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Tomatoes, Lycopene Associated with Low Risk of Different Forms of Cancer

A diet rich in tomatoes and tomato products can greatly reduce the risk of many different types of cancer. That's the finding of the most comprehensive review of studies on this theme published to date.

The red carotenoid lycopene may account for many or most of the cancer-preventing benefits of tomatoes, though the fruit is rich in other carotenoids and nutrients, according to Edward Giovannucci, MD, ScD, of the Harvard School of Public Health, Boston.

Giovannucci identified 72 published studies on tomatoes or lycopene and cancer risk. Of these, 57 studies had found inverse relationships between tomatoes or lycopene and cancer, and the findings of 35 of these studies were statistically significant. About half of the studies found that people who ate a lot of tomatoes or who had high blood levels of lycopene were at least 40 percent less likely to develop cancer.

Both tomato intake and high lycopene blood levels were strongly associated with low risks of cancer of the prostate, lung, and stomach. Tomato consumption or lycopene levels were also associated with lower risks of cancer of the pancreas, colon and rectum, esophagus, mouth, breast, and cervix.

Although the studies did not demonstrate a direct cause and effect in cancer protection, Giovannucci noted that the "consistency of the results" argued in favor of the nutrient's benefits.

Among the findings cited by Giovannucci:

- Elderly people consuming large amounts of tomatoes and tomato food products had a 50 percent lower risk of all cancers, compared with people who ate few tomatoes.

- Ten of 14 studies on tomato and lycopene found them to protect against lung cancer. One study also reported that high tomato intake was associated with longer survival after the diagnosis of lung cancer.

- Ten of 12 studies found that tomato consumption was linked to lower risk of stomach cancer. "While other fruits and vegetables have frequently been inversely associated with gastric cancer, inverse associations with tomatoes have been among the most consistent and strongest," Giovannucci wrote.

- Studies in Italy and China found that high intake of

tomatoes was associated with a 60 percent reduction in both colon and rectal cancers.

- An Iranian study reported that tomatoes reduced the risk of esophageal cancer in men by 39 percent but had no apparent benefits among women.

- An earlier study by Giovannucci found that consumption of tomato sauce reduced the risk of prostate cancer by 34 percent. "High intake of tomatoes and tomato products, which accounted for 82% of lycopene, reduced risk of total prostate cancer by 35 percent and aggressive prostate cancer by 53%," he wrote.

- Other studies have found that high blood levels of lycopene may be related to significant decreases in the risk of breast cancer. Cell and animal studies have demonstrated anti-breast cancer effects of lycopene.

Lycopene may protect against cancers partly by functioning as an antioxidant, according to Giovannucci. For example, *Helicobacter pylori* infection is a known risk factor for stomach cancer (as well as ulcer), and chronic infections may increase the risk of cancer by generating free radicals. "Dietary antioxidants, including lycopene, may potentially reduce the impact of oxidative load from *H. pylori* infections in the stomach," Giovannucci wrote.

Reference: Giovannucci E, "Tomatoes, tomato-based products, lycopene, and cancer: review of the epidemiologic literature," *Journal of the National Cancer Institute*, 1999;91:317-331. □

Finnish Study: Alpha-Carotene May Reduce Lung Cancer Risk

A study of more than 4,500 Finnish men ages 20-65 has found a diet rich in alpha-carotene, abundant in carrots and pumpkins, is associated with a relatively low risk of developing lung cancer.

The same study also found that the consumption of fruits and root vegetables were also associated with a reduced risk of lung cancer.

Paul Knekt, Dr PH, of the National Institute of Public Health, Finland, reanalyzed data from an earlier study to determine whether carotenoids other than beta-carotene might have a bearing on lung cancer risk.

Men consuming large quantities of alpha-carotene

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in food had a 39 percent lower risk of lung cancer, compared with men consuming little or none of the nutrient. Fruits and vegetables reduced lung cancer risk by 40 percent, and root vegetables (mostly carrots) reduced the risk by 44 percent.

Among nonsmokers, high alpha-carotene intake reduced lung cancer risk by 67 percent, and high beta-carotene intake reduced risk by 62 percent. Among smokers, high alpha-carotene consumption reduced lung cancer risk by 30 percent, while beta-carotene had a slight nonsignificant reduction in risk.

Reference: Knekt P, Jarvinen R, Teppo L, et al., "Role of various carotenoids in lung cancer prevention," *Journal of the National Cancer Institute*, 1999;91:182-183. □

Mediterranean Diet Slashes Risk of Second Heart Attack

People who have had a heart attack can greatly reduce their risk of a second one by switching to a Mediterranean diet rich in vegetables, fruit, fish, and beans. That's the finding of a study of more than 400 men and women whose eating habits were tracked for almost four years after suffering a heart attack.

The study demonstrates that such dietary changes can be adopted relatively easily and do more to prevent heart disease than cholesterol-lowering drugs.

Michel de Lorgeril, MD, of Saint Etienne, France, found that subjects who started eating a Mediterranean-style diet were 50-70 percent less likely to have a second heart attack during the 46 months covered by the study, compared with people who continued to eat a conventional diet. Lorgeril wrote that "the data confirm the impressive protective effect of the Mediterranean diet."

An earlier analysis of the study data, published last summer, found that people eating a Mediterranean diet were 56 percent less likely to die and 61 percent less likely to develop cancer during the study.

Physical and lifestyle characteristics of the subjects who followed the Mediterranean and conventional diets were similar. About 18 percent of both groups continued to smoke tobacco.

Both groups also ate relatively high-fat diets, though the types of fats were somewhat different. On average, "control" subjects obtained almost 34 percent of their calories from fat, 12 percent of it from saturated fat. The Mediterranean diet group consumed an average of 30 percent fat, with 8 percent from saturated fat.

People eating the Mediterranean diet consumed more alpha-linolenic acid (likely from leafy green vegetables) and less linoleic acid (found in soy and sunflower oils). Alpha-linolenic acid is an essential fatty acid known to reduce the risk of heart disease.

"This study shows that several years [later]...most...

patients were still closely following the Mediterranean diet recommended to them," wrote Lorgeril. "This suggests, in contrast to the current opinion, that the adoption of and compliance with new dietary habits is not so difficult, provided that the instruction of patients (and that of their families) and surveillance are properly (professionally) conducted."

"At a time when health professionals, the pharmaceutical industries, and the research funding and regulatory agencies are almost totally focused on lowering plasma cholesterol levels by drugs, it is heartening to see a well-conducted study finding that relatively simple dietary changes achieved greater reductions in risk of all-cause and coronary heart disease mortality...than any of the cholesterol-lowering studies to date," wrote Alexander Leaf, MD, of the Harvard Medicine School, in a related editorial.

Reference: Lorgeril M de, Salen P, Martin J-L, et al., "Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction," *Circulation*, 1999;99:779-785. □

Regularly Eating Nuts Reduces Risk of Heart Disease

A study of 86,000 female nurses has found that eating 5 ounces of nuts weekly can reduce the risk of heart disease and fatal and nonfatal heart attacks by 35 percent.

The nuts included, but were not limited to, almonds, walnuts, and peanuts, according to lead researcher Frank B. Hu, MD, PhD, of the Harvard Medical School.

Nuts are rich in many important nutrients, including alpha-linolenic acid, the amino acid arginine, magnesium, potassium, copper, folic acid, vitamin E, and fiber. They are also a key part of the Mediterranean diet, which can reduce the risk of coronary heart disease.

Reference: Hu FB, Stampfer MJ, Manson JE, et al., "Frequent nut consumption and risk of coronary heart disease in women: prospective cohort study," *British Medical Journal*, 1998;317:1341-1345. □

Creatine Supplementation Shows Promise in Reversing ALS

Creatine, a virtual staple of body builders, may slow the progression of amyotrophic lateral sclerosis (ALS), a crippling disease known also as Lou Gehrig's disease, according to a recent animal study.

Creatine plays a crucial role in mitochondria, the cellular organelles that convert glucose and fat to energy. Mitochondria are especially susceptible to free radical damage, which can interfere with energy production. According to lead researcher M. Flint Beal, MD, of the Harvard Medical School, Boston, "buffering intracellular energy levels could exert neuroprotective effects."

Beal and his colleagues used mice specifically bred to develop ALS. They fed them either regular diets or diets containing 1 or 2 percent oral creatine.

Unsupplemented mice had reductions in neurons ranging from 49 to 95 percent. Meanwhile, mice receiving creatine developed better physical motor activity and lived longer than mice on the diet without creatine. In addition, mice getting more creatine did better than those receiving less of the supplemental nutrient. Creatine-supplemented mice "showed complete protection and did not differ significantly from control [normal] mice," according to Beal's report in *Nature Medicine*.

Creatine also outperformed a key pharmaceutical drug used to treat ALS. Mice receiving 1 percent creatine lived 13 days longer and mice getting 2 percent creatine lived 26 days longer than untreated animals. The drug riluzole extended survival by only 13 days.

According to Beal, "Our results indicate that creatine supplementation might be a new therapeutic strategy for the treatment of ALS."

Reference: Klivenyt P, Ferrante RJ, Matthews RT, et al., "Neuroprotective effects of creatine in a transgenic animal model of amyotrophic lateral sclerosis," *Nature Medicine*, 1999; 5:347-350. □

Animal Study Finds that Plant Sterols May Ease Prostate Problems

Natural hormone-like substances in plants may reduce the risk of prostate cancer, according to an animal study by researchers at the University of Buffalo, N.Y.

All plants contain at least some phytosterols, and beta-sitosterol is the most common of these substances. While they do not function as hormones in people, they do interact with steroids and can reduce cholesterol levels.

In the current study, Atif Awad, PhD, fed groups of laboratory rats a standard diet, a diet containing cholic acid to stimulate absorption of vegetable fats, and a diet containing phytosterols and cholic acid.

Animals consuming the phytosterol-containing diet had reductions of 33-48 percent in blood testosterone levels. In addition, activity of the enzyme 5-a reductase dropped by 44 percent in the liver and 33 percent in the prostate, and the enzyme aromatase dropped by 57 percent in the prostate gland.

High levels of testosterone, 5-a reductase, and aromatase are strongly associated with the development of prostate cancer. According to Awad, some studies have found that phytosterol supplements reduce symptoms of benign prostatic hyperplasia (enlarged prostate).

Reference: Awad A, Hartati MS, Fink CS, "Phytosterol feeding induces alteration in testosterone meta-

bolism in rat tissues," *Journal of Nutritional Biochemistry*, 1998;9:712-717. □

This Time British Researchers Find Vitamin C Reduces DNA Damage

Vitamin C supplements significantly reduced indicators of DNA damage, according to the same team of British researchers that last year reported it increased DNA damage.

Marcus S. Cooke, PhD, and his colleagues at the University of Leicester, England, measured levels of the DNA fragment 8-oxo-2'-deoxyguanosine (8-oxodG) in 30 men and women before, during, and after they took 500 mg of vitamin C daily for six weeks.

High levels of 8-oxodG, which have been found in cancer patients, indicate oxidative stress (high levels of free radicals) and DNA damage. 8-oxodG is removed from DNA and excreted through the urine.

In Cooke's study, levels of 8-oxodG in the blood and urine of the subjects decreased as vitamin C levels increased. Seven weeks after stopping vitamin C supplementation, 8-oxodG returned to prestudy levels.

According to Cooke, vitamin C appears to stimulate the repair of 8-oxodG in DNA.

Reference: Cooke MS, Evans MD, Podmore ID, et al., "Novel repair action of vitamin C upon in vivo oxidative DNA damage," *FEBS Letters*, 1998;363:363-367. □

NADH Supplements Help Patients with Chronic Fatigue Syndrome

Nicotinamide adenine dinucleotide (NADH), a vitamin B3-dependent coenzyme involved in energy production, can lessen symptoms of Chronic Fatigue Syndrome (CFS).

CFS is a debilitating condition characterized by extreme fatigue, muscle and skeletal pain, problems with concentration and short-term memory, and sleep disorders. It is often triggered by infection with the Epstein-Barr virus and aggravated by allergies and stress.

"Nicotinamide adenine dinucleotide...is known to trigger energy production through ATP production," wrote Joseph A. Bellanti, MD, and colleagues at Georgetown University. "This knowledge has provided the rationale for the present study. It consists of the ability of the coenzyme to replenish depleted stores of ATP, thus improving the fatigue and cognitive dysfunction characteristic of the disorder."

In the study, Bellanti and his colleagues gave 13 CFS patients supplements of 10 mg NADH daily for four weeks while another 13 patients received a placebo. After a four-week "washout period," the NADH and placebo were switched among the patients.

Eight of the 26 patients (31 percent) responded to

Continues on next page

Quick Reviews of Recent Research

• Antioxidants protect against UV damage

In an experiment using human lung cells, researchers found that beta-carotene was far superior to vitamins E and C in protecting against damage from ultraviolet-A wavelengths. However, a combination of all three antioxidants was even better than beta-carotene alone. When nutrient-enriched cells were exposed to UV-B wavelengths, the rate of normal cell growth increased.

Bohn F, et al., *Journal of Photochemistry and Photobiology*, 1998;44:211-215.

• Isoflavones increase natural killer cell activity

Natural killer (NK) cells help the body identify and kill cancer cells and viruses. In a cell-culture study, researchers found that genistein and daidzein glucuronides increased the cancer-fighting ability of NK cells. Genistein and daidzein glucuronides are metabolites of genistein and daidzein, the two principal isoflavones found in soy foods.

Zhang Y, et al., *Journal of Nutrition*, 1999;129:399-405.

• Thiamine deficiency common in elderly

Researchers found thiamine (B1) deficiency to affect almost 40 percent of hospitalized elderly patients. Patients deficient in the vitamin were more likely to suffer from Alzheimer's disease, depression, heart failure, and falls. Furosemide, a diuretic drug, was often taken by thiamine-deficient patients; the drug interferes with thiamine metabolism.

Pepersack T, et al., *Gerontology*, 1999;45:96-101.

• Selenium aids zinc activity

Both selenium and zinc are essential dietary minerals. Selenium-containing compounds trigger the release and activation of zinc. According to the research,

the release of zinc by selenium is one reason why the latter has antiinflammatory and anticancer properties.

Jacob C, et al., *Proceedings of the National Academy of Sciences of the USA*, 1999;96:1910-1914.

• Whole grains reduce risk of death

In a study of more than 38,000 middle-age women in Iowa, researchers found that the risk of death was inversely related to intake of whole grain food products. In contrast, the risk of death was strongly associated with consumption of refined grains.

Jacobs DR Jr, et al., *American Journal of Public Health*, 1999;89:322-329.

• Coenzyme Q10 reduces lipoprotein(a)

Elevated levels of lipoprotein(a) constitute a risk factor for coronary heart disease. Forty-seven patients with acute coronary heart disease were given either 120 mg of "hydrosoluble" CoQ10 daily or placebo for 28 days. Subjects taking CoQ10 benefited from a 22.6 percent reduction in lipoprotein(a) levels.

Singh RB and Niaz MA, *International Journal of Cardiology*, 1999;68:23-29.

• Overweight children low in antioxidants

In a study of more than 6,000 children, researchers found that consumption of vitamin E and beta-carotene was comparable among obese and normal-weight children. However, blood levels of these two nutrients were significantly lower among obese children. Both antioxidants have been documented to reduce free radical damage to low-density lipoprotein (LDL) cholesterol, an early step in the development of coronary heart disease. Obese children are twice as likely as normal to develop heart disease when they reach adulthood.

Strauss RS, *Journal of Pediatrics*, 1999;134:160-165.

• Zinc supplements improve brain development

The addition of zinc to prenatal supplements increased neurobehavioral development in fetuses, as measured by fetal movement in the womb.

Meriardi M, et al., *American Journal of Obstetrics and Gynecology*, 1999;180:483-490.

NADH and Chronic Fatigue...

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NADH supplements with about a 10 percent reduction in CFS symptoms. Only 2 of the 26 subjects (8 percent) responded favorably.

"Four times as many patients responded to NADH in contrast to placebo," Bellanti wrote. "This response was characterized by improvement in fatigue, decrease of symptoms, and improvement in quality of life.

"In these preliminary studies, although we employed a dosage of 10 mg of NADH per day, it should be emphasized that different patients may have different needs."

Bellanti also noted allergies often worsen symptoms of CFS. Twenty-one of the 26 patients had allergies.

Reference: Forsyth LM, Preuss HG, MacDowell AL, et al., "Therapeutic effects of oral NADH on the symptoms of patients with chronic fatigue syndrome," *Annals of Allergy, Asthma, and Immunology*, 1999;82:185-191. □

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