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Adding Soy to Diet Eases Menopausal Hot Flashes, Reduces Breast Cancer Risk

Adding about 2 ounces of soy protein daily to the diet can substantially reduce the number of hot flashes experienced by menopausal women, according to a study by Italian researchers.

Paola Albertazzi, MRCOG, and her colleagues at the University of Bologna, asked 104 women to add 60 grams of soy protein or casein (milk protein) to their diet each day for three months. All of the women, ages 45-62, suffered at least seven moderate to severe hot flashes (including night sweats) daily before taking the supplemental soy or casein.

After three weeks, women eating the soy protein had a 26 percent reduction in their average number of hot flashes (also known as "hot flushes"). By four weeks they had 33 percent fewer hot flashes, and after 12 weeks 45 percent fewer.

Women consuming the casein also had fewer hot flashes, but the decline was not as significant as it was among the women eating soy.

The researchers attributed the beneficial effects of soy to its high content of naturally occurring estrogen-like substances, called isoflavones. The daily 60 gram dose of soy protein contained 76 mg of isoflavones, including 40 mg of genistein and 28 mg of daidzein.

"In Japan," the researchers wrote, "the consumption of phytoestrogens is estimated to be approximately 200 mg a day and the incidence of hot flushes, hormone-related cancers, and osteoporosis is reported to be one of the lowest in the world."

Conventional hormone-replacement therapy can reduce hot flashes by 83 percent, according to the researchers. But they also noted that many women are reluctant to take hormones because of the increased risk of breast cancer and blood clots.

Constipation was the most common side effects reported by women consuming the soy and casein proteins.

Reference: Albertazzi P, Pansini F, Bonaccorsi G, et al., "The effect of dietary soy supplementation on hot flushes," *Obstetrics & Gynecology*, 1998;91:6-11.

Several other recent studies have explored the roles of plant estrogens on health.

• Australian researchers reported that women with high levels of equol and enterolactone had a substantially lower risk of developing breast cancer. Women consuming large amounts of equol were one-fourth as likely to develop breast cancer, compared with women who consumed little of this isoflavone. Equol is formed in the intestine when bacteria break down daidzein during digestion. Enterolactone is a lignan found in soy fiber, whole grains, and flax seed. (Ingram D, et al., *Lancet*, 1997;350:990-994.)

• In an animal study, high doses of the isoflavone daidzein increased the activity of macrophages, a type of white blood cell. In addition, the weight of the thymus gland, which produces immune T cells, also increased. (Zhang R, et al., *Nutrition and Cancer*, 1997;29:24-28.)

• In a second animal study, high doses of daidzein increased the activity of lymphocytes and interleukin (IL) 2 and 3. IL-2 is essential for the growth of T cells and maintaining immune function, and IL-3 is needed for the production of all types of blood cells. (Wang W, *Nutrition and Cancer*, 1997;29:29-34.) □

N-Acetylcysteine Boosts Immunity, Reduces Influenza Symptoms

Supplementing with N-acetylcysteine (NAC) can dramatically reduce the frequency and severity of flu-like symptoms in elderly high-risk individuals, according to a study by Italian researchers.

Two hundred and sixty-two men and women were asked to take 600 mg of NAC or a placebo twice daily for six months covering the peak wintertime flu season. NAC is a well-absorbed and safe form of the amino acid cysteine.

Each of the subjects was given a diary and asked to make note of such symptoms as fever, muscular weakness, loss of appetite, headache, aches and pains, nasal discharge, sore throat, and cough. Researchers defined "influenza-like episodes" as when two or more of the symptoms occurred at the same time.

"The overall frequency of patients suffering from influenza-like episodes...was significantly lower in NAC-treated subjects than in placebo-treated subjects," wrote S. De Flora, MD, of the Universiy of Genoa in the *European Respiratory Journal*. Of those subjects with laboratory-confirmed flu antibodies, only 25 percent of the NAC group developed symptoms, compared with 79 percent of the placebo group.

Similarly, of the "flu-like" cases among people taking

Continues on next page

NAC, 72 percent were mild, 26 percent were moderate, and 2 percent were severe. In the placebo group, 48 percent of the infections were mild, 47 percent were moderate, and 6 percent were severe.

"An additional criterion for evaluating the severity of influenza-like episodes was the length of time in bed which, irrespective of the age of patients, was remarkably shorter in NAC-treated subjects," De Flora wrote. "In fact, in the 10 subjects suffering from influenza-like episodes who were not bedridden, nine were under NAC treatment."

NAC also increased the activity of the immune system, encouraging a more vigorous response to infection, according to De Flora.

Reference: De Flora S, Grassi C, Carati L, "Attenuation of influenza-like symptomology and improvement of cell-mediated immunity with long-term N-acetylcysteine treatment," *European Respiratory Journal*, 1997;10:1535-1541. □

Vitamins C and E Limit Damage After Balloon Angioplasty

Balloon angioplasty, one of the most common procedures for stretching out clogged arteries, increases the production of damaging free radicals in heart cells.

However, that damage can be prevented with supplemental vitamins C and E, which also promote the development of more normal blood vessels, according to a study at the University of Washington, Seattle.

Bradford C. Berk, MD, PhD, used an oversize balloon to stretch and damage the arteries in 25 pigs (an accepted model for studying balloon angioplasty). Some of the animals, which weighed between 44 and 75 pounds were given 500 mg supplemental vitamin C, 1,000 IU vitamin E, or both vitamins daily for one week before and two weeks after angioplasty.

The angioplasty-induced injury increased levels of superoxide radicals in the media and neointima cells of coronary arteries. However, all of the animals receiving vitamins had a 45 percent reduction in superoxide radical levels, compared with untreated animals.

The vitamins also promoted normal blood vessel remodeling—that is, enlarging the blood vessel or preventing its narrowing. Together, the results strongly suggest that antioxidants might limit restenosis and heart disease after balloon angioplasty in people.

In an accompanying editorial, Kathy K. Griendling PhD, and R. Wayne Alexander, MD, PhD, of the Emory University School of Medicine, Atlanta, noted the beneficial effects of antioxidant vitamins in heart disease. "Taken together, the weight of the clinical evidence appears to be in favor of a beneficial effect of antioxidant vitamins on cardiac disease, a finding in agreement with the apparent increase in oxidative stress that accompanies vascular dysfunction."

Reference: Nunes GL, Robinson K, Kalynych A, et al., "Vitamins C and E Inhibit O_2 production in the pig coronary artery," *Circulation*, 1997;96:3593-3601. □

Folate and Vitamin B6 Lower Risk of Heart Disease

A new study has shown that high intake of folate (folic acid) and vitamin B6—from either diet or supplements—is associated with a significant decrease in the risk of coronary heart disease among women. The study adds further evidence that these two vitamins protect against homocysteine, a risk factor for cardiovascular disease.

Eric B. Rimm, ScD, and his colleagues from Harvard University, tracked the health and dietary habits of 80,000 nurses for 14 years in the ongoing Nurses' Health Study. According to their article in the *Journal of the American Medical Association*, women consuming the greatest amounts of either folate (approximately 700 mcg or more daily) or vitamin B6 (4.6 mg or more daily) reduced their risk of heart attack by about one-third, compared with women who ate little of these nutrients. Women consuming high levels of both folic acid and vitamin B6 were 45 percent less likely to have a heart attack.

"For folate, lower risks were seen for higher intake from either food or supplement sources and for intake well above the current RDA of 180 mcg/d," Rimm wrote. "For vitamin B6, the risk was lowest with higher intake of food and supplement sources combined."

Rimm pointed out that "the current RDA for folate...may not be sufficient to minimize risk of coronary disease."

Most of the folate in the nurses' diets came from multivitamin supplements, cold cereal, orange juice, and lettuce. The vitamin B6 came predominantly from beef, cold cereal, potatoes, and bananas.

In a related editorial, Kilmer S. McCully, MD, of the Veteran's Hospital in Providence, R.I., wrote that the results of the Harvard study "support the view that current recommended dietary allowances for these nutrients are too low to provide optimal protection against cardiovascular disease and need to be revised accordingly for the population as a whole."

McCully was the first researcher to propose, in 1969, that elevated blood levels of homocysteine and low intake of the B vitamins were a cause of coronary heart disease. Homocysteine, a byproduct of protein metabolism that attacks blood vessel walls, is broken down by folate and B6.

He wrote that dietary deficiencies of folate and vitamin B6 are common and are "caused by insufficient intakes of foods containing these nutrients and by losses of these nutrients in the processing, preservation, and

marketing of foods...including white flour, white rice, sugars, fats, and oils."

McCully attributed the steady decline in heart disease deaths since the 1960s to food fortification with vitamin B6, but added that with further "intervention through supplementation, fortification, improved dietary intakes of folate and vitamin B6, and better food processing and distribution methods, the decline in US cardiovascular mortality and morbidity will continue."

References: Rimm EB, Willett WC, Hu FB, et al., "Folate and vitamin B6 from diet and supplements in relation to risk of coronary heart disease among women," *JAMA*, 1998;279:359-364 and McCully KS, "Homocysteine, folate, vitamin B6, and cardiovascular disease," *JAMA*, 1998;279:392-393. □

Different Types of Dietary Fat Affect Breast Cancer Risk

The type of fat a woman eats may increase or decrease her risk of developing breast cancer.

Alicja Wolk, PhD, of the Karolinska Institute, Sweden, analyzed the diets of 61,471 women, ages 40 to 76 years. She and her colleagues found that overall fat intake did not seem to be related to the risk of breast cancer.

However, Wolk found that monounsaturated fats, such as those in olive and canola oils, decreased the risk of breast cancer. In addition, she reported that polyunsatured fats, such as the omega-6 fatty acids found in vegetable cooking oils, increased the risk of cancer.

Saturated fats, found in beef, were not associated with a risk of developing breast cancer.

On average, women eating 10 grams (about one-third of an ounce) of monounsaturated fats daily had a 55 percent lower risk of breast cancer. Women eating 5 grams of polyunsatured fats daily had a 69 percent increased risk of cancer.

The opposite effects of monounsaturated and polyunsaturated fatty acids could have "profound public health implications," Wolk wrote in *Archives of Internal Medicine*.

"Long-term compliance with reduction in total fat may be difficult for the general population because a substantial decrease in total fat intake requires major changes in dietary practices," she added. "In contrast, changes in the type of dietary fats may be more realistic because dietary advice for food preparation may focus on substitution of margarine and different vegetable oils (with the monosaturated-polyunsaturated fat ratio most often being 1:2) by olive oil (with the monosaturated-polyunsaturated fat ratio 5:1)."

Reference: Wolk A, Bergstrom ER, Hunter D, et al., "A prospective study of association of monounsaturated fat and other types of fat with risk of breast cancer," *Archives of Internal Medicine*, 1998;158:41-45. □

Spinach Turns Out To Be Rich Source of Alpha-Lipoic Acid

Researchers have long believed that animal protein is the richest natural source of alpha-lipoic acid, an antioxidant. But an analysis by researchers at the University of California, Berkeley, has identified other important sources of the nutrient.

Lester Packer, PhD, and his colleagues found that, of about 18 foods tested, spinach was the richest natural source of alpha-lipoic acid. It was followed by heart, broccoli, liver, and tomato. Garden peas and Brussel sprouts contained trace amounts of alpha-lipoic acid, but none could be detected in banana, orange peel, or soybeans.

The alpha-lipoic acid in these foods was bound to the protein lipoyllysine. Packer wrote that alpha-lipoic acid levels in these foods may be slightly higher, because not all of the lipoyllysine could be assayed. He also cautioned that the protein-bound alpha-lipoic acid may not be as biologically active as the "free" alpha-lipoic acid found in supplements.

Lodge JK, Youn H-D, Handelman GJ, et al., "Natural sources of lipoic acid: determination of lipoyllysine released from protease-digested tissues by high performance liquid chromatography incorporating electrochemical detection," *Journal of Applied Nutrition*, 1997;49:3-11. □

Arthritics Low in Micronutrients

People with rheumatoid arthritis are deficient in many vitamins and minerals, New Zealand researchers reported in *Seminars in Arthritis and Rheumatism*.

Dr. Alan Doube of Waikato Hospital, Hamilton, N.Z., and his colleagues assessed the diets of 48 men and women with rheumatoid arthritis. "The percentage of patients who achieved the RDI [recommended dietary intake] was 23% for calcium, 46% for folic acid, 29% for vitamin E, 10 percent for zinc, and only 6% for selenium," Doube wrote.

Only 52 percent of patients obtained recommended levels of vitamin A, 46 percent for riboflavin, and 27 percent for magnesium.

"Disability, fatigue, and pain can interfere with the purchase, preparation, and consumption of food," Doube wrote. "Temporomandibular pain can impair mastication. Antiinflammatory and antirheumatic medications commonly lead to nausea, dyspepsia, and altered taste."

Reference: Stone J, Doube A, Dudson D, et al., "Inadequate calcium, folic acid, vitamin E, zinc, and selenium intake in rheumatoid arthritis patients: results of a dietary survey," *Seminars in Arthritis and Rheumatism*, 1997;27:180-185. □

Quick Reviews of Recent Research

• Nutrients and mental function in the elderly

Researchers analyzed the diets of 260 healthy people, ages 65-90, and drew correlations between specific nutrients and cognitive function. Higher scores on cognitive tests were associated with diets relatively low in fat, saturated fat, and cholesterol, and higher in fruits and vegetables, fiber, folic acid, vitamins C and E, beta-carotene, iron, and zinc. Such diets, the researchers wrote, "may be advisable not only to improve the general health of the elderly but also to improve cognitive function."

Ortega RM, et al., *American Journal of Clinical Nutrition*, 1997;66:803-809.

• Pycnogenol® quenches radicals

In an experiment using bovine endothelial (heart) cells, researchers found that Pycnogenol, a complex of flavonoid antioxidants derived from French maritime pine bark, reduced cell levels of superoxide radicals and hydrogen peroxide. It also up-regulated production of antioxidant enzymes, including glutathione, superoxide dismutase, and catalase.

Wei A, et al., *Redox Report*, 1997;3:219-224.

• Aloe extract enhances immune system

Acemannan, an extract of aloe vera, increased the activity of white blood cells against *Candida* yeast cells. In experiments, white blood cells exposed to acemannan, significantly increased their ability to capture and kill yeast cells.

Stuart RW, et al., *International Journal of Immunopharmacology*, 1997;19:75-82.

• Alpha-lipoic acid improves glucose utilization

Alpha-lipoic acid increased the uptake of glucose by an average of 78 percent in lean laboratory rats and by 48 percent in obese rats. Insulin further enhanced glucose uptake by an average of 30-55 percent. The researchers concluded that alpha-lipoic acid worked, at least in part, by improving the efficiency of insulin.

Henriksen EJ, et al., *Life Sciences*, 1997;61:805-812.

• Ginkgo protects against radiation damage

Researchers found that workers who helped clean up the Chernobyl nuclear meltdown suffer chromosome damage at a level 10 times above normal. After taking supplements of *Ginkgo biloba* extract for two months, chromosome damage in blood cells was reduced to near normal levels, with the benefits lasting for up to a year. However, chromosome damage in one-third of the workers increased after *Ginkgo* supplementation ceased.

Emerit I, et al., *Adaptive Effects of Ginkgo Biloba Extract (EGb 761)*, 1997:21-29.

• Antioxidants protect against zinc deficiency

In a laboratory experiment, researchers increased the fragility of red blood cell membranes by depriving them of zinc. However, cell-membrane fragility decreased when the animals were given supplemental vitamins C and E and beta-carotene. Antioxidants can compensate somewhat for the oxidative effects of zinc deficiency.

Kraus A, et al., *Journal of Nutrition*, 1997;127:1290-1296

• Ginseng may protect against stroke.

In an animal study, the flavonoid ginsenoside Rb1, extracted from ginseng, protected neurons from death during stroke-like ischemia. The herb extract probably helped by quenching free radicals.

Lim JH, et al., *Neuroscience Research*, 1997;28:191-200.

• Dietary changes boost carotenoid levels

In a study of breast cancer patients, intensive individual counseling led to greater consumption of fruits and vegetables and higher blood levels of lutein, alpha-carotene, beta-carotene, and vitamin A. The researchers will eventually report whether dietary changes reduced the risk of recurrent breast cancers.

Rock CL, et al., *Cancer Epidemiology, Biomarkers & Prevention*, 1997;6:617-623.

• Free radicals, antioxidants, and gene expression

Both free radicals and antioxidants influence cell behavior and gene expression. The implications of this research is profound in that free radicals and antioxidants may regulate disease processes at the genetic level.

Palmer HN and Paulson KE, *Nutrition Reviews*, 1997;55:353-361.

• Vitamin E supplements lower cancer risk

After analyzing 59 human studies on vitamin/mineral supplements and cancer risk, researchers concluded that there is "modest evidence for protective effects of nutrients from supplements against several cancers." Of the many supplements studied, vitamin E was most strongly associated with a reduced cancer risk.

Patterson RE, et al., *Cancer Causes and Control*, 1997;8:786-802.

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