

The NUTRITION REPORTER™

Vol. 6 No. 11

THE INDEPENDENT NEWSLETTER THAT REPORTS VITAMIN AND MINERAL THERAPIES

November 1995

Higher Intake of B Vitamins Could Slash Risk of Heart Disease and Stroke

Folic acid and other B vitamins reduce the risk of coronary heart disease and stroke, according to a detailed analysis of more than three dozen scientific studies.

These nutrients work by quenching homocysteine, an amino acid in the blood that attacks blood vessel walls and promotes cardiovascular disease.

Homocysteine (pronounced hō•mō•sis•teen) has emerged after 25 years of research as the "new cholesterol," and researchers estimate that it is a major risk factor in 10 to 40 percent of heart attacks and strokes in the United States. Under normal circumstances, this amino acid is a short-lived byproduct of methionine metabolism, but inadequate levels of B vitamins prevent its breakdown.

The latest study, published in the *Journal of the American Medical Association*, analyzed 38 previous studies on homocysteine, folic acid, and cardiovascular diseases. Lead investigator Shirley A. A. Beresford, PhD, of the University of Washington, confirmed that high blood levels of homocysteine were clearly associated with cardiovascular diseases and that folic acid lowered levels of the amino acid. Other studies have reported that vitamins B6, B12, and choline also lower homocysteine levels.

High blood levels of homocysteine, also known as hyperhomocysteinemia, pose a risk of cardiovascular disease independent of other risk factors, such as cholesterol, triglyceride, smoking, and so forth. Beresford estimated that up to 50,000 coronary heart disease deaths could be prevented by increasing folic acid

intake—by eating more fruit and vegetables, fortifying foods with the vitamin, or taking supplements.

Large doses of folic acid are not needed to reduce hyperhomocysteinemia, according to Beresford. She wrote in *JAMA* (Oct 4, 1995;274:1049-57) that 650 mcg daily reduced homocysteine levels by 42 percent in men with hyperhomocysteinemia.

Folic Acid Essential for Healthy Infants, Too

Folic acid has also been gaining momentum as a means of preventing neural-tube birth defects—and, now, cleft palate.

Researchers and physicians have known since the 1960s that folic acid is critical during the first several months of pregnancy, and that a deficiency prevents the neural tube from closing in fetuses. Public health recommendations based on this knowledge, however, have been slow in coming.

"At least 50 percent of the annual number of 2500 cases of neural tube defects in the United States can be prevented if 400 mcg of folic acid is taken daily before and during the first four weeks of pregnancy," observed Shirley A. A. Beresford, PhD, of the University of Washington in *JAMA* (Oct 4, 1995;274:1049-57).

There are, however, additional and interesting aspects of folic acid in pregnancy.

Women who take folic acid and other vitamins for one month before and two months after conception are 25 to 50 percent less likely to give birth to infants with cleft palate, according to a study of almost 1,500 women by Gary M. Shaw, DrPH, of the California

The *JAMA* study is the most recent of several published in 1995. In an investigation of 21,826 Norwegian men and women, Egil Arnesen, MD, of the University of Tromsø, Norway, reported in the *International Journal of Epidemiology* (1995;24:704-9) homocysteine was strongly associated with coronary heart disease.

Another study, involving
Continued on page 4

Birth Defects Monitoring Program.

Cleft palate often results in speech impairments and higher frequency of ear infections. In California, medical and surgical expenses related to cleft palate add up to an estimated \$86 million a year, according to Shaw's article in *Lancet* (Aug 12, 1995;346:393-6).

As with cardiovascular disease, women at risk of giving birth to children with neural-tube defects might be identified by elevated blood levels of homocysteine. Both folic acid and vitamin B12 may normalize homocysteine levels and reduce the risk of such defects, contended James L. Mills, MD, in *Lancet* (Jan 21, 1995;345:149-51).

Premature infants also appear to have a need for supplemental folic acid and B12. Diana A. Worthington-White, MD, of the University of Florida, initially treated 184 anemic infants with iron and vitamin E according to standard medical procedures. Infants subsequently given B12 or a combination of B12 and folic acid had the highest increase in blood hemoglobin, according to a study in

Continued on page 4

Vitamin A Supplements Help Infants Infected with HIV

Vitamin A supplements may be an inexpensive way to improve the health of infants infected with the AIDS virus.

Anna Coutsooudis, PhD, a professor of pediatrics at the University of Natal, South Africa, gave high-dose vitamin A supplements to 118 infants of HIV-infected women. Both mothers and infants (at age one month) had normal vitamin A levels.

Half of the infants received vitamin A supplements at one and three months, six and nine months, and at 12 and 15 months of age. Eighty-five of the infants were later diagnosed with HIV infections.

The HIV-infected children who received vitamin A supplements

suffered approximately 50 percent less diarrhea than those who did not take the vitamin, according to Coutsooudis' article in *American Journal of Public Health*, (Aug 1995;85:1076-1081). Diarrhea is a common cause of death among infants infected with HIV.

Infants without HIV did not have any reduction in diarrhea with vitamin A supplements. However, all of the infants who received vitamin A supplements suffered fewer illnesses, ranging from simple rashes to respiratory infections.

Because the study lasted for only 18 months, the researchers were not able to determine whether vitamin A extended the life of HIV-infected infants.

Vitamin A has long been known for its role in boosting immunity. In 1928, it was referred to as the "anti-infective vitamin" (Green HN, *British Medical Journal*, 1928;2:691-696). It is well established as a nutrient capable of preventing death from measles (American Academy of Pediatrics, *Pediatrics*, May 1993, 91;1014-1015).

In a previous study, Coutsooudis reported that measles prompted a rapid (though temporary) decline in T cells, but that vitamin A supplements increased T cell numbers and antibody responses. (*Pediatric Infectious Diseases Journal*, 1992;11:203-209)

Note: Do not give vitamin A to infants without guidance from a physician. Also, see article below. □

Caution Urged with Vitamin A in Pregnancy, Beta-Carotene Okay

SEE RELATED EDITORIAL IN THE DECEMBER ISSUE OF THE NUTRITION REPORTER.

Women who take large doses of vitamin A around the time of conception or early in their pregnancy run a higher than average risk of delivering infants with birth defects.

That's the finding of a study that flashed across hundreds of newspaper headlines in early October. The *New England Journal of Medicine* released the findings more than a month ahead of the study's scheduled Nov 23, 1995, publication date.

The epidemiological study, which analyzed the dietary and vitamin supplement habits of 22,748 pregnant women, was conducted by Kenneth J. Rothman, DrPH, of the Boston University School of Medicine. Rothman found that women taking more than 10,000 IU of vitamin A daily, either in food or supplements, were three times more likely to deliver infants with deformities of the head, heart, and brain.

Such amounts of vitamin A are found in some multivitamin formulas. Over the past few years, however, many vitamin companies have switched from vitamin A to beta-carotene, which is safe and does *not*

cause birth defects. A 3-ounce serving of liver provides about 30,000 IU of vitamin A.

In Rothman's retrospective study, women were queried about their eating and vitamin supplement habits before becoming pregnant and during the first three months of pregnancy. After delivery, either the women or their physicians completed a questionnaire about the health of the baby.

The researchers found that 121 cases of "cranial neural crest" deformities occurred. These deformities include cleft lip, cleft palate, water on the brain, and heart defects.

Women taking more than 10,000 IU of vitamin A during the first three months of pregnancy were 2.4 times more likely to deliver children with the birth defects. Women taking 20,000 IU were four times more likely to deliver children with birth defects.

While the risk of birth defects increased with high vitamin A, only 1 baby in 57 actually developed defects because of its mother's use of the vitamin. Conversely, 56 of 57 infants born to mothers consuming large doses of vitamin A had no birth defects.

Vitamin A is essential for normal cellular differentiation and in

regulating organ development in the fetus. The researchers recommended that pregnant women either limit their vitamin A consumption to 4,000 to 8,000 IU daily or, alternatively, take beta-carotene.

Researchers responded to the study with a number of criticisms. Pre-publication release of research is discouraged in the scientific community and, in this case, many detailed criticisms of the vitamin A study will not be possible until it's actually published. (The NUTRITION REPORTER received an advance copy.)

Richard Miller, PhD, director of the Prenatal Environmental and Drug Exposure Consultation Service at the University of Rochester, felt the study would discourage pregnant women from taking vitamin supplements in general. This, he told THE NUTRITION REPORTER, was particularly disturbing because he and other researchers have been trying to get women to increase their consumption of vitamins, particularly folic acid.

At a press conference, Rothman emphasized the safety of beta-carotene. "Beta-carotene, a constituent of many fruits and vegetables, can also be

Continued on page 3

Lowering Fat Intake Slows Growth of Prostate Cancer

Slashing fat consumption can dramatically slow the growth of prostate cancer, according to experiments at the Memorial Sloan-Kettering Cancer Center in New York City.

The number of clinically detected prostate cancer varies tremendously from country to country, with 120 times more cases identified in the United States than in China. Based on autopsies, 30 percent of men over age 50 have mild cases of prostate cancer—and usually die of other causes.

However, population-based and laboratory studies have suggested that diet influences the severity of prostate cancer. For example, the incidence of prostate cancer among Japanese men increases after they move to the United States. In addition, some studies have suggested that omega-3 fatty acids (fish oils) might be protective, whereas omega-6 fatty acids (vegetable oils) might promote cancer growth.

In the Sloan-Kettering experiment, Warren D. W. Heston, MD, and his

colleagues transplanted human prostate cancers into mice. Once the cancers started growing, Heston divided the mice into several groups. Their diets were the same except for fat intake, which was 40.5, 30.8, 21.2, 11.6, or 2.3 percent of dietary calories. The 40.5 percent fat (corn oil) was comparable to the typical American diet.

After 11 weeks, Heston measured the size of the tumors. Mice on the 40.5 percent fat diet had tumors 2.5 times the size of those in mice eating the lowest fat diet. Mice consuming only 21.2 percent fat had tumor sizes roughly half those of mice on the high-fat diet. Heston's wrote in the *Journal of the National Cancer Institute* (Oct 4, 1995;87:1456-62) that "dietary modification from high to low fat resulted in slower tumor growth even after the formation of measurable tumors."

Heston's team also measured

Continued on page 4

Drinking Green Tea Lowers Blood Fats

Elderly men who drank 10 or more cups of green tea daily had lower blood levels of cholesterol and triglyceride than men who drank less of the tea, according to a report from the Saitama Cancer Research Center, Japan.

K. Imai, PhD, and K. Nakachi, PhD, studied 1,371 men enrolled in a 40-year study of eating habits and health. "Consumption of green tea was significantly associated with lower serum concentrations of lipids and lipoproteins," they wrote in the *British Medical Journal* (March 18, 1995;310:693-6). An increase in consumption substantially decreased serum total cholesterol and triglyceride concentrations, and this strong

association remained almost unaltered even after age, cigarette smoking, alcohol consumption, and relative body weight were controlled for."

The heavy tea drinkers also benefited from higher blood levels of the "good" high-density lipoprotein and lower levels of the "bad" low-density lipoprotein forms of cholesterol. In addition, they had lower levels of certain liver enzymes, suggesting a reduced risk of liver disease.

"Green tea has many advantages over chemical preventive agents—tea is non-toxic and thus readily available to the general population, Imai and Nakachi wrote. □

Low Vitamin C Linked to Risk of Stroke

Researchers in Britain have known that the incidence of stroke and coronary heart disease are highest in areas where people consume relatively few fruits and vegetables. Such foods provide a virtual cornucopia of nutrients, including vitamins, minerals, and flavonoids.

But the most critical nutrient for preventing stroke may be none other than vitamin C, according to a recently published study.

A research team headed by Christopher N. Martyn, PhD, of the University of Southampton, England, analyzed dietary data gathered from 730 people during the early 1970s in light of their ultimate cause of death.

All of the people were at least age 65 when the study began.

During 20 years of follow up, 643 of the people died, 124 of them from strokes. Martyn found that people who consumed the highest amounts of vitamin C had only one-half the risk of stroke compared with those who consumed only small amounts of the vitamin, according to his report in the *British Medical Journal* (June 17, 1995;310:1563-6).

In general, the subjects' intake of vitamin C decreased with age. People in their late 60s consumed from 28 to 53 mg of vitamin C daily, but only 20 to 40 mg daily after age 85. □

Vitamin A, Pregnancy...

Continued from page 2

converted to vitamin A in the body," he explained. "Other studies show, however, that high beta-carotene intake does not elevate vitamin A levels in the body enough to surpass the threshold for teratogenic effects [birth defects]. Supplements that contain high levels of beta-carotene should not pose a problem with respect to birth defects, nor should high levels of beta-carotene in the diet. We know of no reason for anyone to avoid eating carrots, tomatoes, or other carotene-containing foods, and we know of no adverse effect associated with beta-carotene dietary supplements."

"We stress that there is no indication of any adverse effect of vitamin A at recommended levels, nor do our findings relate to any other vitamin," Rothman added. "Vitamin supplements in general are important dietary adjuncts for those whose diet is deficient in vitamins. We hope that our findings will enable women to maintain levels of intake that are neither too high nor too low." □

B Vitamins, Homocysteine, Heart Disease...

Continued from page 1

researchers from several U.S. universities and medical centers, examined the relationship between homocysteine, folic acid, and B6 in the narrowing of the carotid artery. This artery feeds blood to the head and neck, and its condition is indicative of coronary and cerebrovascular disease.

Lead researcher Jacob Selhub, PhD, of the USDA Human Nutrition Research Center on Aging, Tufts University, analyzed data from 1,041 elderly participants in the well-known Framingham Heart Study. He and his colleagues found that people with high blood levels of homocysteine were twice as likely to suffer from clogged arteries than were people with low levels of the amino acid, according to an article in the *New England Journal of Medicine* (Feb 2, 1995;332:286-91).

At University Hospital in Lund, Sweden, Bo Israelsson, MD, reported

that homocysteine levels increased in the weeks following a heart attack in 68 patients. Folic acid was far more effective than either B6 or B12 in lowering these homocysteine levels, Israelsson wrote in the *Journal of Internal Medicine* (April 1995;237:381-8).

Homocysteine is increasingly recognized as an indicator of folic acid intake, just as testing for methylmalonic acid is increasingly being used to identify B12 status. The higher the blood levels of these substances, the lower the vitamin intake.

A number of studies have found widespread elevations of homocysteine and deficiencies of folic acid. One study found that 25 percent of middle-age men were deficient in vitamin B6, 56 percent in B12, and 59 percent in folic acid (Ubbink JB, *American Journal of Clinical Nutrition*, Jan 1993;57:47-53.). A Tufts University analysis found 30 percent of elderly men and women to have elevated homocysteine levels. (Selhub J et al, *JAMA*, Dec 8, 1993, 270:2693-2698.) In Atlanta, at the 1995 meeting of the Federation of American Societies for Experimental Biology, M. René Malinow, MD, of Oregon Health Sciences University commented that 30 to 40 percent of people with cerebrovascular and peripheral artery disease had high levels of homocysteine.

More recently, researchers from the United States, Germany, and Belgium reported that deficiencies of folic acid, B6, and B12 were far more common than previously thought. They measured homocysteine, methylmalonic acid (an indicator of B12 levels), and other indicators of vitamin status in 300 elderly subjects.

Although the people had apparently "normal" blood levels of vitamins, the researchers gave them intramuscular injections of folic acid, B6, and B12. Levels of homocysteine, methylmalonic acid, and the other vitamin markers began dropping—

indicating that their vitamin levels had increased. "The response rate to vitamin supplements supports the notion that metabolic evidence of vitamin deficiency is common in the elderly, even in the presence of normal serum vitamin levels," Hans J. Naurath, MD, and his colleagues wrote in *Lancet*, (July 8, 1995;346:85-9).

Folic acid, which is water soluble and not stored by the body, is exceptionally safe. The Recommended Dietary Allowance (RDA) has been kept low (currently 200 mcg) because of a remote risk of folic acid masking some signs of B12 deficiency. Beresford, writing in *JAMA* suggested a simple and elegant solution: adding 1 mg of B12 to each 400 mcg tablet of folic acid.

Unlike cholesterol, homocysteine is not found in foods and, consequently, dietitians cannot recommend low-homocysteine diets. In contrast, folic acid is found in dark green leafy vegetables and organ meats. □

Folic Acid, Infants...

Continued from page 1

the *American Journal of Clinical Nutrition* (Dec 1994;60:930-5).

Yet another study discovered that vitamin levels dropped during pregnancy and normalized soon after delivery—with the exception of folic acid, researchers reported in the *European Journal of Obstetrics & Gynecology and Reproductive Biology* (1995;61:31-37). It took more than 6 months for folic acid levels to normalize in 45 percent of the women, according to H.W. Bruinse, MD, of University Hospital Utrecht, Netherlands.

Finally, a study conducted by the Centers for Disease Control and Prevention (CDC) found that the vast majority of women knew that reducing smoking and alcohol would reduce the risk of birth defects. Only 52 percent of women had heard about folic acid, and only 9 percent knew that it prevented birth defects, according to an article in the *Morbidity and Mortality Weekly Report* (Sept 29, 1995;44:716-8). □

Prostate, Fat...

Continued from page 3

blood levels of prostate-specific antigen (PSA), an indicator of prostate tumor risk. Levels of PSA decreased along with tumor size. □

THE NUTRITION REPORTER™ (ISSN 1079-8609) is published monthly except for August and December. Vol. 6, No. 11. Copyright November 1995 by Jack Challeng and Renate Lewin. All rights reserved. Reproduction without written permission is prohibited. Phone: (503) 642-1372. Fax: (503) 649-8948. Internet: jack_challeng@ortel.org CompuServe: 74543,2122. This newsletter is strictly educational and not intended as medical advice. For diagnosis and treatment, consult your physician. Subscriptions must be prepaid: U.S., \$25 per year; Canada, \$32 U.S. or \$43 CAD; all other nations, \$38 U.S. funds payable through a U.S. bank.

THE NUTRITION REPORTER™

Post Office Box 5505
Aloha, OR 97006-5505 USA

Editor and Publisher: **Jack Challeng**
Associate Publisher: **Renate Lewin**

Medical Advisors:

London H. Smith, MD

Portland, Oregon

Richard P. Huemer, MD

Vancouver, Washington

Ralph K. Campbell, MD

Polson, Montana

G. Edward Desaulniers, MD

The Shute Institute Medical Clinic
London, Ontario, Canada