BETA CAROTENE

by Gary Null, Ph.D.

Editor's comment: Following the *NEJM's* critical report of lack of benefit of beta-carotene in preventing lung cancer in smokers, it is appropriate to review this nutrient's scientific literature.

In the past decade, beta-carotene has gained tremendous stature in the nutrition world. This carotenoid, which gives many fruits and vegetables their yellow pigmentation, has always played an important role in health because it *becomes* vitamin A in the body. But in recent years, researchers have discovered that beta-carotene not only functions as a precursor to vitamin A but also works on its own to maintain health. Unlike vitamin A, which has limited antioxidant properties, beta-carotene is among the most powerful of antioxidant nutrients. As such, it can help to guard against the development of cancer cells.

How does beta-carotene *function* in the body?

Pro-vitamin A function. Beta-carotene enables the body to produce vitamin A as this nutrient is needed. For this reason, it is often referred to as pro-vitamin A. While other carotenoids (there are more than 500 in total) also perform this function, they can only create one molecule of vitamin A. The ambitious beta-carotene, on the other hand, generates two molecules of vitamin A because the body splits it in half.[1]

Antioxidant function. In the antioxidant department, beta-carotene is a highly effective quencher of singlet oxygen (the unstable oxygen metabolites with altered energy states) and a direct scavenger of free radicals. What's more, beta-carotene survives the process of absorbing singlet oxygen intact. Therefore, a single molecule of beta-carotene can arrest up to 1,000 molecules of singlet oxygen.[2]

What *specific locations* in the body does beta-carotene affect?

In the 1970's, researchers found that beta-carotene can protect the skin from the damaging effects of erythropoietic protoporphyria, an inherited disease in which the skin becomes red and swollen when exposed to sunlight. As S.K. Gaby and V.N. Singh report in *Vitamin Intake and Health*, this use of beta-carotene followed the discovery that carotenoids protect plants from free radicals that are generated during photosynthesis.

As an antioxidant, beta-carotene has proven to be protective against many types of cancer, but especially cancer of the lungs. Studies also indicate that it may help to protect the eyes from the damage that can lead to cataracts.[3]

What *foods* are good sources of beta-carotene?

The menu for beta-carotene is simple: eat plenty of fresh fruits and vegetables. Some excellent sources of this nutrient are sweet potatoes, carrots, spinach, yellow squash, turnip greens, collard greens, beet greens, red peppers, tomatoes, apricots, peaches, prunes and oranges.

How is beta-carotene *absorbed* in the body?

The fat-soluble beta-carotene is converted to vitamin A in the body as it is needed. For the most part, this conversion takes place in the small intestine. Any remaining beta-carotene in the blood will be converted by the liver. Unlike vitamin A, which has potentially toxic effects if taken in excess, beta-carotene threatens no such toxicity. If you consume amounts in excess of the body's immediate needs, the extra beta-carotene may be stored in fat tissues or it may circulate in the blood.[4]

How much beta-carotene is needed to *prevent a deficiency?*

The government has not established a recommended level for beta-carotene. As a precursor to vitamin A, beta-carotene itself is not considered to be an essential nutrient. But as Richard Passwater points out in *Beta-Carotene: The Backstage Nutrient Now Universally Recognized for Cancer Prevention,* the National Academy of Sciences suggests that adults need 500 to 600 micrograms of retinol (vitamin A) or twice as much beta-carotene to prevent deficiency and to achieve the beneficial effects of storing beta-carotene in the liver.[5]

Who is likely to require a *higher quantity* of beta-carotene?

Smokers. Smokers may benefit from extra beta-carotene for several reasons. First and foremost, beta-carotene has a protective effect against lung cancer. And many studies have found that smokers have lower than normal levels of beta-carotene.[6,7] In fact, the problem seems to be that smoking increases the body's need for beta-carotene, not that smokers eat less foods containing the nutrient than do non-smokers. A study reported in the *Journal of the American College of Nutrition* found that even when smokers and non-smokers had an equivalent intake of beta-carotene, the smokers had lower levels of the nutrient in their plasma.[8]

Alcohol consumers. Studies of people who drink alcohol regularly have determined that they had lower serum levels of beta-carotene. Their blood levels were even lower if they were also cigarette smokers.[9]

How does beta-carotene aid the *immune system?*

Certain aspects of cellular immunity may be enhanced by beta-carotene. According to Gaby and Singh, other carotenoids that do not become vitamin A in the body appear to have these same beneficial effects:

Healthy Adults. In a 1985 study, people who took beta-carotene had an increased number of T-helper cells, which assist in critical aspects of the host immune response. The two-week treatment of 180 mg a day did not affect the number of T suppressor cells.[4]

Similarly, a recent study of older adults found that beta-carotene supplements of 30 mg or more a day significantly increased the number of T-helper cells and natural killer cells. In this case, the levels of retinol (vitamin A) did not increase along with beta-carotene in the plasma. This finding suggests that beta-carotene enhances the immune system independently of its pro-vitamin A function. The researchers concluded: "These results support the role of immunostimulation as a potential mechanism of action of beta-carotene with cancer prevention potential."[10]

Chronically ill adults. In a study of beta-carotene's effects on people with precancerous lesions of the mouth, researcher Harinder S. Garewal and colleagues decided to measure some indicators of immune response as well. They noted a significant increase in the percentage of natural killer cells in the supplemented patients, along with a smaller increase in the number of T-helper cells. Finally, the patients had "modest increases" in the percentage of cells with antigen, transferrin and interleukin 2 receptors.[11]

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Test tube. A 1988 study by Adrianne Bendich found that beta-carotene played a role in immune enhancement. Again, both beta-carotene and other carotenoids were beneficial, indicating that they work independently rather than through vitamin A.[12]

Animals. Animal studies have shown that beta-carotene improves the body's resistance to tumors and both specific and nonspecific immune responses.[13,14] One study, for example, found that beta-carotene increased the phagocytic activity of neutrophils in the peripheral blood.[15]

As an *antioxidant*, how does beta-carotene help to protect the body?

Beta-carotene's most powerful role is to quench singlet oxygen, the reactive oxygen species that can generate free radicals by unloading its excess energy onto other molecules. According to Passwater, beta-carotene may put singlet oxygen out of business before it can initiate skin and lung cancer. In fact, beta-carotene is in a class by itself when it comes to combatting singlet oxygen. Unlike vitamin E, which is destroyed in the process of returning singlet oxygen to its normal state, beta-carotene can come through the battle unharmed. "Beta-carotene can quench the singlet oxygen without damage to itself and thus can be used over and over again," states Passwater.[16]

How does beta-carotene carry off this feat? Gaby and Singh attribute this ability to beta-carotene's structure. It is a rather large molecule, consisting of a long string of 11 double bonds with single bonds in between. Thus, beta-carotene can absorb the singlet oxygen's energy and spread it throughout this long chain of bonds. Beta-carotene then releases the energy as heat and returns to its usual state.[17]

How does beta-carotene affect free radical activity? As if quenching singlet oxygen were not enough, beta-carotene also acts as a direct scavenger of free radicals. It comes on the scene after free radicals are formed to trap the maverick molecules and break the chain reaction. Vitamin E, by contrast, can prevent free radicals from being formed in the first place.

Gaby and Singh offer an interesting footnote on beta-carotene: It seems to do its best antioxidant work in areas of the body that have low concentrations of oxygen, such as the capillary beds. Meanwhile, antioxidants such as vitamins C and E, glutathione peroxidase and catalase are not especially effective in these low-oxygen areas. As a result, beta-carotene's actions may be complementary to those of other nutrients.[18]

Dr. Derrick Lonsdale warns, however, that this relationship can be tricky. While beta-carotene is effective in tissues that are removed from the blood supply, the beta-carotene molecule itself can undergo auto-oxidation in areas of the body where the oxygen pressure is high. *"In fact, beta-carotene and related compounds may act as prooxidants at higher oxygen pressures and contribute to oxygen-induced cellular damage,"* states Dr. Lonsdale in *Free Oxygen Radicals and Disease.* Therefore, he says, supplementation with beta-carotene should be balanced by vitamin E, which works well at high oxygen concentrations.[19]

Does beta-carotene contribute to *cardiovascular health?*

When most people think of beta-carotene, its protective effects against cancer come to mind. But this nutrient also plays a role in maintaining cardiovascular health. Here's how beta-carotene affects heart functioning:

Oxidative stress. Beta-carotene may offer some protection against the oxidative damage associated with low density lipoproteins, which transport cholesterol through the arteries and contribute to blocked vessels. At a conference of the New York Academy of Sciences, Charles H. Hennekens, M.D. reported on his study of 333 physicians who had experienced chest pain but had not suffered a heart attack or stroke. Among the doctors who took 50 mg of beta-carotene every other day, the number of heart attacks, strokes and deaths due to heart disease was only about half that of the doctors who did not take supplements.[20]

Ischemic heart disease. In one animal study of myocardial infarction, beta-carotene was able to reduce the size of the post-infarct scar by 34%. Better yet, the beta-carotene did not inhibit the effects of myocardial antioxidant enzymes, thus enhancing its cardioprotective properties.[21]

Do any *disease states* respond to the use of beta-carotene?

Cataract development. As with other antioxidant nutrients, the blood level of beta-carotene may be linked to the incidence of cataracts. In one study conducted by Paul Jacques and others, participants with low serum carotene levels had more than 5½ times the risk of developing cataracts as the group with high levels.[22] Interestingly, however, the lens of the eye does not contain much beta-carotene. Therefore, the nutrient may be helping to ward off cataracts by decreasing the level of oxidation throughout the body.[23]

Gastric ulcers. It seems that free radical activity may even play a role in gastric ulcers. In one animal study, beta-carotene reduced both the number and the severity of gastric ulcers only 30 minutes after it was injected into the body. By measuring the activity levels of antioxidant enzymes, the researchers concluded that the gastric ulcer produced free radicals and that beta-carotene's "scavenger" properties were involved in its cytoprotective effects.[24]

Can beta-carotene help to *prevent or treat cancer?*

The evidence proving beta-carotene's protective effects against cancer has been piling up for decades now. Without a doubt, the studies have shown that people who consume a lot of beta-carotene are less likely to develop cancer. This correlation is especially strong with lung cancer.[25]

Does beta-carotene's role as an antioxidant help to reduce cancer risk?

Clearly, free radicals and other oxygen metabolites can damage DNA, causing the cell mutations that lead to cancer. Beta-carotene can prevent this

damage by trapping and deactivating free radicals.[26]

Does it help to defend the body against mutagens? Beta-carotene provides a powerful defense against mutagenic and carcinogenic toxins. One example is its protection against the mutagenic effects of snuff and chewing tobacco. As Gaby and Singh report, two studies conducted by researcher H.F. Stitch in the mid-1980s showed that snuff and tobacco chewers who took beta-carotene had much lower levels of micronucleated cells, which form in the mouth due to the chromosome damage caused by tobacco. In both cases, the participants took 180 mg of beta-carotene a week for nine to 10 weeks. They had 66 to 70% fewer micronucleated cells than control subjects.[27]

How does beta-carotene assist the immune system in preventing cancer?

By enhancing the immune system, beta-carotene can contribute to the body's watch over developing cancer cells. As stated earlier, for example, a study of older people found that beta-carotene increased the number of natural killer cells and T-helper cells. This stimulation of the immune system suggests that beta-carotene has cancer-prevention potential.[28]

According to Adrianne Bendich, studies have also shown that beta-carotene and canthaxanthin (another carotenoid) can boost the aspects of the immune system needed to kill tumor cells. "The enhancement of immune responses to cancer cells may be one mechanism by which carotenoids act as chemopreventive agents," states Bendich.[29]

Have epidemiological studies found a link between beta-carotene and cancer prevention?

Following more than a decade of extensive research, it is clear that beta-carotene helps to protect the body against many types of cancer. As Gaby and Singh report, more than 50 epidemiological studies have established this connection. With lung cancer, in particular, the evidence of beta-carotene's protective effects has been strong and consistent. The incidence of cancer in other sites—including the stomach, esophagus, digestive tract and cervix—also has been firmly correlated with low beta-carotene levels.[30]

Interestingly, many studies conducted in the 1980s began to answer a nagging question about beta-carotene and cancer prevention: Is it the beta-carotene itself that provides this protection, or is it vitamin A (which beta-carotene becomes in the body)? According to Gaby and Singh, 17 studies distinguishing between these two nutrients found that beta-carotene offered significant protection but that preformed vitamin A (from animal sources) was not associated with the incidence of cancer.

With cancer of the lung, esophagus and cervix, for example, vitamin A did not act as a protective agent. "These findings suggest that beta-carotene may have specific protective effects at these cancer sites independent of its provitamin A activity," state the authors.[31] With that in mind, here's a brief summary of the research on beta-carotene and specific cancer sites:

Oral-cavity. As mentioned above, beta-carotene can reduce the number of micronucleated cells in the mouth of people who chew snuff and tobacco. In the *American Journal of Clinical Nutrition,* author Harinder S. Garewal says that beta-carotene not only helps to prevent oral cancer but also may be active in reversing a precancerous condition called leukoplakia.[32]

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In a recent study conducted by Garewal, for example, 17 of 24 patients treated with beta-carotene (30 mg a day for three months) showed a significant decrease in the size of lesions in their mouths. Garewal and his colleagues concluded: "Beta-carotene is an excellent candidate for potential application to the chemoprevention of oral cancer because of its lack of toxicity and the possibility of increasing its intake through nutritional supplementation."[33]

Esophagus. Gaby and Singh report on a number of studies that found a link between the dietary consumption of beta-carotene and the risk of esophageal cancer. One study in France found that a high intake of beta-carotene foods was associated with a lower risk of esophageal cancer.[34] In another study by A. Decarli, people with a high intake of carotene (through carrots, green vegetables and fruits) were four times less likely to develop this cancer than participants with the lowest intake.[35]

Lung. In the past 15 years, more than 25 epidemiological studies have found that beta-carotene has a protective effect against lung cancer. At the same time, only a handful of studies did not find a correlation between the level of beta-carotene and the risk of cancer.[36]

One landmark study on beta-carotene and lung cancer risk was published in 1981, following a 19-year analysis of more than 1,950 male workers at Western Electric Co. As Richard Passwater reports in *Beta-Carotene*, this study showed that a "below-average intake of beta-carotene *preceded* the development of cancer and that low blood levels of vitamin A were therefore not a consequence of cancer." The outcome: The men in the lowest one-fourth of beta-carotene levels were seven times as likely to develop cancer as those in the highest category.[37]

Stomach. As early as 1963, studies were showing the positive effects of fruits and vegetables in the prevention of stomach cancer.[38] Since then, more than 10 other studies have suggested a correlation between low beta-carotene intake and an increased risk of developing stomach cancer.[39]

Breast. Studies on beta-carotene and breast cancer also point to a protective effect of a high dietary consumption of carotene or a high blood level of the nutrient. In a study reported in *The British Journal of Cancer,* for example, there was less occurrence of breast cancer among women who had high blood levels of beta-carotene than those who had low levels.[40]

Cervix. The risk of both cervical and endometrial cancer also may be reduced by high levels of beta-carotene. At least 7 epidemiological studies have established this connection, while one study did not find the beta-carotene to be protective.[41] In a 1988 study reported in the *Journal of the National Cancer Institute,* the risk of cervical cancer was reduced by 80% for women whose beta-carotene level ranked in the highest one-fourth of all blood levels.[42]

What are the results of beta-carotene's use in "intervention trials"? When taken alone or with vitamin A, beta-carotene was found to significantly reduce precancerous lesions of the mouth. If treatment was discontinued, the lesions recurred. Likewise, the early results on a study of cancerous lesions of the upper respiratory tract and the esophagus indicate that beta-carotene may be effective at both inhibiting and reducing the lesions.[43]

Is there evidence that beta-carotene has harmful *side effects*?

When it comes to safety, beta-carotene has a major advantage over preformed vitamin A: While excess amounts of vitamin A can prove toxic, beta-carotene is a completely nontoxic substance. In fact, beta-carotene seems to pass every safety test: It is nontoxic, nonmutagenic, noncarcinogenic and nonharmful to developing embryos, according to Gaby and Singh. One harmless side effect of a high beta-carotene blood level is that the skin may take on a yellowish cast.[44]

Does beta-carotene function *synergistically* with other nutrients?

Beta-carotene complements the antioxidant action of vitamin E, with beta-carotene working well at low oxygen concentrations and vitamin E excelling at higher oxygen concentrations.[45] There may even be a synergistic effect between beta-carotene and vitamin A (retinol). In one study, women with severe premenstrual breast pain were treated with both nutrients for six months. They showed a marked reduction in the pain and, in some cases, a recovery from the condition.[46]

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Published Books on Health and Nutrition:
Complete Guide to Sensible Eating
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Clearer, Cleaner, Safer, Greener
Complete Guide to Health and Nutrition
The Complete Handbook of Nutrition
Vegetarian Cooking for Good Health
Healing Your Body Naturally
No More Allergies
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