts, capsules and tablets.

Flavonoids in general exhibit a wide range of antioxidant effects including scavenging superoxide, the hydroxyl radical and singlet oxygen. Generally speaking, there is a direct relationship between the consumption of flavonoids and decreased risks of cardiovascular disease and various forms of cancer.

HERBS

There are literally thousands of herbs that, when ingested, produce a wide range of beneficial biological effects. It is actually the phytochemicals (phyto is a Greek root word meaning plant) in the herbs that produce these effects. There are hundreds of thousands of biologically active phytochemicals with many more still to be discovered. In many cases, some of the beneficial effects from herbs are due to phytochemical antioxidants. As was the case for phytochemical antioxidants, it is far beyond the scope of this newsletter to try to cover all the herbs that contain antioxidant phytochemicals. However, I will discuss **ginkgo biloba** as a representative example of an herb with important antioxidant components.

Ginkgo biloba is a unique herb with a wide range of biological effects. Some of its benefits are due to its phytochemical antioxidants. Commercial ginkgo products are generally standardized to contain 24% ginkgo-flavone glycosides, which are flavonoids that are only found in ginkgo. Although it is convenient to use the ginkgo-flavone glycosides for standardization purposes, ginkgo contains numerous other antioxidant constituents. It contains several other antioxidant flavonoid components such as quercetin, myricetin and proanthocyanidins. Ginkgo contains another important group of antioxidants called terpene lactones. Research from Germany has determined that some of the following ginkgo terpene lactones are able to scavenge superoxide, including **ginkgolide B, ginkgolide C, ginkgolide J, ginkgolide M and bilobalide**.

Oxygen is a very unique substance. It can both generate and neutralize free radicals. When levels of oxygen in cells is optimal, oxygen's ability to generate and neutralize free radicals is essentially the same so there is a minimum of free radical damage taking place. However, when there is less than optimal oxygen in the cells and tissues, oxygen's ability to generate FRs remains the same while its ability to neutralize FRs decreases substantially. Thus, when there is less than optimal oxygen in cells and tissues, there is a substantial increase in free radical damage. This is why **exercise is so important to health**. Exercise stimulates circulation, which carries blood and oxygen to all the tissues of the body.

Conclusion: Fresh foods should be our primary source of antioxidant nutrients. However, many health professionals feel it is wise to supplement with additional antioxidant nutrients. The reasons for this advice include evidence of a decline in the nutritional content of the commercially available food supply. Many people require greater levels of protection because they are under high levels of stress. Another reason for antioxidant supplementation is that greater levels of environmental pollution also substantially increase our need for antioxidant protection; for antioxidant nutrients that have RDAs, these values are thought to be too low.

When people are under any kind of stress, whether it is physical or emotional, **antioxidant nutrients are depleted at a much faster rate**. Thus, higher levels of stress require intake of higher levels of antioxidant nutrients to insure protection. My rule of thumb with antioxidants is that if I am ever going to err, I want my intake to err on the high side of protection rather than on the low side of depletion. I do not

ever want the Mousetrap and Ping-Pong ball chain reaction of destruction going on in my cells and tissues. Antioxidant nutrients are one of the most important aspects of a nutritional supplement program. They represent one of the best ways we can improve our health and take control of our own aging process.

As a review, following is a partial list of people who should, at a minimum, take antioxidants as a regular part of their daily supplementation:

- People who work around or are exposed to **nuclear radiation**
- People who are exposed to **x-rays**
- People who work outside in the sun
- Cancer patients (mouth, throat, vagina, cervix, lungs, colorectal, prostate)
- Patients with sunburn
- Patients with wounds, cuts, abrasions, contusions
- Smokers
- People who regularly experience high stress
- Burn patients
- Athletes, particularly those who participate in triathlons and long-distance events
- People whose diets include a lot of fried foods
- People who work on farms or who are exposed to pesticides
- People who work in nurseries or feed stores and are exposed to pesticides
- People who have had cardiac bypass surgery
- People who have the following conditions:

  - Cancer
  - High LDL Cholesterol
  - Elevated Blood Pressure
  - Diabetes
  - Diabetic Neuropathy
  - Colds
  - Herpes
  - Cervical Dysplasia
  - Cataracts
  - Macular Degeneration
  - Asthma
  - Heart Disease Prevention
  - AIDS
  - Arthritis
  - Candidiasis (yeast infection)
  - Intermittent claudication
  - Atherosclerosis
  - Ischemic Reperfusion injuries
  - Lowered Immunity
  - Viral Infections
  - Insomnia
  - Jet Lag