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Report

# Antioxidants and Aging

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Aging is part of life. But nurture the body with a diet and lifestyle that promote health and prevent cell damage and you can delay aging and extend a healthy life.

"You can't help getting older but you don't have to get old," said George Burns, who lived well into his nineties. To be sure, multiple genetic and environmental influences affect aging.

Genes in our cells determine the hereditary aspects of life, including susceptibility to disease. Environmental factors, such as diet and lifestyle modify genetic patterns. Among the many theories that try to explain why we age, the free radical theory of aging is a leading one. Its basic concept is that toxic substances called free radicals that are produced in

our body, can damage cell components in ways that over time lead to aging and disease.

## What are free radicals?

Free radicals are produced in normal metabolism when oxygen is used to burn food for energy. Free radicals are also produced in certain disease states and in response to toxins and trauma. A free radical is a molecule with an unpaired electron. This feature makes a free radical unstable and highly reactive, trying to capture an electron that will stabilize it. By capturing electrons from molecules nearby, the free radical converts other molecules to free radicals, thereby initiating a destructive chain reaction. By producing oxidative damage in DNA, free radicals can produce mutations that, over time, can lead to cancer.

Oxidative changes in fats (lipids) and proteins injure cell membranes, weaken blood vessels, affect immune cells, modify protective enzymes - among others - and damage many other molecules. These injuries alter cell functions and increase the risk of heart disease, stroke, cancer and brain disease. Oxidation of Low Density Lipoprotein (LDL), the "bad" cholesterol, causes it to stick more easily to blood vessel walls, facilitating the formation of plaques in arteries, leading to atherosclerosis. If plaques detach as clots and travel in the circulation they can block vessels in the heart, causing a heart attack, or in the brain, causing stroke. Vascular damage and other forms of oxidant damage to brain cells are associated with Alzheimer's disease. Free radical injury increases the risk of wrinkles, cataracts, blindness and arthritis.

The most important free radicals made in cells are superoxide, hydroxyl radical and nitric oxide. Other reactive oxygen species that are not free radicals are singlet oxygen - from ultraviolet light - hydrogen and lipid peroxides, and the air pollutant ozone that is high in smog.

Free radical levels rise in the body during rigorous exercise and from exposure to pollutants, radiation, UV light and smoking. During infection and chronic inflammation, massive amounts of nitric oxide and superoxide radicals form in immune cells to fight off invading bacteria and viruses. Made in excess, these oxidants can harm and combine to form

another toxic chemical that produces further damage in DNA and brain cells.

## The antioxidant defense force

Antioxidants are chemical substances that donate an electron to the free radical and convert it to a harmless molecule. In this way, antioxidants intercept free radicals and protect cells from the oxidative damage that leads to aging and disease. Antioxidants prevent injury to blood vessel membranes, helping to optimize blood flow to the heart and brain, defend against cancer-causing DNA damage, and help lower the risk of cardiovascular disease and dementia, including Alzheimer's disease.

Some antioxidants are made in our cells and include enzymes and the small molecules glutathione, uric acid, coenzyme Q10 and lipoic acid. Other essential antioxidants such as vitamin C, E and selenium must be obtained from our diet. Fruits, vegetables and grains are rich sources of antioxidant vitamins, minerals and phytochemicals (botanicals).

## Antioxidant enzymes

The enzyme superoxide dismutases (SOD) converts superoxide radicals into hydrogen peroxide, which is converted into water by the enzymes catalase or glutathione peroxidase. Defense mechanisms against oxidative changes in lipid peroxidation that severely damage membranes depend heavily on glutathione, an efficient free radical scavenger, and on glutathione peroxidase and other peroxidases that destroy peroxides.

A newly reported study in worms suggests that catalase may help increase longevity. When worms were modified genetically in the lab to lose catalase function the worms died earlier than those with normal catalase. The work shows that catalase, which destroys hydrogen peroxide in the body and defends against oxidative damage, slowed aging in the worms and extended their lives.

## Antioxidant vitamins and minerals

Vitamins and minerals cannot be produced by our cells and are obtained from the food we eat and the supplements we take. Vitamins E and C, provitamin A (beta carotene) and selenium are the main antioxidants- they are needed in higher amounts during free radical level increases that occur, for instance, during vigorous exercise, exposure to sunlight or smoking. Smokers require two to three times as much vitamin C to achieve the same blood levels as non-smokers. Increased intake of beta carotene adds protection against the harmful effects of sunlight on skin. In older people, absorption of nutrients from the digestive system into the blood circulation slows down and higher intake of antioxidants is needed. The importance of vitamins and minerals in aging is also due to actions that are unrelated to antioxidant activity. For example, vitamin C is essential for producing collagen in bones, joints and skin. Beta carotene converts to vitamin A that is needed for many functions, including vision.

Antioxidant minerals are cofactors of antioxidant enzymes. Selenium for glutathione peroxidase; zinc and copper for SOD in cells; manganese for SOD in mitochondria; iron for catalase and some peroxidases. These minerals have additional metabolic functions.

## Vitamin C

Vitamin C (ascorbic acid) is needed for most bodily metabolic functions. It is abundant in fruits and vegetables, especially high in citrus and the cabbage family. Other than preventing oxidative damage to DNA and other molecules, vitamin C blocks the production of cancer-causing nitrosamines in the stomach. Epidemiological studies show that diets rich in fruits and vegetables decreased the incidence of some cancers, including stomach cancer, by half. Fruits and vegetables are rich in other protective antioxidants including carotenoid and flavonoid phytochemicals, elements that may have also contributed to the observed anti-cancer effects.

Studies have been conducted on the role of vitamin C in atherosclerosis and heart disease, and some of their results show a protective effect. Vitamin C is soluble in water and is not stored in cells, requiring a daily

dietary intake to maintain sufficient protection in the body.

## Vitamin E

Of the eight forms of vitamin E found in nature as tocopherols and tocotrienols, alpha tocopherol is the major free radical scavenger in fatty tissues and the main defense against the oxidation of lipids. In contrast to vitamin C, vitamin E is stored in the body, in membranes. The richest sources of vitamin E are oils, nuts and grains. Because a high intake of vitamin E from theses sources would require a high caloric diet, which is not recommended, vitamin E supplements offer a good alternative.

Vitamin E has been shown to protects against heart disease. A study of 87,000 nurses showed that a daily intake of 200 IU of vitamin E, for more than two years, reduced heart disease by 41%. Another study in 2002 men found that those with existing heart disease who took 400-800 IU/day of vitamin E reduced their risk of non-fatal heart attacks by 77%.

Vitamin E supplements can increase some immune functions in the elderly. Able to destroy reactive oxygen from sunlight and air pollutants, vitamin E has a protective effect on the skin and guards against cataracts and macular degeneration. Similar to vitamin C, vitamin E blocks nitrosamine formation. Low intake of vitamin E correlates with an increased risk of lung, stomach, breast and cervical cancer. In the Iowa Women's Study, supplementation with vitamin E reduced colon cancer risk. A large six-year clinical trial (the ATBC trial) on 29,133 Finnish male smokers, which intended to investigate the effects of beta carotene and low-dose vitamin E (50IU/day) on lung cancer, showed that the supplements did not reduce lung cancer in these high risk groups, but vitamin E did reduce the risk of prostate cancer by 34%.

## Selenium

Selenium levels in plants depend on soil content. Selenium can be high in garlic compared to other vegetables. Other sources are seafood and meats.

Selenium has long been known as an anti-cancer nutrient in animal and cell models. Selenium fed to cells prevents their conversion to cancer cells by radiation, as it increases levels of catalase and glutathione peroxidase and destroys peroxides. Selenium deficiency in humans correlates with high rates of cancer of the colon, breast, ovary, prostate, lung, bladder and skin. Proof of the ability of selenium to prevent cancer in humans came from a clinical trial, reported from the Arizona Cancer Center. The five year trial followed 1312 older people, who once had skin cancer. When given 200 micrograms of selenium daily (about five times higher than the amount consumed by most Americans) and compared to people taking a placebo, selenium cut the occurrence of overall cancer by 42% and lowered the occurrence of lung, colon and prostate cancer. Selenium did protect against skin cancers in the people who had skin cancer in the past. This shows the importance of selenium in preventing the onset of disease. In another clinical intervention study on prostate cancer, men who received 200 micrograms selenium a day had one third of the occurrence compared to placebo.

## CoQ10

CoQ10, coenzyme Q10 or ubiquinone, is found in the cells' mitochondria, and has two known functions. CoQ10 transports electrons in energy production and is also an antioxidant that protects against free radicals formed during metabolism.

CoQ10 decreases in some tissues, with age. The heart, brain and muscles, which are high in mitochondria, may be most affected by the falling levels of CoQ10. In animal studies, supplemental doses of CoQ10 were introduced into the brains of older animals and were increased to the same levels found in the brains of the young. The results showed that CoQ10 supplementation prolonged life in animals that had defective mitochondria and would otherwise have died. These findings suggest that CoQ10 supplementation may restore CoQ10 in the tissues that have lower levels.

Several clinical trials show the benefits of CoQ10 for patients with heart trouble. In one study, 73 patients, who had suffered a severe heart attack, were given 120mg CoQ10 per day for 28 days, while 71 patients

served as the placebos. CoQ10 protected the heart of patients who had suffered a heart attack from additional symptoms. In addition, lipid peroxides-markers of oxidative stress-were reduced in the blood of the CoQ10 group and the antioxidant vitamins E and C were increased. The study concluded that if CoQ10 is given three days after the onset of symptoms to patients who had previously experienced a heart attack, rapid cardiac protection is achieved.

## Lipoic acid

Lipoic acid is needed for mitochondrial function and is also an antioxidant. It is made in our cells and participates as a co-factor in the conversion of carbohydrates to energy. As an antioxidant, lipoic acid is unusual because it is both water and fat soluble. It can eliminate free radicals in the water compartment of the cell, similar to vitamin C, and protect lipids again oxidation, similar to vitamin E. Animal experiments show that lipoic acid protects animals deficient in vitamin E and helps compensate for reduced levels of vitamin C in aging animal tissues.

## Folate and vitamin B12

High blood levels of homocysteine, a sulfur-containing amino acid, are linked to age-related disease. Homocysteine generates oxygen free radicals that play a role in some of its harmful effects. With the help of vitamin B12, folate-a member of the B vitamin family-converts homocysteine to methionine, an essential amino acid necessary for protein and DNA synthesis. Folate deficiency results in increased homocysteine, DNA damage and a higher risk of heart disease, stroke and cancer, including colon cancer. A 16-year study of 88,818 women showed that women who drank alcohol (15 mg a day, about 6 oz of wine) reduced their risk of breast cancer by half when they took 600 micrograms/day of folate.

Folate and vitamin B12 deficiency are linked to dementia, loss in cognitive function and depression, especially in the elderly. Folate deficiency is a contributing cause in Alzheimer's disease. A recent study in 164 patients with Alzheimer's disease showed that the patients had a high level of

homocysteine and low levels of folate, compared to controls.

Folate levels are high in green leafy vegetables, liver, kidney, wheat germ and beans. To assure adequate intake, daily supplements of 400 micrograms are recommended. Vitamin B12 is present in animal food - vegetarians must obtain it in supplemental form.

## Phytochemicals

Phytochemicals are plant chemicals that are neither vitamins nor minerals, yet they have health-enhancing effects: phytochemicals help protect against cancer, cardiovascular disease and dementia, and aid in the prevention of cataracts and macular degeneration. Many phytochemicals are antioxidants, including carotenoids and flavonoids. Among the flavonoids, isoflavonoids in soy and other legumes have estrogen-like effects. Some phytochemicals, such as isothiocyanates in the cabbage family and organo sulfur compounds in garlic, block the carcinogenic action of chemical carcinogens by helping the body dispose of them.

## Flavonoids

Flavonoids are phenolic compounds that give vegetables, fruits, grains, seeds, leaves, flowers and bark their colors. Grapes, grape juice and wine contain large amounts of flavonoids including catechin, anthocyanin and resveratrol. In animals, resveratrol acts as an anti-carcinogen and blocks the production of inflammatory substances.

Catechins are the most active antioxidants in green and black tea. High consumption of green tea may partly explain why Japanese men who smoke more than American men have lower lung cancer rates. Catechins in tea protect against lipid peroxidation in cells and suppress the growth of many types of cancers produced by chemicals and radiation, including UV light. Epidemiological studies on the cancer preventive effects of tea in humans are not conclusive. A preliminary report in 1995 showing that daily tea consumption reduced esophageal cancer by 50% has yet to be

confirmed.

Soybeans contain isoflavones that have weak estrogenic activities-the most actively studied is genistein. In Japan, the rates of breast and prostate cancers are lower than in the West and are thought to be partly due to the high consumption of soy products in Japan. A number of epidemiological studies show an association between a high intake of soy and reduced cancer risk including breast cancer.

Garlic contains flavonoids, an organo sulfur substance with antioxidant activity that has anti-carcinogenic properties and helps protect against cardiovascular disease. Epidemiological observations in Italy and China have shown an association between high consumption of garlic and onion and low rates of stomach cancer.

Cabbage, broccoli and other cruciferous vegetables are high in the antioxidant vitamin C and flavonoids, and contain indoles and isocyanates that in animals block carcinogen activity. Epidemiological and experimental studies show consistently that consumption of cruciferous vegetables protects against several forms of cancer, including colon cancer.

Ginkgo biloba has been known in China for thousands of years and its leaf extracts used to improve brain function. In Europe, it is widely used to improve blood circulation. Ginkgo contains flavonoids including quercetin and ginkgolides that, like other antioxidants, protect against oxidant damage.

Recent studies have shown that ginkgo may help restore some cognitive functions in people with dementia. Ginkgo biloba extract was given to 202 patients with severe dementia, some with Alzheimer's disease, at daily doses of 120 milligrams, for 52 weeks. The patients receiving ginkgo improved social performance compared to placebo-the effects that lasted six months to a year are likely due to the antioxidant effects of ginkgo.

## Carotenoids

Carotenoids are the fat soluble colors in fruits and vegetables and are a family of more than 600 antioxidants. Beta carotene, which is rich in carrots and other yellow/orange vegetables and fruits, converts to vitamin A when the body lacks enough of the vitamin. Alpha carotene is high in carrots and green beans, lycopene, high in tomatoes and lutein and zeaxantin is high in spinach and other dark greens.

Similar to vitamin E, carotenoids trap reactive oxygen species from sunlight, break free radical chain reactions and prevent oxidative damage. There is no agreement on the benefits of beta carotene in protection from heart disease. In healthy humans, consumption of fruits and vegetables that are high in beta carotene has shown reduced risk of cancer, heart disease and stroke, but clinical trials have not been conclusive in showing that beta carotene itself can prevent heart attacks. Combined supplementation did protect against some forms of cancer. In a six-year study in Lixian, China, 29,584 adults given daily supplements of 50 micrograms selenium, 30 milligram vitamin E (alpha tocopherol) and 15 milligram beta carotene had a 21% reduction in stomach cancer and a 42% reduction in esophageal cancer.

Though beta carotene is the most studied carotenoid, it is by no means the most efficient antioxidant. Lycopene, found in abundance in tomatoes and responsible for their red color, is at least ten times more effective as an antioxidant compared to beta carotene. A diet high in tomatoes and tomato products protected against prostate cancer. Luteine and zeaxantin, found in high levels in spinach, protect the eye from free radical macular degeneration that causes blindness.

## Making the best of it

The health protective effects of a low fat, antioxidant-rich diet are well recognized. Oxidant damage begins at birth. It is a cumulative risk factor for aging and disease. Stress, infections, inflammation and exposure to pollutants and sunlight, which produce free radicals and deplete the protective antioxidants in the body, increase the danger of oxidant stress and cell damage. Furthermore, as people age, vitamins and minerals are absorbed less efficiently into the body. Consequently, plasma antioxidants decrease with age, paving the way for aging and age-related diseases.

A diet high in fruits, vegetables and grain, which provides varied antioxidant vitamins, minerals and phytochemicals, is important to keep up defenses. Populations that consume diets high in fruits, vegetables and grains tend to have higher plasma levels of vitamins E, C, carotenoids and certain flavonoids. They are at lower risk of developing cancer and cardiovascular disease. A daily diet containing 29 mg flavonoids-a level obtained by consuming apples and onions and drinking wine-was more effective in reducing heart disease than people taking 0-19 mg a day.

Though each antioxidant has its specific protective action, when combined they increase their effectiveness as a protective network by enhancing each other's actions. Vitamin E is synergistic with selenium. Beta carotene joins forces by preserving the antioxidant state of vitamin E, and vitamin C does the same for beta carotene. Phytochemicals in our diet, many of them antioxidants, add protection that complements the effects of the vitamins and minerals.

People with lower health risks tend to live longer and have fewer disabilities. A healthy way of life and diet help extend the health span to match the lifespan.

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