

# The NUTRITION REPORTER™

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## Breathing Easy: Studies Find that Vitamins Enhance Lung Function and Health

Three new medical journal reports indicate that high levels of vitamins and other micronutrients contribute to healthy lungs, whereas low levels of these nutrients increase the risk of lung diseases.

In the first report, Linda Grievink, PhD, and her colleagues at Wageningen Agricultural University, The Netherlands, studied the occurrence of pollution-related breathing problems in 227 men and women ages 50-70.

Grievink found that large air-pollution particles and black smoke reduced lung function, as measured daily by "peak expiratory flow," among subjects with low blood levels of beta-carotene.

However, subjects with high blood levels of beta-carotene levels—from supplements or foods—were less likely to suffer impaired breathing. High dietary intake of beta-carotene combined with vitamin C also protected the lungs, though not to the same extent as did high blood levels of beta-carotene alone.

"This study suggests that subjects with chronic respiratory symptoms and with low serum beta-carotene levels were more affected by air pollution than those with high serum beta-carotene levels," Grievink wrote.

Meanwhile, Frank J. Kelly, PhD, of the University of Southampton, England, compared antioxidant levels in fluids obtained from the nasal and bronchial passages and in blood samples from 40 people with or without asthma. Previous research indicates that asthmatics may have high levels of free radicals (a sign of inflammation) and lower levels of antioxidants. "Moreover," Kelly noted, "inflammatory cells from asthma patients generate more reactive oxygen species than those from controls."

Kelly found that bronchial levels of vitamin C were very low or undetectable in asthmatics, even though they had near-normal blood levels of the vitamin. Levels of oxidized glutathione—a sign of excess free radicals—were higher in these tissues.

"These findings provide a basis for understanding why antioxidant intake may have an important role in the cause and severity of asthma and why these patients are more susceptible to inhaled irritants and allergens," Kelly wrote.

Finally, Eduardo De Stefani, PhD, of the Registro

Nacional de Cancer, Uruguay, reported that diets rich in fruits and vegetables—and specific antioxidants in those foods—greatly reduced the risk of lung cancer.

In a comparison of 541 cases of lung cancer and 540 patients hospitalized for other reasons, De Stefani found that diets high in beta- and alpha-carotene, lutein, vitamin E, flavonoids, and glutathione were protective.

People who ate the largest quantities of fruits and vegetables had about one half the risk of lung cancer, compared with people who consumed the least amount of these foods. Carrots, spinach, sweet potatoes, and oranges were also protective. In terms of specific antioxidants, alpha-carotene, glutathione, beta-carotene, total carotenoids, and lutein were associated with a reduced risk of lung cancer.

"Elevated vitamin E intake was associated with a significant reduction in risk...as was glutathione intake," wrote De Stefani. The principal food sources of glutathione were beef, potatoes, winter squash, oranges, and tomatoes.

References: Grievink L, van der Zee SC, Hoek G, et al. Modulation of the acute respiratory effects of winter air pollution by serum and dietary antioxidants: a panel study. *European Respiratory Journal*, 1999;13:1439-1446. Kelly FJ, Mudway I, Blomberg A, et al. Altered lung antioxidant status in patients with mild asthma. *Lancet*, 1999;354:482-483. De Stefani E, Boffetta P, Denco-Pelligrini H, et al. Dietary Antioxidants and lung cancer risk: a case-control study in Uruguay. *Nutrition and Cancer*, 1999;34:100-110. □

### Vitamin D May Help Slow Growth of Some Types of Prostate Cancer

The biologically active form of vitamin D—known technically as D3 or 1,25-D—may be useful in the prevention and treatment of cancer.

The vitamin, a member of the steroid hormone family, has been shown to inhibit the growth of breast cancer and leukemia cells. Now, a team of researchers from the University of Pittsburgh has found that it stops the growth of some types of prostate cancer cells.

Prostate cancer is diagnosed in about 200,000 American men annually. Conventional treatment of

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advanced prostate cancer entails removal of the gland or depressing levels of cancer-stimulating male hormones.

In the study, Michael J. Becich, MD, PhD, and his colleagues exposed human prostate epithelial (surface) and stromal (internal) cells to dihydrotestosterone, the active form of testosterone in the prostate. Some of the cells were also exposed to vitamin D.

Vitamin D slowed the proliferation of prostate epithelial cells by 40 percent, even in the presence of dihydrotestosterone. However, vitamin E increased the proliferation of prostate stromal cells.

Reference: Krill D, Stoner J, Konety BR, et al. Differential effects of vitamin D on normal human prostate epithelial and stromal cells in primary culture. *Urology*, 1999;54:171-177. □

## Carotenoids May Reduce Risk of Developing Stomach Cancer

Diets high in carotenoids and vitamin E, and possibly vitamin C, may reduce the risk of gastric cancer, according to Japanese researchers.

Yoshitaka Tsubono, PhD, of the National Cancer Center Research Institute, Japan, studied the relationship between diet and the risk of gastric cancer in five Japanese regions. Although gastric cancer is a leading cause of death in that nation, its prevalence varies from region to region.

The researchers focused on diet because epidemiological studies have found that high intake of fruits and vegetables are associated with a low risk of gastric cancer.

In Tsubono's study, the lowest rate of death from gastric cancer was in Okinawa, where subjects had the highest dietary levels of alpha-carotene, lycopene, total carotenoids, and vitamin E. The highest rate of mortality from gastric cancer was in Akita. Subjects from this region had the lowest levels of beta-carotene, alpha-carotene, lutein, lycopene, and total carotenoids.

In analyzing the data, Tsubono found that high intake of beta-carotene and vitamin E were associated with the greatest protection against gastric cancer. Alpha-carotene, lycopene, and vitamin C appeared to reduce the risk of gastric cancer somewhat.

"The observed inverse correlation for plasma beta-carotene was consistent with our previous analysis of data from this study that showed inverse associations between gastric cancer rates and the consumption of green vegetables, yellow vegetables, and carotene," Tsubono wrote.

Reference: Tsubono Y, Tsugane S, Gey F. Plasma antioxidant vitamins and carotenoids in five Japanese populations with varied mortality from gastric cancer. *Nutrition and Cancer*, 1999;34:56-61. □

## Vitamin Supplements Reduce Risk of Preeclampsia, Lancet Study Finds

Daily supplements of natural vitamin E and vitamin C can reduce the risk of developing preeclampsia by 76 percent in high-risk pregnant women.

The study, reported in *Lancet*, involved giving 160 pregnant women supplements of 400 IU natural vitamin E and 1,000 mg of vitamin C daily or a placebo starting between 16-22 weeks' gestation.

Preeclampsia is a dangerous condition that sometimes occurs late in pregnancy and, if untreated, can result in injury or death to pregnant women and their fetuses. Doctors believe it is caused by a placenta that produces toxic chemicals, which raise blood pressure and results in other complications.

According to lead researcher Lucilla Poston, PhD, of St. Thomas' Hospital, London, free radicals appear to promote preeclampsia. This observation led her and her colleagues to the hypothesis "that early supplementation with antioxidants may be effective in decreasing oxidative stress and improving vascular endothelial function, thereby preventing, or ameliorating the course of, preeclampsia.

Of the 79 women taking vitamin supplements, only six (8 percent) developed preeclampsia. In contrast, 21 (26 percent) of the 81 women taking placebos—more than three times the number—eventually experienced preeclampsia.

In addition, women taking the vitamin supplements benefited from a 21 percent decrease in the ratio of PAI-1 to PAI-2. PAI stands for plasminogen-activator inhibitor, and a high PAI-1 to PAI-2 ratio is a risk factor for preeclampsia and cardiovascular disorders.

Reference: Chappell LC, Seed PT, Briley AL. Effect of antioxidants on the occurrence of preeclampsia in women at increased risk: a randomised trial. *Lancet*, 1999;354:810-816. □

## Fish Oil Supplements Reduce Risk of Cardiovascular Deaths

Taking a fish oil capsule every day can reduce the risk of a fatal cardiovascular disease by 30 percent among people who have already suffered a heart attack, according to Italian researchers.

Robert Marchioli, MD, of the Consorzio Mario Negri Sud research center, and his colleagues treated more than 11,000 people who had recently suffered a heart attack with one of four protocols: 1 gram daily of omega-3 fish oils, 300 mg of synthetic vitamin E, both nutrients, or placebo. Their end points were a reduction of death, nonfatal heart attack, and stroke.

Over a three-year period, subjects taking the omega-3 fish oils reduced the combined risk of heart attack, stroke, and death by 15 percent. However, most of the benefits resulted from a 30 percent reduction in the risk of heart-related deaths.

"The regimen we used for omega-3 polyunsaturated fatty acids corresponds to a diet that contains a large amount of fatty fish, to be maintained every day (e.g. 100 grams of fatty fish/day..." Marchioli and his colleagues wrote.

Vitamin E did not reduce the risk of cardiovascular-related deaths in this study.

Reference: GOSSI-Prevenzione Investigators. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. *Lancet*, 1999;354:447-455. □

## Coenzyme Q10 Reduces Free Radical Risk During Valve Surgery

The risk of complications during cardiac valve replacement can be reduced through intravenous administration of coenzyme Q10, Chinese researchers report.

CoQ10, a vitamin-like substance found in food and produced by the body, plays a key role in cellular energy production, particularly among heart cells. It is also a powerful antioxidant that scavenges free radicals, which age cells.

Ming Zhou, MD, of the China-Japan Friendship Hospital, Beijing, gave CoQ10 to 12 patients undergoing surgery to replace cardiac valves. The dosage, beginning one week before the operation, ranged from 100 to about 700 mg daily.

"Intravenous CoQ10 has another beneficial action because it can be given in the operative period to maintain therapeutic blood levels and can therefore enter the myocardial cells through the collateral blood supply," Zhou wrote.

Levels of malondialdehyde, a marker of free radical damage, rose less in the CoQ10 group than in the placebo group. In addition, levels of superoxide dismutase, an antioxidant made by the body, decreased less in the CoQ10 group than in the placebo group, suggesting that CoQ10 helps maintain antioxidant levels.

In a separate laboratory experiment, Zhou found that CoQ10 scavenged hydroxyl radicals, considered the most dangerous type.

Zhou concluded that CoQ10 could provide "superior myocardial protection" for patients undergoing valve replacement.

In a separate report, Peter H. Langsjoen, MD and Alena M. Langsjoen, MA, reviewed the clinical use of

CoQ10 in treating cardiovascular disease, particularly heart failure. They noted that the "rationale behind the use of CoQ10 in heart failure has focused primarily on the correction of a measurable deficiency of CoQ10 in both blood and myocardial tissue, with the degree of CoQ10 deficiency correlating directly with the degree of impairment in left ventricular function."

In their review, the Langsjoens discussed the CoQ10-lowering effect of "statin" drugs (lovastatin, pravastatin, simvastatin), which are commonly prescribed to reduce cholesterol levels. They observed that the "concern over the long term consequences of statin-induced CoQ10 deficiency is heightened by the rapidly increasing number of patients treated and the increasing dosages and potencies of the statin drugs.

"As the 'target' or 'ideal' cholesterol level is steadily lowered, the CoQ10-lowering effect will be more pronounced and the potential for long term adverse health effects enhanced. Before the results of this vast human experiment become obvious over the next decade, it is incumbent upon the medical profession to more closely evaluate the clinical significance of this drug-induced CoQ10 depletion."

Reference: Zhou M, Zhi Q, Tang Y, et al. Effects of coenzyme Q10 on myocardial protection during cardiac valve replacement and scavenging free radical activity in vitro. *Journal of Cardiovascular Surgery*, 1999;40:355-361. Langsjoen PH and Langsjoen AM. Overview of the use of CoQ10 in cardiovascular disease. *BioFactors*, 1999;9:273-284. □

## Flavonoids May Help Control Glucose, Risk of Diabetes

People eating diets rich in fruits and vegetables have a relatively low risk of developing adult-onset diabetes. Researchers believe that such foods may reflect a good overall diet.

Now, a cell study points to another mechanism: that the flavonoids found in fruits and vegetables reduce cells' uptake of glucose—in effect, preventing cells from becoming diabetic.

In studies with cells, Jae B. Park, PhD, of the U.S. Department of Agriculture, tested 10 flavonoids commonly found in fruits and vegetables. In general, about half of the glucose uptake of cells was blocked by the dosage of flavonoids used in Park's experiments. The greatest glucose-blocking effect was attributed to fisetin, followed by myricetin, quercetin, apigenin, genistein, cyanidin, daidzein, hesperetin, naringenin, and catechin.

Reference: Park JB. Flavonoids are potential inhibitors of glucose uptake in U937 cells. *Biochemical and Biophysical Research Communications*, 1999;260:568-574. □

## Quick Reviews of Recent Research

### • Hazelnuts improve cholesterol profile

Researchers performed blood chemistries on 30 medical students before and after they consumed roughly 2 ounces of hazelnuts daily for one month. The hazelnuts lowered total cholesterol, reduced low-density lipoprotein (LDL) levels, and raised high-density lipoprotein (HDL) levels, which reduce the risk of heart disease. However, the hazelnuts also raised triglyceride levels, which increase the risk of heart disease. Significantly, the hazelnuts increased antioxidants and decreased free radicals in the blood.

Durak I, et al. *Clinica Chemica Acta*, 1999;284:113-115.

### • Vitamin C lowers stress hormones

Researchers confined laboratory rats to increase their stress, giving some of the animals 200 mg of vitamin C daily (equivalent to several thousand mg in a human). Animals receiving vitamin C had lower levels of glucocorticoids—stress hormones—compared with unsupplemented rats. Vitamin C also helped the animals maintain normal weight and normal size of their thymus and spleen. Glucocorticoids suppress the immune system, and vitamin C supplements can protect against this stress-induced effect.

O'Keefe M, et al. American Chemical Society meeting, New Orleans, August 22, 1999.

### • Genistein protects against squamous cell cancer

Squamous cell carcinoma of the head and neck affects approximately 40,000 Americans annually. In a study, researchers exposed squamous cell cancer cells to genistein, an antioxidant found in soy. Genistein stopped the reproductive cycle of these cells, and the extent of the effect was dependent on dose. Genistein did not affect normal skin cells in a comparative experiment. The cancer-inhibiting effect on squamous cells continued even after the cells were placed in a genistein-free medium.

Alhasan SA, et al. *Nutrition and Cancer*, 1999;34:12-19.

### • St. John's wort has antibacterial effect

The herb St. John's wort (*Hypericum perforatum*) is widely used to treat depression. Low levels of hyperforin, a compound found in the herb, can kill some strains of *Staphylococcus aureus*, a cause of strep throat and skin infections. Hyperforin was also effective against antibiotic resistant *S. aureus*.

Schempp CM, et al. *Lancet*, 1999;353:2129.

### • Alpha-lipoic acid protects against diabetes

Researchers exposed fat cells to glucose oxidase to induce "oxidative stress," and noted a consequential 50-70 percent reduction in glucose transport into cells (which in a person would be a sign of diabetes). By

adding alpha-lipoic acid to the cell medium, researchers were able to normalize glucose transport.

Bashan N, et al. *Diabetes*, 1999;48 (Suppl):A261.

### • Coriander has anti-diabetic benefits

Coriander, a common culinary herb, is a folk remedy for diabetes. In an experiment, researchers added coriander to the diet and drinking water of diabetic mice. The herb improved the utilization of glucose in the animals. In cell-culture experiments, coriander improved glucose uptake and burning, as well as the secretion of insulin.

Gray AM and Flatt PR. *British Journal of Nutrition*, 1999;81:203-209.

### • Plant polysaccharides have anticancer effect

Researchers tested polysaccharides from aloe and three types of medicinal mushrooms (Shiitake, Reishi, and Coriolus) for anticancer properties. In cell-culture studies, they found that Aloe was the most effective in preventing the formation of adducts, which attach carcinogens to DNA. Reishi mushrooms were the most effective in boosting levels of glutathione-S-transferase, an enzyme involved in detoxifying carcinogens. Aloe and Coriolus significantly reduced levels of superoxide radicals. Shiitake had the weakest effects of the plant polysaccharides.

Kim HS, et al. *Carcinogenesis*, 1999;20:1637-1640.

### • Eggs good source of lutein and zeaxanthin

Kale and broccoli are considered excellent sources of lutein and zeaxanthin, two carotenoids that reduce the risk of macular degeneration. In a study of people with moderately high cholesterol levels, researchers found that egg yolks were an excellent, bioavailable source of these carotenoids. However, eating a little more than one egg yolk daily for 4.5 weeks increased LDL-cholesterol levels by 8-11 percent.

Handelman GJ, et al., *American Journal of Clinical Nutrition*, 1999;70:247-251.

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